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Natural Background Radiation in Uranium Mining Areas and Radiation Mapping

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Kazakhstan is currently the world's leading producer of natural uranium extracted by the in-situ recovery (ISR) method. According to the World Nuclear Association (WNA), Kazakhstan produced 21,225 tonnes of uranium in 2022, accounting for 45.14% of global uranium production. National Atomic Company Kazatomprom JSC, together with its subsidiaries, affiliated companies, and joint ventures, develops 26 uranium deposits across the Republic of Kazakhstan, organized into 14 mining assets. The objective of this study was to investigate the natural background radiation in uranium mining areas and to develop a radiation map of the study sites for the purpose of environmental and public protection.

The research focused on contaminated soil collected near production and injection wells, as well as ambient gamma dose rates measured within the territory of JV Inkai LLP (Suzak District, Turkistan Region, Kazakhstan). Gamma radiation measurements were performed using an MKS/SRP-08A dosimeter-radiometer, while the UMF-2000 alpha-beta radiometer was employed to determine the specific alpha activity of contaminated soil samples. Measurements were conducted at intervals of 3–4 days throughout the monitoring period. The MKS/SRP-08A dosimeter-radiometer is designed to detect gamma- and X-ray-emitting sources and to measure the ambient dose equivalent rate of gamma and X-ray radiation. The UMF-2000 alpha-beta radiometer is intended for measuring the total activity of alpha-emitting radionuclides in both thick and thin environmental samples. In addition, it enables the determination of alpha activity in counting samples obtained after selective radiochemical extraction, provided that the corresponding analytical procedures are available.

The principal ore bodies of the deposit are associated with interstratal fault zones intersected by boreholes. These ores exhibit similar mineralogical compositions but differ primarily in the proportions of their major constituents (sulfur, nitrogen, and iron) and in uranium content.

Accordingly, ore samples with varying concentrations of S, Fe, N, and U were collected for analysis. At the wellheads of production wells, the average ambient dose equivalent rate (ADER) was 0.17 μSv/h, ranging from 0.13 to 0.23 μSv/h. The average specific alpha activity of contaminated soil was 810.61 Bq/kg, with values ranging from 211 to 1,865 Bq/kg. At the wellheads of injection wells, the average ambient dose equivalent rate was 0.19 μSv/h, varying between 0.13 and 0.27 μSv/h. The average specific alpha activity reached 980 Bq/kg, with measured values ranging from 94 to 2,856 Bq/kg. Analysis of the obtained data revealed a relationship between the specific alpha activity of contaminated soil and elevated gamma radiation

levels. Areas exhibiting increased gamma dose rates generally corresponded to locations with higher specific alpha activity.

In addition, a pedestrian gamma survey was carried out using the MKS/SRP-08A dosimeter-radiometer. The collected data were used to investigate the relationship between ambient gamma dose equivalent rates (μSv/h) and the specific alpha activity (Bq/kg) of the corresponding soil samples. The identified correlation is presented in Figure 1.

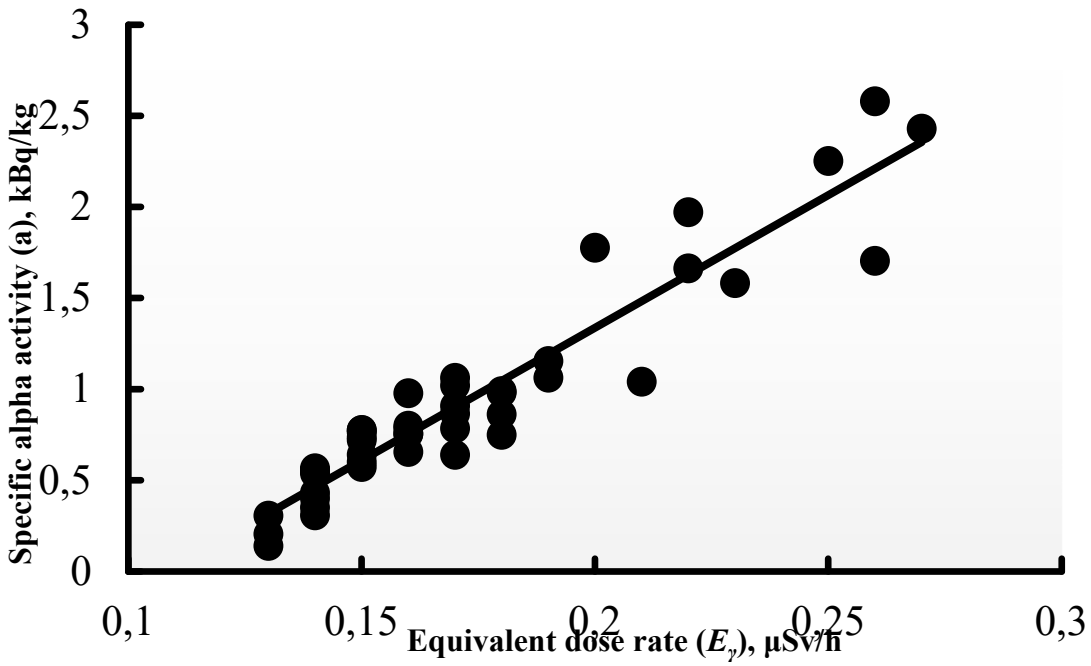

Fig. 1. – Plot of specific alpha activity versus dose rate.

The plot demonstrates a clear positive correlation between the ambient dose equivalent rate and the specific alpha activity of contaminated soil. Nevertheless, further confirmation of this relationship requires a larger dataset, including additional field measurements and laboratory determination of the specific alpha activity of soil samples collected directly at the gamma survey measurement locations.

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AI Readiness Assessment for Small and Medium-Sized Enterprises in Kazakhstan: Methodology, Challenges and Future Perspectives

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Artificial Intelligence (AI) is increasingly recognized as a strategic driver of digital transformation, operational efficiency, and sustainable economic growth. Across the world, AI technologies are reshaping business models, improving decision-making, and increasing organizational competitiveness. In Kazakhstan, national digitalization initiatives have created favorable conditions for AI adoption; however, most small and medium-sized enterprises (SMEs) remain insufficiently prepared to implement AI effectively because of limited digital maturity and the absence of a structured readiness assessment framework.

Existing international AI readiness frameworks have primarily been developed for large organizations operating in technologically advanced economies. Consequently, they do not fully reflect the financial capacity, regulatory environment, and operational characteristics of Kazakhstan's SMEs. To address this gap, this paper proposes the AI Ready Kazakhstan methodology, a context-specific framework designed to evaluate organizational preparedness for AI adoption while considering technological, organizational, and legal factors relevant to Kazakhstan.

The proposed methodology consists of five interrelated dimensions: digital infrastructure readiness, data readiness, organizational readiness, human capital readiness, and legal readiness. Digital infrastructure assesses the availability of information systems, cloud technologies, cybersecurity mechanisms, and digital resources. Data readiness evaluates data quality, accessibility, governance, and consistency. Organizational readiness examines strategic commitment, innovation culture, and change management. Human capital readiness measures employees' AI competencies and digital skills, whereas legal readiness focuses on compliance with personal data protection, information security, intellectual property, and ethical AI principles.

Based on the integrated evaluation of these dimensions, each enterprise receives an AI Readiness Score that reflects its overall preparedness for AI implementation. The assessment results form the basis for an individualized implementation roadmap containing recommendations for improving digital capabilities, strengthening data management, developing employee competencies, and selecting appropriate AI solutions.

Despite considerable opportunities, Kazakhstan's SMEs continue to face several barriers to AI adoption, including insufficient digital infrastructure, fragmented organizational data, limited financial resources, a shortage of AI-qualified professionals, and uncertainty regarding cybersecurity and legal compliance.

The future development of the proposed framework involves the creation of the AI Ready Kazakhstan SaaS platform, enabling enterprises to conduct online AI readiness assessments, automatically calculate readiness scores, identify business processes suitable for AI integration, and generate customized implementation recommendations.

In conclusion, the AI Ready Kazakhstan methodology provides a practical and comprehensive framework for assessing SME readiness for artificial intelligence implementation. By integrating technological, organizational, human, and legal dimensions into a single assessment model, the methodology can support sustainable digital transformation, improve business competitiveness, and contribute to the development of Kazakhstan's digital economy.

The role of technological evolution and social dynamics in modern world

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Abstract: Every aspect of our lives has been impacted by technology, the most important and rapidly evolving dynamic of our time. This technological revolution encompasses everything from the devices in our homes and smartphones to the software used in workplaces and the latest advancements in medical science. This transformation presents both new possibilities and new questions for humanity. In our view, one of the greatest advancements in human history has been the progress of technology. While the agricultural society industrialized during the Industrial Revolution, the information society was created during the Digital Revolution. In addition to libraries and encyclopedias, we can now access information at our fingertips. Every sector, including art, economics, health, and education, has undergone a profound transformation as a result of this change. Technological power, once exclusive to governments or large corporations, is now readily accessible to everyone. Technologies like cloud computing, AI-powered applications, and faster communication, unimaginable just a few years ago, have come together to make our lives more connected and efficient. E-commerce sites are fundamentally changing our purchasing habits, while social media platforms reinforce the idea that we live in a global village. People and societies must constantly adapt to this rapid change. While some traditional professions are changing or disappearing, a new generation of professionals is emerging. Throughout this process, technological literacy is transforming from a benefit to a fundamental necessity.
Keywords: technology, revolution, digital era, artificial intelligence, technological devices.

The future of technology holds many developments that both surprise and worry us. Fields such as artificial intelligence, robotics, nanotechnology, and bioengineering are turning science fiction stories into reality. Technologies like smart urban systems, self-driving cars, and personalized healthcare offer opportunities to improve human well-being. However, such advancements raise significant ethical and societal concerns. The role of AI in decision-making, the potential for algorithms to discriminate, and the protection of personal information are among the concerns driving current debates in technology circles. The replacement of jobs by machines, such as robots and AI, is becoming a major issue shaping upcoming labor laws (Murshed, A.et.al, 2026). The convenience and speed of technology may lead us to neglect interpersonal connections and authentic life experiences. Just as advancements in technology, including VR and AR, offer new avenues for exploration, these innovations also carry the potential risk of drifting towards an artificial presence instead of remaining connected to our physical environment. Therefore, it is imperative that both individuals and societies use technological advancements consciously and ethically.

A technological device serves as a tool for the efficient execution of tasks. How we use something will determine its impact on shaping our destiny in the years to come. Maximizing technological potential while upholding human ethics allows us to create a better tomorrow. In this endeavor, an educational process enriched with innovation, analytical skills, and technological advancements serves as the fundamental tools for the success of the participants.

In the past, our quest for knowledge involved immersing ourselves in the quiet confines of library corridors, where books abounded but were often overlooked due to their age and weariness.

Today, search with an internet search tool, and you'll find every detail at your fingertips. Thus, just as the Industrial Revolution revolutionized industry through steam technology, the Digital Revolution is redefining consciousness and social structures by disseminating data (Brey, 2003).

Today, technological devices are no longer solely in the hands of large corporations or under state control; they are accessible to individuals. I repeat: advancements unimaginable a short time ago, such as faster internet connections, AI-powered devices, and remote data storage systems, now facilitate smoother routines and improved connectivity in daily life. The internet now functions less as an international community and more as our virtual community. The way we shop has changed significantly due to the easy payment features offered by online retailers. Old professions still hold value but demand updated skills; others have disappeared entirely. Today, technical proficiency is not only useful; it is now considered fundamental in guiding our contemporary society (Volti, et.al. 2024, Edward , 2003).

The most exciting stories about the future are no longer being written in science fiction films, but in laboratories. Fields like artificial intelligence, robotics, and biotechnology are redrawing not only the boundaries of devices but also those of humanity itself. Applications such as autonomous vehicles, smart cities, and personalized gene therapies could take our quality of life to unimaginable levels.

However, every step forward brings with it important questions. When can artificial intelligence become a “decision-maker”? Is it possible for algorithms to produce biased results? Are all our personal data bargaining chips? The increasing role of robots in the workforce stands before us as one of the greatest challenges of the future. The comfort and speed offered by technology can sometimes cause us to overlook our most basic human connections and the natural world. While virtual and augmented reality offer us new worlds, they also risk making us forget the magic of the real world.

One of the greatest impacts of technology on culture is its radical transformation of communication methods. Technological innovations such as writing, telephone, radio, television, and ultimately the internet have become tools that bring people together and accelerate cultural exchange. The internet and social media, in particular, facilitate individuals' expression and sharing of their own cultural identities while also enabling interaction with different cultures. This increases cultural diversity and accelerates the formation of a global culture (Koch et.al, 2014).

However, this also brings challenges. With globalization, local cultures may face the risk of being assimilated by dominant cultural trends. Therefore, it is crucial that the cultural exchange facilitated by technology progresses in a balanced and reciprocal manner.

Conclusion: In the future, the impact of technology on culture will deepen even further. Innovations such as artificial intelligence, virtual reality, and blockchain may lead to a completely different dimension in cultural interactions and forms of expression. For example, virtual reality technologies can allow people to have cultural experiences in environments where they are not physically present. Thus, cultural boundaries are redefined, and culture exists independently of physical spaces. Artificial intelligence, on the other hand, can automate cultural production and create personalized cultural content. This could initiate a new era in cultural production, but it also increases the risk of the commercialization of culture. The personalization of cultural content can lead to individuals being trapped in their own cultural bubbles and a decrease in cultural diversity.

Technology has always played and will continue to play a significant role in shaping culture. The radical changes it makes in areas such as communication, media, and cultural production profoundly affect how societies think, behave, and interact. In the future, this role of technology will become even stronger, and new cultural dynamics and value systems will emerge. However, consciously managing the effects of technology and protecting cultural diversity will be crucial for sustainable cultural development.

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ПРИМЕНЕНИЕ ГЕНЕРАТИВНОГО ИСКУССТВЕННОГО ИНТЕЛЛЕКТА ДЛЯ АВТОМАТИЗАЦИИ АНАЛИЗА СОБЫТИЙ ИНФОРМАЦИОННОЙ БЕЗОПАСНОСТИ В ИНФОРМАЦИОННЫХ СИСТЕМАХ

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Аннотация

Рост объема и семантической неоднородности телеметрии информационной безопасности формирует разрыв между скоростью регистрации событий и возможностью аналитика установить их причинную связь, критичность и требуемую реакцию. Генеративный искусственный интеллект способен преобразовывать журналы, оповещения, сведения об активах, уязвимостях и тактиках нарушителя в связное объяснение, однако вероятностная природа языковых моделей создает риск конфабуляций, подмены доказательств гипотезами, утечки конфиденциальной информации и выполнения ошибочных действий. Цель работы - разработать теоретически обоснованную архитектуру контролируемого применения генеративного искусственного интеллекта для автоматизации анализа событий информационной безопасности без передачи языковой модели функций первичной регистрации фактов и без неконтролируемого исполнения защитных действий. Методология объединяет структурированный сравнительный анализ, функциональную декомпозицию процесса SIEM/SOC, сопоставление результатов исследований языковых моделей для журналов и инцидентов, моделирование угроз и архитектурный синтез. Результатом стала семислойная модель доказательно контролируемого генеративного анализа событий информационной безопасности. В нее включены неизменяемый слой первичных свидетельств, нормализация и корреляция, доверенный контекст, генеративный синтез, верификация утверждений, риск-адаптивный шлюз решений и контур обратной связи. Новизна состоит в разделении факта, машинной интерпретации и управленческого решения посредством карточки доказательности, а также в сочетании двух независимых допусков - достаточности доказательств и допустимости операционного воздействия. Предложены четыре уровня автономии, при которых необратимые либо высокорисковые действия сохраняются за уполномоченным специалистом. Практическая значимость определяется возможностью встроить модель между SIEM, средствами контекстного обогащения и SOAR, повысив воспроизводимость триажа и аудируемость решений.

Ключевые слова: генеративный искусственный интеллект, информационная безопасность, событие безопасности, SIEM, SOC, большая языковая модель, анализ журналов, реагирование на инциденты.

Введение

Событие информационной безопасности существует первоначально не как готовый инцидент, а как фрагмент наблюдаемого поведения: вход в учетную запись, изменение привилегий, сетевое соединение, запуск процесса, обращение к файлу, срабатывание средства защиты или изменение конфигурации. Инцидент возникает после установления значимой связи между такими фрагментами, активом, субъектом, уязвимостью, временем и возможным ущербом. Масштаб проблемы отражен в отчете Verizon за 2025 г.: исследовательская группа обработала 22 052 реально зарегистрированных инцидента, из которых 12 195 были подтвержденными утечками данных. Совокупность охватила потерпевшие организации из 139 стран. Эксплуатация уязвимостей достигла 20% подтвержденных утечек и увеличилась на 34% по сравнению с предыдущим отчетным периодом. В образовательных организациях было зарегистрировано 1 075 инцидентов, включая 851 подтвержденную утечку. На System Intrusion, Miscellaneous Errors и Social Engineering пришлось 80% утечек в этом секторе [1]. Эти значения не описывают поток событий одной организации, но показывают разнообразие сценариев, которые должна различать современная аналитическая инфраструктура.

Искусственный интеллект одновременно становится средством защиты и элементом угрозы. По данным IBM Cost of a Data Breach Report 2026, средняя мировая стоимость утечки достигла 4,99 млн долл. США, что на 12% выше значения предыдущего года. Каждая четвертая злонамеренная утечка в исследованной совокупности была связана с применением искусственного интеллекта, число таких случаев увеличилось на 56%, а их средняя стоимость составила 6 млн долл. США. Организации с широким применением искусственного интеллекта и автоматизации в защите сократили средние издержки утечки почти на 2 млн долл. США по сравнению с организациями, не применявшими такие средства [2]. Коммерческая природа отчета требует осторожной интерпретации: показатели не заменяют отраслевую статистику отдельной страны, однако фиксируют экономическую значимость своевременного обнаружения и корректного реагирования.

Для Республики Казахстан журналирование и мониторинг являются не только технологической практикой, но и нормативным требованием. Постановление Правительства Республики Казахстан от 20 декабря 2016 г. № 832 предписывает регистрацию событий операционных систем, систем управления базами данных, антивирусной защиты и прикладного программного обеспечения, синхронизацию времени, защиту журналов и применение системы управления инцидентами и событиями информационной безопасности. Журналы регистрации хранятся в течение срока, установленного технической документацией по информационной безопасности, но не менее трех лет, причем не менее двух месяцев должны находиться в оперативном доступе [3]. Следовательно, интеллектуальная автоматизация должна работать поверх доказательного журнала и не изменять первичные записи, иначе ускорение анализа будет достигнуто ценой утраты проверяемости.

Цифровой кодекс Республики Казахстан от 9 января 2026 г. № 255-VIII определяет алгоритмическую систему как цифровую систему, принимающую решение либо влияющую на него посредством автоматизированной обработки данных. Статья 43 закрепляет право получить информацию о применении такой системы, объяснение ключевых факторов и критериев полностью автоматизированного решения и потребовать его пересмотра уполномоченным специалистом, если решение влечет юридические последствия или

способно повлиять на права и законные интересы лица [4]. Решение SOC о блокировке учетной записи, изоляции узла или прекращении сервиса может затронуть трудовые, договорные и операционные интересы. Поэтому объяснимость генеративного вывода должна обеспечиваться не литературной убедительностью текста, а ссылками на конкретные записи и правила.

Закон Республики Казахстан от 17 ноября 2025 г. № 230-VIII «Об искусственном интеллекте» классифицирует системы по степени риска, а также по режиму использования на открытые, закрытые и локальные. Для систем высокого риска, относимых к критически важным объектам информационно-коммуникационной инфраструктуры, действуют требования информационной безопасности, применимые к государственным информационным системам [5]. Из этого положения вытекает архитектурное требование к локализации чувствительного контекста, разграничению доступа, регистрации запросов и результатов модели, управлению версиями и непрерывному контролю владельцем или оператором.

Международная логика управления киберриском представлена в NIST Cybersecurity Framework 2.0 шестью функциями: Govern, Identify, Protect, Detect, Respond и Recover. Генеративный анализ не образует седьмую автономную функцию. Он служит связующим аналитическим слоем прежде всего между категориями непрерывного мониторинга, анализа неблагоприятных событий, управления инцидентами и анализа инцидентов. Положение этого слоя в полном цикле показано на рисунке 1.

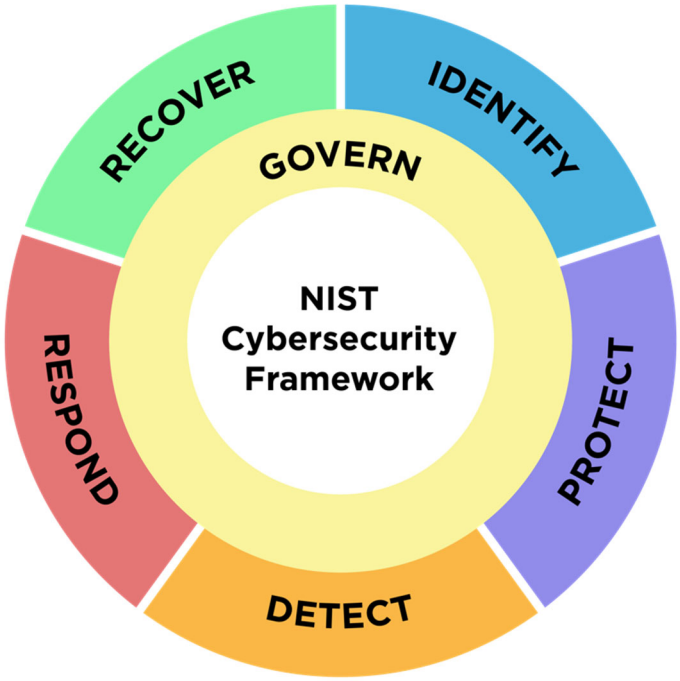

Рисунок 1 - Шесть функций NIST Cybersecurity Framework 2.0
Источник: National Institute of Standards and Technology, графика NIST/Natasha Hanacek [6].

Кольцевая композиция рисунка 1 имеет методологическое значение. Анализ события не заканчивается формированием краткого описания. Результат должен перейти в Respond, затем в Recover, а сведения о качестве обнаружения и реагирования возвращаются в Govern и Identify. NIST SP 800-61 Rev. 3, опубликованный в апреле 2025 г., связывает подготовку к реагированию с функциями Govern, Identify и Protect, непосредственное обнаружение и обработку - с Detect, Respond и Recover, а извлеченные уроки - с категорией Improvement [7].

Поэтому ценность генеративной системы определяется не красотой резюме, а ее способностью сохранять происхождение фактов, помогать объявлять инцидент по установленным критериям и документировать решение для последующего улучшения защиты.

Мировая научная литература быстро расширяется, однако ее результаты неоднородны по задачам, данным и метрикам. Систематический обзор J. Zhang, H. Bu, H. Wen и соавторов охватил более 300 работ с 2023 г. и сгруппировал применения больших языковых моделей в кибербезопасности от построения специализированных моделей до обнаружения уязвимостей, анализа угроз и генерации защитных решений [8]. Широта поля не устраняет ключевую проблему переноса: результат на публичном наборе журналов или в лабораторной задаче не доказывает надежность автономной реакции в производственной информационной системе.

Российский систематический обзор А.А. Конева и Т.И. Паюсовой включил 50 публикаций за период с января 2023 г. по март 2024 г., отобранных по процедуре PRISMA. Авторы связывают потенциал языковых моделей с автоматизацией анализа, тестированием на проникновение и поддержкой специалистов, но фиксируют ограничения, связанные с устареванием знаний, конфабуляциями, jailbreak-воздействиями и отсутствием самостоятельного целеполагания [9]. Для SOC это означает, что модель может формулировать гипотезу и объяснение, но не должна единолично определять истинность события или допустимость воздействия на актив.

Казахстанская научная школа сформировала значимый задел в машинном обнаружении вторжений. A. Imanbayev, S. Tynymbayev, R. Odarchenko, S. Gnatyuk, R. Berdibayev, A. Baikenov и N. Kaniyeva исследовали алгоритмы машинного обучения для IDS в сетях 5G и последующих поколений, сопоставив методы на наборах сетевых данных и связав выбор алгоритма со спецификой виртуализированной инфраструктуры [10]. S. Rysbekov, A. Aitbanov, Z. Abdiakhmetova и A. Kartbayev сравнили методы машинного обучения для обнаружения вторжений на NSL-KDD с предварительным снижением размерности методом главных компонент до 20 компонент [11]. Эти работы подтверждают наличие национальной компетенции в классификации сетевых событий, но оставляют открытой проблему доказательно контролируемого преобразования машинного сигнала в объяснение, приоритет и проект решения SOC. Научная проблема состоит в противоречии между семантической гибкостью генеративного искусственного интеллекта и строгой доказательностью анализа событий информационной безопасности. Традиционная SIEM хорошо сохраняет и коррелирует факты, машинное обучение выделяет статистические отклонения, а языковая модель связывает разнородный контекст и формирует понятный текст. Ни один из трех механизмов по отдельности не обеспечивает одновременно полноту контекста, проверяемость, устойчивость к манипуляциям и безопасное исполнение реакции.

Цель работы - разработать архитектуру доказательно контролируемого применения генеративного искусственного интеллекта, которая автоматизирует контекстуализацию, приоритизацию и объяснение событий информационной безопасности, но сохраняет первичные свидетельства, проверяемость выводов и человеческий контроль над высокорисковыми действиями.

Материалы и методы

Методологическая основа объединяет сравнительный анализ, контент-анализ, функциональную декомпозицию, моделирование угроз и архитектурный синтез. Сравнительный анализ применялся к трем классам средств: детерминированным правилам SIEM, алгоритмам машинного обучения и большим языковым моделям. Сопоставление

проводилось по типу входных данных, назначению, зависимости от обучающей выборки, форме результата, проверяемости вывода и допустимой степени автоматизации.

Функциональная декомпозиция разделила обработку события на регистрацию, нормализацию, корреляцию, обнаружение отклонения, контекстуализацию, построение гипотезы, формирование рекомендации и выполнение действия. Такое разделение позволяет определить операции, где вероятностная генерация создает аналитическую ценность, и операции, где необходим строго детерминированный механизм.

Контент-анализ применялся к зафиксированным в публикациях ограничениям языковых моделей: конфабуляциям, устареванию знаний, косвенной инъекции подсказок, утечке конфиденциальных данных, дрейфу качества и автоматизационному смещению. Моделирование угроз использовалось для установления границ доверия между журналами, базой знаний, языковой моделью, аналитиком и средствами оркестрации. Архитектурный синтез объединил эти границы в последовательность контрольных слоев.

Функциональная декомпозиция опиралась на базовый принцип SIEM как централизованной системы сбора, нормализации, корреляции, хранения и представления событий. Академическая монография D.R. Miller, S. Harris, A. Harper, S. VanDyke и C. Blask описывает развертывание SIEM, настройку источников, корреляцию и снижение ложноположительных оповещений, что позволяет отделить детерминированные функции платформы от добавляемого генеративного слоя [12].

Для унификации контекста использовано структурное сопоставление с OASIS STIX 2.1. Стандарт, утвержденный 10 июня 2021 г., задает язык представления информации о киберугрозах и наблюдаемых объектах, включая идентичности, индикаторы, вредоносное программное обеспечение, инфраструктуру, уязвимости, взаимосвязи и наблюдения [13]. В авторской архитектуре STIX рассматривается как машиночитаемый источник проверяемого контекста, а не как текст, который языковая модель должна воссоздавать по памяти.

Поведенческая интерпретация событий соотнесена с MITRE ATT&CK. Эта база систематизирует тактики, техники, подтехники и наблюдаемые процедуры нарушителей на основе реальных наблюдений и используется для построения моделей угроз и детектирующей аналитики [14]. Сопоставление с ATT&CK в разработанной модели выполняется как гипотеза с указанием признаков и версии базы. Одного совпадения техники недостаточно для атрибуции группировки или подтверждения инцидента.

Архитектурный синтез выполнялся в четыре шага. Сначала были определены операции, которые должны оставаться детерминированными: прием телеметрии, отметка времени, хеширование, нормализация, контроль схемы, применение правил доступа и исполнение команд. Затем выделены операции, для которых полезна генерация: резюмирование, межисточниковое связывание, объяснение, формирование альтернативных гипотез и подготовка проекта отчета. На третьем шаге для каждой генеративной операции сформированы проверочные барьеры. На четвертом шаге операции распределены по уровням автономии с учетом обратимости и потенциального влияния на доступность, конфиденциальность, целостность и права пользователей.

Результаты и обсуждение

Первый результат состоит в строгом разграничении трех аналитических механизмов. Детерминированные правила отвечают на вопрос, выполнено ли формально заданное условие. Машинное обучение оценивает, насколько наблюдение похоже на известный класс или отклоняется от изученного распределения. Генеративная модель преобразует найденные связи в контекстуальное объяснение и проект решения. Подмена одного механизма другим создает системную ошибку: языковая правдоподобность принимается за доказательство, а статистическая аномалия - за установленный злонамеренный умысел.

Таблица 1 - Разграничение функций SIEM, машинного обучения и генеративного искусственного интеллекта

Этап	Детерминированная SIEM-аналитика	Машинное обучение	Генеративный искусственный интеллект	Недопустимая подмена
Прием события	Проверка формата, времени, источника, подписи, обязательных полей	Выявление нетипичного профиля потока	Пояснение содержания нестандартного сообщения	Генерация отсутствующего поля как факта
Нормализация	Приведение к схеме, устранение технических дубликатов	Кластеризация сходных шаблонов	Предложение соответствия незнакомого поля известной семантике	Изменение оригинальной записи
Обнаружение	Правило, сигнатура, порог, последовательность условий	Классификация и обнаружение аномалии	Семантическая связь между разнородными сигналами	Объявление инцидента только по тексту модели
Контекстуализация	Запрос CMDB, IAM, реестра уязвимостей и сетевой топологии	Ранжирование признаков риска	Сводка об активе, пользователе, уязвимости и возможной технике ATT&CK	Использование внутренних знаний модели вместо актуального реестра
Объяснение	Вывод сработавшего правила и полей	Значимость признаков, если метод ее предоставляет	Причинная гипотеза, альтернативы, понятное резюме	Представление гипотезы как установленной причины
Реагирование	Исполнение заранее утвержденного сценария SOAR	Оценка вероятности результата	Подготовка проекта действий и отчета	Самостоятельное необратимое действие без внешнего допуска

Разграничение в таблице 1 определяет целевую роль генеративного компонента как семантического оркестратора, но не регистратора фактов и не конечного субъекта полномочий. Наиболее сильная зона применения находится между машинным обнаружением и человеческим решением: модель сокращает объем чтения, связывает контекст, формирует несколько проверяемых гипотез и переводит технические признаки на язык операционного риска. Наименее допустимая зона - непосредственное изменение инфраструктуры по свободно сформированному тексту.

Трансформерные методы развивались от обнаружения аномальных последовательностей к генеративному объяснению и рекомендациям. Диссертация H. Guo описывает LogBERT, обучаемый на нормальных журналах посредством маскированного предсказания ключей событий и минимизации объема гиперсферы. Сравнение проводилось с четырьмя традиционными и двумя глубокими моделями на HDFS, BGL и Thunderbird [15]. Метод выявляет отклонение, но не решает проблему безопасного управленческого действия.

LogGPT, предложенный X. Han, S. Yuan и M. Trabelsi, использует авторегрессионное предсказание следующего события журнала и дополнительную настройку с подкреплением для сближения языковой цели с задачей обнаружения аномалии [16]. Переход от BERT к GPT в этой постановке касается способа моделирования последовательности, а не автоматического получения достоверной причины инцидента.

Наиболее информативные для проектирования SOC количественные результаты сопоставлены в таблице 2. Проценты из разных работ нельзя ранжировать в одной шкале: исследования различаются данными, задачами, базовыми методами и метриками. Таблица используется для установления границ доказанного, а не для объявления универсального превосходства генеративного подхода.

Таблица 2 - Количественные результаты языковых моделей в анализе журналов и инцидентов

Работа и задача	Материал и дизайн	Подтвержденный результат	Ограничение переноса
LogPrompt, разбор журналов и обнаружение аномалий	9 публичных наборов, 2 задачи, без внутридоменного обучения; человеческая оценка 6 специалистов со стажем более 10 лет	Улучшение до 380,7% относительно простых подсказок; превосходство обученных подходов до 55,9%; средняя оценка полезности и читаемости 4,42 из 5 [17]	Максимальные приросты зависят от набора и базовой линии; публичные журналы не воспроизводят полномочия и последствия реального SOC
Генерация причин и мер для облачных инцидентов	44 340 инцидента из 1 759 сервисов Microsoft; человеческая проверка 25 владельцами инцидентов	Тонкая настройка GPT-3.5 повысила среднее лексическое сходство на 45,5% для причин и на 131,3% для мер относительно режима zero-shot; более 70% владельцев поставили полезности не менее 3 из 5 [18]	Лексическое сходство не равно фактической корректности; авторы зафиксировали неполноту сведений об отдельных инцидентах и риск замедления при неверной рекомендации

Microsoft Copilot for Security, типовые аналитические задачи	Две итерации рандомизированного контролируемого исследования: 147 специалистов безопасности и 149 пользователей без профессионального опыта в кибербезопасности	Специалисты выполнили задания на 22% быстрее и на 7% точнее; резюмирование инцидента ускорилось на 39%, анализ скрипта на 14%, анализ отчета на 19%. У начинающих пользователей точность по трем задачам с множественным выбором повысилась на 35%, а время при сопоставимом качестве сократилось на 25,9%. Повторно использовать систему хотели 97,2% специалистов и 93,2% начинающих пользователей [19]	Исследование проведено производителем; в регрессионном сравнении при сопоставимом качестве одна задача ответа выполнялась группой Copilot на 26,3% медленнее
Масштабируемое обнаружение аномалий в журналах	Частные и публичные журналы; четыре метода; наборы BGL, Thunderbird, ICard и VReg	Для SCLAD recall менялся от 0,73 до 1,00, precision - от 0,72 до 0,95; LMLAD требовал около 30 ГБ памяти GPU, большинство других исследованных алгоритмов - менее 2 ГБ [20]	Лучший метод зависит от формата журнала, набора данных, требуемой полноты и доступных вычислительных ресурсов

Сопоставление выявляет три устойчивых положения. Первое - языковые модели полезны там, где требуется интерпретировать не встречавшиеся при обучении сообщения и представить объяснение. Второе - адаптация к домену, обогащение контекстом и специализированные подсказки оказывают существенное влияние на результат, поэтому универсальная модель без актуальных данных организации недостаточна. Третье - среднее ускорение не распространяется автоматически на каждую операцию. Негативный результат по задаче ответа в исследовании Microsoft особенно значим: генеративная поддержка способна увеличить время, если интерфейс, задержка или контроль качества не соответствуют краткой операции.

Центральный авторский результат - модель доказательно контролируемого генеративного анализа событий информационной безопасности, сокращенно ДКГА-СИБ. Термин «доказательно контролируемый» означает, что каждое существенное утверждение генеративного вывода либо связано с доступным источником, либо явно маркировано как гипотеза, а каждое воздействие проходит независимую проверку полномочий и операционного риска. Архитектура представлена на рисунке 2. Семь слоев образуют не линейный конвейер, а контролируемый цикл: обратная связь аналитика улучшает правила, справочники, шаблоны запросов и тестовый корпус, однако не переписывает первичные свидетельства.

Рисунок 2 - Семислойная архитектура ДКГА-СИБ
Источник: авторская разработка.

Первый слой сохраняет первичную телеметрию в неизменяемом виде. Минимальный набор метаданных включает идентификатор источника, время получения и время возникновения события, схему, контроль целостности, уровень доступа и ссылку на место хранения. Генеративной модели передается не произвольный массив журналов, а минимально необходимое представление с маскированием секретов и персональных данных.

Второй слой выполняет детерминированную обработку: проверяет формат, приводит поля к общей схеме, устраняет технические дубликаты, связывает события по времени, субъекту, активу и сетевой сессии, применяет утвержденные правила корреляции. Смысл слоя состоит в снижении энтропии до обращения к модели. Если десять тысяч одинаковых оповещений можно объединить точным правилом, использование генерации для каждого сообщения экономически и методологически неоправданно.

Третий слой извлекает сведения из доверенных источников: критичность актива из CMDB, владельца и роль учетной записи из IAM, уязвимости и статус исправления из сканера, сетевую зону, бизнес-сервис, утвержденные политики, сведения STIX и актуальную версию ATT&CK. Извлечение должно сохранять идентификатор записи и время актуальности. Такая организация заменяет неконтролируемое «знание модели» проверяемой выборкой из среды организации.

Четвертый слой формирует структурированный результат. Свободный ответ заменяется схемой с обязательными полями: краткое резюме; подтвержденные факты; основная гипотеза; альтернативные гипотезы; признаки за и против; возможная техника ATT&CK; недостающие сведения; предлагаемые запросы; проект мер; ожидаемый операционный эффект; источники каждого утверждения. Отсутствие обязательного поля вызывает техническую ошибку, а не автоматическое заполнение правдоподобным текстом.

Пятый слой проверяет происхождение утверждений. Каждое утверждение классифицируется как факт, вычисленный признак, справочная связь, гипотеза или рекомендация. Факт без ссылки исключается из итоговой карточки; противоречащие источники сохраняются одновременно; неизвестное значение остается неизвестным. Самооценка уверенности языковой моделью не используется как достаточное основание, поскольку числовая уверенность текста не является калиброванной вероятностью истинности.

Шестой слой отделяет аналитическое качество от права действовать. Даже полностью подтвержденный факт не означает, что предложенная мера допустима. Блокировка привилегированной учетной записи может остановить атаку, но также нарушить работу критического сервиса; изоляция узла может уничтожить доступ к оперативной памяти, нужной для расследования. Поэтому отдельно проверяются роль инициатора, критичность актива, обратимость, наличие утвержденного сценария, окно изменений и способ отката.

Седьмой слой передает карточку уполномоченному аналитику либо в SOAR. После решения фиксируются одобренное действие, отклоненные варианты, фактический результат и причина расхождения с рекомендацией. Обратная связь используется для корректировки правил и тестов только после контроля качества. Автоматическое дообучение на каждом решении аналитика опасно: ошибочная локальная практика может закрепиться как систематическое смещение.

Российская работа И.О. Прохорца, В.А. Шматока и М.А. Попова также размещает большую языковую модель над SIEM и машинным обучением как слой семантической интерпретации, контекстной агрегации и поддержки аналитика [21]. Отличие ДКГА-СИБ состоит не в самом добавлении LLM, а в формальном разделении первичного свидетельства, проверяемого утверждения, гипотезы и исполняемого решения, а также в наличии двух независимых допусков. Первый подтверждает достаточность доказательств, второй - правомерность и операционную допустимость воздействия.

Второй авторский результат - карточка доказательности, представляющая результат генеративного анализа как набор проверяемых объектов. Ее состав приведен в таблице 3.

Таблица 3 - Структура карточки доказательности ДКГА-СИБ

Раздел карточки	Обязательное содержание	Правило контроля	Назначение
Идентификация	Уникальный ID, время, источники, связанный инцидент, версия схемы	Поля создаются детерминированно	Исключение смешения разных расследований
Подтвержденные факты	Субъект, актив, действие, объект, время, результат	У каждого факта есть ссылка на первичную запись	Воспроизводимость вывода
Контекст	Критичность актива, роль субъекта, уязвимость, сетевой сегмент, бизнес-сервис	Указываются источник и время актуальности	Оценка значения одного и того же события для разных активов
Основная гипотеза	Предполагаемая причинная цепочка	Маркировка «гипотеза», перечень подтверждающих и опровергающих признаков	Предотвращение подмены факта интерпретацией
Альтернативы	Не менее одной доброкачественной или технической альтернативы, если она логически возможна	Запрещено удалять альтернативу без основания	Снижение эффекта преждевременного закрепления на одной версии
Покрытие доказательствами	Утверждения со ссылками, утверждения без подтверждения, противоречия	Неподтвержденное утверждение не переходит в раздел фактов	Контроль конфабуляций
Таксономия угроз	Тактика, техника или подтехника ATT&CK и признаки сопоставления	Отдельно фиксируется версия базы; атрибуция группы не выводится только из техники	Сопоставимость расследований
Недостающие сведения	Какие данные нужны для различения гипотез	Запрос должен быть выполнимым и минимально необходимым	Управление следующим шагом расследования
Проект решения	Действие, цель, объект, предусловия, побочный эффект, откат	Команда не формируется из свободного текста	Безопасная передача в SOAR
Согласование	Уровень автономии, ответственная роль, решение, время	Неизменяемый журнал одобрения или отклонения	Подотчетность

Карточка меняет единицу качества. Оценивается не сходство с эталонным абзацем, а полнота покрытия существенных утверждений источниками, корректность ссылок, разделение факта и гипотезы, наличие альтернативы и исполнимость следующего шага. Такой подход учитывает вывод исследования облачных инцидентов: автоматические лексические метрики могут слабо соответствовать экспертному восприятию корректности. Для безопасности более релевантен вопрос «может ли аналитик проверить и опровергнуть вывод», чем вопрос «насколько ответ похож на ранее написанный текст».

Третий авторский результат - алгоритм допуска, представленный на рисунке 3. Он реализует принцип fail-closed: недостаток доказательств, прав или механизма отката прекращает автоматическое исполнение, но не мешает сохранить наблюдение и передать его человеку.

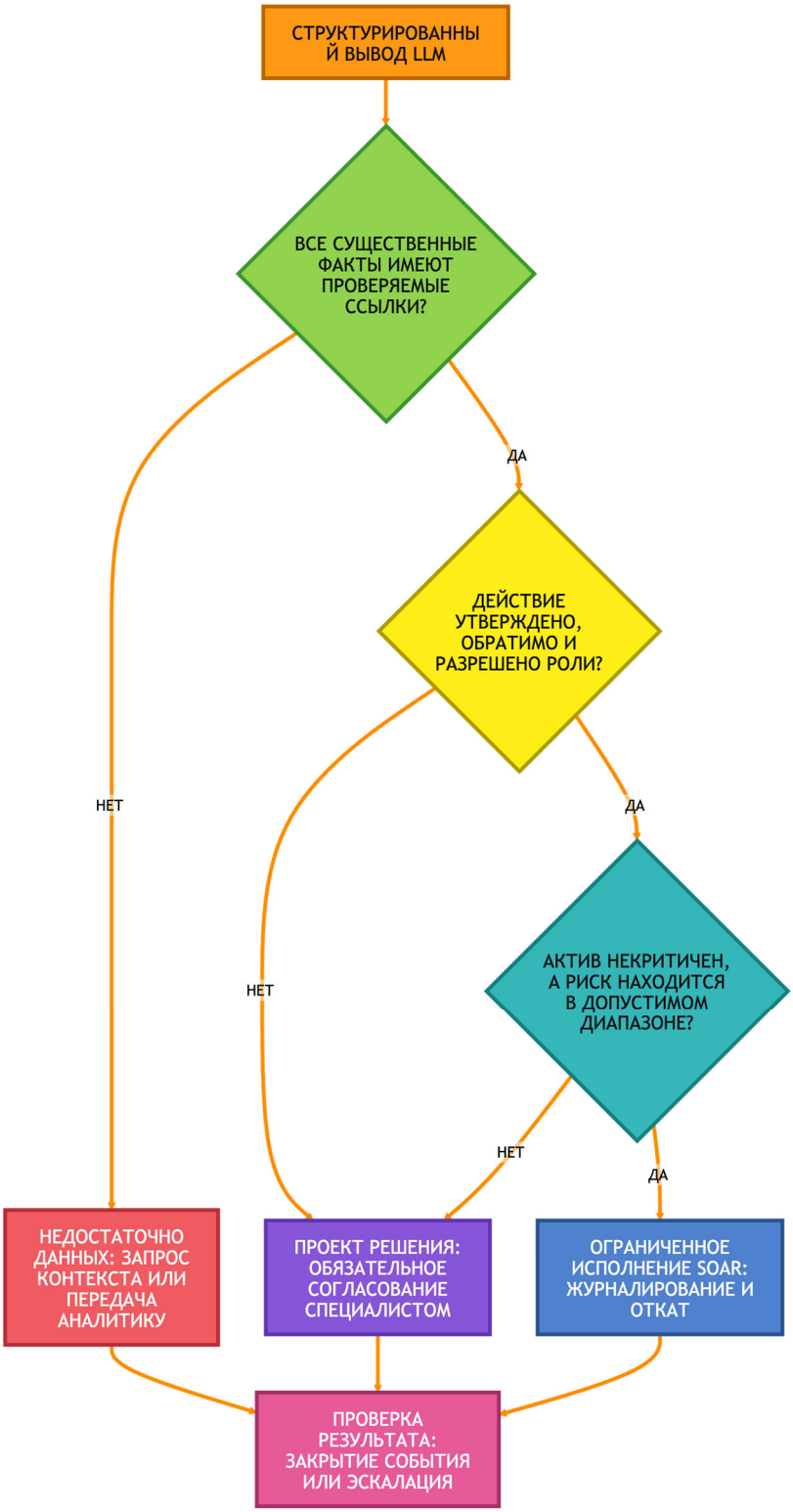

Рисунок 3 - Алгоритм допуска генеративной рекомендации к исполнению
Источник: авторская разработка.

Первый вопрос шлюза относится к эпистемической надежности: достаточно ли доказательств. Второй - к управлению полномочиями и изменениям: разрешено ли действие. Третий - к операционному риску конкретного актива. Последовательность принципиальна. Даже низкорисковая команда не должна исполняться на основе неподтвержденного факта; даже доказанный инцидент не отменяет требований к полномочиям и сохранению доступности.

Таблица 4 - Уровни автономии ДКГА-СИБ

Уровень	Разрешенная функция генеративного ИИ	Исполнение	Пример	Обязательный контроль
A0 - справочный	Поиск, резюмирование и перевод терминов	Отсутствует	Краткое описание группы оповещений	Ссылки на источники, маскирование данных
A1 - рекомендательный	Гипотезы, приоритет, проект запроса и отчета	Только аналитиком	Предложение проверить входы с нового устройства и историю привилегий	Карточка доказательности, экспертное решение
A2 - оркестрационный	Подготовка параметризованного сценария SOAR	После явного согласования	Проект временной блокировки токена или сбора дополнительной телеметрии	Проверка схемы команды, полномочий, объекта и отката
A3 - ограниченно автоматический	Выбор из закрытого набора заранее утвержденных обратимых действий	Автоматически в заданном диапазоне	Добавление низкорискового индикатора во временный список наблюдения	Детерминированные предусловия, лимит времени, журнал, автоматический откат

Уровень A3 не равен свободной автономии агента. Языковая модель не создает команду произвольного содержания и не расширяет собственные права. Она может выбрать только один из заранее описанных сценариев с типизированными параметрами. Удаление данных, изменение сетевой архитектуры, остановка критического сервиса, постоянная блокировка привилегированной учетной записи, изменение политик доступа и иные труднообратимые меры остаются за уполномоченным специалистом независимо от уверенности модели.

Встраивание LLM в SOC создает самостоятельную поверхность атаки. События, отчеты об угрозах, описания уязвимостей, электронные письма и результаты поиска относятся к внешним данным, часть которых может контролироваться нарушителем. Если модель получает одновременно инструкции и недоверенный текст, содержащаяся в тексте команда способна изменить ее поведение.

Российские исследователи И.С. Величко и С.В. Беззатеев систематизировали методы противодействия атакам на языковые модели, включая фильтрацию запросов, изоляцию контекста и обучение с учетом состязательных воздействий [22]. Эти меры полезны, но ни одна фильтрация не заменяет архитектурного запрета на прямое исполнение свободного текста.

K. Greshake, S. Abdelnabi, S. Mishra, C. Endres, T. Holz и M. Fritz экспериментально показали возможность косвенной инъекции подсказки в приложения, где LLM обрабатывает внешние данные: вредоносная инструкция поступает не от непосредственного пользователя, а из документа или другого источника, прочитанного системой [23]. Для SOC это особенно опасно, поскольку содержание журнала, доменное имя, имя файла, заголовок сообщения или текст отчета могут быть сформированы противником.

Таблица 5 - Риски генеративного анализа и обязательные барьеры

Риск	Проявление в SOC	Технический барьер	Остаточное ограничение
Конфабуляция	Несуществующий процесс, IP-адрес, CVE, техника или причинная связь	Генерация только по извлеченному контексту; обязательные ссылки; запрет факта без источника	Ссылка подтверждает происхождение, но аналитик все равно оценивает смысловую достаточность
Косвенная инъекция	Инструкция нарушителя внутри журнала, письма, имени файла или CTI-отчета	Разделение инструкций и данных; экранирование; маркировка происхождения; недоверенный контент не управляет инструментами	Универсального детектора всех семантических инъекций нет
Утечка данных	Передача секретов, персональных данных или внутренней топологии внешнему сервису	Локальная или закрытая модель; минимизация; токенизация; DLP; запрет секретов; договорные и технические границы хранения	Остаточный риск зависит от реализации и режима развертывания
Отравление контекста	Ложная запись в базе знаний или скомпрометированный источник RAG	Белый список источников; подпись; версия; репутация; двухисточниковая проверка критичных сведений	Два зависимых источника могут воспроизводить одну ошибку

Избыточная автоматизация	Ошибочная блокировка, изоляция или изменение политики	Уровни A0-A3; закрытый каталог действий; RBAC; обратимость; подтверждение человека	Формально обратимое действие может иметь необратимый бизнес-эффект
Автоматизационное смещение	Аналитик принимает убедительный текст без проверки	Отображение доказательств до рекомендации; обязательная причина согласия; выбор альтернативы	Организационная культура не обеспечивается одной интерфейсной мерой
Дрейф модели	Изменение качества после обновления модели, подсказки или базы знаний	Версионирование; регрессионный набор; поэтапный выпуск; возможность отката	Тестовый набор не охватывает все будущие сценарии
Отказ и перегрузка	Задержка ответа, рост стоимости, недоступность провайдера	Тайм-аут; кэш; очередь; локальная резервная модель; детерминированный режим деградации	При деградации глубина семантического анализа уменьшается
Манипуляция инструментами	Подмена параметров вызова API или команды SOAR	Строгая схема параметров; отдельный policy engine; подпись запроса; минимальные права	Ошибка в политике допуска остается критическим риском
Невоспроизводимость	Один запрос дает разные формулировки и решения	Фиксация версии модели, системной инструкции, контекста и параметров; сохранение результата	Полная детерминированность не гарантируется для всех моделей и сред

NIST AI 600-1 группирует 12 категорий риска генеративного искусственного интеллекта и предлагает более 200 действий по управлению ими. Среди прямо релевантных SOC категорий находятся конфабуляция, конфиденциальность данных, целостность информации, информационная безопасность, взаимодействие человека и модели, а также интеграция цепочки создания ценности [24]. Таблица 5 переводит эти общие риски в технические границы анализа событий: источник важнее красноречия, внешний policy engine важнее самоограничения модели, а сохраненный журнал решения важнее субъективного ощущения уверенности аналитика.

Переход к ДКГА-СИБ целесообразно выполнять поэтапно. Начальная стадия не требует передачи модели исполнительных полномочий. На уровне A0 выбирается один узкий сценарий с измеримым результатом, например резюмирование коррелированной группы оповещений или подготовка перечня недостающих данных. Вход ограничивается

обезличенными карточками, а результат сравнивается с решением аналитика по полноте фактов, корректности ссылок и времени проверки.

Вторая стадия вводит уровень A1 и карточку доказательности. Для каждого типа события задается минимальный набор контекста. Для подозрительного входа это могут быть история аутентификаций, устройство, география, фактор MFA, роль учетной записи, состояние сессии и критичность ресурса. Для запуска процесса - родительский процесс, командная строка, хеш, подпись, пользователь, сетевые соединения и история на узле. Единый универсальный запрос уступает специализированным шаблонам, потому что доказательная достаточность различается по классам событий.

Третья стадия связывает генеративный слой с SOAR только через типизированный контракт. Контракт должен содержать идентификатор сценария, объект, параметры, срок действия, ожидаемый результат, способ проверки и процедуру отката. Значение, отсутствующее в карточке, не может быть дополнено моделью. Policy engine независимо проверяет роль, критичность актива, окно изменений и разрешенный диапазон параметров.

Четвертая стадия допускает A3 для ограниченного набора обратимых мер после накопления реальных результатов A0-A2. Решение о переходе принимается не по средней удовлетворенности пользователей, а по отдельным критериям качества и безопасности. Минимальная программа проверки должна включать:

1. Полноту доказательств - долю существенных утверждений, имеющих корректную ссылку на доступный источник.
2. Фактическую точность - долю проверенных утверждений, подтвержденных первичной телеметрией и реестрами.
3. Различающую способность - способность отделять вредоносную гипотезу от доброкачественной альтернативы.
4. Время до проверенного решения - интервал от создания карточки до одобрения аналитиком, а не только время генерации текста.
5. Коэффициент исправлений - долю полей, которые аналитик изменил до принятия решения.
6. Безопасность действия - число предотвращенных исполнений из-за недостатка прав, доказательств или обратимости.
7. Устойчивость - качество при изменении формата журнала, появлении неизвестных событий, недоступности источника и наличии враждебного текста.
8. Ресурсную эффективность - задержку, стоимость запроса, потребление памяти и влияние на пропускную способность контура.

Для этих показателей нельзя заранее подставлять желательные проценты. Пороговые значения устанавливаются владельцем процесса с учетом критичности активов и текущего качества ручного триажа. Эмпирическая программа должна использовать реальные обезличенные события, раздельные обучающую, настроечную и контрольную совокупности, слепую экспертную проверку и регистрацию всех исключенных случаев. Если межэкспертное согласие низкое, система не может считаться некачественной только из-за расхождения с единственным экспертом. Сначала требуется уточнить операционное определение правильного решения.

Новизна состоит в разработке ДКГА-СИБ как архитектуры, где генеративная модель не занимает центральное положение источника истины. Ее роль ограничена семантическим синтезом между доказательным контекстом и независимым шлюзом полномочий. Новизна конкретизирована тремя взаимосвязанными конструкциями:

1. Семислойная архитектура отделяет неизменяемые свидетельства и детерминированную корреляцию от генерации, верификации и исполнения.
2. Карточка доказательности преобразует свободный ответ в проверяемую структуру, где факты, гипотезы, альтернативы, пробелы и рекомендации имеют различный эпистемический статус.
3. Двойной допуск разделяет вопрос об истинности аналитического основания и вопрос о допустимости операционного воздействия. Высокая доказательность не расширяет полномочия, а низкий операционный риск не компенсирует отсутствие доказательств.

Авторский вклад в научный результат состоит в функциональном разграничении детерминированной, статистической и генеративной аналитики; разработке семислойной архитектуры ДКГА-СИБ; конструировании карточки доказательности; введении двойного шлюза допуска и четырех уровней автономии; формулировании критериев будущей эмпирической проверки. Все элементы образуют единую систему и непосредственно отвечают установленному противоречию между семантической гибкостью LLM и доказательными требованиями SOC.

Отличие от подходов, оценивающих модель преимущественно по F1, лексическому сходству или средней скорости решения задачи, заключается в переносе центра оценки на трассируемость и безопасность перехода от события к действию. Такая постановка не отменяет метрики обнаружения, но добавляет критерии, без которых производственное применение в SOC остается методологически неполным.

Практическая ценность модели определяется совместимостью с существующей инфраструктурой. SIEM продолжает собирать и хранить события; ML-модуль выделяет статистические сигналы; CMDB, IAM, сканер уязвимостей, STIX и ATT&CK предоставляют контекст; LLM формирует структурированную карточку; policy engine проверяет допуск; SOAR выполняет только разрешенный сценарий. Поэтому внедрение не требует замены всей системы мониторинга одной генеративной платформой.

Границы применимости связаны с качеством телеметрии, актуальностью справочников, полнотой временной синхронизации, доступностью контекста и зрелостью управления изменениями. Если исходные журналы неполны или источник скомпрометирован, генеративный слой не восстанавливает достоверную картину. Он способен лишь явно показать пробел и сформировать запрос на дополнительные сведения. Архитектура также не решает автоматически проблему юридической квалификации инцидента, атрибуции нарушителя или оценки ущерба без соответствующих данных и компетентного решения.

Основное ограничение работы - отсутствие апробации ДКГА-СИБ на обезличенной телеметрии действующего SOC. Поэтому модель имеет концептуальный уровень доказательности. Подтвержденных данных о ее влиянии на MTTD, MTTR, число ложноположительных срабатываний, полноту расследования и стоимость обработки нет. Следующий этап исследования должен включать проспективное сравнение обычного триажа и триажа с ДКГА-СИБ на одной совокупности реальных событий при одинаковом доступе к данным, с раздельной оценкой опытных и начинающих аналитиков и обязательным тестированием косвенной инъекции подсказок.

Заключение

Автоматизация анализа событий информационной безопасности требует четкого разграничения детерминированных, статистических и генеративных операций. Регистрация события, фиксация времени, контроль целостности, нормализация полей, корреляция по установленным правилам и исполнение защитных команд должны выполняться механизмами с воспроизводимым результатом. Генеративный искусственный интеллект целесообразно применять на следующем аналитическом уровне - для объединения разнородного контекста, подготовки содержательного резюме, формулирования конкурирующих гипотез, выявления недостающих сведений и разработки проекта реагирования. При таком распределении функций языковая модель дополняет SIEM и SOAR, но не подменяет их базовые механизмы.

Результаты опубликованных исследований подтверждают практический потенциал языковых моделей, однако не дают оснований считать их универсальным средством автоматизации SOC. LogPrompt оценивался на девяти публичных наборах данных и в двух аналитических задачах. Исследование генерации причин и мер реагирования на облачные инциденты охватило 44 340 инцидентов из 1 759 сервисов Microsoft. В двух итерациях рандомизированного исследования Copilot for Security участвовали 147 специалистов по информационной безопасности и 149 пользователей без профессионального опыта в этой области. Зафиксированное ускорение отдельных операций сочеталось с зависимостью результатов от характера задания, качества контекста и выбранной методики оценки. Лексическое сходство с эталонным ответом не гарантировало фактической корректности, а в одной из кратких задач применение генеративной поддержки увеличило продолжительность работы. Следовательно, оценка должна охватывать не только скорость и формальное сходство текстов, но также проверяемость утверждений, полноту доказательств и безопасность предлагаемого действия.

Предложенная архитектура ДКГА-СИБ объединяет семь последовательно контролируемых слоев: первичные свидетельства, нормализацию и корреляцию, доверенный контекст, генеративный синтез, верификацию утверждений, риск-адаптивный шлюз, решение и обратную связь. Такое построение сохраняет способность языковой модели интерпретировать семантически неоднородные данные, одновременно исключая ее использование в качестве источника первичных фактов. Первичные журналы остаются неизменяемым доказательным основанием, а вывод модели приобретает рабочую ценность только после сопоставления с телеметрией, сведениями об активах, учетных записях, уязвимостях, политиках безопасности и наблюдаемом поведении.

Карточка доказательности переводит генеративный ответ из свободной текстовой формы в проверяемую аналитическую структуру. Подтвержденные факты, вычисленные признаки, справочный контекст, основная гипотеза, альтернативные объяснения, недостающие сведения и рекомендации получают различный эпистемический статус. Утверждение, для которого отсутствует ссылка на первичную запись или доверенный источник, не включается в фактическое основание решения. Неопределенность при этом сохраняется как самостоятельный результат анализа, а не скрывается за убедительной формулировкой. Такой принцип снижает риск конфабуляций и позволяет аналитику не только принять, но и аргументированно опровергнуть машинную интерпретацию.

Двойной шлюз допуска разделяет достаточность доказательств и допустимость операционного воздействия. Даже достоверно установленное событие не создает автоматического права на блокировку учетной записи, изоляцию узла, изменение сетевой политики или остановку сервиса. До исполнения проверяются полномочия инициатора, критичность актива, обратимость меры, наличие утвержденного сценария, срок действия ограничения и возможность отката. Автоматическое выполнение допустимо только для

заранее определенного каталога низкорисковых и обратимых операций. Необратимые действия, вмешательство в работу критических сервисов и изменение привилегированных учетных записей сохраняются за уполномоченным специалистом.

Предложенный подход согласуется с действующими требованиями Республики Казахстан к регистрации и длительному хранению событий, защите журналов, объяснимости полностью автоматизированных решений, человеческому пересмотру и риск-ориентированному управлению системами искусственного интеллекта. Трассируемость происхождения фактов, фиксация версии модели и контекста, регистрация согласования и сохранение результата исполнения формируют единый механизм технической и организационной подотчетности.

Практическое внедрение ДКГА-СИБ целесообразно начинать со справочного и рекомендательного уровней А0-А1, не предоставляя языковой модели исполнительных полномочий. Качество системы должно оцениваться по полноте доказательств, фактической точности, времени до проверенного решения, доле исправленных аналитиком полей, устойчивости к изменению форматов журналов и враждебным инструкциям, безопасности предлагаемых действий и ресурсной эффективности. Переход к ограниченному автоматическому исполнению может рассматриваться только после апробации на реальных обезличенных событиях действующего SOC. До получения таких результатов ДКГА-СИБ представляет собой теоретически обоснованную авторскую архитектуру, практическая эффективность которой требует самостоятельной эмпирической проверки.

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Pedagogical Sciences

IDENTIFYING NOVICE PROGRAMMING MISCONCEPTIONS AND AI UNDERSTANDING GAPS AMONG KAZAKHSTANI 7TH-GRADERS

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ABSTRACT

This article presents a qualitative and quantitative analysis of typical syntactic, logical, and conceptual errors, as well as naive mental models of artificial intelligence among 7th-grade students (N = 24) who completed a 34-hour elective course "Python Artificial Intelligence Programming." Unlike summative evaluations of course effectiveness, this study focuses on the internal mechanisms of student difficulties during the transition from basic Python syntax to applied libraries (NumPy, Pandas, OpenCV, scikit-learn). Based on the analysis of 120+ saved digital code artifacts (Thonny IDE log files and GitHub Classroom), tests, and semi-structured interviews (n = 8), a systematic error classification was derived. It was established that the most frequent problems were array dimension mismatches (70.8%), confusion between return and output statements (return vs print, 54.2%), and input data types (37.5%). Regarding AI perception prior to the course, 79.2% of students demonstrated anthropomorphic misconceptions ("AI thinks like a human"), which shifted after the course to an understanding of AI as a mathematical model trained on datasets (in 91.7% of students). The findings form a foundation for adapting instructional materials and reducing cognitive load in K-12 IT education.

Keywords: novice programmers, Python misconceptions, mental models, artificial intelligence, K-12, misconceptions, qualitative analysis, cognitive load, K-12 computer science.

Introduction

Stating a general growth in student performance following course completion (as demonstrated in previous study stages) does not provide a complete answer to how competencies are formed and what specific barriers a 12–13-year-old student's mind encounters. The introduction of complex applied fields such as Python programming and fundamentals of artificial intelligence (AI) in 7th grade inevitably causes cognitive overload.

Students simultaneously master text-based programming syntax, the logic of abstract algorithmic structures, and the specific mathematical-structural logic of data processing libraries (NumPy, Pandas, OpenCV). Furthermore, deeply ingrained everyday stereotypes and popular media depictions of AI "omnipotence" create mental barriers that hinder an objective understanding of machine learning principles.

Studying and classifying specific errors (programming misconception profiling) and shifts in AI understanding are necessary for instructional design. Understanding precisely where a student experiences a logical failure allows for designing targeted scaffolding, revising learning tasks, and preventing the reinforcement of incorrect mental models.

The objective of this article is to conduct a detailed categorical analysis of students' syntactic and conceptual errors when writing code in Python, as well as to trace the transformation of their perceptions regarding the essence and limitations of artificial intelligence technologies before and after completing a 34-hour course.

Literature Review

The methodological foundation of this study is the work by Sally Hamouda and co-authors (Virginia Tech, 2025) [1]. In their study, the authors presented a detailed taxonomy of conceptual gaps among 105 K-12 students, proving that 31.4% of novice learners systematically confuse the concepts of variables and data types, and only 20% are capable of correctly constructing and debugging composite conditional statements (if/else) on the first attempt [1]. Hamouda's approach demonstrated that quantitatively counting the frequency of specific syntactic and logical error patterns makes it possible to identify fundamental flaws in the educational curriculum [1].

The concept of the "notional machine" described by J. Sorva [2] explains that novice programmers' errors stem from an incorrect internal model of how a computer executes code. R. D. Pea, in his classic work [3], highlighted the "superbug"—the tendency of novices to attribute human intelligence and the ability to "guess" the author's intentions to the computer. In the context of modern education, this superbug extrapolates to AI systems: students tend to anthropomorphize machine learning algorithms [5].

Works by M. Guzdial [4] and D. S. Touretzky et al. [5] emphasize that forming adequate mental models of AI at school age requires a shift from the concept of a "magic black box" to an understanding of AI as a mathematical function converting input data into output predictions based on trained parameters.

Methods and Materials

Context and Participants: The study was conducted at "PhysTech School Almaty" as part of piloting an author-designed 34-hour elective course titled "Python Artificial Intelligence Programming." A total of N = 24 7th-grade students participated in the study (pilot group).

Data Collection: To conduct a mixed (qualitative-quantitative) analysis, a set of methods was utilized:

• Analysis of digital code artifacts: Over 120 saved scripts and debugging log files from the Thonny IDE environment and GitHub Classroom platform were collected and analyzed, generated by students during practical mini-projects.

• Semi-structured interviews: 8 individual interviews with students were conducted (sample formed considering different academic achievement levels: 2 high-performing, 4 average, 2 low-performing). Interviews were carried out in two stages—at Week 4 (after the "Python Basics" module) and at Week 34 (after defending the "Smart School System" project).

• Written diagnostic tests and questionnaires: Open-ended questions asking students to explain code execution and AI mechanisms before and after the course.

Analysis Procedure: Code errors were classified into 5 main categories. The frequency of each error type was calculated as the percentage of students in the group (N = 24) who committed that error at least three times in independent practical tasks. Qualitative interview data were coded using thematic analysis to identify mental models of AI.

Results: Categorical Analysis of Python Code Misconceptions

Based on the analysis of collected artifacts, 5 key categories of syntactic and logical difficulties were identified. Summary statistics of error frequencies are presented in Table 1.

Table 1. Categories and frequency of programming errors among 7th-grade students (N = 24)

Error Category	Specific Error Manifestation	% of Students
1. Syntax and Indentation	IndentationError, missing colons : after if/for/def	62.5%
2. Data Types and Input	Implicit type conversion issues (string from input() instead of int/float)	37.5%
3. Conditional Logic	Confusion between assignment = and comparison ==, complex if/else	45.8%
4. Functions & Scope	Replacing return with print(), using local variables outside scope	54.2%
5. Dimensions & Data Structures	Format mismatches in OpenCV/NumPy, incorrect file path errors	70.8%

Below is a detailed qualitative breakdown of each category with real student code examples.

Category 1: Indentation and Syntactic Blocks (IndentationError)

Unlike languages with curly braces, Python requires strict indentation discipline. 7th-grade students accustomed to text editors did not perceive indentation as a syntactic structure.

Student Code Example (Week 3):

```
def check_temperature(temp):
if temp > 37.5: # IndentationError: expected an indented block
print("ALERT: High temperature!")
else:
print("Normal")
```

Typical Misconception: Students believed that line breaks alone implied subordination of a block to a conditional statement. 62.5% of students regularly encountered IndentationError. After introducing indentation highlighting in Thonny IDE by session 10, this error persisted in only 8.3% of students.

Category 2: Variables, Data Types, and Input (TypeError)

Similar to findings by S. Hamouda (2025) [1], where 31.4% of students confused data types, in our sample 37.5% of students failed to account for the fact that the input() function always returns a string type (str).

Student Code Example (Week 2):

```
age = input("Enter your age: ")
if age >= 18: # TypeError: '>=' not supported between instances of 'str' and 'int'
    print("Access granted")
```

Qualitative observation (Interview with Student B., age 12):

"I entered the number 15 from the keyboard! It says 15 on the screen, so Python should understand that it's a number, not a word."

This quote illustrates the absence of a concept regarding internal data encoding in computer memory within the student's mental model.

Category 3: Comparison Operators and Conditional Logic

45.8% of students faced difficulties writing conditional statements, confusing the assignment operator = with logical comparison ==.

Student Code Example (Week 4):

```
user_role = "admin"
if user_role = "admin": # SyntaxError: invalid syntax
    print("Welcome, System Administrator")
```

Additionally, when constructing complex conditions, students wrote expressions in natural language style: if x and y > 10: instead of if x > 10 and y > 10:, which led to subtle semantic bugs.

Category 4: Functions: Confusion between print() and return

This issue proved to be one of the most persistent (54.2% of students). Students perceived print() as the final result of a function's execution.

Student Code Example (Week 6):

```
def calc_grade_average(grades):
    avg = sum(grades) / len(grades)
    print(avg) # Error: function returns None

final_score = calc_grade_average([5, 4, 5, 3])
if final_score > 4.0: # TypeError: '>' not supported between instances of 'NoneType' and 'float'
    print("Excellent student")
```

Students struggled to understand why final_score evaluated to None when 4.25 was successfully printed to the console. This confirms an immature mental model of data passing across function stack frames.

Category 5: Array Dimensions and Specifics of AI Libraries (OpenCV, NumPy)

When transitioning to computer vision and machine learning modules, 70.8% of students encountered barriers related to matrix type and dimension mismatches (2D/3D arrays).

Student Code Example (Week 18, OpenCV module):

```
import cv2

img = cv2.imread("student.jpg")
# Error 1: img is None because the path is incorrect
gray = cv2.cvtColor(img, cv2.COLOR_BGR2GRAY)
# cv2.error: Severe error in cvtColor (src is empty)
```

Students failed to verify whether the file was successfully loaded from disk, expecting that "the function would find the picture on the desktop itself." In scikit-learn, a frequent error was passing a 1D list [1, 2, 3] to model.predict(), which expected a 2D array [[1, 2, 3]] (ValueError: Expected 2D array, got 1D array instead).

Results: Dynamics of Mental Models and AI Misconceptions

Analysis of diagnostic answers and interview transcripts revealed significant changes in how students understood AI principles. Prior to the course, anthropomorphic and magical mental models dominated (see Table 2).

Table 2. Dynamics of mental models and AI misconceptions pre- and post-course (N = 24)

Misconception Category / Mental Model	Pre-Course %	Post-Course %	Change (Δ)
Anthropomorphism: "AI thinks, feels, and makes decisions like a human"	79.2%	8.3%	-70.9%
Absolute Infallibility: "AI never makes errors, it knows everything"	66.7%	12.5%	-54.2%
Magical Spontaneous Generation: "AI works on its own, it doesn't need data"	83.3%	4.2%	-79.1%
Mathematical-Algorithmic Understanding: "AI is a model trained on datasets"	8.3%	91.7%	+83.4%

Qualitative Illustrations of Thinking Transformation:

From Anthropomorphism to Algorithms:

Pre-course (Student D., age 12): "The phone camera recognizes me because the smartwatch and neural network memorized my face and miss me when I don't look at the screen."

Post-course (same student, Week 34): "The camera doesn't know who I am. The OpenCV library just crops a square of pixels, converts the image to grayscale, and uses Haar cascades to look for contrast matches in shadows. It's just a matrix of numbers."

Understanding the Role of Training Data (Garbage In, Garbage Out):

Pre-course (Student A., age 13): "AI always gives the correct answer because it's connected to the whole internet."

Post-course (same student, Week 30): "Our grade prediction model made a mistake because we only gave it 10 rows in the dataset, and with garbage values too. If you load bad data into train_test_split, the model will learn incorrectly and output nonsense."

Distinguishing Rules from Machine Learning:

After completing the chatbot project (Week 25) and scikit-learn classifier (Week 30), 87.5% of students clearly delineated hardcoded algorithms (if/else rules) from statistical machine learning.

Interview Quote (Student K., age 13):

“I used to think a Telegram chatbot was already AI. But when we wrote a bot using if/elif ourselves, I realized it's just a brancher. But when we trained DecisionTreeClassifier to recognize activity—that's real AI because it found the weights on its own.”

Discussion

A comparative analysis of our findings with data from Sally Hamouda (2025) [1] shows a similar distribution of basic syntactic errors in novices (type conversion, conditions). However, incorporating applied AI libraries in 7th grade adds a specific layer of cognitive load related to spatial and matrix thinking (NumPy and OpenCV data structures).

The key pedagogical takeaway is that hands-on programming of AI elements serves as the best antidote against technology mythologization. As long as AI remains an abstract media

concept, students view it through sci-fi lenses. Once a student personally encounters a ValueError while training a K-Nearest Neighbors (KNN) model, the "magical" mental model breaks down, making way for engineering thinking.

Recommendations for Future Course Iterations:

• Stack-frame visualizers: To overcome confusion between print() and return, visual debuggers (e.g., Python Tutor) should be used in early stages.

• Pre-validation of data: OpenCV and file handling modules must include file existence checks (try/except or os.path.exists) before calling processing functions.

• Graphical shape diagrams: When teaching ML models, visual maps of array shapes (array.shape) should be used to prevent tabular dimension mismatch errors.

The results of this study advance the overall design of doctoral research, providing qualitative justification for developing adaptive instructional materials and debugging exercises for secondary schools in the Republic of Kazakhstan.

Conclusion

The qualitative and quantitative analysis of errors and mental models among 7th-grade students yields the following conclusions:

1. The most frequent technical barriers for students learning AI in Python are array dimension mismatches (70.8%), lack of understanding of function return values (54.2%), and indentation syntax (62.5%).

2. Completing the 34-hour elective course facilitated a radical transformation in students' perceptions of AI: anthropomorphic misconceptions dropped from 79.2% to 8.3%, while the proportion of students understanding AI as a mathematical-algorithmic model rose from 8.3% to 91.7%.

3. The detailed error map establishes an empirical basis for creating specialized instructional guides aimed at preventing typical misconceptions in novice programmers.

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Medical Sciences

The State of Hand Microsurgery in the Republic of Kazakhstan

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Abstract. Hand microsurgery, encompassing digit and limb replantation, revascularization, and microvascular reconstructive procedures, has developed into a specialized field within Kazakhstan's trauma and reconstructive surgery services, concentrated primarily in Almaty-based national centers with more limited regional distribution. This paper reviews the existing published literature describing the epidemiology of hand trauma and the practice of reconstructive hand microsurgery within the Republic of Kazakhstan, situating these findings against the substantially larger body of published experience from the United States, where digit replantation rates and provider volume have been extensively tracked at a national level. The review identifies a consistent gap: while individual Kazakhstani centers have published detailed single-center case series, no unified national registry or standardized outcome-reporting framework currently exists to track hand microsurgery volume, technique, or long-term functional outcomes across the country's treatment centers. To address this gap, the paper proposes a structured, retrospective, multi-center data-collection protocol, modeled on comparable national-level studies conducted in the United States, intended to generate the descriptive foundation for future prospective and registry-based research. This paper is conceptual and methodological; it does not report newly collected patient outcome data.

Keywords: hand microsurgery; digit replantation; reconstructive microsurgery; Kazakhstan; hand trauma epidemiology; outcome standardization; national registry

Introduction

Injuries to the hand and upper extremity remain among the most frequent categories of traumatic presentation to emergency and trauma services worldwide, and their consequences extend well beyond the immediate injury, frequently affecting a patient's long-term occupational capacity, functional independence, and quality of life. Among the surgical techniques available for managing severe hand trauma, microsurgery, defined by the use of an operating microscope, specialized micro-instrumentation, and fine suture material to repair vessels and nerves often no larger than one to two millimeters in diameter, has become the technical foundation for digit and limb replantation, revascularization, and complex reconstructive procedures following traumatic amputation or severe soft-tissue loss.

Within the Republic of Kazakhstan, reconstructive and plastic microsurgery has developed as a distinct clinical service concentrated in a small number of specialized national and regional centers, most prominently the Department of Reconstructive and Plastic Microsurgery of the National Scientific Center of Surgery named after A.N. Syzganov in Almaty, alongside hand-trauma services at the Batpenov National Scientific Center for Traumatology and Orthopaedics. Kazakhstani surgeons affiliated with these centers have published case-series and single-center retrospective analyses describing their institutional experience with hand injury treatment, including a recent comprehensive review of 295 patients treated between 2021 and 2022 (Mukhamedkerim et al., 2025), as well as reports on technically demanding procedures such as heterotopic finger

replantation presented at international hand-surgery meetings (Muradov et al., 2014, as reported in AAHS conference proceedings).

At the same time, national-level epidemiological data specific to hand and upper-extremity trauma in Kazakhstan remains comparatively limited. A broader epidemiological study of traumatic injury in the country found that upper- and lower-extremity injuries were especially frequent among adolescents aged fifteen to seventeen, that surgical intervention was undertaken in approximately one in three of all recorded injuries, and that surgical intervention rates were higher in the country's two largest cities, Almaty and the capital, than in other regions, with osteomyelitis identified as the most frequent infectious complication following trauma and orthopedic care (Pliska, 2022). While informative, this study addressed traumatic injury broadly rather than hand microsurgery specifically, leaving an incomplete picture of how replantation and reconstructive microsurgery outcomes vary across Kazakhstan's treatment centers.

This contrasts with the situation in the United States, where digit replantation practice has been the subject of sustained, national-level epidemiological surveillance for more than two decades. Using large administrative claims and inpatient-sample databases, American researchers have tracked trends in replantation attempts and success rates, provider and hospital volume, and the economic dimensions of upper-extremity replantation care, generating a detailed, quantitatively grounded picture of how the availability and quality of microsurgical services have evolved over time (Cho et al., 2018; Friedrich et al., 2011; Hustedt et al., 2016). This body of American literature offers not only substantive comparative findings but also a methodological template, grounded in registry-style retrospective data extraction, that has not yet been systematically applied within the Kazakhstani context.

The present paper pursues two aims. First, it reviews and synthesizes the existing literature describing hand trauma epidemiology and microsurgical practice in Kazakhstan, situating these findings within the broader international, and specifically American, literature on digit replantation and hand microsurgery outcomes. Second, it proposes a structured, retrospective, multi-center data-collection protocol intended to establish, for the first time at a national level, a standardized descriptive foundation for hand microsurgery outcomes in Kazakhstan. Consistent with its conceptual and methodological character, the Materials and Methods section of this paper is written in the future and conditional tense, describing a protocol that has not yet been executed rather than reporting completed empirical findings.

Literature Review

Institutional Development of Hand Microsurgery in Kazakhstan

Published accounts of hand microsurgery practice in Kazakhstan center overwhelmingly on a small number of specialized institutions, reflecting the concentration of microsurgical expertise typical of a technically demanding subspecialty in a country of Kazakhstan's population and geographic scale. The Department of Reconstructive and Plastic Microsurgery at the National Scientific Center of Surgery named after A.N. Syzganov in Almaty represents the most extensively documented such center in the peer-reviewed literature, with a recent retrospective analysis summarizing the department's experience treating 295 patients with hand injuries between the beginning of 2021 and the end of 2022 (Mukhamedkerim et al., 2025). Complementing this single-center case series, Kazakhstani microsurgeons from the same institution have also presented technically specialized procedures, including heterotopic replantation of amputated fingers to alternative recipient sites as a reconstructive strategy for otherwise unsalvageable injuries, at international hand-surgery meetings (Muradov et al., 2014, as reported in AAHS conference proceedings).

Epidemiology of Hand and Upper-Extremity Trauma in Kazakhstan

Beyond institution-specific case series, epidemiological characterization of traumatic injury in Kazakhstan more broadly has identified several patterns relevant to hand microsurgery service planning. An analysis of injury patterns and associated infectious complications found that upper- and lower-extremity injuries were disproportionately common among adolescents, that roughly one in three recorded injuries required surgical intervention, and that surgical treatment rates were concentrated in Almaty and the capital relative to other regions of the country, with osteomyelitis representing the most frequently observed post-traumatic infectious complication and staphylococcal species the most common causative organisms (Pliska, 2022). These findings suggest both a geographically uneven distribution of surgical, and by extension microsurgical, capacity, and a need for infection-control considerations specific to the regional trauma-care context to be incorporated into any future microsurgery outcome-reporting framework.

Comparative International Context: Digit Replantation Practice in the United States

The American literature on hand microsurgery offers a substantially more extensive and quantitatively detailed body of evidence, generated primarily through large national administrative and inpatient-sample databases rather than single-center case series. A national-level survey of members of the American Society for Surgery of the Hand found that although the majority of surveyed hand surgeons had received residency training in orthopedic or plastic surgery, the extent to which microsurgical techniques were incorporated into routine practice varied considerably, with survey responses received from 561 of 1,238 contacted members (Payatakes et al., 2007). Subsequent national-level analyses using inpatient-sample data spanning 2001 to 2014 documented a continued decline in the rate of attempted and successful digit replantation despite expert advocacy for the procedure, finding that in 2012 only fifty-five percent of Level-I and twenty-nine percent of Level-II trauma centers offered immediate access to a digit replantation service, and that only about half of hand surgeons certified in microsurgery actually performed the procedure, with most of those who did completing fewer than five cases annually (Cho et al., 2018).

Related American research has examined the structural and economic drivers underlying this pattern, including evidence that decentralization of replantation services away from high-volume centers has had a measurable detrimental effect on national replantation outcomes (Hustedt et al., 2016), that hospital and surgeon case volume is significantly associated with successful thumb replantation (Mahmoudi & Chung, 2017), and that the economics of upper-extremity replantation, including reimbursement structures, have shaped where and how often the procedure is performed (Chen & Narayan, 2009). A national epidemiological description of upper-extremity replantation surgery in the United States has further mapped how replantation caseload is distributed across hospital types and geographic regions (Friedrich et al., 2011). Earlier technical case reports, such as an early account of cross-hand replantation following a severe mining accident, illustrate the long developmental history of complex microsurgical salvage techniques within American academic surgical centers (Kutz et al., 1982).

Synthesis and Identified Gap

Considered together, the Kazakhstani and American literatures reveal markedly different evidentiary foundations for describing hand microsurgery practice. Kazakhstani publications, while clinically detailed, remain confined to single-center retrospective case series and conference-presented technical reports, without a unifying national data-collection framework. American research, by contrast, has been able to draw on large, standardized administrative databases to generate national-level estimates of replantation rate, provider volume, and outcome trends over multi-decade periods. This asymmetry does not necessarily imply a difference in the quality of clinical care; the case series from the National Scientific Center of Surgery named after A.N. Syzganov describe technically sophisticated procedures, including heterotopic replantation, that are reported comparatively rarely even in the American literature. Rather, it identifies a specific

methodological gap: the absence, within Kazakhstan, of a standardized, multi-center retrospective or registry-based data-collection framework analogous to those that have enabled the American national-level analyses reviewed above. Section 3 proposes such a framework.

Workforce and Training Considerations

A further theme relevant to comparing hand microsurgery systems concerns the surgical workforce itself. The American survey of hand-surgery society members found considerable heterogeneity in prior microsurgical training and current practice patterns, with the majority of respondents having trained through orthopedic surgery residency and only a minority through plastic surgery pathways, and with many respondents reporting that they did not routinely incorporate microsurgical techniques into practice despite having received some formal training in them (Payatakes et al., 2007). Related American research has similarly found that case volume per surgeon remains low even among those who do perform replantation, with most active replant surgeons completing fewer than five cases annually, a pattern that has been linked to the broader national decline in replantation rates over time (Cho et al., 2018).

Comparable workforce data specific to Kazakhstani hand and microsurgery practitioners have not, to the knowledge of the present review, been published in a form allowing direct comparison with these American findings. The existing Kazakhstani literature instead documents institutional experience at the department level, such as the 295-patient case series from the National Scientific Center of Surgery named after A.N. Syzganov (Mukhamedkerim et al., 2025), without disaggregating outcomes by individual surgeon volume or training background. This represents a further specific gap that the data-collection framework proposed in Section 3 is designed to help address, by explicitly incorporating surgeon-level experience as a candidate variable alongside center-level case volume.

Materials and Methods

Proposed Study Design and Participating Centers

A retrospective, multi-center descriptive study would be proposed, encompassing the principal Kazakhstani institutions known from the published literature to provide hand microsurgery services, including the Department of Reconstructive and Plastic Microsurgery of the National Scientific Center of Surgery named after A.N. Syzganov in Almaty and the microsurgery and hand-trauma department of the Batpenov National Scientific Center for Traumatology and Orthopaedics, together with any additional regional centers identified through a structured survey of the Kazakhstani Ministry of Healthcare's registered trauma and reconstructive surgery departments. The proposed study period would extend across at least five consecutive calendar years to capture sufficient case volume for meaningful comparison across centers, extending and standardizing the two-year single-center window used in the most recent published Kazakhstani case series (Mukhamedkerim et al., 2025).

Center identification would proceed in two stages. First, all institutions already represented in the published Kazakhstani hand-microsurgery literature would be invited to participate, given their demonstrated capacity and willingness to document and report clinical experience. Second, a supplementary survey of regional trauma and orthopedic departments would be conducted, modeled on the approach used in the American national society survey (Payatakes et al., 2007), to identify any additional centers performing hand microsurgery procedures that have not yet published their experience, thereby reducing the risk that the proposed dataset would simply reproduce the existing publication bias toward the country's most research-active institutions. Each participating center would be asked to designate a local data coordinator responsible for chart identification and de-identified data extraction, with a centralized study team providing a standardized data-collection instrument and periodic data-quality review.

Proposed Inclusion Criteria and Data Sources

Eligible cases would include all patients presenting with traumatic digit or hand amputation, or with severe hand or upper-extremity soft-tissue and vascular injury requiring microsurgical intervention, at a participating center during the defined study period. Data would be drawn from existing hospital medical records, operative reports, and, where available, departmental case logs, rather than from newly conducted clinical examinations, consistent with the retrospective chart-review design used in comparable published studies (Mukhamedkerim et al., 2025; Pliska, 2022).

Cases would be excluded where documentation was insufficient to determine the injury mechanism, the procedure performed, or the immediate postoperative outcome, in order to preserve the reliability of the resulting descriptive dataset. Pediatric cases (patients under eighteen years of age) would be recorded separately from adult cases given the distinct injury patterns and healing characteristics previously noted in the broader Kazakhstani adolescent trauma literature (Pliska, 2022), allowing age-stratified analysis without conflating pediatric and adult outcome patterns. Where a participating center's records distinguish between primary replantation performed at initial presentation and delayed or staged procedures, this distinction would be preserved in the extracted dataset, consistent with the level of procedural detail reported in existing single-center Kazakhstani case series.

Proposed Data Extraction Framework

Table 1 below summarizes the proposed categories of data to be extracted from participating centers' records, together with the rationale or published precedent supporting each category. This framework is intended to allow direct comparison, where methodologically appropriate, against the American national-level replantation literature reviewed in Section 2.3, while remaining sensitive to the more limited scale and differing organization of Kazakhstan's hand-trauma treatment system.

Data extraction would be performed using a standardized electronic case report form, piloted at a single center before wider deployment to identify and resolve ambiguities in variable definitions across institutions with differing documentation practices. Particular attention would be given to operationalizing ischemia time (the interval between injury and restoration of blood flow), given its recognized importance as a predictor of replantation success in the American literature (Friedrich et al., 2011), since this interval may be documented inconsistently across Kazakhstani centers depending on regional emergency-transport infrastructure and record-keeping practice. Where exact ischemia time could not be reliably determined from existing records, a categorical estimate (for example, under six hours, six to twelve hours, or over twelve hours) would be recorded instead, preserving analytic value while accommodating documentation limitations.

Table 1. Proposed Multi-Center Data Extraction Framework for Hand Microsurgery Outcomes in Kazakhstan (illustrative planning framework; not yet applied to patient-level data)

Data category	Proposed extraction variables	Rationale / precedent
Demographics	Age, sex, occupation, region/center	Consistent with variables reported in Mukhamedkerim et al. (2025) and Pliska (2022)
Injury characteristics	Mechanism, digit(s)/level involved, time from injury to surgery (ischemia time)	Ischemia time is a recognized predictor of replantation success in the U.S. literature (Friedrich et al., 2011)
Procedure type	Replantation vs. revision amputation, tendon/nerve/vascular repair type	Mirrors classification used by Mukhamedkerim et al. (2025)
Center/provider experience	Annual case volume per center, surgeon years of microsurgical experience	Volume-outcome relationship established by Mahmoudi & Chung (2017)
Outcome	Digit/limb survival, early complications, reoperation	Primary outcome in FRONT study framework (Cho et al., 2018)
Follow-up	Duration and completeness of functional follow-up, where recorded	Highlighted as a data gap in existing regional literature

Proposed Outcome Measures and Comparative Benchmarking

The primary proposed outcome would be digit or limb survival following replantation or revascularization, defined consistently with the classification used in the American FRONT study framework (Cho et al., 2018), allowing direct rate comparison. Secondary proposed outcomes would include early complication rate, reoperation rate, and, where medical records permit, duration and completeness of functional follow-up, an area explicitly identified above as under-documented in the existing regional literature. Center-level case volume and surgeon years of microsurgical experience would additionally be recorded as candidate explanatory variables, given the volume-outcome relationship previously demonstrated in the American thumb-replantation literature (Mahmoudi & Chung, 2017).

Where a comparable outcome definition exists in the American literature, the proposed protocol would adopt it directly rather than defining a Kazakhstan-specific alternative, in order to maximize the interpretability of any resulting cross-national comparison; for instance, revision amputation would be recorded as a distinct outcome category rather than as a subtype of failed replantation, mirroring the categorical distinction maintained throughout the American national-trend literature (Cho et al., 2018; Chen & Narayan, 2009). Economic variables, including approximate procedure cost and reimbursement source where documented, would also be recorded as a secondary descriptive category, informed by the American literature's demonstration that economic factors meaningfully shape replantation service availability (Chen & Narayan, 2009), even though Kazakhstan's state-grant-based financing model for microsurgical procedures differs structurally from the American insurance-based system.

Proposed Statistical Approach

Descriptive statistics (frequencies, percentages, means with standard deviations, or medians with interquartile ranges as appropriate to data distribution) would be calculated for all extracted variables, both overall and stratified by participating center. Comparative analysis across centers would employ chi-square or Fisher's exact tests for categorical outcome variables and appropriate parametric or non-parametric tests for continuous variables, with a significance threshold of $p < 0.05$. Given the retrospective, multi-center design, appropriate adjustment for clustering by center

would be considered, for example through multilevel or generalized estimating equation models, where sample size permits.

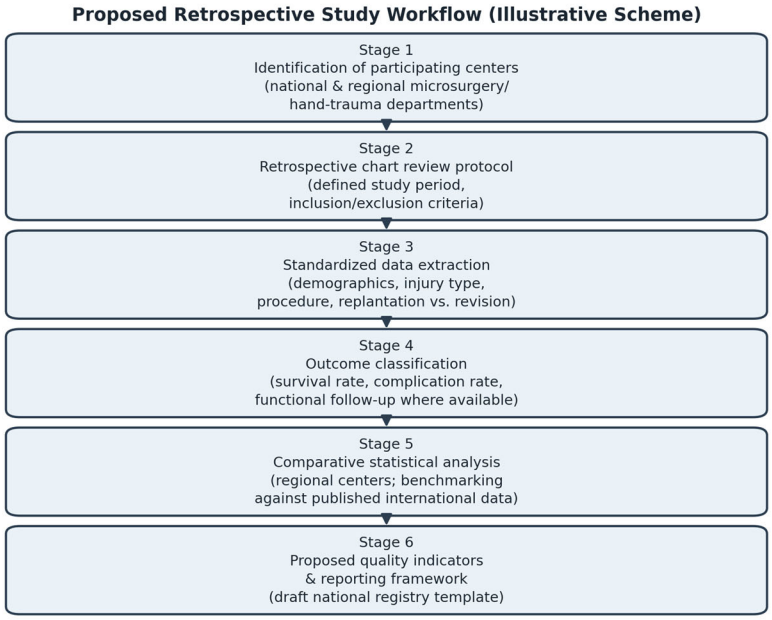
Time trends across the proposed five-year study period would additionally be examined using simple linear regression of annual replantation attempt and success rates, modeled directly on the trend-analysis approach used in the American national inpatient-sample literature (Cho et al., 2018; Hustedt et al., 2016), to determine whether Kazakhstan's replantation practice has been increasing, decreasing, or remaining stable over the study interval, and whether any such trend differs meaningfully between the country's most research-active center and other participating institutions. All statistical analyses would be pre-specified in a written analysis plan prior to data extraction, and any post-hoc analyses arising from unanticipated patterns in the data would be clearly identified as exploratory in any resulting publication.

Proposed Ethical and Governance Considerations

Any future execution of this protocol would require institutional ethics committee approval at each participating center, together with formal data-sharing agreements consistent with Kazakhstani patient-data protection requirements. De-identification of all extracted records prior to centralized analysis would be considered a mandatory safeguard. Successful completion of this proposed protocol would generate the descriptive foundation upon which a prospective national hand microsurgery registry, analogous in function to the administrative databases underlying the American literature reviewed in Section 2.3, could subsequently be built.

Given that several participating centers, including the National Scientific Center of Surgery named after A.N. Syzganov, have already demonstrated institutional capacity to conduct and publish retrospective outcome research (Mukhamedkerim et al., 2025), the proposed multi-center protocol would be designed to build directly on existing local research infrastructure and ethics-review experience rather than requiring entirely new institutional capacity. A designated multi-center steering committee, comprising a representative from each participating institution, would oversee protocol adherence, resolve cross-center data-definition discrepancies identified during the piloting phase described in Section 3.3, and coordinate eventual dissemination of findings, with the explicit long-term goal of transitioning from this retrospective descriptive protocol toward a sustained, prospectively maintained national registry.

Figure 1. Proposed retrospective, multi-center study workflow for characterizing hand microsurgery practice and outcomes in Kazakhstan.



Conclusion

The published literature indicates that hand microsurgery in Kazakhstan is practiced with considerable technical sophistication at a small number of specialized national centers, most notably the Department of Reconstructive and Plastic Microsurgery of the National Scientific Center of Surgery named after A.N. Syzganov, whose surgeons have reported both routine hand-injury management across a substantial single-center case series and technically demanding procedures such as heterotopic digit replantation. At the same time, this review has identified a clear structural gap: unlike the United States, where multi-decade, national-level administrative data have allowed detailed tracking of replantation rates, provider volume, and outcome trends, Kazakhstan currently lacks an equivalent standardized, multi-center framework for describing hand microsurgery practice and outcomes at a national scale.

The retrospective, multi-center data-collection protocol proposed in this paper is intended to begin addressing that gap. By adapting the data categories and comparative logic of established American national-level studies to the specific institutional landscape of Kazakhstani hand-trauma and reconstructive microsurgery services, the proposed framework offers a methodologically grounded starting point for future descriptive research. Because this paper is conceptual and methodological rather than empirical, the data-extraction categories and illustrative workflow presented here should be understood as a planning framework rather than as reported outcomes; any future study built upon this protocol would need institutional ethics approval, formal inter-center data-sharing arrangements, and careful attention to the regional and infrastructural differences, such as the uneven geographic distribution of surgical capacity previously documented in the broader Kazakhstani trauma literature (Pliska, 2022), that distinguish Kazakhstan's hand-trauma care system from the more centralized administrative data environment available in the United States.

Should this protocol be executed, the resulting descriptive dataset could support the development of a prospective national hand microsurgery registry, inform targeted investment in regional microsurgical capacity where current case-volume and outcome data suggest the greatest need, and provide Kazakhstani hand surgeons and health policymakers with an evidence base comparable in structure, if not yet in scale, to that which has guided two decades of replantation-service planning in the United States. Such a development would represent a meaningful step toward the broader modernization and standardization of hand trauma and reconstructive microsurgery services within the Republic of Kazakhstan.

Several limitations of the present conceptual synthesis and proposed protocol should be acknowledged. The Kazakhstani literature reviewed here is drawn from a small number of published sources, concentrated in Almaty-based institutions, and may not fully represent practice patterns at smaller or less research-active regional centers; the proposed supplementary center-identification survey described in Section 3.1 is intended to mitigate, though not fully eliminate, this limitation. Direct quantitative comparison with the American literature must also be interpreted cautiously, given substantial differences in health-system financing, population scale, and the underlying administrative data infrastructure available for research in each country; the American national inpatient-sample and claims-based studies reviewed above draw on data sources with no direct Kazakhstani equivalent, meaning that the proposed retrospective chart-review protocol, while methodologically sound, would necessarily yield a smaller and less granular dataset than its American counterparts. Finally, because retrospective chart review depends entirely on the completeness and consistency of existing clinical documentation, variables such as functional follow-up, already identified as inconsistently recorded in the existing regional literature, may remain incompletely characterized even after this protocol's execution, underscoring the longer-term value of moving toward prospective, registry-based data collection once this initial descriptive foundation has been established.

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Organic disease, as a general risk factor of criminal behavior

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Abstract: The fact of connection between organic diseases and criminal behavior is the subject of investigation by psychologists, as the reasons of triggering aggressive feeling causing the criminal tendencies and behavior can serve as an valuable information for maintaining organic diseases especially in teenagers, as a risk factor for criminal behavior and rhus, choose an appropriate preventive psycho-correctional intervention. In this research we decided to compare two groups of aggressive teenagers, such as criminal minor and teenagers having diabetes mellitus.
It appeared that diabetes mellitus can in fact trigger an aggressive behavior, that can transform into a criminal one, in case of low level of socialized value orientations, thus confirming the idea of checking the medical data of teenagers in combination with their value orientation of and starting early psycho-correctional intervention to prevent future criminal behavior.
Key words: organic disease, risk-factor, criminal behavior, diabetes mellitus, aggressive behavior, criminal prevention, psycho-correctional intervention.

Introduction

Despite the fact, that there is no direct link between an organic disease and criminal behavior per se; however, an organic disease can serve as a risk factor for criminal behavior, given that behavior is generally a multifactorial phenomenon comprising medical, psychological, and social components. Naturally, impairment of cognitive functions constitutes a risk factor for engaging in criminal behavior, as during such times, a person struggles to assess the situation or predict their own behavior and is unable to control impulses. Emotional instability diminishes the perception of moral and ethical norms, while paroxysmal episodes give rise to sudden outbursts of aggression and agitation.
Crime often results from the convergence of an organic condition and other factors. For instance, alcohol intoxication can act as a situational trigger: in a person who already struggles with impulse control, alcohol further impairs that ability, leaving the individual unable to restrain their aggression. We must also mention non-compliance—instances where an individual fails to adhere to the treatment schedule, disregards it, or discontinues treatment, potentially leading to a relapse of the condition.
Individuals with organic mental disorders face a higher risk of committing violent crimes—such as murder, bodily injury, rape, theft, and robbery—a topic we have already addressed in the section dedicated to the link between mental illness and crime.
Furthermore, brain damage and dysfunction lead to impaired control and serve as a contributing factor to the commission of crimes by individuals with distorted values.

Endocrine disorders and crime

We have to mention again, that there is no direct link between endocrine diseases and criminal behavior—meaning the disease itself cannot compel a person to commit a crime—but endocrine disorders alter one's psyche and behavior, thereby increasing the risk of deviant behavior.For example, fluctuations in testosterone levels are associated with increased aggression. Certain forms of hyperthyroidism, polycystic ovaries, and adrenal gland dysfunction lead to depression, which in itself constitutes a risk factor for deviant behavior.

Certain endocrine disorders alter a person's basic needs, desires, aspirations, and instincts; the ability to foresee the consequences of one's actions is impaired, and volitional control is diminished. This can drive an individual toward impulsive, risky, and antisocial behavior.

During the prolonged and severe course of certain endocrine diseases, a psycho-organic syndrome may develop—that is, an impairment of mental functions—which also creates the conditions for the emergence of deviant behavior.

For quite some time, the so-called endocrine theory of criminal predisposition existed. Proponents of this theory—such as R. Funes (1889–1953)—believed that anomalies in the endocrine glands create a predisposition toward antisocial behavior. This theory also faced numerous critics, and the reason for this is logical.

Endocrine disorders are considered alongside other factors, such as social, psychological, and mental health issues. Behavioral patterns change in such cases, and it is precisely this shift that can lead an individual to engage in criminal behavior.

An endocrine disorder does not make a person a criminal; however, it can be a factor that disrupts internal regulation, exacerbates emotional issues, and increases the likelihood of an individual engaging in behavior they otherwise would not have committed. The task of specialists—such as psychiatrists, psychologists, and criminologists—is to identify such connections to ensure a timely response, encompassing both correction and prevention.

As previously mentioned, diabetes does not directly cause the development of an antisocial personality; however, unstable blood sugar levels or the psychological stress associated with the disease can lead to temporary behavioral changes.

The mechanism behind behavioral changes in diabetes is as follows:

1) Hypoglycemia (a drop in blood sugar levels) – a glucose deficit leads to oxygen deprivation, causing a loss of self-control, irritability, impulsivity, and outbursts of aggression known as "Diabetic Rage." In this state, the individual behaves provocatively or antisocially and is unaware of their actions.

2) Behavioral disorders in type 1 diabetes (data from the Czech registry, published in the journal *Nature Mental Health*): This study links childhood-onset diabetes to an increased risk of developing personality disorders and deviant behavior in adulthood, a risk driven by chronic stress. When evaluating antisocial behavior, doctors recommend ruling out chronic medical conditions.

Organic and neurological causes to be ruled out:

1) Traumatic brain injury – damages the frontal lobes, which are associated with impulse control, aggressive outbursts, and a lack of empathy.

2) Neurological disorder: conditions such as epilepsy (particularly temporal lobe epilepsy), dementia, or a brain tumor significantly alter behavior.

3) Infectious diseases, such as neurosyphilis—or any other acute systemic infection—can cause delirium or personality changes and mimic antisocial traits.

4) Autoimmune disease – a lupus-like condition causes cognitive impairment or sudden behavioral changes.

There is also organic personality disorder, where changes in personality and behavior are directly linked to another medical condition.

Therefore, when evaluating behavior that is new, sudden, or uncharacteristic for an individual, undergoing a standard medical examination is essential. The diagnostic procedure includes checking blood hormone and glucose levels, obtaining neuroimaging to rule out tumors or structural brain damage, and analyzing electroencephalogram (EEG) data to detect any predisposition to epileptic spasms or other forms of pathological activity.

It is well-known, that diabetes mellitus causes aggression and aggression in its turn can serve as a trigger of criminal behavior especially in those whose value orientations is not socialized.

Therefore, we decided to study the connection of the level of aggression and the criminal tendency in diabetic teenagers and criminal minor and the reasons causing aggression.
As we mentioned above, the trigger of criminal behavior very often especially in case of teenagers, is the choice of aggressive behavior and lack of socialized value orientations and we decided to compare the groups of criminal minor and teenagers having diabetes mellitus.
In the research participated 13-14 aged subjects, 24 subjects having diabetes mellitus and 40 criminal minor.
For the research were used Szondi test for studying psychological features and original inventory stugying different reasons ttigeering agressive behavior and valur oerientations as wel as hand test srudying the level of agression.

It apperad that the level of aggression in high in the both groups, but in the criminal minor the reason of aggression is named insult, the desire of being dominant and reaction to others' aggression. In teenagers having diabtes the reason of aggression was named fear of life, as they feeled themselves phisically weak and unable to confront others' aggression, but in those who had socialized value orientations aggression never transformed into the criminal behavior desire. Those two groups were indentical in the feeling of deprivation in hedonistic shpere, but for the minor this feeling was situational and for the desased teenagers it was a parmanent feeling.

Naturally, for crime prevention it is of a paramount importance to choose and appropiate and effective psycho-correctional method and maintaining such factors, as endocrinal disbalance and anti-social valuer oriantations and study of personality features and social factors in every individual case, as it gives us a possibility of controlling manifestation of aggression and preventing future impulsive behavior.

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АМБУЛАТОРНАЯ ДИАГНОСТИКА И ВЕДЕНИЕ ПАЦИЕНТОВ С АЛЛЕРГИЧЕСКИМ РИНИТОМ НА УРОВНЕ ПЕРВИЧНОЙ МЕДИКО-САНИТАРНОЙ ПОМОЩИ

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Аннотация

Аллергический ринит (АР) занимает одно из ведущих мест среди хронических заболеваний верхних дыхательных путей, затрагивая от 10 до 40% взрослого и детского населения во всем мире. Несмотря на кажущуюся простоту симптоматики, АР нередко остается нераспознанным или неправильно классифицированным на уровне первичной медико-санитарной помощи (ПМСП), где он маскируется под острые респираторные вирусные инфекции, вазомоторный или хронический ринит. Цель настоящего обзора - систематизировать актуальные данные о диагностике и ведении АР в амбулаторных условиях с акцентом на практику первичного звена. Поиск литературы проводился в базах PubMed, Scopus и Web of Science за период 2021-2026 годов. В обзор включены 10 источников, соответствующих критериям: наличие DOI, связь с амбулаторной диагностикой, первичной помощью, клиническим ведением или цифровым мониторингом АР. Анализ литературы показал, что разрыв между актуальными рекомендациями и реальной практикой врачей ПМСП сохраняется: недостаточная осведомленность об алгоритмах диагностики, недооценка тяжести симптомов и несвоевременное направление к аллергологу остаются ключевыми проблемами. Перспективным инструментом для улучшения контроля АР в амбулаторных условиях является внедрение электронных дневников симптомов и образовательных моделей с участием фармацевтов.

Ключевые слова: *аллергический ринит; первичная медико-санитарная помощь; амбулаторная диагностика; специфический IgE; кожные пробы; оценка симптомов; электронный дневник; ведение пациента.*

ВВЕДЕНИЕ

Пациент приходит на прием с жалобами на заложенность носа, водянистые выделения и приступообразное чихание. Врач первичного звена фиксирует «ОРВИ» или «хронический ринит», назначает сосудосуживающие капли и рекомендует прийти через неделю. Ситуация повторяется несколько раз в год, нередко в одни и те же сезоны. Именно в этой банальной клинической картине скрывается один из наиболее частых диагнозов, которые остаются нераспознанными на амбулаторном приеме: аллергический ринит.

По различным оценкам, АР страдает от 10 до 40% населения в разных странах, однако реальный охват диагностикой существенно ниже этих цифр [1]. Причины недодиагностики многообразны: сходство симптомов с вирусной инфекцией, отсутствие у части врачей ПМСП четкого алгоритма опроса, бытовое представление пациентов о насморке как о несерьезном

состоянии. Между тем АР оказывает прямое влияние на качество сна, продуктивность на работе и учебе, психоэмоциональный фон, а при ненадлежащем контроле повышает риск формирования бронхиальной астмы [2].

Международный консенсус 2023 года рассматривает АР не как локальную проблему носа, а как заболевание с выраженным влиянием на сон, работоспособность и качество жизни [3]. В рамках этой концепции оценка тяжести симптомов и их влияния на повседневную деятельность становится частью стандартного приема, а не дополнительным исследованием. Между тем исследования, посвященные реальной практике врачей ПМСП, фиксируют иную картину: диагностика нередко ограничивается расспросом об основных симптомах, а стандартизированные шкалы оценки применяются редко [4].

Проблема усугубляется тем, что аллергический ринит - диагноз, который во многих системах здравоохранения остается в компетенции врача общей практики или педиатра, тогда как направление к аллергологу происходит лишь при явно выраженном или осложненном течении. В этих условиях именно врач ПМСП несет основную ответственность за первичное распознавание, дифференциацию формы (интермиттирующая или персистирующая, легкая или среднетяжелая/тяжелая), подбор базовой терапии и мониторинг ответа. Ошибки на каждом из этих этапов не только снижают качество жизни пациента, но и влекут избыточные затраты системы здравоохранения [5].

Цель настоящего обзора - систематизировать актуальные данные о диагностике и ведении АР в амбулаторных условиях с акцентом на практику первичного звена, выявить разрывы между рекомендательными документами и реальной клинической практикой, а также оценить возможности современных инструментов мониторинга симптомов для улучшения ведения пациентов с АР.

МАТЕРИАЛЫ И МЕТОДЫ

Настоящая работа представляет собой нарративный обзор литературы. Поиск источников проводился в трех базах данных: PubMed, Scopus и Web of Science. Временные рамки поиска ограничены периодом с 2021 по 2026 год включительно. Использовались следующие ключевые слова и их комбинации: allergic rhinitis, primary care, outpatient diagnosis, ambulatory care, diagnosis, management, specific IgE, skin prick test, symptom score, e-diary. Поиск проводился на английском языке; в случае выявления релевантных источников на других языках они рассматривались при условии наличия полнотекстового перевода.

Критерии включения источников в обзор: наличие DOI, публикация в рецензируемом журнале, индексирование в Scopus и/или Web of Science, тематическая связь с амбулаторной диагностикой, первичной медицинской помощью, клиническим ведением или цифровым мониторингом аллергического ринита. Рассматривались клинические рекомендации, международные консенсусы, систематические и нарративные обзоры, оригинальные исследования, посвященные практике врачей ПМСП, многофазные исследования образовательных программ, а также работы по валидации инструментов оценки симптомов.

Критерии исключения: отсутствие DOI, публикация до 2021 года, тематика, не связанная с амбулаторным уровнем помощи (исключительно стационарные исследования, хирургические вмешательства, специфические популяции пациентов с иммунодефицитными состояниями). Исключались также тезисы конференций, письма в редакцию и рукописи без рецензирования. Логика отбора источников представлена в таблице 1.

Таблица 1. Стратегия отбора источников для обзорной статьи

Параметр	Описание	Итог
Базы данных	PubMed, Scopus, Web of Science	3 базы
Период поиска	2021-2026 гг.	5 лет
Ключевые слова	allergic rhinitis, primary care, outpatient diagnosis, ambulatory care, specific IgE, skin prick test, symptom score, e-diary	8 запросов
Критерии включения	Наличие DOI, индексирование в Scopus/WoS, клинические рекомендации, консенсусы, обзоры, исследования первичной помощи, диагностики, ведения, цифрового мониторинга	Включено 10 источников
Критерии исключения	Без DOI, до 2021 г., стационарный уровень, тезисы, письма в редакцию	Исключены нерелевантные работы

Как видно из таблицы 1, отбор был сфокусирован не на всех публикациях об аллергическом рините, а на работах, которые имеют значение для амбулаторной диагностики и первичного ведения пациента. Итоговая выборка составила 10 источников, опубликованных в период с 2021 по 2024 год.

РЕЗУЛЬТАТЫ

Диагностика аллергического ринита в первичном звене

Анализ литературы позволяет выделить несколько ключевых проблем, с которыми сталкивается врач ПМСП при работе с пациентом, предъявляющим симптомы ринита. Первая из них - дифференциальная диагностика. Симптомы АР (водянистая ринорея, зуд в носу, чихание, заложенность) во многом перекрывают клиническую картину острых респираторных инфекций и вазомоторного ринита [2]. Специфическим признаком, указывающим на аллергический генез, является их сезонность и/или четкая связь с конкретными триггерами: пыльцой, шерстью животных, домашней пылью. Однако без целенаправленного расспроса пациент может не упомянуть эту связь самостоятельно [1].

Второй проблемой является оценка тяжести. Международная классификация ARIA (Allergic Rhinitis and its Impact on Asthma) делит АР на интермиттирующий и персистирующий, а по тяжести - на легкий и среднетяжелый/тяжелый. Тяжесть определяется не столько интенсивностью симптомов, сколько их влиянием на сон, профессиональную деятельность и повседневную активность пациента [3]. На амбулаторном приеме этот вопрос нередко упускается: врач фиксирует факт симптомов, но не оценивает их функциональные последствия. Данные международного Дельфи-опроса показывают, что эксперты в области аллергологии рассматривают оценку влияния АР на качество жизни как обязательный компонент первичного обследования, тогда как в реальной практике ПМСП эта оценка проводится непоследовательно [5].

Третья проблема - лабораторная верификация. В условиях первичного звена определение специфических IgE в сыворотке крови или проведение кожных прик-тестов нередко недоступно непосредственно на приеме у врача общей практики; пациентов необходимо направлять к аллергологу. Исследование по Саудовской Аравии зафиксировало, что значительная часть врачей ПМСП либо не используют стандартизированных диагностических инструментов, либо не осведомлены об актуальных

рекомендательных документах [6]. Схожая картина описана для стран Юго-Восточной Азии, где реальная практика диагностики и лечения АР существенно отличается от протоколов [7].

Основные признаки, которые позволяют врачу первичного звена заподозрить аллергический ринит уже на первом приеме, обобщены в таблице 2.

Таблица 2. Ключевые диагностические признаки аллергического ринита на амбулаторном уровне

Признак	Характеристика	Клиническое значение
Анамнез симптомов	Чихание, водянистая ринорея, заложенность, зуд в носу и глазах	Сочетание всех четырех симптомов повышает вероятность АР
Сезонность	Симптомы появляются в определенное время года или при контакте с триггером	Указывает на сенсибилизацию к сезонным аллергенам (пыльца, споры плесени)
Связь с аллергенами	Домашняя пыль, шерсть животных, профессиональные факторы	Круглогодичный АР; важен бытовой анамнез
Семейный анамнез	АР, астма, атопический дерматит у родственников	Генетическая предрасположенность к атопии
Оценка тяжести (ARIA)	Влияние на сон, работу/учебу, повседневную активность	Определяет необходимость интенсификации терапии и направления к аллергологу
Осмотр полости носа	Отечная, бледная/синюшная слизистая, прозрачный секрет	Физикальное подтверждение ринита; исключение полипоза
Специфический IgE / кожные пробы	Проводятся при нечеткой клинической картине или перед началом иммунотерапии	Верификация сенсибилизации; выбор стратегии лечения

Данные таблицы 2 показывают, что амбулаторная диагностика должна начинаться не с лабораторного теста, а с правильно собранного анамнеза и оценки связи симптомов с аллергенной экспозицией. Лабораторная верификация необходима для уточнения диагноза, выбора тактики лечения и подготовки к аллерген-специфической иммунотерапии, но не является обязательным стартовым шагом при типичной клинической картине.

Алгоритм диагностики аллергического ринита в амбулаторных условиях

На основе анализа литературы был составлен пошаговый алгоритм диагностики АР, применимый на уровне первичного приема. Схема алгоритма представлена на рисунке 1.

Рисунок 1. Алгоритм амбулаторной диагностики аллергического ринита

Алгоритм, представленный на рисунке 1, не претендует на замену клинического суждения, но задает структуру приема, при которой каждый шаг закономерно вытекает из предыдущего. Такой подход согласуется с рекомендациями международного консенсуса 2023 года и данными педиатрического руководства по ПМСП: диагностика строится от анамнеза к осмотру и только при необходимости - к лабораторной верификации [1, 3].

Основные направления ведения аллергического ринита в амбулаторной практике

Анализ литературы позволяет выделить несколько ключевых компонентов ведения АР на уровне первичного звена. Их сравнительная значимость по частоте упоминания в рассмотренных источниках представлена на диаграмме 1.

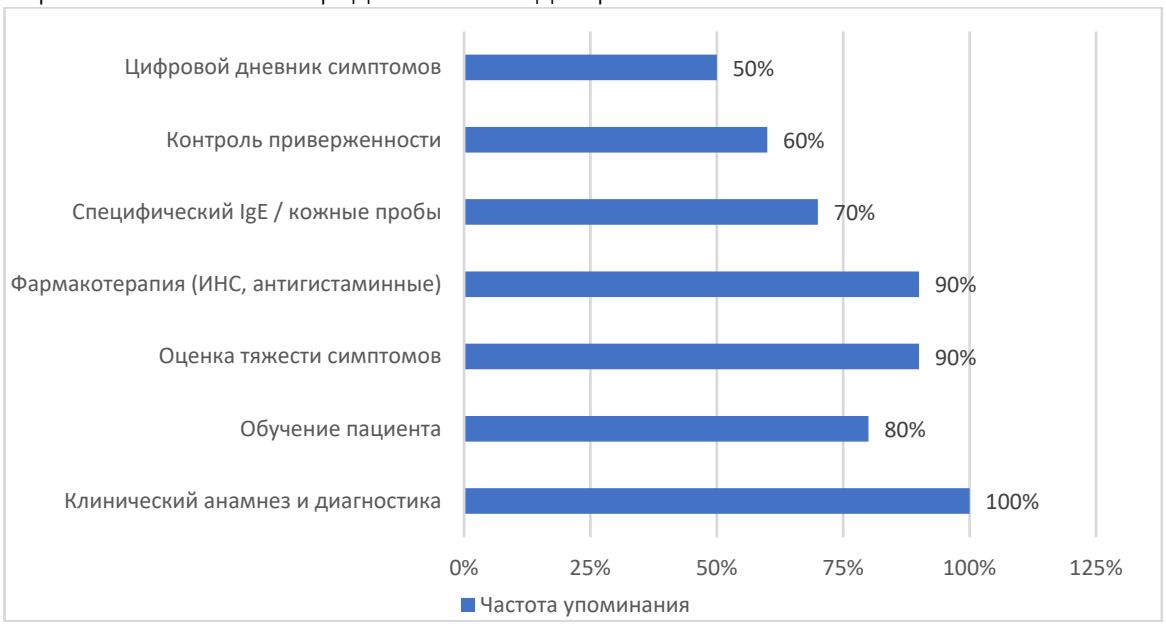

Рисунок 2. Основные направления амбулаторного ведения аллергического ринита по данным литературы

Рисунок 2 наглядно показывает, что клинический анамнез и диагностика, а также оценка тяжести симптомов и фармакотерапия присутствуют практически в каждом из

рассмотренных источников. Цифровой мониторинг симптомов упоминается реже, однако именно это направление демонстрирует наибольший потенциал для повышения качества амбулаторного ведения АР в долгосрочной перспективе.

Фармакотерапия и образовательные модели на уровне первичного звена

Ведение АР в амбулаторных условиях строится на нескольких фармакологических группах: интраназальные кортикостероиды (ИНС) являются препаратами первой линии при среднетяжелом и тяжелом персистирующем течении, антигистаминные препараты второго поколения - при интермиттирующих и преимущественно легких симптомах. Деконгестанты допускаются кратким курсом и не должны применяться длительно [2, 3]. При сопутствующем аллергическом конъюнктивите рассматривается добавление местных антигистаминных или стабилизаторов тучных клеток.

Канадское руководство 2024 года особо указывает на то, что приверженность терапии у пациентов с АР низка: пациенты нередко прекращают прием ИНС при первом улучшении симптомов, не понимая, что препарат требует регулярного применения для достижения эффекта [4]. Образовательный компонент, встроенный в амбулаторный прием, способен существенно улучшить ситуацию. В этом контексте показательна многофазная работа по разработке образовательной модели с участием фармацевта: обучение пациентов технике использования назальных спреев, разъяснение природы АР и необходимости длительной поддерживающей терапии достоверно повышали приверженность и общую удовлетворенность лечением [9].

Цифровые дневники симптомов представляют собой отдельный и перспективный инструмент мониторинга. Исследование с применением электронного дневника AllergyMonitor выявило неоднородность данных, которые пациенты вносят в режиме реального времени: пропуски записей, задержка внесения и вариабельность оценок оказались значимыми ограничениями для интерпретации собранных данных [8]. Тем не менее сама концепция ежедневного самомониторинга симптомов остается ценной: при условии правильного внедрения она позволяет врачу первичного звена получить более полную картину динамики состояния пациента, чем единственный расспрос на приеме раз в несколько месяцев [10].

ОБСУЖДЕНИЕ

Разрыв между рекомендациями и реальной практикой

Если консенсусные документы описывают оптимальную модель ведения, то исследования первичного звена показывают, где именно эта модель ломается. Международный консенсус 2023 года детально регламентирует диагностику и лечение АР, устанавливая стандарты оценки тяжести, выбора препаратов и условий для аллерген-специфической иммунотерапии [3]. Однако исследование среди врачей ПМСП Саудовской Аравии зафиксировало, что осведомленность о действующих рекомендациях недостаточна: часть врачей не применяла классификацию ARIA и не использовала стандартизированные шкалы при оценке пациентов [6]. Аналогичные данные получены на Филиппинах, где реальная практика диагностики и лечения АР в значительной мере отклонялась от рекомендательных документов [7].

Это согласуется с общей закономерностью, характерной для внедрения клинических рекомендаций: разрыв между тем, что написано в консенсусе, и тем, что происходит на приеме, определяется не столько качеством самих рекомендаций, сколько условиями их применения - продолжительностью амбулаторного приема, доступностью диагностических инструментов и уровнем постдипломной подготовки специалистов ПМСП. В отличие от стационарного звена, где диагностика может занимать несколько дней с использованием широкого набора инструментов, врач первичного приема вынужден принимать решение в

течение 10-15 минут, нередко при отсутствии экспресс-тестов для определения специфических IgE.

Для наглядного сравнения данных различных исследований, вошедших в настоящий обзор, ниже представлена таблица 3.

Таблица 3. Сопоставление данных ключевых источников обзора

Источник	Страна / регион	Фокус исследования	Выявленные проблемы	Предлагаемые решения
Loke et al. [1]	Сингапур	Ведение АР у детей в первичном звене	Недодиагностика у детей	Структурированный алгоритм педиатрического приема
Siddiqui et al. [2]	Великобритания	Диагностика и ведение АР в стационарной и амбулаторной практике	Перегрузка системы из-за поздних направлений	Усиление роли ПМСП в первичной диагностике
Wise et al. [3]	Международный	Международный консенсус ICAR:AR 2023	Вариабельность практик в разных странах	Единые стандарты диагностики и лечения
Larenas-Linnemann et al. [5]	Международный (Delphi)	Взгляды экспертов на классификацию и терапию АР	Несогласованность классификаций между странами	Глобальный экспертный консенсус по фармакотерапии
Almousa et al. [6]	Саудовская Аравия	Знание рекомендаций врачами ПМСП	Низкая осведомленность о рекомендациях ARIA	Постдипломное обучение врачей ПМСП
Dramburg et al. [8]	Германия	Валидность данных электронного дневника симптомов	Пропуски данных, задержки, вариабельность оценок	Совершенствование UX электронных инструментов
Chew et al. [9]	Малайзия	Образовательная модель с участием фармацевта	Низкая приверженность терапии	Фармацевтическое обучение пациентов

Данные таблицы 3 показывают, что при всем разнообразии дизайнов, стран и фокусов все рассмотренные исследования указывают на единый паттерн: потенциал амбулаторного звена в ведении АР реализуется не полностью из-за структурных ограничений системы и недостаточной образовательной подготовки как врачей, так и пациентов.

Роль цифровых инструментов мониторинга

Электронные дневники симптомов привлекают внимание как инструмент, способный восполнить информационный пробел между визитами к врачу. При сезонном АР самомониторинг в течение нескольких недель дает возможность оценить динамику симптомов в реальных условиях, выявить пиковые периоды и скорректировать терапию превентивно. Однако данные другого исследования показывают, что гетерогенность вносимых пациентами данных является значимым ограничением: пропущенные записи и субъективная интерпретация шкал снижают надежность результатов [8]. Это не означает, что от цифровых дневников следует отказаться, но указывает на необходимость их правильного внедрения: обучение пациента работе с приложением, четкая структура вопросов и встроенные напоминания являются обязательными условиями.

В отличие от традиционного ретроспективного сбора анамнеза на приеме, дневник симптомов фиксирует данные проспективно, в режиме реального времени. Это принципиально меняет информационную ценность собираемых данных: врач получает возможность оценить не субъективное воспоминание пациента о «прошлой неделе», а фактическую динамику состояния. Такой подход согласуется с концепцией мониторинга АР, изложенной в международном консенсусе 2023 года, где регулярная оценка контроля симптомов рассматривается как неотъемлемая часть ведения [3, 10].

Особого внимания заслуживает образовательное направление. Исследование многофазной модели с участием фармацевта показало, что структурированное обучение пациентов с АР повышает правильность использования интраназальных спреев, понимание природы заболевания и готовность к длительной терапии [9]. В отличие от единственного разговора с врачом на приеме, консультация фармацевта при отпуске препарата предоставляет дополнительную возможность для закрепления образовательного сообщения в момент, максимально приближенный к началу применения лекарства. Эта синергия между врачом и фармацевтом пока остается слабо использованной в большинстве систем ПМСП.

Наш обзор показал, что проблема АР в амбулаторном звене - это не проблема отдельного инструмента или препарата. Сопоставление источников показывает, что речь идет о системном разрыве: рекомендации существуют и они детальны, диагностические инструменты доступны, фармакотерапия стандартизирована, а цифровые решения разрабатываются. Разрыв возникает на уровне внедрения: недостаточная осведомленность врачей ПМСП, короткий прием, отсутствие встроенных алгоритмов в электронных медицинских записях, слабая коммуникация между врачом и пациентом о природе заболевания и необходимости соблюдения режима терапии.

ЗАКЛЮЧЕНИЕ

Аллергический ринит - одно из наиболее частых хронических заболеваний, с которым сталкивается врач первичного звена, и одно из наиболее недооцененных по реальному влиянию на качество жизни пациента. Анализ литературы позволяет выделить четкий практический алгоритм, применимый в условиях амбулаторного приема: тщательный сбор анамнеза с оценкой сезонности и связи с триггерами, физикальный осмотр полости носа, стратификация тяжести по критериям ARIA, базовая терапия с выбором препарата в соответствии с формой заболевания, регулярная оценка ответа на терапию и своевременное направление к аллергологу при тяжелом, персистирующем или неконтролируемом течении.

Ключевая проблема состоит не в отсутствии инструментов, а в их последовательном применении. Рассмотренные исследования фиксируют устойчивый разрыв между уровнем рекомендаций и уровнем повседневной практики, устранение которого требует совершенствования постдипломной подготовки врачей ПМСП, интеграции образовательных программ для пациентов и внедрения цифровых инструментов мониторинга симптомов.

Роль фармацевта как дополнительного звена в образовании и контроле приверженности заслуживает более активного использования. Будущие исследования должны быть направлены на разработку и валидацию практических протоколов для врачей первичного звена, включая регионально адаптированные алгоритмы диагностики и мониторинга, применимые в условиях стран с различным уровнем ресурсного обеспечения.

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COMPREHENSIVE REVIEW OF ANTIPSYCHOTIC AGENTS: MECHANISMS OF ACTION, CLINICAL UTILITY, ADVERSE EFFECTS, TOXICITY MANAGEMENT, PHARMACOGENOMICS, PRECISION MEDICINE, PHARMACOVIGILANCE, THERAPEUTIC DRUG MONITORING, EVIDENCE-BASED CLINICAL PRACTICE AND EMERGING THERAPEUTIC INNOVATIONS

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Abstract
Antipsychotic agents remain the cornerstone of pharmacological management for schizophrenia spectrum disorders and are increasingly utilized in bipolar disorder, major depressive disorder, autism spectrum disorder-associated irritability, Tourette syndrome, delirium, dementia-related behavioral disturbances, and several off-label neuropsychiatric conditions. Over the past seven decades, substantial advances in psychopharmacology, molecular neuroscience, pharmacogenomics, and precision medicine have transformed the understanding of antipsychotic drug mechanisms, therapeutic applications, safety profiles, and individualized

treatment strategies. Despite remarkable progress, antipsychotic therapy continues to present considerable clinical challenges, including treatment resistance, variable therapeutic response, metabolic complications, extrapyramidal symptoms, cardiovascular toxicity, neuroendocrine disturbances, cognitive impairment, and medication non-adherence. Consequently, optimizing antipsychotic therapy requires an integrated evidence-based approach that combines neurobiological understanding, pharmacokinetic monitoring, pharmacogenomic-guided prescribing, pharmacovigilance, and patient-centered clinical decision-making. This comprehensive review critically evaluates the current scientific evidence regarding conventional (first-generation) and atypical (second- and third-generation) antipsychotic medications, emphasizing their molecular pharmacology, receptor-binding characteristics, intracellular signaling pathways, neurochemical modulation, and mechanisms underlying therapeutic efficacy and adverse reactions. Particular attention is devoted to dopamine, serotonin, glutamate, gamma-aminobutyric acid (GABA), acetylcholine, histamine, adrenergic, and neuroinflammatory pathways that collectively contribute to psychosis pathophysiology and antipsychotic pharmacodynamics. The review further examines the expanding role of partial dopamine agonists, multimodal receptor modulators, long-acting injectable formulations, and novel investigational compounds designed to improve efficacy while minimizing toxicity. Clinical applications across schizophrenia, schizoaffective disorder, bipolar disorder, psychotic depression, treatment-resistant psychosis, pediatric psychiatry, geriatric psychiatry, and consultation-liaison psychiatry are comprehensively discussed. Comparative analyses of efficacy, relapse prevention, functional recovery, cognitive outcomes, quality of life, and long-term disease management are integrated with recommendations from contemporary international clinical practice guidelines. The review also explores individualized therapeutic selection according to patient-specific characteristics, psychiatric comorbidities, medical illnesses, age-related considerations, pregnancy, hepatic and renal dysfunction, and polypharmacy. A substantial focus is placed on adverse drug reactions and toxicity management, including extrapyramidal syndromes, tardive dyskinesia, neuroleptic malignant syndrome, metabolic syndrome, obesity, diabetes mellitus, dyslipidemia, hyperprolactinemia, QT interval prolongation, myocarditis, agranulocytosis, seizures, hepatic dysfunction, and anticholinergic toxicity. Current evidence regarding early recognition, prevention strategies, emergency management, supportive care, therapeutic drug monitoring, laboratory surveillance, and multidisciplinary interventions is critically synthesized. Special consideration is given to clozapine monitoring protocols, individualized dose optimization, drug-drug interactions mediated through cytochrome P450 enzymes, and strategies for minimizing preventable medication-related harm. The review additionally highlights emerging advances in pharmacogenomics, biomarker-guided therapy, artificial intelligence-assisted clinical decision support, digital psychiatry, real-world pharmacovigilance systems, population pharmacokinetic modeling, machine learning prediction of treatment response, and precision psychiatry. Genetic polymorphisms involving CYP2D6, CYP1A2, CYP3A4, CYP2C19, dopamine receptor genes, serotonin receptor genes, and transporter proteins are examined as potential determinants of efficacy, adverse events, and individualized dosing strategies. Furthermore, recent developments in therapeutic drug monitoring, pharmacometric modeling, personalized medicine, and translational neuroscience are evaluated for their potential to optimize treatment outcomes and reduce healthcare burden. The contemporary antipsychotic pharmacotherapy is evolving toward highly individualized, evidence-based, and precision-oriented clinical practice. Integration of neuropharmacology, pharmacogenomics, pharmacovigilance, therapeutic drug monitoring, and innovative therapeutic technologies provides unprecedented opportunities to enhance efficacy, improve long-term safety, reduce treatment-related morbidity, and promote functional recovery among individuals with severe mental illness. Continued multidisciplinary

research, international collaboration, biomarker validation, and implementation of personalized treatment algorithms will be essential for advancing the next generation of antipsychotic therapeutics and improving global psychiatric care.

Keywords: Antipsychotic agents; Precision psychiatry; Pharmacogenomics; Therapeutic drug monitoring; Pharmacovigilance.

INTRODUCTION

Global Burden of Psychotic Disorders and the Evolution of Antipsychotic Pharmacotherapy

Psychotic disorders represent some of the most complex, disabling, and clinically challenging conditions within the field of neuropsychiatry. Characterized by disturbances in perception, cognition, emotional regulation, thought organization, and behavioral control, psychotic illnesses substantially affect individual functioning, social relationships, occupational capacity, and overall quality of life. Among these disorders, schizophrenia remains the prototypical psychotic illness, affecting approximately 1% of the global population and contributing significantly to disability-adjusted life years, premature mortality, healthcare utilization, and socioeconomic burden. Beyond schizophrenia, psychotic symptoms occur in a broad spectrum of psychiatric and medical conditions, including schizoaffective disorder, bipolar disorder, major depressive disorder with psychotic features, substance-induced psychosis, neurodegenerative disorders, autoimmune encephalitis, and neurological diseases.

The clinical manifestations of psychosis are traditionally categorized into positive symptoms, negative symptoms, cognitive symptoms, and affective disturbances. Positive symptoms, including hallucinations, delusions, disorganized speech, and abnormal behavioral patterns, represent the most recognizable features and remain the primary therapeutic targets of antipsychotic medications. Negative symptoms, such as social withdrawal, anhedonia, reduced motivation, emotional blunting, and impaired interpersonal functioning, are often more resistant to treatment and are strongly associated with long-term disability. Cognitive impairment involving attention, working memory, executive function, and information processing represents another critical determinant of functional outcomes and remains an area of unmet therapeutic need.

The introduction of antipsychotic medications in the mid-twentieth century marked one of the most transformative developments in psychiatric medicine. Before the availability of effective pharmacological treatments, individuals with severe psychotic disorders frequently required prolonged institutional care, with limited therapeutic options beyond supportive interventions. The discovery of chlorpromazine in the early 1950s initiated the era of modern psychopharmacology and fundamentally changed the management of schizophrenia and related disorders. Chlorpromazine demonstrated that pharmacological modulation of central nervous system pathways could significantly reduce psychotic symptoms, leading to the development of numerous compounds targeting neurotransmitter systems involved in psychosis.

The evolution of antipsychotic pharmacotherapy reflects a continuous effort to improve therapeutic efficacy while reducing adverse effects. First-generation or typical antipsychotics, including haloperidol, chlorpromazine, fluphenazine, and trifluoperazine, primarily exert their therapeutic effects through dopamine D2 receptor antagonism. These medications remain effective for controlling acute psychotic symptoms, particularly positive symptoms; however, their clinical utility has been limited by extrapyramidal adverse effects, tardive dyskinesia, hyperprolactinemia, and poor tolerability in many patients.

The development of second-generation or atypical antipsychotics represented a major advancement in psychiatric therapeutics. Agents such as clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole demonstrated broader receptor activity profiles

involving dopamine, serotonin, histamine, muscarinic, and adrenergic systems. These medications generally provide improved tolerability regarding movement disorders compared with many first-generation agents and introduced new possibilities for addressing treatment-resistant schizophrenia, affective symptoms, and relapse prevention. Particularly, clozapine remains the most effective pharmacological intervention for treatment-resistant schizophrenia and reduction of suicide risk, although its clinical application requires rigorous monitoring due to potentially severe adverse reactions, including agranulocytosis, myocarditis, seizures, and metabolic complications.

The emergence of third-generation antipsychotics, including dopamine partial agonists such as aripiprazole, brexpiprazole, and cariprazine, has further expanded therapeutic strategies. Unlike conventional dopamine antagonists, partial dopamine agonists provide functional stabilization of dopaminergic neurotransmission by reducing excessive dopamine activity in mesolimbic pathways while maintaining sufficient dopamine signaling in other brain regions. This pharmacological approach aims to achieve antipsychotic efficacy with reduced risks of extrapyramidal symptoms, hyperprolactinemia, and metabolic disturbances. More recent innovations include long-acting injectable formulations, multimodal receptor agents, and investigational compounds targeting alternative neurobiological pathways.

Despite major advances in antipsychotic drug development, significant therapeutic limitations persist. A considerable proportion of patients demonstrate incomplete response, persistent functional impairment, or intolerance due to adverse effects. Approximately one-third of individuals with schizophrenia may experience treatment-resistant illness, requiring complex pharmacological strategies, including clozapine therapy, augmentation approaches, electroconvulsive therapy, or emerging biological interventions. Furthermore, variability in individual response to antipsychotic treatment remains a major challenge, as patients receiving identical medications at comparable doses may experience substantially different therapeutic outcomes and adverse reactions.

This variability reflects the complex interaction between genetic, molecular, environmental, developmental, and psychosocial factors influencing psychiatric disorders and drug response. Traditional approaches to antipsychotic prescribing have largely relied on symptom profiles, clinical experience, and trial-and-error medication selection. However, advances in molecular psychiatry, pharmacogenomics, computational biology, and precision medicine are progressively transforming this paradigm toward individualized treatment strategies. Identification of genetic variants affecting drug metabolism, receptor sensitivity, transporter activity, and intracellular signaling pathways may allow clinicians to predict therapeutic response, optimize dosing, reduce adverse reactions, and improve long-term outcomes.

Modern antipsychotic pharmacotherapy is therefore undergoing a transition from standardized treatment algorithms toward personalized, evidence-based models integrating clinical characteristics, biological markers, pharmacokinetic parameters, and patient preferences. Pharmacogenomic testing, therapeutic drug monitoring, artificial intelligence-based prediction models, digital health technologies, and real-world pharmacovigilance databases represent emerging tools capable of enhancing treatment precision and safety.

The increasing complexity of antipsychotic treatment requires a multidisciplinary approach involving psychiatrists, clinical pharmacologists, pharmacists, neuroscientists, geneticists, primary care providers, and healthcare policymakers. Comprehensive understanding of antipsychotic mechanisms, receptor pharmacology, adverse effect profiles, toxicity management strategies, and innovative therapeutic approaches is essential for optimizing patient care and reducing the global burden associated with severe mental illness.

Historical Development of Antipsychotic Agents: From First-Generation to Novel Therapeutics

The history of antipsychotic medication development reflects the broader evolution of neuroscience, molecular pharmacology, and psychiatric therapeutics. Prior to the discovery of antipsychotic drugs, treatment approaches for schizophrenia and related psychotic disorders were primarily supportive and frequently involved institutionalization, psychotherapy, behavioral interventions, and non-specific biological treatments. The introduction of effective pharmacological agents revolutionized psychiatric practice by demonstrating that pathological brain signaling pathways underlying psychosis could be modified through targeted chemical interventions.

The accidental discovery of chlorpromazine's antipsychotic properties in 1952 represented a landmark moment in medicine. Initially developed as an antihistamine and anesthetic adjunct, chlorpromazine was observed to produce a distinctive calming effect without causing complete sedation. Subsequent clinical observations demonstrated its ability to reduce hallucinations, delusions, agitation, and behavioral disturbances among individuals with psychotic disorders. This discovery led to the concept of neuroleptic pharmacology and stimulated intensive research into neurotransmitter mechanisms involved in schizophrenia.

The first-generation antipsychotics were primarily developed during the 1950s–1970s and shared a common pharmacological characteristic: potent antagonism of dopamine D2 receptors. The dopamine hypothesis of schizophrenia, proposed in the 1960s and later refined through neurochemical and imaging studies, suggested that excessive dopaminergic signaling, particularly within mesolimbic pathways, contributed to positive psychotic symptoms. The clinical efficacy of D2 receptor antagonists provided strong support for this hypothesis and established dopamine modulation as the central principle of antipsychotic therapy.

However, dopamine blockade alone could not fully explain the complexity of schizophrenia or the limitations of conventional antipsychotic drugs. While D2 antagonism effectively reduced positive symptoms, it demonstrated limited efficacy against negative and cognitive symptoms. Additionally, excessive dopamine inhibition within nigrostriatal pathways produced movement disorders, while blockade of tuberoinfundibular dopamine pathways resulted in increased prolactin secretion. These limitations stimulated the search for pharmacological approaches capable of achieving broader therapeutic effects with improved safety profiles.

The limitations of first-generation antipsychotics stimulated the development of second-generation or atypical antipsychotic agents during the late twentieth century. The term "atypical" initially referred to medications that produced antipsychotic effects with a lower propensity for extrapyramidal motor adverse effects compared with conventional dopamine receptor antagonists. Although the distinction between typical and atypical antipsychotics has become increasingly complex, second-generation agents introduced a broader pharmacological perspective by targeting multiple neurotransmitter systems simultaneously.

The reintroduction of clozapine into clinical practice during the 1980s represented a pivotal advancement in antipsychotic pharmacotherapy. Originally synthesized in the 1960s, clozapine demonstrated superior efficacy in individuals who failed to respond adequately to conventional antipsychotics. Unlike many first-generation agents, clozapine exhibits relatively weak dopamine D2 receptor antagonism combined with strong serotonin 5-HT2A receptor antagonism and activity at multiple additional receptors, including 5-HT2C, D4 dopamine, muscarinic acetylcholine, histamine H1, and adrenergic α1 receptors. This unique receptor profile contributed to improved efficacy for treatment-resistant schizophrenia and reduced risk of severe extrapyramidal symptoms. However, the emergence of potentially life-threatening adverse effects, particularly agranulocytosis, required the establishment of strict hematological monitoring systems and contributed to the development of modern pharmacovigilance practices.

Following the clinical success of clozapine, numerous atypical antipsychotics were introduced, including risperidone, olanzapine, quetiapine, ziprasidone, amisulpride, and later aripiprazole, brexpiprazole, and cariprazine. These medications represented significant progress in receptor-selective pharmacology and expanded therapeutic possibilities across psychiatric disorders. Risperidone demonstrated strong serotonin 5-HT2A and dopamine D2 receptor antagonism and became widely used for schizophrenia, bipolar disorder, and irritability associated with autism spectrum disorders. Olanzapine provided strong antipsychotic efficacy but was associated with substantial metabolic risks, including weight gain, insulin resistance, dyslipidemia, and increased risk of type 2 diabetes mellitus. Quetiapine showed efficacy across schizophrenia, bipolar depression, and major depressive disorder augmentation while producing comparatively lower extrapyramidal liability but significant sedative and metabolic effects.

The development of dopamine partial agonists represented another important milestone in antipsychotic drug discovery. Aripiprazole introduced a novel pharmacological concept described as dopamine system stabilization. Rather than completely blocking dopamine signaling, aripiprazole acts as a partial agonist at dopamine D2 and D3 receptors, reducing excessive dopaminergic activity in mesolimbic regions while maintaining physiological dopamine transmission in nigrostriatal and mesocortical pathways. This mechanism contributes to reduced risks of hyperprolactinemia, metabolic abnormalities, and movement disorders compared with many dopamine antagonists. Subsequent agents, including brexpiprazole and cariprazine, further refined this approach by modifying receptor affinity and intrinsic activity profiles.

The evolution of antipsychotic therapy has also been influenced by the development of long-acting injectable (LAI) formulations. Medication non-adherence remains one of the most significant barriers to successful treatment outcomes in schizophrenia and related disorders, contributing to relapse, hospitalization, suicide risk, and increased healthcare costs. LAI formulations of several antipsychotic agents provide sustained plasma concentrations, improve adherence monitoring, reduce fluctuations associated with oral administration, and may enhance long-term disease management. Contemporary clinical practice increasingly incorporates LAI medications as an important component of relapse prevention strategies, particularly among individuals with recurrent episodes associated with poor adherence.

Recent decades have witnessed a transition from receptor-based drug discovery toward more complex neurobiological models of psychosis. Although dopamine dysfunction remains central to current understanding, schizophrenia is now recognized as a disorder involving multiple interacting systems, including glutamatergic transmission, γ-aminobutyric acid (GABA) signaling, neuroinflammation, oxidative stress, synaptic dysfunction, immune regulation, and neurodevelopmental abnormalities. These discoveries have stimulated research into novel therapeutic targets beyond dopamine and serotonin pathways.

Investigational antipsychotic strategies increasingly focus on glutamate modulation, particularly through N-methyl-D-aspartate (NMDA) receptor-associated mechanisms. The observation that NMDA receptor antagonists such as phencyclidine and ketamine can induce psychosis-like symptoms provided evidence for glutamatergic involvement in schizophrenia pathophysiology. Research into agents influencing glutamate receptors, glycine transporters, metabotropic glutamate receptors, and synaptic plasticity pathways represents a promising direction for future treatment development, particularly for negative symptoms and cognitive dysfunction that remain inadequately controlled by existing medications.

Another emerging area involves the development of multifunctional compounds capable of simultaneously regulating multiple neurotransmitter systems. The complexity of psychiatric disorders suggests that single-target pharmacological approaches may be insufficient for achieving optimal outcomes. Therefore, contemporary drug development increasingly

emphasizes balanced receptor interactions, reduced toxicity profiles, improved cognitive outcomes, and enhanced functional recovery.

Neurobiological Foundations of Psychosis and Molecular Targets of Antipsychotic Drugs

Understanding the mechanisms underlying psychosis is essential for rational antipsychotic drug development and individualized therapeutic selection. Psychosis is not considered a consequence of a single neurotransmitter abnormality but rather the result of complex interactions among genetic vulnerability, neurodevelopmental processes, environmental stressors, immune alterations, and disruptions in neural circuitry.

The classical dopamine hypothesis remains one of the most influential models explaining psychotic symptoms. According to this framework, excessive dopamine transmission within the mesolimbic pathway contributes primarily to positive symptoms such as hallucinations and delusions. Neuroimaging studies using positron emission tomography have demonstrated altered dopamine synthesis capacity, increased dopamine release, and enhanced dopamine receptor sensitivity in subsets of individuals with schizophrenia. The relationship between dopamine dysfunction and antipsychotic efficacy is strongly supported by the observation that therapeutic antipsychotic effects generally require adequate dopamine D2 receptor occupancy.

However, the dopamine hypothesis has evolved considerably. Contemporary models recognize that dopamine abnormalities may represent a final common pathway influenced by upstream disturbances involving glutamate, GABA, stress hormones, inflammation, and developmental processes. Dysfunction within the mesocortical dopamine pathway has been associated with negative symptoms and cognitive impairment, while nigrostriatal dopamine modulation contributes to motor adverse effects associated with antipsychotic therapy.

Serotonergic mechanisms have become increasingly important in understanding atypical antipsychotic pharmacology. Serotonin 5-HT2A receptor antagonism differentiates many second-generation antipsychotics from first-generation agents and contributes to reduced extrapyramidal effects. Serotonin pathways also influence mood regulation, cognition, anxiety, and emotional processing, providing a theoretical basis for the broader clinical effects observed with atypical medications.

The glutamatergic system represents another major area of investigation. NMDA receptor hypofunction has been proposed as a potential mechanism contributing to cognitive deficits, negative symptoms, and abnormal neural connectivity in schizophrenia. Interactions between glutamate and dopamine systems suggest that antipsychotic effects may depend on restoring balance between excitatory and inhibitory neurotransmission rather than simply suppressing dopamine activity.

GABAergic dysfunction has also been implicated in schizophrenia, particularly through alterations in inhibitory interneuron function. Reduced activity of parvalbumin-positive GABAergic interneurons may contribute to impaired gamma oscillations, cognitive deficits, and abnormal information processing. Future therapeutic strategies targeting GABAergic regulation may therefore provide opportunities for addressing symptoms inadequately treated by current antipsychotics.

Neuroinflammatory and immune mechanisms have gained increasing recognition in psychiatric neuroscience. Elevated inflammatory markers, microglial activation, oxidative stress, and altered immune signaling have been reported in subsets of individuals with schizophrenia. These findings have stimulated research into anti-inflammatory strategies, immune-modulating therapies, and biomarkers capable of identifying biologically distinct patient subgroups.

The molecular complexity of psychosis highlights the necessity of integrating neuropharmacology with systems biology, genomics, and personalized medicine approaches. Future antipsychotic development will likely depend on identifying biologically meaningful

subtypes of psychiatric disorders and matching specific therapeutic interventions to individual molecular profiles.

Classification and Pharmacological Characteristics of Antipsychotic Agents

Antipsychotic medications represent a heterogeneous group of centrally acting psychotropic compounds characterized by their ability to reduce psychotic symptoms through modulation of neurotransmitter systems involved in perception, cognition, motivation, and emotional regulation. Although traditionally classified into first-generation (typical) and second-generation (atypical) antipsychotics, contemporary pharmacological understanding recognizes a broader spectrum of receptor activity, molecular mechanisms, and therapeutic applications. This expanded classification includes dopamine receptor antagonists, serotonin–dopamine antagonists, dopamine partial agonists, and emerging multimodal agents with novel mechanisms of action.

First-Generation Antipsychotic Agents

First-generation antipsychotics (FGAs), also known as typical antipsychotics, were the first successful pharmacological treatments for schizophrenia and remain clinically relevant in many healthcare systems worldwide. These agents primarily exert their therapeutic effects through antagonism of dopamine D2 receptors within mesolimbic pathways. Their efficacy is strongly associated with reduction of positive psychotic symptoms, including hallucinations, delusions, and severe behavioral disorganization.

FGAs are commonly divided according to their potency:

High-potency first-generation antipsychotics, such as haloperidol and fluphenazine, demonstrate strong dopamine D2 receptor antagonism and are highly effective for acute psychosis, agitation, and relapse prevention. However, their strong dopamine blockade increases the risk of extrapyramidal adverse effects, including acute dystonia, akathisia, parkinsonism, and tardive dyskinesia.

Low-potency first-generation antipsychotics, including chlorpromazine and thioridazine, exhibit weaker dopamine D2 antagonism but greater activity at histamine H1, muscarinic M1, and adrenergic α1 receptors. Consequently, they are associated with increased sedation, anticholinergic effects, orthostatic hypotension, and metabolic complications. Chlorpromazine remains historically significant because its introduction initiated modern biological psychiatry and transformed the management of institutionalized patients with severe mental illness.

Despite limitations, first-generation antipsychotics continue to have therapeutic roles, particularly in acute psychiatric emergencies, treatment of severe agitation, and settings where cost considerations influence medication selection. Long-acting injectable formulations of haloperidol and fluphenazine remain valuable options for maintenance therapy when adherence difficulties are present.

Second-Generation Antipsychotic Agents

Second-generation antipsychotics (SGAs), also referred to as atypical antipsychotics, were developed to overcome the limitations of conventional dopamine antagonists. Their defining pharmacological characteristic is combined serotonin 5-HT2A receptor antagonism and dopamine D2 receptor modulation. This receptor profile contributes to reduced extrapyramidal symptoms and improved therapeutic effects in selected symptom domains.

SGAs include clozapine, risperidone, olanzapine, quetiapine, ziprasidone, amisulpride, paliperidone, and others. Although these medications share common pharmacological properties, individual agents demonstrate distinct receptor-binding profiles that influence clinical efficacy and adverse-effect patterns.

Clozapine remains the reference medication for treatment-resistant schizophrenia. Its superior efficacy compared with other antipsychotics has been demonstrated in patients who fail

adequate trials of conventional treatments. Clozapine also reduces suicidal behavior among individuals with schizophrenia and schizoaffective disorder. However, its use requires careful monitoring due to risks of neutropenia, myocarditis, seizures, metabolic syndrome, gastrointestinal hypomotility, and severe inflammatory complications.

Risperidone exhibits potent dopamine D2 and serotonin 5-HT2A antagonism and has demonstrated efficacy in schizophrenia, bipolar mania, maintenance therapy, and irritability associated with autism spectrum disorder. However, dose-dependent dopamine blockade may produce extrapyramidal symptoms and increased prolactin concentrations.

Olanzapine provides strong antipsychotic efficacy and broad symptom control but is associated with significant metabolic adverse effects, including weight gain, insulin resistance, hyperglycemia, and dyslipidemia. These complications require proactive monitoring of body mass index, glucose metabolism, and cardiovascular risk factors.

Quetiapine possesses relatively lower dopamine D2 receptor affinity combined with strong histamine H1 and adrenergic α1 receptor activity. It is widely used for schizophrenia, bipolar disorder, bipolar depression, and augmentation treatment in major depressive disorder. Sedation, orthostatic hypotension, and metabolic effects remain important clinical considerations.

Ziprasidone demonstrates relatively favorable metabolic characteristics compared with several SGAs but requires attention to potential QT interval prolongation. Paliperidone, the active metabolite of risperidone, offers advantages in pharmacokinetic predictability and availability in long-acting injectable formulations.

Third-Generation Antipsychotics and Dopamine Partial Agonists

Third-generation antipsychotics represent a conceptual shift from dopamine receptor blockade toward dopamine system stabilization. The most clinically established agents include aripiprazole, brexpiprazole, and cariprazine.

Aripiprazole acts as a partial agonist at dopamine D2 and D3 receptors and serotonin 5-HT1A receptors while antagonizing serotonin 5-HT2A receptors. This unique mechanism enables reduction of excessive dopamine signaling without complete suppression of physiological dopamine activity. Clinically, aripiprazole is associated with lower risks of metabolic complications and hyperprolactinemia compared with many dopamine antagonists.

Brexpiprazole was developed as a serotonin–dopamine activity modulator with lower intrinsic dopamine agonist activity than aripiprazole. It demonstrates efficacy in schizophrenia and as adjunctive therapy for major depressive disorder.

Cariprazine has selective affinity for dopamine D3 receptors, which may provide advantages in addressing negative symptoms and cognitive dysfunction. Its pharmacological profile has stimulated interest in improving functional outcomes beyond traditional symptom reduction.

Mechanisms of Action: Dopaminergic, Serotonergic, Glutamatergic, and Multireceptor Modulation

The therapeutic effects of antipsychotic medications arise from complex interactions between multiple neurotransmitter systems. Although dopamine receptor modulation remains central, modern neuropharmacology recognizes that successful treatment requires regulation of interconnected neural circuits rather than inhibition of a single molecular target.

Dopamine Receptor Modulation

Dopamine signaling involves four major pathways relevant to antipsychotic pharmacology:

Mesolimbic pathway: Excessive dopamine activity within this pathway is strongly associated with positive psychotic symptoms. Antipsychotic-induced D2 receptor blockade reduces hallucinations, delusions, and behavioral disturbances.

Mesocortical pathway: Reduced dopamine activity in prefrontal regions contributes to negative symptoms and cognitive impairment. Excessive dopamine suppression in this pathway may worsen motivation and cognitive functioning, highlighting the importance of balanced dopamine modulation.

Nigrostriatal pathway: Dopamine inhibition within motor pathways produces extrapyramidal symptoms, including rigidity, tremor, bradykinesia, dystonia, and tardive dyskinesia.

Tuberoinfundibular pathway: Dopamine normally inhibits prolactin secretion. D2 receptor blockade increases prolactin concentrations, potentially causing galactorrhea, sexual dysfunction, infertility, and bone mineral density reduction.

The concept of optimal dopamine receptor occupancy is critical for antipsychotic effectiveness. Clinical studies suggest that approximately 60–80% dopamine D2 receptor occupancy is generally required for therapeutic effects, whereas excessive occupancy increases the probability of adverse motor effects.

Serotonergic Modulation

Serotonin receptors, particularly 5-HT2A receptors, play a major role in differentiating atypical from typical antipsychotics. Serotonin–dopamine receptor interactions influence cortical dopamine release, cognition, mood regulation, and motor control.

5-HT2A antagonism enhances dopamine release in nigrostriatal pathways, thereby reducing extrapyramidal toxicity associated with dopamine blockade. Additionally, serotonergic mechanisms may contribute to improved affective symptoms, anxiety reduction, and broader therapeutic effects.

Glutamate and Cognitive Function

Increasing evidence indicates that glutamatergic dysfunction contributes significantly to schizophrenia pathophysiology. NMDA receptor hypofunction may lead to impaired cortical connectivity, cognitive deficits, and negative symptoms. Current antipsychotics provide limited benefits for these domains, creating a major area of unmet medical need.

Novel pharmacological strategies targeting glutamate receptors, glycine modulation, synaptic plasticity, and neuroprotective pathways are being investigated to develop next-generation therapies capable of improving cognitive and functional outcomes.

Histaminergic, Cholinergic, and Adrenergic Receptor Effects

Antipsychotic receptor interactions beyond dopamine and serotonin contribute substantially to therapeutic profiles and adverse effects.

Histamine H1 receptor antagonism produces sedation and increased appetite, contributing to weight gain observed with several SGAs.

Muscarinic acetylcholine receptor antagonism causes anticholinergic effects, including dry mouth, constipation, urinary retention, blurred vision, and cognitive impairment.

Adrenergic α1 receptor blockade contributes to orthostatic hypotension and dizziness, particularly during dose initiation or escalation.

Understanding these receptor interactions is essential for individualized medication selection, especially in older adults and patients with cardiovascular, metabolic, or neurological comorbidities.

Antipsychotic medications have become fundamental components of modern psychiatric practice due to their ability to reduce psychotic symptoms, prevent relapse, improve behavioral control, and support functional recovery across a wide range of psychiatric disorders. Although originally developed for schizophrenia treatment, their clinical applications have expanded considerably over recent decades. Contemporary evidence supports their use not only in primary psychotic disorders but also in bipolar disorder, psychotic depression, treatment-resistant mood disorders, neurodevelopmental conditions, neurocognitive disorders associated with behavioral disturbances, and several psychiatric emergencies requiring rapid symptom stabilization.

Clinical Utility of Antipsychotic Agents in Contemporary Medicine

Schizophrenia remains the primary clinical indication for antipsychotic therapy. The disorder is characterized by persistent abnormalities in thought processes, perception, emotional regulation, and social functioning, often resulting in substantial disability. Antipsychotics represent the most effective pharmacological intervention for controlling acute psychotic episodes and reducing the probability of future relapse. Early initiation of appropriate antipsychotic treatment following the onset of psychosis is associated with improved clinical outcomes, reduced symptom severity, and enhanced long-term functional recovery.

The selection of an appropriate antipsychotic medication requires careful consideration of multiple factors, including symptom profile, previous treatment response, adverse effect susceptibility, comorbid medical conditions, patient preferences, adherence patterns, pharmacokinetic characteristics, and potential drug interactions. Although most antipsychotic agents demonstrate comparable efficacy for positive symptoms in many patients, meaningful differences exist regarding tolerability, metabolic effects, cognitive outcomes, impact on negative symptoms, and effectiveness in treatment-resistant cases.

Treatment-resistant schizophrenia represents one of the greatest challenges in psychiatric pharmacotherapy. Defined by inadequate improvement despite appropriate trials of at least two antipsychotic medications, this condition affects a substantial proportion of individuals with schizophrenia and is associated with chronic disability and increased healthcare burden. Clozapine remains the most effective evidence-based intervention for treatment-resistant schizophrenia and occupies a unique position in clinical practice. Beyond symptom reduction, clozapine demonstrates benefits in reducing suicidal behavior, aggression, and hospitalization frequency. However, the requirement for continuous hematological monitoring and management of metabolic and cardiovascular risks limits its broader utilization.

Antipsychotic medications are also essential in the management of bipolar disorder, particularly during acute manic episodes characterized by elevated mood, increased energy, impulsivity, reduced need for sleep, and psychotic features. Several second-generation antipsychotics, including quetiapine, olanzapine, risperidone, aripiprazole, cariprazine, and lurasidone, have demonstrated efficacy in bipolar mania and maintenance therapy. Some agents, particularly quetiapine and lurasidone, have shown effectiveness in bipolar depression, an area where therapeutic options have historically been limited.

In major depressive disorder, antipsychotics have gained importance as augmentation strategies for patients with inadequate response to conventional antidepressant therapy. Low-dose atypical antipsychotics may enhance antidepressant efficacy through modulation of dopaminergic, serotonergic, and noradrenergic pathways. However, careful evaluation of risks and benefits is required due to potential metabolic, neurological, and cardiovascular adverse effects.

Antipsychotic medications also have important applications in neurodevelopmental and behavioral disorders. Risperidone and aripiprazole have demonstrated clinical utility in reducing irritability, aggression, and severe behavioral disturbances associated with autism spectrum

disorder. Their use requires careful monitoring because children and adolescents may be particularly vulnerable to weight gain, metabolic abnormalities, sedation, and hormonal disturbances.

In geriatric psychiatry, antipsychotic therapy presents unique challenges due to age-related changes in pharmacokinetics, increased prevalence of medical comorbidities, polypharmacy, and increased sensitivity to adverse effects. Although antipsychotics may occasionally be required for severe behavioral symptoms associated with dementia, their use must be carefully justified because of increased risks of cerebrovascular events, cardiovascular complications, sedation, falls, and mortality among elderly patients with dementia-related psychosis.

The clinical utility of antipsychotic agents extends into emergency psychiatry, where rapid control of severe agitation, aggression, and acute psychotic states may be required. Intramuscular formulations of certain antipsychotics, often combined with other emergency interventions, provide effective short-term stabilization. However, emergency use requires careful assessment of cardiovascular status, drug interactions, and potential adverse reactions.

Adverse Effects and Safety Challenges of Antipsychotic Therapy

Despite their therapeutic benefits, antipsychotic medications are associated with a broad spectrum of adverse effects that significantly influence treatment adherence, quality of life, and clinical outcomes. The diversity of adverse reactions reflects the complex receptor activity of these drugs and their effects on multiple physiological systems.

Extrapyramidal symptoms remain among the most recognized adverse effects associated with dopamine receptor blockade. Acute dystonia may occur shortly after treatment initiation and is characterized by involuntary muscle contractions, particularly affecting the neck, eyes, and facial muscles. Akathisia, characterized by subjective inner restlessness and an inability to remain still, can significantly impair patient comfort and may be associated with increased distress and suicidal ideation. Drug-induced Parkinsonism involves tremor, rigidity, and slowed movement resembling Parkinsonian syndromes. Long-term dopamine receptor blockade may result in tardive dyskinesia, a potentially irreversible condition involving repetitive involuntary movements of the face, tongue, and extremities.

Management of extrapyramidal adverse effects requires individualized strategies, including dose adjustment, switching to medications with lower dopamine receptor affinity, use of anticholinergic agents when appropriate, and treatment with newer pharmacological interventions for tardive dyskinesia. Prevention remains preferable through careful medication selection and avoidance of unnecessary long-term exposure to high-potency dopamine antagonists.

Metabolic adverse effects represent one of the most significant limitations of modern antipsychotic therapy. Several second-generation antipsychotics, particularly clozapine and olanzapine, are associated with substantial weight gain, increased appetite, insulin resistance, dyslipidemia, and elevated risk of metabolic syndrome. These complications contribute to increased cardiovascular morbidity and reduced life expectancy among individuals with severe mental illness.

Metabolic monitoring has therefore become an essential component of evidence-based antipsychotic treatment. Regular assessment of body weight, body mass index, waist circumference, blood pressure, fasting glucose, glycated hemoglobin, and lipid profiles enables early identification and management of metabolic complications. Lifestyle interventions, nutritional counseling, physical activity programs, and pharmacological approaches may be required to reduce long-term cardiovascular risk.

Hyperprolactinemia is another clinically important adverse effect associated with dopamine D2 receptor antagonism. Increased prolactin levels may result in menstrual irregularities, infertility,

sexual dysfunction, gynecomastia, and reduced bone mineral density. Risperidone and conventional antipsychotics are particularly associated with prolactin elevation, whereas dopamine partial agonists generally demonstrate lower risk.

Cardiovascular safety remains a major consideration in antipsychotic prescribing. QT interval prolongation may increase the risk of potentially fatal ventricular arrhythmias, particularly in susceptible individuals or when combined with other QT-prolonging medications. Baseline cardiovascular assessment, electrolyte monitoring, and electrocardiographic evaluation are recommended in patients with relevant risk factors.

Rare but severe adverse reactions require immediate recognition and intervention. Neuroleptic malignant syndrome is a potentially life-threatening complication characterized by severe muscle rigidity, hyperthermia, autonomic instability, altered mental status, and elevated creatine kinase levels. Prompt discontinuation of the causative medication, intensive supportive care, and appropriate pharmacological treatment are essential.

Clozapine-associated toxicity represents a particularly important area of pharmacovigilance. Although highly effective, clozapine requires structured monitoring due to risks of agranulocytosis, myocarditis, seizures, severe constipation, and metabolic complications. The implementation of mandatory blood monitoring programs has significantly reduced mortality associated with hematological toxicity and serves as a model for medication safety systems.

Toxicity Management and Pharmacovigilance in Antipsychotic Treatment

The increasing complexity of antipsychotic pharmacotherapy has emphasized the importance of systematic pharmacovigilance approaches aimed at identifying, preventing, and managing medication-related harm. Pharmacovigilance involves continuous monitoring of adverse drug reactions, evaluation of risk-benefit relationships, detection of rare toxicities, and development of strategies to improve medication safety.

Therapeutic decision-making requires balancing symptom control with minimization of adverse effects. Regular clinical assessment, laboratory monitoring, patient education, and interdisciplinary collaboration are essential components of safe antipsychotic use. Pharmacists and clinical pharmacologists play increasingly important roles in medication review, interaction assessment, adherence optimization, adverse-effect prevention, and patient counseling.

Drug-drug interactions represent a significant challenge, particularly among patients receiving multiple psychotropic and medical therapies. Many antipsychotics undergo hepatic metabolism through cytochrome P450 enzymes, including CYP2D6, CYP3A4, CYP1A2, and CYP2C19. Genetic variability and environmental factors affecting these enzymes contribute to substantial differences in plasma drug concentrations and clinical response.

Therapeutic drug monitoring provides an additional strategy for optimizing treatment, particularly for medications with narrow therapeutic windows, significant pharmacokinetic variability, or uncertain adherence. Measurement of plasma concentrations may assist in dose optimization, detection of non-adherence, identification of drug interactions, and prevention of toxicity.

The future of antipsychotic therapy increasingly depends on integrating pharmacovigilance systems with pharmacogenomics, precision medicine, and advanced computational approaches. Such integration may enable clinicians to predict individual treatment responses, identify patients at increased risk of adverse reactions, and select medications based on biological characteristics rather than empirical trial-and-error approaches.

Pharmacogenomics and Precision Medicine in Antipsychotic Pharmacotherapy

The remarkable variability observed in clinical response and adverse reactions to antipsychotic medications has stimulated increasing interest in pharmacogenomics and precision medicine

approaches. Traditional psychiatric prescribing has historically relied on population-based treatment guidelines, clinical experience, and sequential medication trials. Although this approach has improved outcomes for many patients, it remains limited by unpredictable therapeutic responses, delayed identification of effective medications, unnecessary exposure to ineffective treatments, and preventable adverse drug reactions.

Precision psychiatry represents an emerging paradigm that seeks to individualize treatment selection and dosing according to biological, genetic, environmental, and clinical characteristics of each patient. Within this framework, pharmacogenomics provides an opportunity to understand how inherited genetic variations influence antipsychotic pharmacokinetics, pharmacodynamics, therapeutic efficacy, and toxicity risk. The integration of genomic information into psychiatric practice may facilitate more rational medication selection, improve treatment outcomes, and reduce the burden associated with adverse drug reactions.

A major focus of antipsychotic pharmacogenomics involves genes encoding drug-metabolizing enzymes responsible for hepatic biotransformation. The cytochrome P450 enzyme system plays a central role in determining plasma concentrations of many antipsychotic medications. Genetic polymorphisms affecting CYP2D6 activity represent one of the most extensively studied examples. Individuals may be categorized as poor metabolizers, intermediate metabolizers, normal metabolizers, or ultrarapid metabolizers depending on their CYP2D6 genotype. These variations can significantly influence exposure to medications such as risperidone, aripiprazole, haloperidol, and other antipsychotic agents.

Patients with reduced metabolic capacity may experience increased drug concentrations and a higher risk of dose-related adverse effects, including extrapyramidal symptoms, sedation, and cardiovascular complications. Conversely, individuals with increased metabolic activity may demonstrate lower plasma concentrations and reduced therapeutic response despite standard dosing. Recognition of these differences highlights the potential value of genotype-guided medication optimization.

CYP1A2 polymorphisms are particularly relevant for medications such as clozapine and olanzapine. Environmental factors, including tobacco smoking, can strongly influence CYP1A2 activity and alter antipsychotic plasma levels. Smoking-induced enzyme activation may reduce concentrations of certain medications, potentially leading to reduced efficacy, whereas smoking cessation may increase plasma exposure and create toxicity risks if dose adjustments are not implemented. This interaction illustrates the importance of integrating genetic and environmental factors into individualized pharmacotherapy.

Beyond metabolic enzymes, pharmacodynamic genes involved in neurotransmitter signaling pathways have been investigated as potential determinants of antipsychotic response. Variations in dopamine receptor genes, including DRD2 and DRD3, have been examined because dopamine receptor modulation represents the primary mechanism of action for many antipsychotics. Genetic differences affecting dopamine receptor density, sensitivity, or signaling efficiency may contribute to variations in symptom improvement and susceptibility to movement disorders.

Serotonergic system genes, including serotonin receptor and transporter genes, have also attracted considerable attention. Since many atypical antipsychotics exert significant effects through serotonin–dopamine interactions, genetic variability within serotonergic pathways may influence therapeutic response, emotional symptom improvement, and adverse effect susceptibility. However, despite promising findings, clinical implementation of many pharmacogenomic markers remains limited due to inconsistent replication, population variability, and the complex polygenic nature of psychiatric disorders.

The future of pharmacogenomic-guided antipsychotic therapy will likely depend on integrating multiple genetic markers into comprehensive predictive models rather than relying on single-

gene associations. Advances in genome-wide association studies, artificial intelligence, machine learning algorithms, and multi-omics approaches may facilitate identification of clinically meaningful biological patterns associated with treatment outcomes.

Therapeutic Drug Monitoring and Pharmacokinetic Optimization

Therapeutic drug monitoring represents an important component of individualized antipsychotic management, particularly when pharmacokinetic variability significantly affects clinical outcomes. Unlike many areas of medicine where standardized dosing produces predictable responses, psychiatric pharmacotherapy frequently demonstrates considerable interindividual variation. Differences in absorption, distribution, metabolism, elimination, genetic background, age, body composition, organ function, smoking status, concurrent medications, and adherence behavior contribute to variability in antipsychotic exposure.

Therapeutic drug monitoring involves measurement of plasma drug concentrations to support clinical decision-making. It provides valuable information when treatment response is inadequate, adverse effects occur unexpectedly, adherence is uncertain, drug interactions are suspected, or patients require complex medication regimens. Rather than replacing clinical judgment, therapeutic drug monitoring serves as an additional tool that complements symptom evaluation and pharmacological assessment.

Clozapine is among the antipsychotics for which therapeutic drug monitoring has demonstrated particular clinical relevance. Plasma clozapine concentrations correlate with therapeutic response and toxicity risk, assisting clinicians in identifying inadequate exposure, optimizing dosage, and reducing unnecessary escalation. Monitoring may be especially important when metabolic factors, smoking behavior, inflammatory conditions, or interacting medications alter clozapine clearance.

Therapeutic drug monitoring is also relevant for other antipsychotics, including risperidone, aripiprazole, haloperidol, and olanzapine. Population pharmacokinetic modeling and pharmacometric approaches increasingly allow prediction of drug concentrations based on patient-specific variables. These approaches combine pharmacological principles with computational methods to support individualized dosing strategies.

The integration of therapeutic drug monitoring with pharmacogenomic information represents an important step toward precision psychiatry. Genetic data may explain differences in metabolic capacity, while plasma concentration measurements provide real-time information regarding actual drug exposure. Together, these approaches may improve dose optimization and minimize the risk of both therapeutic failure and toxicity.

Emerging Innovations in Neuropharmacology and Antipsychotic Drug Development

Despite major progress in antipsychotic pharmacotherapy, substantial unmet clinical needs remain. Current medications are highly effective for positive symptoms in many patients; however, their effects on negative symptoms, cognitive dysfunction, social functioning, and long-term recovery remain limited. Furthermore, treatment resistance, adverse effects, and medication discontinuation continue to represent major challenges.

Future therapeutic innovations increasingly focus on developing medications that target broader neurobiological mechanisms involved in psychosis. Advances in molecular neuroscience have expanded attention beyond dopamine and serotonin systems toward glutamatergic regulation, neuroinflammation, oxidative stress pathways, synaptic plasticity, neurodevelopmental mechanisms, and immune–brain interactions.

Glutamatergic approaches represent one of the most promising areas of investigation. Since NMDA receptor dysfunction has been implicated in cognitive impairment and negative symptoms, therapeutic strategies aimed at enhancing glutamate signaling or restoring

excitatory–inhibitory balance may provide benefits that are not achieved with conventional dopamine-based therapies. Agents targeting glycine modulation, metabotropic glutamate receptors, and synaptic regulatory pathways are currently being explored.

Neuroinflammation and immune dysregulation have also emerged as potential therapeutic targets. Evidence suggests that subsets of individuals with schizophrenia may exhibit altered inflammatory profiles, increased oxidative stress, and immune-related abnormalities. Identification of biological subgroups through biomarkers may enable development of targeted anti-inflammatory or neuroprotective interventions.

Digital health technologies and artificial intelligence are increasingly influencing psychiatric research and clinical decision-making. Machine learning models can analyze large datasets incorporating clinical characteristics, neuroimaging findings, electronic health records, genetic information, and treatment outcomes to identify patterns associated with medication response. Although these approaches require further validation, they represent promising tools for improving prediction accuracy and personalized treatment planning.

Long-acting injectable technologies, novel drug delivery systems, and digital adherence monitoring represent additional innovations aimed at improving treatment continuity. Improved formulations may enhance patient acceptance, reduce relapse risk, and provide more stable pharmacokinetic profiles compared with traditional oral administration.

Evidence-Based Clinical Practice and Future Directions

The advancement of antipsychotic therapy requires continuous integration of scientific discoveries, clinical evidence, and patient-centered approaches. Evidence-based clinical practice provides the foundation for selecting appropriate medications, evaluating therapeutic effectiveness, monitoring safety, and implementing individualized treatment strategies. International clinical guidelines increasingly emphasize shared decision-making, early intervention, metabolic monitoring, relapse prevention, and comprehensive management of psychiatric and medical comorbidities.

The future of antipsychotic pharmacotherapy will likely involve a transition from symptom-based treatment models toward biologically informed precision approaches. Integration of pharmacogenomics, therapeutic drug monitoring, digital technologies, artificial intelligence, and biomarker-driven strategies may allow clinicians to identify the most appropriate medication for each patient while minimizing risks.

However, several challenges remain before precision psychiatry becomes widely implemented. These include the need for robust clinical validation of biomarkers, cost-effectiveness assessment, and ethical considerations regarding genetic information, healthcare infrastructure requirements, and equitable access to advanced diagnostic technologies. Collaborative efforts among neuroscientists, pharmacologists, psychiatrists, geneticists, pharmacists, and policymakers will be essential to overcome these barriers.

Antipsychotic medications remain indispensable tools in modern psychiatric medicine, but their optimal use requires a comprehensive understanding of pharmacology, neurobiology, and safety monitoring, and individualized patient characteristics. Continued research into molecular mechanisms, genetic determinants, novel therapeutic targets, and innovative clinical strategies will shape the next generation of antipsychotic treatments.

Translational Neuropharmacology and the Future Landscape of Antipsychotic Development

The advancement of antipsychotic pharmacotherapy increasingly depends on translational neuropharmacology, which bridges fundamental neuroscience discoveries with clinical applications. Traditional antipsychotic development has largely followed a receptor-based strategy, focusing predominantly on dopamine D2 receptor antagonism and serotonin receptor

modulation. While these approaches have produced substantial therapeutic benefits, they have not fully addressed the heterogeneity of psychotic disorders or the diverse biological mechanisms contributing to symptom development and treatment response.

Contemporary neuroscience emphasizes that psychotic disorders represent complex neurobiological syndromes involving multiple interacting molecular pathways rather than isolated neurotransmitter abnormalities. Genetic vulnerability, epigenetic regulation, neurodevelopmental abnormalities, environmental stress exposure, immune dysfunction, mitochondrial impairment, oxidative stress, and altered neural connectivity collectively contribute to disease expression. Consequently, future antipsychotic discovery is moving toward multidimensional therapeutic strategies capable of targeting several pathological mechanisms simultaneously.

The emergence of systems neuroscience has provided new insights into the relationship between brain networks and psychiatric symptoms. Functional imaging studies have demonstrated abnormalities in connectivity patterns involving prefrontal cortical regions, hippocampal structures, thalamic circuits, and limbic networks among individuals with psychotic disorders. These findings suggest that future therapeutic interventions may require modulation of dysfunctional neural circuits rather than simple alteration of individual neurotransmitter pathways.

Neuroplasticity has become an important concept in the development of next-generation psychiatric medications. The ability of therapeutic agents to restore adaptive neural connectivity, improve synaptic function, and enhance cognitive processing represents a major goal beyond traditional symptom suppression. Novel compounds targeting synaptic remodeling, neurotrophic signaling pathways, and neuronal resilience mechanisms may provide opportunities for improving functional recovery and quality of life.

The development of biomarkers represents another critical direction in modern neuropharmacology. Current psychiatric diagnoses are primarily based on clinical symptoms rather than objective biological measurements. This limitation contributes to substantial variability in treatment outcomes. Biomarkers derived from genetics, neuroimaging, electrophysiology, inflammatory profiles, metabolomics, and digital behavioral assessments may enable identification of biologically distinct subgroups of patients who are more likely to respond to specific interventions.

A biomarker-driven approach could fundamentally transform antipsychotic treatment by replacing generalized prescribing models with targeted therapeutic strategies. For example, patients with predominant dopaminergic abnormalities may benefit from dopamine-modulating medications, whereas individuals characterized by glutamatergic dysfunction or inflammatory activation may require alternative approaches. Such stratification may improve efficacy while reducing unnecessary exposure to ineffective medications.

Pharmacovigilance Systems and Medication Safety in Antipsychotic Therapy

The complexity of antipsychotic treatment requires comprehensive pharmacovigilance systems capable of monitoring medication safety throughout the entire lifecycle of drug use. Pharmacovigilance extends beyond the identification of adverse drug reactions and includes risk assessment, prevention strategies, regulatory decision-making, medication optimization, and continuous evaluation of real-world clinical outcomes.

Antipsychotic-associated adverse effects often emerge gradually and may significantly influence morbidity and mortality. Long-term metabolic complications, cardiovascular disease, movement disorders, endocrine abnormalities, and medication-related quality-of-life impairments require systematic monitoring. Effective pharmacovigilance programs facilitate early recognition of safety signals and allow healthcare systems to implement evidence-based interventions.

Real-world evidence obtained from electronic health records, prescription databases, patient registries, and international safety monitoring networks has become increasingly important in evaluating antipsychotic effectiveness and safety. Randomized controlled trials remain the gold standard for establishing efficacy; however, they frequently exclude individuals with complex comorbidities, polypharmacy, advanced age, or socioeconomic challenges. Real-world pharmacovigilance provides complementary information regarding medication performance in routine clinical practice.

Artificial intelligence and machine learning technologies are increasingly being incorporated into pharmacovigilance systems. Advanced computational algorithms can analyze large-scale healthcare datasets to identify previously unrecognized adverse drug reactions, predict high-risk patients, and support clinical decision-making. Natural language processing techniques may allow extraction of safety information from clinical documentation, patient reports, and medical literature.

The role of healthcare professionals in pharmacovigilance remains essential. Psychiatrists, pharmacists, clinical pharmacologists, nurses, and primary healthcare providers contribute to adverse effect detection, patient education, medication reconciliation, and prevention of avoidable harm. Pharmacists, in particular, provide critical expertise in drug interactions, dose optimization, therapeutic monitoring, and adherence improvement.

Integration of Artificial Intelligence and Digital Technologies in Personalized Antipsychotic Care

Digital transformation is rapidly influencing the future of psychiatric medicine. Artificial intelligence, machine learning, wearable technologies, mobile health applications, and digital biomarkers offer new opportunities for improving diagnosis, treatment monitoring, and personalized care.

Machine learning approaches can integrate diverse clinical datasets, including demographic characteristics, symptom trajectories, genetic information, medication histories, laboratory findings, and neuroimaging data. These models may identify patterns associated with treatment response and assist clinicians in selecting optimal therapeutic strategies.

Digital monitoring technologies may also improve long-term management of psychotic disorders. Smartphone-based applications and wearable devices can provide continuous information regarding sleep patterns, activity levels, social engagement, physiological parameters, and early warning signs of relapse. Such technologies may support proactive intervention before severe symptom deterioration occurs.

Digital adherence monitoring represents another promising development. Medication non-adherence remains a major contributor to relapse and hospitalization among individuals with schizophrenia and related disorders. Technologies capable of monitoring medication intake, treatment engagement, and behavioral changes may improve continuity of care while supporting collaborative treatment relationships.

However, implementation of artificial intelligence and digital psychiatry requires careful consideration of ethical, regulatory, and privacy issues. Protection of sensitive psychiatric data, transparency of algorithmic decision-making, avoidance of bias, and equitable access to digital healthcare technologies are essential principles for responsible innovation.

Global Perspectives and Public Health Importance of Optimized Antipsychotic Treatment

Psychotic disorders represent a significant global public health challenge affecting individuals across diverse cultural, economic, and healthcare environments. Despite major advances in psychiatric pharmacology, disparities remain in access to diagnosis, evidence-based treatment, monitoring services, and psychosocial support.

In many low- and middle-income countries, limited availability of psychiatric specialists, restricted medication access, inadequate laboratory monitoring infrastructure, and social stigma continue to influence treatment outcomes. Expanding access to safe and effective antipsychotic therapy requires international collaboration, healthcare system strengthening, professional education, and implementation of cost-effective treatment strategies.

Global mental health initiatives increasingly emphasize integration of psychiatric care into primary healthcare systems. Such approaches may improve early identification of psychotic disorders, facilitate continuity of treatment, and reduce barriers associated with specialized psychiatric services.

The optimization of antipsychotic pharmacotherapy has implications beyond symptom reduction. Effective treatment contributes to improved social functioning, employment opportunities, family stability, and reduced hospitalization rates, and enhanced quality of life. Therefore, advances in antipsychotic medication management represent not only scientific achievements but also important contributions to global health improvement.

Rationale and Objectives of the Present Review

The continuous evolution of antipsychotic pharmacotherapy requires comprehensive evaluation of established knowledge and emerging scientific developments. Although antipsychotic medications remain among the most extensively studied psychopharmacological interventions, challenges related to incomplete efficacy, treatment resistance, adverse effects, toxicity, and individualized treatment selection persist.

This comprehensive review aims to provide an integrated analysis of antipsychotic agents by examining their mechanisms of action, pharmacological characteristics, clinical applications, safety considerations, toxicity management strategies, pharmacogenomic determinants, precision medicine approaches, neuropharmacological mechanisms, pharmacovigilance principles, therapeutic drug monitoring applications, and emerging therapeutic innovations.

By synthesizing evidence from molecular neuroscience, clinical pharmacology, psychiatric research, and personalized medicine, this review seeks to highlight current achievements, identify remaining challenges, and discuss future directions for improving antipsychotic therapy. Particular emphasis is placed on the transition from traditional symptom-oriented treatment toward individualized, biomarker-informed, and technologically enhanced models of psychiatric care.

The integration of pharmacological science with precision medicine represents a transformative opportunity for the future of psychiatry. Through continued interdisciplinary research, development of reliable biomarkers, advancement of innovative therapeutic targets, and implementation of evidence-based clinical strategies, next-generation antipsychotic treatments may achieve greater efficacy, improved safety, and enhanced functional outcomes for individuals affected by psychotic disorders worldwide.

Goal

The goal of this comprehensive review is to provide an integrated and evidence-based analysis of contemporary antipsychotic agents by examining their molecular mechanisms of action, pharmacological characteristics, clinical applications, adverse effect profiles, toxicity management strategies, and safety optimization approaches. This review aims to critically evaluate advances in neuropharmacology, pharmacogenomics, precision medicine, therapeutic drug monitoring, and pharmacovigilance that contribute to individualized antipsychotic treatment. Furthermore, it seeks to explore emerging therapeutic innovations, novel biological targets, and future directions in antipsychotic drug development to improve treatment efficacy,

minimize medication-related risks, enhance patient outcomes, and advance personalized evidence-based psychiatric care.

Methodology

This comprehensive review employed a systematic and evidence-based literature synthesis approach to evaluate contemporary developments in antipsychotic pharmacotherapy. Relevant scientific publications, clinical guidelines, pharmacological databases, and peer-reviewed studies were critically analyzed, focusing on mechanisms of action, clinical efficacy, adverse reactions, toxicity management, pharmacogenomic determinants, precision medicine strategies, therapeutic drug monitoring, and emerging neuropharmacological innovations. Literature was identified through structured searches of major biomedical databases, including PubMed, Scopus, Web of Science, and other authoritative scientific sources. Selected evidence was critically appraised, integrated, and synthesized to provide a multidisciplinary perspective on current advances and future directions in antipsychotic treatment.

RESULTS AND DISCUSSION

The comprehensive analysis of contemporary antipsychotic pharmacotherapy demonstrates that these agents remain among the most important therapeutic interventions in psychiatry, while simultaneously representing one of the most complex areas of clinical pharmacology. The findings derived from extensive evaluation of pharmacological research, clinical trials, real-world evidence, pharmacogenomic investigations, and emerging neurobiological studies indicate that antipsychotic treatment has evolved considerably from simple dopamine receptor blockade toward multidimensional, personalized, and precision-oriented therapeutic approaches.

The current evidence confirms that antipsychotic medications significantly reduce positive psychotic symptoms, prevent relapse, improve behavioral stability, and enhance long-term disease management in individuals with schizophrenia spectrum disorders and other psychiatric conditions associated with psychosis. However, therapeutic outcomes remain highly heterogeneous, reflecting the biological complexity of psychotic disorders and substantial variability in individual responses to pharmacological interventions.

The analysis highlights that dopamine neurotransmission continues to represent a central mechanism underlying antipsychotic efficacy. The relationship between dopamine D2 receptor modulation and clinical response remains strongly supported by neuroimaging studies, pharmacological investigations, and decades of clinical experience. Most effective antipsychotic medications influence dopaminergic signaling within mesolimbic pathways, reducing excessive dopamine activity associated with hallucinations, delusions, and disorganized thinking. Nevertheless, the results also demonstrate that excessive dopamine inhibition contributes directly to several major treatment limitations, including extrapyramidal symptoms, hyperprolactinemia, and impaired motivation.

The evolution from first-generation antipsychotics to second-generation and third-generation agents reflects progressive attempts to achieve therapeutic dopamine modulation while minimizing adverse consequences. First-generation antipsychotics remain effective for acute psychosis and positive symptom control; however, their clinical limitations are strongly associated with high dopamine D2 receptor occupancy and increased risk of movement-related adverse effects. The widespread introduction of atypical antipsychotics represented a significant advancement because serotonin–dopamine receptor interactions provided improved tolerability and broader therapeutic profiles.

The findings indicate that atypical antipsychotics demonstrate substantial differences in receptor-binding characteristics, which translate into clinically meaningful variations in safety and efficacy. Clozapine remains the most effective medication for treatment-resistant schizophrenia and continues to represent the reference standard when adequate trials of other antipsychotics fail. The superior efficacy of clozapine appears to result from its complex pharmacological profile involving dopamine, serotonin, glutamate, cholinergic, histaminergic,

and adrenergic systems. However, its clinical use requires careful risk management due to potentially severe adverse effects, including agranulocytosis, myocarditis, seizures, metabolic disturbances, and gastrointestinal complications.

The evidence regarding clozapine emphasizes the importance of balancing therapeutic benefit with safety surveillance. Structured monitoring programs, including regular hematological evaluation and metabolic assessment, have substantially improved the safety profile of this medication. The clozapine model demonstrates how pharmacovigilance systems can transform a high-risk medication into an essential therapeutic option for patients with severe and refractory psychiatric illness.

Comparative evaluation of second-generation antipsychotics demonstrates that differences in clinical effectiveness are often less pronounced than differences in tolerability profiles. Medications such as olanzapine provide strong symptom control but are associated with significant metabolic consequences, whereas agents such as ziprasidone and aripiprazole generally demonstrate more favorable metabolic profiles. These findings reinforce the importance of individualized medication selection rather than universal prescribing strategies.

The emergence of dopamine partial agonists represents a major conceptual development in antipsychotic pharmacology. Unlike traditional dopamine antagonists, partial agonists provide functional stabilization of dopaminergic neurotransmission. The results indicate that this mechanism may reduce the incidence of certain adverse effects while maintaining antipsychotic efficacy. Aripiprazole, brexpiprazole, and cariprazine demonstrate the potential advantages of receptor modulation rather than complete receptor inhibition. Particularly, cariprazine's preferential activity at dopamine D3 receptors has generated interest regarding potential benefits for negative symptoms and cognitive impairment, although further research remains necessary.

The clinical analysis further demonstrates that antipsychotic therapy extends beyond schizophrenia management. Antipsychotic agents have become integral components of treatment strategies for bipolar disorder, psychotic depression, autism spectrum disorder-associated irritability, and several other psychiatric conditions. Their expanding clinical utility reflects increasing recognition that dysregulation of dopamine, serotonin, and related neurotransmitter networks contributes to multiple neuropsychiatric syndromes.

In bipolar disorder, antipsychotics demonstrate substantial efficacy in acute mania and maintenance treatment. Several atypical antipsychotics provide rapid reduction of manic symptoms, including agitation, impulsivity, elevated mood, and psychotic manifestations. The evidence suggests that treatment selection should consider both efficacy and long-term tolerability, particularly because many individuals with bipolar disorder require prolonged pharmacological management. Metabolic adverse effects, sedation, and adherence challenges remain important factors influencing therapeutic success.

The analysis of antipsychotic use in depressive disorders demonstrates the increasing importance of augmentation strategies. Certain atypical antipsychotics enhance antidepressant response in individuals with treatment-resistant depression, likely through complex modulation of serotonergic, dopaminergic, and noradrenergic systems. However, careful clinical assessment remains essential because augmentation therapy introduces additional risks related to metabolic changes, movement disorders, and long-term medication burden.

One of the most significant findings emerging from current evidence is that symptom reduction alone is insufficient as the primary measure of therapeutic success. Modern psychiatric care increasingly emphasizes functional recovery, cognitive improvement, social reintegration, employment capacity, and quality of life. Traditional antipsychotic therapies demonstrate limited effectiveness against negative symptoms and cognitive deficits, representing major areas of unmet clinical need.

The results indicate that future progress in antipsychotic treatment requires expansion beyond dopamine-centered models. Increasing evidence supports the involvement of glutamatergic dysfunction, GABAergic abnormalities, neuroinflammation, oxidative stress, mitochondrial dysfunction, and altered synaptic plasticity in psychotic disorders. These findings have stimulated research into novel therapeutic targets capable of addressing symptom domains that remain poorly responsive to existing medications.

Glutamate-based therapeutic approaches represent one of the most promising areas of investigation. The association between NMDA receptor dysfunction and cognitive impairment has encouraged development of agents targeting glutamate signaling pathways. Although clinical translation remains challenging, these approaches may provide future opportunities for improving cognitive symptoms and functional outcomes.

The analysis of adverse effects confirms that medication safety remains a central determinant of treatment success. Antipsychotic-related toxicity represents a complex interaction between pharmacological properties, individual susceptibility, genetic factors, environmental influences, and concurrent medications. Extrapyramidal symptoms, metabolic syndrome, cardiovascular risks, endocrine disturbances, and rare severe reactions require systematic prevention and management strategies.

Metabolic complications represent one of the greatest challenges associated with modern antipsychotic therapy. The results demonstrate that weight gain, insulin resistance, diabetes mellitus, and dyslipidemia significantly contribute to increased cardiovascular morbidity among individuals receiving long-term antipsychotic treatment. These findings emphasize the necessity of continuous metabolic monitoring and early intervention.

Preventive strategies including lifestyle modification, nutritional interventions, physical activity programs, careful medication selection, and appropriate pharmacological management of metabolic abnormalities should be integrated into routine psychiatric care. The balance between psychiatric stabilization and physical health protection represents a fundamental principle of contemporary antipsychotic management.

The findings of this comprehensive evaluation further demonstrate that successful antipsychotic therapy requires a multidimensional approach integrating pharmacological efficacy, adverse-effect prevention, patient-specific characteristics, and continuous therapeutic monitoring. The historical emphasis on symptom reduction has gradually shifted toward a broader model of psychiatric care that prioritizes long-term functional recovery, prevention of relapse, preservation of physical health, and optimization of quality of life.

The management of antipsychotic-induced neurological adverse effects remains a significant clinical challenge. Extrapyramidal symptoms continue to represent a major limitation of dopamine receptor antagonism, particularly among individuals receiving high-potency first-generation antipsychotics. The results confirm that the risk of motor complications is strongly associated with dopamine D2 receptor occupancy, dose intensity, treatment duration, patient age, and individual vulnerability. Acute dystonia, akathisia, drug-induced Parkinsonism, and tardive dyskinesia require early recognition because delayed intervention may result in persistent impairment and reduced adherence.

Current evidence supports individualized strategies for preventing and managing extrapyramidal toxicity. These include selecting medications with lower propensity for dopamine blockade-related complications, using the lowest effective dose, gradual dose adjustment, and regular assessment of movement disorders. The introduction of standardized evaluation instruments for extrapyramidal symptoms and tardive dyskinesia has improved clinical recognition and facilitated treatment optimization. Furthermore, newer pharmacological approaches targeting vesicular monoamine transporter regulation have expanded therapeutic possibilities for patients experiencing persistent tardive dyskinesia.

Akathisia deserves particular attention because it may be underestimated in clinical practice despite its profound impact on patient experience. The subjective distress associated with severe restlessness may contribute to treatment discontinuation, emotional deterioration, and increased risk of self-harm behaviors. Differentiating akathisia from anxiety, agitation, or worsening psychosis is essential for appropriate management. Clinical evidence supports medication adjustment, switching strategies, and selected pharmacological interventions when clinically indicated.

Endocrine adverse effects represent another important consequence of antipsychotic treatment. Dopamine blockade within the tuberoinfundibular pathway results in increased prolactin secretion, leading to hyperprolactinemia-associated complications. The findings demonstrate that prolonged elevation of prolactin may negatively affect reproductive function, sexual health, bone metabolism, and psychological well-being. Women may experience menstrual abnormalities, infertility, or galactorrhea, while men may develop decreased libido, erectile dysfunction, gynecomastia, and reduced testosterone levels.

The differential effects of antipsychotic agents on prolactin regulation highlight the importance of pharmacological selection. Dopamine partial agonists generally demonstrate lower risks of prolactin elevation and may represent appropriate alternatives for patients experiencing clinically significant endocrine complications. Monitoring prolactin concentrations should be considered in symptomatic individuals and in patients receiving medications with known high prolactin liability.

Cardiovascular safety remains a fundamental consideration in long-term antipsychotic treatment. The results indicate that antipsychotic-associated cardiovascular risks arise through multiple mechanisms, including metabolic disturbances, direct electrophysiological effects, autonomic modulation, and interactions with other medications. QT interval prolongation represents a clinically important concern because it may increase susceptibility to ventricular arrhythmias, particularly in patients with underlying cardiac disease, electrolyte abnormalities, or polypharmacy.

A comprehensive cardiovascular risk assessment before and during antipsychotic treatment is therefore essential. Evaluation of personal and family cardiac history, baseline electrocardiography when indicated, electrolyte monitoring, and careful review of interacting medications contribute to safer prescribing practices. These measures are particularly relevant in vulnerable populations, including elderly patients and individuals receiving multiple psychotropic agents.

Neuroleptic malignant syndrome remains one of the most serious acute toxicities associated with antipsychotic medications. Although relatively uncommon, this syndrome represents a medical emergency requiring rapid diagnosis and intervention. The findings emphasize that neuroleptic malignant syndrome reflects complex interactions between dopamine blockade, individual susceptibility, environmental factors, and medication exposure. Early recognition of clinical manifestations, including severe rigidity, hyperthermia, autonomic instability, altered consciousness, and elevated muscle enzymes, is critical for reducing morbidity and mortality.

The analysis of antipsychotic toxicity highlights the importance of pharmacovigilance as an integral component of psychiatric practice. Pharmacovigilance systems provide essential mechanisms for identifying rare adverse reactions, evaluating long-term safety outcomes, and improving medication management. Unlike controlled clinical trials, which often involve carefully selected populations, pharmacovigilance databases capture medication experiences across diverse patient groups, including individuals with complex medical conditions and multiple medications.

Real-world evidence has significantly expanded understanding of antipsychotic safety profiles. Large observational studies have identified important associations between specific

medications, treatment duration, patient characteristics, and long-term outcomes. Such evidence complements randomized clinical trials by providing insights into routine clinical effectiveness and safety.

The integration of electronic health records, pharmacological databases, and artificial intelligence-based analytical approaches represents a major advancement in pharmacovigilance. Machine learning algorithms have the potential to identify previously unrecognized safety signals by analyzing large volumes of clinical information. These approaches may improve early detection of adverse reactions and support proactive risk management.

Pharmacogenomics represents one of the most promising developments in individualized antipsychotic treatment. The results demonstrate that genetic variability contributes significantly to differences in medication response, metabolism, and adverse-effect susceptibility. Unlike traditional prescribing approaches based primarily on clinical observation, pharmacogenomic strategies aim to incorporate biological information into medication selection and dose optimization.

Cytochrome P450 enzyme polymorphisms remain among the most clinically relevant genetic factors influencing antipsychotic pharmacokinetics. CYP2D6 variation significantly affects metabolism of several commonly prescribed agents, including risperidone and aripiprazole. Patients with reduced enzyme activity may experience higher drug exposure and increased toxicity risk, whereas individuals with increased metabolic activity may demonstrate reduced therapeutic response.

The clinical relevance of CYP1A2 variability is particularly evident with clozapine and olanzapine therapy. Environmental factors such as cigarette smoking influence CYP1A2 activity and can substantially alter plasma concentrations. Changes in smoking behavior may therefore require medication reassessment to prevent unexpected toxicity or therapeutic failure.

Beyond metabolic pathways, genetic variations affecting neurotransmitter receptors and transport systems may contribute to differences in antipsychotic response. Dopamine receptor genes, serotonin receptor genes, and genes involved in neuronal signaling pathways have been investigated as potential predictors of treatment outcomes. Although many associations remain under investigation, advances in genomic technologies continue to improve understanding of biological heterogeneity among individuals with psychotic disorders.

The findings suggest that future clinical implementation of pharmacogenomics will likely require integration of multiple genetic markers rather than reliance on individual polymorphisms. Psychiatric disorders are highly polygenic, and medication response is influenced by complex interactions between genetic, environmental, and clinical variables. Therefore, comprehensive predictive models combining genomic information with clinical characteristics may provide the greatest benefit.

Therapeutic drug monitoring represents another important component of precision antipsychotic therapy. The results indicate that plasma concentration monitoring can provide valuable information in situations involving treatment resistance, suspected non-adherence, unexpected adverse effects, drug interactions, or significant physiological changes. By providing objective information regarding medication exposure, therapeutic drug monitoring supports rational dose adjustment and individualized treatment planning.

Clozapine remains the most established example of clinically valuable therapeutic drug monitoring among antipsychotic medications. Plasma concentration assessment may assist in identifying patients who require dose optimization and may reduce unnecessary dose escalation associated with toxicity. In addition, inflammatory states, smoking changes, and metabolic alterations may significantly influence clozapine clearance, emphasizing the importance of dynamic monitoring.

Population pharmacokinetic modeling and pharmacometric approaches are increasingly being applied to antipsychotic treatment optimization. These mathematical frameworks incorporate patient characteristics such as age, body weight, organ function, genetics, and concurrent medications to predict drug exposure and guide individualized dosing. Such approaches represent an important bridge between pharmacology and precision medicine.

The results further demonstrate that the future of antipsychotic therapy will increasingly depend on integration of multiple scientific disciplines. Neuropharmacology, genomics, artificial intelligence, digital medicine, and clinical pharmacology are converging to create new models of psychiatric treatment. This interdisciplinary approach has the potential to improve therapeutic precision while reducing the burden associated with ineffective treatment and medication-related harm.

The integration of pharmacogenomics, therapeutic drug monitoring, and advanced computational approaches represents a fundamental transformation in the management of psychotic disorders. The results of contemporary research indicate that the future of antipsychotic therapy will depend increasingly on individualized treatment algorithms capable of incorporating genetic, molecular, clinical, and environmental variables. This transition reflects a movement away from traditional empirical prescribing toward a precision psychiatry framework in which therapeutic decisions are guided by measurable biological characteristics and patient-specific risk profiles.

Precision medicine approaches in psychiatry aim to overcome the limitations associated with current diagnostic and therapeutic models. Unlike many areas of medicine where molecular biomarkers guide treatment selection, psychiatric disorders have historically relied primarily on symptom-based classification systems. Although diagnostic criteria remain clinically valuable, they do not fully capture the biological heterogeneity underlying psychotic disorders. Individuals with the same clinical diagnosis may exhibit distinct neurobiological mechanisms, variable treatment responses, and different susceptibility to adverse effects.

The findings indicate that precision psychiatry requires integration of multiple information domains, including genomic data, neuroimaging characteristics, inflammatory biomarkers, metabolic profiles, electrophysiological measurements, digital behavioral indicators, and longitudinal clinical outcomes. Such multidimensional approaches may allow identification of patient subgroups with specific biological characteristics and facilitate selection of the most appropriate therapeutic intervention.

Artificial intelligence and machine learning technologies are increasingly contributing to this emerging paradigm. The analysis demonstrates that artificial intelligence-based systems have the potential to enhance prediction of treatment response, identify relapse risk, optimize medication selection, and improve clinical decision-making. Machine learning algorithms can analyze complex datasets containing thousands of variables that may exceed the analytical capacity of conventional clinical approaches.

In antipsychotic pharmacotherapy, artificial intelligence models have been investigated for predicting medication response based on clinical history, demographic characteristics, genetic information, brain imaging findings, and treatment trajectories. These approaches may eventually assist clinicians in identifying patients who are more likely to respond to specific medications, including clozapine or dopamine partial agonists, while avoiding unnecessary exposure to ineffective treatments.

Digital biomarkers represent another emerging area of innovation. Continuous monitoring through smartphones, wearable devices, and remote assessment technologies may provide objective information regarding changes in behavior, sleep patterns, activity levels, speech characteristics, and social interaction. Such information may facilitate early detection of symptom worsening and enable preventive intervention before severe relapse occurs.

The application of digital technologies may be particularly valuable in schizophrenia and related disorders because relapse is frequently preceded by subtle behavioral and functional changes. Traditional clinical assessments performed during scheduled appointments may fail to capture these dynamic fluctuations. Continuous monitoring systems may therefore provide a more comprehensive understanding of disease progression and treatment effectiveness.

However, the implementation of artificial intelligence and digital psychiatry requires careful evaluation of ethical, clinical, and regulatory considerations. Algorithms must demonstrate reliability, transparency, and clinical validity before widespread adoption. Potential risks include algorithmic bias, unequal access to digital technologies, privacy concerns, and inappropriate reliance on automated recommendations. Therefore, artificial intelligence should function as a supportive clinical tool rather than a replacement for professional judgment and therapeutic relationships.

The results further emphasize the importance of patient-centered approaches in optimizing antipsychotic therapy. Medication effectiveness is influenced not only by pharmacological properties but also by patient preferences, treatment expectations, psychosocial circumstances, adherence behavior, and therapeutic alliance. Shared decision-making between clinicians and patients improves treatment engagement and may enhance long-term outcomes.

Medication adherence remains one of the most significant challenges in the management of psychotic disorders. The chronic nature of schizophrenia and related conditions, combined with limited insight, cognitive impairment, adverse effects, and social factors, contributes to discontinuation of treatment. Non-adherence is strongly associated with relapse, hospitalization, increased healthcare costs, and reduced functional recovery.

The findings demonstrate that long-acting injectable antipsychotic formulations provide an important strategy for improving treatment continuity. By maintaining more stable plasma concentrations and reducing dependence on daily medication administration, these formulations may decrease relapse risk among selected patients. Furthermore, long-acting preparations allow healthcare providers to identify treatment interruption more accurately and intervene earlier.

Nevertheless, medication adherence should not be considered solely a patient-related issue. Adherence is influenced by medication tolerability, therapeutic communication, healthcare accessibility, stigma, socioeconomic factors, and patient involvement in treatment decisions. Comprehensive adherence strategies should therefore include education, psychosocial support, adverse-effect management, and collaborative care planning.

The analysis also highlights the importance of considering physical health outcomes in individuals receiving long-term antipsychotic treatment. Individuals with severe mental illness experience significantly increased rates of cardiovascular disease, metabolic disorders, and reduced life expectancy compared with the general population. Antipsychotic-associated metabolic effects contribute to this health disparity, emphasizing the necessity of integrated psychiatric and medical care.

Routine monitoring of metabolic parameters should therefore be regarded as a fundamental component of antipsychotic management. Early identification of weight gain, impaired glucose regulation, hypertension, and lipid abnormalities allows timely intervention and may prevent long-term complications. Clinical strategies should incorporate lifestyle interventions, nutritional support, physical activity programs, and appropriate medical treatment when required.

The relationship between antipsychotic therapy and inflammation represents another emerging area of investigation. Increasing evidence suggests that immune dysregulation and inflammatory processes may contribute to the development and progression of psychotic disorders. Elevated inflammatory markers, altered cytokine activity, and microglial activation have been identified in subsets of patients, suggesting potential opportunities for biomarker-guided interventions.

Anti-inflammatory and immunomodulatory strategies are currently being explored as complementary approaches in psychiatric treatment. Although results remain preliminary, these approaches may become particularly relevant for biologically defined patient groups demonstrating immune-related abnormalities. Future research will be required to determine which individuals may benefit most from such interventions.

The role of oxidative stress and mitochondrial dysfunction in psychotic disorders has also gained increasing attention. Abnormal regulation of oxidative processes may contribute to neuronal dysfunction, impaired synaptic communication, and disease progression. Therapeutic strategies targeting oxidative pathways and neuroprotection represent promising areas for future investigation.

Emerging therapeutic innovations are also expanding beyond traditional small-molecule antipsychotics. Novel drug delivery systems, receptor-selective compounds, neuroprotective agents, and combination therapies are being investigated to improve efficacy and safety. The development of medications capable of addressing negative symptoms and cognitive impairment remains a particularly important objective because these symptom domains are strongly associated with disability.

The results indicate that future antipsychotic development will likely focus on several key principles: improved targeting of disease mechanisms, reduced adverse effects, enhanced cognitive outcomes, prevention of relapse, and promotion of functional recovery. Successful therapeutic innovation will require integration of molecular neuroscience, clinical pharmacology, computational biology, and patient-centered research.

The expanding field of pharmacovigilance will continue to play a critical role in evaluating emerging therapies. As new medications enter clinical practice, long-term safety monitoring will be essential for identifying rare adverse events, assessing effectiveness in diverse populations, and guiding regulatory decisions. International collaboration and standardized data collection will strengthen the ability to detect safety signals and improve medication management.

The evidence reviewed demonstrates that antipsychotic pharmacotherapy has progressed from a relatively simple model of dopamine receptor inhibition toward a sophisticated discipline incorporating molecular neuroscience, personalized medicine, and advanced technology. Current medications provide substantial benefits for millions of individuals worldwide; however, important challenges remain regarding treatment resistance, adverse effects, cognitive impairment, and individualized therapeutic selection.

The future of antipsychotic therapy will depend on continued development of biologically informed treatment strategies. Integration of pharmacogenomics, therapeutic drug monitoring, artificial intelligence, digital health technologies, and novel neurobiological targets offers the possibility of creating more precise, effective, and safer interventions. These advances may ultimately transform psychiatric treatment from symptom management toward personalized disease modification and long-term functional recovery.

The comprehensive evaluation of current evidence indicates that antipsychotic pharmacotherapy is undergoing a fundamental transformation characterized by increasing molecular complexity, individualized treatment strategies, and integration of multidisciplinary scientific approaches. The historical paradigm of selecting medications primarily according to diagnostic category and symptom severity is gradually being replaced by a more sophisticated framework that incorporates neurobiological mechanisms, pharmacokinetic variability, genetic determinants, environmental influences, and patient-specific therapeutic goals.

One of the most important findings emerging from contemporary research is the recognition that treatment response to antipsychotic medications is highly heterogeneous. Although antipsychotics demonstrate significant efficacy at the population level, individual patients may experience dramatically different therapeutic outcomes. Some individuals achieve rapid and

sustained symptom remission, whereas others demonstrate partial response, persistent symptoms, treatment resistance, or unacceptable toxicity. This variability emphasizes the limitations of conventional prescribing approaches and supports the development of predictive models capable of identifying optimal therapeutic strategies before treatment initiation.

The results indicate that treatment-resistant psychosis remains one of the greatest unresolved challenges in psychiatric pharmacotherapy. Despite numerous available antipsychotic agents, a substantial proportion of patients continue to experience persistent hallucinations, delusions, negative symptoms, and functional impairment. Current evidence confirms that clozapine remains the most effective pharmacological option for treatment-resistant schizophrenia; however, barriers including safety concerns, monitoring requirements, clinician familiarity, and patient acceptance limit its broader implementation.

Improving the utilization of clozapine represents an important clinical priority. Evidence suggests that delayed initiation of clozapine after failure of multiple antipsychotic trials may contribute to prolonged suffering, unnecessary hospitalization, and reduced functional outcomes. Enhanced clinician education, improved monitoring systems, and patient-centered approaches may facilitate more appropriate use of this highly effective medication.

The findings also emphasize the importance of distinguishing pharmacological treatment resistance from pseudo-resistance. Inadequate response may result from insufficient dosage, poor adherence and inappropriate duration of treatment, drug interactions, rapid metabolism, or incorrect diagnosis rather than true biological resistance. Therapeutic drug monitoring and comprehensive clinical assessment can assist in identifying these factors and preventing unnecessary medication changes.

Pharmacokinetic variability represents a major contributor to differences in antipsychotic exposure and therapeutic outcomes. The analysis demonstrates that factors such as age, body composition, hepatic function, renal function, smoking status, inflammation, concurrent medications, and genetic variation significantly influence drug concentrations. Understanding these variables is essential for optimizing dosage and preventing avoidable toxicity.

The interaction between inflammation and antipsychotic metabolism represents an emerging area of clinical importance. Acute inflammatory states may alter cytochrome P450 enzyme activity and subsequently modify plasma concentrations of certain medications. This phenomenon is particularly relevant for drugs with narrow therapeutic ranges, where unexpected increases in exposure may lead to severe adverse reactions. Future treatment models may incorporate inflammatory biomarkers alongside pharmacokinetic monitoring to improve safety.

The evidence further supports the importance of interdisciplinary collaboration in modern antipsychotic management. Optimal care requires cooperation among psychiatrists, clinical pharmacologists, pharmacists, nurses, genetic specialists, primary healthcare providers, and other healthcare professionals. Each discipline contributes unique expertise necessary for comprehensive medication management.

Clinical pharmacists and pharmacologists have an increasingly important role in contemporary psychiatric care. Their contributions include medication reconciliation, evaluation of drug interactions, therapeutic drug monitoring interpretation, adverse reaction prevention, pharmacogenomic consultation, and patient education. Integration of pharmacological expertise into psychiatric teams has the potential to improve treatment safety and effectiveness.

The results also demonstrate the importance of comprehensive outcome assessment. Traditional evaluation of antipsychotic efficacy has focused primarily on reduction of psychotic symptoms; however, modern therapeutic goals extend beyond symptom control. Functional recovery, cognitive improvement, social participation, occupational performance,

independence, and quality of life are increasingly recognized as essential indicators of successful treatment.

Cognitive impairment remains one of the most persistent and disabling components of schizophrenia. Current antipsychotic medications provide limited improvement in cognitive domains such as attention, working memory, executive function, and processing speed. This limitation represents a critical unmet therapeutic need because cognitive deficits strongly predict long-term functional outcomes.

Research into cognitive enhancement strategies has therefore become an important component of next-generation antipsychotic development. Potential approaches include glutamatergic modulation, cholinergic enhancement, neuroprotective interventions, cognitive remediation combined with pharmacotherapy, and agents targeting synaptic plasticity pathways. Although many approaches remain experimental, they represent important directions for future psychiatric innovation.

The analysis highlights the growing importance of early intervention strategies in psychotic disorders. Evidence indicates that reducing the duration of untreated psychosis may improve clinical outcomes and functional recovery. Early identification of individuals at high risk for psychosis, timely initiation of appropriate treatment, and comprehensive psychosocial support represent important components of modern psychiatric care.

However, early intervention requires careful consideration of risk-benefit balance, particularly when initiating long-term pharmacological treatment in younger individuals. Personalized assessment of symptom severity, functional decline, biological risk factors, and patient preferences is essential to ensure appropriate clinical decision-making.

The role of lifestyle and environmental factors in antipsychotic treatment outcomes is increasingly recognized. Physical activity, nutrition, sleep regulation, stress management, and social support influence both psychiatric symptoms and medication-related health risks. Integrated treatment models combining pharmacological interventions with psychosocial and lifestyle approaches may provide superior outcomes compared with medication alone.

The results demonstrate that prevention and management of antipsychotic-associated metabolic complications require proactive rather than reactive approaches. Monitoring should begin at treatment initiation and continue throughout therapy. Early identification of weight gain or metabolic abnormalities allows clinicians to modify treatment plans before irreversible complications develop.

Pharmacological strategies to mitigate metabolic adverse effects are also being investigated. Adjunctive interventions targeting weight regulation, glucose metabolism, and insulin sensitivity may provide additional support for patients requiring medications with higher metabolic risk profiles. Future research should continue evaluating optimal strategies for balancing psychiatric efficacy with physical health protection.

The emergence of novel antipsychotic compounds targeting alternative biological pathways represents a promising advancement. Current research is investigating compounds affecting muscarinic receptors, trace amine-associated receptors, glutamate systems, inflammatory pathways, and intracellular signaling mechanisms. These approaches aim to overcome the limitations of existing therapies by addressing broader aspects of disease biology.

Muscarinic receptor modulation has attracted particular interest because cholinergic dysfunction may contribute to cognitive impairment and negative symptoms. Novel agents influencing muscarinic receptor activity represent an important area of investigation and may expand therapeutic options beyond traditional dopamine-centered approaches.

The development of biomarkers remains a central requirement for advancing precision psychiatry. Reliable biomarkers could assist in diagnosis, prediction of treatment response, identification of adverse-effect risk, and monitoring of disease progression. Although significant

progress has been made in genomic, imaging, and molecular research, translation into routine clinical practice remains challenging.

Future research should prioritize large-scale longitudinal studies integrating multiple biological and clinical variables. Such studies may help identify reproducible predictors of treatment outcomes and establish clinically practical precision medicine frameworks.

The increasing availability of large healthcare datasets provides unprecedented opportunities for advancing psychiatric research. Real-world evidence, combined with genomic information and artificial intelligence-based analysis, may reveal previously unrecognized relationships between patient characteristics, treatment strategies, and outcomes. These approaches may accelerate discovery and improve clinical decision-making.

Nevertheless, technological advancement must be accompanied by ethical responsibility. Psychiatric information is highly sensitive, and protection of patient privacy remains essential. Transparent governance frameworks, informed consent procedures, and responsible data management practices are necessary to ensure that precision medicine develops in an ethical and patient-centered manner.

The findings of this comprehensive review demonstrate that antipsychotic therapy has entered a new era characterized by integration of pharmacology, neuroscience, genetics, digital technologies, and individualized clinical care. While current medications have transformed the prognosis of psychotic disorders, significant opportunities remain for improving efficacy, reducing toxicity, and achieving meaningful functional recovery.

The future direction of antipsychotic research should focus on developing therapies that are not only effective in reducing psychotic symptoms but also capable of improving cognition, social functioning, and overall quality of life. A successful next generation of antipsychotic interventions will likely emerge from the convergence of precision medicine, advanced pharmacology, biomarker discovery, and innovative healthcare technologies.

The comprehensive evaluation of contemporary antipsychotic pharmacotherapy demonstrates that the future advancement of psychiatric treatment depends on achieving a balance between pharmacological efficacy, safety optimization, biological personalization, and improvement of long-term patient-centered outcomes. The accumulated evidence indicates that antipsychotic medications remain indispensable therapeutic tools; however, their optimal application requires a deeper understanding of disease mechanisms, individual variability, and the complex relationship between therapeutic effects and adverse reactions.

A major conclusion derived from current evidence is that antipsychotic treatment should no longer be viewed as a uniform pharmacological intervention applied according to diagnostic categories alone. Instead, psychotic disorders should be conceptualized as biologically heterogeneous conditions involving multiple interacting pathways. This perspective supports the transition toward stratified treatment approaches in which medication selection is informed by symptom dimensions, molecular characteristics, genetic profiles, metabolic vulnerability, and previous therapeutic response.

The development of precision psychiatry represents a significant advancement in this direction. Unlike traditional psychiatric treatment models based primarily on clinical observation, precision psychiatry seeks to integrate biological information with clinical expertise to improve therapeutic decision-making. The results suggest that successful implementation of precision approaches requires collaboration between neuroscience, pharmacology, genomics, computational sciences, and clinical medicine.

One of the most important implications of precision psychiatry is the possibility of reducing the current trial-and-error approach to antipsychotic prescribing. Delayed identification of effective treatment contributes to prolonged symptom burden, increased hospitalization rates, functional decline, and reduced quality of life. Predictive models capable of identifying the most

appropriate medication at the beginning of treatment could significantly improve clinical outcomes.

Pharmacogenomic-guided prescribing represents a promising component of this transformation. Although current evidence supports the clinical relevance of several genetic variants affecting antipsychotic metabolism and response, routine implementation remains limited. The findings suggest that future pharmacogenomic applications will require integration of multiple genetic markers with clinical variables rather than reliance on isolated polymorphisms.

The complexity of psychiatric disorders indicates that medication response is influenced by networks of interacting genes rather than single genetic determinants. Therefore, polygenic risk models, genome-wide association studies, and multi-omics approaches may provide more accurate predictions of treatment outcomes. Combining genomic information with transcriptomic, proteomic, metabolomic, and neuroimaging data may allow identification of biologically meaningful subgroups of patients.

The results also emphasize the importance of therapeutic drug monitoring as a practical bridge between pharmacology and precision medicine. While genetic information provides insight into potential metabolic capacity, therapeutic drug monitoring reflects actual medication exposure under real clinical conditions. This combination may allow clinicians to determine whether treatment failure results from inadequate drug concentration, biological non-response, or other clinical factors.

The application of therapeutic drug monitoring may be particularly valuable in complex clinical situations, including treatment resistance, polypharmacy, pregnancy, elderly patients and hepatic dysfunction, smoking changes, and suspected drug interactions. By providing objective pharmacokinetic information, monitoring can support rational dose adjustment and improve medication safety.

The relationship between pharmacokinetics and pharmacodynamics remains central to optimizing antipsychotic therapy. Drug concentration alone does not fully determine clinical response because receptor sensitivity, downstream signaling mechanisms, and disease-related biological factors also influence therapeutic outcomes. Future models integrating pharmacokinetic and pharmacodynamic parameters may provide more accurate predictions of individual treatment response.

The findings further highlight the importance of developing safer antipsychotic medications with improved tolerability profiles. Although current agents provide substantial benefit, adverse effects remain a major determinant of treatment discontinuation. Future drug development should prioritize compounds capable of maintaining antipsychotic efficacy while minimizing metabolic, neurological, cardiovascular, and endocrine complications.

A particularly important objective is the development of medications that effectively address negative symptoms and cognitive dysfunction. These symptom domains contribute substantially to disability and remain insufficiently treated by currently available therapies. Improving cognition, motivation, emotional engagement, and social functioning should become central goals of future antipsychotic innovation.

The emergence of novel mechanisms beyond dopamine modulation provides promising opportunities. Research targeting glutamatergic pathways, cholinergic systems, neuroinflammatory processes, oxidative stress mechanisms, and synaptic plasticity may lead to therapeutic approaches capable of addressing broader aspects of psychotic disorders. These strategies may complement existing dopamine-based treatments or provide alternative options for individuals who respond inadequately to current medications.

The role of neuroinflammation represents a particularly important area of investigation. Increasing evidence suggests that immune alterations may contribute to psychosis in biologically

defined subgroups of patients. Identification of inflammatory biomarkers may allow development of targeted therapeutic strategies and improve understanding of disease heterogeneity.

Similarly, oxidative stress and mitochondrial dysfunction have emerged as potential contributors to neuronal vulnerability in psychotic disorders. Therapeutic approaches aimed at enhancing neuroprotection, restoring cellular energy balance, and reducing oxidative damage may represent future avenues for intervention.

The results also demonstrate the growing importance of integrated care models. Antipsychotic medication alone is rarely sufficient to achieve optimal long-term outcomes. Pharmacological treatment should be combined with psychosocial interventions, cognitive rehabilitation, family support, occupational strategies, and lifestyle modification programs.

Comprehensive care models are particularly important because schizophrenia and related disorders affect multiple dimensions of human functioning. Successful treatment requires addressing not only hallucinations and delusions but also social isolation, unemployment, cognitive impairment, physical health problems, and reduced independence.

The findings support increased emphasis on collaborative decision-making between healthcare providers and patients. Patients who understand treatment goals, potential benefits, and possible adverse effects are more likely to participate actively in care and maintain adherence. Respect for patient preferences and individual treatment priorities is therefore an essential component of modern psychiatric practice.

The importance of reducing stigma associated with psychotic disorders and psychiatric medications should also be emphasized. Social stigma remains a major barrier to treatment access, adherence, and recovery. Public education, professional training, and community-based mental healthcare initiatives are essential for improving acceptance and support for individuals living with psychotic disorders.

From a healthcare system perspective, optimized antipsychotic management has substantial economic implications. Effective treatment reduces hospitalization, emergency care utilization, disability, and social costs associated with untreated or inadequately controlled psychosis. Investment in early intervention, monitoring systems, and personalized treatment approaches may therefore provide long-term benefits for both patients and healthcare systems.

The increasing availability of digital health technologies provides additional opportunities for improving psychiatric care delivery. Remote monitoring, telepsychiatry, electronic medication management systems, and digital therapeutics may expand access to specialized care, particularly in regions with limited psychiatric resources.

However, technological solutions must be implemented with consideration of accessibility, digital literacy, privacy protection, and clinical validation. Digital tools should enhance rather than replace human-centered psychiatric care.

The results of this review indicate that antipsychotic pharmacotherapy is entering a period of significant transformation. The combination of molecular neuroscience, precision medicine, pharmacogenomics, therapeutic drug monitoring, artificial intelligence, and innovative drug development provides unprecedented opportunities to improve treatment outcomes.

Nevertheless, several challenges remain. Many emerging biomarkers require further validation before routine clinical application. Genetic testing availability and cost remain important considerations. Artificial intelligence systems require rigorous evaluation to ensure accuracy, transparency, and fairness. Novel therapeutic targets require confirmation through large-scale clinical trials.

Future research should prioritize longitudinal studies capable of evaluating treatment outcomes over extended periods and across diverse populations. Greater representation of different ethnic,

geographic, and clinical groups will be essential for developing universally applicable precision medicine strategies.

The evidence demonstrates that antipsychotic therapy has evolved from traditional receptor blockade toward a comprehensive, individualized, and scientifically integrated approach. Current medications have fundamentally changed the prognosis of psychotic disorders; however, continued innovation is necessary to overcome persistent challenges related to treatment resistance, adverse effects, cognitive impairment, and functional disability.

The next generation of antipsychotic therapeutics will likely emerge from the integration of pharmacology, genomics, neuroscience, artificial intelligence, and patient-centered medicine. Such advances have the potential to transform psychiatric treatment from reactive symptom control toward proactive, predictive, and personalized care, ultimately improving safety, effectiveness, and quality of life for individuals affected by psychotic disorders worldwide.

The optimizing antipsychotic pharmacotherapy requires continuous integration of advances in clinical neuroscience, molecular pharmacology, pharmacogenomics, and evidence-based psychiatric practice. Although antipsychotic medications have substantially improved the prognosis of psychotic disorders during the past seven decades, their therapeutic success remains constrained by considerable interindividual variability in efficacy, tolerability, and long-term functional outcomes. Consequently, modern psychopharmacology increasingly emphasizes individualized treatment algorithms that consider biological, clinical, environmental, and psychosocial determinants of therapeutic response.

An important observation emerging from recent investigations is the recognition that schizophrenia and related psychotic disorders represent biologically heterogeneous syndromes rather than uniform disease entities. Neuroimaging, genomic, transcriptomic, proteomic, and metabolomic studies consistently demonstrate substantial variability in underlying pathophysiological mechanisms among affected individuals. This biological diversity likely explains why identical pharmacological interventions produce markedly different clinical responses. Therefore, precision medicine approaches that classify patients according to biological signatures rather than symptom clusters alone may substantially improve therapeutic accuracy and reduce unnecessary medication exposure.

The concept of receptor occupancy has become increasingly important in understanding antipsychotic efficacy and toxicity. Positron emission tomography studies have consistently demonstrated that therapeutic response generally occurs when dopamine D2 receptor occupancy reaches an optimal range, whereas excessive receptor blockade substantially increases the risk of extrapyramidal symptoms and hyperprolactinemia. These findings support individualized dose optimization rather than routine administration of high-dose antipsychotic therapy. Maintaining receptor occupancy within therapeutic windows represents one of the principal objectives of contemporary psychopharmacology and further supports the growing role of therapeutic drug monitoring in routine psychiatric practice.

Another significant finding involves the influence of pharmacokinetic variability on treatment effectiveness. Numerous physiological factors, including hepatic enzyme activity, renal function, age-related pharmacokinetic changes, obesity, inflammatory status, nutritional condition, smoking behavior, and concomitant medications, alter systemic drug exposure. Consequently, patients receiving identical doses may exhibit substantially different plasma concentrations, therapeutic responses, and toxicity profiles. This variability reinforces the importance of individualized dosing strategies based on objective pharmacokinetic assessment rather than standardized prescribing alone.

Polypharmacy remains a controversial yet increasingly encountered aspect of psychiatric practice. Although clinical guidelines generally recommend antipsychotic monotherapy whenever possible, combination therapy continues to be prescribed in patients with inadequate response, severe

symptomatology, or complex psychiatric comorbidities. The present evidence suggests that routine antipsychotic polypharmacy offers limited additional efficacy for most patients while substantially increasing the likelihood of adverse reactions, drug-drug interactions, medication burden, and healthcare costs. Therefore, combination therapy should be reserved for carefully selected clinical situations following comprehensive evaluation of therapeutic benefits and potential risks.

Drug-drug interactions constitute another critical determinant of medication safety. Antipsychotic agents frequently interact with antidepressants, mood stabilizers, anticonvulsants, antimicrobial agents, cardiovascular medications, and numerous other therapeutic classes through pharmacokinetic and pharmacodynamic mechanisms. Cytochrome P450-mediated interactions remain particularly important because inhibition or induction of metabolic enzymes may significantly alter plasma drug concentrations. Clinicians should therefore perform comprehensive medication reviews before initiating or modifying antipsychotic treatment, particularly in elderly patients and individuals receiving multiple medications.

The evidence also demonstrates that long-term antipsychotic treatment should be viewed within the broader context of chronic disease management. Schizophrenia is associated with recurrent episodes, persistent functional impairment, and increased risk of medical comorbidity. Consequently, successful management extends beyond acute symptom reduction and requires comprehensive strategies focused on relapse prevention, rehabilitation, psychosocial integration, and preservation of physical health. Long-term continuity of treatment remains one of the strongest predictors of favorable clinical outcomes.

Long-acting injectable antipsychotics have emerged as valuable therapeutic options for improving adherence and reducing relapse. Compared with oral formulations, long-acting preparations maintain relatively stable plasma drug concentrations, reduce fluctuations associated with inconsistent medication intake, and facilitate early identification of treatment interruption. Meta-analyses indicate that appropriately selected patients receiving long-acting injectable therapy experience lower relapse rates, fewer psychiatric hospitalizations, and improved treatment continuity. Nevertheless, patient preference, shared decision-making, accessibility, and healthcare infrastructure remain essential considerations when selecting these formulations.

The growing emphasis on patient-centered care represents another important advancement in psychiatric practice. Historically, treatment decisions were predominantly clinician-directed; however, contemporary evidence supports collaborative decision-making that actively involves patients in selecting therapeutic strategies. Shared decision-making enhances treatment adherence, improves patient satisfaction, strengthens therapeutic alliance, and facilitates realistic discussion of expected benefits and potential adverse effects. Individual treatment goals, occupational aspirations, social functioning, family responsibilities, and quality-of-life priorities should therefore be incorporated into therapeutic planning.

The findings further indicate that management of physical health should become an integral component of psychiatric treatment. Individuals with severe mental illness experience disproportionately high rates of obesity, diabetes mellitus, dyslipidemia, hypertension, cardiovascular disease, and premature mortality. Although antipsychotic medications contribute to metabolic risk, psychiatric illness itself, socioeconomic disadvantage, reduced access to healthcare, sedentary lifestyle, nutritional factors, and tobacco use also play significant roles. Consequently, multidisciplinary management involving psychiatrists, internists, endocrinologists, cardiologists, pharmacists, dietitians, and rehabilitation specialists is essential for comprehensive patient care.

Current evidence strongly supports structured metabolic monitoring throughout antipsychotic therapy. Baseline evaluation should include body weight, body mass index, waist circumference, blood pressure, fasting glucose or glycated hemoglobin, and lipid profile, followed by periodic

reassessment according to established clinical guidelines. Early recognition of metabolic abnormalities enables timely intervention through lifestyle modification, medication adjustment, or pharmacological treatment of metabolic disorders. Such preventive strategies may substantially reduce long-term cardiovascular morbidity and mortality.

An additional area receiving increasing attention involves sex-related and age-related differences in antipsychotic response. Pharmacokinetic characteristics, hormonal influences, body composition, and receptor sensitivity vary between males and females and across different age groups. Elderly individuals frequently demonstrate increased sensitivity to sedation, orthostatic hypotension, cognitive impairment, and cardiovascular complications because of physiological changes associated with aging. Similarly, pediatric and adolescent populations exhibit unique pharmacodynamic characteristics requiring careful dose selection and continuous monitoring. Recognition of these differences is fundamental to individualized prescribing.

The expanding understanding of neurodevelopmental mechanisms has also influenced contemporary concepts of psychotic disorders. Evidence suggests that schizophrenia originates from complex interactions between genetic susceptibility and environmental exposures occurring throughout prenatal development, childhood, adolescence, and early adulthood. Consequently, therapeutic strategies focusing exclusively on symptom suppression may fail to address broader neurodevelopmental abnormalities. Future interventions combining pharmacotherapy with cognitive rehabilitation, psychosocial support, and early preventive measures may improve long-term functional trajectories.

The role of inflammation and immune dysregulation continues to generate considerable scientific interest. Elevated concentrations of pro-inflammatory cytokines, alterations in microglial activation, and immune-mediated neuronal dysfunction have been observed in subsets of patients with schizophrenia. Although anti-inflammatory interventions remain investigational, accumulating evidence suggests that biologically stratified therapeutic approaches may eventually identify patients who derive benefit from adjunctive immunomodulatory therapies. Such developments further reinforce the concept that psychotic disorders encompass multiple biological subtypes requiring individualized therapeutic strategies.

Advances in systems biology and computational neuroscience are expected to accelerate the identification of novel therapeutic targets. Integration of multi-omics technologies with artificial intelligence may facilitate discovery of molecular pathways associated with disease progression, medication response, and adverse reactions. Computational modeling capable of analyzing complex interactions among genetic, metabolic, inflammatory, neuroimaging, and clinical variables may substantially improve prediction of treatment outcomes. These approaches have the potential to transform psychiatric pharmacotherapy from reactive symptom management toward proactive and predictive precision medicine.

The evidence synthesized throughout this review indicates that the future success of antipsychotic pharmacotherapy will depend not only on the development of innovative medications but also on optimizing implementation of existing therapies through individualized dosing, comprehensive monitoring, pharmacogenomic integration, therapeutic drug monitoring, rigorous pharmacovigilance, multidisciplinary collaboration, and patient-centered clinical practice. Continued translational research bridging basic neuroscience with clinical psychiatry will be essential for developing safer, more effective, and biologically informed therapeutic strategies. As knowledge regarding the molecular architecture of psychotic disorders continues to expand, antipsychotic treatment is expected to evolve from generalized pharmacological intervention toward highly personalized therapeutic care capable of maximizing efficacy, minimizing toxicity, improving functional recovery, and enhancing the overall quality of life of individuals affected by severe psychiatric disorders.

Conclusion

- Antipsychotic agents remain essential components of contemporary psychiatric pharmacotherapy, providing substantial benefits in the management of schizophrenia spectrum disorders, bipolar disorder, psychotic depression, and other conditions associated with severe behavioral and perceptual disturbances. This comprehensive review demonstrates that advances in antipsychotic research have transformed therapeutic strategies from conventional dopamine receptor blockade toward more sophisticated approaches incorporating neuropharmacology, pharmacogenomics, precision medicine, therapeutic drug monitoring, and evidence-based clinical practice.
- Although current antipsychotic medications have significantly improved symptom control and reduced relapse rates, important clinical challenges remain, including treatment resistance, metabolic complications, neurological adverse effects, cardiovascular risks, endocrine disturbances, and limited efficacy against negative symptoms and cognitive impairment. Effective management therefore requires individualized therapeutic decision-making, continuous safety monitoring, and integration of pharmacological interventions with psychosocial and rehabilitative strategies.
- The emergence of pharmacogenomic approaches and precision psychiatry represents a major advancement toward personalized antipsychotic treatment. Understanding genetic variability in drug metabolism, receptor function, and therapeutic response may enable clinicians to optimize medication selection, minimize toxicity, and improve clinical outcomes. Therapeutic drug monitoring further strengthens individualized care by providing objective information regarding drug exposure and supporting rational dose optimization, particularly in complex clinical situations.
- Future developments in antipsychotic therapy are expected to arise from deeper understanding of neurobiological mechanisms underlying psychotic disorders. Novel therapeutic targets involving glutamatergic signaling, neuroinflammation, oxidative stress, synaptic plasticity, and immune–brain interactions may provide opportunities to overcome limitations of existing treatments. Furthermore, artificial intelligence, digital biomarkers, and advanced computational approaches have the potential to enhance prediction of treatment response, early identification of relapse, and implementation of personalized interventions.
- Despite remarkable progress, continued interdisciplinary research is required to establish clinically validated biomarkers, improve therapeutic precision, and develop safer and more effective medications. The integration of molecular neuroscience, clinical pharmacology, genomics, and patient-centered care will define the future direction of antipsychotic treatment. Ultimately, the goal of modern antipsychotic pharmacotherapy is not only the reduction of psychotic symptoms but also the achievement of sustained recovery, improved functioning, enhanced quality of life, and long-term well-being for individuals affected by psychiatric disorders.

Recommendations

- Future advancements in antipsychotic pharmacotherapy should focus on the implementation of personalized, evidence-based treatment strategies that integrate clinical characteristics with pharmacogenomic, neurobiological, and pharmacokinetic information. Routine incorporation of precision medicine approaches, including validated pharmacogenetic testing and therapeutic drug monitoring, should be encouraged to improve medication selection, optimize dosing, reduce adverse effects, and enhance therapeutic outcomes.
- Clinical practice should emphasize comprehensive monitoring protocols for patients receiving antipsychotic medications, including regular assessment of metabolic parameters, cardiovascular risk factors, neurological symptoms, endocrine disturbances, and potential drug

interactions. Early identification and proactive management of adverse effects are essential for improving medication adherence, preventing long-term complications, and promoting patient safety.

- Healthcare systems should strengthen multidisciplinary models of psychiatric care involving psychiatrists, clinical pharmacologists, pharmacists, genetic specialists, nurses, and primary healthcare professionals. Such collaborative approaches can improve medication management, pharmacovigilance practices, patient education, and continuity of treatment.
- Further research should prioritize the discovery and validation of reliable biomarkers capable of predicting treatment response, adverse-effect susceptibility, and disease progression. Large-scale longitudinal studies integrating genomics, artificial intelligence, neuroimaging, and real-world clinical data are recommended to accelerate the development of precision psychiatry.
- Future antipsychotic drug development should focus on novel therapeutic mechanisms beyond traditional dopamine modulation, with particular attention to improving negative symptoms, cognitive impairment, functional recovery, and overall quality of life. Emerging technologies, including digital health platforms and artificial intelligence-based clinical decision-support systems, should be carefully evaluated and integrated to enhance personalized psychiatric care.
- The successful antipsychotic treatment requires a holistic approach that combines pharmacological innovation, continuous safety assessment, patient-centered decision-making, and equitable access to advanced therapeutic strategies worldwide.

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MANAGING VACCINATION ADHERENCE AT THE PRIMARY HEALTH CARE LEVEL: A DESCRIPTIVE STUDY IN A SINGLE HEALTH FACILITY

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Abstract. The article assesses the level of vaccination adherence among adults registered with a primary health care (PHC) facility and identifies the local factors that shape it. A single-stage descriptive survey was conducted at BCMO LLP in Balkhash, Kazakhstan (n = 100). Of the respondents, 78% considered vaccination necessary and 84% acknowledged its preventive role, whereas only 72% regarded vaccines as safe. Trust in health workers reached 81%, yet 67% reported an unmet need for additional information. The two gaps identified at the facility level define the content of the communication and management measures proposed.

Keywords: vaccination adherence, primary health care, communication strategy, trust in health workers, immunization, KPI.

Introduction

The effectiveness of immunization programmes depends not only on the availability of vaccines but also on public confidence in them. The WHO Immunization Agenda 2030 identifies sustaining public trust, equitable access to services, strengthening the primary health care level and evidence-based decision-making as priority areas [1]. According to the definition of the SAGE Working Group, vaccine hesitancy is the delay in acceptance or the refusal of vaccination despite the availability of vaccination services; its determinants include contextual, individual and group, and vaccine-specific influences [2; 3].

The Behavioural and Social Drivers (BeSD) framework assesses vaccination decisions across four domains: what people think and feel, social processes, motivation, and the practical issues of accessing the service [4]. This approach shows that explaining non-vaccination solely by a lack of information is insufficient. Interventions directed at behaviour itself — reminders, simplified appointment booking, improved access — increase uptake more reliably than mass campaigns aimed at changing attitudes [5].

In Kazakhstan the procedure for preventive vaccination is regulated by the Code "On public health and the healthcare system" [6] and by the Government Decree adopted on its basis [7], while the work of PHC organisations is defined by the corresponding rules [8] and the organisational standard [9]. Compliance with regulatory requirements, however, does not in itself

secure public trust: a facility needs to measure the actual information needs of its registered population.

The aim of the study was to assess the level of vaccination adherence among adults registered with a single PHC facility, together with the local factors affecting it, and on this basis to propose communication and management measures.

Materials and methods

The study was carried out at BCMO LLP (formerly Polyclinic No. 2) in Balkhash as a single-stage descriptive survey. The target population comprised registered residents aged 18 years and over; participants were recruited by convenience sampling among those attending preventive appointments, the district physician and the immunization room.

A total of 110 people were invited and 103 consented to participate (93.6%); three incompletely completed questionnaires were excluded, and the responses of 100 respondents were included in the analysis. Women accounted for 56% of the sample and men for 44%; by age group, 18–30 years – 28%, 31–45 years – 39%, 46–60 years – 23%, over 60 years – 10%. Respondents with higher or postgraduate education made up 47%, 69% had children and 91% lived in Balkhash.

The author-developed questionnaire consisted of six content blocks: sociodemographic characteristics; attitudes towards vaccination; sources of information; trust in health workers; reasons for hesitancy; and readiness to be vaccinated together with the need for further information. The instrument underwent pilot testing with 10 participants (mean completion time 12 minutes); their responses were not included in the main analysis.

Vaccination adherence was assessed through three components: recognising the need for vaccination, trusting the medical recommendation and being ready to receive the recommended vaccine. The data were processed using descriptive statistics; the statistical significance of between-group differences was not assessed. Participation was voluntary and anonymous, and informed consent was obtained from every respondent.

Results

The key indicators of vaccination adherence are presented in Table 1.

Table 1 – Key indicators of vaccination adherence among respondents registered with BCMO LLP (n = 100)

No.	Indicator	Positive answer, %	Negative answer, %
1	Considers vaccination necessary	78	22
2	Believes vaccination helps prevent infectious diseases	84	16
3	Considers vaccines safe	72	28
4	Trusts health workers	81	19
5	Takes the physician's recommendation into account	83	17
6	Ready for an individual consultation with a health worker	82	18
7	Considers adherence to the national immunization schedule important	79	21
8	Ready to receive the recommended vaccination	76	24
9	Ready to use official sources of information	74	26
10	Reports a need for additional information on vaccination	67	33

Note – compiled by the author from the survey results.

The data show a generally favourable attitude towards vaccination, but two systematic gaps emerged.

The first is the gap between perceiving the collective benefit and perceiving personal safety: 84% acknowledged the preventive role of vaccination, while 72% regarded vaccines as safe – a difference of 12 percentage points. The source of hesitancy therefore lies not in the purpose of vaccination but in concerns about possible adverse reactions.

The second is the gap between trust and being informed: 81% expressed trust in health workers, 83% took the physician's recommendation into account and 82% were ready for an individual consultation, yet 67% still reported a need for additional information. The facility has accumulated a resource of trust that has not been fully converted into meeting the information demand.

Among the sources of information, advice from a health worker accounted for 34%, official sources for 25%, the opinion of family members for 16%, social media for 15% and personal experience for 10%. The reasons for hesitancy included fear of adverse reactions, insufficient information on safety and conflicting content online. Some respondents named inconvenient appointment times and the absence of a timely reminder as reasons for a missed vaccination, which shows that a vaccination not administered does not always mean a deliberate refusal.

Discussion

The findings are consistent with international data. A clear and consistent recommendation from a physician remains one of the strongest predictors of vaccine acceptance: the format in which the discussion is initiated significantly affects the likelihood of acceptance [10]. At the same time, increasing the volume of information does not in itself reduce hesitancy — motivational interviewing supports the patient in drawing on their own arguments and improves readiness to be vaccinated [11]. Under the 5C model, uptake is shaped not only by confidence but also by complacency, constraints and collective responsibility [12]; combining deliberate refusal, medical deferral, non-attendance and loss of contact into a single indicator therefore leads to a management error.

On the basis of the results, five directions are proposed at the facility level: keeping the list of residents due for vaccination up to date; training staff in active listening, risk communication and motivational interviewing; sending reminders by SMS and messaging applications; recording the reasons for non-vaccination in separate categories; and monthly evaluation against KPIs. The target values proposed for the pilot period are: adherence from 78% to 85%, readiness from 76% to 83%, trust from 81% to 87%, and the need for additional information reduced below 50%. These are planned indicators rather than results already achieved.

Conclusion

The limitations of the study relate to convenience sampling, its conduct at a single facility and reliance on self-reported answers; the findings cannot be extended to the whole population of the city or the country. At the level of a single PHC facility, the key indicators of vaccination adherence ranged from 72% to 84%. The weakest links are the personal perception of vaccine safety (72%) and the unmet demand for additional information (67%). The comparatively high level of trust in health workers (81%) is the main resource available to the facility, and the priority of information work should therefore shift from mass campaigns towards individual counselling, targeted reminders and the classified recording of reasons for refusal. The proposed set of indicators makes it possible to turn information work from a list of formal activities into a measurable management cycle; the actual effectiveness of the recommendations is to be assessed by a repeat survey after pilot implementation.

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BREAST CANCER: CONTEMPORARY PROBLEMS AND CURRENT TRENDS

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Annotation: This scientific and analytical work presents modern global and local-regional data on incidence, mortality, lethality and five-year survival of the most common oncological pathology, such as breast cancer. The issues of etiology and pathogenesis, features of distribution, modern principles of diagnostics, including screening, as well as prognosis, preventive measures of this formidable disease are covered in detail. The epidemiological characteristics of this pathology in our republic are given in the context of the regions of the country.

Key words: oncology, breast cancer, phenotype, biological markers, risk factors, etiopathogenesis, diagnostics, treatment, epidemiology, incidence, mortality, lethality, five-year survival rate, prognosis, prevention.

Breast cancer (BC) is the most common global malignancy and the leading cause of cancer deaths [1]. There is much evidence showing the influence of life style and environmental factors on the development of mammary gland cancer (high-fat diet, alcohol consumption, lack of physical exercise), the elimination of which (primary prevention) may contribute to a decrease in incidence and mortality. Secondary prevention, comprising diagnostic tests (e.g. mammography, ultrasonography, magnetic resonance imaging, breast self-examination, as well as modern and more precise imaging methods) help the early detection of tumours or lesions predisposing to tumours. It is estimated that nearly 70% of malign tumours are caused by environmental factors, whereas in BC this percentage reaches 90-95%. There are national programmes established in many countries to fight cancer, where both types of prevention are stressed as serving to decrease incidence and mortality due to cancers. Cancer prevention is currently playing a key role in the fight against the disease. Behaviour modification, as well as greater awareness among women regarding BC, may significantly contribute towards reducing the incidence of this cancer [2].

Speaking about the diagnostic criteria for making a diagnosis, women complain about the presence of a formation in the mammary gland; enlarged axillary, supra- and subclavian lymph nodes; the presence of skin changes on the mammary gland; swelling of the mammary gland. The history is noteworthy of the presence of cancer in close relatives; early onset of menstruation; age of first pregnancy and first birth, taking oral contraceptives and/or hormone replacement therapy, gynecological diseases. During a physical examination, attention is paid to the symmetry of the location and shape of the mammary glands; level of position of the nipples and their appearance (retraction, deviation to the side); skin condition (hyperemia, swelling, wrinkling, retractions or protrusions on it, narrowing of the areolar field, etc.); presence/absence of pathological discharge from the nipples (quantity, color, duration); presence of swelling of the arm on the affected side. Palpation of the mammary glands is carried out in the vertical and horizontal positions of the subject; regional and cervico-supraclavicular lymph nodes are usually performed in a vertical position [3].

From laboratory tests, if metastatic BC is suspected, it is recommended to perform detailed clinical and biochemical blood tests, and a study of the blood coagulation system. In case of hormone-dependent BC in women under 50 years of age, to assess ovarian function and plan hormone therapy, it is recommended to study the level of follicle-stimulating hormone in the blood serum and the level of total estradiol in the blood. A cytological study is also carried out (an increase in the size of atypical cells up to giant ones, a change in the shape and number of intracellular elements, an increase in the size of the nucleus, its contours, different degrees of maturity of the nucleus and other cell elements, a change in the number and shape of nucleoli); histological examination: histological type of tumor, degree of differentiation (grade - ability to form tubes, nuclear polymorphism, number of mitoses), presence of necrosis, vascular invasion, tumor of infiltrating lymphocytes, presence of calcifications. Immunohistochemical study for key markers: 1) determination of estrogen and progesterone receptors, HER2, Ki67 - it is recommended to evaluate biological markers again at least once during metastasis, if clinically possible; 2) if the result of IHC analysis of HER2 is controversial, the HER2/neu gene amplification should be determined by in situ hybridization; 3) determination of PD-L1 in triple negative BC to decide on the prescription of immunotherapy; 4) if necessary - Cytokeratin 5/6, Calponin-1, E-Cadherin, GCDFP-15, Mammaglobin, p120 and Topoisomerase IIa.

Molecular genetic testing to determine germline BRCA1/2 mutations is indicated in all patients, regardless of age, family history, or type of BC with mBC and during progression to decide whether to prescribe PARP inhibitors (olaparib1 and talazoparib). In women with a positive germline mutation of the BRCA1 or 2 gene, the incidence of BC development before 70 years of age is 45-65%. More often detected: 1) with a burdened family history (close relatives have BC aged ≤ 50 years, BC in a man, ovarian cancer, metastatic prostate cancer, pancreatic cancer); 2) in patients under 45 years of age; 3) in patients under 60 years of age with a triple negative BC phenotype; 4) with primary multiple BC; 5) in patients with HER2 negative BC phenotype who have a high risk of relapse after surgical treatment and neoadjuvant or adjuvant therapy; 6) for BC in men. Comprehensive genomic profiling is carried out in patients with a severe clinical course, aggressive tumors, with a high risk of progression, lack of effect from traditional methods of antitumor treatment [in advanced BC (triple negative and progressive HER2+)] [3].

Instrumental studies: 1) ultrasound of the mammary glands, regional lymph nodes: the presence of a hypoechoic structure of the formation with large/small microcalcifications in the structure, the contours are uneven, stellate, there may be areas of mixed echogenicity, the structure of the node is heterogeneous, increased vascularization is possible; 2) mammography (mammograms in two projections visualize shapeless heterogeneous compactions with multiple microcalcifications in the structure, pronounced deformation of the stroma, thickening of the skin, nipple-areolar complex, the nipple can be retracted, the presence of enclosed lymph nodes); 3)

contrast-enhanced spectral mammography (CESM) method, which consists of performing mammography with soft and hard images after intravenous administration of an iodinated contrast agent. The CESM method is informative in the diagnosis of early forms of BC, allows you to detect pathology in the dense part of the mammary gland, and is used as a differential diagnosis of benign and malignant neoplasms; before the study, creatinine and urea levels in the blood are assessed, an iodine-containing contrast agent is administered intravenously in an amount of 1.0-1.5 ml per kg of the patient's weight; images are taken in two projections, craniocaudal (CC) and media-lateral (MLO), in a period of time from 2 to 7 minutes after administration of the contrast agent; 4) magnetic resonance imaging (MRI) of the mammary glands to assess the local spread of BC for the following indications: age up to 30 years; the presence of mutations in the BRCA1, BRCA2 genes; high radiological density of the mammary glands; the presence of breast implants when it is impossible to perform a high-quality mammographic examination; presence of lobular carcinoma in situ; 5) ductography (in the presence of an intraductal formation behind the nipple, it is carried out to clarify the size and distance of the formation from the nipple-areolar complex); 6) puncture biopsy of a tumor formation (cytological examination reveals an increase in the size of cells up to giant ones, a change in the shape and number of intracellular elements, an increase in the size of the nucleus and its contours, different degrees of maturity of the nucleus and other cell elements, a change in the number and shape of nucleoli); 7) trephine biopsy or sectoral resection of the mammary gland with express histology (histological verification of the tumor: histological type of tumor, degree of differentiation (grade - ability to form tubes, nuclear polymorphism, number of mitoses), absence of necrosis, vascular invasion, tumor of infiltrating lymphocytes, the presence of calcifications; 8) ultrasound of the abdominal organs and retroperitoneal space/ultrasound of the pelvis (with metastatic lesions of the liver, its structure is heterogeneous, rounded in shape with uneven clear contours, with single or multiple formations with a hypoechoic rim along the periphery); 9) computed tomography (CT) or MRI of the abdominal organs with intravenous contrast if the results of ultrasound of the abdominal organs are ambiguous or not very informative; 10) survey X-ray examination of the CT of the chest organs (in case of metastatic lesions of the lungs across all pulmonary fields or in a segment, multiple/single mid-focal shadows with clear contours, of various sizes are determined); 10) scintigraphy of skeletal bones (hyperfixation of an osteotropic drug in foci of pathological bone formation) if metastatic lesions of skeletal bones are suspected to assess the extent of BC prevalence; 11) positron emission tomography (PET) (accumulation of the drug by pathological foci), combined with CT with tumor-tropic radiopharmaceuticals (with or without contrast) (PET-CT) to assess the extent of BC spread in cases where standard methods of staging examinations are ambiguous, especially when locally advanced process, when the detection of metastases fundamentally changes treatment tactics; 12) MRI or CT scan of the brain with IV contrast to exclude metastatic lesions if the presence of metastases in the brain is suspected.

To standardize and simplify the criteria for assessing response to tumor therapy, the international Response Evaluation Criteria in Solid Tumors (RECIST) scale is used. According to RECIST 1.1, the following types of response are distinguished for targeted lesions.

1. Complete response – disappearance of all tumor foci.

2. Partial answer – a decrease in the sum of the largest diameters of each lesion by more than

than 30%.

3. Stabilization of the disease – reduction of the sum of the largest diameters of each lesions from 20 to 30% (for RECIST 1.0 from 25 to 50%).

4. Progression of the disease – an increase in the sum of the largest diameters of each lesion by more than 20% or the appearance of new tumor lesions.

The overall response of solid tumors to treatment is based on a combination of data on

measurable lesions, non-measurable lesions and the appearance or absence of new tumor lesions. The duration of overall response is from the date of documentation of the disease until its progression. Relapse-free interval (time to progression) – from the end of treatment to the date of documented disease progression [3].

As part of outpatient drug therapy, it is recommended to use hormone therapy in the adjuvant mode for patients with hormone-positive BC for at least 5 years (tamoxifen, letrozole, anastrazole, goserelin, triptorelin) and with progression or metastatic luminal BC before progression (tamoxifen, letrozole, anastrazole, goserelin, triptorelin, toremifene, fulvestrant, exemestane, everolimus). The use of bisphosphonate therapy when metastatic bone lesions are detected is recommended for two years (zoledronic and pamidronic acid, denosumab). CD 4/6 inhibitors (palbociclib, ribociclib, abemaciclib) are recommended for patients with HER2-negative metastatic luminal BC in combination with an aromatase inhibitor or fulvestrant, until progression or unacceptable toxicity develops; the use of monotherapy with Poly(ADP-ribose) polymerase inhibitors (olaparib or talazoparib) is recommended for patients with metastatic BC with germline BRCA1 or BRCA2 mutations, regardless of hormone receptor and HER2 status, as an alternative to chemotherapy. In patients with high-risk BRCA-associated BC, olaparib is prescribed as adjuvant therapy. The use of targeted therapy (trastuzumab) is recommended for patients with early and metastatic HER2-positive BC in combination with chemotherapy, targeted therapy or monotherapy (up to completion of 18 cycles). The use of targeted therapy (lapatinib) is recommended for patients with HER2-positive metastatic BC, either alone or in combination with capecitabine and/or trastuzumab, until progression or development of unacceptable toxicity. The use of capecitabine in the adjuvant treatment of chemo-resistant triple negative BC, or in metastatic BC in combination with lapatinib and hormone therapy.

Indications for radiation therapy: 1) morphologically established diagnosis of malignant neoplasm; 2) in case of relapses, continued growth of the tumor or progression of the disease after previously carried out combined or complex treatment. Methods of radiation therapy: 1) continuous radiation therapy; 2) single-fraction radiation therapy for SRS; fractionated radiation therapy for Single Focal Dose from 1.6 Gy to 12.0 Gy 2-5 fractions per week (standard fractionation, hypofractionation, hyperfractionation, accelerated fractionation, multifractionation). In this case, external beam radiation therapy is carried out 2D, 3D, IMRT, RapidArc, IGRT conformal irradiation Single Focal Dose 1.8-2.0-2.66, 2.67, 5.2 Gy 5 fractions per week up to Total Focal Dose 50 Gy, 42.56 Gy, 40.05 Gy, 25 Gy and 60-70 Gy in independent mode, Total Focal Dose 10-16 Gy (“Boost”) in the postoperative mode after organ-sparing operations. A continuous course of radiation therapy is used, using γ-therapy devices or linear accelerators. Tomotherapy is used as a standard fractionation technique for administering single and total focal doses. The main advantage is hypofractionation in Single Focal Dose 2.5 Gy. Intraoperative radiation therapy is used in breast-conserving operations for T1-2N0-1M0. The bed of the removed tumor is irradiated with an electron beam at a dose of 10-20 Gy in order to devitalize the remaining malignant cells [3].

Now, regarding chemotherapy. There are several types of chemotherapy that differ in purpose: 1) neoadjuvant chemotherapy of tumors is prescribed before surgery, in order to reduce an inoperable tumor for surgery, as well as to identify the sensitivity of cancer cells to drugs for further use after surgery; 2) adjuvant chemotherapy is prescribed after surgical treatment to prevent metastasis and reduce the risk of relapse; 3) curative chemotherapy is given to shrink metastatic cancers. Depending on the location and type of tumor, chemotherapy is prescribed according to different regimens and has its own characteristics.

Indications for chemotherapy: 1) cytologically and histologically verified BC; 2) in the treatment of locally advanced tumors; 3) metastases in regional lymph nodes/distant organs - lungs, liver, brain, bone structure; 4) tumor recurrence; 5) a satisfactory blood picture in the

patient: normal hemoglobin and hemocrit, the absolute number of granulocytes is more than 200, platelets are more than 100,000; 6) preserved function of the liver, kidneys, respiratory system and cardiovascular system; 7) the possibility of converting an inoperable tumor process into an operable one; 8) patient's refusal to undergo surgery; 9) improvement of long-term treatment results in unfavorable tumor phenotypes (triple negative, HER2-negative cancer).

Contraindications to chemotherapy can be divided into two groups: absolute and relative. Absolute contraindications: hyperthermia >38 degrees; disease in the stage of decompensation (cardiovascular system, respiratory system, liver, kidneys); the presence of acute infectious diseases; mental illness; the ineffectiveness of this type of treatment, confirmed by one or more specialists; tumor decay (threat of bleeding); the patient's serious condition according to the Karnofsky Performance Scale is 50% or less. Relative contraindications: pregnancy up to 16-18 weeks; intoxication of the body; active pulmonary tuberculosis; persistent pathological changes in blood composition (anemia, leukopenia, thrombocytopenia); cachexia.

The rationale for prescribing neoadjuvant systemic therapy for BC is: high probability of latent (micrometastatic) spread; the ability to reduce the amount of surgical intervention within the "clean" resection margins; the ability to evaluate the clinical response to therapy in vivo; availability of accurate pathomorphological assessment of the degree of tumor regression; the possibility of special studies of biopsy tumor material before, during and after completion of primary systemic treatment. For medullary carcinoma and adenoid cystic carcinoma, adjuvant chemotherapy may not be required (in the absence of lymph node involvement).

And a very important and decisive aspect when prescribing adjuvant/neoadjuvant systemic therapy is the molecular biological subtype of BC:

1. Luminal type A. In early BC (T1-2N0M0), hormone therapy is carried out only in the presence of severe concomitant diseases and/or there are absolute contraindications to surgical treatment until the maximum effect is achieved, followed by radiation therapy. For T2-4N1-3M0 locally advanced inoperable BC, it is recommended to prescribe hormone therapy with antiestrogens and aromatase inhibitors; it is advisable to carry out treatment until the maximum effect is achieved with clinical and instrumental assessment every 3 months. At the same time, in most cases, the appointment of adjuvant/neoadjuvant chemotherapy (in addition to hormonal therapy) is possible in the presence of at least two parameters: widespread process (≥ 4 regional lymph nodes affected by metastases; ≥T3); GIII; young age; presence of pregnancy; increase in initial Ki67 values during repeat biopsy/postoperative material after neoadjuvant hormone therapy.

2. Luminal B (HER2 negative). Hormone therapy + chemotherapy in most cases. For T1a (≤ 5 mm) and N0 - only adjuvant hormonal therapy. In other cases, chemotherapy with anthracycline- and taxane-containing regimens in addition to hormone therapy. Adding platinum drugs to adjuvant chemotherapy only in the presence of a BRCA1/2 gene mutation.

3. Luminal type B (HER2 positive). Chemotherapy + anti-HER2 therapy + hormone therapy. For T1a (≤ 5 mm) and N0: adjuvant hormone therapy only; chemotherapy and trastuzumab are not indicated. For T1b, c (> 5 mm but ≤ 20 mm) and N0: chemotherapy with paclitaxel (without anthracyclines) in combination with trastuzumab (followed by hormone therapy) is possible. For T2-T4 (> 20 mm) or N+: the first step is anthracyclines, then taxanes + trastuzumab ± pertuzumab (followed by hormone therapy).

4. HER2 positive (non-luminal). Chemotherapy + anti-HER2 therapy. For T1a (≤ 5 mm) and N0: systemic therapy is not indicated. For T1b (> 5 mm but ≤ 10 mm) and N0: taxane chemotherapy (without anthracyclines) in combination with trastuzumab is possible. For T1c-T4 (> 10 mm) or N+: the first step is anthracyclines, then taxanes + trastuzumab ± pertuzumab.

5. Triple negative (ductal). Chemotherapy including anthracyclines and taxanes. For T1a (≤ 5 mm) and N0, systemic therapy is not indicated. Adding platinum drugs to adjuvant

chemotherapy only in the presence of a BRCA gene mutation. There are also features when prescribing adjuvant chemotherapy to patients who have received neoadjuvant chemotherapy in full.

Also, a very important section is the use of hormone therapy in the adjuvant or neoadjuvant mode. In the premenopausal period, hormone therapy is used as follows. After completion of systemic chemotherapy and continued menstrual function, bilateral oophorectomy or ovarian suppression with luteinizing gonadotropin releasing hormone agonists followed by an anti-estrogen for 5 years is indicated. When menstrual function ceases after receiving courses of chemotherapy and the level of estradiol in the blood is determined, an anti-estrogen is prescribed to confirm true menopause. The following regimens with tamoxifen are used: 1) tamoxifen 20 mg/day orally daily for 5 years; 2) tamoxifen 20 mg/day orally daily, for 10 years, in the presence of at least one unfavorable prognosis factor: age ≤ 35 years, preserved ovarian function after adjuvant chemotherapy, T3-4, involvement of ≥ 4 axillary lymph nodes, GIII, positive HER2, high Ki67; 3) tamoxifen 20 mg/day orally daily for 5 years, then aromatase inhibitors (letrozole 2.5 mg/day orally daily, or anastrozole 1 mg/day orally daily, or exemestane 25 mg/day orally daily) for 5 years. For patients who have achieved stable menopause by the time they stop taking tamoxifen, with at least one poor prognostic factor: age ≤ 35 years, preserved ovarian function after adjuvant chemotherapy, T3-4, involvement of ≥ 4 axillary lymph nodes, GIII, HER2 positive, high Ki67; 4) ovarian suppression1 + tamoxifen 20 mg/day orally daily / aromatase inhibitors (letrozole 2.5 mg/day orally daily, or anastrozole 1 mg/day orally daily, or exemestane 25 mg/day orally daily) for 5 years, and also if there are indications for adjuvant chemotherapy and preserved ovarian function after completion of chemotherapy; 5) bemaciclib 150 mg 2 times a day in combination with endocrine therapy for the adjuvant treatment of hormone receptor positive (HR+) and human epidermal growth factor receptor type 2 (HER2) negative BC in early stages with involvement of regional lymph nodes and a high risk of relapse [3].

In pre- or perimenopausal women, endocrine therapy with aromatase inhibitors should be combined with a luteinizing hormone-releasing hormone agonist. To achieve ovarian suppression, it is possible to use the following methods: 1) surgical castration (bilateral oophorectomy); the most effective method, causes irreversible shutdown of ovarian function; 2) medicinal (analogues of luteinizing gonadotropic hormone: goserelin 3.6 mg intramuscularly once every 28 days or 10.8 mg subcutaneously once every 12 weeks; or buserelin 3.75 mg intramuscularly once every 28 days; or leuprorelin 3.75 mg IM 1 time in 28 days): causes reversible suppression of ovarian function; does not always provide complete suppression of ovarian function, especially in young women; to confirm complete ovarian suppression, it is necessary to determine estradiol in the blood serum; determination of follicle-stimulating hormone during treatment with luteinizing gonadotropic hormone analogues is not informative; aromatase inhibitors should be started 6-8 weeks after the first administration of luteinizing gonadotropin hormone analogues; luteinizing gonadotropin hormone analogues are administered monthly; 3) radial; causes irreversible shutdown of ovarian function. The optimal method of ovarian suppression has not been determined; it is usually prescribed for a period of 2-5 years.

Hormone therapy for BC for menopausal patients is carried out in the following variations: 1) tamoxifen 20 mg/day orally daily for 5 years; 2) aromatase inhibitors (letrozole 2.5 mg/day orally daily, or anastrozole 1 mg/day orally daily, or exemestane 25 mg/day orally daily) for 5 years; in the presence of at least one unfavorable prognosis factor: preserved ovarian function after adjuvant chemotherapy, T3-4, involvement of ≥ 4 axillary lymph nodes, GIII, positive HER2, high Ki67; 3) tamoxifen 20 mg/day orally daily for 10 years; in the presence of at least one unfavorable prognosis factor: preserved ovarian function after adjuvant chemotherapy, T3-4, involvement of ≥ 4 axillary lymph nodes, GIII, positive HER2, high Ki67; 4) tamoxifen 20 mg/day orally daily for 5 years, then aromatase inhibitors (letrozole 2.5 mg/day orally daily, or anastrozole 1 mg/day orally

daily, or exemestane 25 mg/day orally daily) for 5 years. For patients who have reached stable menopause by the time they stop taking tamoxifen, in the presence of at least one unfavorable prognosis factor: preserved ovarian function after adjuvant chemotherapy, T3-4, involvement of ≥ 4 axillary lymph nodes, GIII, positive HER2, high Ki67; 5) abemaciclib 150 mg 2 times a day in combination with endocrine therapy for the adjuvant treatment of hormone receptor-positive (HR+) and human epidermal growth factor receptor type 2 receptor-negative (HER2-) BC in the early stages with involvement of regional lymph nodes and a high risk of relapse - continuously for 2 years or until disease relapse or intolerable toxicity develops [3].

And, of course, the surgical method remains one of the leading methods in the treatment of this pathology, and in some cases, it is the only method of treatment (cancer in situ). For BC, the following types of surgical interventions are performed: 1) radical mastectomy according to Halstead - single-block removal of the mammary gland along with the pectoralis major and minor muscles and their fascia, subclavian, axillary and subscapular tissue with lymph nodes within the anatomical cases; 2) extended axillary-thoracic radical mastectomy, single-block removal of the mammary gland with the pectoral muscles, subclavian-axillary and subscapularis tissue, as well as a section of the chest wall with parasternal lymph nodes and internal mammary vessels; 3) functionally sparing operations (modified radical mastectomy - differs from Halstead mastectomy by preserving the pectoralis major muscle; modified Madden mastectomy - differs from Halstead mastectomy by preserving both pectoral muscles; 4) simple mastectomy - removal of the mammary gland with the fascia of the pectoralis major muscle (indications: decaying tumor, advanced age, severe concomitant diseases; 5) radical sectoral resection - removal of the sector along with the tumor, part of the underlying fascia of the pectoralis major and minor muscles, subclavian, axillary, subscapular tissue with lymph nodes in one block; 6) sectoral resection - removal of the breast sector to the underlying fascia (performed only for diagnostic purposes or in combination with radiation therapy for cancer in situ); 7) biopsy of the sentinel lymph node is carried out for diagnostic and therapeutic purposes in the early stages of the disease (1st level lymph nodes are removed with a histological express study to determine the presence of elements of a malignant tumor); detection of sentinel lymph nodes is possible using radioactive colloid and/or blue dye; a combined determination method is preferred.

Indications for performing organ-preserving operations: the presence of a nodular form of cancer up to 2.0 cm in size; absence of multicentricity and multifocality of tumor growth (on mammograms, ultrasound data, clinical examination); slow and moderate growth rate, doubling of tumor size no faster than 3 months (according to medical history); a favorable ratio of the size of the mammary gland and the tumor to obtain a good cosmetic result of the operation; absence of distant metastases; the presence of single metastases in the axillary region is acceptable; the patient's desire to preserve the mammary gland; satisfactory objective tumor response (partial and complete tumor regression) to previous neoadjuvant systemic treatment.

Reconstructive operations can be performed for stages I-III of BC at the request of the patient at any tumor location: 1) reconstruction (primary or delayed) of the mammary gland using an endoprosthesis (implant) (this type of operation involves the installation of a temporary (expander) or permanent prosthesis under the pectoralis major muscle, which allows compensation for the defect due to its volume, after mastectomy); 2) one-stage reconstruction: a skin-skin-sparing mastectomy is performed with the fascia of the pectoralis major muscle (if tumor cells are detected in the tissue behind the nipple during express histological examination, the nipple with the areola is removed); 3) reconstruction (primary or delayed) of the mammary gland using one's own tissues (autoplasty); this type of reconstruction involves replacing the defect using one's own tissues; basically, 2 types of operations are used - breast reconstruction by replacing with a TRAM flap (using a flap based on the rectus abdominis muscles) and breast reconstruction by replacing with a thoracodorsal flap, which is used in combination with an endoprosthesis.

Types of surgical interventions for metastatic BC: 1) sanitary/simple mastectomy (if there is a threat of bleeding for health reasons); 2) open liver biopsy (diagnostic surgery for suspected liver metastases); 3) other diagnostic manipulations on the liver (liver resection in the presence of single metastatic foci in the liver); 4) excision of the affected area or tissue of the meninges (in the presence of solitary metastatic foci of the meninges); 5) other types of excision or destruction of the damaged area or brain tissue (in the presence of solitary metastatic foci in the brain); 6) precision resection of a segment of the lung (in the presence of solitary metastatic foci in the lungs); 7) laparoscopic salpingo-oophorectomy (prophylactic bilateral removal of appendages for hormone-dependent BC tumors in premenopausal patients); 8) total hysterectomy with appendages (for metastatic lesions of the ovaries, uterine body); 9) electrochemotherapy for intradermal metastatic lesions (combination treatment that uses the administration of chemotherapeutic drugs in association with electroporation of the cell membrane).

Contraindications to surgical treatment for BC: the patient has signs of inoperability and severe concomitant pathology; distant metastases, the presence of a disseminated tumor process; synchronously existing and widespread inoperable tumor process of another localization, for example lung cancer, etc.; chronic decompensated and/or acute functional disorders of the respiratory, cardiovascular, urinary system, gastrointestinal tract; allergy to drugs used in general anesthesia.

Also, a very important point is preventive measures for BC. Primary prevention of BC is the prevention of the disease by studying the etiological and risk factors (normalization of family life, timely implementation of childbearing, breastfeeding the baby, avoiding marriages in cases of mutual cancer). Secondary prevention of BC is the early detection and treatment of precancerous diseases of the mammary glands. Tertiary prevention is prevention, early diagnosis and treatment of relapses and metastases; using a nutritious diet rich in vitamins and proteins, giving up bad habits (smoking, drinking alcohol), preventing viral infections and concomitant diseases, regular preventive examinations with an oncologist, regular diagnostic procedures (radiography of the lungs, ultrasound of the liver, kidneys, neck lymph nodes).

Prophylactic mastectomy - risk-reducing surgeries, such as mastectomy with reconstruction, may be offered to women at risk. The risk of developing BC is reduced by approximately 90-95%, however, absolute guarantees regarding the occurrence of BC in the future are impossible. Indications for performing bilateral prophylactic mastectomy in women who do not currently have BC (in order to reduce the risk of developing primary BC): mutations of the BRCA1 and BRCA2 genes; family history (presence of BC in first- and second-line relatives) without a proven mutation; histological risk factors are atypical ductal or lobular hyperplasia. Indications for performing prophylactic contralateral mastectomy in women with current or past BC: newly diagnosed unilateral BC stage I-II, or a history of stage I-II BC (in order to reduce the risk of developing cancer in the contralateral mammary gland and achieving symmetry with the operated mammary gland); lobular carcinoma in situ. Contraindications for use: age over 70 years; general contraindications to surgical treatment; synchronous and metachronous malignant tumors, with the exception of skin cancer [3].

Next, of course, it is necessary to discuss in detail the issue of BC screening. The key concept of BC screening is the detection of oncological pathology in the early stages, when the prognosis is most favorable and allows you to get the best long-term treatment results. A preventive examination always has advantages over a diagnostic examination when symptoms of the disease are already present. At the same time, upon receipt of the M2 and M3 indices according to the BI-RADS classification, it is possible to timely additionally examine these patients and, if necessary, take them to the dispensary record by a district mammologist with effective dispensary examinations and treatment of precancerous breast diseases. Along with this, it must be understood that the main conditions for screening for BC are the availability of trained

personnel and a standardized approach to identifying the trait under study and evaluating the results. The methods used should be sufficiently simple, reliable and reproducible, and also have sufficient sensitivity and high specificity. Such qualities are fully possessed by modern digital mammography [4,5,6].

Now, regarding this pathology in our country at the republican level. BC ranks first in the structure of the frequency of malignant neoplasms in both sexes in the population with a share of 14.9% (14.7% in 2022). This situation has been stable since 2004, in addition, BC ranks first and stably remains in this position in the structure of female oncopathology.

The incidence of BC in 2023 as a whole in the country increased to 27.7 per 100 thousand of the population with a growth rate of 4.3% compared to the previous year (in 2022 - 26.5). In the structure of cases, BC ranks first in the absolute majority of regions and cities of the country [7].

The incidence of BC in 12 regions of the country is higher than the national average (27.7 per 100 thousand of the population). The top three regions by this indicator are North Kazakhstan - 45.1; East Kazakhstan - 41.7 and Karaganda - 40.4. Next come: Kostanay - 39.1; Abay - 38.1; Pavlodar - 37.5; the city of Almaty - 36.2; Akmola - 35.9; the city of Astana - 34.3; Ulytau - 33.4; West Kazakhstan - 28.7 and Aktobe - 28.4 regions. This indicator is below the national average in 8 regions: Turkestan - 11.4 (the lowest level); Zhambyl - 15.8; Mangistau - 16.7; the city of Shymkent - 17.9; Almaty - 20.0; Kyzylorda - 20.2; Atyrau - 22.5 and Zhetysu - 22.8 per 100 thousand population. Mortality from this pathology was 5.3 per 100 thousand population. In the structure of causes of death in women in 2023, this pathology continues to occupy a leading position (1st rank place), amounting to 17.3% or 1056 people (17.2% and 1060 women, respectively).

The regions with the BC mortality rate above the national average (5.3 per 100,000 population) are: East Kazakhstan - 9.6 (maximum level); Pavlodar - 8.2; the city of Almaty - 7.8; Abay - 6.7; the city of Astana - 6.5; West Kazakhstan - 6.2; Kostanay - 6.1; Karaganda and North Kazakhstan - 5.6 and Akmola - 5.5 regions of the country. The lowest rates were recorded in Turkestan - 2.3 (minimum level); Ulytau - 3.2; Aktobe - 3.4; Atyrau - 3.6; Zhetysu - 3.7; Mangistau - 4.0; Kyzylorda - 4.3; Almaty - 4.6; in the city of Shymkent - 4.7; in Zhambyl - 4.8 regions per 100 thousand population [7].

The number of deaths from BC, not registered with oncology organizations and established posthumously in the Republic of Kazakhstan in 2023 amounted to 4 people; at the same time, the specific weight was 0.1% and this is the 22nd ranking place, as in the previous year.

At the same time, the one-year mortality rate was 3.4%. At the same time, the ratio between one-year mortality and neglect (stage IV) was, as in 2022, 0.7. At the same time, we recall that the farthest from "1" is the worst ratio between the indicators of one-year mortality and neglect.

Now, regarding preventive examinations. It should be noted that during large-scale preventive examinations of the population in 2023, significantly more patients with malignant neoplasms were actively identified than in 2022. This is 25,193 patients against 23,623 patients identified in 2022, i.e. +6.6%. This is due to the further abatement of the epidemiological situation with coronavirus and the increased availability of preventive care for the population. The proportion of patients identified during routine examinations increased from 62.0% to 62.4% of the total number of patients identified per year.

The number of newly identified BC patients registered with oncology organizations in 2023 amounted to 5,426 people (5,101 in 2022).

As for preventive examinations. The absolute number of BC patients identified during routine examinations amounted to 3,072 people (2,822 a year earlier). At the same time, the proportion of those identified during routine examinations increased from 55.3% in 2022 to 56.6% in 2023. At the same time, despite the fact that the absolute number of people diagnosed with

this pathology increased from 2474 to 2636 people, the proportion of patients diagnosed with BC at early (I, II) stages decreased from 87.7% to 85.8%. Of course, when analyzing the epidemiological situation, early diagnostic indicators are very important issues.

The regions where the proportion of patients with early stage I of the pathology in question is above the national average (35.8% and 9th place) include the following: Ulytau - 56.8% (the best indicator); Kyzylorda - 50.3%; Turkestan - 47.3%; the city of Shymkent - 46.0%; West Kazakhstan - 45.4%; the city of Astana - 44.6%; Mangistau - 44.2%; North Kazakhstan - 41.4%; Karaganda - 38.7%; Almaty - 38.5%; Pavlodar - 38.1% and East Kazakhstan - 36.1%. The lowest rates of early diagnosis were recorded in the Zhambyl region - only 14.0%; Atyrau - 24.4%; Akmola - 25.2%; the city of Almaty - 26.2%; Kostanay - 27.4%; Zhetysu - 31.4%; Aktobe - 35.0% and Abay - 35.7% regions of the country [7].

The average indicator in the country for detecting patients with BC at early (I and II) stages was 88.4%, and this is a high 4th rank place among all nosological forms of malignant neoplasms.

The regions where the proportion of patients with BC detected at stages I-II is above the average in the republic include the following regions: Atyrau - 94.2%; Aktobe - 92.4%; Kyzylorda - 92.3%; Pavlodar - 92.1%; the city of Shymkent - 92.0%; West Kazakhstan - 91.8%; North Kazakhstan - 91.6%; the city of Astana - 91.3%; Turkestan - 90.9; Ulytau - 90.5%; Almaty and the city of Almaty - 89.0%; Abay - 88.5%. Mangistau region is on par with the national average. Below the national average are: Karaganda - 79.8%; Kostanay - 81.1%; Akmola - 82.4%; Zhetysu - 86.2%; East Kazakhstan - 86.6%; and Zhambyl - 87.6% of the regions [7].

As can be clearly seen from the above data, there is a very wide range in early diagnosis rates (at stage I of the disease) across the country, from very good to dismal. Of course, it is necessary to take into account migration processes and other factors affecting the early diagnostic rates, but nevertheless, the obtained results give a reason not to stop there, both for oncologists and mammologists, obstetricians-gynecologists, radiologists, and, naturally, for general practitioners, since improving the early diagnostic rates of malignant tumors, as one of the main postulates and one of the main tasks of medicine in general, continues to be relevant today. Among the visual localizations of malignant tumors in the reporting year, the proportion of seven main forms determines the picture of late diagnostics (stages III-IV) and amounts to 13.3% in total, with a decrease compared to the level of the previous year (2022 - 14.2%). At the same time, with BC, the neglect rate was 11.6% (13.8% - in 2022).

The proportion of stage IV BC among all nosological forms of malignant neoplasms was 4.3%. The following indicators were noted by regions of our country: in East Kazakhstan - 8.4% (the worst result); Karaganda - 7.4%; Mangistau - 6.2%; Kyzylorda - 5.9%; Almaty - 5.3%; Atyrau - 5.1%; Akmola and Kostanay - 5.0%. At the same time, the lowest neglect of this cancer localization was established in the West Kazakhstan region - 2.1% [7].

The morphological verification rate of the disease in the country was 99.4%. At the same time, the leaders in this aspect with a 100% indicator are Almaty, Zhambyl, Mangistau, North Kazakhstan, Ulytau regions and the city of Shymkent. Next come: the city of Astana and the Karaganda region (99.8%); East Kazakhstan (99.7%); the city of Almaty, Turkestan and Abay regions (99.6%); West Kazakhstan (99.5%). At parity with the national average are Kostanay and Atyrau regions. Then come: Aktobe (98.9%); Pavlodar (98.2%); Zhetysu (98.1%); Akmola (97.8%); Kyzylorda (97.0% - the worst indicator in the republic) regions.

The total number of patients with malignant neoplasms registered with specialized oncology organizations of the republic continued to grow and by the end of 2023 amounted to 218,186 people, with an increase of 6.0% compared to the level of the previous year (2022 - 205,822, +5.8%). The overall incidence rate of malignant neoplasms increased by 3.9%, from 1055.3 to 1096.4 per 100 thousand people. The growth of this indicator is due to both the increase in the incidence and detection of pathology, and the increase in the survival rate of cancer

patients. In addition, statistical data on patients diagnosed with malignant neoplasms, who have been under observation for 5 years or more, and continue to be observed in 2023, showed that the number of patients under observation by oncological organizations in Kazakhstan for over five years continued to grow and at the end of the reporting year amounted to 117,616 people, with an increase of 6.2% (2022 - 110,790 people, +6.6%) (form. No. 7).

It is impossible to ignore such an important clinical aspect as the coverage of patients with a diagnosis of BC in the Republic of Kazakhstan with special treatment.

In 2023, the number of hospitalizations for all nosological forms of malignant tumors in the country's oncology organizations amounted to 108,252 cases (2022 - 101,095), with an increase of 7.1% compared to the previous year, which is associated with a constant increase in the number of cancer patients, improved standardization of oncology care, and the development of palliative and rehabilitation services.

At the end of 2023, the absolute number of BC patients who completed specialized treatment amounted to 3,419 people, continuing treatment - 1,729 patients. The following results were obtained in percentage terms by methods and types of treatment: 40.9% of patients received complex treatment, 21.8% received only surgical treatment, 20.0% received only drug treatment, 12.6% received combined treatment, 1.1% received only radiation treatment, 0.7% received chemoradiation treatment.

Next, regarding the five-year survival rate of patients. As for BC, at the end of 2023, 48,496 people were registered with the dispensary, or 243.7 per 100 thousand of the population. At the end of 2022, there were 45,728 patients, or 234.5 per 100 thousand of the population, respectively.

At the same time, the lethality of the observed contingents decreased slightly from 2.3% in 2022 to 2.2 in 2023.

The five-year survival rate of patients with BC was 57.7% in 2023 and 57.1% in 2022 [7].

Mass screening to identify BC patients should mainly involve healthy women without any signs of the disease or symptoms. Screening not only helps to detect hidden forms of cancer that can be treated, but also has psychological value for women. As a result of screening, women are convinced that they do not have BC, and this is the most important potential success of such programs. While the ultimate goal of screening is to reduce BC mortality, its immediate goal is to detect cancer before clinical manifestation. However, BC is a heterogeneous disease, which can significantly affect the effectiveness of screening. Screening models for BC are usually based on the fact that the majority of detected tumors are invasive cancers in the early stage of progression. In addition, it must be taken into account that the detection of cancer (or its precursors) before clinical manifestation increases the risk of false positive diagnosis [8,9].

Mammography has a sensitivity of 95% and a specificity of 97%. These indicators decrease when examining women with denser mammary glands (young age, use of hormone therapy), with low quality mammography, and also with insufficient qualifications of the radiologist. Detection of high-grade invasive cancer by screening, when the tumor is not yet detected by clinical examination (palpation), means the possibility of reducing mortality from BC [10].

Preventive screening for early detection of BC in the Republic of Kazakhstan includes [11]:

1) mammography of both mammary glands in two projections - direct and oblique in the mammography room of the city, district polyclinic (mobile medical complex). All digital mammograms in the presence of a system for archiving and transferring medical images are copied to CDs and other electronic media and transferred to the server of the mammography room of the Cancer Center using specialized licensed software integrated between medical organizations; in case of impossibility of digital transmission - they are printed on X-ray film at a scale of 1:1 - 100% (1 patient - 1 set - 2 or 4 mammograms) with subsequent transfer to the mammography room of the Cancer Center;

2) interpretation of mammograms according to the BI-RADS classification (M0t, M0d, M1, M2, M3, M4, M5) by two or more independent radiologists of the same medical organization - double reading or different medical organizations: a radiologist of the mammography room city, district polyclinic (mobile medical complex) - the first reading, and the radiologist of the mammography room of the Cancer Center - the second reading;

3) in-depth diagnostics - targeted mammography, ultrasound examination (hereinafter - ultrasound) of the mammary glands, trepanobiopsy, including under ultrasound or stereotaxic control for histological examination, which is carried out in case of detection of pathological changes on mammograms (M0d) in the mammography room of the Cancer Center.

√ An average medical worker or a responsible person of the organization of outpatient care sends the patient for mammography to the district, city polyclinic.

√ The X-ray laboratory assistant of the mammography room of the city, district polyclinic (mobile medical complex) performs mammography, fills out a referral for double reading of mammograms and transmits the referral through information interaction.

√ Radiologist of the mammography office of the city, district polyclinic (mobile medical complex): fulfills the requirements for the safety and quality of mammographic examinations; evaluates the quality of the images provided and the correctness of the installation; performs repeated mammography in the M0t category (technical errors of mammography); determines the radiological density of the mammary glands on the ACR scale (A, B, C, D) indicating this parameter in the study protocol; conducts the first reading of mammograms with interpretation of the BI-RADS classification results. In the M0d category (undetermined or suspicious radiological changes requiring additional examination), the study protocol indicates the predominant pathology: education, asymmetry, violation of architectonics, microcalcifications; sends mammograms, electronic copies of mammograms through the archiving system and transfer of medical images to the workplace of the mammography office of the Cancer Center together with directions for double reading of mammograms; directs low-dose CT images through the system of archiving and transferring medical images to the workplace of the CT office of the Cancer Center together with copies of images recorded on CD-ROMs or other electronic media and directions for double reading.

√ The radiologist of the mammography room of the Cancer Center: evaluates the quality of the provided images and the correctness of the styling. Viewing digital X-ray images transferred to the server or on digital media (CD, DVD) is carried out on a monitor for interpreting digital X-ray images with a resolution of at least 5 megapixels, which has a certified grayscale transmission in accordance with the DICOM standard; conducts a double (second) reading of mammograms with the interpretation of the results according to the BI-RADS classification, using, if necessary, archival images. Organizes the third reading according to indications. With double reading, an independent interpretation of the images is carried out (blinding method - the second radiologist does not know the results of the first reading); in the M0m category (technical errors in mammography), recommends repeat mammography; in the M0d category (uncertain or suspicious radiographic changes requiring additional examination), the study protocol indicates the predominant pathology: education; asymmetry, violation of architectonics, microcalcifications; recommends that the outpatient care organization, according to indications, invite the patient for in-depth diagnostics (targeted mammography, ultrasound of the mammary glands, trephine biopsy, including under ultrasound or stereotaxic control, followed by histological examination of the material); collects and archives all mammograms (films and electronic media) made as part of the examination. The shelf life of mammograms is at least 3 years after leaving the age subject to a screening study; the results of the double (second) reading are transferred to the outpatient care organizations through information exchange.

√ Indications for in-depth diagnostics are the conclusions of double reading mammograms

M0d (uncertain or suspicious X-ray changes requiring additional examination).

√ In-depth diagnostics is carried out in two stages. At the first stage, ultrasound is performed, according to indications, targeted mammography, possibly with an increase (with asymmetry, violation of architectonics and the presence of microcalcifications). When visualizing a suspicious pathology (M4 and M5), the second stage is performed - trepanbiopsy, including under ultrasound control and stereotaxic control for histological examination.

√ Histological examination is carried out in the laboratory of pathomorphology or pathological bureau. Morphological interpretation of the biopsy is carried out in accordance with the recommendations of the World Health Organization.

√ Physician or responsible person of the outpatient care organization:

1) upon receipt of a mammography result according to the BI-RADS classification:

- in case of M0t (technical errors in mammography) - sends the patient for a second X-ray examination to the mammography room of the city, district polyclinic (mobile medical complex);

- with M0d (undefined or suspicious X-ray changes requiring additional examination) - sends the patient for in-depth diagnostics to the mammography room of the Cancer Center;

- with M1 (no changes detected) - recommends that the patient undergo a follow-up mammography examination after 2 years. With radiological density of the mammary glands, C and D are sent for ultrasound of the mammary glands to exclude a false-negative result of mammography;

- with M2 (benign changes), refer the patient for a consultation with an oncologist (mammologist) of the clinical diagnostic department, followed by a screening mammography examination after 2 years;

- with M3 (probable benign changes) - sends the patient for short-term dynamic radiation observation to the local doctor with the recommendation of control mammography or ultrasound in 6 months;

- with M4 (signs that cause suspicion of malignancy), M5 (practically reliable signs of malignancy) and if it is technically impossible to perform a trepanbiopsy or a biopsy is refused, a referral to an oncologist (mammologist) of the clinical diagnostic department for dynamic observation and decision on the verification of the identified pathology;

2) upon receipt of the result of a histological examination:

- benign education - refers the patient to an oncologist (mammologist) of the clinical diagnostic department for dynamic monitoring, followed by a screening mammography examination after 2 years;

- formation with an indeterminate malignant potential or carcinoma in situ - refers the patient to the Cancer Center for consultation and treatment, followed by dynamic observation by an oncologist (mammologist) of the clinical diagnostic department at the place of her attachment;

- malignant neoplasm - refers the patient to the Cancer Center for treatment and follow-up;

3) communicates the results of the screening examination to the patient in any available way (by telephone, in writing, through electronic means of communication);

4) enters the results of double reading, in-depth diagnostics, histological examination, recommendations of the radiologist of the Cancer Center mammography room into the information system.

Establishing the size of the primary tumor is especially important in screening. Tumor size is an important criterion for evaluating the quality of screening and determining the ability of X-ray mammography to detect non-palpable tumors. Therefore, it is extremely important that pathologists measure tumor diameter as accurately as possible. The smaller the size of the primary tumor, the greater the likelihood of error in determining its size.

In 2023, the number of patients identified during screening examinations increased by

22.5%, from 2,230 to 2,731 people, as a result, the detection rate during screenings increased from 5.9 to 6.8%. During mammographic screening for BC in 2023, 918,464 women of the target group aged 40 to 70 were examined (a year earlier - 808,503 women). During mammographic screening in 2023, 1,875 cases of BC were detected (2022 - 1,570 cases). The cancer detection rate increased from 1.94 to 2.04 per 1,000 examined. The best result is in the North Kazakhstan region - 3.11 per 1,000 examined women (2022 - 2.31). High detection rates of BC were observed in Aktobe, Almaty, Atyrau, West Kazakhstan, Karaganda, Kostanay regions and in two megacities - the cities of Astana and Almaty. Low detection rates per 1000 examined, compared with the national average, were observed in Abay, Akmola, East Kazakhstan, Zhambyl, Kyzylorda, Mangistau, Pavlodar, Turkestan, Ulytau regions and the city of Shymkent. The lowest result was in Zhambyl region - 0.96 per 1000 examined women (2022 - 0.58). Compared to 2022, an increase in the detection of BC was noted in all regions, with the exception of Akmola (from 2.42 to 1.99), East Kazakhstan (from 2.21 to 1.93), West Kazakhstan (from 2.29 to 2.28), Karaganda (from 2.63 to 2.15), Pavlodar (from 2.15 to 1.51) regions, where a deterioration in results was allowed [7].

Summarizing the above, we can conclude that BC, along with lung cancer, continues to firmly occupy a leading place from year to year among all existing malignant tumors of other localizations. At the same time, taking into account a number of factors, the indicators of early diagnostics do not allow oncologists to "sleep peacefully". Despite the attitude to visually accessible localizations, the percentage of locally advanced forms of this type of tumors still remains quite high. The variability and veiled nature of symptoms, their similarity with various non-core processes (for example, the mastitis-like form of BC, often imitating mastitis), leads to the neglect of the disease. All this requires oncologists, and first of all, primary health care workers and, of course, mammologists, obstetricians and gynecologists, as well as radiologists to increase the level of oncological alertness, inform the population about early symptoms that may indicate this pathology or the onset of proliferative changes and conduct high-tech diagnostic measures, including for the purpose of differential diagnosis and, as a result, timely treatment.

Patients registered with various forms of so-called mastopathy need to regularly visit specialized specialists and, if necessary, undergo examination.

An epidemiological assessment of the situation with BC in our country allows us to say that in the regions there are sometimes significant differences not only in morbidity rates, but also in the parameters of early diagnosis and mortality from this pathology. In connection with the above, this pathology continues to be a serious problem of modern clinical oncology.

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Сепсис с нейротоксикозом у детей: современные подходы к интенсивной терапии

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Аннотация

Педиатрический сепсис представляет собой инфекционно-ассоциированное критическое состояние, при котором дисрегулированный ответ организма приводит к потенциально жизнеугрожающей органной дисфункции. Особую диагностическую и терапевтическую сложность формирует острый церебральный синдром, традиционно обозначаемый в клинической практике термином «нейротоксикоз». Нарушение сознания, судороги, очаговая неврологическая симптоматика и церебральный отёк при тяжёлой инфекции могут быть связаны с системным нейровоспалением, нарушением гематоэнцефалического барьера и церебральной перфузии, прямой нейроинфекцией, гипоксией, метаболической дисфункцией или сочетанием нескольких механизмов. Цель исследования состояла в формировании клинически ориентированной модели интенсивной терапии сепсиса с неврологической дисфункцией у детей, учитывающей современные критерии Phoenix, контроль инфекции, возраст-специфическую гемодинамическую и респираторную поддержку, нейрокритическую диагностику, функцию почек и показания к экстракорпоральной терапии. Предложена нейро-септическая матрица, разделяющая системную органную дисфункцию и непосредственное поражение центральной нервной системы и связывающая каждое вмешательство с измеримой физиологической целью и обязательной повторной оценкой. Клиническая применимость концепции иллюстрируется ранее описанной траекторией ребёнка с сепсисом, менингоэнцефалитом, церебральным отёком и транзиторным нарушением функции почек. Положительная динамика после многокомпонентной интенсивной терапии не позволяет выделить причинный эффект отдельного вмешательства. Наиболее перспективной стратегией является переход от фиксированных лечебных алгоритмов к динамической оценке взаимосвязанных органных траекторий.

Ключевые слова: педиатрический сепсис; нейротоксикоз; неврологическая дисфункция; сепсис-ассоциированная энцефалопатия; менингоэнцефалит; церебральный отёк; интенсивная терапия; органная дисфункция; непрерывная заместительная почечная терапия.

Введение

Современная концепция педиатрического сепсиса принципиально отличается от прежней модели, основанной преимущественно на признаках системной воспалительной реакции. Международный консенсус 2024 г. определяет сепсис у ребёнка как предполагаемую или подтверждённую инфекцию в сочетании с потенциально жизнеугрожающей органной дисфункцией. Практическим инструментом этой концепции стал Phoenix Sepsis Score, включающий респираторный, сердечно-сосудистый, коагуляционный и неврологический домены. При инфекции сумма 2 балла и более соответствует критериям сепсиса; септический шок определяется при наличии сепсиса и как минимум одного сердечно-сосудистого балла. В неврологическом домене оценка по шкале комы Глазго 10 баллов и менее имеет самостоятельный диагностический вес. Это положение существенно меняет клиническое восприятие нарушения сознания: церебральная дисфункция рассматривается как один из компонентов органной недостаточности, а не как неспецифическая «интоксикация» [1].

Критерии Phoenix были получены на педиатрическом массиве, масштабы которого значительно превосходят доказательную основу прежних определений. L.N. Sanchez-Pinto, T.D. Bennett, P.E. DeWitt и соавт. использовали данные 3 049 699 обращений в наборе разработки и 581 317 обращений при внешней валидации. Среди 172 984 детей с предполагаемой инфекцией в первые 24 ч четырёхорганная модель показала лучшие характеристики, а площадь под ROC-кривой Phoenix Sepsis Score в различных валидационных выборках составляла 0,71-0,92. Порог 2 балла и более имел более высокую положительную прогностическую ценность при сходной или более высокой чувствительности по сравнению с критериями International Pediatric Sepsis Consensus Conference 2005 г. При этом Phoenix является системой определения органной дисфункции, а не готовым механизмом этиологической атрибуции каждого поражённого органа [2].

Обновлённая Surviving Sepsis Campaign 2026 г. усилила другую сторону современной парадигмы - лечение должно быть ранним, но не механическим. Международная группа из 68 экспертов, представлявших 13 профессиональных организаций, при участии шести методологов сформулировала 61 положение, из которых только пять получили статус сильных рекомендаций, 24 - условных, десять - положений надлежащей клинической практики; ещё по 22 PICO-вопросам самостоятельная рекомендация не была сформирована. При предполагаемом септическом шоке антимикробную терапию рекомендуется начинать максимально быстро, предпочтительно в пределах первого часа после распознавания. При вероятном сепсисе без шока допустима ограниченная во времени быстрая диагностическая оценка, однако при подтверждении клинического подозрения начало лечения желательно в пределах 3 ч. При септическом шоке в условиях доступной интенсивной терапии жидкость предлагается вводить отдельными болюсами по 10-20 мл/кг до суммарных 40-60 мл/кг в первый час, причём после каждого болюса требуется переоценка гемодинамики, а дальнейшее введение прекращается при разрешении шока или появлении признаков перегрузки жидкостью. Таким образом, даже базовая ресусцитация представляет управляемый физиологический процесс, а не выполнение заранее заданного объёма [3].

Глобальная значимость проблемы определяется не только госпитальной летальностью. По данным R.S. Watson, E.D. Carrol, M.J. Carter, N. Kissoon, S. Ranjit и L.J. Schlapbach, приблизительно половина из около 50 млн случаев сепсиса, возникающих ежегодно в мире, приходится на новорождённых, детей и подростков младше 19 лет. Авторы подчёркивают существенные региональные различия заболеваемости, микробиологической структуры и исходов, которые не объясняются одним уровнем дохода страны. Современное понимание бремени болезни также включает постсептическую заболеваемость, нейроразвитие и качество жизни, поэтому выживание в отделении

интенсивной терапии больше не рассматривается как единственная достаточная конечная точка [4].

Возрастная биология определяет принципиальные ограничения прямой экстраполяции взрослой интенсивной терапии на ребёнка. M.J. Carter, E.D. Carrol, S. Ranjit, R. Mozun, N. Kissoon, R.S. Watson и L.J. Schlapbach связывают современную помощь с ранним распознаванием, стабилизацией и последующим индивидуальным титрованием органной поддержки. Различия иммунного ответа, сердечно-сосудистого резерва, сосудистого тонуса, распределения жидкости, фармакокинетики и фоновой патологии означают, что фиксированные взрослые гемодинамические цели не являются универсальными педиатрическими ориентирами [5].

Именно неврологический фенотип наиболее наглядно демонстрирует ограничения линейных алгоритмов. Термин «нейротоксикоз» сохраняет клиническую узнаваемость в русскоязычной педиатрической и реанимационной традиции, но не соответствует одной современной международной нозологической категории. У ребёнка с тяжёлой инфекцией угнетение сознания может быть следствием системной сепсис-ассоциированной церебральной дисфункции, прямого инфекционного поражения оболочек или вещества мозга, гипоксемии, недостаточной церебральной перфузии, судорожной активности, электролитных и метаболических расстройств, лекарственного воздействия или нескольких механизмов одновременно.

Научная проблема поэтому состоит не в поиске ещё одного универсального «нейропротектора», а в корректном разделении причин церебральной дисфункции и синхронном управлении системной физиологией. Цель исследования заключалась в разработке клинической модели интенсивной терапии сепсиса с нейротоксикозом у детей, в которой инфекционный контроль, органная поддержка и этиологическая диагностика неврологического синдрома объединены общей системой повторной оценки.

Литературный обзор

J.S. Dumbuya, S. Li, L. Liang и Q. Zeng определяют paediatric sepsis-associated encephalopathy - педиатрическую сепсис-ассоциированную энцефалопатию - как церебральную дисфункцию, возникающую при сепсисе без очевидного непосредственного инфекционного поражения центральной нервной системы. Клинический спектр включает изменения поведения и сознания, судороги и кому, однако эти проявления неспецифичны. Диагностическая логика имеет принципиальное значение: непосредственная инфекция центральной нервной системы, метаболическая, токсическая, сосудистая и гипоксическая энцефалопатия должны быть исключены до окончательной атрибуции симптоматики сепсис-ассоциированной энцефалопатии. Для педиатрической практики особенно важно, что доказательная база SAE значительно уступает взрослой, а развивающийся мозг ограничивает механическое перенесение взрослых патофизиологических моделей [6].

Патогенетическая архитектура септической церебральной дисфункции не сводится к циркуляции одного цитокина. D. Xiao, X. Wang, W. Liang, Y. Yang, Y. Du, C. Liu, F. Xu, Y. Yang, M. Wei и G. Yang описывают параллельное участие нарушения гематоэнцефалического барьера, нейровоспаления, церебральной ишемии, митохондриальной дисфункции и расстройства нейротрансмиссии. Микроглия в этой системе выполняет роль функционального связующего звена между системным воспалительным сигналом, эндотелиальной дисфункцией, астроцитарной реакцией и нейрональным повреждением. Авторы отдельно подчёркивают взаимодействие активированной микроглии с цитокиновыми каскадами, активными формами кислорода, оксидом азота и глутаматергической передачей [7].

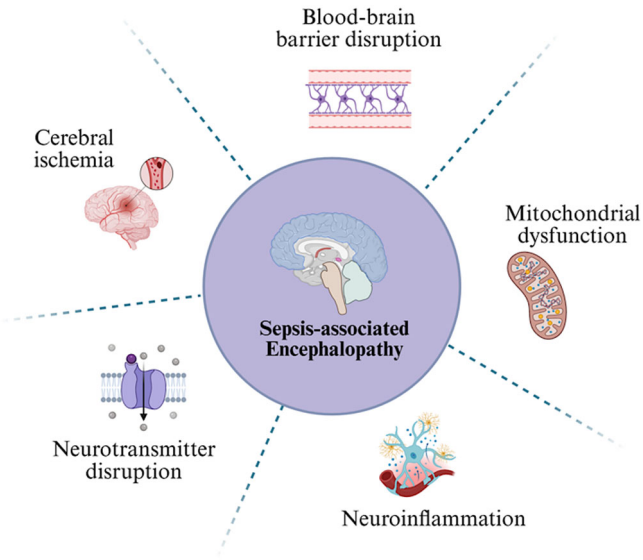

Рисунок 1. Многофакторный патогенез сепсис-ассоциированной энцефалопатии: нарушение гематоэнцефалического барьера, нейровоспаление, церебральная ишемия, митохондриальная дисфункция и нарушение нейротрансмиссии.
Источник: Xiao D., Wang X., Liang W. et al., 2025.

Физиологическое значение схемы, указанной на рисунке 1 выходит за пределы терминологии. Повреждение гематоэнцефалического барьера увеличивает взаимодействие периферического воспалительного ответа с церебральным микроокружением; эндотелиальная дисфункция нарушает микроциркуляцию и ауторегуляцию; воспалительная активация микроглии меняет межклеточную сигнализацию; митохондриальная недостаточность снижает энергетический резерв нейрона. Прямое воспалительное поражение мозга при энцефалите способно развиваться параллельно с этими системными механизмами. Поэтому наличие сепсиса не исключает нейроинфекцию, а наличие нейроинфекции не исключает септическую органную дисфункцию.

К.М. Быкова, И.А. Саввина, Н.В. Бодарева и Ю.М. Забродская также связывают сепсис-ассоциированную энцефалопатию с комплексом нейровоспалительных, сосудистых и метаболических механизмов и подчёркивают ограниченную диагностическую специфичность отдельного лабораторного или инструментального признака. В русскоязычной практике это имеет особое значение, поскольку термин «нейротоксикоз» исторически описывает клинический синдром, тогда как сепсис-ассоциированная энцефалопатия является более узкой патофизиологической категорией. Их автоматическое отождествление способно скрыть менингит, энцефалит, метаболическую патологию или другое самостоятельное поражение головного мозга [8].

Дифференциальная диагностика становится особенно важной при решении вопроса о люмбальной пункции. Рекомендации Всемирной организации здравоохранения 2025 г. не поддерживают рутинное выполнение компьютерной или магнитно-резонансной томографии каждому пациенту перед исследованием цереброспинальной жидкости. Однако предварительная нейровизуализация требуется при клинических признаках, повышающих вероятность опасной внутричерепной патологии, включая выраженное нарушение сознания и очаговый неврологический дефицит. Если выполнение люмбальной пункции откладывается, предполагаемый бактериальный менингит не должен оставаться без своевременной антибактериальной терапии. Рекомендации охватывают детей старше одного месяца и взрослых и рассматривают не только диагностику, но и ведение долгосрочных последствий [9].

Практическое руководство ВОЗ 2026 г. развивает эту модель в форме последовательных клинических алгоритмов. Основным объектом является острый бактериальный менингит у детей старше одного месяца, подростков и взрослых, однако начальная диагностическая логика предусматривает дифференциацию вирусных, туберкулёзных и других инфекционных поражений. Существенным остаётся принцип параллельности: стабилизация жизненно важных функций, этиологическая диагностика и эмпирическая терапия развиваются одновременно, если промедление создаёт дополнительный риск [10].

Органная взаимозависимость является центральной особенностью педиатрической реаниматологии. Шестое издание *Fuhrman and Zimmerman's Pediatric Critical Care* под редакцией J.J. Zimmerman и A.T. Rotta построено по органно-системному принципу и объединяет сепсис, нейрокритические состояния, механическую вентиляцию, гемодинамику, острое повреждение почек и экстракорпоральные технологии. Издание содержит 1664 страницы и 860 иллюстраций; официальный издатель указывает дату публикации 2021 г. и copyright year 2022. Для нейро-септического фенотипа эта взаимосвязь имеет прямое физиологическое содержание: изменение вентиляции воздействует на $PaCO_2$ и церебральный сосудистый тонус, нарушение системной перфузии отражается на доставке кислорода головному мозгу, почечная дисфункция меняет водный и электролитный баланс, а седация изменяет возможность серийной оценки сознания [11].

Дополнительную информацию о церебральной гемодинамике дают данные транскраниальной допплерографии. H. Algebaly, S. ElSherbini, A. Galal, R. Hamdi, A. Baz и A. Elbeleidy в проспективном исследовании 75 детей с тяжёлым сепсисом или септическим шоком выделили 45 пациентов с сепсис-ассоциированной энцефалопатией и 30 детей без неё. Медиана пульсационного индекса составляла соответственно 1,15 и 1,0, резистивного индекса - 0,68 и 0,62; площадь под ROC-кривой для прогнозирования SAE достигала 0,72 и 0,73. Эти результаты не превращают транскраниальную допплерографию в самостоятельный диагностический тест, но подтверждают наличие измеримых изменений цереброваскулярного сопротивления при септическом поражении мозга. Исследование опиралось на критерии тяжёлого сепсиса предыдущей эпохи, что необходимо учитывать при переносе результатов в современную систему Phoenix [12].

Почечная и экстракорпоральная поддержка требует не меньшей терминологической точности. G. Cortina, M. Daverio, D. Demirkol, R. Chanchlani и A. Deep рассматривают continuous renal replacement therapy - непрерывную заместительную почечную терапию - как управляемый метод удаления жидкости и растворённых веществ у критически больных детей. Continuous venovenous hemofiltration - непрерывная вено-венозная гемофильтрация - преимущественно использует конвекцию; continuous venovenous hemodialysis - непрерывный вено-венозный гемодиализ - диффузию; continuous venovenous hemodiafiltration - непрерывная вено-венозная гемодиафильтрация - сочетает диффузию, конвекцию и ультрафильтрацию. Авторы подчёркивают, что выбор режима зависит не только от патофизиологии пациента, но и от технических возможностей и опыта центра [13].

D.Y. Fuhrman, K.M. Gist и A. Akcan-Arikan показали масштаб существующей доказательной неопределённости. Основой их международного двухраундового modified Delphi стали 172 публикации 2012-2022 гг., однако только 12% включённых работ были непосредственно педиатрическими. В первом раунде приняли участие 147 специалистов, во втором - 126; консенсус был достигнут по 26 положениям. Наибольшее согласие наблюдалось относительно начала непрерывной заместительной почечной терапии, дозирования, антикоагуляции и удаления жидкости, тогда как методы контроля антикоагуляции и фактически доставленного лечения оставались более вариабельными.

Следовательно, технологическая распространённость CKRT существенно опережает объём высококачественных детских данных [14].

H. Miao, J. Shi, C. Wang, G. Lu, X. Zhu, Y. Wang, Y. Cui и Y. Zhang исследовали 324 ребёнка с тяжёлым сепсисом в четырёх педиатрических отделениях интенсивной терапии. Госпитальная летальность составляла 35,6% среди 180 пациентов, получавших CRRT, и 47,9% среди 144 пациентов без неё. После propensity score matching сравнивались по 136 пациентов в каждой группе, а летальность составляла соответственно 21,3% и 32,4%. Наблюдательный дизайн, отсутствие рандомизации, клинический отбор пациентов и вероятность остаточного конфаундинга не позволяют использовать эту ассоциацию как доказательство причинного эффекта процедуры у отдельного ребёнка. Особенно показательно, что в подгрупповом анализе статистически значимое снижение относительного риска смерти было получено для пациентов с острым респираторным дистресс-синдромом, но не для подгрупп с шоком, острым повреждением почек, энцефалопатией или жидкостной перегрузкой более 10% [15].

Долгосрочный исход также не может быть сведен к выживанию при выписке. E.F. Carlton, A. Gebremariam, A.B. Maddux и соавт. исследовали 101 511 госпитализаций критически больных детей. Среди 5150 выживших после сепсиса 670 детей, или 13,0%, в течение шести месяцев получили новое состояние из четырёх заранее определённых категорий: хроническая дыхательная недостаточность, судорожное расстройство, зависимость от дополнительного питания или хроническая болезнь почек. Среди 1834 детей с уже существовавшим состоянием у 385, или 21,0%, зарегистрировано прогрессирование. В целом новое или прогрессирующее заболевание было отмечено у 998 из 5150 выживших, то есть у 19,4% [16].

Неврологическая перспектива особенно важна для ребёнка школьного возраста. J. Kaur, P. Singhi, S. Singhi, P. Malhi и A.G. Saini проспективно обследовали 50 детей с сепсис-ассоциированной энцефалопатией и сравнили их с контрольной группой. После критического состояния отмечались более низкие показатели вербального и общего коэффициента интеллекта, а снижение школьной успеваемости регистрировалось у 44% пациентов. Частота низкого интеллекта составила 52% против 32% в контрольной группе. Исследование невелико и относится к более ранней системе определения сепсиса, однако оно убедительно отделяет восстановление бодрствования от восстановления когнитивной функции [17].

D.C. de Souza, R. Paul, R. Mozun, J. Sankar, R. Jabornisky, E. Lim и соавт. рассматривают качество помощи при детском сепсисе через всю клиническую траекторию - от профилактики и распознавания заболевания семьёй до своевременной медицинской оценки, транспортировки, интенсивной терапии и помощи после выписки. По состоянию на 2024 г. системные педиатрические программы повышения качества были реализованы лишь в ограниченном числе стран. Для нейро-септического фенотипа организационные факторы имеют непосредственное клиническое значение, поскольку время доступа к антибиотикам, специализированной реанимационной помощи, нейровизуализации и безопасной транспортировке способно изменять весь последующий ход критического состояния [18].

L.N. Sanchez-Pinto, M.D.P. Arias López, H. Scott, K. Gibbons, M. Moor, R.S. Watson, M.O. Wiens, L.J. Schlapbach и T.D. Bennett связывают следующий этап развития педиатрической септологии с анализом траекторных данных. Электронные медицинские записи, мобильные технологии, носимые сенсоры и системы поддержки клинических решений дают возможность анализировать не единичный пороговый показатель, а последовательность изменений во времени. Авторы подчёркивают одновременно существенное неравенство цифровизации между высокоресурсными и низкоресурсными системами и необходимость клинической валидации алгоритмов на той популяции, где они будут использоваться [19].

Российские федеральные клинические рекомендации 2025 г., подготовленные А.У. Лекмановым, П.И. Мироновым, Ю.С. Александровичем, Д.К. Азовским, Д.А. Поповым, К.В. Пшенисновым и А.Л. Музуровым, утверждены Министерством здравоохранения России 10 октября 2025 г. Документ включает антимикробную терапию, гемодинамическую и респираторную поддержку, питание, заместительную почечную терапию, экстракорпоральную гемокоррекцию и адъювантные методы. Для педиатрической практики принципиален отказ от безусловного использования взрослых фиксированных гемодинамических ориентиров и необходимость возрастной интерпретации физиологических параметров [20].

Казахстанское направление исследований в 2026 г. представлено работой G. Sabitova, Z. Makhammajanov, M. Khvan, P. Tarlykov и V. Sazonov из Nazarbayev University, National Center for Biotechnology и University Medical Center. В анализ были включены четыре оригинальных протеомных исследования детского сепсиса. Среди молекулярных кандидатов представлены интерлейкин-27, STAT3, гаптоглобин, сывороточный амилоид A1/2, растворимый CD25 и LRG1. Для отдельных маркеров чувствительность варьировала от 60% до 86%, специфичность - от 75% до 92%; мультимаркерные панели демонстрировали более высокую диагностическую информативность, чем отдельные маркеры. Авторы одновременно указывают на малые и неоднородные выборки, возрастную вариабельность и недостаток внешней валидации. Следовательно, протеомика представляет перспективное направление стратификации, но пока не заменяет клиническую диагностику и серийную оценку органной дисфункции [21].

Национальный организационный контекст педиатрической помощи в Казахстане определяется приказом Министра здравоохранения Республики Казахстан от 15 марта 2022 г. № ҚР ДСМ-25 «Об утверждении стандарта организации оказания педиатрической помощи в Республике Казахстан». Официальная система «Әділет» обозначает документ как обновлённый; его редакция изменялась, в том числе приказом от 21 февраля 2025 г. № 11, зарегистрированным 24 февраля 2025 г. № 35745. Нормативная база регламентирует организацию и преемственность педиатрической помощи, что имеет значение для маршрутизации ребёнка с критической инфекцией между уровнями медицинской системы [22].

R. Tennant в докторской диссертации University of Waterloo 2026 г. рассматривает педиатрический сепсис как область структурной клинической неопределённости: исходное физиологическое состояние детей, клинические определения, скорость ухудшения и маршруты оказания помощи варьируют настолько существенно, что бинарная автоматическая классификация способна скрывать важную информацию. Предложенный автором constraint-based approach ориентирован на отображение границ физиологического функционирования и ограничений клинической среды. Этот принцип применим и без использования искусственного интеллекта: неизвестный показатель должен оставаться неизвестным, а не превращаться в предположительно нормальное или расчётное значение [23].

Материалы и методы

Объектом исследования являлись терапевтические решения при сепсисе у детей, сопровождавшемся острым нарушением функций центральной нервной системы. Аналитической единицей служило отдельное клиническое решение, для которого сопоставлялись четыре характеристики: объективное показание, непосредственная физиологическая цель, измеримый признак ответа и условие, требующее пересмотра или прекращения вмешательства.

Системную органную дисфункцию оценивали по четырём доменам, положенным в основу Phoenix Sepsis Score: респираторному, сердечно-сосудистому, коагуляционному и

неврологическому. Неврологический фенотип дополнительно характеризовали уровнем сознания, реакцией зрачков, наличием менингеальных симптомов, очагового двигательного дефицита и судорог, результатами компьютерной и магнитно-резонансной томографии и характеристиками цереброспинальной жидкости. Такая схема позволяла разделять тяжесть системного состояния и этиологию церебральной дисфункции.

Нейротоксикоз рассматривался как синдромная характеристика инфекционно-ассоциированной церебральной дисфункции. Сепсис-ассоциированная энцефалопатия классифицировалась отдельно и предполагала отсутствие установленного непосредственного инфекционного поражения центральной нервной системы. Менингит, энцефалит и менингоэнцефалит относились к прямой патологии центральной нервной системы. Токсико-метаболическая энцефалопатия связывалась с установленным системным метаболическим или токсическим фактором. Церебральный отёк оценивался как морфофункциональный феномен, не определяющий этиологию самостоятельно.

Интенсивная терапия была разделена на инфекционный, гемодинамический, респираторный, церебральный, метаболически-нутритивный и почечный контуры. Для антимикробного лечения физиологической целью считался контроль предполагаемого инфекционного процесса с последующей возможностью сужения спектра после этиологического уточнения. Для инфузионной и вазоактивной поддержки оценивалось восстановление системной перфузии при одновременном контроле признаков жидкостной перегрузки. Для респираторной терапии анализировались газообмен и безопасность дыхательных путей. Для нейрокритической поддержки сопоставлялись сознание, очаговые признаки, судорожная активность, нейровизуализация и системные факторы, способные вторично повреждать головной мозг. Для заместительной почечной терапии учитывались почечная функция, электролитный и кислотно-основной статус и жидкостный баланс.

Клиническую согласованность модели сопоставляли с обезличенной траекторией ранее описанного ребёнка школьного возраста, у которого на фоне тяжёлого инфекционного процесса зарегистрированы ШКГ 9-10 баллов, менингеальная симптоматика, очаговое снижение двигательной активности справа и диффузный церебральный отёк; в последующем выявлен лимфоцитарный плеоцитоз, отмечено транзиторное ухудшение почечных показателей и проведена ПВВГДФ. Подробная история заболевания повторно не воспроизводилась.

Для оценки клинической траектории использовались только объективно зарегистрированные переменные: уровень сознания, число лейкоцитов, С-реактивный белок, прокальцитонин, мочевина, нейровизуализационные изменения, результаты исследования ликвора и факт применения органной поддержки. Значения, единицы измерения которых нельзя было достоверно подтвердить по первичному лабораторному результату, не использовались для формального стадирования органной недостаточности. Полный ретроспективный Phoenix Sepsis Score не рассчитывался при отсутствии синхронного исходного набора всех необходимых параметров.

Изменение состояния после лечения рассматривалось как временная последовательность, а не как доказанная причинность. Отдельному вмешательству не приписывался самостоятельный эффект, если в тот же период продолжались или изменялись антибактериальная терапия, респираторная поддержка, гиперосмолярное лечение, седация, питание или экстракорпоральная терапия.

Результаты

Сопоставление системного и неврологического контуров показало, что интенсивная терапия сепсиса с нейротоксикозом не может быть сведена к одному набору мероприятий для всех пациентов. Одинаковое снижение уровня сознания способно занимать принципиально разное место в патогенезе. При отсутствии признаков прямого

воспалительного поражения центральной нервной системы оно может соответствовать системной сепсис-ассоциированной церебральной дисфункции. Менингеальные симптомы, очаговый дефицит, судороги, воспалительные изменения ликвора или структурная патология требуют параллельного нозологического поиска.

Из этого различия следует терапевтически значимый вывод: тяжесть неврологической дисфункции и её происхождение являются двумя самостоятельными координатами. ШКГ может характеризовать тяжесть органной недостаточности, но не определяет, вызвана ли она нейроинфекцией, сепсис-ассоциированной энцефалопатией, гипоксией, метаболической декомпенсацией или фармакологической седацией.

Таблица 1. Нейро-септическая матрица интенсивной терапии у детей

Клинический домен	Ключевой объект оценки	Физиологическая цель	Тактика интенсивной терапии	Обязательная повторная оценка	Клинически опасная ошибка
Инфекционный процесс	Вероятный очаг, микробиология, эпидемиология, предшествующие антибиотики	Максимально ранний контроль инфекции	Забор микробиологического материала без клинически значимой задержки лечения, эмпирическая терапия достаточного спектра, контроль источника	Клиническая динамика, результаты посева/ПЦР, чувствительность, возможность деэскалации	Продолжение необоснованно широкого спектра или задержка первой дозы при жизнеугрожающем состоянии
Системная органная дисфункция	Phoenix-домены, лактат, динамика функций органов	Раннее распознавание прогрессирующей недостаточности	Поддержка поражённых органов одновременно с этиологическим лечением	Изменение числа и выраженности органных нарушений	Интерпретация сепсиса только по лихорадке, лейкоцитозу или одному биомаркеру
Гемодинамика	Перфузия, АД с учётом возраста, капиллярное наполнение, диурез, температура конечностей	Достаточная доставка кислорода без перегрузки жидкостью	Титрованная инфузия, своевременная вазоактивная поддержка при сохраняющейся циркуляторной недостаточности	Ответ после каждого вмешательства, признаки перегрузки, динамика перфузии	Механическое достижение заранее заданного суммарного объёма жидкости
Респираторный статус	Оксигенация, вентиляция, работа дыхания, сознание, защитные рефлексы	Достаточный газообмен и предупреждение вторичного церебрального повреждения	Кислородная, неинвазивная или инвазивная поддержка по физиологическим показаниям	SpO_2, газовый состав крови, $PaCO_2$, гемодинамика, неврологический статус	Оценка ИВЛ исключительно как метода коррекции гипоксемии без учёта защиты дыхательных путей и влияния $PaCO_2$ на мозг

Сознание и фокальная неврология	ШКГ, зрачки, очаговый дефицит, менингеальные признаки	Выявление прогрессирования церебрального поражения	Серийный неврологический осмотр, нейровизуализация по показаниям, коррекция системных факторов	Динамика до и после седации, новых вмешательств и изменения системной физиологии	Приписывание любого снижения ШКГ «нейротоксикозу» или SAE
Прямая нейроинфекция	Менингеальные признаки, ликвор, КТ/МРТ, микробиология	Раннее этиологическое лечение при безопасной диагностике	Параллельная стабилизация и диагностика; люмбальная пункция с учётом внутричерепного риска	Этиологические результаты, неврологическая и нейровизуализационная динамика	Задержка антибиотиков ради диагностической процедуры
Церебральный отёк	Сознание, зрачки, КТ/МРТ, натрий, осмолярность, вентиляция	Предотвращение вторичного повреждения мозга	Коррекция причины, гипоксии, гипоперфузии, температуры и осмотического дисбаланса; гиперосмолярная терапия при соответствующих показаниях	Неврологический статус, электролиты, осмолярность, гемодинамика, нейровизуализация	Представление отёка мозга как самостоятельного этиологического диагноза
Судорожная активность	Клинические приступы, ЭЭГ при соответствующих показаниях	Прекращение электрической и метаболической нагрузки на мозг	Противосудорожная терапия при документированной или обоснованно предполагаемой активности	Сознание, повторные приступы, ЭЭГ, фармакологическое влияние	Рутинная профилактическая полипрагмазия без подтверждённого показания
Метаболический статус	Глюкоза, натрий, калий, кальций, кислотно-основное состояние	Предупреждение вторичной токсико-метаболической дисфункции мозга	Коррекция клинически значимых нарушений	Серийные лабораторные показатели и неврологическая реакция	Атрибуция метаболически обратимого нарушения прямому поражению мозга
Питание	Гемодинамическая стабильность, функция ЖКТ, переносимость питания	Поддержание энергетического и белкового обеспечения	Энтеральный путь после стабилизации при отсутствии противопоказаний	Переносимость, энергетическая обеспеченность, желудочно-кишечные осложнения	Необоснованная задержка энтерального питания после стабилизации
Почки и жидкость	Диурез, азотистые показатели, электролиты, кислотно-основное состояние, баланс жидкости	Сохранение гомеостаза и предотвращение жидкостной перегрузки	Коррекция нефротоксических факторов, баланса жидкости и метаболических нарушений	Динамика функции почек и накопленной жидкости	Позднее распознавание жидкостной перегрузки

ПВВГДФ / CKRT	Почечные, метаболические и жидкостные показания; технические параметры процедуры	Управляемое удаление жидкости и растворённых веществ	Выбор режима и дозы относительно массы тела и клинической задачи	Фактически доставленная доза, простои контура, электролиты, гемодинамика, баланс	Использование понятия «детоксикация» как замены конкретным показаниям
Деэскалация	Траектория функций органов	Снижение лечебной нагрузки после стабилизации	Отмена ненужной поддержки, сужение антибактериального спектра, уменьшение седации	Стабильность после уменьшения вмешательства	Продолжение лечения только потому, что оно было назначено ранее
После выписки	Моторика, когнитивные функции, питание, почки, качество жизни	Выявление скрытой постсептической заболеваемости	Неврологическое и функциональное наблюдение по индивидуальному риску	Возврат к исходной активности и обучению	Приравнивание госпитальной выживаемости к полному восстановлению

Матрица отражает принцип управляемой интенсивной терапии: вмешательство без определённой физиологической цели и точки повторной оценки превращается в ритуальную процедуру. Для жидкости такой точкой является перфузионный ответ и появление признаков перегрузки; для вазоактивного препарата - гемодинамика; для ИВЛ - газообмен, безопасность дыхательных путей и церебральные условия; для антибактериальной терапии - клинический и микробиологический ответ; для ПВВГДФ - почечная, метаболическая или жидкостная задача и фактически доставленная интенсивность процедуры.

Рисунок 3. Двухконтурная модель атрибуции неврологической дисфункции при педиатрическом сепсисе

Двухконтурная модель устраняет методологическую ошибку, при которой наличие сепсиса автоматически определяет происхождение церебральных симптомов. Первый контур устанавливает тяжесть инфекционно-ассоциированной органной дисфункции. Второй отвечает на другой вопрос - существует ли самостоятельное воспалительное, структурное, метаболическое или другое поражение центральной нервной системы. Эти контуры не конкурируют друг с другом. Ребёнок с менингоэнцефалитом может одновременно иметь сепсис; наоборот, ребёнок с сепсисом и нарушением сознания не обязательно имеет прямую нейроинфекцию.

Таблица 2. Дифференциальная атрибуция неврологической дисфункции при тяжёлой инфекции у детей

Клиническая категория	Патофизиологическое содержание	Признаки, усиливающие диагностическую вероятность	Признаки, требующие другой атрибуции	Значение для интенсивной терапии
Нейротоксикоз	Синдромное обозначение тяжёлой инфекционно-ассоциированной церебральной дисфункции	Нарушение сознания, гипертермия, судороги, вегетативные и системные проявления тяжёлой инфекции	Наличие более конкретно установленного механизма требует уточнения нозологии	Термин характеризует тяжесть, но не определяет единственную этиологию
Сепсис-ассоциированная энцефалопатия	Диффузная дисфункция мозга при системном сепсисе без установленной прямой инфекции ЦНС	Нарушение сознания или когнитивных функций на фоне сепсиса после исключения альтернатив	Воспалительный ликвор, доказанная инфекция ЦНС, самостоятельное структурное поражение	Приоритетны контроль сепсиса, перфузии, оксигенации, метаболизма и вторичных церебральных факторов
Бактериальный или вирусный менингит	Воспаление оболочек мозга	Менингеальные симптомы, воспалительные изменения ликвора, этиологические данные	Паренхиматозный очаговый дефицит может свидетельствовать о более широком поражении	Требуется своевременное этиотропное лечение; диагностическая процедура не должна создавать опасную задержку
Энцефалит / менингоэнцефалит	Воспалительное поражение вещества мозга, изолированное или вместе с оболочками	Очаговый дефицит, судороги, выраженное нарушение сознания, нейровизуализационные и ликворологические изменения	Изолированная метаболическая причина без признаков воспаления	Этиотропное лечение сочетается с нейрокритической и системной поддержкой
Токсико-метаболическая энцефалопатия	Вторичная церебральная дисфункция вследствие системного нарушения	Значимая гипо-/гипергликемия, электролитные расстройства, печёночная или почечная дисфункция, токсическое воздействие	Стойкая очаговая симптоматика или воспалительный ликвор требуют расширения поиска	Коррекция системного фактора является терапевтически определяющей
Гипоксически-ишемическая дисфункция	Недостаточная доставка кислорода и/или нарушение церебральной перфузии	Гипоксемия, тяжёлая циркуляторная недостаточность, соответствующая временная связь	Воспалительные признаки ЦНС не объясняются только гипоксией	Необходимы оптимизация оксигенации и системной гемодинамики
Лекарственно-ассоциированное угнетение сознания	Фармакологическое влияние седативных, анальгетических и других препаратов	Временная связь с введением, дозозависимость, отсутствие прогрессирующих объективных неврологических признаков	Новая анизокория, очаговый дефицит, судороги требуют немедленной альтернативной оценки	Неврологический осмотр интерпретируется только с учётом фармакологического контекста

Церебральный отёк	Морфофункциональное состояние с увеличением содержания воды в ткани мозга	Нейровизуализационные изменения, прогрессирование нарушения сознания, признаки внутричерепной гипертензии	Сам по себе отёк не устанавливает инфекционную или септическую этиологию	Требуется лечение причины и предупреждение вторичного повреждения

Клиническое наблюдение, использованное для проверки согласованности модели, демонстрировало сочетание сразу нескольких признаков второго контура. На раннем этапе зарегистрированы ШКГ 9-10 баллов, ригидность затылочных мышц и снижение двигательной активности справа; КТ от 30.03.2025 выявила диффузный церебральный отёк. В последующем исследование цереброспинальной жидкости показало цитоз 48 клеток с лимфоцитарным преобладанием до 80%, а клинический диагноз включал менингоэнцефалит, нейроинфекцию и сепсис. Такая комбинация не позволяет корректно свести неврологический синдром только к сепсис-ассоциированной энцефалопатии.

При поступлении в описанной клинической траектории лейкоциты составляли 20,4 × 10^9/л, С-реактивный белок - 400 мг/л, прокальцитонин - 35 нг/мл. На третьи сутки лечения соответствующие значения составляли 18,6 × 10^9/л, 210 мг/л и 12 нг/мл. К 05.04.2025 лейкоциты снизились до 7,3 × 10^9/л, С-реактивный белок - до 15 мг/л, прокальцитонин - до 0,05 нг/мл; ШКГ достигла 14 баллов. В этот же период ПВВГДФ проводилась три дня, однако параллельно продолжалась многокомпонентная интенсивная терапия. К третьим суткам С-реактивный белок уменьшился на 47,5% относительно исходного значения, тогда как прокальцитонин - приблизительно на 65,7%. К 05.04.2025 снижение относительно исходного уровня составляло соответственно 96,25% и около 99,86%. Одновременно в промежуточной точке ухудшались почечные показатели, то есть воспалительная и почечная траектории изменялись несинхронно. Этот факт подтверждает принцип, положенный в основу нейро-септической матрицы: изменение одного лабораторного домена не должно использоваться как эквивалент общего органного восстановления.

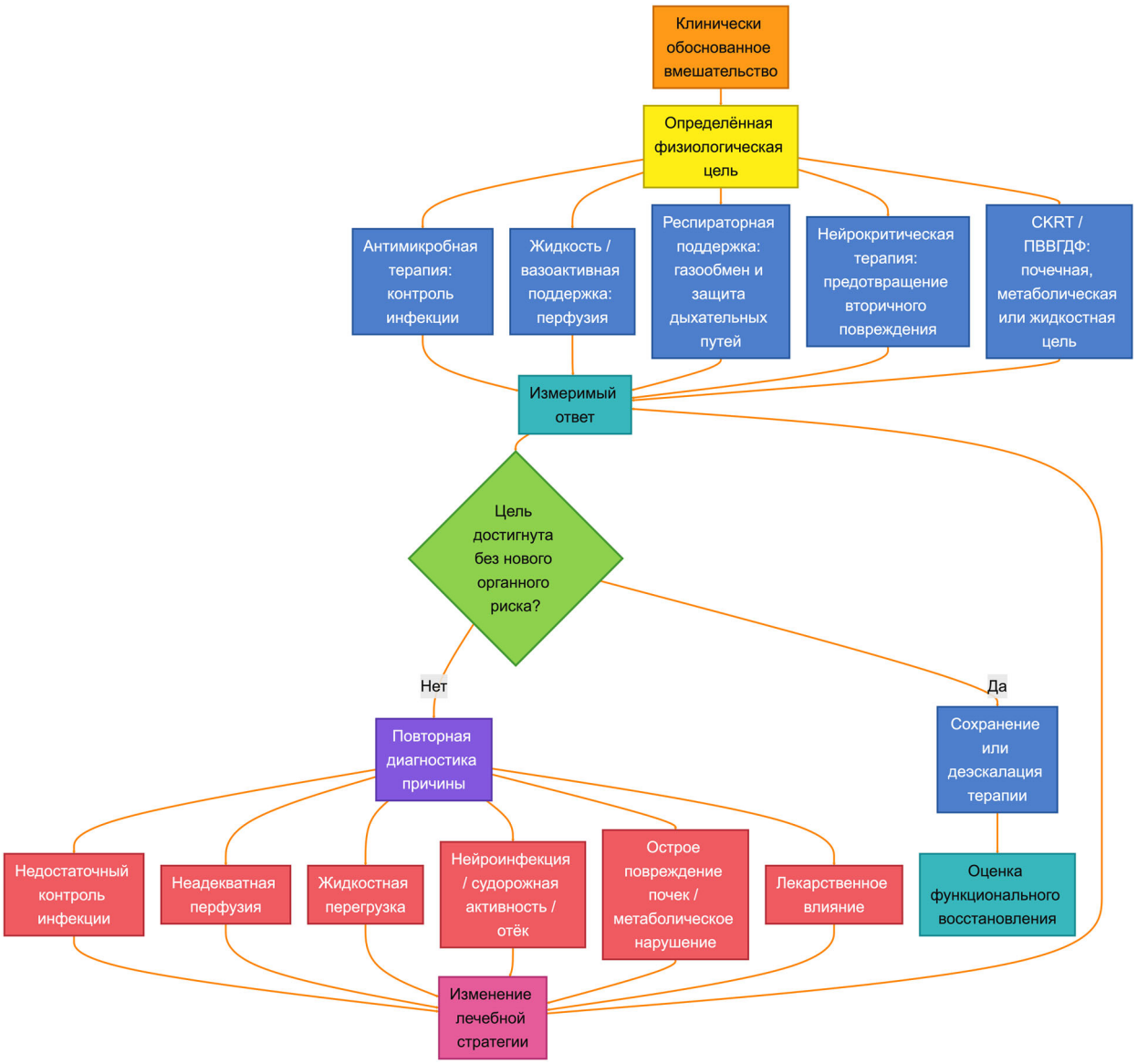

Рисунок 4. Контур физиологически управляемой интенсивной терапии при сепсисе с неврологической дисфункцией у детей

Ключевым результатом является переход от логики «назначение - ожидание результата» к циклу «показание - физиологическая цель - измеримый ответ - повторная диагностика - деэскалация или изменение стратегии». Такая конструкция особенно важна в педиатрической реанимации, где усиление одного компонента терапии способно ухудшить другой: дополнительная жидкость может увеличить интерстициальную перегрузку, чрезмерная седация затрудняет неврологическую оценку, изменение вентиляции влияет на церебральную гемодинамику, а увеличение интенсивности экстракорпорального клиренса способно изменить фармакокинетику антимикробных препаратов.

Обсуждение

Современная интенсивная терапия детского сепсиса развивается в направлении, противоположном прежней универсализации. Ранее тяжесть инфекции часто пытались выразить одной категорией, а лечебную стратегию - фиксированным набором целевых значений. Phoenix Criteria и Surviving Sepsis Campaign 2026 г. формируют более сложную картину: органная дисфункция должна быть объективизирована, однако значительная часть конкретных лечебных решений остаётся условной и требует клинической адаптации. Это не

слабость современной доказательной медицины, а отражение биологической неоднородности сепсиса.

Особенно очевидна эта неоднородность при церебральной дисфункции. Термин «нейротоксикоз» полезен как клинический сигнал тяжести, но недостаточен как окончательный диагноз. Он не отвечает на вопрос, поражена ли центральная нервная система непосредственно, является ли мозговая дисфункция следствием системного воспаления, или сознание изменено преимущественно из-за гипоксемии, перфузионной недостаточности, метаболического нарушения или лекарственного воздействия.

Поэтому наиболее существенным результатом настоящего анализа является не новая нозологическая категория, а изменение диагностической последовательности. Сначала устанавливается наличие инфекционно-ассоциированной системной органной дисфункции. Параллельно, а не после неё, определяется происхождение неврологического синдрома. Такая логика предотвращает два противоположных вида ошибки. Первый возникает, когда прямой менингоэнцефалит растворяется в понятии «септическая энцефалопатия». Второй - когда всё системное ухудшение объясняется нейроинфекцией и недооценивается нарастающая полиорганная недостаточность.

Клинический случай хорошо иллюстрирует именно первое ограничение. Ригидность затылочных мышц, одностороннее снижение двигательной активности, выраженный церебральный отёк и последующий воспалительный характер ликвора формируют существенно более специфичный неврологический профиль, чем изолированное снижение ШКГ. Поэтому современная ретроспективная интерпретация должна сохранять менингоэнцефалит как самостоятельный патологический компонент.

Оценка по шкале комы Глазго остаётся важной количественной переменной, но требует временного контекста. Значение до интубации и седации отличается по диагностическому содержанию от значения после введения пропофола, бензодиазепина, опиоида или другого седативного средства. Неврологическая траектория должна поэтому фиксировать не только число баллов, но и фармакологический фон.

Респираторная поддержка при нейро-септическом фенотипе также выполняет несколько задач одновременно. Защита дыхательных путей становится самостоятельным основанием для интубации при глубоком нарушении сознания, даже если гипоксемия не является ведущей проблемой. После интубации параметры вентиляции приобретают церебральное значение, поскольку $PaCO_2$ участвует в регуляции мозгового кровотока. Рутинная длительная гипервентиляция поэтому не должна рассматриваться как универсальная «противоотёчная» стратегия вне конкретной нейрокритической ситуации.

Гемодинамическая поддержка требует ещё большей возрастной дисциплины. Среднее артериальное давление 65 мм рт. ст., которое часто фигурирует во взрослых рекомендациях, не является универсальной целью для ребёнка любого возраста. Уже сама шкала Phoenix использует различные возрастные диапазоны среднего артериального давления: физиологический смысл одного и того же абсолютного давления у младенца и подростка различен. Фиксированные взрослые показатели ЦВД также не способны заменить клиническую оценку перфузии и жидкостного статуса.

Современная жидкостная терапия фактически представляет серию коротких физиологических экспериментов у постели пациента. Болюс вводится не для достижения административно заданного количества миллилитров, а для улучшения перфузии. Если ожидаемый ответ отсутствует или появляются признаки жидкостной перегрузки, логика лечения должна измениться. Продолжение инфузии только потому, что «целевой объём» ещё не достигнут, противоречит принципу повторной оценки.

Это особенно важно для ребёнка с церебральным отёком. Системная гиповолемия способна ухудшать церебральную перфузию, но чрезмерная положительная жидкостная

нагрузка одновременно осложняет лёгочную и тканевую физиологию. Оптимальная стратегия находится не между двумя фиксированными числами, а между признаками недостаточной и избыточной циркуляторной поддержки.

Антимикробная терапия, напротив, относится к вмешательствам, где временной фактор имеет наиболее непосредственное значение. При предполагаемом септическом шоке задержка стартовой терапии не оправдана ожиданием полного комплекса лабораторных результатов. Одновременно высокая скорость старта не отменяет последующего antimicrobial stewardship - рационального управления антимикробной терапией. После уточнения возбудителя, источника и чувствительности широкий эмпирический спектр должен перестать восприниматься как неизменная часть «интенсивности» лечения.

При предполагаемой нейроинфекции это приобретает особую сложность. Потребность в цереброспинальной жидкости для этиологической диагностики не должна конфликтовать с безопасностью пациента. Угнетение сознания и очаговый дефицит изменяют последовательность диагностических процедур. Антимикробная терапия и диагностическая работа поэтому должны развиваться параллельно, а не строго последовательно.

Отдельного обсуждения требует использование кортикостероидов. Доказательная поддержка кортикостероидной терапии при определённых вариантах бактериального менингита не означает универсальной эффективности высокодозного метилпреднизолона при любом септическом церебральном отёке. Для оценки конкретной схемы необходимы предполагаемая этиология, время относительно первой дозы антибиотика, характер воспаления центральной нервной системы и наличие других специфических показаний. В единичной клинической траектории регресс отёка на фоне комплексной терапии не позволяет выделить эффект одного препарата.

Аналогичное ограничение относится к гиперосмолярной терапии. Маннитол и гипертонический раствор NaCl изменяют осмотические градиенты, однако выбор препарата, концентрации и режима должен учитывать гемодинамику, натрий, осмолярность, функцию почек и общий водный баланс. Наличие отёка на КТ не является достаточным основанием для бесконечного воспроизведения одной схемы без контроля физиологического эффекта.

Особенно важна переоценка экстракорпоральных методов. Термин «экстракорпоральная детоксикация» создаёт впечатление широкой неспецифической очистки организма, хотя реальная процедура работает по конкретным физическим механизмам и имеет измеримые технические параметры. В клинической документации предпочтительнее указывать режим CKRT, кровоток, диализат, замещающий раствор, чистую ультрафильтрацию, антикоагуляцию, длительность и доставленную дозу, а не ограничиваться словом «детоксикация».

ПВВГДФ действительно сочетает диффузионный и конвективный клиренс, что создаёт биологическую возможность удаления ряда растворённых веществ. Однако вопрос «может ли мембрана удалить молекулу?» принципиально отличается от вопроса «улучшает ли такое удаление выживаемость или неврологический исход?». Последний требует клинических сравнительных исследований.

Наблюдательная работа Miao и соавт. представляет интересный сигнал, но не закрывает этот вопрос. Даже propensity score matching балансирует только измеренные смешивающие переменные и не создаёт рандомизацию. Время назначения CRRT, степень органной дисфункции, решение клинициста, наличие ресурсов и множество неучтённых факторов способны влиять на исход. Именно поэтому результат такого исследования формирует гипотезу и основание для дальнейших исследований, но не доказательство универсального назначения ПВВГДФ каждому ребёнку с сепсисом.

В рассматриваемой клинической траектории после подключения ПВВГДФ действительно отмечались снижение температуры, улучшение сознания и дальнейшая положительная лабораторная динамика. Однако почти в тот же период продолжались антимикробная терапия, вентиляционная поддержка, гиперосмолярное лечение, противовоспалительная терапия, питание, а антибактериальная схема была изменена. Контрфактического состояния того же ребёнка без ПВВГДФ не существует. Поэтому научно корректно фиксировать временную ассоциацию и невозможно доказательно утверждать самостоятельный причинный эффект.

Эта логика не обесценивает процедуру. Напротив, она позволяет точнее определить её место. При остром повреждении почек, неконтролируемом нарушении водного баланса, значимых электролитных и кислотно-основных расстройствах CKRT является полноценной органной поддержкой. Дискуссия начинается тогда, когда физический клиренс воспалительных медиаторов превращается в самостоятельное клиническое показание без достаточной доказательной опоры.

Важный технический вывод касается расчёта дозы CKRT. Абсолютные потоки аппарата сами по себе мало сопоставимы между пациентами. Один и тот же поток имеет совершенно различную физиологическую интенсивность у ребёнка массой 10 кг и подростка массой 50 кг. Поэтому исследовательская регистрация должна обязательно включать массу тела и фактически доставленный эффлюент в мл/кг/ч, а также простои контура и накопленный баланс жидкости.

Лабораторные биомаркеры также следует вернуть на их физиологическое место. С-реактивный белок и прокальцитонин характеризуют различные аспекты воспалительной реакции, но не являются прямыми измерителями функции головного мозга, почек или системы кровообращения. Быстрое снижение прокальцитонина может сосуществовать с продолжающейся органной дисфункцией. В клиническом наблюдении именно такой феномен прослеживался на промежуточном этапе, когда воспалительные маркеры уже уменьшались, а почечные показатели ухудшались.

Следовательно, наиболее информативным объектом является не значение, а траектория. Для ребёнка с сепсисом и нейротоксикозом целесообразно синхронно представлять температуру, состояние сознания, зрачки, фокальный неврологический статус, судороги, артериальное давление, признаки перфузии, диурез, баланс жидкости, параметры вентиляции, газовый состав крови, лактат, С-реактивный белок, прокальцитонин, микробиологические результаты и время ключевых лечебных вмешательств.

Именно такая траекторная структура может стать практическим развитием нейро-септической матрицы. В электронном интерфейсе она должна показывать не только текущее значение, но и направление его изменения. Падение артериального давления, рост кислородной потребности, ухудшение сознания и сокращение диуреза, происходящие в одном временном окне, несут иной объём информации, чем четыре отдельно выведенных «красных» лабораторных или мониторных сигнала.

На этом уровне работа Tennant приобретает практическое значение. Структурная неопределённость не должна маскироваться. Если масса пациента не зарегистрирована, нельзя создавать точную дозу CKRT в мл/кг/ч. Если единица креатинина сомнительна, нельзя формально стадировать острое повреждение почек. Если возбудитель не идентифицирован, нельзя превращать клиническое определение «вирусно-бактериальный» в микробиологически доказанную коинфекцию. Такая дисциплина повышает качество научного текста сильнее, чем увеличение числа формальных числовых показателей.

Перспектива протеомики усиливает, а не отменяет эту необходимость. Казахстанские данные 2026 г. показывают привлекательность мультимаркерных панелей, однако диагностическая ценность новых белков зависит от возраста, времени забора и фенотипа

сравнения. Один и тот же биомаркер не обязательно имеет одинаковый порог у младенца и подростка. Следующим этапом должна стать интеграция молекулярного профиля с клинической траекторией, а не замещение врача одним лабораторным сигналом.

Новизна нейро-септической матрицы состоит в соединении двух независимых решений. Первое отвечает на вопрос, какие органы потеряли функциональный резерв в структуре инфекции. Второе устанавливает происхождение церебрального синдрома. Контур повторной оценки добавляет третье измерение - время. Таким образом, ребёнок описывается не статической категорией «тяжёлый сепсис», а направлением изменений функций нескольких органов под воздействием заболевания и лечения.

Практическая новизна заключается в возможности стандартизировать передачу таких пациентов между медицинскими организациями. При межбольничной транспортировке особенно ценна не длинная история назначений, а компактная динамическая информация: исходный и текущий уровень сознания, неврологические признаки, вентиляционная поддержка, состояние перфузии, тренд диуреза, основные лабораторные изменения, предполагаемый очаг и время последней антимикробной терапии.

Для Казахстана перспективным является многоцентровый регистр педиатрического сепсиса, совместимый с Phoenix Criteria, но не ограниченный ими. Отдельный нейрологический модуль такого регистра должен включать менингит, энцефалит и менингоэнцефалит, ШКГ до седации, судорожную активность, результаты ликвора, КТ и МРТ, а также функциональный исход. Почечный модуль должен фиксировать массу тела, диурез, жидкостную перегрузку, режим CKRT и фактически доставленную дозу.

Наблюдение после выписки требует аналогичного расширения. Для ребёнка школьного возраста ясное сознание и отсутствие грубой гемиплегии ещё не означают возвращения к исходному состоянию. Клиническое значение имеют внимание, память, скорость обработки информации, исполнительные функции, эмоциональная регуляция, сон, утомляемость и способность выдерживать прежнюю учебную нагрузку.

Структурированное наблюдение после тяжёлого нейро-септического эпизода поэтому должно быть риск-ориентированным. Выраженное исходное угнетение сознания, судороги, прямое поражение центральной нервной системы, длительная органная поддержка или субъективные изменения после выписки создают основания для неврологической и при необходимости нейропсихологической оценки. Такой подход соответствует современному пониманию исхода как функционального восстановления, а не только выживания.

Ограничение настоящей аналитической модели связано с отсутствием проспективной валидации на независимой серии пациентов. Единичная ранее описанная клиническая траектория подтверждает логическую применимость двухконтурной атрибуции, но не позволяет оценить чувствительность, специфичность или влияние матрицы на клинические исходы. Следующим исследовательским этапом должно стать проспективное использование модели в нескольких отделениях интенсивной терапии с регистрацией времени распознавания нейроинфекции, продолжительности органной поддержки, частоты диагностической переклассификации и функционального исхода.

Заключение

Сепсис с нейротоксикозом у детей следует рассматривать не как единую нозологическую конструкцию, а как клинический фенотип, в котором инфекционно-ассоциированная системная органная дисфункция сочетается с различными механизмами церебрального повреждения. Неврологический домен Phoenix позволяет объективизировать тяжесть нарушения сознания, но не определяет его этиологию.

Сепсис-ассоциированная энцефалопатия, менингит, энцефалит, менингоэнцефалит, токсико-метаболическая дисфункция и церебральный отёк не являются

взаимозаменяемыми понятиями. Менингеальные признаки, очаговая симптоматика, судороги, воспалительные изменения цереброспинальной жидкости и патологическая нейровизуализация требуют самостоятельного анализа непосредственного поражения центральной нервной системы.

Интенсивная терапия должна быть построена вокруг физиологических целей. Антимикробная терапия обеспечивает контроль инфекции; гемодинамическая поддержка - адекватную перфузию без избыточной жидкостной нагрузки; респираторная терапия - газообмен и безопасность дыхательных путей; нейрокритическая помощь - предупреждение вторичного церебрального повреждения; заместительная почечная терапия - решение конкретной почечной, метаболической или жидкостной задачи.

Ни С-реактивный белок, ни прокальцитонин, ни отдельный показатель гемодинамики не характеризуют восстановление всего организма. Клинически более информативна синхронная траектория сознания, перфузии, дыхания, диуреза, воспалительных показателей, нейровизуализации и потребности в органной поддержке.

ПВВГДФ является технологически мощным методом экстракорпоральной поддержки, однако возможность удаления воспалительных медиаторов не должна отождествляться с доказанным самостоятельным эффектом на исход сепсиса. У ребёнка её назначение, интенсивность и продолжительность должны связываться с конкретными показаниями и измеримыми физиологическими целями.

Предложенная нейро-септическая матрица объединяет системный, церебральный и временной контуры критического состояния. Её практическая ценность заключается в том, что каждое вмешательство получает показание, физиологическую цель и точку обязательной повторной оценки, а отсутствие ожидаемого ответа становится основанием для пересмотра диагноза и стратегии, а не для автоматического усиления прежней терапии.

Перспективой является проспективная многоцентровая валидация такой модели с интеграцией Phoenix Criteria, нейровизуализации, ликворологических данных, параметров CKRT, молекулярных маркеров и долгосрочного нейрокогнитивного исхода. Именно траекторный, а не статический подход наиболее полно соответствует биологической неоднородности педиатрического сепсиса и современной логике персонализированной интенсивной терапии.

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Philological Sciences

Экотекст в постмодернистской прозе А.Жаксылыкова

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Аннотация. В статье исследуются специфика и поэтика экотекста в контексте постмодернистской парадигмы на материале прозы казахстанского писателя Аслана Жаксылыкова. Рассматривается деконструкция традиционного пейзажного дискурса, анализируется лингвосемантическое наполнение водных образов (река, исток, родник), их мифопоэтическая и метатекстуальная природа. Особое внимание уделено интертекстуальным связям и коммуникативным стратегиям экотекста, а также возможностям его использования в образовательной практике для формирования экологического мышления.

Ключевые слова: постмодернизм, экотекст, Аслан Жаксылыков, казахстанская проза, экологический дискурс, интертекстуальность, лингвосемантика

Введение

Современное литературоведение стремительно развивается в сторону междисциплинарного подхода, позволяющего рассматривать художественный текст не только как эстетическую категорию, но и как средство познания мира, культурного и социального взаимодействия, а также экологической рефлексии. Одним из актуальных направлений в этом контексте выступает изучение **экотекста**, в котором экосмысл становится не просто тематическим фоном, но центральной структурообразующей единицей. Особенно интересным представляется анализ экотекста в рамках **постмодернистской парадигмы**, которая разрушает традиционные границы жанров, стилей и идеологий, формируя новые способы взаимодействия текста с читателем и окружающей действительностью.

Постмодернистская литература, обладая выраженной метатекстуальностью, иронией, интертекстуальностью и установкой на деструкцию смыслов, находит новое прочтение в свете экологической проблематики. В ней экотема подаётся не в виде прямолинейного морализаторства, а через сложную систему образов, аллюзий, игровых стратегий и нарративной многослойности. Это позволяет говорить о появлении особого феномена — **постмодернистского экотекста**, который одновременно является и эстетической категорией, и коммуникативной, и идеологической конструкцией.

Особую актуальность приобретает изучение постмодернистского экотекста в казахстанской литературе, где процессы глобализации, экологического кризиса и культурной трансформации тесно переплетаются. В этом контексте произведения **Аслана Жаксылыкова** представляют собой уникальный материал для анализа. Жаксылыков — автор, сочетающий глубокую философскую рефлексию, внимание к экологическим и нравственным аспектам современности и постмодернистскую стилистику. Его тексты насыщены природными образами, символикой воды, земли, воздуха, и в то же время демонстрируют многослойную структуру, богатую на цитаты, метатекстовые включения, иронию и скрытую полемику с классическими традициями.

Целью настоящего исследования является **выявление поэтики постмодернистского экотекста в произведениях А. Жаксылыкова**, а также **анализ его коммуникативной функции** в контексте современной литературы.

В ходе работы будут рассмотрены следующие задачи:

- дать характеристику постмодернизма как литературного явления;
- определить специфику экотекста в постмодернистской прозе;
- выявить связь между постмодернистской стилистикой и экологической проблематикой;
- проанализировать структуру, стилистику, метатекстовые и коммуникативные приёмы в произведениях А. Жаксылыкова;
- рассмотреть динамику изменения экотекста и его коммуникативной функции в современной литературе;
- предложить возможные пути использования экотекста в образовательной практике.

Научная новизна данного исследования заключается в комплексном подходе к изучению постмодернистского экотекста на материале казахстанской прозы и в попытке описания новой жанрово-коммуникативной модели, актуальной как для литературоведческого анализа, так и для лингводидактики.

Практическая значимость работы состоит в возможности использования её результатов в учебном процессе, в разработке методических материалов, направленных на развитие экологического мышления и коммуникативной компетенции обучающихся.

Характеристика постмодернизма в литературе

Постмодернизм как эстетико-философская парадигма занимает особое место в истории мировой литературы второй половины XX — начала XXI века. Возникший как реакция на утопизм модернизма и разочарование в идеях просвещенческого разума, постмодернизм ознаменовал собой переход к новому типу художественного мышления, основанному на плюрализме, деконструкции и интертекстуальности.

Литературный постмодернизм характеризуется рядом устойчивых признаков, среди которых:

- отказ от авторитарности авторской инстанции и всеведущего рассказчика;
- размывание жанровых границ;
- игра со смыслами и знаками;
- активное использование иронии, пародии, пастиша;
- наличие метатекста и саморефлексии текста;
- фрагментарность повествования;
- симулякризация реальности и утрата идеи «истинного» смысла.

Одним из ключевых понятий постмодернистской эстетики становится интертекстуальность, когда каждый новый текст воспринимается как результат бесконечной цепочки цитат и аллюзий. Таким образом, постмодернистский текст существует не в изоляции, а в постоянном диалоге с культурным, философским и литературным контекстом. Это делает восприятие постмодернистской прозы сложным, требующим от читателя высокой степени подготовки и интеллектуальной вовлечённости.

В постмодернизме происходит радикальный сдвиг в понимании истины: она больше не считается объективной и универсальной. Вместо этого предлагается множественность точек зрения, релятивизм, отказ от метанарративов. Эта философская установка напрямую влияет на структуру и содержание литературных произведений, в которых разрушается линейность времени, нарушается причинно-следственная логика, а повествование становится открытым, «неоконченным» и часто парадоксальным.

В постсоветской литературе постмодернизм стал не просто стилистическим направлением, а способом осмысления травматичного исторического опыта, социальной и культурной

трансформации. Особенно это касается казахстанского литературного пространства, где постмодернизм позволил авторам заново интерпретировать национальные традиции, исторические события и ментальные коды.

Появление постмодернистского подхода в казахстанской прозе обусловлено рядом факторов: с одной стороны — глобализацией культурных процессов, с другой — внутренними изменениями в общественном и интеллектуальном сознании. Принципиально важным является то, что казахстанские авторы не копируют западные постмодернистские модели, а адаптируют их к собственному культурному и языковому контексту, формируя уникальную версию постмодернизма.

Таким образом, понимание постмодернизма в литературе как многоуровневой системы эстетических и философских установок является необходимым условием для дальнейшего анализа экотекста в произведениях А. Жаксылыкова. Именно в рамках постмодернистской парадигмы возникает особый тип экологического письма, в котором традиционные формы репрезентации природы подвергаются деконструкции и переосмыслению.

Особенности экотекста в постмодернистской прозе

Экотекст — это форма художественного дискурса, в центре которой находится тема взаимодействия человека и природы. Он может включать в себя описания ландшафтов, экологических катастроф, водных, лесных и климатических систем, а также этико-философские размышления о сущности природы, её месте в культурной и антропоцентрической системе координат. Экотекст — это не просто тематическое поле, но и способ мышления, проявляющийся на структурном, семантическом и прагматическом уровнях текста.

С начала XXI века понятие экотекста приобретает всё большую значимость в связи с глобальным экологическим кризисом и возрастанием интереса к устойчивому развитию. Художественная литература становится пространством, где происходит не только фиксация экологической тревоги, но и формирование нового взгляда на мир, основанного на экологической этике, симбиотическом сосуществовании человека и природы, переосмыслении роли потребления и технического прогресса.

Постмодернистская проза, с её склонностью к иронии, деконструкции и полифонии, вносит в представление об экотексте ряд новых черт. В ней природный ландшафт теряет статус внешнего и стабильного фона — он становится равноправным участником повествования, метафизическим субъектом, носителем смысла. Природа в постмодернистском экотексте не изображается как идеализированное пространство «вне цивилизации», напротив — она часто представляется фрагментированной, разрушенной, символически опустошённой. Это отражает постструктуралистский скепсис по отношению к любой цельности и гармонии.

Характерные особенности экотекста в постмодернистской прозе можно сформулировать следующим образом:

- **Деконструкция традиционного природного пейзажа.** В классической литературе природа нередко выступала как источник красоты, покоя или вдохновения. В постмодернистском экотексте эти смыслы размываются, заменяются тревожными, амбивалентными образами.
- **Интертекстуальность экологических кодов.** Тексты насыщаются отсылками к научным, мифологическим, религиозным и литературным источникам, связанным с природной символикой, что создаёт полисемантическое пространство.
- **Полифония голосов природы и человека.** Природа говорит в экотексте не как фон, а как субъект, иногда наделённый речью, памятью, протестом.
- **Ирония и гротеск.** Природные катастрофы, загрязнение, экологическое разрушение часто описываются с элементами пародии, чёрного юмора, что, с одной стороны, снижает трагизм, а с другой — усиливает эффект отчуждения.

- **Симуляция и искусственность.** В некоторых текстах природа представлена как конструкция, медийный продукт или даже пародия на «натуральность», что соответствует постмодернистской критике реальности как симулякра.

Таким образом, экотекст в постмодернистской прозе — это не только способ изображения природы, но и форма экзистенциальной и культурной рефлексии. Он позволяет автору размышлять о разрушительных последствиях технологического вмешательства, дегуманизации, кризисе идентичности, предлагая новые модели взаимодействия между человеком и окружающей средой.

Следует подчеркнуть, что в казахстанской литературе постмодернистский экотекст несёт в себе также глубоко национальный смысл. Природный ландшафт часто кодирует этническую память, связь с родом, сакральное восприятие земли как живого организма. Именно в таком контексте следует рассматривать экотексты Аслана Жаксылыкова, в которых природа — не просто тема, а центральный экзистенциальный и философский стержень повествования.

Общая характеристика художественного мира Аслана Жаксылыкова

Творчество Аслана Жаксылыкова занимает особое место в казахстанской литературе конца XX — начала XXI века. Его проза отличается философской глубиной, экспериментами с формой и стилем, активным использованием символических и аллегорических образов. В произведениях писателя природа — не просто декорация, а самостоятельная сущность, носитель культурных и метафизических смыслов. Природная среда (особенно воды, степи, горы) выступает в роли зеркала, в котором отражаются внутренние состояния человека, его сознание и подсознание, его духовные искания и заблуждения.

Жаксылыков органично соединяет черты постмодернистской прозы — фрагментарность, полифонию, интертекстуальность — с глубоко национальным мировосприятием. Природа в его текстах всегда многослойна: это и экосистема, и культурный код, и философская категория. Таким образом, его произведения можно с полным основанием рассматривать как образцы постмодернистского экотекста.

Водные ресурсы как символ и мотив в прозе писателя

Особое место в творчестве Жаксылыкова занимают водные мотивы. Вода в его текстах многозначна: она может быть символом жизни и очищения, метафорой памяти, опасности, разрушения или забвения. Этот мотив выполняет не только образную, но и структурообразующую функцию — он объединяет фрагменты повествования, формирует внутреннюю логику текста, наделяет повествование ритуальными, философскими и культурными смыслами.

В рассказах и повестях писателя можно обнаружить разные проявления водной стихии:

- **реки** — как символ времени, истории, течения судьбы;
- **родники и источники** — как образ первозданной чистоты, традиции, родовой памяти;
- **болота и застойные воды** — как метафора застоя, деградации, утраты;
- **дождь, ливень, вода как разрушительная стихия** — как проявление гнева природы, ответ на человеческое вмешательство.

Вода у Жаксылыкова всегда эмоционально заряжена: она говорит с героем, напоминает, предупреждает, очищает или наказывает. Это делает водную тематику важнейшим элементом экотекста, усиливая тревожность, философичность и интроспективность повествования.

Анализ повести «Өзендер қайда ағады?» («Куда текут реки?»)

Повесть «Өзендер қайда ағады?» является ключевым текстом для анализа экологической тематики в творчестве писателя. Уже само название задаёт важнейший философский и экологический вопрос — о направлении, цели и судьбе природных потоков, о том, как эти потоки отражают судьбу народа и самого человека. Это произведение насыщено символами, метафорами и аллюзиями, связанными с водой.

Сюжетное ядро повести — судьба героев, чьё существование тесно связано с рекой, с её изменениями, иссяканием, загрязнением. Река здесь — не только фон, но и участник повествования, своего рода хронист и судья. Она «наблюдает» за человеком, «говорит» через сны, мифы, предчувствия. Герои испытывают чувство утраты, потому что вода — как и память, традиция, честь — уходит, исчезает, становясь бесплотной.

Структурные и художественные особенности повести:

- Фрагментарность и монтажность повествования создают эффект хронотопического расслоения: прошлое, настоящее и будущее сливаются в водной метафоре.
- Повторяющиеся водные образы создают эффект водоворота — времени и памяти, в котором тонут судьбы людей.
- Использование фольклорных элементов и мифологем придаёт повести метафизическую глубину.

Таким образом, «Куда текут реки?» — это не только экологическое высказывание, но и экзистенциальная метафора: автор говорит о катастрофе не только природной, но и духовной, культурной.

Семантика водных образов: метафора, символ, архетип

Одним из ключевых элементов экотекста у Аслана Жаксылыкова являются водные образы, обладающие глубокой семантической нагрузкой. Вода в его текстах — это не просто природная субстанция, а универсальный символ с множеством культурных и философских значений.

На лингвосемантическом уровне водная лексика реализуется в виде:

- метафорических переносов («память текла, как иссякающая река», «время мутное, как вода весной»);
- символических конструкций, в которых река или родник обозначают судьбу, жизнь, движение, очищение;
- архетипических образов, уходящих корнями в традиционные мифы и культурные сценарии (образ «вечной воды», «воды жизни», «речного стража» и т.д.).

Эти образы функционируют как ключевые семантические узлы, формирующие структуру текста, придающие ему ритуальный, мифопоэтический характер. Водная семантика также способствует эмоциональной экспрессии текста, передаёт тревожность, тоску, надежду и покаяние.

Лексико-семантические поля: вода, исток, исчезновение

Лексико-семантические поля, связанные с водной тематикой, в произведениях Жаксылыкова отличаются высокой частотностью и смысловой насыщенностью. Ключевые семантические кластеры:

- Поле «вода»: су, өзен, бұлақ, тамшы, тасқын, теңіз, жауын;
- Поле «движение/изменение»: ағады, жоғалады, сорғалайды, шайып кетеді, сарқылады;
- Поле «исчезновение/утрата»: жоқ болды, тартылды, құрғады, өшті, буланды.

Особое внимание заслуживает словоупотребление с глаголами исчезновения: «өзен жоғалды», «бұлақ сарқылды», «су буланып кетті» — эти конструкции несут не только фактический, но и метафорический смысл, говоря о потере не только водных ресурсов, но и культурных корней, духовной связи с землёй.

Такой подход позволяет рассматривать экотексты писателя как высокоорганизованные лингвосемантические системы, в которых экологическая проблематика выражена средствами языка глубоко и многослойно.

Языковые средства создания экологического дискурса

Анализ речевых стратегий Аслана Жаксылыкова показывает, что он использует широкий спектр языковых средств для создания экологически заряженного дискурса:

- **Эмоционально-оценочные эпитеты** («сарқылған өзен», «у дауысты су», «мұңды бұлақ») усиливают трагизм описания.
- **Аллюзии на народные поверья и легенды** (образ «бұлақ иесі», «су перісі», «су аруағы») связывают природные явления с культурной памятью.
- **Синтаксические повторы и параллелизмы** придают тексту ритмичность, близкую к заклинанию или молитве.
- **Контекстуальные антонимы** («су – құрғақ», «ағыс – тоқырау») акцентируют контрасты между жизнью и смертью природы.

Таким образом, языковая организация экотекстов у Жаксылыкова направлена на создание сильного эмоционального и этического воздействия на читателя. Его тексты призывают не только к размышлению, но и к внутреннему отклику, к экологическому сознанию.

Заключение

Исследование экотекстов Аслана Жаксылыкова, в частности произведений, связанных с водной тематикой, позволяет сделать несколько значимых выводов как в теоретическом, так и в прикладном аспектах:

1. **Экотематика** в творчестве Жаксылыкова — не вспомогательная, а **системообразующая категория**, в которой природа выступает не только как среда действия, но как равноправный участник повествования, духовный и культурный субъект.
2. **Водные образы** функционируют как универсальные символы, охватывающие сферу личного, социального и космического. Через них писатель выражает тревогу за судьбу земли, народа, культуры, самого человека.
3. **Лингвосемантический анализ** показывает, что экологическая проблематика реализуется через тонко организованную систему водной лексики, мифопоэтических мотивов, стилистических приёмов и культурных аллюзий. Это подтверждает, что тексты Жаксылыкова представляют собой подлинные **экологические послания**, направленные не только на констатацию проблемы, но и на её этическое переосмысление.
4. **Постмодернистская форма** не ослабляет, а напротив — усиливает влияние экотекста на читателя, предлагая ему интерпретативную свободу, диалогичность и включённость.

Таким образом, произведения Аслана Жаксылыкова представляют собой уникальное явление в казахстанской литературе, где художественное, экологическое и философское сплетаются в единую текстовую ткань. Его экотексты — это не просто литературные произведения, а **экологическое мышление в художественной форме**, способное формировать новое мировоззрение, основанное на гармонии, памяти и ответственности.

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Political Studies

Трансшекаралық өзендер дипломатиясы: Қазақстан және Қытай

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Аннотация

Мақалада Қазақстан мен Қытай арасындағы трансшекаралық өзендерді бірігіп пайдалану мәселесінің қазіргі жағдайы, келісімдік-құқықтық негізі және екі ел арасында осы өзендерге қатысты атқарылып жатқан жұмыстар мен проблемалық мәселелер қарастырылған. Зерттеуде траншекаралық өзендерге қатысты екі мемлекеттің ұстанымдары талданып, қазіргі кезде жүргізіліп жатқан келіссөздердің нәтижесі жан-жақты пайымдалған. Екі елдің арасында осы мәселеге қатысты атқарылып жатқан нақты жұмыстар легі ашып көрсетілген. Сонымен бірге екі мемлекет арасында ең ірі өзендерге қатысты келісім шарттардың осы уақытқа дейін жасалмай отырған себептері талданып, Қытайдың өзінің Шыңжаң-Ұйғыр ауданын дамытуға арналған Стратегиясын жүзеге асыруға байланысты келісімге келуді созып жібергені, Қазақстан жағы өз экономикасында өзен суларын үнемдеудің жаңартылған технологиясын шаруашылыққа енгізіп жатқандығы туралы пайымдаулар жасалған.

Кілт сөздер: Траншекаралық өзендер, Қазақстан-Қытай диплломатиясы, Ертіс және Іле өзендері, Қорғас және Сүмбе өзендері, Бірлескен комиссия.

Қазіргі әлемде халықты сумен қамтамасыз ету мәселесі ең өзекті мәселе болып отырғаны анық. Сарапшылардың пікірінше, болашақта мемлекеттер арасында көмірсутегі ресурстары үшін емес, адамзатқа қажетті су ресурстары үшін талас күшеюі мүмкін. Сондықтан Қазақстан дипломатиясы үшін елімізді су көздерімен қамтамасыз етіп отырған траншекаралық өзендер мәселесін құқықтық негізде шешуді ұйымдастыру кезек күттірмейтін өзекті мәселе екендігі белгілі. Себебі географиялық орналасу жағдайына байланысты Қазақстан өзін су ресурстарымен табиғи жолмен 56 пайыз қамтамасыз ете алады. Ал қалған 44 пайыз су ресурстары көрші елдерден ағып келетін тарнсшекаралық су көздерінен алынады. Соның ішінде еліміздің саясатында Қытай мемлекетімен екі арадағы өзен сулары өте маңызды орын алады. Осы бағытта қазақстан дипломатиясы ұзақ жылдар бойы бір бағытты, сындарлы, табанды жұмыс жасап келе жатқандығын атап өтсе болады.

Осы уақытқа дейін трансшекаралық өзендер мәселесі екі жақты дипломатияда мемлекет басшыларының жоғарғы деңгейінде, парламент, министрліктер мен ведомстволар арасында үздіксіз маңызды мәселе ретінде көтеріліп келеді. Осы мәселеге қатысты екі мемлекет арасында келіссөздер басталғанда тараптар екі елдің арасында 20-дан астам ірі трансшекаралық өзендер бар екендігі және соларды бірігіп пайдалануды келісу керектігін белгілен болатын.

Осы ретте Қытай мен екі арадағы траншекаралық өзендер мәселесінің біздің еліміздің сыртқы саясатындағы басты мәселе болуының бірнеше себептері бар екендігін атап өткіміз келеді.

Біріншіден, Қытайдан Қазақстанға ірілі-ұсақты мыңнан астам өзеннің ағып келетіндігі және олардың 23-і ірі өзендердің болуы. Бұл ретте Тянь-Шань, Алтай тауларының биік бөлігі Қытай жағында орналасқандықтан және өзендердің бастауы сол жерден басталатындықтан Қазақстан жағы осы мәселеде Қытай жағына тәуелді жағдайда болып отыр. Өйткені осы өзендер Қазақстанның экономикалық жағдайында үлкен орын алып отырған су ресурстары болып табылады. Осыған байланысты Қазақстан дипломатиясының алдында тұрған маңызды мәселе - халықаралық құқық нормаларына сүйене отырып осы мәселені заңды түрде реттеу болып отыр.

Екіншіден, Қазақстан жағын алаңдататын жағдай, 90-шы жылдардан былайғы уақытта Қытай басшылығының біздің елмен іргелес жатқан Шыңжаң-Ұйғыр автономиялы өлкесіне үлкен назар аудырып, ол өңірді өте тез жылдамдықпен дамытуға деген ұмтылысы болып отыр. Оның дәлелі 2000 жылдардың басында Қытай басшылығы осы өңірді игерудің 2050 жылға дейін арналған арнайы «Батыстың үлкен дамуы» Стратегиясын қабылдауы десек болады.

Қабылданған бұл Стратегия 2050 жылға дейін қойылған мақсаттарға қол жеткізуді үш кезеңге бөліп жүзеге асыруды көздеп отыр. Бірінші кезең (2001-2010 жылдар) қазіргі күні іске асырылды. Соның арқасында Қытайдың батыс провинцияларын бастапқы индустрияландыруға және орташа жылдық ЖІӨ 10% өсуіне әкелді. Екінші кезеңде (2010-2030 жылдар) өңірде өнеркәсіптің жаңғыруына басымдық берілуде. Үшінші кезеңде (2050 жылға дейін) өңірде ғылым мен техниканың соңғы жетістіктерін пайдалан отырып, жоғары деңгейдегі заманауи өндіріс орындарын құруды көздейді [1].

Көріп отырғанымыздай бұл стратегияны жүзеге асыру аталған өңірге ішкергі аймақтан халықтарды қоныстандыру және осы аймақты ірі өндіріс орталығына айналдыруды мақсат етіп отыр. Ал мұның өзі трансшекаралық өзендердің суын аймақ экономикасына кеңірек пайдалануды тудыратын жағдай екені белгілі.

Үшіншіден, кейінгі кезде Шыңжаң-Ұйғыр автономиялы облысының әлеуметтік-экономикалық жағынан белсенді дамуы өзен суларын ауыл шаруашылығына, өндіріске және көбейіп жатқан халықтың тұрмысына көбірек пайдалану қажеттігін тудырып отыр. Қытай жағы осы өзендерде бөгеттер салып, су қоймаларын жасап және суды бұру құрылыстарын т.б. жүргізуде. Сонымен бірге кейінгі кезде осы аймақтағы Қарамай жерінде көмірсутегі кенінің ашылуы және оны жылдамдата игеру жұмыстарына трансшекаралық өзен суларын кеңінен пайдалануы біздің елімізді алаңдатып отырғаны анық. Осы себепті Қазақстан жағында траншекаралық өзендердің суы азайып кетпей ме, елді сумен қамтамасыз ету жағдайына қатер төнбей ме деген қауіп күшеюде.

Осыған байланысты Қазақстан басшылығы Қытаймен екі арадағы траншекаралық өзендер мәселесін шешу бағытында табанды түрде келіссөз жүргізіп келе жатыр. Сарапшылардың пікірінше Қытай тек Қазақстанмен ғана өзен суларын ортақ пайдалануға қатысты келіссөздер жүргізуде дейді. Негізінен Қытай трансшекаралық өзендерді елдердің өзара бірігіп пайдалануын құқықтық негізде реттейтін «Траншекарлық су ағындарын және халықаралық көлдерді қорғау және пайдалану туралы» 1992 жылғы Конвенцияға және 1997 жылғы «Халықаралық су ағындарын пайдалану құқығы туралы» халықаралық Конвенцияларға қол қоймаған елдердің бірі.

Бізді алаңдататын мәселе - осы екі елдің арасындағы трансшекаралық өзендердің қазіргі жағдайы мен осы бағытта жүргізіліп жатқан дипломатиялық келіссөздер және атқарылып жатқан іс-шаралардың барысы, нәтижесі болып отыр. Сондықтан мақалада Қазақстан мен Қытай арасында траншекаралық өзендерге қатысты мәселе қалай шешілуде, оның құқықтық базасы және екі ел арасында осы мәселеге қатысты қандай іс-шараларға қол жеткізілді, оның тиімділігі, нәтижесі және оның болашағы қандай деген сұрақтар төңірегінде

зерттеу жүргізіп, осы бағыттағы қазақстан дипломатиясының жұмысының нәтижесін анықтау және бағалау болып табылады.

Қазақстан мен Қытай мемлекеттері арасындағы трансшекаралық өзендерді бірігіп пайдаланудың құқықтық-келісімдік жағдайы.

Өзімізге белгілі Қазақстан мен Қытай арасында траншекаралық өзендерге қатысты келіссөздер ресми негізде тұрақты түрде 1998 жылдан бастап жүргізіліп келеді. Екі ел траншекаралық өзендерді бірігіп пайдаланудың құқықтық негізін біртіндеп келісіп жүзеге асыруда. Ұзақ келіссөздердің нәтижесінде қол жеткен алғашқы негізгі келісім шарттардың бірі 2001 жылы қыркүйек айында «Қазақстан Республикасы Үкіметі мен Қытай Халық Республикасы Үкіметі арасында трансшекаралық өзендерді пайдалану және қорғау саласындағы ынтымақтастық туралы» 14 баптан тұратын Келісімге қол қойылуы болды. Бұл қазақстан дипломатиясының жұмысының бір нәтижесі және екі жақты су мәселесін шешудің негізгі құқықтық шартының бірі деп білуге болады. Аталған Келісімнің 5-ші бабында су мөлшері мен сапасын бақылау, табиғи апаттардың алдын алу сияқты міндеттемелер белгіленген. Сонымен бірге маңыздысы - келісімде осы қызметтерді атқару үшін Бірлескен комиссия құрылатындығы және оның мәжілісі жыл сайын өткізіп отыру келісілген [2].

Дегенмен, бұл келісім екі елдің арасындағы траншекаралық өзендер мәселесінің негізгі деген сұрақтарын шешкен жоқ, сонда да ең маңыздысы, екі елдің министрліктері мен ведомстволары арасында траншекаралық өзендер мәселесін тұрақты түрде қарастырып, белгілі бір дәрежеде нақты келісімдерге қол жеткізуге үлкен мүмкіндік тудырды және осы мәселені құықтық негізде шешуге жол ашты десе болады. Тағы бір маңызды жағдай Келісімде атап көрсетілген Қазақстан-Қытай Бірлескен комиссия кейіннен құрылып, 2003 жылдан бастап жұмыс істей бастады. Бірлескен Комиссияның құрамында трансшекаралық өзендердің техникалық және ғылыми мәселелерін анықтаумен айналысатын сарапшылар тобы да жұмыс жасайды.

Оның бірінші мәжілісі 2003 жылы 31 қазанда Пекин қаласында өтті. Онда Бірлескен Комиссияның қызметі туралы Ереже қабылданды және келесі жылға жұмыс жоспары келісілді. Одан кейін де комиссияның мәжілісі жыл сайын өткізіліп отырды. Бірлескен комиссияның жұмысының нәтижесінде бірнеше келісімдерге қол жеткізілгенін және бірқатар нақты шаралар жүзеге асырылғанын атап өтуге болады. 2020 жылғай дейін Бірлескен комиссияның 17 мәжілісі және эксперттік жұмысшы топтың 16 кездесуі өткізілген [3]. 2008 жылы 31 қазанда Бірлескен комиссия ҚР-ҚХР Ынтымақтастық комитетінің құрамына енгізілген болатын.

Осы мәселеге қатысты тағы бір маңызды құжат - 2011 жылы ақпан айында Пекин қаласында қол қойылған екі елдің арасында «Қазақстан Республикасы Үкіметі мен Қытай Халық Республикасы Үкіметі арасында трансшекаралық өзендердің су сапасын қорғау туралы» Келісім болып табылады. Мұның өзі жұмыс топтарының екі елдің де жағалық жердегі өндірістік орындардың зиянды қалдықтарынан өзен суларының құрамы өзгеріп, сапасы нашарлауы мүмкін деген қорытындыларынан кейін қол жеткізілген жетістік болды.

Сол 2011 жылы тағы да бір Келісімге қол қойылды, яғни екі елдің арасында өзендер ағып өтетін аудандардың экологиясын жақсарту бағытында «Қазақстан Республикасы Үкіметі мен Қытай Халық Республикасы Үкіметі арасында қоршаған ортаны қорғау саласындағы ынтымақтастық туралы» Келісім де екі елдің өзен суларына қатысты өзара ынтымақтастықты жалғастыруға дайын екендігін көрсетті.

Сонымен бірге екі елдің министрліктері арасында да траншекаралық өзендердегі табиға апаттар туралы тараптарды төтенше жағдайда хабардар ету (2005 ж.), осы өзендер бойынша ғылыми-зерттеу жұмыстарын жүргізу бағытында ынтымақтастықты дамыту (2006 ж.) және ірі трансшекаралық өзендердің шекаралық бақылау бекеттерінің гидрологиялық және гидрохимиялық құрамы туралы ақпаратты өзара алмасу туралы (2006 ж.) Келісімдер

жасалған. Бұл келісімдердің жасалуы траншекаралық өзендерді бірігіп пайдалану бағытындағы айтарлықтай жетістік деп айтуға келеді.

Жоғарыда көрсетілген келісімдер екі елдің арасындағы трансшекаралық өзендер мәселесін толықтай шешкен жоқ, дегенмен осы мәселені шешуге жасалған дайындық, басты қадамдар болып табылады деп білеміз. Бұл жағдай екі жақтың да өзендер суы мәселесін бірігіп шешуге ниетті екендігінің көрінісі десек те болады.

Осыған байланысты екі жақты қатынастардың даму барысында байқалған тенденция осы келісімдердің негізінде Қазақстан мен Қытай арасындағы траншекаралық өзендерге қатысты нақты іс-шаралардың біртіндеп жүзеге асырылуы болып табылады. 2003 жылы құрылған Бірлескен комиссияның 2015 жылғы дейінгі аралықта 13 мәжілісі өткізіліп, бірқатар шаралар жүзеге асырылған. Атап айтқанда, осы Бірлескен комиссия аясында бірнеше жұмыс топтары құрылған: бірінші топ 2003 жылы құрылған сарапшылар тобы, екіншісі 2002 жылы құрылған Қорғас өзені суларын бөлу бойынша бақылау комиссиясы, үшіншісі Сүмбе және Қайшыбұлақ өзендерінің суын пайдалану мен жинау бойынша тұрақты су комиссиясы (2008), төртінші топ трансшекаралық өзендерде су бөлу бойынша техникалық жұмыстарды іске асырушылар тобы (2010), бесіншісі Достық су торабын пайдалану бойынша біріккен қызмет тобы (2013) және алтыншысы 2014 жылы құрылған су бөлу туралы келісім жобасын дайындау бойынша Арнайы жұмыс тобы.

Сонымен бірге Қазақстанның Сыртқы істер министрілігінің мәліметі бойынша Бірлескен комиссияның шеңберінде трансшекаралық өзендердің гидрологиялық және гидрохимиялық мәліметтермен алмасу жұмыстары келесі су бекеттері бойынша жүргізіледі:

- Ертіс өзенінде – Боран (ҚР) – Наньвань (ҚХР) гидро бекеттері;
- Іле өзенінде - Добын (ҚР) – Саньдаохэцзы (ҚХР) гидро бекеттері;
- Текес өзенінде - Текес (ҚР) – Цзефандацяо (ҚХР) гидро бекеттері [4].

Осы аталған шаралар екі мемлекеттің арасында тек келісімдер ғана жасалып қоймай, біртіндеп екі аралықтағы өзендер суларын біріге отырып игерудің механизмі қалыптаса бастағанын көрсетеді.Трансшекаралық өзендердің су ресурстарын қорғау мәселесі, сондай-ақ ҚР-ҚХР Қоршаған ортаны қорғау саласындағы ынтымақтастық жөніндегі комиссиясы қызметінің шеңберінде де қарастырылады.

Осының өзі екі ел арасында өзендер бойынша нақты жұмыс жүріп жатқандығының айғағы болып табылады. Екі мемелекет арасындағы қол қойылған құжаттар трансшекаралық өзендер суларын пайдалану бағытындағы нақты қадамдар болып табылады. Дегенмен, Қазақстан жағы әсіресе, ірі деп саналатын Ертіс пен Іле өзені бойынша келісімге келу бағытында тынбай жұмыс жасап келеді. Бүгінгі күні Ертіс өзенінің су көлемінің азаюы және Іле өзенінің де суы тартыла бастағаны, ал оның суы азайса Балқаш көлі апатқа ұшырайтыны туралы баспасөз беттерінде жариялануда. Сондықтан екі мемлекет арасында ірі өзендер бойынша келіссөздер жасалып келісімге келу аймақтық қауіпсіздікке қосылар үлкен үлес болар еді.

Осы ретте назар аударатын мәселе 2015 жылдан бастап екі елдің арасында Ертіс пен Іле өзендерінің суларын ортақ пайдалануға қатысты Келісім жобасын әзірлеу жұмысы жүргізілуде екендігі. Қазақстан жағының мәлімдеуінші бүгінгі күні 31 баптан тұратын Келісімнің жобасы дайындалған, енді әрбір баптары бойынша қайтадан қарап, нақтылау жұмыстары жүргізілуде [5].

Сонымен, жоғарыда айтылғандарды зерделесек, екі мемлекеттің арасында трансшекаралық өзендерді өзара келісіп пайдаланудың келісімдік-құқықтық базасының іргесі қаланғанын көреміз. Ендігі жерде бұл құқықтық негізді одан әрі күшейтіп, негізгі деген су ресурстары бойынша нақты келісімдердің жасалуы екі ел үшін де, аймақ үшін де маңызды жағдай болар еді.

Келесі кезекте екі елдің арасында құрылған Бірлескен комиссия мен жұмыс топтары осыған дейін нақты қандай жұмыстарды жүзеге асырғаны туралы сұрақ туындауы орынды, енді осы мәселені анықтасақ.

Қазақстан-Қытай арасындағы траншекаралық өзендерге қатысты жүргізіліп жатқан жұмыстардың нәтижесі.

Қазақстан жағын алаңдатып отырған жағдай Қытайдың әсіресе Ертіс және Іле өзендеріне қатысты жүргізіп жатқан шаралары. Бүгінгі күні Қытай Қара Ертіс-Қарамай және Қара Ертіс-Үрімжі каналдарын салып, Ертіс өзенінің су ресурсын аймақтағы өндірісті дамытуға пайдалануды жүзеге асырып жатыр. Сонымен бірге қазіргі кезде Қытай Іле өзенінде 13 су қоймасын және 59 гидроқондырғыларды орналастырып оның суын кеңінен пайдалануда [6].

Осының бәрі Қазақстан үшін елді сумен қаматамсыз ету, су ресурстарына қатысты қауіпсіздікті сақтау бағытында үнемі жұмыс жасауға итермелеп отырған көрсеткіш.

Жоғарыда атап өткендей осы уақытқа дейін екі елдің арасында трансшекаралық өзендерге қатысты келіссөздер тоқтаған жоқ және Бірлескен комиссия тұрақты түрде жұмыс жасауда. Екі жақтың осы уақытқа дейін нақты жүзеге асырған шаралары келесідей болып табылады.

Екі жақты комиссия мен жұмыс топтарының ең басты қол жеткен жетістіктері - ол 2013 жылы Қорғас өзені бойынша және 2022 жылы Сүмбе өзенінін бірігіп пайдалану бойынша қол жеткен келісімдер мен осы өзендерде нақты қойылған гидротехникалық қондырғылар болды. Қорғас өзеніндегі бірлескен «Достық» гидроқондырғыны басқару және пайдалану туралы Үкіметаралық келісімге 2013 жылдың қыркүйек айында қол қойылған болатын. Ал Сүмбе өзеніндегі гидроқұрылым 2019 жылы салынып бітті, ал оны ортақ пайдалану туралы келісімге 2022 жылы қол жеткізілді.

Бүгінгі күні Қорғас өзенінде де, Сүмбе өзенінде де Қытай жағымен келісе отырып арнайы гидротехникалық құрылыс - шлюздер салынған. Бұл шлюздер автоматты түрде жұмыс жасайды және өзеннің суын екі елге бірдей пайдаланатындай етіп бөліп беріп отыр. Бұл шлюздердің тиімділігі сондай, егерде бір ел өзеннен алатын судың мөлшерін өзгерткенде, ол су екінші жаққа да сол мөлшерде бөлінеді. Сонымен бірге ендігі кезекте осындай қондырғыны Шығыс Қазақстан облысына ағып келетін Үлкен Үласты өзеніне орнату туралы келісім бар, ол да біртіндеп жүзеге асады деген ойдамыз [7].

Әрине мұндай жетістіктерге қол жеткізу оңай болған жоқ. Екі жақ та бұл мәселеде мүдделі болғандықтан және ұзақ келіссөздер жүргізу барысында бұл жұмыстарды жүзеге асыруға қол жеткізілді.

Сонымен бірге қазіргі кезде Бірлескен комиссия мен жұмыс топтарының өзара әрекеттесуінің нәтижесінде келесі өзендердегі гидро бекеттердің мәліметтері бойынша екі ел өзендердің гидрогеологиялық және гидро химиялық жағдайы туралы бір-бірімен мәліметтер алмасуды жолға қойған. Атап айтқанда, Ертіс өзеніндегі Қазақстан жағының Боран және Қытай жағындағы Наньвань гидро бекеттері арасында, Іле өзеніндегі қазақстандық Добын және Қытайдың Сандаохези, Текес өзеніндегі қазақстандық Текес пен қытайлық Цзефандацяо бекеттері арасында судың құрамы туралы мәліметтер алмасу нақты жүргізілуде [7].

Осының өзі Қытаймен екі арада тек келісім шарттар ғана жасалып қоймай, нақты жұмыстар жүргізіліп жатқанының айғағы. Екі жақты комиссия және жұмыс топтары үздіксіз осы бағытта жұмыс жасап жатқанынының көрсеткіші. Келесі кезекте Қазақстан жағы Іле-Балқаш су бассейні бойынша Қытаймен екі арадағы траншекаралық өзендер мәселесін осындай құқықтық негізде шешуді алдына мақсат етіп отыр. Өйткені бұл бассейнде еліміздің территориясына ағып келетін Ертіс және Іле сияқты маңызды өзендер бар. Іле өзені Балқаш

көлінің 70 пайыз су қорын қамтамасыз ететін болса, Ертіс өзені бойында еліміздің Өскемен, Павлодар, Қарағанды сияқты өндірістік орындары орналасқан.

Екі ел арасындағы осы өзендер суын бөлісу туралы келіссөздер 2013 жылы қыркүйек айында Қытайдың төрағасы Си Цзинпиннің Қазақстанға келген мемлекеттік сапарынан бастап жаңадан жандана бастады. Осы сапар барысында Қытай басшысы осы мәселені арнайы екі жақты комиссия 2015 жылдан бастап зерттеп, қосымша келісімнің жобасын дайындауы керек екендігіне келісті. Осыған байланысты сол кезде арнайы комиссия құрылып жұмыс жасай бастады және 2024 жылға дейін осы комиссияның 17 отырысы өткені белгілі болды. Екі ел арасындағы осы өзендердің суын пайдалануды шешуге арналған жоба әлі күнге дейін талқылануда. Жоба кіріспеден және 31 баптан тұрады.

Осы мәселе бойынша 2024 жылы қараша айында Қазақстанның су ресурстары және ирригация министрлігінің басшысы Н.Нұржігітов Қазақстандағы Қытайдың Төтенше және Өкілетті Елшісі Чжан Сяомен кездесті. Осы кездесуде министр Н.Нұржігітов Іле-Балқаш су бассейні бойынша өзен суларын бірігіп пайдалану, балық аулау ісі мен аумақтың экологиясын сақтау, туризмді дамыту мәселесін көтере отырып, осы жағдайға қазақстан жағы ерекше мән бертінін атап өтті. Қытай дипломаты Қазақстан жағындағы мамандарды егістік жерлерді суарудың жаңа, үнемді технологияларымен таныстырып, үйрету үшін білім көтеру, тәжірибе алмасу ісін ұйымдастыруға дайын екендіктерін білдірді. Өз кезегінде Министр қазіргі кезде қытайдың Power China компаниясымен қазақстан мамандарын біліктілік курстарынан өткізу туралы келісім бар екенін атап өтті [8].

Осы себепті екі елдің арасында қол жеткізілген тағы бір үлкен жұмыс – Қытай жағының қазақстандық мамандарды суды үнемдеп қолданатын технологияларды игеру үшін біліктілікті көтеру курстарын өткізуінде. Қытай жағы үнемі су ресурстарын егістікті суаруда жаңа жетілдірілген технологиялық құрылғыларды қолдана отырып суаруды ұсынып келеді. Бұл әрі суды үнемдеп пайдалануға әсерін тигізетін тәсіл.

Осыған байланысты екі жақты келіссөздер барысында қытай жағы осы мәселеге басты назар аударып келді. Осы әрекеттің нәтижесі ретінде 2026 жылдан бастап қазақстандық су шаруашылығы мамандарының Қытайға барып біліктілікті көтеру курстарынан өтуі болып отырғандығын атап өткіміз келеді. Бұл да екі жақты өзендерге қатысты атқарылып жатқан дұрыс шаралардың бірі деп пайымдауға болады.

Деректерге қарағанда осы жылдың мамыр айында қазақстандық су шаруашылығы мамандарының алғашқы тобы Қытайдың су ресурстарын басқару жүйелерін жоспарлау және енгізу тәжірибесімен, сондай-ақ кешенді су ортасын жақсарту технологияларымен танысу үшін Қытайға семинарға барды. Семинар «Қазсу шаруашылығы» мемлекеттік кәсіпорны мен Power China International Group Limited арасындағы өзара түсіністік және ынтымақтастық туралы меморандум, сондай-ақ Қазақстан Республикасы Су ресурстары және суару министрлігі және Қытай Халық Республикасының Су ресурстары министрлігі арасындағы өзара түсіністік және ынтымақтастық туралы меморандум аясында ұйымдастырылған. Барлық шығындарды Қытай тарапы көтерді. Жалпы алғанда, осы жылдың соңына дейін шамамен 200 адам Қытайда оқудан өтетін көрінеді [9].

Жоғарыдағы айтылғандарды нәтижелесек, Қазақстан мен Қытай арасында трансшекаралық өзендерге қатысты бірқатар нақты шаралардың жүзеге асырылып жатқанын көреміз. Екі елдің арасында осы жұмыс тоқтамай, барлық өзендер бойынша келісімдер жасалып, өзен суларын екі жаққа да тиімді пайдалану тетігі қалыптасатынына үмітіміз зор.

Қытайдың өзендерге қатысты саясаты.

Қытай жағы траншекаралық өзендер мәселесін, әсіресе бізге ең қажетті Ертіс және Іле өзендері бойынша келіссөздерді ұзартып отыр. Жоғарыда атап өткеніміздей, кейінгі кезде Қытай Шыңжаң-Ұйғыр автономиялы облысын дамытуға арнайы Стратегия әзірледі

және оның белгілеген жоспар бойынша кезең-кезеңімен жүзеге асырып жатыр. Стратегияда белгілегендей осы аймақтағы қытай халқының санын көбейтуді жоспарлап, оны біртіндеп жүзеге асыруда. Өзімізге белгілі КСРО ыдырағанға дейін бұл аймақ халқының негізінен қазақ, ұйғыр, дүнген және қырғыз ұлттары құраған болатын. КСРО-ның ыдырауы ұйғырлардың бұл өлкеде өзінің мемлекетін құруға деген қозғалысын белсендірді. Бұл әрине Қытай үкіметін алаңдатып, Шыңжаң өлкесіне ерекше назар аудару қажеттігін тудырды. Екінші назар аударатын жағдай кейінгі кезде Шыңжаң өлкесіне іргелес жатқан Ауғанстандағы саяси тұрақсыздық жағдайы болып отыр. Бұл жағдай Қытайдың ол жақтан мұсылмандық экстремистік, сепаратистік топтардың жергілікті мұсылман халқына ықпал етіп, бұл аймақта тұрақсыздық жағдайын тудыруы мүмкін деген қауіпін ұлғайтты. Мұның салдары қытай басшылығының бұл аймаққа ерекше назар аударып, арнайы Стратегия қабылдап, бұл аймақты кеңінен игеріп, қадағалап отыру керектігін күшейтті.

Сонымен бірге кейінгі кезде Шыңжаң өлкесінде Қарамай деген жерде көмірсутегі кен орындары табылуы бұл өңірді қытай жағының кеңінен игеріп, жандандыруға деген ұмтылысын тудырды. Осыған байланысты бұл ауданда логистикалық құрылымдар салынып, ішкергі өңірден мамандарды, жұмысшыларды қоныс аудартып бұл аумақты өндірісті өңірге айналдыру жұмыстары қарқынды жүргізілуде. Ал мұның өзі онсыз да су жағынан тапшы аймаққа траншекаралық өзендерді кеңінен пайдалануға деген ұмтылыстарын тудырып отырғаны сөзсіз.

Осы қарқынмен 2005 жылы Қытай көмірсутегін молынан игеру мақсатында Қарамай жерінде ұзындығы 300 км. қамтитын Қара Ертіс-Қарамай суару каналын салып бітірді. Ертістің жылдық ағыны 7-9 м/куб болса, осы канал арқылы қытай жағы Ертіс өзенінен жылына 1 м/куб алып отыр. Эксперттердің пікірінше болашақта қытай жағы 5м/кубқа дейін алуы мүмкін. Одан басқа олар Іле өзенінің бойында 15 су қоймасы мен 59 су электр станциясын орнатқан және сол арқылы жыл сайын өзен суының 15 текше шақырымын алып отыр [10].

Осындай жағдайда Қытайдың бұл ісіне Ресей алаңдатушылық нотасын жіберсе, біздің еліміз 2009 жылы БҰҰ Бас Ассамблеясының 64-ші сессиясында Ертіс өзені мәселесін бүкіл әлемдік деңгейде көтерді. Өйткені дәл осы сессияда көптеген экологиялық мәселелер қаралған болатын.

Ресей зерттеушісі В.Прохватиловтың пайымдауынша Қытай жағы Шыңжаң өлкесіндегі халықтың санын қазіргі 20 миллионнан 100 миллионға жеткізуді көздеп отыр дейді. Сонымен бірге Қытай бұл аймақты игеруде 1999 жылдан «Батысқа барамыз», 2013 жылдан «Жібек жолының экономикалық белдеуі» жобаларын жүзеге асырып келеді.

Қарамай кен орнын игеру және Шыңжаң өлкесін сепараттық қақтығыстардан сақтау үшін Қытай басшылығы бұл аймақты игерудің барлық шараларын жасап, көлемді жобаларды жүзеге асыруға тырысып жатыр. Осыған байланысты Қазақстанмен екі арадағы трансшекаралық өзендерді пайдалануды реттеу мәселесін асықпай шешуде. Осыған байланысты сарапшылардың көбі Шыңжаң өлкесіндегі саяси, экономикалық және әлеуметтік жағдайды біршама реттеп алмай, Қытай жағы трансшекаралық өзендер туралы нақты келісімдерге әлі де болса келе қоймайма деген ойда.

Осы мәселедегі Қазақстанның ұстанымы.

Қазақстан жағы траншекаралық өзендер мәселесінде Қытайға тәуелді жағдайда болғандықтан, бұл мәселені өзара келіссөздер нәтижесінде және құқықтық негізде шешуді көздейді. Оның нәтижесі жоғарыда айтылған келісім шарттар, Бірлескен комиссияның және жұмыс топтарының құрылуы және бірқатар жүзеге асқан шаралардан көрінеді.

Бүгінгі күнге дейін өз тарапынан Қазақстан жағы суды үнемдеп жұмсау бағытында ауыл шаруашылығы болсын, өндіріс орындары болсын қажетті техника мен технологияларды енгізуде. Оның нәтижесінде тамшылатып және жаңбырлатып суару сияқты

заманауи технологиялар бүгінде-ақ су шығынын 50%-ға дейін азайтып, сонымен қатар өнімділікті арттыруға мүмкіндік беріп отыр, бірақ оларды кең көлемде енгізу жұмыстарын жеделдету қажеттігі анық. Сонымен бірге биылғы жылдан бастап суды үнемдеп жұмсау технологиясын меңгеру үшін қазақстандық су шаруашылығы мамандары Қытайда арнайы курстарды өтуде.

Тағы бір назар аударатын жағдай Ертіс және Іле сияқты өзендерді бірігіп пайдалану бойынша Қазақстан жағы 31 баптан тұратын Келісімнің жобасын дайындап Қытай жағына ұсынған болатын, келісім жобасын талқылау баяу да болса жүргізілуде. Ертіс өзені бойынша келісім жасау үдерісіне қазақстандықтар Ресей жағын да қосқысы келеді. Өйткені аталған проблемалар бұл елге де қатысты болып отыр.

Қытайдың трансшекаралық су мәселесін шешудегі уақытты созуы, Қазақстанды біртабан шешімдерді қабылдауына алып келіп отыр. Атап айтқанда, 1 млрд. АҚШ долларына бағаланатын Ақ – Қабы және Қара – Қабы өзендерін басқа арнаға бұрып алу жобасы кеңінен зерттелуде. Аталған өзендерге тоннель жүргізу арқылы шекараға жеткізбей бұрып алу және де Қазақстан территориясындағы Ертіс өзеніне бағыттау мәселесі қарастырылуда.

Ескере кететін жағдай Қазақстан мен Қытай арасында 2001 жылы жасалған келісімнің 4-ші бабында: тараптардың ешқайсы өзара мүдделерді ескере отырып, екінші тарапқа трансшекаралық өзендердің су ресурстарын ұтымды пайдалану мен қорғауды шектемейді – деп жазылған. Осы бабқа сүйенсек, Іле және Ертіс өзендері Қытайдың территориясынан басталатындықтан, Қазақстан аталған өзендердегі Қытайдың су бөлу жоспарларына кедергі келтіре алмайтын болып шығады. Осының өзі Қытай жағына екі ел арасындағы өзен суларын еркін пайдалануға мүмкіндік бермей ме? – деген сұрақ тууы орынды.

Қазақстан 2007 жылы келісімшарт бойынша азық-түлікті жеңілдіктермен траншекаралық өзердер арқылы, бірінші кезекте, Ертіс және Іле трансшекаралық өзендері арқылы тасымалдауды Қытайға ұсынды. Ондағы мақсаты егер Қытай жағы келіссе, Ертіс және Іле өзендерімен жүк тасымалы жүзеге асырылатын болса, екі өзеннің де суының деңгейі бірқалыпты болуына Қытай жағы да мүдделі болар еді. Алайда Қытай елі бұл ұсынысқа әзірге қолдау көрсете қойған жоқ.

2025 жылы қыркүйек айында Қытайда өткен Шанхай Ынтымақтастық Ұйымының мәжілісінде біздің еліміздің Президенті Қасым-Жомарт Тоқаев осы Ұйымның аясында Су ресурстарын зерттеу Орталығын құруды ұсынды. «Климат өзгерісі шекара таңдамай, әлемнің көптеген елі мен өңіріне қауіп төндіріп отыр. Нақты қатерлерге, мәселен, шөлейттенуге, құрғақшылыққа, су қоймаларының тартылуына, мұздықтардың еруіне және басқа да экологиялық мәселелерге қарсы күрес стратегиясын бірлесіп әзірлеу өзекті. Сондықтан Қазақстанда ШЫҰ-ның Су мәселелерін зерттеу орталығын ашуды қолдаймыз» – деді Қасым-Жомарт Тоқаев [11]. Осының бәрі Қазақстан жағының екі ел арасындағы өзендер мәселесін шешудің әр түрлі жолдарын жан-жақты қарастырып жатқандығының көрінісі болып табылады. Осындай Су мәселесін зерттеу орталығы ашылса, онда Орталық Азия елдері мен Қытай мемлекетінің мамандары бірігіп жұмыс жасаса, бұл теңдесі жоқ, маңызы зор, әрі барлық елдер үшін тиімді жоба болатындығы анық.

Қарап отырсақ, Қазақстан жағы трансшекаралық өзендер суын екі елге де тиімді жағдайда пайдалану бағытында бірқатар шараларды жүзеге асырып, үнемі осы бағытта барынша нәтижеге бағытталған жұмыс жасап келе жатқандығын көруге болады.

Проблемалар

Қытай мен екі арада келіссөздер жүргізуде әр түрлі проблемалар да жоқ емес. Соның бірі Үлкен Ұласты өзеніне қатысты мәселе. Деректерге қарағанда 2007 жылы Қытай жағы біржақты тәртіппен осы өзенінің суын бұрып алған. Сол себепті Шығыс Қазақстан облысының Майқапшағай, Досым және Үмбетай шаруашылығы іс жүзінде сусыз қалған. Осыған байланысты Зайсан ауданының Әкімдігі Шыңжаң өлкесіндегі Іле-Қазақ автономиялы

облысының әкімшілігімен келіссөздер жүргізуге тырысып баққан, бірақ қытай тарапы қандай болмасын түсініктеме беруден бас тартқан, ал бұл өз кезегінде 2002 жылғы үкіметаралық келісімді бұзу болып саналатыны сөзсіз [12].

Кейіннен 2012 жылы Қазақстанның ауыл шаруашылығы министрлігінің сол кездегі вице-министр қызметін атқарған М.Төлибаев 2004 жылдан бері Қазақстан-Қытай шекарасынан ағып өтетін Үлкен Ұласты өзені бойынша түбегейлі дау жалғасып келе жатқанын атап өтті. Қытай өзеннен өздеріне қарай канал салып бұрып алған, соған байланысты қазір оның суының көп бөлігі Қытайға ағып жатқандығын. Осы өзен бойынша келіссөз 8 жыл бойы жүргізіліп, тек 2012 жылы ғана өзен суын теңдей бөліп алу туралы келісімге қол жеткізілгендігін атап өтті.

Назар аударатын қызықты жағдай осы өзен туралы келіссөз барысында Қытай жағы Үлкен Ұласты өзені бойында өз елдері жағында 80 мың адам тұратындығы, ал Қазақстан жағында тек адамы санаулы малшы қоныстары (5 отбасы) ғана бар екендігін көлденең қойып, өзен суын адам санына байланысты бөлейік деген ұсыныс жасаған көрінеді. Оған Қазақстан делегациясы қарсы болған [13].

Тағы бір басты мәселе Ертіс және Іле өзеніндеріне қатысты жағдай. Өзімізге белгілі Ертіс өзені екі мемлекеттен басқа Ресей территориясына қарай ағып өтеді. Сондықтан Ертіс өзеніне қатысты мәселені шешуге Ресейдің де қатысы бар. Қазақстан жағы Ертіс өзеніне қатысты мәселені осы үш мемлекет бірігіп келіссөз жүргізіп шешуді қолдайды, алайда Қытай жағы өзендер мәселесін тек екі жақты келіссөздер жүргізу арқылы шешуді жақтайды. Тіпті өзендер мәселесін Шанхай Ынтымақтастық Ұйымының аясында шешу жөнінде қазақстан жағы ұсыныс жасауда, бірақ қытай жағы оны қолдамай отыр.

Дегенмен, бұл мәселені ресейлік зерттеушілер де қадағалап отырғаны сөзсіз. Ресей сарапшылары осы мәселені зерттей отырып, өздерінің мақалаларында Ертіс пен Іле өзені бойынша екі мемлекеттің арасындағы келіссөздердің нақты шешімге келмей жатқандығының себебін ашып көрсетуге тырысуда. Бірнеше жыл бұрын, 2018 жылы Ресей Ғылым академиясының Океанология институтының, Бүкілресейлік Гидравликалық инженерия және мелиорация ғылыми-зерттеу институтының және Мәскеудің Витте университетінің бір топ ресейлік ғалымдары осы мәселеге қатысты өздерінің зерттеулерін жариялады. Онда зерттеушілер Қатый билігінің қазақстанмен траншекаралық өзендер бойынша келіміге келуді тежеп, кешіктіріп отырған себептерін түсіндіреді. Олардың пайымдауынша Қытай билігі біз басында атап өткен Шыңжаң өлкесін дамытудың стратегиясын кезең-кезеңмен жүзеге асыруда. Сарапшылар бүгінгі күні Шыңжаң-Ұйғыр автономиялы ауданында халықты тұрақта түрде сумен қамтамасыз етудің бірнеше жобаларын тездетіп жүзеге асырып жатқандығын. Қазіргі кезде нақты түрде Қара Ертісте Цяобэта су электр станциясының құрылысы, 13 шағын және орта сыйымдылықтағы су қоймалары және өнеркәсіптік мақсатта пайдаланатын мұнай өндіруге қажетті су қоймасын құрып жатқандығын атап өтеді. Сонымен бірге Ресей сарапшылары егер Қытай Қара Ертіс пен Іленің суын өздерінің Батыс өлкесін қамтамасыз етуге тұрақты түрде көп көлемде пайдаланатын болса, онда Балқаш көліне үлкен қауіп төніп тұрғанына атап өтеді [14].

Осыдан біз түптеп келгенде Ертіс өзенінің мәселесі ресейліктер үшін де маңызды екендігін және олардың Қазақстан мен Қытай арасындағы өзендердің жағдайын зерттеп, бақылап отырғанын көреміз. Қажет жағдайда ресейліктердің бұл жағдайды реттеуге араласуы мүмкін екендігі анық байқалады.

Шын мәнінде Қазақстан мен Қытай арасындағы трансшекаралық өзендерге қатысты шешілмей отырған мәселе қазақстан халқын алаңдатады. Сондықтан қазақстан дипломатиясының алдында осы өзендер мәселесін табандылықпен, үлкен біліктілік және құқықтық негізде шешу жағдайы бірінші кезекте тұрған мәселе екендігін тұжырымдағымыз келеді.

Қорытынды және пайымдаулар.

Жоғарыда айтылғандарды қорытындылай келе, мәселенің тездетіп шешілмей жатқанының бір негізгі себебі - Қытай жағының Үйғыр-Шыңжаң өлкесін дамыту жұмыстарына басымдық беріп, өздері белгілеген Стартегия бойынша осы өлкенің әлеуметтік-экономикалық жағдайын тездетіп дамытып реттемейінше, екі жақты өзендер мәселесін шешуді баялатуында болып отыр деп білеміз. Өйткені өзендер суын осы өлкенің экономикасын дамытуға кеңірек пайдалануға, оның қанша көлемде қажет болатынын пайымдауға тырысуында болып отырма дейміз.

Екіншіден, Қазақстан жағы Қытайды трансшекаралық өзендер бойында көптеп су электр станцияларын, су қоймаларын, суару каналдарын салуда және өзен суларын өндірістік өнімдерді өндіруге пайдалану судың құрамын бұзып, экологиялық қауіптер төндіреді деп айыптаса, Қытай жағы қазақстандықтарды өзен суларын үнемдемей, егін суаруда көбіне бұрынғы арықтық жүйені пайдаланып отырғандығын алға тартады.

Осыған дейін екі елдің де осы өзендер мәселесін шешуге мүдделі екендігін жасалған келісімдер мен атқарылып жатқан іс-шарлар арқылы көруге болады. Дегенмен, Қытай жағы бір-екі өзен бойынша келісімдер жасап, қазақстан жағын соған қанағаттандырып, әрі үміттендіріп отыр ма деген ойдамыз.

Кейінгі кезде Қытай тек Қазақстанмен трансшекаралық өзендер бойынша келіссөздер жүргізіп отыр деген мәліметтер жарық көруде. Оның себебіне үңілсек, Қытай үшін өзінің әлемдік деңгейдегі мақсаттарын орындау бағытында Қазақстанның геосаяси маңызы жоғары екендігін пайымдауға болады:

Біріншіден, Қазақстан Қытайдың Батыс елдерімен байланыстарын жоғары деңгейге жеткізуде, «Бір жол-бір белдеу» ғаламдық жобасын жүзеге асыруда логистикалық негізде маңызды болып отыр. Қазіргі кезде Қытайдың Батысқа бағытталған тауарының 85 пайызы біздің еліміз арқылы өтеді.

Екіншіден, Қазақстан Қытайдың саяси тұрақсыз деп есептелетін Шыңжаң-Үйғыр автономиялы өлкесімен іргелес орналасқандықтан, екі арадағы шекарадағы қауіпсіздікті қамтамасыз етуде қытай үшін қазақстанмен бейбіт ынтымақтастықты одан әрі жалғастыру маңызды.

Үшіншіден, Қазақстан Қытай үшін маңызды көмірсутегі шикізатын арзан бағада жеткізетін бірден бір ел және Түркменстанның газы біздің ел арқылы өтетіні де қытай жағын бірқатар жеңілдіктерге баруға итермелеп отырғаны сөзсіз. Сонымен бірге Қазақстан дайын өнеркәсіп өнімдерін игеретін нарық көзі болуы да Қытай үшін тиімді.

Осы аталған жағдайларды Қазақстан дипломатиясы тиімді пайдалану қажет және келіссөздер барысында Қытай үшін Қазақстанның маңызды тұстарын алға тартып, тездетіп осы мәселені реттеу керек деп пайымдаймыз.

Екі мемлекеттің арасындағы траншекаралық өзендер мәселесін реттеуде көптеген ұсыныстары бар екендігі сөзсіз. Солардың бірі ретінде қоршаған орта және климаттың өзгеруі бойынша халықаралық сарапшы Болат Есекин Кеңестік дәуірдегі саясатты пайдалау қажет деген пікірін атап өтуге болады. Оның ұсынысы бойынша бұл мәселеге Қырғызстанды да тарту қажет болады, өйткені Қырғызстаннан бірқатар өзендер Қытайға қарай ағады екен. Осыны пайдаланып, Қытай жағы траншекаралық өзендерден суды алуды арттырмаққа әрекет жасағанда, Кеңестер Одағы бұл өзендердің суын жауып тастайтынын ескертеді екен. Сарапшы Іле өзені бойынша келіссөзге біз Қырғызстанды тартсақ болады, өйткені ол да осы Балқаш-Іле су бассайніне кіреді, сонда белгілі бір нәтижеге қол жеткізуге болады - деген ұсынысын білдіріп отыр.

Осы мәселені шешуде Ресей сарапшылары да өздерінің ұсыныстарын білдіруде. 2016 жылы мамыр айында Ресейдің ауыл шаруашылығы министрі А.Ткачев Алтай өлкесіндегі өзен суларын Қазақстан арқылы Шыңжаң-Үйғыр өлкесіне жеткізу туралы ойын білдірді. Алайда

бұған қарсы ғалымдардың көпшілігі оның экологиялық жағынан тиімсіз екенін айтысты. Бұл да бір үлкен мәні бар ұсыныс, дегенмен, тұтастай өзен суларын бұрып басқа арнаға жіберу үлкен материалдық шығындар тудыруы және экологиялық апаттарға әкелуі де мүмкін. Сондықтан, бұл ретте жасалып жатқан ұсыныстарды ескеріп, олардың тиімділігін анықтау Бірлескен комиссияның құзыретінде болуы керек екендігі түсінікті.

Зерттеу барысында негізгі анықтағанымыздай, Қытай жағы Шыңжаң-Ұйғыр өлкесін дамытуда көрші елдердің, әсіресе Қазақстанның мүдделерін ескеру керек деп ойлаймыз, ал Қазақстан жағы барынша өзендер суларын тиімді және үнемді пайдаланудың техникалық және технологиялық жағын жаңарта дамытып, ел экономикасына кеңінен енгізуді ұйымдастырғаны дұрыс деп білеміз.

Қорытындылай келе, Қазақстан дипломатиясы ұзақ жылдар бойы тынбастан Қытай жағымен трансшекаралық өзендерді бірігіп пайдалануды реттеу бағытында біршама нәтижелі жұмыстарды атқарғанын пайымдауымызға болады. Атап айтқанда траншекаралық өзендерді пайдаланудың алғашқы Келісімдеріне қол қойылып, осы мәселеде екі жақты ынтымақтастықтың құқықтық базасы қалыптаса бастағанын және Қорғас және Сүмбе өзендері бойынша Келісімдер жасалып, осы өзендерде суды теңдей бөлетін жаңа гидроқондырғылардың жұмыс жасауы екі елдің арасындағы осы мәселеге қатысты ортақ мүдделері бар екенін көрсетеді. Сонымен бірге Қорғас және Сүмбе өзендерін бірігіп пайдалану тәжірибесі екі елдің арасындағы барлық өзендерді бірігіп пайдалануды шешуде үлгі болатын шара екендігі сөзсіз. Сондықтан Қытай жағының осы тәжірибені одан әрі жалғастырып, басқа өзендер жағдайын да осылай реттеуді тездетіп жүзеге асыруға ықпал етуіміз қажет дегіміз келеді. Осыған байланысты қазақстан дипломатиясы әлі де болса қолдағы барлық мүмкіндіктерді пайдаланып, Қазақстанның Қытай үшін геосаяси, геоэкономикалық маңызын ұстана отырып, аймақтағы қауіпсіздікті қамтамасыз етудегі рөлін маңыздай отырып, еліміз үшін маңызды өзендер бойынша қажетті келісімдерді жасауға қол жеткізеді деген үміттеміз.

Траншекаралық өзендерді екі елдің өзара тиімді пайдалануы туралы келісімдердің жасалуы екі ел үшін де, аймақ елдері үшін де, тіпті әлемдік қауіпсіздік үшін де маңызы зор болатыны сөзсіз. Өйткені халықаралық тәжірибе көрсеткендей, трансшекаралық су ресурстарын ортақ пайдалануды бақылайтын бірлескен комиссия құрылып, сол комиссия арқылы барлық мәселелерді реттеп отыруға мүмкіндік туар еді және екі ел үшін де өзара достық қатынастарды одан да жоғары деңгейде әрі қарай дамытуға үлкен жағдай жасалары сөзсіз.

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Economic Sciences

The Role of the „Middle Corridor“ Global Project in the Economic Development of Georgia

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Abstract. Georgia’s geopolitical location determines the prospects for the country's economic development. In this context, it is imperative that the international "Middle Corridor" project be transformed into one of the key drivers of Georgia's economic development. As a result of global geoeconomic transformation, the Trans-Caspian International Transport Route has emerged as a major alternative to the "Northern Corridor."

This paper analyzes the challenges and strategic opportunities facing the Georgian economy through the country's involvement in this large-scale international project. Although the project offers Georgia a unique opportunity to attain the status of a regional logistics hub and attract foreign direct investment, this process unfolds against a backdrop of significant structural and institutional barriers.

The research subject of this paper encompasses crucial challenges such as geopolitical risks, infrastructural constraints, coordination and digital integration, economic inclusivity, and others. It is essential to examine how Georgia's transit function can be converted into sustainable economic growth. To achieve this, the country must not remain merely a "transit corridor," but must develop local high-value-added manufacturing and logistics services.

In the concluding section, concrete recommendations are formulated regarding the optimization of state policy, public-private partnership, and synchronized collaboration with international partners—all of which are required to maximize Georgia's economic benefits within the "Middle Corridor." The presented simulation mathematical model enables the forecasting of Georgia's economic growth within the framework of the "Middle Corridor" project.

Keywords: Georgia, geopolitical location, advantage, "Middle Corridor", economic development, forecasting, mathematical model.

Introduction

Until 2022, the most important transport and logistics route in the region was the "Northern Corridor," also known as the "Eurasian Land Bridge." The latter constitutes a network of transcontinental rail and road routes connecting East Asia with Europe, with the main section passing through the territory of the Russian Federation. The "Northern Corridor" includes:

- The Trans-Siberian Railway: Cargo moves from China deep into Russia, crosses Siberia, and enters Belarus and the EU (Poland) via Moscow.
- The Trans-Mongolian Railway: Originates in China, crosses Mongolia, and joins the Trans-Siberian Railway.
- The Kazakhstan Route: Freight enters Kazakhstan from China and flows into Russia from Central Asia, eventually reaching Europe.

Prior to the outbreak of Russia's war in Ukraine in 2022, 90% of overland freight transport between China and Europe utilized the "Northern Corridor" (Shengelia, 2025). Following the full-

scale war launched by Russia in Ukraine, the situation shifted dramatically: the European Union and Western nations imposed severe sanctions on Russian and Belarusian railways. Major logistics companies (e.g., Maersk, DHL) refused to use Russian territory, while international insurance companies ceased insuring cargo passing along this route. This crisis created an urgent need to develop overland trade between China and Europe that bypasses Russia.

Due to these and other objective reasons, global trade logistics networks shifted toward the "Middle Corridor." This route passes through the Caspian Sea, Georgia, Azerbaijan, and Türkiye. Thus, the Trans-Caspian International Transport Route acts as a vital nexus connecting China, Central Asia, and Europe via the Caspian Sea, the Caucasus, and the Black Sea. As a consequence of the Russia–Ukraine war, the "Northern Corridor" lost its appeal, causing a sharp surge in demand for the alternative southern route (Shengelia, Berishvili, 2026).

For Georgia, this represents a unique opportunity to transform from a simple transit country into a regional logistics hub. However, fully realizing this potential involves addressing numerous economic, infrastructural, and geopolitical challenges. The efficiency of the "Middle Corridor" depends heavily on its capacity and speed. In this regard, our country is not yet adequately meeting these new challenges, as evidenced by the following issues:

1. Infrastructural Bottlenecks: Delays in the Anaklia Deep Sea Port project create a significant barrier to the country's full integration into this initiative. The ports of Poti and Batumi lack sufficient depth to accommodate large vessels, which restricts cargo turnover and increases shipping costs.
2. Rail and Road Capacity: The capacity and modernization rate of Georgian Railway remain limited, and bringing the Baku–Tbilisi–Kars railway to full operational capacity poses ongoing difficulties. Completing the East–West highway—particularly through the Rikoti Pass—is critical for rapid freight transit.
3. Multimodal Complexity: The "Middle Corridor" is inherently a complex, multimodal route where cargo must alternate between land and sea transport multiple times. Therefore, seamless logistical execution and infrastructural perfection are paramount—standards that the Georgian transit node currently cannot fully guarantee (Cornell, Frederick, 2006).

It is equally important for Georgia to establish a unified digital platform and tariff policy alongside Azerbaijan and Kazakhstan to render the corridor competitive. The absence of modern logistics centers (and deep-sea ports) significantly limits the country's potential. As a result, the transit function currently yields limited economic benefit, as transit revenues (road fees, port tariffs) constitute only a small fraction of GDP and generate relatively few jobs. Georgia faces a crucial challenge: processing cargo locally to create added value. The country must enhance the efficiency of its Free Industrial Zones (FIZs). It is vital that raw materials arriving from China are processed in Georgia and exported to European nations at zero tariffs by utilizing the Deep and Comprehensive Free Trade Area (DCFTA) agreement with the EU (Shengelia, Berishvili, 2024).

The stability of the "Middle Corridor" is directly linked to regional security. In this respect, the key problems and challenges facing Georgia include:

- Geopolitical Pressure & Regional Risks: Russia has a strong economic and political interest in preventing an alternative corridor bypassing its territory from operating effectively.
- Occupied Territories: The existence of occupied territories and creeping occupation represent major risk factors for potential investors.
- Black Sea Security: Military activities and naval mine threats in the Black Sea complicate maritime transport and inflate shipping costs.
- Institutional Hurdles: Further hurdles include limited port capacity, railways with weak logistical capabilities, delays in constructing the Anaklia Port, inadequate digital integration, and bureaucratic delays at customs checkpoints (World Bank, 2025).

Despite these difficulties, the "Middle Corridor" offers the country a historical chance to modernize its economy, firmly integrate into the global economic architecture, and secure substantial economic growth and social development (Shengelia, Gelashvili, 2020). Achieving this requires consistent approaches and strategic action from the government.

Fully operationalizing the "Middle Corridor" promises not merely a transit effect for Georgia, but a strategic economic transformation. The country has the chance to evolve from a basic "transit corridor" into a regional economic center. To do so, several key objectives must be resolved swiftly and consistently:

- Large-Scale Infrastructure Investments: Billions of dollars in foreign capital must be invested in infrastructure. The construction of the Anaklia Deep Sea Port, the expansion of the Poti and Batumi ports, and the establishment of modern warehousing facilities in Tbilisi and Kutaisi require significant capital that must be attracted from foreign investors, given the country's limited domestic capabilities.
- Leveraging Free Trade Agreements: Georgia holds Free Trade Agreements (DCFTA) with both the EU and China. An operational "Middle Corridor" will allow international companies to establish manufacturing facilities in Georgia (e.g., within Free Industrial Zones). They can import raw materials from China or Central Asia, process them in Georgia, and export finished products to Europe tariff-free. Thus, driving domestic production and expanding exports of Georgian-made goods should become the highest economic priority, promising the creation of thousands of new, well-paying jobs.
- Increased Fiscal Revenues: State budget revenues will grow through higher transit fees (road usage charges, maritime and rail tariffs) and increased tax revenues generated by newly established enterprises.
- Monetary System Resilience: One of the main vulnerabilities of the Georgian economy is monetary instability, caused in part by an asymmetric trade balance. Exporting logistics and transit services (where foreign entities pay for local services) provides a continuous inflow of hard foreign currency. This will strengthen the Lari (GEL) and make the country's monetary system more resilient against external shocks.

Ultimately, the "Middle Corridor" grants Georgia the chance to break free from the "small market" mindset. The country can become more than just a market of 3.7 million people—it can serve as a vital gateway upon which a vast portion of global trade depends (Shengelia, Kozak, Kirkitadze, 2020).

In order to scientifically evaluate the impact of the "Middle Corridor" on Georgia's economy at a structural level, we must construct a macroeconomic structural model. This model expands the classical Keynesian aggregate demand framework by directly integrating parameters for transit trade, foreign investment, and digital efficiency.

Below are the mathematical structure, behavioral equations, and multiplier analysis of the model.

Basic Model Equation (Output Volume)

Taking into account the effects of the "Middle Corridor," the country's total output (GDP- Y) is expressed as follows:

$$Y = C + I(FDI_{mc}) + G + \left[X_g + X_s(T_{mc})\right] - M$$

Where:

Y – Gross Domestic Product (Real GDP);

C – Private domestic consumption;

I(FDI mc) – Aggregate investments that react endogenously to foreign direct investment entering within the framework of the Middle Corridor (FDI mc);

G – Government purchases (including capital expenditures on transport infrastructure);

Xg – Export of goods;

Xs (Tmc) – Export of services, directly linked to the cargo traffic volume transported through the Middle Corridor (T mc);
M – Aggregate imports, which depend on the level of domestic income.
Functional Dependencies Between Variables:
a) Service Export and Transit Function. The primary direct channel for the activation of the "Middle Corridor" is the commercial realization of transport, port, and logistics services:

$$Xs = X0 + \alpha \cdot Tmc$$

Where: Xo – Autonomous export of services (tourism, financial services, etc.);
Tmc – Annual volume of cargo transported via the Middle Corridor (expressed in millions of tons or TEUs/containers);
α – Marginal transit effect (α>0), representing the revenue generated by Georgia per each additional unit of cargo handled (railway tariffs, port fees, dispatching).
b) Investment Stimulus Function. Investments react to the development of major strategic assets within the framework of the Middle Corridor (e.g., Anaklia Port, Free Industrial Zones, dry ports):

$$I = I0 + \beta \cdot FDI\ mc$$

Where:

- I_0– Autonomous domestic investment (capital expenditures of local businesses);
- FDI_{mc}– Targeted foreign direct investment attracted by the Middle Corridor;
- β– Domestic capital stimulation coefficient ($\beta \geq 1$), reflecting the extent to which major foreign projects induce local investments in supplier, construction, and supporting sectors (the crowding-in effect).

c) Domestic Consumption Function. Consumption depends on disposable income, which in turn grows alongside increases in employment and wages:

$$C = Co + c \cdot (Y - T)$$ Co – Autonomous consumption

Co – Autonomous consumption;
c – Marginal propensity to consume (0<c<1);
T – Taxes.

3. The Multiplier Effect (Mid-Corridor Multiplier) By solving the system of equations for Y, we obtain the model of the Middle Corridor economic multiplier. For a simplified structure, assuming that taxes and imports are proportional to GDP (T=t·Y and M=m·Y), the formula takes the following form:

$$\frac{1}{1 - c(1 - t) + ml} \cdot [C\,0 + I\,0 + G + X\,0 + X\,g + \beta \cdot FDI\ mc + \alpha \cdot T\ mc]$$

Where:
The coefficient $\frac{1}{1-c(1-t)+ml}$ represents the macroeconomic multiplier.

4. Dynamic Effects (Time Factor t) In the long run, elements of neoclassical (Solow) growth are integrated into the model, where the volume of production depends on technological progress and capital accumulation:

$$Yt = A\,t \cdot Kt\gamma \cdot L\,t\,1-\gamma$$

Where:
At – Total Factor Productivity (TFP). The operationalization of the Middle Corridor and the implementation of digital technologies (logistics platforms) increase A t (enhancing national overall efficiency).
Ktγ – Capital stock, which expands through the accumulation of annual FDI mc : K t+1 =K t +It −δK t (where δ is the depreciation rate).

"The Middle Corridor" is not merely a geopolitical project for Georgia, but a real economic engine. To see how the development of this corridor impacts the country's economy, let us construct a dynamic macroeconomic model. This model will help us establish the connection between infrastructure investments, freight turnover growth, and the Gross Domestic Product (GDP) multiplier.

Model Variables and Parameters

Let us define the main components that correspond to Georgia's current economic reality:

Yt – Georgia's GDP in year t (baseline GDP of USD 25 billion).

Vt – Cargo turnover on the Georgian section of the Middle Corridor (in million tonnes).

It – Investment in logistics infrastructure (Anaklia Port, railway modernization, highways).

Rt – Direct and indirect revenue generated from transit.

P – Average revenue per 1 tonne of cargo handled (tariff, employment, and services effect; conditionally USD 25/tonne).

B – Keynesian economic multiplier (indicates how the increase in transit revenues impacts other sectors, such as services and trade).

Mathematical Formulation

The model relies on three interconnected equations:

a) Freight Capacity Function:

Logistics capacity depends on the investments made. After a certain period of time (accounting for the time lag), investment increases freight turnover:

V t =Vt−1 (1+G n)+α·I t−1

where:

G n is the natural growth rate of freight turnover (without additional investments, e.g., 3%),

α is the investment efficiency coefficient (e.g., every $100 million invested increases throughput capacity by 1 million tons, i.e., α=0.01).

b) Transit Revenue Equation:

$$R_t = V_t \times P$$

c) GDP Growth Model:

The country's total product consists of baseline economic growth and an additional multiplied effect derived from the Middle Corridor:

$$Y_t = Y_{t-1}(1 + g_{\text{GDP}}) + b(R_t - R_{t-1})$$

where:

(g_{GDP}) is the baseline growth rate of Georgia's economy (e.g., 5%).

3. Practical Simulation (Example)

Suppose that in the initial year (0), we have the following baseline data:

Baseline GDP (Y_0) is $25,000 million USD, current cargo turnover (V_0) is 15 million tons, and in Year 1, the government and the private sector make a major infrastructure investment (I_1) of $1,000 million USD.

Let's see how the parameters will change in Year 2, when this investment becomes operational:

Step 1: Calculation of Cargo Turnover (V2)

V2 =15(1+0.03)+0.01×1000=15.45+10=25.45 million tons

Step 2: Revenue Growth (ΔR) Initial Revenue: R 0 =15×25=$375 million

New Revenue: R 2 =25.45×25=$636.25 million

Net Increase: ΔR=636.25−375=$261.25 million

Step 3: Impact on GDP (Y 2) Assuming a baseline economic growth rate of 5%, taking into account the new infrastructure:

Y 2 =25,000×(1+0.05)+1.4×261.25 Y 2 =26,250+365.75=$26,615.75 million

Summary of Results

Parameter	Base year	post-investment (2nd year)	change (%)
cargo turnover	15 million tonnes	25.45 million tonnes	+69.6%
transit income	$375 million	$636.25 million	+69.6%
Georgia's GDP	$25,000 million	$26,615.75 million	+6.46% (instead of the baseline 5%)

Here is the precise English translation of the remaining section, clearly organized with formatted bullet points and headers:

As the model demonstrates, under conditions of an effective multiplier and proper investment, the expansion of the Middle Corridor can accelerate Georgia's annual economic growth rate by an additional 1.46%.

Despite the fact that the "Middle Corridor" holds immense economic potential for Georgia, the country faces numerous serious obstacles, barriers, and challenges on the path to its full operationalization. These obstacles can be categorized into four main groups: infrastructure, logistics & technology, geopolitics, and finances.

Infrastructure Barriers

Georgia's current transport network is not prepared to handle the scale of cargo flows implied by trade between China and Europe.

- Absence of a Deep-Sea Port (The Anaklia Factor): This is the single biggest weakness. The inability to handle transshipment for large cargo vessels increases transportation costs and delays the process. Meanwhile, the construction of the Anaklia Port has been stalled for years due to political and financial disagreements.
- Limited Railway Capacity: "Georgian Railway" is mostly single-track, which limits train traffic frequency. Despite ongoing modernization, the complex terrain (mountain passes) significantly hinders transit speed. The Baku–Tbilisi–Kars railway line, connecting Georgia to Turkey, undergoes continuous reconstruction and has yet to operate at full capacity.

Logistics & Technological Barriers

- Absence of a "Single Window" Principle: Customs and transit procedures among corridor member states (Kazakhstan, Azerbaijan, Georgia, Turkey) are still not fully synchronized. Due to the lack of a unified digital management platform, documentation processing and border crossings require significant time.
- Uncompetitive Tariffs: Due to a lack of coordination, shipping cargo through the Middle Corridor is often more expensive than via maritime routes (the Suez Canal) or the older Northern Route (through Russia).
- Deficit of Logistics Centers: Georgia practically lacks top-tier "Class A" dry ports and warehouse facilities where cargo could be efficiently managed and sorted.

Geopolitical & Security Risks

The region through which the corridor runs is characterized by high political instability, which deters major international carriers.

- The Russia Factor: Russia has economic and political interests in ensuring this alternative corridor does not succeed, so as not to lose leverage over China and Europe. Georgia's occupied territories and creeping occupation represent a constant source of risk.
- Black Sea Security Crisis: Due to the ongoing war in Ukraine, the Black Sea remains a zone of military action. The threat of naval mines and military risks drastically increases ship insurance premiums, making the route less attractive.
- Balancing Between the West and China: The involvement of Chinese state-owned enterprises in the construction of Anaklia Port raises concerns for the US and the European Union. Georgia is forced to navigate a complex geopolitical balancing act to avoid losing the support of its Western partners.
- The Caspian Sea Problem: Water levels in the Caspian Sea are dropping critically, hindering operations at Kazakh and Azerbaijani ports. Additionally, there is a deficit of ships and ferries on this sea, leading to cargo backlogs.
- Infrastructure Disconnect with Turkey: Turkey's rail network from Kars deeper into the country requires modernization to handle large volumes bound for Europe.

Consequently, due to the absence of the Anaklia Port, Georgia cannot accommodate high-capacity vessels; high financial/administrative tariffs and heavy bureaucracy undermine the route's competitiveness; and Russian occupation alongside rising insurance costs leads to a decline in investor confidence.

The barriers facing the Middle Corridor require Georgia not only to upgrade its domestic infrastructure, but also to engage in active, well-considered diplomacy—both with neighboring countries (to reduce tariffs) and with the West (to attract security and investment).

Conclusions and Recommendations

The international "Middle Corridor" project is not merely a transit route for Georgia; it represents a historic opportunity for geopolitical and economic transformation. However, as the analysis presented in this paper demonstrates, a favorable geographical location alone is insufficient for the country to extract maximum benefit from this global project. Achieving a real economic breakthrough requires the timely and effective overcoming of existing challenges.

1. Infrastructure Modernization: Georgia's transport arteries (railways, highways) and seaports (including the strategic project of the Anaklia Deep-Sea Port) require urgent modernization. Capacity deficits and logistical bottlenecks threaten to divert cargo flows toward alternative routes.
2. Digitalization: Physical infrastructure alone cannot ensure competitiveness; full digitalization of customs and logistics procedures is imperative. Establishing a unified, transparent, and fast digital platform with Middle Corridor member states will critically reduce cargo transit times and costs.
3. Value Creation Beyond Transit: Georgia's primary economic challenge is to avoid remaining a passive transit territory. By developing modern logistics centers, free industrial zones, and processing facilities, the country can generate new jobs and foster dynamic economic development.

The success of the Middle Corridor in Georgia depends on the consistency of state policy, the ability to attract private investment, and synchronized collaboration with international partners. Provided there is prudent management of geopolitical risks and execution of internal structural reforms, this project will become the primary guarantor of Georgia's long-term, sustainable economic development and further integration into the Euro-Atlantic space.

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Insurance-Enabled Resilience in Global Manufacturing Supply Chains: A Qualitative Analysis of Political Risk Insurance Policy Documents

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Abstract

The intensification of geopolitical tensions, the deepening of climate-related risks and the continuous restructuring of global supply chains after the COVID-19 epidemic have made the overseas supply chain risks faced by manufacturing enterprises increasingly complex. As a risk transfer and risk management tool, insurance has a significant impact on the resilience of overseas supply chains of manufacturing enterprises through mandatory and voluntary arrangements (Faure, 2006; Christopher & Peck，2004）。 Based on the theory of supply chain risk management (Ponomarov & Holcomb, 2009; Sahab & Oulfarsi, 2026) and international business theory, using qualitative literature analysis method (Bowen, 2009), taking the open access policy publication Investment Policy Monitoring 30: Political Risk Insurance of UNCTAD (UNCTAD, 2025) as the main analysis text, supplemented by peer-reviewed literature on supply chain resilience that can be retrieved through the open academic platform. This analysis clarifies the specific path of embedding political risk insurance and export credit insurance into the risk management system of overseas supply chain of manufacturing enterprises, and compares the different contributions of compulsory insurance arrangements and voluntary insurance arrangements. The analysis shows that: (1) export credit agencies are the main providers of political risk insurance, accounting for 78% of the total circulation in the past decade, while manufacturing projects account for 20% of all insured projects from 2019 to 2023, which is the highest among all industries (UNCTAD, 2025); (2) Insurance mechanism enhances the adaptability and resilience of supply chain through risk identification, risk mitigation and liquidity support (Pettit, Croxton and Fiksel, 2013; El Baz and Ruel, 2021). (3) In the high-risk market with significant information asymmetry and externalities, policy-based (quasi-compulsory) insurance arrangements bear disproportionate risks, while commercial (voluntary) arrangements provide enterprises with a more flexible and complementary risk management tool (Faure, 2006; UNCTAD, 2025). Finally, this study puts forward the management enlightenment to insurance companies, manufacturing enterprise managers and policy makers, and expounds the limitations of the study and the future research direction.

Keywords: Political Risk Insurance; Export Credit Insurance; Supply Chain Resilience; Manufacturing Enterprises; Document Analysis

1. Introduction

1.1 Research Background

In recent years, the operating environment of global supply chain has undergone profound changes, and the uncertainty of international trade and cross-border investment continues to intensify. Geopolitical tensions, including Sino-US trade disputes, regional armed conflicts,

international sanctions, global public health emergencies and increasingly frequent extreme weather events, have seriously disrupted global production networks and supply chains. Therefore, manufacturing enterprises engaged in overseas production, procurement, logistics and market expansion are facing unprecedented political, commercial and institutional risks. In this context, the traditional cost-effective global supply chain management model has gradually revealed its limitations in dealing with large-scale external shocks. Therefore, supply chain resilience has become the key ability for manufacturing enterprises to maintain international competitiveness and ensure sustainable operation.

Supply chain resilience refers to the ability of supply chain to maintain operational continuity, quickly recover from interruption and dynamically adapt to changing environmental conditions after encountering unexpected external shocks. With the evolution of supply chain risks from isolated events to systematic interruptions, it is not enough to effectively cope with the increasingly complex international business environment only by relying on internal organizational resources and inter-enterprise cooperation. Therefore, integrating external risk management mechanism into supply chain management has become an important research direction to improve the resilience of supply chain.

As a market-oriented risk transfer tool, insurance plays an increasingly important role in promoting international investment and cross-border trade. Political risk insurance provides protection for investment losses caused by political events such as war, expropriation, currency convertibility and government default, while export credit insurance mainly covers commercial credit risks and specific political risks related to international trade. In recent years, governments around the world have increasingly taken political risk insurance and export credit insurance as strategic policy tools to support foreign direct investment and international business expansion. Therefore, insurance has gradually evolved from the traditional financial compensation mechanism to an important part of supply chain risk management.

Under the background of global supply chain reorganization, it is of great theoretical significance and practical value to systematically study how insurance mechanism can enhance the resilience of overseas manufacturing supply chain. This kind of research can provide valuable insights for enterprise risk management, international investment decision-making and the formulation of national policy framework to support overseas business activities.

1.2 Research Significance

Theoretical Significance

Existing research on this topic has primarily evolved within three interconnected fields: supply chain risk management, supply chain resilience, and insurance economics. Studies on supply chain risk management mainly emphasize internal governance mechanisms, including risk identification, risk assessment, risk mitigation, and recovery capabilities. Meanwhile, insurance economics has largely focused on issues such as insurance system design, information asymmetry, moral hazard, adverse selection, and the economic rationale for compulsory insurance.

As a risk transfer tool, insurance is one of the ways for enterprises to deal with external uncertainty. Export credit insurance and political risk insurance have become policy tools for many countries to support foreign investment and trade, and purchasing such products also constitutes a part of supply chain risk management practice. The existing researches on the mandatory and voluntary dimensions of green insurance are mainly discussed from the perspectives of insurance

economics (Faure, 2006) and the relationship between climate change and insurance industry (Savitz & Gavriletea, 2019), but the systematic analysis on how the insurance mechanism can be specifically integrated into the process of building the resilience of overseas supply chains of manufacturing enterprises is still limited. The purpose of this study is to solve this specific management problem and link the supply chain risk management literature with the insurance mechanism literature.

Despite the substantial progress achieved in these research streams, limited attention has been devoted to understanding how insurance mechanisms function as external governance instruments that can be integrated into the resilience-building process of manufacturing supply chains. Consequently, insufficient theoretical linkage exists between supply chain resilience and insurance-based risk governance.

This study seeks to bridge this research gap by incorporating political risk insurance and export credit insurance into the analytical framework of supply chain resilience. Specifically, it investigates how insurance mechanisms enhance supply chain resilience through multiple governance pathways, including risk identification, risk mitigation, financial support, and institutional assurance. By doing so, this research extends the theoretical boundaries of supply chain resilience and contributes to a more comprehensive understanding of external risk governance mechanisms.

Practical Significance

From a practical point of view, China's manufacturing enterprises have accelerated their international expansion in the past decade, which has led to a substantial increase in overseas investment activities. At the same time, enterprises are also facing increasing international market challenges such as political uncertainty, business risks and institutional instability. The effective use of political risk insurance and export credit insurance can not only reduce the possible financial losses caused by overseas investment, but also enhance the continuity of enterprise operations and enhance the risk management ability at the enterprise level.

Therefore, the findings of this study are of practical significance to many stakeholders. Insurance companies can use the research results to optimize the political risk insurance products and service system; Manufacturing enterprises can improve overseas risk management strategies by bringing insurance into supply chain governance; Policymakers can take the research results as theoretical support, improve the policy insurance system and promote the effective coordination between public insurance and commercial insurance arrangements.

1.3 Research Objectives and Scope

Based on the research background presented above, this study investigates how insurance mechanisms contribute to the resilience of overseas manufacturing supply chains. Specifically, the research addresses the following three questions:

What are the structural characteristics of political risk insurance providers and the industrial distribution of political risk insurance in international practice, and what position does the manufacturing sector occupy within the global political risk insurance system?

Through what specific mechanisms do political risk insurance and export credit insurance enhance the resilience of overseas manufacturing supply chains, and what are the principal

pathways through which these effects are realized?

What are the differences between policy-based (quasi-mandatory) insurance arrangements and commercial (voluntary) insurance arrangements in supply chain risk governance, and how do their governance functions vary across different risk environments?

To address these research questions, this study adopts a qualitative document analysis approach. The primary source of analysis is Investment Policy Monitor No. 30: Political Risk Insurance, published by the United Nations Conference on Trade and Development (UNCTAD) in 2025. The policy document is further triangulated with representative literature in supply chain risk management, supply chain resilience, and insurance economics to ensure analytical rigor and theoretical validity.

The scope of this study focuses specifically on political risk insurance and export credit insurance. Other insurance products, such as property insurance and liability insurance, are beyond the scope of the analysis. Moreover, this research does not employ enterprise-level quantitative data or econometric models. Instead, it concentrates on interpreting institutional arrangements reflected in international policy documents and explaining their theoretical implications for enhancing the resilience of overseas manufacturing supply chains.

2. Literature Review

2.1 Theoretical Foundations of Mandatory and Voluntary Insurance Arrangements

Insurance system is an important institutional mechanism for risk sharing and loss compensation in market economy. According to the mode of participation, insurance arrangements can usually be divided into compulsory insurance and voluntary insurance.

From the perspective of insurance economics, Faure (2006) believes that the economic rationality of compulsory insurance mainly comes from market failures such as information asymmetry, moral hazard, adverse selection and externalities. When the potential responsible party is unable to fully compensate the social losses due to insufficient financial capacity, compulsory insurance can effectively reduce the social costs caused by market failure and improve the overall efficiency of risk management.

In contrast, voluntary insurance follows the market-oriented principle, allowing enterprises to decide whether to buy insurance and choose the scope of insurance according to their own risk preferences, business characteristics and risk tolerance. Commercial insurance is characterized by flexible product design, wide coverage and market-based pricing mechanism, which is more suitable for a relatively stable market environment with sufficient risk management capabilities.

In recent years, political risk insurance and export credit insurance are increasingly showing a complementary mode of combining policy insurance with commercial insurance. As a government-supported institution, export credit agencies mainly provide insurance protection for overseas investment and international trade in high-risk markets, thus achieving national policy objectives. In contrast, private insurance companies respond to market demand by providing more flexible and customized insurance products. These two insurance arrangements together constitute a comprehensive international investment risk protection system, which provides institutional support for the stable operation of the global manufacturing supply chain.

2.2 Theoretical Foundations of Supply Chain Risk Management and Supply Chain Resilience

Supply chain resilience has become one of the most prominent research topics in contemporary supply chain management literature. Ponomarov and Holcomb (2009) defined the supply chain resilience as the ability of the supply chain to recover from the interruption while continuously learning and adapting to the changing environment. Different from the robustness of supply chain that emphasizes maintaining normal operation under interference, the resilience of supply chain focuses on recovery speed, adaptability and the ability to maintain long-term operation after external shocks.

The existing research agrees that supply chain risk management is the basic premise of supply chain resilience. Tang (2006) proposed that supply chain risk management includes four core processes: risk identification, risk assessment, risk mitigation and risk control. Craighead et al. (2007) further pointed out that the severity of supply chain interruption depends not only on the scale of external events, but also on the ability of organizations to effectively mitigate risks. Pettit et al. (2008) further pointed out that the supply chain toughness is closely related to the severity of supply chain interruption on the basis of previous studies. Wieland and Wallenburg (2013) constructed a comprehensive resilience framework covering preparedness, response and resilience, which has become one of the most influential theoretical foundations for the subsequent supply chain resilience research.

With the global supply chain risks evolving into increasingly complex and systematic challenges, scholars have emphasized the importance of collaborative governance among supply chain partners. Wieland and Wallenburg (2013) emphasized that collaborative relationship contributes to resource sharing and collective risk management, thus enhancing the overall resilience of the supply chain. Recently, Ivanov and Dolgui (2020) put forward the concept of supply chain viability, arguing that under the continuous systematic interference, enterprises must not only strengthen their resilience, but also develop the ability to dynamically reconstruct the supply chain network to ensure the sustainability of long-term operations.

2.3 The Relationship Between Insurance Mechanisms and Supply Chain Resilience

Although remarkable progress has been made in the study of supply chain resilience and insurance economics, most of the previous studies focused on enhancing the internal capabilities of enterprises, while the attention to insurance as an external risk management mechanism was relatively limited. Political risk insurance and export credit insurance reduce the risk of overseas investment through risk sharing, financial support and institutional guarantee. Therefore, their role has gradually surpassed the traditional financial compensation and become an increasingly important part of modern supply chain risk management.

Political risk insurance mainly protects investors from losses caused by political events such as war, expropriation, currency transfer restrictions and government default. The main providers of political risk insurance include export credit institutions, multilateral development institutions and private insurance companies. In contrast, export credit insurance mainly protects enterprises from commercial credit risks and specific political risks arising from international trade, while improving the channels for enterprises to obtain trade financing and enhancing the continuity of cross-border business.

A review of the existing literature shows that there is a close theoretical relationship between insurance mechanism and supply chain resilience. On the one hand, insurance can help enterprises identify and evaluate the political and commercial risks related to overseas operations, thus reducing the potential economic losses caused by major emergencies. On the other hand, insurance compensation and trade financing support can provide funds for enterprises during the interruption of operations, enhance their resilience, and enable the supply chain to resume normal operations more quickly after external shocks.

However, at present, systematic research on how insurance mechanism can enhance the resilience of overseas manufacturing supply chain is still limited. Especially in the risk management of international supply chain, the difference of governance functions between policy insurance and commercial insurance has not been fully compared and studied. In order to make up for this research gap, this study takes Investment Policy Monitoring Report No.30: Political Risk Insurance (UNCTAD, 2025) as the main analysis document. This study combines the theories of supply chain risk management, supply chain resilience and insurance economics, systematically investigates the mechanism of insurance enhancing the resilience of manufacturing supply chain, and further discusses the governance function and management significance of various insurance arrangements under different risk environments.

3. Methodology

3.1 Research Design

This study adopts document analysis, a qualitative research method, to systematically examine political risk insurance policy documents and explore the mechanisms through which insurance enhances the resilience of overseas manufacturing supply chains. Document analysis is a widely recognized qualitative research approach that involves the systematic collection, classification, coding, and interpretation of policy documents, legal regulations, industry reports, and other authoritative sources in order to identify key themes and theoretical relationships. According to Bowen (2009), document analysis not only reveals the institutional arrangements and governance logic embedded in policy documents but also enhances the credibility and explanatory power of research findings through triangulation with multiple sources of evidence.

Compared with quantitative surveys and case studies, document analysis is particularly appropriate for policy-oriented research. On the one hand, political risk insurance constitutes an important component of national risk governance systems, and its institutional arrangements are primarily reflected in official policy documents and international reports. On the other hand, publicly available enterprise-level data concerning political risk insurance adoption and supply chain performance remain limited, making large-scale empirical analysis difficult. Consequently, using authoritative international policy documents as the primary source of analysis enables a comprehensive understanding of the development, institutional characteristics, and governance functions of political risk insurance.

Based on these considerations, this study employs Investment Policy Monitor No. 30: Political Risk Insurance, published by the United Nations Conference on Trade and Development (UNCTAD) in 2025, as the principal analytical document. The policy document is further triangulated with representative studies in supply chain risk management, supply chain resilience, and insurance economics to investigate how insurance mechanisms contribute to the resilience of overseas manufacturing supply chains.

3.2 Data Sources

The data employed in this study consist of two complementary sources: policy documents and academic literature.

The primary policy document is Investment Policy Monitor No. 30: Political Risk Insurance, published by UNCTAD in 2025. This report provides a comprehensive overview of the global political risk insurance market, including major insurance providers, product categories, industry coverage, and policy support mechanisms. As one of the most authoritative international references on political risk insurance, it serves as the principal source for the document analysis conducted in this study.

The theoretical foundation is established through a review of representative academic literature retrieved from major international databases, including Web of Science and Scopus. The literature primarily covers four research domains: supply chain risk management, supply chain resilience, insurance economics, and risk governance. Representative studies include Christopher and Peck (2004), Tang (2006), Ponomarov and Holcomb (2009), Pettit et al. (2013), Ivanov and Dolgui (2020), and Faure (2006). These studies provide the theoretical basis for interpreting the relationship between insurance mechanisms and supply chain resilience.

To enhance the reliability and validity of the findings, this study adopts a triangulation strategy, whereby evidence derived from the UNCTAD policy document is systematically interpreted and cross-validated using established theoretical perspectives from the academic literature. This approach minimizes the potential bias associated with relying on a single documentary source and strengthens the robustness of the analytical conclusions.

3.3 Data Analysis Procedure

Following the document analysis framework proposed by Bowen (2009), this study conducts the analysis through four sequential stages: document collection, content coding, thematic analysis, and theoretical interpretation.

First, the UNCTAD (2025) policy report was thoroughly reviewed to identify information concerning the development of political risk insurance, institutional arrangements, and operational characteristics. Particular attention was devoted to content directly related to overseas manufacturing investment and supply chain risk governance.

Second, an open coding process was conducted to classify relevant textual information according to the research objectives. Coding categories included insurance providers, industry coverage, risk protection mechanisms, financial support instruments, and institutional arrangements.

Third, the initial coding results were consolidated into four overarching analytical themes:

Structure of the Political Risk Insurance Market
Industry Coverage Characteristics
Insurance Mechanisms Supporting Supply Chain Resilience
Comparison between Policy-Based and Commercial Insurance Arrangements

This thematic categorization improved the consistency and coherence of the qualitative analysis.

Finally, the identified themes were interpreted through the theoretical lenses of Supply Chain Risk Management Theory, Supply Chain Resilience Theory, and Insurance Economics. The analysis examined how insurance mechanisms enhance overseas manufacturing supply chain resilience through four principal governance pathways: risk identification, risk mitigation, liquidity support, and institutional assurance. Furthermore, the study compared the governance functions of policy-based insurance and commercial insurance under different risk environments.

3.4 Research Framework

Based on the literature review and qualitative analysis of the policy document, this study develops an analytical framework linking policy documents, insurance mechanisms, and supply chain resilience.

Specifically, the UNCTAD (2025) policy report serves as the primary analytical source for identifying the institutional characteristics of political risk insurance and export credit insurance. Building upon the theoretical foundations of supply chain risk management, the study investigates four principal mechanisms through which insurance contributes to supply chain resilience: risk identification, risk mitigation, liquidity support, and institutional assurance.

Subsequently, the study compares the governance functions of policy-based insurance and commercial insurance in international supply chain risk management and summarizes their managerial implications for enhancing the resilience of overseas manufacturing supply chains.

This research is exploratory in nature and does not involve questionnaire surveys or econometric analysis. Instead, it employs a rigorous qualitative document analysis approach based on internationally recognized policy documents to explain the theoretical logic through which insurance mechanisms contribute to manufacturing supply chain resilience. The proposed analytical framework also provides a theoretical foundation for future case studies and quantitative empirical research.

4. Analysis and Findings

4.1 Provider Structure and Sectoral Distribution of Political Risk Insurance

UNCTAD (2025) data show that export credit agencies are the dominant providers of political risk insurance, with multilateral institutions and private insurers accounting for the remaining shares; developing countries are the primary beneficiaries, and Asia receives the largest share of coverage from export credit agencies and private insurers alike, a pattern linked to China's dual role as both a recipient and a provider of political risk insurance (UNCTAD, 2025). Table 1 summarizes the provider structure.

TABLE 1

Provider	Institutional Characteristics	Primary Target	Role in Supply Chain Resilience
Export Credit Agencies (ECAs)	Government-supported institutions providing investment and trade risk protection	Overseas investment and export projects	Reduce sovereign and political risks, improve investment stability
Multilateral Development Banks (MDBs)	International financial institutions offering political risk guarantees	Cross-border infrastructure and development projects	Enhance investment confidence and facilitate international financing
Private Insurers	Commercial insurance companies operating on a market basis	Enterprises with diversified international operations	Provide flexible and customized risk protection

Regarding sectoral distribution, manufacturing accounted for the largest share of political risk insurance-covered projects between 2019 and 2023, as shown in Table 2.

TABLE 2

Industry	Typical Risk Exposure	Insurance Demand	Implications for Supply Chain Resilience
Manufacturing	Political instability, supply disruption, asset expropriation	High	Maintain production continuity and international operations
Infrastructure	Government intervention, project interruption	High	Ensure long-term project implementation
Energy and Natural Resources	Regulatory uncertainty and geopolitical conflicts	High	Secure strategic resource supply
Telecommunications and Digital Services	Policy changes and cyber-related risks	Moderate	Improve digital supply chain stability
Other Industries	Sector-specific political risks	Moderate	Support overseas business expansion

Table 2 indicates that manufacturing has become a leading sector for political risk insurance, with a project share exceeding that of infrastructure, natural resources, and energy-related projects.

4.2 Pathways Through Which Insurance Mechanisms Enable Supply Chain Resilience

Drawing on the supply chain risk management literature, this study identifies three pathways through which insurance mechanisms enable manufacturing supply chain resilience, summarized in Table 3.

TABLE 3

Insurance Mechanism	Functional Description	Contribution to Supply Chain Resilience	Supporting Literature
Risk Identification	Assess political and operational risks before investment	Improve risk awareness and decision quality	Tang (2006)
Risk Transfer	Transfer political and commercial losses through insurance contracts	Reduce disruption impacts and financial losses	Christopher & Peck (2004); Craighead et al. (2007)
Financial Support	Claims compensation and trade finance services	Improve liquidity and recovery capability	Pettit et al. (2013)
Institutional Assurance	Strengthen investor confidence in high-risk markets	Enhance long-term supply chain stability	Ivanov & Dolgui (2020)

First, the risk identification pathway: the systematic pre-underwriting assessment of a host country's political environment, sectoral risk, and project characteristics helps manufacturing firms identify potential supply chain disruption risks earlier, corresponding to the risk identification stage of supply chain risk management (Tang, 2006). Second, the risk mitigation and liquidity support pathway: by covering overseas assets and receivables, political risk insurance and export credit insurance reduce the probability of financial loss from political events or buyer default and improve firms' access to bank financing, providing a financial buffer for continued operations and recovery when disruptions occur—corresponding to the recovery and adaptive capacity emphasized in supply chain resilience frameworks (Pettit et al., 2013). Third, the institutional confidence-building pathway: the availability of political risk insurance strengthens manufacturing firms' confidence to enter high-risk markets and maintain existing overseas production footprints, reducing the likelihood of hasty withdrawal from critical supply chain nodes during periods of geopolitical tension—consistent with the view that supply networks must maintain connectivity and viability under systemic shocks (Ivanov & Dolgui, 2020).

4.3 Differentiated Contributions of Mandatory and Voluntary Insurance Arrangements

This study further distinguishes policy-based (quasi-mandatory) arrangements led by export credit agencies from voluntary arrangements led by private insurers. Data show that least developed countries account for only about 15 percent of political risk insurance-covered projects, yet the insured project value is equivalent to roughly 28 percent of total foreign direct investment flowing into those countries, compared with about 6 percent for developing countries and about 2 percent for developed countries (UNCTAD, 2025). Table 4 compares the two types of arrangement.

TABLE 4

Dimension	Policy-Based Insurance	Commercial Insurance
Provider	Export Credit Agencies and public institutions	Private insurance companies
Participation	Government-supported or quasi-mandatory	Voluntary purchase by enterprises
Primary Objective	Address market failures and political risks	Meet firm-specific risk management needs
Target Market	High-risk countries and strategic investments	General international business activities
Pricing Mechanism	Policy-oriented	Market-oriented
Product Flexibility	Relatively standardized	Highly customized
Governance Function	Public risk sharing and policy support	Complementary commercial risk management
Contribution to Supply Chain Resilience	Strengthen baseline resilience under extreme uncertainty	Improve operational flexibility and adaptive capability

Table 4 shows that policy-based arrangements absorb a disproportionately large share of risk in high-risk markets where information asymmetries and externalities are most pronounced, consistent with the insurance economics argument that mandatory insurance is best suited to contexts marked by pronounced information problems and externalities (Faure, 2006). Commercial arrangements, by contrast, offer customized coverage based on firms' own risk appetite and project characteristics, providing manufacturing firms with an established degree of risk-management capability a supplementary tool.

5. Discussion

The analysis above indicates that insurance mechanisms do not merely provide passive financial protection for manufacturing firms operating abroad but are embedded within firms' supply chain risk-governance systems, supporting risk identification, risk mitigation, and liquidity management (Table 3). This finding extends a supply chain risk management literature that has largely focused on internal organizational capability-building (Sahab & Oulfarsi, 2026; Chowdhury & Quaddus, 2017), indicating that external risk-transfer instruments should be incorporated into the analytical framework of supply chain resilience research. The comparative analysis of policy-based versus commercial insurance (Table 4) offers a concrete supply chain management application for the literature on green insurance's mandatory and voluntary dimensions: in high-risk regions marked by pronounced information asymmetries and externalities, policy-based arrangements play an irreplaceable, complementary role (Faure, 2006); in relatively lower-risk market environments, the voluntary purchase of commercial insurance reflects firms' own risk-management initiative.

For insurers, these findings point toward developing more targeted political risk insurance and export credit insurance products addressing manufacturing firms' supply chain disruption risks, and deepening cooperation with host-country investment promotion agencies and multilateral development institutions. For manufacturing managers, insurance purchasing decisions should be integrated into the firm's overall supply chain risk management strategy. For

policymakers, continued refinement of export credit insurance and political risk insurance frameworks is warranted, with an emphasis on a complementary relationship between policy-based and commercial insurance.

6. Conclusion

Using qualitative document analysis and UNCTAD's (2025) Investment Policy Monitor 30: Political Risk Insurance as the primary analytical text, this study has examined the pathways through which insurance mechanisms contribute to the resilience of manufacturing firms' overseas supply chains, and has distinguished the differentiated contributions of mandatory and voluntary insurance arrangements. The findings show that export credit agencies are the dominant providers of political risk insurance and manufacturing is a leading covered sector (Tables 1 – 2); insurance mechanisms enable supply chain resilience through three pathways—risk identification, risk mitigation, and liquidity support (Table 3); and policy-based arrangements absorb a disproportionately large share of risk in high-risk markets, while commercial arrangements provide firms with a more flexible, supplementary risk-management tool (Table 4).

This study has two main limitations. First, as a qualitative document analysis, its conclusions rest on the systematic interpretation of a single authoritative policy text, without interview or case data from specific manufacturing firms. Second, the study did not draw on firm-level quantitative data linking insurance purchasing behavior to supply chain performance outcomes. Future research could adopt a multiple-case-study design, selecting representative manufacturing firms with overseas operations for in-depth interviews to validate the theoretical pathways proposed here; where data permit, quantitative methods could also test the empirical relationship between insurance purchasing and supply chain resilience performance.

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Chemical Sciences

Impact of ozonized water on resveratrol and quercetin in red wine of Georgia (region Bolnisi)

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Winemakers Association "Wine Bolnisi"

Abstract
The effect of aqueous ozone on resveratrol and quercetin levels in red grapevines and wines of Saperavi and the indigenous Tavqveri from Georgia studied. Shown that ozonizing did indeed cause oxidative stress and enhance defense reactions with the formation of adding quantity of resveratrol. The content of resveratrol in wines from ozonated plot increased on 30 %. the distribution of resveratrol and quercetin across the vine is uneven, with the highest concentrations found in the leaves and skins of the berries.
Keywords: *red wine, ozonized water, spraying, resveratrol, quercetin*

Introduction
The use of chemicals for treating grapes and wines is becoming increasingly less popular due to their adverse, and sometimes toxic, impact on the environment and human health. Over the past two decades, the issue of replacing grape treatments with pesticides has become increasingly pressing [1-3]. Now is known that pesticide levels in European wines have increased sharply, particularly the concentration of poorly soluble trifluoroacetic acid (TFA). TFA is a hazardous chemical that accumulates in grapes and [4]. In contrast, no traces of TFA were detected in wines produced before 1988. Data indicate a sharp increase in TFA contamination since 2010. This has created a pressing need to develop new, safe protection methods. One such environmentally friendly method for treating grapes during growth, development, and ripening is aqueous ozonation.
In oenology, ozone has found application in vinification, aging, and equipment sanitization. However, more and more studies are appearing on the use of ozone to combat pathogens at all stages of grapevine growth and ripening, as well as on its effect on important red wine

components such as the polyphenols resveratrol, quercetin, catechin, epicatechin, proanthocyanidins, and other antioxidants. The most attractive of these is resveratrol (3,5,4'-trihydroxy-trans-stilbene) (Fig. 1), whose significant benefits include regulating the human immune system, treating various inflammations, chemopreventing, neuroprotection, cardioprotection, lipid regulation, and treating diseases such as diabetes, Parkinson's disease, and cancer. In addition, it exhibits antibacterial, antiviral and antifungal activity [5, 6]. Quercetin, as a powerful natural antioxidant, has five hydroxyl groups (Fig. 2) and has more pronounced anti-inflammatory and antiallergic properties.

A number of studies on the effects of ozone, a strong oxidizer, on grapes and wine products have noted that, depending on the concentration, time, and number of applications, it can have both positive and negative effects [7.8]: in small doses, it initiates plant defense mechanisms and increases resveratrol levels; in large doses, it causes vine burn.

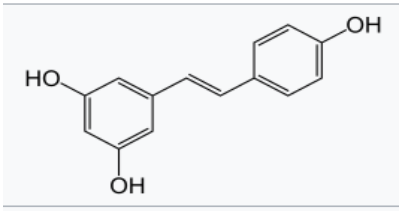

Fig. 1. Resveratrol

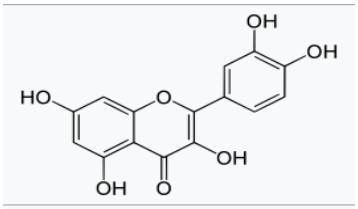

Fig. 2. Quercetin

This study examined the effects of aqueous ozone on resveratrol and quercetin levels in red grapevines and wines of Saperavi and the indigenous Tavqveri from Georgia's oldest region, Bolnisi. The objectives were provided by the Dzmebis Marani winery and its manager, Guram Avkopashvili.

It's worth noting that the Bolnisi microzone is a winemaking region with a rich and unique history, which distinguishes it from the renowned Kakheti region. Bolnisi is known as one of the oldest centers of winemaking, as evidenced by the discovery of Neolithic qvevri. The influence of German colonists, the Swabians, who settled here in the early 19th century, is unique. They brought European methods and techniques to local winemaking, including large wooden vats, which are still used alongside traditional qvevri.

However, the chemical composition of Bolnisi wines remains poorly understood, and the effect of the environmentally friendly ozone-based protection method against vine diseases on the content of the main components is proposed for the first time in this study.

Objectives and Methods

Soil and vine chemical analysis was conducted not in test plots with predetermined ozone or pesticide treatment conditions, but in actual vineyards, managed by winegrowers according to climate conditions and their own experience. Ozone generators (to generate ozonated water immediately prior to grapevine treatments) and water containers were installed in the vineyard. The procedures were carried out for 15 minutes per treatment, with a concentration of 2-3 mg/L early in the morning at a temperature of 18-20^{0}C.

The content of resveratrol and quercetin is determined using high-performance liquid chromatography (HPLC) on the device Agilent 1290 Series UHPLC coupled with 6450 Accurate Mass-Q-TOF-LC-HRMS. Mobil phase: MeOH/Acetic Acid 2% in Water 50:50; Column: Discovery C18, 4.6x250mm, 5um Particle Size; Thermostat temperature: 25 degrees; Initiation volume: 5µl; Flow rate: 1.0 ml/min.

Soil samples and grapevine parts from trunk to seed were collected manually in April and at the end of September. Two key components—resveratrol and quercetin—were selected to monitor the impact of ozone on wine quality and organoleptic properties.

Wine and juice samples were treated by the method of wet mineralization. A sample of 50 ml red wine was put into a glass, 5 ml con. HNO_3 was added and heated on a sand bath. If the sample was not discoloration for 1 hour, it was cooled and then 2 ml con. HNO_3 was added. Heating continued until the solution discoloration, after which the sample was transferred into a graduated 10 ml cylinder and brought to volume. Acid digestion of materials was carried out in a sample decomposition system Microwave Pressure Digestion Labstation MWS-3, BERGHOF. Strong acid 1N HNO_3, ammonium acetate buffer solution with pH = 4.8 and water were used as extractants. Below in Figures 3 and 4 there are shown the chromatograms of a standard mixture of resveratrol and quercetin, and their presence in the studied samples.

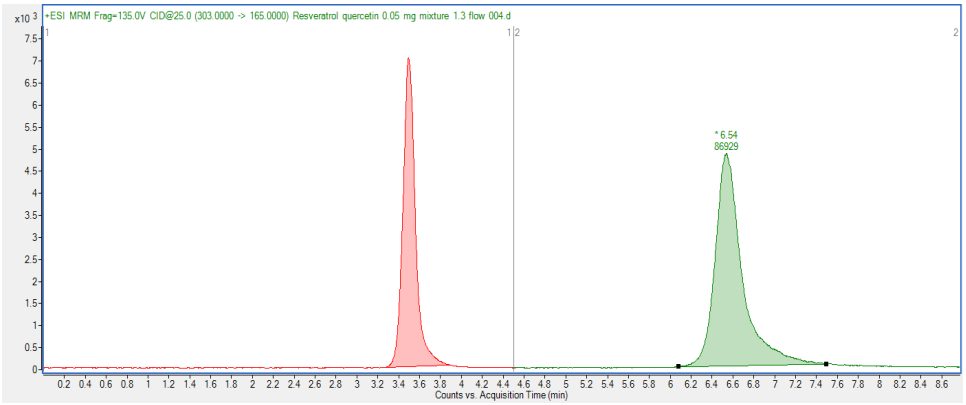

Fig.3. Chromatograms of mix of standards resveratrol and quercetin (0.09 mg/mL concentration)

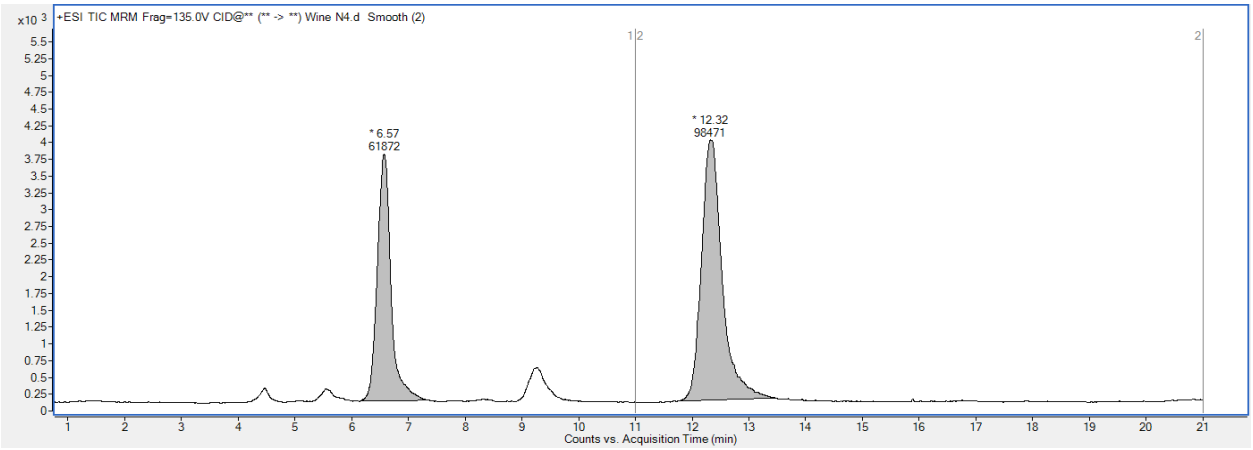

Fig.4. *Chromatograms of resveratrol (left) and quercetin (right) in wine "Saperavi"*

Results and discussion

The results of determining resveratrol and quercetin content in Saperavi grape leaves, pulp, seeds, and skin treated with aqueous ozone throughout the season are presented in Table 1. According to the data, the highest amount of resveratrol is found in the skin, followed by the seeds, but resveratrol is virtually absent from the pulp. The highest amount of quercetin is found in the leaves of ozonated Saperavi grapes and is also absent from the pulp. In the non-ozonated section, resveratrol content is significantly lower in all parts of the vine compared to the ozone-treated section, almost an order of magnitude lower in the skin. Ozonation did indeed cause oxidative stress and enhance defense reactions with the formation of secondary metabolites, particularly resveratrol. Quercetin is highest in the seeds and leaves of ozonated grapes. The concentration of resveratrol in the leaves of ozonated Tavkveri is 5.76 mg/kg, and quercetin is 6.0 mg/kg, which is also higher compared to grapes treated with systemic drugs, in the leaves of which resveratrol was not detected.

Table. The content of resveratrol and quercetin in Saperavi grape from ozonated and non-ozonated sites, mg/kg

Sample	Component	Ozonated site	Non-ozonated site
Leaf	Resveratrol	5.3	3.4
	Quercetin	14.0	9.5
Skin	Resveratrol	26.5	2.4
	Quercetin	4.4	8.2
Pulp	Resveratrol	< 0.01	1.0
	Quercetin	<0.01	0.22
Seed	Resveratrol	10.2	1.0
	Quercetin	4.5	0.4

In wines made from these grapevines, the ratio of Resveratrol to Quercetin remained virtually the same, with more resveratrol and quercetin in the ozone-treated samples.

So, content of resveratrol in Saperavi wine from non-ozonated (control) plot and ozonated were equal to 3.03 and 4.43 mg/l accordingly; quercetin 0.02 in wine, treated with systemic preparations and 0.7 mg/l in ozonated. Therefore, the content of resveratrol in wines from ozonated plot increased on 30 %. Resveratrol content in leaves of Saperavi grape, treated with systemic preparations reached 7.6, quercetin content 20.05 mg/kg.

An interesting fact was that the amount of resveratrol in wines made from the same grape varieties on the same soils decreases over the years: 2022 year - C(RVS) = 18.3 mg/L; 2024 year - C(RVS) = 6.38 mg/L; 2025 year - C(RVS) = 2.31 mg/L; 2026 year - C(RVS) = 0.65 mg/L. This persistent decline in resveratrol content over the years can be explained either by climatic conditions or by the aging of the wine in bottles – wine aged for 4 years has several times higher resveratrol levels.

Conclusion

Based on the obtained results of resveratrol and quercetin analyses, it was shown that seasonal spraying of Saperavi and Tavkveri grape varieties in the Bolnisi region with ozonated water, using the technology used by Georgian winegrowers (7-8 sprays with a concentration of 2-3 mg/L for 15 minutes at 18-20°C), successfully replaces pesticides and sulphur dioxide in the fight against pathogens and does not affect the organoleptic properties of wines. Furthermore, it improves their quality and stability during maceration due to increased resveratrol levels. It was shown that the distribution of resveratrol and quercetin across the vine is uneven, with the highest concentrations found in the leaves and skins of the berries.

However, these data are preliminary. Further research is needed to determine the dosage and frequency of treatments, as well as potential changes in the content of numerous other components, to avoid risks of deteriorating wine quality or damaging the vines.

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Historical Sciences

AZERBAIJAN-UKRAINE RELATIONS

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Keywords: Azerbaijan, Ukraine, diplomatic relations, cooperation and partnership, GUAM, Humanitarian and cultural relations, support of territorial integrity

Summary

The article examines the historical development stages of Azerbaijan-Ukraine relations, diplomatic relations formed during the period of independence, and the main directions of strategic partnership. The study shows that the relations between the two peoples have ancient historical roots, trade and cultural relations have been formed since the Middle Ages, and diplomatic contacts were established between the Azerbaijan Democratic Republic and the Ukrainian People's Republic at the beginning of the 20th century. Special attention is paid to the political relations established between Azerbaijan and Ukraine as independent states after 1991, the activities of diplomatic missions, and the importance of signed bilateral agreements. The article evaluates the mutual visits of heads of state, cooperation within the framework of GUAM, the UN, the OSCE, and other international organizations, mutual support for sovereignty and territorial integrity as the main principles of relations. In addition, the dynamics of the development of cooperation in the fields of energy, trade, transport, humanitarian, education, and culture, the activities of diaspora organizations, and the prospects for economic relations are analyzed. The impact of the Russian-Ukrainian war on Azerbaijani-Ukrainian economic relations, changes in trade turnover and Azerbaijan's humanitarian support to Ukraine are also important aspects of the research. The results of the study show that Azerbaijani-Ukrainian relations are developing based on historical traditions, mutual trust, respect for the principles of international law and strategic partnership and are of significant political and geopolitical importance in terms of strengthening regional cooperation.

Introduction. Relations between Azerbaijan and Ukraine are one of the important directions of the system of interstate relations, which is based on historical roots and has risen to the level of strategic partnership during the period of independence. The foreign policy course of both states, based on the principles of sovereignty, territorial integrity and international law, has created a favorable basis for the development of mutual cooperation. After gaining independence, the establishment of diplomatic relations, expansion of political dialogue, mutual support within the framework of international organizations, as well as cooperation in the economic, energy, transport, humanitarian and cultural spheres have constituted the main directions of Azerbaijan-Ukraine relations. In recent years, geopolitical processes and changes in the security environment in the region have further increased the strategic importance of these relations. The article analyzes the historical stages of development of Azerbaijan-Ukraine relations, their current state and the main directions of cooperation from a historical and political perspective.

Main text. The history of relations between Azerbaijan and Ukraine has deep roots. According to scientific research, the foundation of these relations was laid as early as 1000 years ago, during the time of the Kievan Rus' state, as a result of initial trade relations with the states located in the geography of Azerbaijan. At that time, quite extensive information was published in scientific journals about the arrival of merchants of the Kievan Rus' state to these territories. In

subsequent periods, along with trade relations between the peoples located in both geographical areas, cultural relations also began to form and expand. There is also sufficient information about the arrival of Ukrainian cultural and scientific representatives and scientists to Azerbaijan in the 19th century, their activities in Baku, Ganja and other regions, as well as their contribution to the development of cultural relations between the two peoples. Today, scientific research is being conducted on these issues both in Azerbaijan and Ukraine.[20]

Although official diplomatic relations between Ukraine and Azerbaijan were established on February 6, 1992, the history of the diplomatic presence of Ukrainians on Azerbaijani soil dates back to the struggle of both peoples for independence in the 20th century.

The first Ukrainian consulate in Baku was opened in September 1918, a few months after the proclamation of the Azerbaijan Democratic Republic. On September 21, 1919, the Ministry of Foreign Affairs of the ADR recognized the head of the Ukrainian community living in Baku, Mr. Golova, as the temporary vice-consul of the Ukrainian People's Republic (UPR).

The date when diplomatic relations between Ukraine and Azerbaijan were further strengthened was February 8, 1919. On that day, the head of the UPR Special Diplomatic Mission to Azerbaijan, Ivan Kraskovsky, presented his credentials to the ADR leadership. In October of that year, a Ukrainian diplomatic mission arrived in Baku, the delegation of which included representatives of the UPR government, including attachés and special officers. This page was the first full-fledged example of interstate diplomatic cooperation in our common history.

After Ukraine gained independence in 1991, Azerbaijan was one of the first countries to recognize this independence. Since then, Ukrainian-Azerbaijani relations have been constantly developing on the basis of the principles of friendship, mutual respect and strategic partnership.

The Embassy of Ukraine in Azerbaijan was officially opened on May 5, 1996. Initially, the embassy was located in a rented building of the “Azerbaijan” hotel. Since October 15, 2001, the Embassy has been operating in its own building on the street named after the prominent Azerbaijani figure and the first ambassador of the ADR to Ukraine, Yusif Vazir Chamanzaminli. It is symbolic that the diplomatic mission of Ukraine is located on a street that reflects the historical respect and mutual recognition between our peoples.[22]

Relations between Azerbaijan and Ukraine are based on friendship, mutual respect and beneficial cooperation.

After gaining independence, both countries have attached special importance to developing relations in political, economic, energy, transport, humanitarian and other areas.

These relations are based not only on the official level, but also on mutual sympathy and trust between the peoples. In the political sphere, relations between Azerbaijan and Ukraine are stable and sustainable. Meetings between the leaders of the two countries, mutual visits and negotiations within the framework of international events indicate the high level of relations. Both states support the principles of international law, the sovereignty and territorial integrity of countries. In this regard, the political support provided by the parties to each other is one of the main directions of relations.[15]

Diplomatic relations between the Republic of Azerbaijan and Ukraine were established on January 31, 1992. In 1996, the Embassy of Ukraine was opened in Azerbaijan, and in 1997, the Embassy of Azerbaijan in Ukraine was opened.

The basis of the relations between our states is the Treaty on Friendship, Cooperation and Partnership between the Republic of Azerbaijan and Ukraine dated March 16, 2000 and the Declaration on Friendship and Strategic Partnership between the Republic of Azerbaijan and Ukraine dated May 22, 2008.

Relations between Azerbaijan and Ukraine in political, economic, scientific, educational, cultural and other spheres are developing rapidly, the two states are strategic partners. Inter-parliamentary relations and cooperation in the field of legislation are developing.

Azerbaijan and Ukraine hold consultations within the framework of the UN, the Council of Europe, the BSEC, GUAM, the CIS and other international and regional organizations and traditionally provide mutual support to each other. At the same time, the two countries actively cooperate in the fight against terrorism, organized crime, drug trafficking and other dangerous types of crimes.[13]

It is not enough to view the relations between the Republic of Azerbaijan and Ukraine only as official diplomatic relations; these relations are a deep philosophy of partnership shaped by similar historical destinies, geopolitical challenges and the will to independence. Both nations, having separated from the imperial system at the end of the 20th century, were forced to rebuild their statehood and in this process faced the same problems - economic transformation, political stability and the challenges of protecting territorial integrity. It is this parallelism that gives Azerbaijani-Ukrainian relations a deeper meaning beyond the formal framework.

This path, which began with the establishment of diplomatic relations in 1992, was actually more of a strategic choice than a political act. Because both Azerbaijan and Ukraine, when determining their place in the international system, had to take into account not only their national interests, but also the general security environment. In this regard, the mutual support they demonstrate within the framework of organizations such as the United Nations and the OSCE is not accidental, but an expression of a thoughtful and principled position.[19]

The analogy between today's Ukraine and Azerbaijan of the 1990s - an important leadership phenomenon - in modern international relations, ensuring peace, preventing conflicts and strengthening the security of states directly depends on the strength of political leadership. The discussions surrounding the peace plan presented for Ukraine also show that leadership with a decisive, strategic position plays a decisive role in the fate of countries.[22]

Bilateral relations between Azerbaijan and Ukraine are built on the principles of mutual respect, support for territorial integrity and strategic cooperation in the post-Soviet space. Both countries established diplomatic relations after gaining independence in 1991, and these relations have developed over the years in the political, economic and humanitarian spheres.

On the political level, Azerbaijan and Ukraine closely cooperate within the framework of international organizations, in particular within GUAM (Georgia, Ukraine, Azerbaijan, Moldova). This platform serves to promote respect for the sovereignty, territorial integrity of member states and the principles of international law. Both countries have always supported each other's territorial integrity and advocated the resolution of conflicts within the framework of international law.

Economic relations are also an important aspect of the relationship. Azerbaijan plays a certain role in Ukraine's energy security, especially in the field of oil and oil product exports. At the same time, Ukraine acts as a partner in the non-oil sector of Azerbaijan, including agriculture, mechanical engineering and industry. Although trade turnover has changed at different times, both countries are interested in expanding economic relations.

Humanitarian and cultural relations are also noteworthy. The Azerbaijani diaspora living in Ukraine and the Ukrainian community operating in Azerbaijan play the role of a bridge between the peoples. Cooperation in the fields of education, culture and tourism contributes to the deepening of relations. Various student exchange programs and cultural events further strengthen these relations.

In recent years, against the backdrop of regional and global challenges, relations between Azerbaijan and Ukraine have entered a new stage. The prospects for cooperation in the fields of energy, transport and logistics are expanding, in particular. Azerbaijan's transit opportunities and Ukraine's potential for access to European markets create a favorable basis for mutually beneficial cooperation.[3]

“The strong relations between the parties are not newly formed, they are based on history...The foundation of strong relations between the two countries was laid with the visit of the National Leader Heydar Aliyev to Ukraine in 1995.

Later, with the visits of President Ilham Aliyev to Ukraine, the dynamics of development in these relations began. Also, Ukrainian leaders regularly visit our country. Both countries have always supported each other's territorial integrity and have shown their support on international platforms. In addition, the relations between the peoples of Azerbaijan and Ukraine are quite high.[16]

Historically, the Azerbaijani people have been closely connected with the Crimean Tatars, a Turkic-speaking people living on the Crimean peninsula of the Republic of Ukraine. Crimean Turks Ismail Gaspirali, Mustafa Krimoglu, etc. are still remembered with respect by Azerbaijani intellectuals today. Approximately 500 thousand Azerbaijanis live in Ukraine. A strong Azerbaijani diaspora operates in this country and they actively participate in socio-political processes, including being represented in leadership positions. Ukraine is one of Azerbaijan's main strategic allies in the CIS and relations with this country exist in almost all areas, from socio-economic, educational, cultural to military cooperation. Azerbaijan and Ukraine have also established fairly good relations for many years within the framework of the Organization for Economic Development, GUAM. Ukraine has always demonstrated a position supporting Azerbaijan's position both during and before the Karabakh war. Azerbaijan has also supported the territorial integrity of Ukraine all these years and continues to support the territorial integrity of Ukraine today. Because Azerbaijan is guided by the norms and principles of international law in international relations. In these norms and principles, the issue of sovereignty and territorial integrity of states always comes to the fore.[12]

On the one hand, the Russia-Ukraine war did not remain without an impact on trade and economic relations with Ukraine, which is one of Azerbaijan's important economic partners. This is more clearly reflected in the decline in our trade relations in the first years of the war. Thus, before the war began, that is, in 2021, the volume of trade turnover between Azerbaijan and Ukraine was $922 million. After the war began, in 2022, that is, within one year, trade turnover between Azerbaijan and Ukraine decreased by more than $300 million, or 33 percent, and fell to $618 million. However, in recent years, positive dynamics in trade turnover between Azerbaijan and Ukraine have gradually begun to recover. In 2025, trade turnover between Azerbaijan and Ukraine demonstrated positive dynamics compared to the previous year and exceeded $513 million, including imports of $292.5 million or 1.2 percent of our imports, and exports of $221 million or 0.9 percent of our exports. However, our trade turnover with Ukraine decreased from $922 million to $513 million, or 44 percent, compared to 2021, before the Russia-Ukraine war, including imports from $470 million to $292.5 million, or 38 percent, and exports from $452 million to $221 million, or 51 percent. In 2021, Ukraine ranked 7th among 188 countries with which Azerbaijan has established trade relations in terms of trade turnover and 5th in terms of imports, but in 2025 it will not be among the top ten countries. Official figures show that both Azerbaijan’s exports to and imports from Ukraine have decreased. By effectively utilizing the existing potential in this area, trade turnover between Azerbaijan and Ukraine can be increased to the level before the Russia-Ukraine war in the coming years, and then to over $1 billion.[14]

Today, Azerbaijan undoubtedly has high political relations with Ukraine, and in addition to defending each other on various platforms, one can even recall the speeches of the Ukrainian delegation in the Council of Europe and other platforms in defense of Azerbaijan's position. On the other hand, this shows that relations at the political level also affect economic spheres. Especially before the war, there were very close economic relations, and we clearly saw this in agriculture, trade and various fields. These relations were gradually deepening. However, the

outbreak of the Russian-Ukrainian conflict prevented many processes in a certain sense, but this does not mean that these processes stopped completely.

During this period, the provision of humanitarian and technical support to Ukraine by Azerbaijan, especially in the areas of fuel and emergency assistance, was highly appreciated by the Ukrainian public.

At the same time, the support of the Azerbaijani government in providing state institutions operating in the fields of emergency assistance, emergencies and other services to the population in Ukraine with the necessary means and fuel was highly appreciated by the Ukrainian people.

Also noteworthy are the investment projects implemented by Azerbaijan in Ukraine, including its participation in restoration and reconstruction works. The participation of Azerbaijani companies in the reconstruction of some cities and their contribution to infrastructure projects are real results of the strategic partnership. This shows that relations are developing not only on a political but also on a practical level.[4]

Diplomats, scientists, historians, young people and students joined the online scientific conference “Diplomatic cooperation between Azerbaijan and Ukraine: through the prism of the past and modernity” organized by ADA University and the embassies of the two countries.

Azerbaijani Ambassador to Ukraine Elmira Akhundova gave a speech and reviewed the history of high-level diplomatic relations between the two countries...

The ambassador, who said that relations between the two countries had entered a new stage after the return of the national leader Heydar Aliyev to power, recalled that Ukrainian President Leonid Kuchma paid an official visit to Azerbaijan in July 1995 and 11 documents on cooperation between the two countries were signed. Two years later, in March 1997, the Great Leader paid an official visit to Ukraine. The close friendship of these two leaders laid the foundation for strategic cooperation between Azerbaijan and Ukraine.[1]

In general, Ukraine is considered one of Azerbaijan's main strategic allies in the post-Soviet space. These relations have further developed based on the Treaty of Friendship, Cooperation and Partnership between the two countries on March 16, 2000, the Treaty of Friendship, Cooperation and Strategic Partnership on May 22, 2008, and the "Joint Declaration" between the two countries on January 14, 2022.

The historical visits of the leaders of both countries during the period of independence contributed to these relations. Ukraine has always supported the territorial integrity and sovereignty of Azerbaijan on all platforms. In response to this visit, on March 24, 1997, the President of Azerbaijan, national leader Heydar Aliyev paid an official visit to Kiev. In addition, there were sincere and friendly meetings between the leaders of both countries at all international events. The intensive dynamics of Azerbaijani-Ukrainian relations continued during the term of Ilham Aliyev. It is no coincidence that Ilham Aliyev's first official visit to Kiev took place on June 3, 2004. The meeting discussed in detail the issues of trade and economic cooperation, including cooperation in the oil industry and in the field of transportation of energy carriers to Europe, exchanged views on international problems, issues of cooperation within the framework of GUAM, and mutual relations with the European Union and NATO. In response to this visit, the President of Ukraine Viktor Yushchenko paid his first official visit to Azerbaijan on September 7, 2006. During the visit, trade and economic cooperation, including cooperation in the oil sector and transportation of energy carriers, were discussed. After that, there were mutual visits of the leaders of both countries. Each visit contributed to relations and further developed ties. The first visit of the current President of Ukraine, Volodymyr Zelensky, to Azerbaijan and the South Caucasus took place on December 18, 2019. In response to this visit, Ilham Aliyev paid a working visit to Ukraine on January 14, 2022.[17]

Relations between Azerbaijan and Ukraine are characterized by deep ties, based on both historical roots and a modern strategic partnership. According to the latest data as of April 2026, these relations have entered a new stage, especially in the military-technical and humanitarian spheres.

Azerbaijan and Ukraine consistently support each other's sovereignty and territorial integrity at the international level. On April 25, 2026, Ukrainian President Volodymyr Zelensky paid an official visit to Azerbaijan. This was his first visit to Baku since the start of the war. Both countries cooperate closely within the framework of GUAM and in a bilateral format.

The energy sector forms the backbone of relations. Azerbaijan's state oil company SOCAR is one of the main players in the Ukrainian fuel market and has an extensive network of gas stations throughout the country.

Trade turnover between the two countries has exceeded $500 million, and new logistics projects are planned to increase this figure (for example, through the Alat Free Economic Zone).[18]

Today, the Embassy of Ukraine in Azerbaijan is not only an official diplomatic institution, but also a symbol of ancient friendship, strong partnership, and the common European future of our countries.[2]

Azerbaijani-Ukrainian relations have generally always been at a high level: "After Azerbaijan declared independence, it established very serious economic and political relations with Ukraine. Recently, these relations have expanded even further. Especially after President Ilham Aliyev came to power, these relations have been given greater priority. The Azerbaijani state recognizes the territorial integrity of Ukraine. That is, despite the war between Russia and Ukraine, Azerbaijan always supports official Kiev and provides humanitarian assistance. Recently, humanitarian aid was sent on the instructions of Mr. President. There are very serious relations between Azerbaijan and Ukraine in the energy sector. We know that Azerbaijan carries out the bulk of its oil and gas exports and processing through Ukraine. SOCAR branches operate there. In addition, gas compressor stations also operate there. Recently, Azerbaijan-Russia relations have been somewhat cold. In this regard, Russia has carried out some attacks. As a result of these attacks, some SOCAR facilities, including the gas compressor station, were damaged".[23]

Azerbaijan and Ukraine also work together in international organizations as strong regional partners. Cooperation within the UN, OSCE, GUAM, the Black Sea Economic Cooperation Organization and other organizations has further strengthened bilateral strategic relations. The signing of the Joint Declaration between the two countries, as well as political documents on the development of strategic cooperation, is of great importance for the relations to reach a high peak. Azerbaijan is an independent state, builds and implements its foreign policy, bilateral and multilateral relations in accordance with its national interests. These relations have never been directed against other countries. Azerbaijan supports the territorial integrity and sovereignty of all countries. This is one of the fundamental principles of international law. If these principles are not observed, security, cooperation, and peaceful coexistence become impossible. Azerbaijan has suffered from the violation of its territorial integrity for decades. Therefore, it is well aware of the importance of observing these principles. Azerbaijan does not participate in any form in the conflict between Ukraine and Russia, and is completely far from military components.[21]

Conclusion. Thus, the conducted research shows that Azerbaijan-Ukraine relations have developed based on historical traditions, mutual trust and the principles of strategic partnership. During the period of independence, the establishment of diplomatic relations, mutual visits of heads of state, signing of bilateral agreements and cooperation within the framework of international organizations played an important role in strengthening relations. At the same time, the expansion of cooperation in the political, economic, energy, transport, humanitarian and cultural spheres created conditions for the development of mutually beneficial partnership

between the two countries. Although the Russian-Ukrainian war had a certain impact on economic relations, Azerbaijan continued to support the sovereignty and territorial integrity of Ukraine, and maintained humanitarian assistance and other areas of cooperation. The results of the research show that Azerbaijan-Ukraine relations, based on mutual interests and the principles of international law, will continue to be of great importance in strengthening regional stability and multilateral cooperation in the future.

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Biological Sciences

Sweden's Educational Reversal and the Neurocognitive Cost of Digitalised Childhood

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Abstract
In 2023 the Swedish Government, supported by the Swedish National Agency for Education (Skolverket), announced an unprecedented redirection of public-school policy: hundreds of millions of kronor were allocated to restore printed textbooks as the primary pedagogical medium, a national mobile-phone restriction was enacted in primary and lower-secondary classrooms from 2026 onwards, and the prior "one-to-one digital" strategy was formally re-described as a partial failure. Sweden's reversal is not an isolated administrative gesture; it coincides with a measurable drop in reading literacy on the Progress in International Reading Literacy Study (PIRLS) 2021 and a persistent downward drift on the Programme for International Student Assessment (PISA) 2022, and it echoes converging neuroscientific evidence that extensive screen exposure restructures children's developing brains at the molecular, cellular, and network level. This article reviews the Swedish policy reversal in its socio-political context and synthesises current evidence on how four major gadget categories — smartphones, tablets, laptops, e-readers, televisions, and dedicated gaming consoles — differentially alter reading comprehension, attentional control, sleep, mood, and structural neurobiology in children and adults. We map molecular mechanisms including dopaminergic reward de-sensitisation, brain-derived neurotrophic factor (BDNF) suppression of synaptic plasticity, hypothalamic–pituitary–adrenal (HPA) axis dysregulation, and circadian melatonin suppression, and contrast their effects on the developing and the mature brain. The synthesis supports a graded risk hierarchy in which passive smartphone scrolling and high-tempo action gaming during sensitive windows of cortical maturation confer the largest documented cognitive cost, while static e-reader text and educational television carried under controlled conditions appear comparatively benign. By framing Sweden's "books and pens" decision as an evidence-consistent response to a measurable neurocognitive burden, this review contributes to the scientific basis for educational technology policy.
Kay words: Sweden; educational policy reversal; digitalised childhood; reading literacy; neurocognitive development.

Introduction

Introduction: Why a Technological Leader Pivots Back

Sweden long occupied an enviable position in international comparative education. Its schools ranked at or near the top of OECD reading, mathematics, and science performance throughout the early 2000s, and it was simultaneously the first nation to issue a national strategy of one-to-one digital device provisioning for every pupil (Bäcklund et al., 2026). Between 2011 and 2021 the Skolverket explicitly recommended that tablets, laptops, and learning-management applications replace or supplement printed textbooks in foundational literacy instruction. Yet by

the close of the decade two divergent trends became unmistakable. On the one hand, OECD-coordinated assessments documented a marked drop in reading achievement. PIRLS 2021 placed Swedish fourth graders at 544 points, the lowest score ever recorded for Sweden in that cycle and a 17-point decline since 2016 (Reimers et al., 2025). PISA 2022 confirmed parallel losses in reading, mathematics, and science, and a Ministry of Education commissioned report concluded that heavy classroom use of digital devices was associated with lower — not higher — performance once socioeconomic status was controlled (OECD, 2023). On the other hand, the global neuroscience literature on screen-based media and the developing brain accumulated at unprecedented speed, with the Adolescent Brain Cognitive Development (ABCD) study, the European longitudinal cohorts, and several diffusion tensor imaging cohorts consistently reporting structural and functional correlates of habitual high-intensity screen exposure (Paulus et al., 2019; Hutton et al., 2020). The convergence of these two streams — worsening literacy outcomes in a heavily digitised population, paired with mechanistic neurobiological concern — created the political conditions for the 2023 pivot. This article integrates the policy record with the molecular and systems-level neuroimaging literature to ask three questions: (1) what does the Swedish reversal actually change in classroom practice; (2) what are the documented neurocognitive mechanisms by which digital media produce harm; and (3) which gadget categories and which developmental windows carry the highest risk. The aim is to provide a balanced, scientifically rigorous platform on which future curricular, regulatory, and parental guidance can be built (Fig 1).

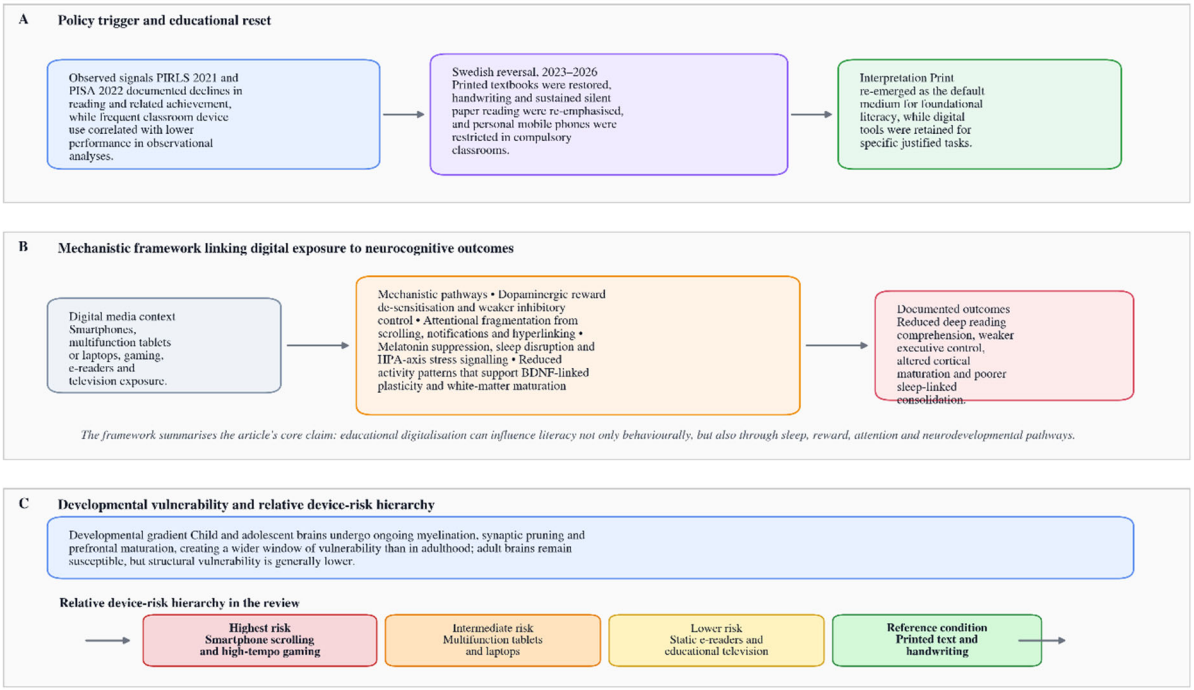

Figure 1. Conceptual framework linking Sweden's educational policy reversal to the neurocognitive consequences of digitalised childhood.
(A) National learning declines and the Swedish policy reset are summarised, including renewed investment in printed textbooks, restoration of handwriting and sustained paper-based reading, and restriction of personal mobile telephones in compulsory classrooms. **(B)** Proposed mechanistic pathways by which screen-based media may influence learning and neurodevelopment are shown, including dopaminergic reward de-sensitisation, attentional fragmentation, melatonin suppression with sleep disruption and HPA-axis stress signalling, and reduced support for BDNF-linked plasticity and white-matter maturation. **(C)** A developmental gradient is illustrated, highlighting greater vulnerability during childhood and adolescence, together with a relative device-risk hierarchy in which smartphone scrolling and high-tempo

gaming occupy the highest-risk position, multifunction tablets and laptops an intermediate position, and static e-readers or educational television a lower-risk position relative to printed text and handwriting.

The Swedish Policy Reversal in Detail

The pivot unfolded across three administrative layers. First, in mid-2023 the Minister for Schools announced a one-off capital allocation of approximately 1.2 billion SEK (~€100 million) earmarked for the purchase of printed textbooks by municipalities, with the explicit goal that every pupil in compulsory grades should have access to a dedicated paper copy in every subject (Bäcklund et al., 2026). Second, in late 2024 the Skolverket issued an updated national digitalization strategy that, while retaining technological competence among its goals, removed the prescription of daily device-based instruction and reintroduced handwriting, dictation, and sustained silent reading on paper as core student skills from year one. Third, in early 2026 a nationwide regulation barred personal mobile telephones from primary and lower-secondary classrooms and required telephones to be kept out of sight throughout the school day, with implementation supported by municipalities and audited via the Schools Inspectorate. Importantly, the policy does not eliminate digital technology in Swedish classrooms; rather, it differentiates the role of the device from the role of the book. Tablets and laptops remain in use for specific didactic activities — coding, language-laboratory work, mathematics software — but the default literacy medium returned to print. Several justifications were cited. The Skolverket referred to international learning-loss trends and national test results showing that the largest declines were concentrated in inferred text comprehension and the construction of written arguments rather than in retrieving discrete facts, suggesting a deficit in deep rather than surface literacy (Reimers et al., 2025). Public-health bodies, including the Public Health Agency of Sweden and research groups at Karolinska Institutet, contributed formal commentaries emphasising sleep, attention, and mood endpoints in children (Mekhail et al., 2024). Although the political narrative sometimes framed the reversal as a repudiation of digital innovation, the policy text itself is more conservative: it positions print as the default for foundational literacy and reserves screens for explicitly justified pedagogical purposes. This nuance matters because it preserves the option of technology where evidence supports it while restoring the load-bearing function of the book.

The International Evidence Base: PIRLS 2021 and PISA 2022

Sweden's pivot cannot be evaluated without the dual quantitative anchor of PIRLS 2021 and PISA 2022. PIRLS assessed 159,425 fourth-grade students in 57 countries and reported an average reading achievement decline of 15 points (≈0.18 standard deviations) since the previous cycle (Reimers et al., 2025). Sweden's drop was among the steepest, and post-stratification analyses showed that students with fewer socioeconomic resources, students with Swedish as a second language, and students in schools with the most aggressive one-to-one device programmes registered the largest losses. PISA 2022 extended the picture to fifteen-year-olds. Across OECD countries reading scores fell by 10 points, mathematics by 15, and — for the first time in the instrument's history — problem-solving by 16 points; Sweden posted declines of comparable magnitude, with the steepest fall in mathematics. OECD analyses specifically dedicated a chapter to "Digital education in Sweden" and concluded that students reporting frequent use of digital devices during lessons scored lower on reading and mathematics once baseline achievement was controlled, while no comparable decrement was observed for students using devices for short discrete tasks (OECD, 2023). It is important to note that PISA does not establish causation: digital-device use and lower achievement may both reflect pre-existing educational disadvantage, lower teacher quality, or reduced exposure to literate cultural capital. Nonetheless, three lines of triangulation support the policy reversal. First, the size of the Swedish loss is larger than can plausibly be attributed to demographic shifts alone, since migrant-origin cohorts grew modestly and school funding per pupil remained stable. Second, countries with comparable digital-intensity

trajectories — including the Netherlands and parts of Germany — reported similar or smaller losses, suggesting that the Swedish decline is not a function of technology per se but of how intensively it was substituted for print in early literacy. Third, intervention studies in which schools reintroduced sustained silent paper reading produced gains that were statistically detectable within a single academic year, implying that the underlying mechanism is at least partially reversible. The combination of large-scale, longitudinal, cross-national evidence on performance and more granular evidence from within-country reversals creates the empirical scaffolding on which the Skolverket's withdrawal from compulsory device-based literacy rests.

Reading on Paper versus Reading on Screens: Cognitive and Ergonomic Evidence

A central neurocognitive argument for the Swedish reset is that reading on paper and reading on screens are not equivalent cognitive tasks. A series of meta-analyses converges on a small but robust advantage of paper over screen for expository, lengthy, and deep-reading tasks. The meta-analysis of Clinton (2019) compiled 33 studies with more than 25,000 participants and reported a moderate effect size favouring paper for reading-comprehension outcomes that require inference and integration rather than literal recall. The independent meta-analysis of Delgado et al. (2018) reached similar conclusions and noted that the gap was largest when reading time was uncontrolled and when the goal of the text was for later recall. Karpinski et al. (2015) extended this finding by demonstrating that even when participants are matched on reading speed and self-reported understanding at the moment of reading, delayed retention is significantly lower for screen-based material. Several candidate mechanisms have been proposed. First, screen reading is associated with higher meta-comprehension calibration errors — readers overestimate how much they have understood, which leads to less strategic re-reading (Mills et al., 2021). Second, screen reading competes with concurrent digital affordances — hyperlinks, scrolling, notifications — that draw on the same executive resources required for deep reading, producing measurable increases in task-irrelevant mind-wandering. Third, embodied ergonomics differ: a paper book provides a spatially stable haptic referent (page corners, overall thickness, known number of pages remaining) which supports situation-model construction, whereas a tablet or laptop ties the text to a virtual frame whose dimensions are continuously reconfigurable. Fourth, screens emit short-wavelength blue light and tend to be associated with later evening use, suppressing melatonin and degrading subsequent sleep-dependent consolidation (Silvani et al., 2022). Fifth, font-rendering variability, line-length changes with resizing, and continuous partial refresh on e-paper versus LCD versus OLED introduce subtle perceptual instability that may consume attentional bandwidth (Nichols, 2016). The aggregate literature does not claim that screens make reading impossible — skilled adult readers can compensate — but it does support the proposition that for novice readers, for habit-formation, and for the construction of deep comprehension, paper offers measurably richer cognitive affordances. The Swedish curricular shift re-weights the early-literacy environment toward the substrate that is most likely to support deep reading.

Mind-Wandering, Hyperlinks, and the "Shallows" of Online Reading

Beyond the comprehension results, a robust finding from cognitive neuroscience is that screen-based reading surfaces more frequent and more disruptive mind-wandering than equivalent paper reading. The classic account, articulated by Carr (2011), argued that the internet's reward structure — rapid task-switching, novelty density, micro-confirmations — conditions neurocognitive networks for shallow rather than deep processing. Empirical support has accumulated. Mills et al. (2021) deployed an "Eye-Mind Reader" that monitors eye movements in real time to detect mind-wandering during expository text reading and showed that screen readers exhibit significantly more off-text gazes, longer gaze durations, and reduced situation-model updating. Kuzmičová et al. (2020) demonstrated that reading fiction on mobile telephones specifically elevated distraction frequency during aesthetic immersion. Nichols (2016) reviewed the literature and concluded that on-screen reading consistently increases extraneous cognitive load relative to print, even when

reading time is strictly controlled. Mechanistically, the phenomenon reflects a competition between bottom-up attentional capture — animations, banners, notifications, autocomplete suggestions — and top-down text-driven attentional control. In functional neuroimaging terms, the default-mode network, normally suppressed during effortful comprehension, intrudes into task-positive networks, producing measurable deactivation of the dorsal attention system and reduced coherence in the frontal eye fields. For adolescents this competition is particularly acute, because the prefrontal cortex — the structural anchor of effortful attention — is still undergoing protracted myelination into the mid-twenties, making it structurally vulnerable to high-frequency attentional interruptions (Barnea-Goraly et al., 2005). Crucially, the effects are not symmetric across modalities. On a static e-paper Kindle without notifications, distraction frequency approximates paper reading. On a multifunction tablet or smartphone, distraction frequency is highest. Sweden's policy reset, by re-establishing print as the default literacy medium, may thus be reducing not only surface cognitive load but also its deeper neurobiological cost — the chronic over-recruitment of attentional control networks and their accelerated depletion.

From Behavioural Effects to Neuroanatomy: Evidence from the ABCD and European Cohorts

Behavioural measures of attention and comprehension are downstream of neural architecture. The Adolescent Brain Cognitive Development (ABCD) study — a longitudinal neuroimaging cohort of more than 11,800 US children recruited at ages nine and ten — has produced the largest dataset on the structural correlates of habitual screen use. Paulus et al. (2019) reported that screen-media activity, particularly media with high entertainment value, was associated with reduced cortical thickness in regions supporting executive function and reward evaluation, with effect sizes comparable to those observed for other known neurodevelopmental risk factors such as sleep curtailment. The most consistent findings localised to the prefrontal cortex, the anterior cingulate, and the insula — regions anatomically central to decision-making, impulse control, and interoceptive awareness. The structural findings have been corroborated by diffusion tensor imaging studies of children under five. Hutton et al. (2020), using a Cincinnati pediatric cohort and parental report of screen exposure, demonstrated that preschool-aged children with higher screen time had lower microstructural integrity of white-matter tracts sub-serving language and emergent literacy skills, including arcuate fasciculus and uncinate fasciculus. The white-matter effect was independent of household income, parental language exposure, and child age, suggesting a direct exposure-outcome pathway. In the European literature, a meta-analysis of neuroimaging studies in adolescents and young adults with Problematic Usage of the Internet or mobile telephones, conducted by Solly et al. (2022), reported a robust pattern of reduced grey-matter volume in bilateral dorsolateral prefrontal cortex, anterior cingulate, and orbitofrontal cortex, with effect sizes in the moderate range. Importantly, these longitudinal structural data are not artefacts of cross-sectional sampling: the ABCD study's within-subject design controls for familial and genetic predisposition, strengthening the inference that excessive screen exposure may actively shape the developing cortex rather than simply correlate with pre-existing neural architecture.

Myelination and White-Matter Integrity

A separate and arguably more concerning line of evidence concerns the integrity of white matter — the myelinated fibre tracts that connect grey-matter regions and whose maturation is the substrate of efficient neural communication. In children and adolescents, myelin deposition accelerates in primary sensorimotor regions during the first years of life and continues through the prefrontal and association cortices well into early adulthood, following an inverted-U trajectory of growth and pruning (Barnea-Goraly et al., 2005). This protracted myelination window is both an opportunity — environments rich in language, music, physical activity and social interaction potentiate tract development — and a vulnerability — environments poor in stimulation or characterised by chronic low-level stress, sleep disruption, or attentional fragmentation may impair it. The Hutton et al. (2020) DTI finding that preschool children with higher screen exposure had

lower fractional anisotropy in language-supporting white matter tracts is one of the clearest mechanistic demonstrations that the structural neural substrate of literacy is itself responsive to media environment during sensitive windows. For adolescents, the meta-analysis of Marciano et al. (2021) summarised structural-magnetic-resonance-imaging findings across several European and US cohorts and reported consistent reductions in prefrontal and anterior-cingulate cortical thickness correlated with discretionary screen time, with effect-size estimates in the small-to-moderate range. Mechanistically, several pathways connect chronic high-frequency screen exposure to impaired myelination: sleep curtailment reduces the pulsatile release of growth hormone that supports oligodendrocyte proliferation; chronic stress elevates glucocorticoids, which suppress oligodendrocyte differentiation; and reduced time spent in reading-anchored, language-rich interaction reduces the neural activity that drives activity-dependent myelination. The clinical implication is that the Swedish reversal — by re-anchoring foundational literacy to print and handwriting — restores a developmentally appropriate pattern of sustained visual-orthographic engagement, motor-orthographic integration through writing, and rich adult-guided discourse, all of which are known drivers of activity-dependent myelination in reading-relevant networks.

Dopaminergic Reward and the "Digital Drug" Hypothesis

A central neurochemical hypothesis connects habitual screen exposure to alterations in mesocorticolimbic dopamine signalling. The pathway involves the ventral tegmental area projecting to the nucleus accumbens (reward evaluation) and to the prefrontal cortex (motivational control and value-guided decision-making). Short-form social media, autoplay video, and loot-box or reward-schedule video games are engineered to deliver highly variable, high-frequency dopaminergic micro-rewards — the same profile that has been associated with developing behavioural addictions in adults. Studies in habitual smartphone users demonstrate that the salience network — comprising the anterior insula and dorsal anterior cingulate cortex — is hyper-responsive to device-related cues, while the executive control network, anchored in the dorsolateral prefrontal cortex, is hypo-responsive to inhibitory demands (Hadar et al., 2017). A neuroimaging meta-analysis of individuals with problematic smartphone use by Lin et al. (2022) reported consistent hypo-activation of the dorsolateral and ventrolateral prefrontal cortex, alongside hyper-activation of striatal reward regions. In adolescents, Chen et al. (2023) demonstrated that children with higher daily screen use showed weaker functional connectivity within the inhibitory control network and stronger reward orientation, measured both behaviourally and via resting-state functional MRI. Over time, repeated exposure to high-frequency dopaminergic micro-rewards is hypothesised to produce a tolerance-like shift, requiring ever more intense or novel stimulation to elicit comparable subjective reward — a phenomenon sometimes called "hedonic down-shift." Critically, this is not merely a motivational problem. Reduced dopaminergic tone within the prefrontal cortex diminishes working-memory gating, increases impulsivity, and reduces the threshold for distraction by sub-salient cues. The implication for schooling is direct: learning tasks — particularly reading, writing, and arithmetic — are intrinsically low-frequency-reward activities; their motivational competition with high-frequency digital stimulation is asymmetric. By strengthening the relative reward of paper-based literacy, the Swedish reversal may be reducing, not eliminating, that asymmetry.

Prefrontal Executive Function: Working Memory, Cognitive Flexibility, and Inhibitory Control

Working memory is the cognitive workspace in which text information is temporarily held, transformed, and integrated into coherent mental models. Its adult capacity of approximately three to four meaningful chunks is supported by sustained firing within recurrent prefrontal circuits and depends critically on the integrity of the dorsolateral prefrontal cortex and its connections to posterior parietal and anterior cingulate regions. In children, working memory is still under construction and is exquisitely sensitive to environmental demand. Cowan (2014) demonstrated

that working memory capacity constrains reading comprehension, mathematical problem solving, and scientific reasoning, with capacity tightly linked to classroom achievement. The chronic attentional fragmentation produced by frequent task-switching between primary tasks and notifications is a structural stressor on this system. Moshel et al. (2024) conducted a meta-analysis of neuropsychological deficits in disordered screen use and reported an effect size of g = 0.50 for attention and 0.31 for executive functioning in affected individuals relative to controls, with the largest decrements observed in inhibitory control and working-memory updating. Oswald et al. (2020), in a systematic scoping review of "screen time" versus "green time" in children and adolescents, found consistent small-to-moderate negative associations between recreational screen exposure and executive-function performance, with the inverse association between outdoor time and dysfunction suggesting that the deficit is partly mediated by displacement. A further contributor is sleep: working-memory performance is highly sensitive to sleep duration, and chronic curtailment of sleep in screen-using adolescents produces additional, additive decrements (Pedersen et al., 2022). The cumulative picture is that routine, multi-hour screen exposure is associated with measurable reductions in the prefrontal systems that underlie deep comprehension. For developing children this is particularly consequential because the prefrontal cortex is not yet fully myelinated, density of dopaminergic receptors is still declining toward adult levels, and lateral prefrontal regions that subserve complex working memory are still undergoing synaptic pruning. Reducing chronic demand on these circuits by re-anchoring early literacy to print — and by removing the mobile telephone from the classroom — is consistent with a developmentally informed model of cognitive load.

Brain-Derived Neurotrophic Factor, Synaptic Plasticity, and the Molecular Substrate

At the molecular level, screen exposure has been hypothesised to influence synaptic plasticity through brain-derived neurotrophic factor (BDNF). BDNF is a small secreted protein highly expressed in the hippocampus, cortex, and basal forebrain, where it supports activity-dependent plasticity, dendritic spine formation, long-term potentiation, and ultimately learning and memory consolidation (Miranda et al., 2019). Reduced BDNF signalling has been linked to cognitive impairment, depressive symptomatology, and impaired structural recovery from stress. Although no direct longitudinal study has measured BDNF in humans exposed to varying levels of screen media, multiple convergent lines of evidence make such a mechanism plausible. First, physical activity — one of the most robust environmental up-regulators of BDNF — is displaced by screen time in children and adolescents (Latomme et al., 2022). Second, sleep curtailment, which is a common co-morbidity of evening screen use, acutely reduces BDNF expression in the hippocampus and impairs memory consolidation (Toader et al., 2025). Third, chronic social isolation or reduced high-quality face-to-face interaction, which is displaced by screen exposure, is itself associated with reduced BDNF signalling. Fourth, in rodent models of intense stimulus exposure and in human neuroimaging studies of disordered internet use, network-level alterations are observed in regions with particularly high BDNF dependence — the hippocampus and the prefrontal cortex. The cumulative molecular argument is not that screens directly suppress BDNF; it is that the lifestyle package typically co-occurring with heavy screen use — reduced exercise, shortened and fragmented sleep, reduced face-to-face discourse, increased sedentary posture — depletes BDNF reserve at a developmental moment when plasticity is maximal. The Swedish educational policy, by restoring handwriting, sustained reading, and physically present classroom discourse, alters this package by design. For adult learners the BDNF story is qualitatively similar but quantitatively attenuated: BDNF continues to support neurogenesis in the dentate gyrus of the hippocampus and to support cortical plasticity in motor and association cortices, but the magnitude of plastic change is smaller than in childhood.

HPA-Axis Activation, Cortisol, and Chronic Stress Physiology

The hypothalamic–pituitary–adrenal (HPA) axis is the body's principal stress-response system, producing cortisol from the adrenal cortex under the regulatory control of hypothalamic corticotropin-releasing hormone and pituitary adrenocorticotropic hormone. Acute cortisol elevation supports adaptive responses — increased alertness, mobilisation of glucose, sharpened attention — but chronic dysregulation of the HPA axis, whether hyper- or hypo-reactive, has been implicated in hippocampal atrophy, impaired executive function, and elevated risk of mood and anxiety disorders. Screen exposure intersects with the HPA axis through multiple pathways. First, exposure to emotionally arousing, novel, or socially evaluative digital content — for example, social-media comparisons — is itself an acute psychological stressor that produces measurable cortisol elevation (Pedersen et al., 2022). Second, blue-light-induced sleep curtailment dysregulates the circadian component of cortisol secretion, blunting the morning awakening response and elevating evening nadir values. Third, displacement of physical activity and outdoor exposure reduces both the immediate stress-buffering effects of exercise and the slow-wave-sleep-dependent consolidation of emotional memory, prolonging stress reactivity. Fourth, the chronic attentional fragmentation and the resulting feeling of never completing tasks, often termed "technostress," sustains low-grade HPA activation. Pedersen et al. (2022) reported that controlled digital-detox interventions produced changes in HPA-axis biomarkers and mood within days, with effect sizes comparable to first-line behavioural interventions for mild depressive symptoms. Effects in children are likely larger because the HPA axis is still maturing and because children's daily schedules have less slack to absorb disruption. For adults the HPA-axis response is qualitatively similar but generally less disruptive in absolute magnitude, partly because the adult prefrontal cortex exerts stronger top-down inhibitory control over the amygdala and partly because adult cortisol patterns are more entrenched. Sweden's classroom policy — by removing the smartphone from the school day — directly targets one of the principal sources of classroom HPA activation for a developmentally vulnerable population.

Melatonin Suppression and Circadian Disruption

Melatonin is the principal hormonal output of the suprachiasmatic nucleus of the hypothalamus and acts as the body's internal time signal, signalling biological night and supporting sleep initiation. Its secretion is acutely inhibited by short-wavelength (≈460–480 nm) blue light, which is precisely the wavelength enriched in the emission spectra of LED-backlit screens, particularly tablets, smartphones, and OLED televisions. Silvani et al. (2022) reviewed the evidence and concluded that evening blue-light exposure produces measurable suppression of melatonin, delay of sleep onset, reduction of total sleep time, and degradation of sleep architecture, particularly slow-wave sleep. The implications extend beyond sleepiness: slow-wave sleep is the principal window for glymphatic clearance of metabolic by-products and for protein synthesis supporting synaptic consolidation. Sleep curtailment also reduces the pulsatile release of growth hormone that supports oligodendrocyte proliferation and therefore myelination. Effects on children are particularly concerning because (a) the crystalline lens transmits more blue light to the retina in young eyes than in adult eyes, (b) children's evening sleep onset tends to be later relative to circadian phase when screens are present, and (c) the homeostatic sleep pressure that accumulates during the day interacts with circadian phase to gate memory consolidation in a sleep-stage-specific manner. Adults are less vulnerable to melatonin suppression in absolute terms because adult circadian amplitude is more robust and because adults tend to engage in fewer late-evening screen activities than adolescents. Nevertheless, the consistent finding that even modest evening screen exposure shifts sleep onset by 20–40 minutes has implications for occupational performance, cardiovascular risk, and metabolic health in adults. The pedagogical implication for Sweden is direct: school-day mobile-phone restrictions extend beyond the classroom because they

reduce the home-evening temptation to scroll; the curriculum focus on handwriting and paper-based reading further displaces evening screen use by restoring a low-arousal wind-down activity.

Sleep Architecture, Glymphatic Function, and Downstream Cognitive Effects

Building on the melatonin story, the consequence of chronic screen-induced sleep curtailment is not simply tiredness but measurable architectural change in the polysomnographic record. Slow-wave sleep — the high-amplitude, low-frequency cortical oscillations generated by synchronised thalamocortical and corticocortical networks — is reduced in duration and reduced in spectral power under chronic sleep curtailment. Slow-wave sleep is the principal substrate for declarative memory consolidation, including the integration of newly learned vocabulary, factual knowledge, and procedural skills. Its reduction predicts impaired next-day learning, as demonstrated in classic sleep-deprivation studies and replicated in modern neuroimaging of memory consolidation. Rapid eye movement (REM) sleep, in turn, supports emotional regulation, abstract reasoning, and the consolidation of implicit procedural patterns. Reduced REM sleep has been associated with impaired affective regulation and elevated negative emotional reactivity. The combination of reduced slow-wave and reduced REM sleep in adolescents with high screen use predicts the daily academic and mood profile that teachers report: distractibility in morning lessons, dysregulated affect during transitions, and a slowing of cumulative literacy gains over the school year. Glymphatic function — the perivascular clearance of β-amyloid, tau, and other metabolic by-products — is also concentrated in slow-wave sleep. Although the long-term neurodegenerative implications for children are speculative, the implication for adults is concrete: chronic curtailment of slow-wave sleep is associated with impaired next-day executive function, elevated amyloid burden in cerebrospinal fluid, and increased cardiovascular risk. By reducing evening screen use and restoring a low-arousal paper-based wind-down, the Swedish reversal may be restoring the conditions under which slow-wave sleep architecture — and the cognitive and metabolic processes that depend on it — can be re-established.

Comparing Gadget Categories: Smartphones, Tablets, Laptops, E-Readers, Televisions, and Gaming Consoles

The term "digital device" obscures substantial variation in cognitive and neurobiological risk. Smartphones combine all the risk factors: high-frequency short-form content, notifications, deep-link hypertext, social comparison, blue light, and bidirectional dopamine-driven reward loops. They are the category most strongly associated with disordered screen-use behaviours (Moshel et al., 2024). Tablets share many of these properties but, because of their larger field of view, are more often used for sustained reading or creative activity; their blue-light emission is comparable to smartphones. Laptops are functionally similar to tablets for content but introduce additional task-fragmentation through multitasking affordances and exposure to work-related notifications; the cumulative attentional cost is higher than for tablets in many observational studies. Dedicated e-readers (e-paper Kindle-type displays), in contrast, emit no intrinsic blue light, deliver text with paper-like luminance and contrast, lack notifications and hypertext, and, when used as a single-purpose reading device, approximate the cognitive ergonomics of paper quite closely. The Clinton (2019) meta-analysis supports this pattern: e-reader vs paper comprehension effects are small and frequently non-significant, whereas general tablet/screen vs paper effects favour paper. Televisions and video-streaming devices present distinct risks: they are typically used at a coarser attentional grain, are often watched passively in the background while other activities occur, and are associated with reduced parent–child discourse time. They are not, broadly, associated with improvements in literacy. Dedicated gaming consoles — particularly those used for fast-tempo multiplayer action games — produce intense cognitive engagement with strong reward schedules. Palaus et al. (2017) reviewed fMRI evidence from habitual gamers and reported both beneficial effects on visuospatial cognition and working memory and, in heavy players, reduced prefrontal activity during cognitive control tasks. Kühn et al. (2014) demonstrated that even brief Super Mario

play produced measurable grey-matter increases in the right hippocampus and the dorsolateral prefrontal cortex in young adults, suggesting that action games can be cognitively enriching when engagement is moderate and well-regulated. The net effect on children, however, depends on dosage, content, and displacement of sleep and exercise.

From Television to Console Gaming: A Sub-Comparative Risk Map

Continuing the gadget comparison, dedicated television viewing for entertainment is associated with the largest within-age-group decrements in reading because it directly displaces the active reading time that the curriculum assumes (Oswald et al., 2020). Effects are stronger in children than in adolescents, and stronger in adolescents than in adults, consistent with a developmentally graded vulnerability model. Console gaming diverges from television in two important respects: first, interactive games engage visuospatial, attentional, and motor systems that passive viewing does not; second, certain genres (action, first-person shooter, multiplayer online battle arena) generate high-frequency reward schedules with documented dopaminergic striatal activation. Weinstein and Lejoyeux (2020) argued that at high dosages these schedules meet behavioural-addiction criteria in a minority of users, with compulsive use accompanied by craving, withdrawal, and functional impairment. Sugaya et al. (2019) reviewed the biopsychosocial profile of internet-gaming-disorder-diagnosed children and adolescents and reported consistently elevated rates of anxiety, depression, social withdrawal, sleep disturbance, and academic difficulty. Moshel et al. (2024) extended these findings and noted that executive-function deficits in disordered gaming populations approximate, in magnitude, those observed in attention-deficit-hyperactivity disorder (Gao et al., 2021). Educational effects of gaming are content-dependent: prosocial, narrative, and problem-solving games can produce moderate gains in executive control and STEM-relevant skills, while loot-box-driven and pay-to-progress games reliably reproduce addictive patterns. The comparative risk ranking emerging from the synthesis is therefore: smartphones > general-purpose tablets and laptops > action and multiplayer online games > social television viewing > educational television > static-purpose e-readers. Adults are partially protected from the highest-risk categories because their prefrontal inhibition is mature, their sleep is less plastic, and their established habits buffer the disrupting effects. Children and early adolescents lack these buffers. Sweden's classroom-level reversal targets the highest-risk categories directly: removing phones from schools eliminates the most disruptive medium during the longest continuous stretch of children's waking time, and re-anchoring foundational literacy to print reduces reliance on general-purpose screens in the developmental window most sensitive to all the mechanisms reviewed here.

Children versus Adults: A Window-of-Vulnerability Model

A consistent theme across the molecular, cellular, network, and behavioural evidence is that children and adolescents are more vulnerable than adults to the cognitive costs of heavy screen exposure. The vulnerability reflects three converging facts. First, cortical maturation is not complete: synaptogenesis peaks in the first years of life, pruning continues through childhood and adolescence, and myelination of prefrontal and association cortices continues into the early twenties (Barnea-Goraly et al., 2005). This implies that the structural targets of screen-induced alteration — prefrontal cortex, anterior cingulate, hippocampus — are simultaneously the regions undergoing the most plastic change. Second, the dopaminergic system is still calibrating: receptor density is high in adolescence and declines through pruning into adulthood. This produces both heightened reward sensitivity and elevated susceptibility to habituation. Third, sleep regulatory mechanisms — particularly the circadian phase response curve and homeostatic sleep pressure dynamics — are still being entrained by environmental cues, making adolescent sleep onset disproportionately vulnerable to evening blue-light exposure. Adults enjoy partially protective factors: they have stable prefrontal myelination; their dopaminergic systems are at adult density; their sleep is more entrenched; and many have already developed habits of deep reading and

reflective work. Nevertheless, adults are not exempt. Mid-career adults routinely report attentional fragmentation under heavy digital workload, and neuroimaging work has demonstrated that habitual multitasking is associated with reduced prefrontal task-evoked activity and reduced performance on working-memory tasks (Moshel et al., 2024). The graded vulnerability model that emerges is consistent with the Swedish policy reversal: for children the stakes are highest and the developmental timing most plastic, justifying the strongest classroom-level restriction; for adolescents the next-highest stakes warrant continued device-management under adult guidance; for adults the evidence supports reasonable screen hygiene but does not require the same degree of regulatory intervention. Importantly, this is not a moral judgement of either children or adults; it is a developmental neuroscience conclusion with explicit molecular and structural grounding.

Anxiety, Depression, and the Affective Cost of Heavy Screen Use

A large and converging literature documents associations between heavy screen exposure and elevated symptoms of anxiety and depression, particularly in adolescent girls. Eirich et al. (2022) conducted a meta-analysis of 87 studies comprising more than 159,000 children aged 12 years or younger and reported a small but statistically reliable association between higher screen time and both internalising and externalising behaviour problems. Oswald et al. (2020) extended the picture across age ranges and reported consistent inverse associations between recreational screen exposure and psychological well-being, with the largest effects observed for social-media and video-streaming use. Mechanistically, four pathways connect heavy screen exposure to affective symptoms: (i) displacement of physical activity, sleep, and face-to-face social interaction by screen time; (ii) direct exposure to socially comparative content, which produces upward social comparison and reduced self-evaluation; (iii) the bright-light/late-evening pathway, in which blue-light-induced sleep curtailment dysregulates emotional regulation; and (iv) attentional fragmentation, which reduces the cognitive resources needed to engage in effortful mood-management strategies. In adolescents the picture is complicated by the well-documented developmental peak in social-comparison sensitivity, which intersects with the lifetime peak in screen exposure. The Swedish reversal reduces exposure to (i) and (iv) directly by restoring time-rich, paper-based activities and reduces exposure to (ii) in the high-density school-day period by removing phones. Effects on (iii) are downstream consequences of (i). For adults the picture is similar but quantitatively smaller; nevertheless, occupational screen intensification during and after the COVID-19 pandemic has been associated with measurable increases in burnout, anxiety symptoms, and sleep disturbance, indicating that protective structural changes are needed even in adult life (Swider-Cios et al., 2023). The afferent signal to the policy reversal is therefore not only cognitive but affective: a measurable net improvement in child and adolescent mood is a credible outcome of broad classroom-level screen reduction.

Towards a Risk Hierarchy and Predictive Mitigation Framework

Synthesising the evidence reviewed above, a graded risk hierarchy can be proposed. At the top, habitual use of multifunction smartphones during school years, with frequent short-form video and social-comparison content, simultaneously activates multiple neurocognitive disruption pathways: dopaminergic reward de-sensitisation, HPA-axis dysregulation, attentional fragmentation, myelin vulnerability, and melatonin suppression. The cumulative cost in this age group is the highest documented. Next, general-purpose tablets and laptops used intensively for both school and entertainment share most of the same risks minus the social-comparison cue density; they remain a moderate-to-high concern. Third, action-genre video gaming on consoles or personal devices shares reward-schedule risks with smartphones but, when played in moderation, may exert neurocognitive benefits via visuospatial and motor training. Fourth, social television viewing carries the displacement risks with comparatively lower direct neurocognitive load. Fifth, educational television, particularly when adults engage with children in co-viewing

discourse, retains developmental benefits under controlled dosage (Hirsh-Pasek et al., 2015). Sixth, static-purpose e-readers approximate paper in cognitive ergonomics and blue-light load and can substitute for print in mobility-constrained contexts (e.g., commuting) without substantially compromising comprehension. Within each category, content matters: an hour of paper reading is not equivalent to an hour of passively viewed fast-cut video, and an hour of puzzle gameplay is not equivalent to an hour of social media. Mitigation strategies follow the hierarchy: prioritise removal of smartphones from classrooms for primary pupils; restrict social media until mid-adolescence; preserve sufficient daily outdoor and physical-activity time; enforce evening screens-off periods; preserve reading-anchored, paper-based literacy as the dominant medium in early schooling; and reserve dedicated e-readers as the highest-quality screen analogue when mobility demands (Chmiliar et al., 2017). Sweden's current policy implements the first two recommendations directly and the others indirectly through curricular restructuring (Fig 2).

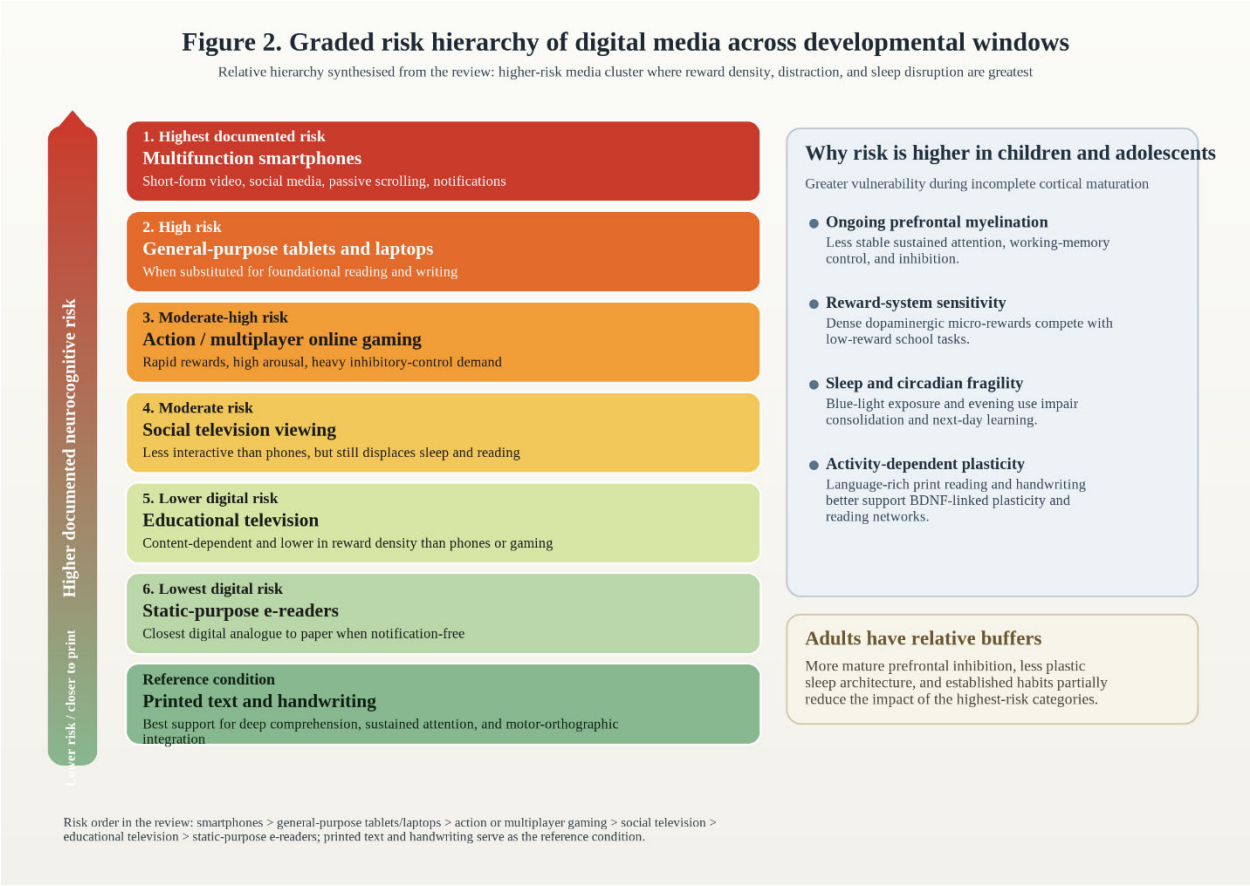

Figure 2. Graded risk hierarchy of digital media across developmental windows.

This figure presents a vertical risk hierarchy ranking media from highest to lowest documented neurocognitive risk in developing learners. From top to bottom, it places multifunction smartphones, general-purpose tablets and laptops, action or multiplayer online gaming, social television viewing, educational television, static-purpose e-readers, and finally printed text and handwriting as the reference condition. A right-side panel explains why children and adolescents are more vulnerable, emphasizing ongoing prefrontal myelination, greater reward-system sensitivity, sleep and circadian fragility, and the importance of activity-dependent plasticity for reading development

Conclusion: From a National U-Turn to a Globally Relevant Model

Sweden's educational reversal — the systematic return of printed textbooks, the renewed emphasis on handwriting, the nationwide mobile-phone restriction in primary and lower-secondary classrooms, and the rebalancing of the curriculum toward deep, paper-based literacy — is a coherent response to a converging body of evidence. PIRLS 2021 and PISA 2022 documented declines that sub-stratification analyses specifically attributed to the most device-intensive

learning environments (Reimers et al., 2025; OECD, 2023). The ABCD study, the European diffusion tensor imaging cohorts, and the meta-analyses of disordered smartphone use and internet use converge in identifying structural and functional correlates of heavy screen exposure precisely in the regions that underlie attention, working memory, literacy, and impulse control (Paulus et al., 2019; Hutton et al., 2020; Solly et al., 2022). The molecular literature on BDNF, HPA-axis stress reactivity, and melatonin suppression provides plausible mechanistic links between the behavioural/cognitive observations and underlying cellular biology (Miranda et al., 2019; Pedersen et al., 2022; Silvani et al., 2022). The gadget-comparison literature distinguishes the high-risk categories (smartphones, general-purpose tablets, action games) from the lower-risk categories (e-readers, educational television, paper) in a graded way that supports targeted rather than blanket restrictions (Clinton, 2019; Delgado et al., 2018; Palaus et al., 2017). Crucially, the vulnerability gradient between children and adults — strongest in early adolescence, still elevated in late adolescence, smaller but real in adults — maps onto a developmentally graded policy response that Sweden's classroom-level regulations implement. As the first major OECD country to formally pivot back from universal digital literacy to a print-default model while reserving devices for justified pedagogical purposes, Sweden offers a globally relevant experiment. If the predicted cognitive gains, reading gains, sleep gains, and mood gains materialise over the next PIRLS and PISA cycles, the model will warrant serious consideration in other high-screen education systems. If they do not, the experiment will, at minimum, narrow the evidential base for further escalation. Either outcome is valuable; what is no longer scientifically defensible is digital maximalism in early literacy without reference to the neurocognitive evidence reviewed here.

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Agricultural Sciences

Evaluation of Selected Early-Maturing Chinese Soybean (Glycine max L.) Varieties under the Conditions of Northern Kazakhstan

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Abstract. The successful cultivation of soybean in Northern Kazakhstan requires early-maturing varieties capable of completing their growth cycle under the region's relatively short growing season. This study aimed to evaluate selected early-maturing soybean varieties of Chinese origin under the environmental conditions of Northern Kazakhstan and to identify promising genotypes for further cultivation and breeding. Field experiments were conducted during the 2023–2025 growing seasons at the experimental fields of the A.I. Barayev Research and Production Centre for Grain Farming. Six Chinese soybean varieties (Beidou 14, Beidou 36, Beidou 41, Beidou 53, Heihe 35 and Heike 59) were evaluated in comparison with the standard variety Ivushka. Agronomic traits, including plant height, grain yield and vegetation period, were assessed. Considerable variation among the studied varieties was observed. Beidou 14 and Heike 59 were characterized by vigorous plant growth. Higher grain productivity was recorded for Beidou 14 and Heike 59 under favorable environmental conditions. The obtained results indicate that several Chinese soybean varieties possess valuable agronomic characteristics and can be recommended as promising genetic resources for soybean breeding and cultivation in Northern Kazakhstan.

Keywords: soybean, Glycine max, early-maturing varieties, Chinese germplasm, yield, Northern Kazakhstan.

Introduction. Soybean (*Glycine max (L.)* Merr.) is one of the world's most important legume crops due to its high protein (35–45%) and oil (18–22%) content [1]. Soybean products are widely used in the food industry, animal nutrition, and biofuel production, resulting in a continuously increasing global demand for this crop. Therefore, expanding soybean cultivation into new agricultural regions has become an important objective of modern crop production.

Soybean is among the most protein-rich crops of major agricultural importance, and its expanding production has been driven largely by increases in both sown area and yield. According to USDA data, approximately 80% of the world's soybean area is concentrated in three leading countries: Brazil (156.0 million t), the USA (113.3 million t), and Argentina (50.0 million t) [2]. In 2025, the soybean cultivation area in Kazakhstan reached approximately 200 thousand ha. Nevertheless, soybean production remains geographically concentrated. Northern Kazakhstan accounts for only 2.8% (3.2 thousand ha) of the national soybean area, while Almaty Region dominates soybean production with 83.6% (94.7 thousand ha), followed by Kostanay Region

(7.7%) and East Kazakhstan Region (5.0%). These data emphasize the importance of evaluating early-maturing soybean varieties adapted to the climatic conditions of Northern Kazakhstan.

The limited expansion of soybean cultivation in Northern Kazakhstan is primarily attributed to heat and moisture deficiency and to the shortage of locally adapted varieties, since most southern-bred cultivars require a longer vegetation period that is unsuited to the region's shorter frost-free season [3]. As a heat-demanding, short-day plant grown across latitudes of 40-55° N under a sharply continental climate, soybean's photoperiod and temperature requirements constrain its cultivation at higher latitudes. Consequently, breeding priorities differ markedly across Kazakhstan's agroecological zones: late-maturing, drought-tolerant varieties with a well-developed root system (135-145 days, maturity group III) dominate in the south; medium-late varieties (120-130 days, groups I-II) are grown in the southeast; varieties with a 100-110-day cycle (groups 0-00) are used in the east; while only ultra-early and early-maturing varieties (85-95 days, groups 000-00) are suitable for the northern regions.

Grain yield is a complex trait determined by both genotype and environmental conditions. Therefore, comprehensive evaluation of introduced soybean germplasm under local conditions is essential for identifying well-adapted and productive genotypes.

The aim of this study was to evaluate selected early-maturing soybean varieties of Chinese origin under the conditions of Northern Kazakhstan and to identify promising varieties based on vegetation period, plant height, and grain yield. We hypothesized that, despite differences in vegetation period duration, at least some of the Chinese-origin varieties would demonstrate yield and morphological performance comparable to, or exceeding, the local standard under the agroecological conditions of Northern Kazakhstan.

Materials and Methods. The study was conducted during the 2023–2025 growing seasons at the experimental fields of the A.I. Barayev Research and Production Centre for Grain Farming LLP, Akmola Region, Kazakhstan. Six early-maturing soybean varieties of Chinese origin (Beidou 14, Beidou 36, Beidou 41, Beidou 53, Heihe 35 and Heike 59) were evaluated in comparison with the standard variety Ivushka. Field experiments were carried out according to the methodological guidelines of the N.I. Vavilov All-Russian Institute of Plant Genetic Resources (VIR) [4]. Phenological observations were performed following the Fehr and Caviness scale [5]. Plant height, grain yield and vegetation period were evaluated over three growing seasons, and three-year mean values and deviations from the standard were calculated for each trait.

Results and Discussion. Vegetation period turned out to be one of the clearest points of separation between the standard and the introduced material. Ivushka completed its cycle in just 84,3 days, noticeably faster than any of the Chinese accessions, which was expected, since a locally bred standard is selected specifically to fit the short Northern Kazakhstan season, whereas germplasm introduced from lower latitudes often carries a longer inherent cycle.

Table 1. Vegetation period of the studied soybean varieties, days (2023–2025)

No.	Variety	Vegetation period, days				
		2023	2024	2025	Average	± to St.
1	Ivushka	85	85	83	84,3	St.
2	Beidou 14	101	114	96	103,7	+19,3
3	Beidou 36	85	99	95	93,0	+8,7
4	Beidou 41	102	112	82	98,7	+14,3
5	Beidou 53	91	97	95	94,3	+10,0
6	Heihe 35	101	100	114	105	+20,7
7	Heike 59	104	98	95	99	+14,7

What is more encouraging is that Beidou 36 came reasonably close, finishing in 93 days, while Heihe 35 needed a full three weeks longer than Ivushka (105 days), a gap that, in a region where an early autumn frost is always a possibility, can mean the difference between a full harvest and a damaged one.

Table 2. Plant height of the studied soybean varieties, cm (2023–2025)

No.	Variety	Plant height, cm				
		2023	2024	2025	Average	± to St.
1	Ivushka	36,9	25,7	41,1	34,6	St.
2	Beidou 14	67,3	61,0	50,0	59,4	+24,9
3	Beidou 36	50,7	46,4	37,8	44,9	+10,4
4	Beidou 41	52,0	37,0	41,8	43,6	+9,0
5	Beidou 53	51,0	33,3	40,0	41,4	+6,9
6	Heihe 35	50,3	51,0	38,0	46,4	+11,9
7	Heike 59	58,0	39,8	47,4	48,4	+13,8

The morphological data reinforce this picture rather than complicate it. Every Chinese variety grew taller than Ivushka, and Beidou 14 stood out with an average height of 59,4 cm, a trait that plausibly explains part of its yield advantage, since a taller canopy typically supports more pod-bearing nodes.

Table 3. Grain yield of the studied soybean varieties, dt/ha (2023–2025)

No.	Variety	Yield, dt/ha				
		2023	2024	2025	Average	± to St.
1	Ivushka	12,5	15,1	16,5	14,7	St.
2	Beidou 14	11,6	9,4	17,8	12,9	-1,8
3	Beidou 36	6,8	14,6	15,1	12,2	-2,5
4	Beidou 41	6,3	10,1	16,2	10,9	-3,8
5	Beidou 53	4,8	10,4	10,2	8,5	-6,2
6	Heihe 35	6,2	9,5	14,1	9,9	-4,8
7	Heike 59	7,8	11,2	15,3	11,4	-3,3

Yield tells a partly different story. Despite lagging behind in maturity speed, Beidou 14 was the strongest performer among the Chinese varieties, reaching 12,9 dt ha^{-1}, with Beidou 36 close behind at 12,2 dt ha^{-1} and Heike 59 at 11,4 dt ha^{-1}. Beidou 41 and Beidou 53 trailed the standard more noticeably, at 10,9 and 8,5 dt ha^{-1} respectively, both well below Ivushka's 14,7 dt ha^{-1}, and Beidou 53 in particular combined one of the longer vegetation periods with the lowest yield of the whole set. None of the introduced varieties actually matched the standard's yield over the three seasons, but Beidou 14, Beidou 36 and Heike 59 came noticeably closer than the other three, which is consistent with our hypothesis that at least some of the introduced lines would prove agronomically competitive even without matching Ivushka on every trait.

Conclusion. Among the evaluated accessions, Beidou 14, Beidou 36 and Heike 59 were identified as the most promising varieties. Beidou 14 combined high productivity and large seed size, Beidou 36 had the shortest vegetation period among the Chinese accessions, and Heike 59 showed favorable harvesting characteristics. These varieties are recommended for further breeding and cultivation in Northern Kazakhstan.

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Philosophical Sciences

THE IMPORTANCE OF ACADEMIC RESEARCH AND THE ROLE OF RELIGIOUS STUDIES IN POST-COMMUNIST SOCIETY

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Introduction

In the era of contemporary globalization and socio-political transformations, the role and significance of academic research are growing exponentially. Particularly for post-communist societies that have broken free from the influence of former Soviet ideology and chosen their own path, the issues of religion and belief have transformed into a complex and sensitive domain.

The state atheism policy of the Soviet era restricted religious consciousness and hindered the formation of scientific religious studies. In the post-independence period, however, the spiritual renewal of society and the revival of religious consciousness posed new tasks for academic religious studies. This article comprehensively examines the fundamental importance of academic research, the developmental features of religious studies in the post-communist space, and its benefits and impact on social processes.

The Importance and Methodological Foundations of Academic Research

Academic research is the primary tool that determines the intellectual potential of any society and sets the course for socio-economic and spiritual development.

"Scientific-academic research is not limited to accumulating theoretical knowledge; it serves to predict risks in society and propose ways to resolve them."

The significance of academic research in the field of religious studies is characterized by the following factors:

- **Objectivity and Neutrality:** Analyzing religious phenomena from a scientific-methodological perspective, free from any ideological or confessional pressure.
- **Empirical Base:** Examining actual religious trends, traditions, and forms of belief in society through social research (surveys, interviews).
- **Conceptual Foundation:** Providing a scientific basis for conceptual documents and legislative acts that regulate state-religion relations.

The Process of Religious Studies in Post-Communist Society

The religious landscape of states in the post-communist space has undergone a unique transformation. Forced secularization and attempts to push religion out of public life during the Soviet period have given way to the opposite trend—a religious revival (renaissance)—since independence.

The main characteristics of this process:

Stage / Characteristic	Soviet Era	Post-Communist Era
Attitude toward religion	Ideological opponent, a phenomenon to be eradicated	Constitutional right of citizens, spiritual pillar
Status of religious studies	Tool for atheistic propaganda (scientific atheism)	Academic discipline, independent field of science
Religious environment	Closed, controlled communities	Open, diverse movements and missionary organizations

The development of religious studies in post-communist societies has gone through several complex stages:

1. **The Vacuum-Filling Stage (1990s):** The mass dissemination of information about religion due to the removal of ideological restrictions and the necessity to eliminate public religious illiteracy.
2. **The Institutionalization Stage (2000s):** The opening of religious studies majors in higher education institutions, and the establishment of research centers and institutes.
3. **The Security and Expertise Stage (Current Stage):** Developing the institution of religious expertise and improving state-confessional policy with the aim of countering threats of religious extremism and radicalism.

Benefits and Impact of Religious Studies on Society

Religious studies is not a narrow theoretical discipline; it is a practically significant field that directly impacts the stability and security of society as a whole.

Spiritual Security and Prevention of Destructive Movements

The open information space in post-communist countries has paved the way for the spread of external destructive and pseudo-religious movements. Academic religious studies helps prevent radical ideologies among youth and vulnerable segments of the population. Quality research and educational work make it possible to distinguish true traditional values from alien currents.

Formation of Interconfessional Harmony and Tolerance

In multi-confessional and multi-ethnic post-communist societies, the basis of public stability is mutual understanding and harmony. The science of religious studies strengthens the culture of tolerance in society by scientifically explaining the history, worldview, and customs of various religious belief representatives.

Providing Expert Support for State Policy

State agencies rely on the expertise of professional religious scholars when making decisions in the religious sphere. Essential state functions—such as registering religious organizations, monitoring their activities within the framework of the law, and conducting expert analyses of religious literature—are directly based on the achievements of academic religious studies.

Conclusion

In conclusion, academic research and the science of religious studies serve as a guarantee for the spiritual renewal and sustainable development of post-communist society. For these societies, liberated from the ideological shackles of the Soviet era, understanding religion scientifically, properly evaluating its role in public life, and establishing a constructive dialogue between the state and religion are vital matters.

Religious studies remains not only a researcher of the past, but also an important intellectual resource that prevents future risks and paves the way for citizens to make conscious and correct choices. Only by increasing our academic potential can we build a conscious society whose spiritual integrity and security are fully ensured.

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Sociological Sciences

PROFESSIONAL FEMALE SOCIOLOGIST JANE ADDAMS (1860-1935), AND HULL HOUSE MUSEUM

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Jane Addams, and her associates acted in harmony with it, and the Hull House project was a powerful contributor to empirical research in sociology. There was strong resistance to women's academic success, and support for their particular marginalisation in the field of sociology, and the tendency to move their action into the field of social work. In that period, according to Knezevic, it was possible to talk about the existence of a male, and female Chicago school. The project of ecofeminism, as a direction based on the identification of women with nature, focuses on the critique of anthropocentrism in culture and the relation to women and nature. Jane Addams is a representative of the Chicago Sociological School of Thinking, which focuses on connecting urban urban planning, in which the level of social cohesion, and the relationship between the individual, and the society can be considered empirically, while the construction will be adapted to the needs of both sexes, for affirmation in personal, and public life. Within the most important, and prominent schools, the Chicago, and Frankfurt schools were also remake, and male sociologists.
Key terms: men Chicago school, female Chicago school, ecofeminism, Hull House, academic marginalization

Introduction

Traditional patriarchal ideology created an opinion in the dichotomies of nature / culture, I / Other, mind / emotion, private / public, male / female, where the symbols of superiority are always linked to male culture (Mušić 2015), and tradition of thinking. The source of this view of the world is to identify a man with an intellectual principle, and women with emotions and natural, and therefore a subordinated identity (Mušić 2018).The simplest way of explication is related to the phenomenon of the logic of domination that is tacitly related to the male sex, and the logic of care, that is solely related to the principle of femininity, and which completely opposes the rational categories of thought, and action. In this context, it is necessary to consider the relationship with nature(Mušić 2010:180), which is identical to the attitude towards the woman(Mušić 2011:112). The discourse of the logic of domination(Mušić 2013)is identified with the Western, patriarchal, imperial culture, which goes all the way differently, and is distinguished by a special concept in the perception of power, and the hierarchy of values. The ethics of care, as a category that femininity, in a certain way makes women adaptable to understanding the discourses of oppressed groups, and thus are a powerful potential, that helps the advancement of ecological culture, ecological nationalism(Mušić 2014) as an advanced form of awareness of the ecological problems of the modern age, and which has received its reflection even in the aforementioned project of multifunctional homes, for the unemployed moved from Addams, and its associates. This period was characterised not by the existence of adequate space for the academic work of women, and their creative activity, which would be outside the sphere of the family. Jane Addams was a

representative of the Chicago School of Sociology, and Hannah Arendt as a member of the Erasmus Society, was a representative of the Frankfurt School, although this school is considered a fundament of Marxist and socialist feminism, while Walter Benjamin is considered the Frankfurter who had the greatest influence on the feminist movement. Chicago's sociological school of thought included women, some of whom worked in Chicago, and Jane Addams sharply opposes the unfortunate ambience of work, at academic institutions of that time. Although tied to school, she never wanted to work at the University. Park, as one of the most important representatives of this school, had strong animosity towards the work of women, especially in the field of sociology (Knežević 2009). Although there was mutual academic co-operation, and continuous correspondence with Jane Addams, within empirical research, and her associates had the most significant academic qualifications, the academic work of women, was not sufficiently appreciated. The mapping technique was invented by the Doctor of Science of Sociology, the American Nobel Prize winner, Jane Addams, which is rarely mentioned in the works of sociologists, and sociological works. She was in contact with members of the Chicago Sociological School, and is known for establishing a kind of commune for the lives of homeless people, in which there were all kinds of lives, from cafes, libraries, shops to the rest, and where she wanted to emporium method of examining the relationship of an individual, with his environment, always emphasising, that the way of organising social relations is structured, by the person from within. However, Hull House did not just present this, a strong academic activity was taking place, within this multifunctional house, and there were professional sociologists, and social workers who studied the ways of life, in this organised community (how adolescent poor living conditions behave in changed circumstances). An interesting approach to Mary Jo Deegan, in the book Jane Addams and the sociologists of the Chicago School 1892-1918 / *Jane Addams, and the men of the Chicago School 1892-1918*, dealt with the analysis of the relationships of other representatives of the Chicago sociological school, against the sociological research of Addams. It was emphasised that the first generation was highly respected, and supported the work, and personality of this author, while while only the Park declares, that she knows only a little about the author, and Burgess (supporting the doctrine of the divided spheres), when asked about her, replies that she always admired the characters of women on the pedestals. Park's attitude towards women's work in academic institutions, however, was discriminatory. Turner, in his work *Sociology*, mentions the features of her theory and its orientation in the views, and determinations of the Chicago School, which emphasises, that it is precisely the period of the eighteenth, and nineteenth centuries, is marked by the difficulty of entering into social institutions for women. Jane Addams sees herself as a sociologist, and according to some authors like Knežević ((Chicago Society of Sociology - Social Work Sociology and Social Theory for Social Work, http://hrcak.srce.hr/35337, accessed 12.03.2010), Addams is considered the pioneer of the Chicago Women's School, which linked sociology, and social work. The Hull House building project was created , and created by Jane Addams, and Ellen Star for direct research, in the field of social work, whereby the influence of the women's Chicago school, of thought on the male. The school was run by women of a higher and middle class, and at the same time they were tied up with some of the most prominent academic workers of that time, and this school was the strongest female school of modern times. Jane Addams was known as a person of homosexual orientation, so it is assumed, that the animosity towards her existed for that reason. Among sociologists, one of the founders of sociology in general is known, Harriet Martineau is the first woman to be known for translating Comte's work Course of Positive Philosophy, or Sociology into English, and a number of significant works, and studies. She was the most sociologist of the period, but due to the marginalisation of female academic, literary, and every other form of creativity, her works were not mentioned in the older depictions, in researches of the sociological thought. A professor at the University of California, Turner points out that she did in sociology as much as Comte, and that her thought can be

compared to the most important classical sociological thinkers, of that period, such as Durkheim, and Weber.. The focus of the Martineau study included the intersection of family, marriage, and religion, with the emphasis on combating not only gender, but also racial, and religious discrimination. After Martineau, in sociology, Jane Addams occupies the most prominent place. Turner (2009: 46-47) emphasises that Addams was one of the most important, and most famous authors in this field, who managed to achieve a sociology, as a career. Among other things, she became the winner of the Nobel Peace Prize, she was influenced by Mead, and the theory of interactionism, and wrote about the relationship between society, and personality, for example the relationship between the personality, his family and society, for examples of everyday interaction from clubs, and cafes to way of spending free time. Mary Jo Deegan (1990: 37), emeritus Nebraska Lincoln of the American University, about Jane Addams wrote the following: "Jane Addams is the most important sociologist for many reasons. In the period between 1890-1920, she was the leader of dozens of women in sociology, and was one of the sisters founders in Sociology(Mušić 2019:181).

Hull House

Her social housing, Hull House, was an institutional port for this network, of female founders in Sociology (Mušić 2016). Serving as a focus for women's work, and as a link to the most important male sociological centre during this period, the Chicago University. Jane Addams's ideas of cultural feminism, and critical pragmatism led the works of many other women, and articulated their ideas, at the same time.

Photo 1. Hull House Museum(available at https://michaelminn.net/cities/chicago/hull_house_museum/index.html, accessed on 05/15/2026/)

" In studying individual cases of domestic violence, in which parents called children, children who are devouring domestic violence, to take over economic resources, Addams includes the topic of domestic violence in their sociological and feminist analyses (Addams, Jane, biography, www.stanfordencyclopediaofphylosophy .com accessed: 02/22/2017). The non-decadent approach, in sociology will affect that Caroline Bartlett Crane, founded his house, in the former church in Kalamazoo, Michigan, where lectures of different types for the poor, and migrant will be organised, with professional sociologists present. Unlike other male sociologists who have been misconstrued, or ambivalent about the academic work of women, in sociology, Lester Ward, as the first president of the American Society of Sociologists, supported the inclusion of sociologists, considering (despite supporting the doctrine of divided spheres in the sociology of sociology and sociologists) that sociologists are the dominant first (Ward, Lester. /http://www.newworldencyclopedia.org/entry/Lester_Frank_Ward, accessed 08.02.2017). The first section, within which professional sociologists participated, was a family, in the 1900s, and on the panel which was called the "delinquent girl", seven panelists participated, three of whom were women (Deegan, Mary Jo, Early Women Sociologists and The American Sociological Society: The Patterns of Exclusion and Participation. The American Sociologist available at: http://www.asanet.org/sites/default/files/savvy/images/members/docs/pdf/special/as/AS_16_1_Article_2_Deegan. pdf (accessed 20 May 2015) Migration is a historically important topic, in the field of sociology, and has its source in the work of the first group of professional sociologists. Jane Addams graduated in 1881, and faced a number of problems experienced, by her contemporaries, and colleagues, such as George Herbert Meade, and William James, attempted to attend the Women's Medical College in Philadelphia, but left that same year and returned to Chicago to travel to Europe, seeing Toynbee Hall,(at the same time eastern part of London), inspires the work for the poor. "Years later, she theorised that one of the most difficult tasks for women was the realisation of conflicting demands, between" family "and" social "demands. For Addams, this resolution was achieved through social institutions, where it could have been a "lady", while it also made a social, and political impact. At the same time, it was independent of traditional women's roles, and responsibilities, in the family, and at home. Because of these personal benefits, for those who helped others, she always emphasised subjectively, and objectively, the need for social housing. This emphasis on the dual importance of the habitation, prevented her from becoming a sentimental, or insensitive advocate of matriarchy, as is was usually presented. With her own internal struggle in the uncertainty about awarding honorary titles, she quickly advanced to gain leadership in the US social movement, and gradually left the course of American epistemology, and politics "(Deegan, 1990: 38). This dramatic role came, after she returned to America, in January, 1889.

Conclusion

The Hull House House, 1890, was the place where anarchists, Marxists, socialists, unionists, and the most important sociological theorists, came together. Some of them were John Dewey, and George Herbert Mead, who sought to generate a just, and free society by linking scientific, and objective observations, with ethical, and moral values. The fundamental sociological text, Hull House maps and papers, are published by Hull House residents in 1893, as a fundamental sociology paper, transnationally (Mušić 2022: 257). "Focused on social change, they articulated the American dream, especially adapted to smart, educated anglo-women, who wanted a new role in life, and society. Addams surrounded herself with brilliant, and dedicated people, especially women. These women formed a key group living in the countryside, writing together, collecting

statistics, examining factories and industries, examining health conditions, examining sanitary conditions, lobbying for legislative, and political reforms, and organising social improvement in their overpopulated, immigrant district working class. Outside this vast, and poorly organised space of activity, Addams(Mušić 2025) was a charismatic leader, who translated "facts" into everyday language, articulating the problems, and needs of the community, and forming American ideals, and social thoughts"(Mušić 2017). An author of eleven books, and hundreds of articles, Addams(Mušić 2021) continued her efforts, in lectures, and education, through the lectures across the country, and at Hull House.

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Femina Academica, Female Professionals in Sociology

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Femina Academica as a concept, a research project idea, and book investigation theme is defined in 2016 (Spano), inside the Higher Educational Female Leadership position, precisely focused on towards female leadership inside Higher University positions. Femina Sociologica, Femina Ecologica, and Femina Xenologica(along with Femina Academica, constitute educative tetralogy, dedicated to investigational research practices of Feminine identity in the Contemporary. Spano explains the importance of Female leadership through the notion of basis in legal documents. "The UNESCO (1998) Declaration on Higher Education" includes a statement that Higher Education (HE) 'should promote solidarity and equity', and it also includes equality of access. Femina Academica, and Empowering of Women, in Higher Institutional Education, is complex, historically remarkable, and especially developed inside the contemporary professional female Sociology and, in American Sociology because of distinguished the Sociologists for Women in Society organisation, while in Europe, still we find less dominant female professional positions , and perplexities of selections of Females in Academia.

Key terms: Femina Academica, Black Feminist Sociology, Female Centred Sociology, Academic Conviviality, Feminist Eco criticism

Introduction

As a sub-discipline of Sociology, Professional Female Sociologists(Mušić 2016) are a very significant theme inside the sub discipline of Sociology, that is extraordinarily multidisciplinary, based on a plural perspective , and important for the professional organisations as well. Theme *Sister founders in Sociology(*Mušić 2017a) is, a concept defined by Mary Jo Deegan, professor Emerita from Nebraska Lincoln University (USA). This concept (Mušić 2014) , is connected with the demarcation, and reconstruction of female establishment in Sociology. Museum of famous today, Sister founders in Sociology(Mušić 2017b), include Ida Wells Barnett's Museum, Jane Addams's Museum , and Caroline Bartlett Crane's Museum. Well known for black feminism, and Sociology of Empowerment, and Black Female Emancipation, W.E.B. Du Bois, incorporated into his very celebrated Museum exhibits, the multimedia representations inherited inside the freedom of Speech, Vote, and debates around the discrimination of Black Females.

" Du Bois's(Mušić 2022) limited views of black women inhibit his ability to imagine African American women as race leaders.Du Bois's descriptions of black women unintentionally re-inscribed patriarchal ideals as he sought racial equality. To Du Bois, black women held moral power over men, and thrived in the domestic sphere" (24). "The Damnation of Women," similarly to this letter, Du Bois finds that black women's damnation lies in their inability, to be deemed respectable, delicate, and worthy of the same admiration, as white women. Yet unlike his 1920 essay, the letter demonstrates that as of 1906, Du Bois had not yet articulated how racism affected black women's political or economic standing. His analyses of race, and gender were limited to black women's representation , and their need for protection. The founders action of Black feminist sociology, Ida Wells-Barnett, and Anna Julia Cooper, made Radical social change in biographies, history, and Sociology. They envisioned the African-American female life as what?'s, and as a contemporaries, they founded the sociology of African-American Women, which concentrated on were the special focus towards their real, and practical experiences.(Madoo,

Lengermann, Niebrugge (1998:149-184). Gender Dimension of Comparison in Between Anastasia, Pinocchio, and Tiana Characters , inside the disscussions around first dark princess idea, celebrates the rationality of the dark young women choice, as an afrofuturism idea, globally accepted(Mušić 2024). Intersection of Sociology of Gender, Sociology of Disney(Mušić 2026). Sociology of Afrofuturism, and Animal Sociology(Mušić 2025), and Other subdisciplines of Sociology, emphasize the intradisciplinarity of the field.

Marianne Weber (Mušić 2021) as a wife of Max Weber's wife, founded the idea of Women-centred sociology. Women centred Sociology is , organised around the female standpoint, especially in relation to importance on gender based ideology! She critiques the family structure, and especially working sphere, and domestic life(Mušić 2008), and " that societal harmony is made on the account of female autonomy" (Madoo, Lengermann, Niebrugge, Brantley, 1998:204). Weber argues: "That Women are framed in male-dominated society, with male dominated institutions of law, religion and history of series of male-made events, and by male-dominated analysis of the relations in between this institutions and this events."(1998:204). In her text, "The soil and air of the Academic life ," she writes about the concept of academic conviviality, explaining describing the gatherings in Heidelberg of intellectuals at Weber's family saloon, around the academic themes, in Heidelberg, decades after Weber died. She organised Sunday lectures that looked like this: "the first hour was spent in unguided conversations in small groups, with tea, and cakes. Then the guests settled down, to the talk and discuss, that followed, views of them as vital elements of the intellectual Heidelberg. The scholars who participated with their wives, were from all the faculties of the University, but most of them came from the Humanities, and Social Sciences(1977:4-5). Feminist Eco criticism, according to Vakoch's (2012)theory, represents the plural perspectives that involves pleads of different, and even contradictory positions, since it is not subject of generalisations. Feminist Eco criticism pinions forces Feminism, and Eco critics (feminist literature relation to the environment) into a creative, innovative, enhancing project of multiple perspectives(Mušić 2020) in understanding the feminist , and Ecological structure in different-varying, and even opposed perceptions (Vakoch 2012).

"The origin of female exclusion in theory, in the work of the eco feminist Eislar Rian Eco feminist manifesto (1987)(Mušić 2013), can be traced in following notions that the social system of Minoan period of rule on Greek island Crete, was the only true democracy. The Athenian democracy was the rule of free aristocratic males . Women and slaves (man and women of other colour) were marginalised, and excluded from public sphere. Only free males were subject to obligation of public speeches, as a mark of true citizen. Patricia Shipley holds that Aristotle's scripts on social system represent the origin of misogyny, and subordination of women, especially binary divisions: Femininity / masculinity, Nature / Culture, Emotion / Ratio, Subordination / Dominance(Mušić 2011:113) , Logic of care/Logic of dominance, Pain /Pleasure(Mušić 2009). Small Albion advocates the doctrine of separate spheres believing that men and women are different distinctly, "separate but equal",(Mušić 2010) comparing this difference to difference between two musical instruments having the same relation to the notes in scale, but could not be replaced or supply place in their own separate series (Deegan, 1981: 15).

Methodology

This analyses employs Comparative and historical methods as well as, the content analyses of textbooks , and materials in order to compare the female stream and a male stream in sociological approaches. Some of the methodological goals of this chapter include: the gender equal education, as a significant tool of postmodern education processes, and female stream textbooks involvement, inside the curriculum. During this process the interviews, with the eminent authors of the books, and writers of female sociologists biographies will be preformed (Mary Jo Deegan, prof.emerita Nebraska Lincoln University). The library and archival researches are undertaken to analyses the accessibility of the literature on Female sociologists. Mary Jo Deegan,

in 1990, wrote her significant study- source book on Women founders in sociology, through which she mentioned 53 women founders, in sociology. In the appendix of this work, refers to another even plus 66 women sociologists, who should be subject of are mentioned for further investigations. These women are rarely mentioned, in male stream sociology. Only pro feminist masculine authors mention works of women in sociology. John Peter Scot has written a study on 50 key sociologists, but he only mentions three women. In comparison to Mary Jo Deegan's work on 118 female sociologists, this previously mentioned work is male stream and even discriminating.

FEMALE SOCIOLOGY AS AN ACADEMIC DISCIPLINE

The importance of this project involves, being introduced into the introduction to the significant large amount of the literature written in America about female sociologists(Mušić 2014). First female professional sociologists speakers at ASA conferences : Ward supported the authorship and academic activities of Charlotte Perkins Gilman, and supported the inclusion of women (Mušić 2025). Charlotte Perkins Gilman, as a respectful female sociologists and economist, was even three times involved as discussant during the American Sociological Association (ASA) meetings. The first women included in first ASA meeting was Mrs J. Oldenwalrd-Unger. Small invited Jane Addams to speak as major a prominent speaker during 1911, 1912, and 1913(Mušić 2014), at the ASA conferences, in years 1911, 1912, 1913. The other speakers were Lucy Salmon from Vassar College (1913), and Emily Greene Balch, from Wellesley College, in 1914 (Deegan , 198:16). But in some years , no women were included, because they did not hold important roles, in meetings. Ross invited Jane Addams(Mušić 2023) to speak on sociological aspects of War, and Militarism , in their sociological aspects, in 1915, but Emily Green Balch came instead of her, and spoke on Addams' behalf. , and the 1915 meeting become a controversial meeting. Why was the meeting controversial? Addams and Balch were against war, and supported pacifism, and also were both Nobel Prize Winners. Jane Addams won the award in 1931, and Emily Green Balch in 1946. None of the men from Chicago school wanted to discuss Addams' work. Consequently, after contacting fifteen male sociologists, Ross founded two women,: Lillian Wald (Head, residents of Henry Settlement, NYC) and Anna G. Spencer (Meadville Theological Seminar, Ohio), who would read Addams' papers. The fundamental sociological text, Hull House maps and papers, is published by Hull House residents in 1893, as a fundamental sociology paper. An author of eleven books, and hundreds of articles, Addams continued her efforts in lectures and education through lectures across the country, and at Hull House. She became a spokeswoman for her era, especially for women and immigrants of the working class. "(Deegan, 1990: 39). The origin of these houses became popular in America, and one such was founded by Lillian Wald, Lynn Wald, Henry Settlement in New York, and a sociologist of neoadamsian Orientation, Caroline Bartlet Crane in Kalamazoo, Michigan. In the time before the beginning of the First World War, the Pacifist, Addams, was considered a good and noble woman to become a target of various animosities and personal attacks until the American accession to the war in 1913, when she became socially and publicly marginalised, and after public celebration as a saint, she becomes publicly abused as a violent one."Intimidated by the excitement of speaker platforms, and abandoned by colleagues, and the most prominent, other sociologists / gypsies, Addams has socially become a rogue band. That time was the agony's time for her. Dedicated to her values, basic, feminine ideals, she continued to advocate her pacifist position. The culmination of her politically unbreakable status occurred in 1919, when the US government labeled her the most dangerous woman in America. At that time, her role as a sociologist, which was the main one, was erased. "(Deegan, 1990: 40). After women gained the right to vote, in 1920, Adams and many Suffragettes celebrated as the main victory, in the years to come after 1931, Addams again becomes the spokeswoman of the establishment of social security, and as a dying 1935 , was again mournful around the world, as a great leader , and analyst of American

social reality (Deegan, 1990: 40). Jane Addams, Charlotte Perkins Gilman (Deegan, Podeschi, 2001), Caroline Bartlett Crane (Deegan, Rynbrandt, 2002). Sisters founders in sociology, advocated cultural feminism , and ecofeminist pragmatism(Mušić 2018) . The inclusive momentum of all disputes in her studies was a disagreement between cultural feminism, and critical pragmatism.

Conclusion

Femina Academica(Mušić 2021), Women centred sociology, Academic conviviality, Black feminist sociology, Black male feminism, and Feminist eco criticism, offer academic analysis, that is global, embracive, inclusive, wide ranging, and far reaching in its their academically distinguished results. Sociology of gender uses all of thesis approaches in distinguished, subversive, and always challenging approach.

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