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Table of Contents

Psychological Sciences

Medical Sciences

Economic Sciences

Идентификация и управление рисками в проектах: современный подход

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Управление рисками в области строительства представляет собой важнейший аспект для успешной реализации проектов. В этой статье обсуждаются ключевые риски, оказывающие влияние на строительные процессы, а также современные подходы к их выявлению и снижению. Оценивается воздействие колебаний цен на строительные материалы, задержек в поставках, ошибок в проектной документации, административных препонов и погодных условий. В работе также представлены как количественные, так и качественные методики оценки рисков, такие как SWOT-анализ, метод Дельфи и метод ожидаемой денежной стоимости (EMV). В заключение статьи сформулированы стратегические рекомендации для повышения устойчивости строительных проектов и уменьшения вероятности возникновения серьезных угроз.

Ключевые слова: управление рисками, строительные проекты, анализ рисков, риски, цифровизация строительства, прогнозирование рисков, BIM-моделирование, влияние погодных условий, стратегия минимизации рисков.

Управление строительными проектами невозможно без учета рисков, поскольку данная отрасль характеризуется значительной степенью неопределенности. Факторы, такие как колебания цен на строительные материалы, сбои в поставках, изменения в нормативно-правовой базе, проектные ошибки и неблагоприятные погодные условия, могут существенно повысить расходы и задержать выполнение работ. Необходимость планирования и минимизации этих рисков становится ключевым аспектом эффективного управления проектом. Применение современных подходов к оценке и управлению рисками помогает строителям предвидеть потенциальные проблемы и принимать меры для их снижения. Таким образом, грамотное управление рисками не только способствует более эффективному использованию ресурсов, но и способствует соблюдению сроков выполнения проекта, гарантируя его успешное завершение.

По данным McKinsey Global Institute (2023), более 70% строительных проектов сталкиваются с перерасходом бюджета, а 60% завершаются с задержками. Это указывает на необходимость системного подхода к управлению рисками, основанного на аналитических методах прогнозирования и минимизации негативных факторов.

Цель данной статьи — проанализировать ключевые риски строительных проектов и предложить практические решения, позволяющие минимизировать их последствия.

Классификация и анализ ключевых рисков

В процессе реализации строительных проектов можно выделить несколько наиболее значимых рисков, которые оказывают наибольшее влияние на сроки и бюджет строительства.

1. Рост стоимости строительных материалов

Одним из наиболее распространенных рисков является увеличение цен на строительные материалы. За последние пять лет стоимость ключевых ресурсов, таких как цемент, арматура и металлоконструкции, увеличилась на 20–40%.

Колебания цен на сырье могут привести к перерасходу бюджета на 10–15%, что критично для крупных строительных объектов.

Меры минимизации:

- Заключение долгосрочных контрактов с фиксированной ценой;
- Диверсификация поставщиков для снижения зависимости от одного рынка;
- Использование биржевых инструментов и стратегий хеджирования ценовых рисков.

2. Ошибки в проектной документации

Недостатки проектной документации могут привести к переделке строительных конструкций, увеличению сроков и возникновению дополнительных расходов. По оценкам экспертов, исправление ошибок на этапе строительства увеличивает затраты на 5–8% от общей стоимости проекта.

Меры минимизации:

- Проведение многоуровневой проверки проектной документации перед началом строительства;
- Использование BIM (Building Information Modeling) для выявления возможных коллизий на ранних стадиях;
- Введение строгого контроля качества проектирования с участием независимых экспертов.

3. Задержки поставок и ненадежность подрядчиков

Сбои в поставках строительных материалов и низкая надежность подрядчиков приводят к срыву графика работ. Анализ строительных проектов показывает, что около 50% задержек связано именно с поставщиками и подрядными организациями.

Меры минимизации:

- Контрактная система с четкими условиями поставок и штрафными санкциями;
- Создание резервного запаса критически важных материалов;
- Внедрение цифровых систем мониторинга работы подрядчиков.

4. Регуляторные и бюрократические риски

Изменение законодательства в сфере строительства может потребовать пересмотра проектной документации и корректировки проектных решений. За последние пять лет в строительной отрасли введено более 30 новых нормативных актов, что усложняет процесс согласования.

Меры минимизации:

- Проведение юридического аудита проекта до начала работ;
- Взаимодействие с государственными органами на стадии проектирования;
- Использование электронных систем документооборота для ускорения согласований.

5. Неблагоприятные погодные условия

Климатические условия оказывают значительное влияние на темпы строительства. В зимний период в ряде регионов строительные работы могут быть приостановлены на 30–40% рабочего времени.

Меры минимизации:

- Планирование графика строительства с учетом сезонности;

- Применение современных технологий, позволяющих вести работы в сложных климатических условиях (например, прогрев бетона);
- Разработка альтернативных сценариев выполнения работ.

Методы оценки рисков

Для эффективного управления рисками необходимо применять аналитические методы оценки их вероятности и последствий. В данной работе рассмотрены три ключевых метода: SWOT-анализ, метод Дельфи и метод ожидаемой денежной стоимости (EMV).

SWOT-анализ

SWOT-анализ позволяет выявить сильные и слабые стороны строительного проекта, а также оценить потенциальные угрозы и возможности.

Фактор	Примеры
Сильные стороны	Применение цифровых технологий, контроль качества
Слабые стороны	Высокая зависимость от подрядчиков, риски поставок
Возможности	Государственные субсидии, новые технологии
Угрозы	Рост цен, задержки поставок, изменения в законодательстве

Метод Дельфи

Метод Дельфи используется для оценки рисков путем получения экспертных мнений. Он применяется в ситуациях, когда недостаточно статистических данных или требуется субъективная оценка вероятности и последствий рисков. Данный метод основывается на анонимных опросах группы экспертов, проводимых в несколько этапов, чтобы достичь максимально объективных результатов. Например, вероятность наступления некоторых рисков отличается. Рост стоимости материалов примерно 70%, Ошибки в проекте 50%, Задержка поставок 40%, Погодные условия 60%

Метод Дельфи используется для оценки рисков путем экспертного прогнозирования. В рамках данного исследования данный метод был адаптирован на основе анализа отраслевых отчетов, публикаций консалтинговых компаний и данных международных организаций. Вероятностные оценки рисков основаны на динамике изменений стоимости строительных материалов за последние пять лет, статистике задержек поставок и анализе влияния климатических факторов на строительные процессы. Подход включает комплексную обработку экспертных мнений и статистических данных, что позволяет обоснованно определить вероятность возникновения ключевых рисков и их влияние на реализацию строительных проектов.

Метод ожидаемой денежной стоимости (EMV)

EMV позволяет рассчитать потенциальные финансовые потери при возникновении рисков.

Метод ожидаемой денежной стоимости применяется для количественной оценки рисков, позволяя прогнозировать потенциальные финансовые потери. Расчет основан на данных о вероятности возникновения рисков и оценке их финансовых последствий, полученных на основе анализа бюджетов реализованных строительных проектов. В расчетах учитывались прогнозируемые изменения цен на строительные материалы, возможные затраты на устранение ошибок проектирования, задержки поставок и влияние климатических факторов. Полученные значения позволяют определить финансовую уязвимость строительного проекта и разработать стратегии минимизации рисков.

Риск	Вероятность (P)	Потери (L), млн тг	EMV = P × L (млн тг)
Рост стоимости материалов	0.75	180	135
Ошибки в проекте	0.5	75	37.5
Задержка поставок	0.4	30	12
Погодные условия	0.6	20	12

Стратегии управления рисками

Для эффективного контроля рисков необходимо внедрять комплексные меры управления:

1. Прогнозирование и мониторинг – анализ цен, поставок и нормативных изменений.
2. Цифровизация процессов – применение BIM, автоматизированных систем управления проектами.
3. Финансовая защита – создание резервных фондов и страхование.
4. Контроль подрядчиков – строгие контракты, рейтинговые системы и независимый аудит.

Строительная отрасль характеризуется высокой степенью неопределенности, что делает управление рисками обязательным элементом проектного менеджмента. Анализ ключевых угроз, применение современных методов оценки и стратегическое планирование позволяют снизить потери и повысить устойчивость проектов.

Компании, внедряющие системный подход к управлению рисками, способны реализовывать проекты в срок, в рамках бюджета и с высоким уровнем качества. Это подтверждает, что риск-менеджмент является не только инструментом минимизации потерь, но и важным фактором конкурентоспособности в строительной сфере.

Предложенные методы оценки рисков позволяют повысить предсказуемость строительных проектов, снизить неопределенность и минимизировать потенциальные убытки. Практическая реализация таких инструментов, как цифровое проектирование, оптимизация логистических процессов и применение контрактных механизмов управления рисками, способствует повышению устойчивости строительной отрасли. Внедрение системного подхода к управлению рисками позволяет строительным компаниям достигать поставленных целей в рамках запланированных сроков и бюджета, обеспечивая стабильность и эффективность реализации проектов.

ЭВОЛЮЦИЯ КОНЦЕПЦИИ КОМПЛАЕНС-МЕНЕДЖМЕНТА: ОТ НОРМАТИВНОГО СООТВЕТСТВИЯ К СТРАТЕГИЧЕСКОМУ УПРАВЛЕНИЮ РИСКАМИ

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АННОТАЦИЯ

Исследование направлено на обоснование эволюции комплаенс-менеджмента от нормативного соответствия к стратегическому управлению рисками. Применен сравнительный анализ подходов, изучение международных стандартов и практических кейсов российских, казахстанских и зарубежных компаний. Выявлено, что интеграция комплаенса в стратегическое управление обеспечивает устойчивость бизнеса, а риск-ориентированный подход позволяет оптимизировать ресурсы и снижать угрозы. Комплаенс трансформируется из изолированной функции в стратегический актив, формирующий корпоративную культуру и конкурентное преимущество.

ABSTRACT

The study aims to substantiate the evolution of compliance management from regulatory compliance to strategic risk management. A comparative analysis of approaches has been applied, along with a study of international standards and practical cases from Russian, Kazakhstani, and foreign companies. It has been revealed that integrating compliance into strategic management ensures business sustainability, and a risk-based approach makes it possible to optimize resources and reduce threats. Compliance is transforming from an isolated function into a strategic asset that shapes corporate culture and provides a competitive advantage.

Ключевые слова: комплаенс-менеджмент; риск-ориентированный подход; стратегическое управление рисками.

Keywords: compliance management; risk-based approach; strategic risk management.

В условиях трансформации деловой среды регуляторное давление перестало быть статичным фактором, превратившись в динамическую переменную. Бизнес-модели усложняются, а география деятельности расширяется, что порождает новые, нетривиальные уязвимости. Традиционный подход к комплаенсу как к функции «подчинения» правилам обнаруживает свою недостаточность. Он не позволяет прогнозировать угрозы и интегрировать защитные механизмы в стратегию. На первый план выходит необходимость переосмысления комплаенса как инструмента создания стоимости. Исследование вызвано запросом на проактивные модели управления, способные обеспечить устойчивость организации. В условиях неопределенности пассивное соблюдение норм становится фактором конкурентного риска. Стратегический подход смещает фокус с фиксации нарушений на управление совокупным профилем рисков. Это требует новой методологии и пересмотра роли комплаенс-функции в корпоративном управлении.

В современной научной литературе комплаенс трактуется как комплексная система инициатив. Как указывают А.А. Шегай и А.Е. Фирсов, - «данная система направлена на предупреждение противоправных действий сотрудников» [1, с.463]. Одновременно она обеспечивает внедрение корпоративной бизнес-этики, базирующейся на неукоснительном соблюдении закона. Генеральной целью комплаенс-менеджмента выступает выявление и предотвращение ошибок и правонарушений в деятельности корпорации. Реализация этой цели позволяет минимизировать потенциальный ущерб от возникающих проблем. Кроме того, по мнению Д.В.Ланской, С.В. Фиберт и Е.И. Баркаловой, «комплаенс способствует не только защите, но и улучшению бизнес-процессов и механизмов внутреннего контроля» [2, с.11]. В идеальном состоянии данная система обеспечивает управление организацией персоналом на всех уровнях без инцидентов, связанных с несоблюдением требований.

Эволюция комплаенс-менеджмента знаменует собой сдвиг от восприятия его как обременительной формальности к признанию стратегическим активом. В условиях современной нестабильной среды пассивное следование предписаниям перестало гарантировать безопасность.

Комплаенс-менеджмент прошел развитие от традиционного до современного подхода, различие данных подходов показаны в таблице 1.

Таблица 1.

Сравнительная характеристика этапов эволюции комплаенс-менеджмента

Критерий сравнения	Нормативное соответствие (традиционный подход)	Стратегическое управление рисками (современный подход)
Основная цель	Избежание штрафов и юридических санкций.	Защита репутации и создание долгосрочной стоимости.
Характер действий	Реактивный (реагирование на уже принятые законы и инциденты).	Проактивный (прогнозирование угроз и предупреждение событий).
Роль в компании	Изолированная функция (юридический отдел или безопасность).	Интегрирована в стратегию и все бизнес-процессы.
Объект внимания	Формальное соблюдение буквы закона.	Управление совокупным профилем рисков (репутационных, операционных, этических).
Пример инструментов	Чек-листы, проверки документации, внутренние аудиты.	Комплаенс-аналитика Big Data, системы информирования о нарушениях (whistleblowing), ESG-отчетность.
Ответственные лица	Юристы, внутренние аудиторы.	Комплаенс-офицеры, Совет директоров, Топ-менеджмент.
Результативность	Минимизация ущерба от уже совершенных ошибок.	Повышение устойчивости бизнеса и доверия стейкхолдеров.

Д.В. Борзаков и М.В. Корсакова указывает, что «интеграция комплаенса в систему стратегического управления рисками позволяет организации не только защищать себя от потерь, но и формировать устойчивую корпоративную культуру» [3, с.28]. Такой подход способствует повышению инвестиционной привлекательности и операционной эффективности, превращая нормативные ограничения в фундамент для устойчивого развития и конкурентного преимущества.

Содержательное наполнение комплаенс-менеджмента варьируется в зависимости от конкретной корпорации. Его предметное поле может включать соблюдение законов и внутренних нормативных актов в различных областях. К таковым относятся экологические вопросы, трудовое законодательство и правила оплаты труда. Сюда же входят вопросы безопасности данных, охраны здоровья и труда. Не менее значимыми аспектами являются равные возможности при трудоустройстве, антимонопольное законодательство и правила сбора средств. А.А. Цыбина указывает на существование риска чрезмерной диверсификации комплаенс-инициатив [4, с.59]. Охват слишком многих областей часто приносит меньший результат по сравнению со строго определенной сферой деятельности.

Функциональное распределение обязанностей в данной области дифференцировано. Финансовый комплаенс традиционно контролируется аудиторами. Операционным комплаенсом ранее управляли юристы, специалисты по внутреннему контролю и консультанты по стратегии. В современной практике ответственность за это направление возложена на комплаенс-офицеров. Государство выступает основным, но не единственным источником нормативных актов. Комплаенс-менеджмент взаимодействует с иными формами регулирования. К ним относится внутренняя корпоративная политика и стандарты профессиональных групп, например, Базельского комитета. Также учитываются требования отраслевых ассоциаций.

В качестве примера Базельского стандарта в области комплаенс-менеджмента можно привести документ «Руководство по комплаенс-функции в банках», опубликованное Базельским комитетом по банковскому надзору в апреле 2005 года. Данный документ закрепляет принципы организации эффективной функции комплаенса в кредитных организациях. В соответствии с принципом 2: «функция комплаенса должна быть независимой. Она должна иметь полномочия отчитываться перед высшим руководством и советом директоров. Функция комплаенса должна располагать достаточными ресурсами для эффективного выполнения своих обязанностей» [5]. В этом же документе Базельский комитет подчеркивает, что комплаенс-риск рассматривается как стратегический, а не только операционный. Это перекликается с обозначенной выше эволюцией от нормативного соответствия к стратегическому управлению рисками.

Рассматриваемый феномен правомерно интерпретировать как часть общего перехода от нормативного правоприменения к саморегулированию. Саморегулирование демонстрирует преимущества в скорости, гибкости и эффективности по сравнению с государственным регулированием. Оно позволяет применять накопленные суждения и отраслевой опыт к вопросам, которые правительству трудно формализовать с помощью четких правил. Классическим примером саморегулирующегося механизма выступает сертификация ISO. В качестве классического примера саморегулирующегося механизма, помимо сертификации ISO, можно привести Стандарт ISO 37301:2021 «Системы менеджмента комплаенса. Требования с руководством по применению».Примечательно, что ISO 37301:2021 не просто формализует процедуры нормативного соответствия, но интегрирует комплаенс в общую систему стратегического управления организацией. Стандарт требует от высшего руководства активного участия, оценки рисков и постоянного улучшения, что полностью соответствует эволюционному переходу от пассивного следования предписаниям к проактивному стратегическому управлению рисками. Сертификация по данному стандарту служит для контрагентов и регуляторов сигналом о зрелости комплаенс-культуры компании [6].

Следует подчеркнуть, что государственные стимулы для сертифицированных субъектов являются значимой движущей силой данного процесса. Сторонники корпоративного саморегулирования указывают на снижение издержек при обеспечении эквивалентного уровня защиты [7, с.150].

Комплаенс представляет собой относительно новую организационную функцию, и многие компании не владеют ею в полной мере. Организации сталкиваются с серьезными проблемами при соблюдении международных норм. В связи с этим появились специалисты, должностные лица, менеджеры и поставщики услуг в данной области. Схема специалистов в области комплаенс-менеджмента показана на рисунке 1.

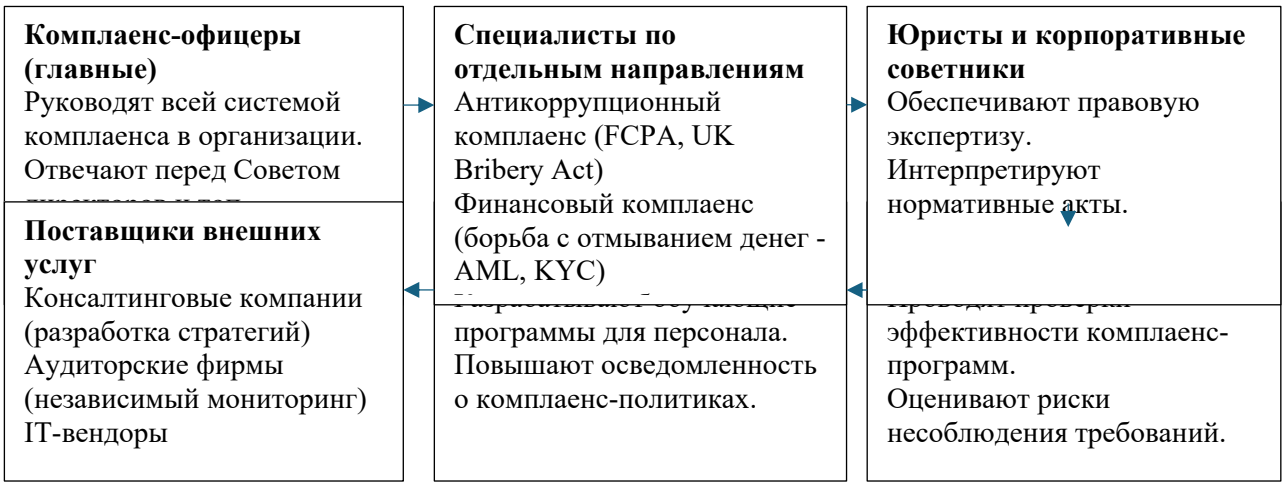

Рисунок 1. Схема специалистов в области комплаенс-менеджмента

Появление широкого спектра комплаенс-специалистов отражает рост сложности регуляторной среды и осознание бизнесом критической важности данной функции. Если изначально комплаенс ограничивался юристами, то сегодня он требует мультидисциплинарного подхода, объединяющего право, финансы, риск-менеджмент, информационные технологии и управление человеческими ресурсами. Разнообразие ролей свидетельствует о зрелости комплаенс-менеджмента как самостоятельной профессиональной области. Однако наличие должностей не гарантирует эффективность – успех определяется реальной интеграцией комплаенса в стратегию и корпоративную культуру.

Тем не менее, уровень информированности о комплаенс-менеджменте остается низким. Нельзя говорить о наличии общих знаний или повсеместного понимания этой проблемы. На сегодняшний день большинство компаний не владеют техникой комплаенс-контроля, что подвергает их значительным рискам [8, с.10].

В основе построения корпоративной комплаенс-культуры лежит комплекс методов «мягкого контроля». Приоритетное значение среди них отводится обучению и тренингам для персонала, а также разработке и имплементации кодекса этики [9, с.11]. Критически важным условием выступает поддержание непрерывного конструктивного диалога между руководством и сотрудниками. Внедрение цифровых технологий позволяет совершенствовать мониторинг и одновременно снижать нагрузку на контролирующие органы. Данный подход также способствует повышению прозрачности контрольной деятельности. Дополнительным инструментом выступает риск-ориентированное регулирование, которое концентрирует усилия на наиболее уязвимых областях. Именно там нарушения норм могут повлечь наиболее серьезные последствия.

Активное применение мягких методов контроля предопределяет закономерный переход к модели риск-ориентированного подхода. Данная трансформация применима, в частности, к контрольной деятельности управления делами региона. Она будет способствовать безболезненному и последовательному совершенствованию корпоративной культуры. Следует констатировать, что риск-ориентированный подход

принципиально ориентирован на профилактику нарушений, а не на карательные меры. Система комплаенса в этом контексте формирует особую среду, где организации и государственные органы действуют сознательно. Она позволяет соблюдать нормы и стандарты на добровольной основе, минимизируя риски и обеспечивая прозрачность. Комплаенс в данной парадигме становится неотъемлемой частью стратегии управления. Его ключевое назначение – предупреждение нарушений до момента их возникновения. Такой подход обеспечивает решение проблем без применения жестких санкций, что соответствует современным стандартам эффективного управления.

В таблице 2 представлены примеры внедрения комплаенс-менеджмента в компаниях. Представленные примеры демонстрируют, что комплаенс-менеджмент является универсальным инструментом, эффективным как в крупных корпорациях с развитыми рынками (Siemens, Walmart), так и в компаниях с формирующимися институтами управления (Россия, Казахстан).

Таблица 2.

Реальные примеры внедрения комплаенс-менеджмента в компаниях

Компания	Ключевые комплаенс-инициативы	Результат
ПАО «Сбербанк»	Внедрение системы антикоррупционного комплаенса, обучение сотрудников, цифровой мониторинг транзакций, Кодекс корпоративной этики.	Снижение операционных рисков, повышение доверия клиентов и регуляторов, включение в индексы устойчивого развития.
АО «Самрук-Казына»	Внедрение системы комплаенс-контроля во всех дочерних организациях, обучение топ-менеджмента, создание Комитета по этике и комплаенсу.	Повышение прозрачности управления, снижение коррупционных рисков, улучшение инвестиционного климата.
Siemens AG	Полный пересмотр комплаенс-системы после коррупционного скандала (2006-2008), создание независимого комплаенс-подразделения, глобальные программы обучения и «whistleblowing».	Восстановление репутации, возвращение доверия инвесторов и государств, признание одной из самых комплаентных компаний мира.
Walmart Inc.	Глобальная программа антикоррупционного комплаенса (FCPA), мониторинг поставщиков и контрагентов, внедрение цифровых инструментов контроля.	Успешное урегулирование многолетних расследований, снижение штрафных рисков, стандартизация контроля в 28 странах.

Внедрение комплаенс-систем в российских и казахстанских компаниях происходит с учетом международных стандартов (включая требования OECD, FCPA, Базельские принципы), что подтверждает глобальную конвергенцию подходов. При этом успешные кейсы показывают, что комплаенс перестает быть исключительно реактивной мерой и превращается в стратегический фактор конкурентоспособности.

Присутствует регуляторная природа комплаенс-риска. Однако измерение данного риска осуществляется посредством различных концептуальных подходов. В этой связи организациям критически важно идентифицировать релевантные требования комплаенса. Данная идентификация служит необходимым условием для эффективного снижения соответствующих рисков. Современные подходы к структурированию нормативной базы комплаенса акцентируют приоритет риска [10, с.431]. Риски подлежат ранжированию от наиболее критичных до операционных и репутационных. К числу критичных относятся

угрозы безопасности организации и общества, а также финансовой стабильности. Подобная концепция фокусирует внимание на законодательных актах с наибольшим потенциальным ущербом. Она согласуется с рекомендациями ведущих регуляторов и отражает современные научные взгляды на природу комплаенса. Структурирование нормативно-правовой базы по приоритетам риска должно носить динамичный и регулярно пересматриваемый характер. Такой подход позволяет организациям целенаправленно управлять возникающими угрозами. В результате минимизируются потенциальные угрозы экономической безопасности и обеспечивается устойчивое развитие компании [11, с.371].

В группе рисков коррупции и взяточничества ключевыми документами выступают Конвенция ООН против коррупции от 31.10.2003 г. [12], Конвенция ОЭСР о борьбе с подкупом иностранных должностных лиц при осуществлении международных коммерческих операций от 21.11.1997 г. [13], а также Закон Республики Казахстан от 18 ноября 2015 года № 410-V «О противодействии коррупции» [14]. Нарушение данных норм влечет уголовно-правовые, административные, финансовые и репутационные последствия. В блоке рисков нарушения персональных данных и кибербезопасности основополагающими актами являются Закон Республики Казахстан от 21 мая 2013 года № 94-V «О персональных данных и их защите» [15], Закон Республики Казахстан от 2 июля 2003 года № 461-II «О рынке ценных бумаг» [16], а также Общий регламент по защите персональных данных Европейского Союза (GDPR) [17].

Структурирование законодательных документов позволяет организациям акцентировать внимание на значимых особенностях каждой группы рисков. Это помогает руководству минимизировать угрозы и рационально распределять ресурсы для формирования надежной комплаенс-системы. Кроме того, такой подход способствует идентификации потенциальных угроз и выявлению зон повышенного риска. Создание и анализ матрицы рисков предоставляет руководству наглядное представление об уровне угроз и вероятности их реализации. Это облегчает принятие управленческих решений и выстраивание приоритетов в работе с нормативными требованиями. Регулярное обновление нормативной базы и адаптация под специфику бизнеса обеспечивают гибкость и актуальность системы. Данная адаптивность особенно важна в условиях динамично меняющегося законодательства и бизнес-среды.

Систематизация законодательной базы в зависимости от группы рассматриваемых рисков способствует повышению эффективности управления рисками. Она снижает вероятность нарушений и обеспечивает устойчивость бизнеса в условиях внешних и внутренних угроз. В современных литературных источниках прослеживается тенденция встраивания работы с рисками в общую систему управления предприятием. Ключевым инструментом методологии действий с рисками выступает риск-ориентированный подход. Он позволяет не только выявлять узкие места правового регулирования, но и целенаправленно структурировать нормативно-правовую базу. Данное структурирование осуществляется в соответствии с уровнем и характером конкретных рисков, идентифицированных на каждом этапе бизнеса. Постоянное усложнение регуляторной среды и стремление оптимизировать ресурсы для обеспечения соответствия требованиям закона обусловили актуальность такого подхода. Нормативно-правовую базу комплаенса невозможно воспринимать как совокупность формальных обязательств. Данный пласт системы позиционируется неразрывно с оценкой и ранжированием рисков, что составляет его сущностную характеристику.

Внутренние документы компаний служат инструментом реализации нормативно-правовой базы комплаенса, позволяя применять системный подход к управлению рисками. Реестр рисков обеспечивает фиксацию и систематизацию угроз, а также реализацию требований законодательства. Определение приоритетов рисков оптимизирует

распределение ресурсов и позволяет прогнозировать проблемные ситуации. Установка факторов риска представляет ключевой этап управления с учетом отраслевой специфики и внешних условий. Разбор практических кейсов выявляет причины нарушений и адаптирует комплаенс-систему под актуальные нормы.

Сопоставление контрольных процедур с правовыми требованиями раскрывает содержание каждого элемента управления. Локальные акты закрепляют процедуры оценки рисков, устанавливают сроки и показатели эффективности. Реестр фиксирует причины нарушений, их уровень и ответственных лиц. Анализ источников рисков формирует основу для проактивного управления. Изучение реальных ситуаций позволяет выявлять несоответствия и повышать эффективность контроля.

Нормативно-правовая база служит фундаментом стратегий управления рисками. Сущность риск-ориентированного подхода заключается в системном анализе требований закона с учетом специфики деятельности. Такой анализ определяет критические зоны и приоритеты контрольных процедур. Он оптимизирует распределение ресурсов и обеспечивает гибкость системы в условиях изменяющегося законодательства. Соотнесение рисков с конкретными правовыми нормами позволяет целенаправленно управлять угрозами. Современные исследования подтверждают, что риск-ориентированный подход адаптирует нормативное регулирование к реальным условиям бизнеса.

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AI-Driven Prediction and Resilience Building in Tourism Risk and Crisis Management

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Abstract. Tourism systems are exposed to health, environmental, geopolitical, technological, and operational disruptions. This conceptual study explains how natural language processing, knowledge graphs, and time-series forecasting can be combined to strengthen early warning and organizational resilience. It uses a structured integrative review and mechanism synthesis rather than presenting original empirical estimates. The resulting framework connects heterogeneous data inputs to signal detection, relational diagnosis, forecasting, human validation, coordinated response, and post-event learning. Three propositions specify when artificial intelligence is most likely to improve preparedness, supply-chain adaptability, and accountable emergency decisions. The analysis also identifies limits involving data drift, rare events, multilingual bias, privacy, cybersecurity, and automation bias. The paper contributes an auditable human-in-the-loop architecture that treats artificial intelligence as decision support rather than an autonomous crisis manager.

Keywords: artificial intelligence; tourism crisis management; early warning; resilience; natural language processing; knowledge graphs; forecasting

1. Introduction

Tourism is unusually sensitive to disruption because mobility, perceived safety, infrastructure, and coordinated service delivery are jointly required. A localized transport failure, health alert, extreme-weather event, or political incident can therefore propagate across accommodation, attractions, intermediaries, and destination organizations. The COVID-19 shock illustrated the global reach and interdependence of such disruption (Gössling et al., 2021). Crisis research consequently treats preparedness, response, recovery, and organizational learning as connected managerial functions rather than isolated emergency tasks (Faulkner, 2001; Ritchie, 2004).

Digital tourism produces large volumes of operational and behavioral traces. News, official alerts, reviews, booking patterns, mobility indicators, and sensor feeds may reveal weak signals earlier than conventional periodic reports. Yet data volume alone does not create resilience. Smart-tourism research stresses that value arises when data are integrated with governance, service ecosystems, and decision processes (Buhalis & Law, 2008; Gretzel et al., 2015). The managerial problem is therefore how to combine complementary analytical techniques without transferring unreviewable authority to an algorithm.

This paper asks: (1) how can natural language processing (NLP), knowledge graphs, and time-series models jointly support tourism early warning; (2) through what mechanisms can they strengthen supply-chain and destination resilience; and (3) what controls are required for responsible emergency use? Its contribution is a mechanism-based architecture linking data, analytical outputs, human validation, organizational action, and learning. No new dataset or measured causal effect is claimed.

2. Method and Scope

The study follows a structured integrative-review logic. It combines foundational tourism crisis and resilience research with peer-reviewed work on smart tourism and the technical foundations of NLP, knowledge graphs, and machine learning. Sources were selected for conceptual relevance, publication traceability, and their ability to define mechanisms or governance constraints. The synthesis proceeded in four steps: defining crisis-management functions; mapping each AI family to an information-processing capability; identifying organizational actions enabled by that capability; and specifying failure modes and safeguards.

The unit of analysis is an AI-assisted destination or tourism-enterprise decision system. The framework is explanatory and propositional, not a systematic meta-analysis and not an empirical evaluation. Accordingly, it does not report accuracy rates, economic losses, adoption shares, or forecasts. Future testing should pre-register outcomes and compare AI-assisted decisions with an appropriate baseline.

3. Theoretical Foundations

3.1 Crisis management and resilience

Faulkner (2001) distinguishes preparation, response, recovery, and resolution in tourism disaster management, while Ritchie (2004) emphasizes strategic flexibility and learning under turbulence. Resilience extends the objective beyond rapid restoration: a system should absorb disturbance, adapt its configuration, and retain essential functions. At destination level this requires redundancy, information sharing, distributed capability, and learning across public and private actors (Hall et al., 2018).

3.2 AI as an information-processing capability

The three selected AI families solve different problems. NLP extracts entities, events, topics, and sentiment from unstructured language. Knowledge graphs represent entities and relationships so that dependencies can be queried and reasoned about. Time-series models estimate temporal patterns and conditional forecasts. Deep learning can improve representation of nonlinear relationships, but its performance remains dependent on training data and distributional stability (LeCun et al., 2015). The techniques should therefore be treated as complementary modules rather than interchangeable tools.

4. Integrated Predictive-Resilience Framework

Layer	Primary function	Tourism application	Required control
NLP	Detect and classify textual signals	Official alerts, news, complaints, multilingual traveler discourse	Source ranking, language validation, false-positive review
Knowledge graph	Represent dependencies and propagation paths	Links among hazards, transport nodes, hotels, attractions, suppliers, and agencies	Versioned ontology, provenance, role-based access
Time-series models	Forecast demand, capacity, and recovery trajectories	Bookings, cancellations, staffing, inventory, mobility, and resource needs	Rolling back-tests, drift monitoring, prediction intervals
Human decision layer	Interpret trade-offs and authorize intervention	Escalation, resource allocation, public communication, and service continuity	Named decision owner, override log, post-event audit

4.1 Signal detection through NLP

NLP can continuously classify incoming text by location, hazard, urgency, and affected service. Entity extraction can connect a report to a destination or transport node; topic and sentiment shifts can flag emerging anxiety or service failure. Because online content is strategically manipulated, unevenly distributed, and multilingual, an alert should include source provenance and confidence. Automated sentiment must not be treated as a direct measure of actual risk. Human analysts should validate high-impact alerts against official bulletins and operational data.

4.2 Relational diagnosis through knowledge graphs

A knowledge graph converts separate alerts into a model of interdependence. A closed airport, for example, can be linked to routes, tour operators, hotels, visitor segments, and alternative transport. Graph queries can identify exposed nodes and possible substitutes. The graph literature emphasizes explicit schemas, provenance, and reasoning over linked entities (Hogan et al., 2021). In crisis use, every edge should therefore record its source and update time; otherwise an apparently precise dependency map may be stale.

4.3 Dynamic forecasting and scenario comparison

Time-series models can estimate short-term bookings, cancellations, capacity needs, and recovery paths. Their role is to present conditional scenarios, not a single certain future. Rolling-origin validation, comparison with simple baselines, prediction intervals, and drift monitoring are essential. Rare crises create structural breaks, so a model trained on normal periods may fail precisely when needed most. Managers should combine model outputs with scenario assumptions and stress tests.

4.4 From analytics to coordinated action

The framework closes the loop by connecting validated signals to predefined playbooks. Alerts are triaged by severity and confidence; graph-based diagnosis identifies exposed actors; forecasts estimate resource implications; and a named human owner selects and records the intervention. Outcomes then update thresholds, data-quality rules, and response procedures. This feedback loop converts one-off prediction into organizational learning.

5. Propositions and Managerial Implications

Proposition 1. AI-assisted early warning will improve preparedness when heterogeneous signals are fused across complementary models and high-impact alerts are verified by accountable human decision makers. A single channel may be fast but brittle; triangulation reduces dependence on platform-specific noise.

Proposition 2. Knowledge-graph visibility will strengthen tourism supply-chain resilience when dependency data are current and participating organizations have agreed escalation and data-sharing protocols. Technical visibility without authority to act cannot reallocate capacity or activate substitutes.

Proposition 3. Forecasting will support adaptive recovery when managers receive uncertainty ranges, baseline comparisons, and model-drift warnings rather than point estimates alone. Transparent uncertainty encourages contingency planning and limits false precision.

Implementation should begin with a narrowly defined decision, such as transport disruption triage, rather than an enterprise-wide platform. Managers should specify the decision owner, accepted data sources, threshold logic, fallback procedure, retention period, and audit record before deployment. Performance should be evaluated using timeliness, false-alert cost, service continuity, recovery time, and equity across traveler groups, not predictive accuracy alone.

6. Governance and Limitations

Tourism data can reveal location, identity, health status, or purchasing behavior. Collection should follow purpose limitation, data minimization, access control, and retention rules. Multilingual and regional imbalance may underrepresent smaller destinations or traveler groups. Cybersecurity is also a resilience issue: a compromised alert pipeline can amplify disruption.

Finally, automation bias may cause staff to accept model output despite contradictory evidence. Mandatory review for consequential actions, documented overrides, and regular exercises are therefore central design requirements.

This study is limited by its conceptual method. The propositions require empirical testing across destinations of different size, institutional capacity, and data maturity. Comparative field studies could evaluate whether the integrated architecture reduces detection delay or recovery time, while simulation studies could examine behavior under missing or adversarial data.

7. Conclusion

AI can strengthen tourism crisis management when it reorganizes information processing and coordination rather than merely automating existing routines. NLP detects weak textual signals, knowledge graphs expose dependencies, and time-series models compare possible trajectories. Their value depends on provenance, validation, uncertainty communication, accountable authorization, and post-event learning. The proposed human-in-the-loop framework offers a testable foundation for building predictive capacity without confusing algorithmic output with managerial responsibility.

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Artificial Intelligence-Assisted Management Decision-Making in the Context of Digital Transformation

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Abstract. Artificial intelligence changes managerial decision-making by redistributing prediction, evaluation, and authorization between algorithms and organizational actors. This conceptual paper develops a governance-oriented framework for AI-assisted decisions under digital transformation. A structured integrative review links machine learning, knowledge-based systems, and predictive analytics to three mechanisms: reducing information asymmetry, augmenting bounded managerial cognition, and accelerating feedback-based organizational learning. The framework distinguishes decision support, sequential hybrid decision-making, and constrained delegation, and maps each mode to suitable task conditions and controls. Four propositions explain how task structure, explainability, data quality, and accountability influence decision quality. The study rejects claims of automatic performance improvement and specifies an implementation cycle covering problem definition, baseline comparison, human review, monitoring, and audit. Its principal contribution is a practical and testable model of responsible human–AI decision architecture for service- and information-intensive organizations.
Keywords: artificial intelligence; managerial decision-making; digital transformation; human–AI collaboration; governance; predictive analytics

1. Introduction

Digital transformation is an organizational change process in which digital technologies reshape value creation, structure, and strategy rather than simply computerize existing activities (Vial, 2019). Artificial intelligence (AI) is central to this process because it can classify observations, predict outcomes, generate recommendations, and standardize repeated decisions. In logistics, tourism, education, accounting, and other information-intensive sectors, such capabilities affect resource allocation, risk control, performance evaluation, and service design.

The managerial consequences are not reducible to automation. Digital innovation is distributed across actors and organizational boundaries (Nambisan et al., 2017), while algorithmic systems alter who may initiate, justify, review, and revise a decision. Research therefore highlights human–AI combinations, ranging from delegation to sequential or aggregated decision structures (Shrestha et al., 2019). Raisch and Krakowski (2021) further show that automation and augmentation are interdependent rather than mutually exclusive.

This paper asks how AI reshapes managerial decision-making, which task conditions favor different human–AI arrangements, and what governance mechanisms preserve accountability. It develops a mechanism-based framework and four propositions. The paper is conceptual: it does not present primary data or claim that AI adoption by itself increases firm performance.

2. Method and Analytical Boundaries

A structured integrative review was used to combine research on digital innovation, organizational decision structures, human–AI collaboration, algorithmic control, analytics capability, and ethics. Sources were retained when their bibliographic identity was traceable and they directly informed a construct, mechanism, or governance condition. The synthesis first

separated the stages of a managerial decision, then mapped AI capabilities to those stages, compared alternative allocations of authority, and identified controls for known failure modes.

The analysis focuses on organizational decisions supported by data-driven models. It excludes autonomous physical systems and does not treat generative output as verified evidence. “Decision quality” refers to a context-specific combination of accuracy, timeliness, consistency, adaptability, fairness, and accountability. These dimensions may conflict; no single metric is presumed sufficient.

3. Conceptual Foundations

3.1 Bounded cognition and algorithmic prediction

Managers operate with incomplete information, limited attention, and established routines. Machine learning can expand pattern recognition and compare more alternatives, thereby augmenting human cognition. Jarrahi (2018) describes a symbiotic arrangement in which computational analytical capacity complements contextual and intuitive judgment. Learning algorithms can also reshape expertise, occupational boundaries, coordination, and control (Faraj et al., 2018). However, prediction does not determine organizational objectives, acceptable trade-offs, or responsibility for consequences.

3.2 Digital innovation and organizational learning

Digital innovation is recombinable and distributed, so models and data frequently cross functional and organizational boundaries (Nambisan et al., 2017). AI outputs also become inputs into new routines: managers act, observe outcomes, and revise thresholds or processes. This feedback can enable learning, but it can also create self-reinforcing bias when decisions influence the data later used for retraining. Learning therefore requires explicit outcome review rather than automatic model updating.

3.3 The automation–augmentation tension

Automation promises speed and consistency, whereas augmentation preserves contextual judgment. Raisch and Krakowski (2021) argue that prioritizing either pole can generate unintended reinforcing effects. An augmented process may gradually become automated as confidence grows; a highly automated process may require more human intervention after drift or exceptional events. Decision architecture must therefore define both normal authority and exception handling.

4. AI Capabilities and Managerial Mechanisms

4.1 Machine learning and information asymmetry

Machine-learning models identify patterns in operational, behavioral, or financial data. They can support demand forecasts, anomaly detection, churn risk, or service prioritization. The managerial mechanism is a reduction in information asymmetry: relevant patterns become visible earlier and more consistently. Yet historical data encode past policies and unequal observation. Before deployment, managers need a simple baseline, out-of-sample validation, subgroup evaluation, and a definition of unacceptable error.

4.2 Knowledge-based systems and coordination

Rule engines and knowledge graphs make decision logic and relationships explicit. They are suited to stable constraints such as eligibility rules, process dependencies, or escalation requirements. Their managerial benefit is coordination: units can share terminology and apply consistent logic. Their principal vulnerability is obsolescence. A named owner, version control, provenance, and scheduled review are needed whenever regulations, products, or organizational structures change.

4.3 Predictive analytics and adaptive control

Predictive analytics links forecasts to operational choices such as staffing, inventory, budgets, or risk limits. Research on big-data analytics suggests that performance effects depend on organizational capabilities rather than data possession alone (Wamba et al., 2017). Adaptive

control therefore requires timely feedback, the authority to respond, and monitoring for drift. Point predictions should be accompanied by uncertainty and scenario assumptions.

5. Human–AI Decision Architecture

Mode	Suitable conditions	Human role	Core safeguard
Decision support	Ambiguous, high-impact, or novel tasks	Frames objectives, interprets output, and authorizes action	Explanations, alternative options, documented rationale
Sequential hybrid	Moderately structured tasks with reviewable cases	Reviews exceptions or confirms model recommendation	Escalation thresholds, sampling audit, override analysis
Constrained delegation	High-volume, low-impact, stable, reversible tasks	Sets limits and monitors aggregate performance	Hard constraints, rollback, drift alerts, periodic reapproval

Shrestha et al. (2019) show that task characteristics such as search-space specificity, interpretability, speed, and replicability shape the appropriate allocation of human and AI authority. Full delegation is therefore not a maturity endpoint. High-impact or poorly specified choices generally require decision support; repeated and reviewable cases may suit a sequential hybrid; only stable, reversible, bounded tasks are candidates for constrained delegation.

Proposition 1. AI assistance will improve decision quality more consistently when the assigned task has a measurable outcome and the model is compared with a relevant human or statistical baseline.

Proposition 2. Human–AI complementarity will be stronger when human reviewers possess both domain authority and the information needed to challenge the model, rather than serving as nominal approvers.

Proposition 3. The benefits of faster prediction will be reduced when organizational routines cannot act on the output or when feedback arrives too late to evaluate the decision.

Proposition 4. Accountability will weaken as decision authority becomes more distributed unless the organization names an owner for data, model performance, operational authorization, and incident response.

6. Applications and Implementation

In logistics, forecasting can inform capacity and routing, but disruption decisions require operational constraints and exception review. In tourism, demand estimates may guide staffing while destination managers retain responsibility for safety and public communication. In education, early-warning systems can prioritize support but must not convert correlations into irreversible judgments about students. In accounting, anomaly detection can direct audit attention while evidence evaluation and professional responsibility remain human functions.

A responsible implementation cycle contains six steps. First, define the decision, affected groups, owner, and success criteria. Second, document the data source, lawful purpose, coverage, and known gaps. Third, compare the model with a simple baseline and test performance across relevant subgroups and time periods. Fourth, select a decision mode and specify escalation, override, and rollback rules. Fifth, monitor outcomes, drift, overrides, complaints, and operational failures. Sixth, conduct periodic reauthorization and retire systems whose benefits no longer exceed their risks.

7. Governance Risks

Algorithmic systems can reproduce bias, obscure responsibility, and enable intensive surveillance. Mittelstadt et al. (2016) show that ethical concerns arise from opacity, evidence quality, unfair outcomes, and traceability. Algorithmic control may also change worker autonomy and the visibility of managerial power (Kellogg et al., 2020). Governance must therefore extend beyond technical explainability to participation, contestability, access control, retention limits, security, and meaningful remedies.

Automation bias and deskilling are additional risks. When reviewers rarely overturn a recommendation, formal human oversight may not be substantive. Organizations should analyze override patterns, rotate manual review samples, train staff on model limits, and run exercises for system failure. A useful audit trail records model version, input provenance, output, uncertainty, reviewer, action, and observed outcome without retaining unnecessary personal data.

8. Discussion and Limitations

The framework contributes by connecting AI capability to an organizational mechanism, authority allocation, and governance control. It explains why identical technology can produce different results across organizations: value depends on task definition, complementary capability, feedback, and accountability. It also reframes “human in the loop” as an institutional design question, not simply a button requiring approval.

The paper is limited by its conceptual scope and cross-industry abstraction. The propositions should be tested using longitudinal field studies that compare decision modes while measuring accuracy, time, reversibility, fairness, and accountability. Research should also examine how regulation, professional norms, data maturity, and organizational power shape the practical ability to challenge AI output.

9. Conclusion

AI-assisted management is most defensible when organizations treat prediction as one component of a governed decision process. Machine learning can reduce information asymmetry, knowledge systems can coordinate rules and dependencies, and predictive analytics can accelerate feedback. These benefits require appropriate authority allocation, validated baselines, uncertainty communication, human challenge, monitoring, and audit. The proposed architecture provides a testable basis for achieving augmentation without abandoning managerial responsibility.

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Pedagogical Sciences

Artificial Intelligence and Intercultural Communicative Competence in EFL Classrooms: A Case Study from Central Asia

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Abstract

Intercultural communicative competence (ICC) the ability to communicate effectively and appropriately across linguistic and cultural backgrounds is a key goal of EFL instruction (Byram, 1997; Deardorff, 2006). This pilot quasi-experimental study examined teacher-mediated, AI-supported roleplay among 30 B1–B2 EFL students in Kazakhstan. Over four weekly sessions, an experimental group (n = 15) used generative AI, while a comparison group (n = 15) completed parallel tasks without AI. Using pre/post questionnaires, roleplay rubrics, and student reflections, the study found greater development in selected ICC dimensions among AI-supported students, particularly adapting language, interpreting cultural differences, managing misunderstandings, and tolerating ambiguity. Findings suggest that teacher-mediated AI can support ICC development by expanding scenarios, linguistic input, and reflection opportunities, although AI content requires critical verification.

Keywords: Intercultural communicative competence (ICC), AI, teacher education, EFL

Introduction

Intercultural communicative competence (ICC) has been recognized for over two decades as a core outcome of foreign language education, extending beyond linguistic accuracy to encompass the knowledge, skills, and attitudes required to communicate effectively across cultural boundaries (Byram, 1997; Deardorff, 2006). As classrooms increasingly incorporate digital tools, researchers have begun to examine whether and how technology-mediated practice can support ICC development, including through virtual reality simulations (Taguchi, 2023), digital games, and mobile-mediated interaction (Sykes & Dubreil, 2019).

Generative AI tools introduce a new possibility for this line of research: the ability to provide EFL learners with on-demand, interactive roleplay partners for practicing intercultural communication scenarios that might otherwise be difficult to arrange in a classroom setting. However, empirical evidence on how such tools affect ICC development remains limited, and almost no research has examined this question in Central Asian higher education contexts, where English is typically the third language after Kazakh and Russian and where intercultural competence has particular significance given the region's position at the crossroads of multiple cultural and linguistic traditions.

This study extends prior classroom-based work on intercultural communicative competence development among EFL students at a Kazakhstani university by examining, through a pilot quasi-experimental design, the specific contribution of teacher-mediated, AI-supported dialogue practice. The study addresses two research questions: (1) How, if at all, does students' intercultural communicative competence differ between a group using AI-supported roleplay practice and a comparison group completing parallel tasks without AI support? (2) How do

students describe their experience of using AI tools to practice intercultural communication scenarios, including their engagement with the accuracy and reliability of AI-generated content?

Literature Review

Intercultural Communicative Competence: Conceptual Foundations

Byram's (1997) foundational model of ICC identifies five components teachers should aim to develop in learners: attitudes of openness and curiosity toward other cultures, knowledge of one's own and other cultures, skills of interpreting and relating cultural phenomena, skills of discovery and interaction in real-time communication, and critical cultural awareness. Deardorff (2006) extended this work by developing a widely used process model of intercultural competence, emphasizing that ICC develops iteratively through cycles of attitude, knowledge, and skill, resulting in both internal outcomes (adaptability, empathy) and external outcomes (effective and appropriate communication and behavior in intercultural situations).

Technology-Supported ICC Development

A growing body of research has examined how technology can create opportunities for intercultural practice that are otherwise difficult to arrange, particularly in foreign language contexts where learners have limited direct access to native speakers or authentic intercultural encounters. Taguchi (2023) used immersive virtual reality to assess learners' ability to mediate intercultural conflict, finding that VR-based simulation offered a viable method for both practicing and assessing intercultural competence. Sykes and Dubreil (2019) reviewed a broader landscape of digital tools including mobile-based games and simulations for developing intercultural and pragmatic competence, arguing that technology-mediated practice can provide learners with low-stakes opportunities to rehearse intercultural interaction before encountering it in real-world settings.

Generative AI chatbots represent a further development in this line of research: unlike fixed simulations, AI dialogue partners can respond dynamically to learner input, potentially offering a more flexible and scalable form of intercultural roleplay practice. However, this possibility remains largely unexamined empirically, particularly outside North American, European, and East Asian contexts.

The Central Asian and Multilingual Context

English language teaching in Kazakhstan occurs within an officially trilingual context alongside Kazakh and Russian (Ahn & Smagulova, 2022), positioning intercultural communicative competence as a particularly salient pedagogical goal: students are routinely required to navigate cultural and linguistic difference not only in relation to English-speaking cultures but within their own multilingual national context. This study is situated within this broader context, extending prior classroom-based work on ICC development among Kazakhstani EFL students to examine the specific contribution of AI-supported practice.

Methodology

Research Design

This study employed a quasi-experimental pretest–posttest design with a comparison group, supplemented with classroom observation and written student reflections, to examine changes in intercultural communicative competence (ICC) following a period of AI-supported roleplay practice. Given the study's exploratory, classroom-embedded scope, it is best characterized as a pilot quasi-experimental study rather than a fully controlled experiment.

Participants and Setting

Thirty second-year undergraduate EFL students (approximately B1–B2 proficiency) at Kazakh Ablai Khan University of International Relations and World Languages participated in the study, divided into two groups of 15. The experimental group completed intercultural roleplay tasks using generative AI tools, while the comparison group completed parallel tasks without AI support. The study was conducted within undergraduate foreign-language instruction in which the

instructor regularly employs communicative, problem-based, and interactive approaches, and had begun piloting AI-assisted learning activities; this instructional context informed the design of the intervention described below.

Intervention

Both groups completed four one-hour sessions over four weeks focused on intercultural communication scenarios (e.g., negotiating a misunderstanding with a foreign colleague, interpreting an unfamiliar communicative norm). The experimental group used ChatGPT and Claude to generate and revise dialogues, scenarios, vocabulary, and alternative response options, and used Gemini primarily to produce visual and illustrative materials supporting the scenarios. Listening materials were deliberately varied to include different regional varieties and accents of English as well as different communicative styles, rather than simply different speaker voices. Pair and small-group work was used throughout both conditions and was deliberately structured to keep students actively engaged rather than passively observing.

Students in the experimental group were explicitly instructed to verify AI-generated content rather than accept it uncritically, since ChatGPT occasionally generated inaccurate or culturally inappropriate information that required checking against reliable sources. Claude was informally perceived by the instructor as somewhat more reliable for certain tasks over the course of the intervention; this is reported here as an instructional observation rather than a systematic or generalizable comparison between tools.

Instruments

ICC was assessed using a mixed-methods approach combining three sources of evidence: (a) a pre/post ICC questionnaire; (b) instructor observation and rubric-based rating of student performance during roleplay tasks, focused on five dimensions recognition of cultural differences, ability to interpret a communication partner's perspective, appropriate adjustment of language and register, management of misunderstanding, and tolerance of ambiguity; and (c) short written reflections completed by students after each session, in which they described what they had found difficult and how they had adapted their communication. In addition, a faculty administrator (the department Dean) observed one of the roleplay demonstrations and provided an informal evaluation of task quality and student engagement, offering a secondary, non-participant perspective on classroom implementation.

Data Analysis

Pre/post questionnaire and rubric data were compared descriptively between the experimental and comparison groups, given the small sample size and pilot scope of the study. Written reflections were analyzed thematically, using the same five ICC dimensions from the observation rubric as an initial coding framework, while remaining open to additional themes, particularly regarding students' engagement with and evaluation of AI-generated content.

Findings

Consistent with the study's pilot, small-sample scope, findings are reported descriptively and thematically rather than as precise numerical gains, and should be interpreted as suggestive rather than conclusive. Table 1 summarizes the observed pattern of change across the five ICC dimensions assessed via rubric-based observation.

Table 1

Observed Change Across ICC Dimensions, by Group (N = 30)

ICC dimension	Experimental (n = 15)	Comparison (n = 15)
Recognition of cultural differences	Moderate–clear gain	Slight gain
Interpreting a partner's perspective	Clear gain	Slight gain
Adjustment of language/register	Clear gain	Moderate gain
Management of misunderstanding	Clear gain	Slight gain
Tolerance of ambiguity	Moderate–clear gain	Minimal change

Note. Ratings reflect instructor rubric-based observation across four sessions rather than a standardized numerical scale; they are reported qualitatively given the pilot scope and sample size of the study.

Differences Between the Experimental and Comparison Groups

Students in the experimental group showed more visible development across several of the five rubric dimensions over the course of the intervention, particularly in recognizing that the same communicative behavior can carry different meanings across cultures, adapting language and register to different interlocutors, managing misunderstanding, and tolerating ambiguity in unfamiliar communicative situations. Students in the comparison group also showed some improvement, consistent with the benefit of repeated structured practice with intercultural scenarios, but changes in these more adaptive, interpretive dimensions of ICC were less pronounced than in the experimental group.

The Role of AI: Variety and Verification

Generative AI tools were particularly useful for expanding the range of scenarios, vocabulary, and alternative response options available to students, and for producing varied listening materials reflecting different regional varieties and communicative styles of English. However, AI use did not translate automatically into ICC development: several students' written reflections and classroom performance indicated that the pedagogical value of the AI-generated material depended on the instructor's mediation selecting, adapting, and framing AI output and on students actively verifying content rather than accepting it uncritically. This verification requirement, prompted by occasional inaccurate or culturally inappropriate AI output, appeared to itself become a productive site of critical engagement with intercultural material rather than simply a limitation of the tools.

Student Reflections

In their written reflections, students most frequently described difficulty in recognizing when a misunderstanding had occurred and in adjusting their language to an unfamiliar communicative style, and described adapting by asking clarifying questions, rephrasing, and paying closer attention to context provided in the AI-generated scenarios. The Dean's observation of one classroom demonstration offered a corroborating, non-participant perspective, noting the quality of task design and the visible engagement of students during the roleplay activity.

Discussion

Rather than supporting the broad claim that AI improves intercultural communicative competence, these findings support a more specific and defensible argument: teacher-mediated use of generative AI can support the development of selected dimensions of intercultural communicative competence by increasing the variety of communicative scenarios, linguistic input, and opportunities for reflection available to students; however, AI-generated content requires critical verification and pedagogical guidance to be pedagogically productive.

This pattern maps onto Byram's (1997) and Deardorff's (2006) models in a specific way: the dimensions that showed the clearest experimental-group advantage recognizing alternative cultural interpretations, adjusting language to interlocutors, tolerating ambiguity correspond closely to Byram's skills of interpreting and relating and Deardorff's emphasis on adaptability, while more foundational attitudinal components appeared to develop similarly across both groups. This suggests that AI-supported practice may be particularly well suited to developing the more interactive, adaptive dimensions of ICC rather than functioning as a general-purpose intervention across all of its components.

The finding that AI's pedagogical value depended on teacher mediation and student verification also extends prior technology-and-ICC research. Where Taguchi (2023) and Sykes and Dubreil (2019) examined largely fixed simulation and game-based environments, the present study's generative AI tools were more flexible but also less predictable, introducing a verification burden consistent with broader concerns raised in the critical AI literacy literature regarding uncritical reliance on generative AI output (Aleman et al., 2025; Baran et al., 2026). Rather than treating this verification requirement as a limitation to be engineered away, the findings suggest it may itself function as a form of critical intercultural and AI literacy practice, worth deliberately incorporating into future intervention designs.

Conclusion and Future Directions

This pilot quasi-experimental study offers early, classroom-based evidence that teacher-mediated, generative-AI-supported roleplay practice can support selected dimensions of intercultural communicative competence among EFL students in Kazakhstan, while underscoring that AI-generated content requires active verification and pedagogical framing rather than unmediated use. Future work should extend this pilot with a larger sample and formal statistical comparison between conditions, examine which specific instructional practices most effectively support students' critical evaluation of AI-generated intercultural content, and investigate how these patterns generalize across other Central Asian higher education contexts.

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ИННОВАЦИОННЫЕ ПОДХОДЫ В ПОДГОТОВКЕ УЧИТЕЛЕЙ МУЗЫКИ В УСЛОВИЯХ ЦИФРОВИЗАЦИИ ОБРАЗОВАНИЯ

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Аннотация

В статье рассматриваются актуальные вопросы подготовки будущих учителей музыки в условиях цифровизации образования. Анализируются современные тенденции интеграции информационно-коммуникационных технологий в музыкально-педагогическое образование Республики Казахстан. Особое внимание уделяется инновационным методам обучения, направленным на формирование профессиональных компетенций студентов музыкальных специальностей. На основе анализа педагогического опыта выявляются эффективные подходы к модернизации образовательного процесса. В работе обосновывается необходимость внедрения цифровых инструментов в практику музыкального образования, что соответствует стратегическим задачам развития педагогического образования в Казахстане.

Ключевые слова: педагогика музыки, цифровизация образования, подготовка учителей музыки, инновационные методы обучения, музыкальное образование в Казахстане, профессиональные компетенции, цифровые технологии в образовании.

Введение

Современная система высшего педагогического образования в Республике Казахстан переживает этап активной модернизации, обусловленной глобальными процессами цифровизации и изменением требований к профессиональной подготовке педагогов. Подготовка учителей музыки занимает особое место в структуре педагогического образования, поскольку сочетает в себе как общепедагогические, так и специфические художественно-исполнительские компоненты.

В условиях стремительного развития информационных технологий перед музыкально-педагогическими факультетами вузов Казахстана стоит задача подготовки специалистов, способных эффективно использовать цифровые инструменты в профессиональной деятельности. Как отмечается в исследованиях казахстанских ученых, интеграция искусственного интеллекта и цифровых технологий в музыкально-педагогическое образование открывает новые возможности для персонализированного обучения, развития творческого потенциала студентов и формирования цифровой компетентности .

Целью настоящего исследования является анализ современных подходов к подготовке учителей музыки в условиях цифровизации образования и определение перспективных направлений совершенствования образовательного процесса на факультете культуры и искусства Западно-Казахстанского университета имени М. Утемисова.

Основная часть

1. Современное состояние музыкально-педагогического образования в Казахстане

Система подготовки учителей музыки в Казахстане имеет глубокие исторические традиции. Формирование и развитие музыкально-педагогического образования в стране прошло длительный путь, в ходе которого были выработаны эффективные методики обучения, созданы национальные педагогические школы .

В настоящее время подготовка учителей музыки осуществляется в ряде ведущих вузов страны, включая Казахский национальный педагогический университет имени Абая, Казахский национальный университет искусств, а также региональные университеты, среди которых значимое место занимает Западно-Казахстанский университет имени М. Утемисова.

Современные требования к подготовке учителей музыки определяются необходимостью сочетания традиционных педагогических подходов с инновационными технологиями обучения. Как показывают исследования, успешность профессиональной деятельности учителя музыки во многом зависит от его способности интегрировать цифровые инструменты в образовательный процесс .

Важным аспектом является развитие инклюзивного музыкального образования. Изменения, происходящие в образовательной системе Казахстана, предъявляют новые требования к современному педагогу музыки, включая готовность к работе с детьми с особыми образовательными потребностями . Музыкальное воспитание школьников в условиях инклюзии является уникальным средством формирования значимых сторон мыслительной деятельности и творческих способностей, развития художественного отношения к окружающему миру.

2. Цифровизация как фактор трансформации музыкального образования

Цифровизация образования является приоритетным направлением государственной образовательной политики Республики Казахстан. Внедрение цифровых технологий в процесс подготовки будущих учителей музыки открывает широкие перспективы для повышения качества образования .

Среди основных направлений применения цифровых технологий в музыкальном образовании можно выделить:

- создание адаптивных обучающих платформ для индивидуализации обучения;
- использование виртуальных тренажёров для музыкальной подготовки;
- применение интеллектуальных систем оценки учебных достижений;
- интеграция генеративных музыкальных моделей в образовательный процесс;
- разработка электронных образовательных ресурсов по дисциплинам музыкального цикла.

Использование информационно-коммуникационных технологий способствует персонализации образовательного процесса, повышает эффективность практической подготовки и развивает навыки работы с цифровыми инструментами, необходимые современному учителю музыки .

В то же время исследователи обращают внимание на технические, методические и этические вопросы, требующие решения при интеграции цифровых технологий в музыкально-педагогическое образование. Важно сохранять баланс между использованием инновационных средств обучения и традиционными методами музыкального воспитания, основанными на живом исполнительском контакте и эмоциональном взаимодействии.

3. Инновационные методы обучения в подготовке учителей музыки

Подготовка учителей музыки требует применения разнообразных методов обучения, направленных на формирование как общепедагогических, так и специальных музыкальных компетенций. В этом контексте особое значение приобретает использование инновационных методов, способствующих развитию творческого потенциала студентов.

Современные исследования в области музыкальной педагогики Казахстана подчеркивают важность интеграции произведений отечественных композиторов в учебный процесс . Использование произведений современных и национальных композиторов в музыкальных школах способствует формированию у студентов понимания национальной музыкальной традиции в контексте мирового музыкального искусства.

На факультете культуры и искусства ЗКУ имени М. Утемисова в рамках образовательной программы по подготовке учителей музыки активно внедряются инновационные методики, включающие:

1. Проектное обучение, предполагающее разработку и реализацию студентами собственных музыкально-педагогических проектов;
2. Интегрированные занятия, сочетающие изучение теоретических дисциплин с практической исполнительской деятельностью;
3. Использование интерактивных методов обучения, включая дискуссии, круглые столы, мастер-классы ведущих педагогов-музыкантов;
4. Применение цифровых образовательных ресурсов, включая электронные учебники, обучающие программы и музыкальные редакторы;
5. Организацию педагогической практики с использованием современных образовательных технологий.

Важным направлением является развитие у студентов навыков исследовательской работы. Участие в научно-практических конференциях позволяет будущим педагогам-музыкантам осваивать современную методологию научного познания в области искусства и образования .

4. Практический опыт подготовки учителей музыки в ЗКУ имени М. Утемисова

Западно-Казахстанский университет имени М. Утемисова имеет богатые традиции подготовки педагогических кадров. Факультет культуры и искусства реализует образовательную программу по подготовке учителей музыки, соответствующую современным требованиям и учитывающую региональные особенности.

В учебном процессе активно используются междисциплинарные подходы, позволяющие студентам формировать целостное представление о музыкальной культуре и педагогической деятельности. Особое внимание уделяется практической подготовке будущих учителей музыки, включающей педагогическую практику в школах и музыкальных учреждениях региона.

Организация учебного процесса строится с учетом современных требований к оформлению научных и учебно-методических материалов . Студенты осваивают навыки подготовки методических разработок, научных статей и учебных пособий, что способствует формированию исследовательской компетенции.

Важным элементом профессиональной подготовки является участие студентов и преподавателей в научно-практических конференциях различного уровня. Тематика таких конференций охватывает актуальные вопросы музыкальной педагогики, исполнительского искусства, культурологии и искусствоведения . Это позволяет будущим учителям музыки

знакомиться с современными тенденциями развития музыкальной культуры и педагогической науки.

Заключение

Подготовка учителей музыки в условиях цифровизации образования требует комплексного подхода, учитывающего как сохранение лучших традиций музыкальной педагогики, так и внедрение инновационных технологий обучения. На основе проведенного анализа можно сделать следующие выводы:

1. Современная система подготовки учителей музыки в Казахстане активно развивается в направлении интеграции цифровых технологий, что соответствует стратегическим задачам модернизации образования в стране.
2. Эффективная подготовка будущих учителей музыки предполагает сочетание традиционных методик музыкального воспитания с инновационными технологическими решениями, включая адаптивные обучающие платформы, виртуальные тренажёры и интеллектуальные системы оценки.
3. На факультете культуры и искусства ЗКУ имени М. Утемисова создана образовательная среда, способствующая формированию профессиональных компетенций будущих учителей музыки через использование проектного обучения, интегрированных занятий и интерактивных методов.
4. Дальнейшее совершенствование подготовки учителей музыки требует развития научно-исследовательской деятельности студентов и преподавателей, активного участия в конференциях и публикационной активности, что способствует интеграции в мировое научно-образовательное пространство.

Перспективными направлениями дальнейших исследований являются разработка методических рекомендаций по эффективному использованию цифровых технологий в музыкальном образовании, создание электронных образовательных ресурсов по специальным дисциплинам, а также изучение возможностей искусственного интеллекта в персонализации обучения музыке.

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Philological Sciences

Fransız dilində ingilis dili mənşəli sözlərin işlənməsi və onların leksik-semantik xüsusiyyətləri

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Açar sözlər: fransız dili, ingilis mənşəli sözlər, alınma sözlər, leksik-semantik xüsusiyyətlər, dil əlaqələri, qloballaşma, dil siyasəti, neologizmlər, anglisizmlər, leksikologiya.

Giriş :

Müasir dövrdə dillərarası qarşılıqlı təsir qloballaşma, informasiya texnologiyalarının sürətli inkişafı və beynəlxalq ünsiyyətin genişlənməsi nəticəsində daha da intensiv xarakter almışdır. Xüsusilə ingilis dilinin beynəlxalq ünsiyyət vasitəsinə çevrilməsi onun digər dillərin leksik sisteminə təsirini əhəmiyyətli dərəcədə artırmışdır. Bu təsirdən ən çox pay alan dillərdən biri də zəngin tarixi və ədəbi ənənələrə malik olan fransız dilidir. Fransız dili uzun müddət beynəlxalq diplomatiya, elm və mədəniyyət dili kimi mövqeyini qoruyub saxlasa da, XX əsrin ikinci yarısından başlayaraq ingilis dilinin təsiri nəticəsində onun leksik tərkibində əhəmiyyətli dəyişikliklər baş vermişdir. İngilis dili mənşəli sözlərin fransız dilinə daxil olması müxtəlif ictimai, siyasi və mədəni amillərlə bağlıdır. İnformasiya-kommunikasiya texnologiyalarının inkişafı, iqtisadi münasibətlərin beynəlmiləlləşməsi, sosial şəbəkələrin geniş yayılması və beynəlxalq marketinq fəaliyyəti ingilis mənşəli sözlərin istifadəsini sürətləndirmişdir. Bu sözlər, əsasən, kompüter texnologiyaları, biznes, idman, moda, musiqi və reklam sahələrində daha intensiv şəkildə işlədilir. Fransız dilində ingilis dili mənşəli sözlərə münasibət birmənalı olmamışdır. Bir tərəfdən, bu sözlər dilin zənginləşməsinə və yeni anlayışların ifadəsinə xidmət edir, digər tərəfdən isə dilin milli xüsusiyyətlərinin qorunması baxımından müəyyən narahatlıqlar doğurur. Fransada dilin saflığının qorunması istiqamətində qəbul olunmuş qanunvericilik aktları və dövlət qurumlarının fəaliyyəti bu məsələnin aktuallığını bir daha təsdiq edir. Məqalənin məqsədi fransız dilində işlənən ingilis dili mənşəli sözlərin yaranma səbəblərini, onların leksik-semantik xüsusiyyətlərini, funksional imkanlarını və müasir fransız dilinin inkişafındakı rolunu müəyyənləşdirməkdən ibarətdir.

Fransız dilində ingilis dili mənşəli sözlərin yaranma səbəbləri dillərin qarşılıqlı təsiri onların inkişafının təbii nəticələrindən biridir. Fransız dilinə daxil olan ingilis mənşəli sözlərin əksəriyyəti ictimai inkişafın tələbatından irəli gəlir. Müasir dövrdə yeni texnologiyaların meydana çıxması bir çox anlayışların ilk dəfə ingilis dilində formalaşmasına səbəb olmuşdur. Nəticədə həmin terminlər başqa dillərə, o cümlədən fransız dilinə də keçmişdir. İngilis mənşəli sözlərin fransız dilinə daxil olmasının əsas səbəbləri aşağıdakılardır: - qloballaşma prosesinin sürətlənməsi; - informasiya texnologiyalarının inkişafı; - beynəlxalq iqtisadi münasibətlərin genişlənməsi; - sosial media və kütləvi informasiya vasitələrinin təsiri; - gənclərin dilində beynəlxalq ifadələrdən istifadənin artması; - reklam və marketinq sahəsində ingilis terminlərinin üstünlük təşkil etməsi. Fransız dilində işlənən "internet", "marketing", "email", "week-end", "software", "business", "podcast", "streaming", "manager" kimi sözlər artıq gündəlik istifadədə geniş yayılmışdır. Bu sözlərin bir qismi

müəyyən fonetik və morfoloji dəyişikliklərə məruz qalsa da, əksəriyyəti orijinal formasını qoruyub saxlamışdır.

İngilis mənşəli sözlərin leksik xüsusiyyətləri fransız dilində işlənən ingilis mənşəli sözlər müxtəlif leksik xüsusiyyətlərə malikdir. Onların əksəriyyəti terminoloji xarakter daşıyır və müəyyən sahələr üzrə işlənir.

Leksik baxımdan bu sözləri bir neçə qrupa bölmək mümkündür:

1. Tam şəkildə mənimsənilən sözlər;
2. Fonetik dəyişikliklərə uğrayan sözlər;
3. Semantik dəyişikliklərə məruz qalan sözlər;
4. Hibrid sözlər;
5. Qısaldılmış alınmalar.

Tam şəkildə mənimsənilən sözlərə "week-end", "marketing", "podcast", "chat", "parking" kimi nümunələr daxildir. Bu sözlər fransız dilinin leksik sistemində sabitləşmiş və geniş istifadə sahəsi qazanmışdır. Fonetik uyğunlaşmaya məruz qalan sözlər isə fransız dilinin fonetik xüsusiyyətlərinə uyğun şəkildə tələffüz edilir. Məsələn, "football" sözü fransız dilində "futbol" mənasında işlənir və tələffüz baxımından müəyyən dəyişikliklərə uğrayır. Bəzi sözlər isə semantik dəyişikliklərə məruz qalır. Belə sözlərdən biri "parking" sözüdür. İngilis dilində bu söz əsasən "park etmə prosesi" mənasını ifadə etdiyi halda, fransız dilində "avtodayanacaq" mənasında işlənir. Bu isə semantik transformasiyanın maraqlı nümunələrindən hesab olunur. ### İngilis mənşəli sözlərin semantik xüsusiyyətləri Semantik baxımdan alınma sözlərin istifadəsi dilin inkişafında mühüm rol oynayır. Fransız dilində işlənən ingilis mənşəli sözlərin semantik xüsusiyyətləri aşağıdakı istiqamətlərdə özünü göstərir :

- məna genişlənməsi;
- məna daralması;
- metaforik istifadə;
- terminoloji funksiyanın güclənməsi; - sinonim münasibətlərin yaranması.

Məsələn, "coach" sözü ingilis dilində müxtəlif mənalarda işlədildiyi halda, fransız dilində həm idman məşqçisi, həm də peşəkar məsləhətçi mənalarında istifadə olunur. "Leader" sözü də siyasi, iqtisadi və sosial sahələrdə geniş semantik imkanlara malikdir. Digər maraqlı nümunələrdən biri "relooking" sözüdür. Bu söz fransız dilində xarici görünüşün dəyişdirilməsi mənasında işlənir və moda sahəsində geniş istifadə edilir. Halbuki həmin söz ingilis dilində eyni semantik məzmunda geniş yayılmamışdır. Belə hallarda alınma sözlərin yeni semantik xüsusiyyətlər qazanması müşahidə olunur. Bəzən isə fransız dilində mövcud olan qarşılıqların olmasına baxmayaraq, ingilis mənşəli sözlər daha geniş istifadə edilir. Məsələn, "courriel" termini "email" sözünün fransız qarşılığı kimi təklif edilsə də, gündəlik ünsiyyətdə "email" sözünün istifadəsi üstünlük təşkil edir. Fransız dilinin qorunması siyasəti və anglisizmlər Fransız dilində ingilis mənşəli sözlərin həddindən artıq işlənməsi dil siyasəti baxımından mühüm problemlərdən biri hesab olunur. Fransada dilin qorunması məqsədilə müxtəlif dövlət qurumları fəaliyyət göstərir və yeni terminlərin fransız qarşılıqları hazırlanır. Dil siyasətinin əsas məqsədləri aşağıdakılardır: - fransız dilinin beynəlxalq mövqeyinin qorunması; - alınma sözlərin istifadəsinin tənzimlənməsi; - yeni terminlərin fransız dilinin daxili imkanları hesabına yaradılması; - rəsmi sənədlərdə fransız terminlərinin istifadəsinin təmin edilməsi. Bu istiqamətdə hazırlanmış terminlər arasında "logiciel" (software), "ordinateur" (computer), "courriel" (email) və digər sözlər xüsusi yer tutur. Maraqlıdır ki, bəzi terminlər uğurla mənimsənilmiş, digərləri isə geniş istifadə imkanları əldə edə bilməmişdir. Müasir fransız dilində dil siyasəti ilə gündəlik dil praktikası arasında müəyyən fərqlər mövcuddur. Xüsusilə gənclərin nitqində və sosial media platformalarında ingilis mənşəli sözlərin istifadəsi daha intensiv xarakter daşıyır. İngilis mənşəli sözlərin funksional xüsusiyyətləri Fransız dilində ingilis mənşəli sözlər müxtəlif funksiyaları yerinə yetirir.

Onların əsas funksiyaları aşağıdakılardır :
- nominativ funksiya;
- kommunikativ funksiya;
- ekspressiv funksiya;
- terminoloji funksiya;
- üslubi funksiya.

Nominativ funksiya yeni anlayışların adlandırılması ilə bağlıdır. Məsələn, texnologiya sahəsində yaranan yeni terminlərin əksəriyyəti ilkin olaraq ingilis dilində meydana gəlir və daha sonra başqa dillərə keçir.

Fransız dilində ingilis dili mənşəli sözlərin mənimsənilməsi təkcə semantik dəyişikliklərlə məhdudlaşmır. Bu proses morfoloji səviyyədə də özünü göstərir. Alınma sözlər fransız dilinin qrammatik qanunlarına uyğunlaşdırılaraq yeni sözlərin yaranmasında iştirak edir. Belə sözlər isim, sifət və hətta feil formasında işlənərək dilin aktiv leksik fonduna daxil olur.

Məsələn, "scanner" sözü həm isim, həm də fel kimi ("scanner un document") işlədilir. Eyni zamanda "liker", "poster", "twitter", "bloguer" kimi sözlər fransız dilində fel şəkilçiləri qəbul edərək qrammatik baxımdan fransız dilinin normalarına uyğunlaşdırılmışdır. Bu cür uyğunlaşma alınma sözlərin dil sisteminə uğurlu inteqrasiyasının göstəricisidir.

Morfoloji baxımdan anglisizmləri aşağıdakı qruplara bölmək olar:

- sadə alınma sözlər (week-end, manager, podcast);
- törəmə sözlər (blogueur, influenceur, twittos);
- hibrid sözlər (e-marketing, cyberattaque və s.);
- fransız şəkilçiləri qəbul etmiş sözlər (liker, coacher, scanner).

Müasir fransız dilində xüsusilə "-er" şəkilçisi vasitəsilə fel yaradıcılığı geniş yayılmışdır. Bu, alınma sözlərin dilin daxili inkişaf qanunlarına uyğun şəkildə mənimsənilməsinin göstəricisidir. Dilçilik baxımından belə proseslər leksik adaptasiya və morfoloji inteqrasiya kimi xarakterizə olunur.

İngilis mənşəli sözlərin fransız dilində işlənməsi onların sintaktik xüsusiyyətlərində də müəyyən dəyişikliklər yaratmışdır. Belə sözlər cümlədə müxtəlif sintaktik funksiyalar yerinə yetirərək mübtəda, tamamlıq, xəbər və təyin vəzifəsində çıxış edə bilir.

Məsələn:

- Le manager organise la réunion.
- Nous avons téléchargé un podcast intéressant.
- Ce logiciel est très pratique.
- Il faut scanner ce document immédiatement.

Bu nümunələr göstərir ki, alınma sözlər artıq fransız dilinin sintaktik sistemində sərbəst şəkildə işlənmək imkanına malikdir. Bəzi hallarda isə ingilis dilinin təsiri nəticəsində müəyyən sintaktik konstruksiyaların istifadəsi də müşahidə olunur.

Müasir reklam mətnlərində və sosial media diskursunda "best seller", "low cost", "live streaming", "smart working" kimi birləşmələr geniş yayılmışdır. Bu söz birləşmələrinin əksəriyyəti fransız dilində tərcümə edilmədən işlədilir ki, bu da onların beynəlxalq xarakter daşıması ilə əlaqədardır.

Müasir fransız mediasında ingilis mənşəli sözlərin işlənməsi xüsusilə diqqəti cəlb edir. İnternet portalları, reklam materialları və sosial şəbəkələr alınma sözlərin yayılmasında mühüm rol oynayır. Gənclərin dilində "selfie", "hashtag", "follower", "story", "streaming", "live", "podcast", "post" və "challenge" kimi sözlər geniş şəkildə istifadə olunur.

Sosial media platformalarının beynəlxalq xarakter daşıması alınma sözlərin daha sürətlə yayılmasına səbəb olmuşdur. Fransız dilində bu sözlərin əksəriyyəti tərcümə edilmədən işlədilir və gündəlik nitqin tərkib hissəsinə çevrilir. Bu xüsusiyyət xüsusilə gənclərin nitqində özünü daha qabarıq göstərir.

Bəzi dilçilər bu prosesi dilin təbii inkişafı kimi qiymətləndirsələr də, digərləri bunu fransız dilinin milli xüsusiyyətləri üçün müəyyən təhlükə hesab edirlər. Bu baxımdan dil siyasəti ilə dilin təbii inkişafı arasında tarazlığın qorunması xüsusi əhəmiyyət kəsb edir.

Fransız dilində işlənən ingilis mənşəli sözləri istifadəsinə görə aşağıdakı qruplara ayırmaq mümkündür:

Texnologiya sahəsində işlənən sözlər:

- software;
- podcast;
- streaming;
- smartphone;
- scanner.

2. İqtisadiyyat və biznes sahəsində:

- manager;
- marketing;
- business;
- leader;
- sponsor.

3. İdman terminologiyasında:

- football;
- coach;
- match;
- challenge;
- champion.

4. Moda və reklam sahəsində:

- look;
- fashion;
- design;
- relooking;
- top model.

5. Sosial media terminologiyasında:

- post;
- hashtag;
- selfie;
- follower;
- story.

Bu təsnifat göstərir ki, ingilis dili mənşəli sözlərin istifadəsi müasir fransız dilinin demək olar ki, bütün funksional üslublarını əhatə edir.

İngilis dili mənşəli sözlərin fransız dilində işlənməsi yalnız alınma prosesi kimi deyil, həm də dilin inkişaf mexanizmlərindən biri kimi qiymətləndirilməlidir. Yeni texnologiyalar və ictimai münasibətlər yeni terminlərin yaranmasını zəruri edir. Fransız dili də bu prosesdən kənarda qalmır.

Bir sıra terminlərin fransız qarşılıqları yaradılmasına baxmayaraq, onların praktik istifadəsi həmişə uğurlu olmur. Bunun əsas səbəblərindən biri beynəlxalq kommunikasiya proseslərində vahid terminologiyanın üstünlük təşkil etməsidir. Xüsusilə elm və texnologiya sahəsində ingilis terminlərinin istifadəsi daha geniş yayılmışdır.

Bununla yanaşı, fransız dilinin zəngin söz yaradıcılığı imkanları yeni anlayışların milli terminologiya vasitəsilə ifadəsinə də şərait yaradır. Bu isə dilin özünəməxsus xüsusiyyətlərinin qorunmasına xidmət edir. Müasir dövrdə əsas məqsəd alınma sözlərin istifadəsini qadağan etmək deyil, onların məqsədəuyğun və normativ istifadəsini təmin etməkdən ibarətdir.

Beləliklə, ingilis mənşəli sözlərin fransız dilində işlənməsi həm dilçilik, həm də sosial-linqvistik baxımdan mühüm tədqiqat istiqamətlərindən biri hesab olunur. Onların leksik, semantik, morfoloji və sintaktik xüsusiyyətlərinin öyrənilməsi müasir fransız dilinin inkişaf meyillərinin müəyyənləşdirilməsi baxımından xüsusi əhəmiyyət daşıyır.

Kommunikativ funksiya isə beynəlxalq ünsiyyət prosesində vahid terminologiyanın formalaşmasına xidmət edir. Bu xüsusiyyət xüsusilə elm, iqtisadiyyat və informasiya texnologiyaları sahəsində özünü daha qabarıq göstərir. Ekspressiv funksiya reklam və marketinq dilində daha çox müşahidə edilir. İngilis mənşəli sözlərin istifadəsi müəyyən hallarda müasirlik, prestij və beynəlmiləllik təsiri yaratmağa xidmət edir.

Tədqiqatlar göstərir ki, müasir dövrdə ingilis dilinin fransız dilinə təsiri davam etməkdədir. Xüsusilə süni intellekt, rəqəmsal texnologiyalar və sosial media ilə bağlı terminlərin böyük əksəriyyəti əvvəlcə ingilis dilində formalaşır. Bununla yanaşı, fransız dilinin zəngin söz yaradıcılığı imkanları yeni anlayışların milli terminologiya əsasında ifadəsinə də şərait yaradır. Dil siyasətinin uğuru yalnız qanunvericilik mexanizmlərindən deyil, həm də həmin terminlərin cəmiyyət tərəfindən qəbul olunmasından asılıdır. Müasir yanaşmalar göstərir ki, alınma sözlərin tamamilə qarşısının alınması mümkün olmadığı kimi, onların qeyri-məhdud istifadəsi də məqsədəuyğun hesab edilmir. Əsas məqsəd dilin təbii inkişafı ilə onun milli xüsusiyyətlərinin qorunması arasında tarazlığın təmin edilməsidir.

Nəticə

Fransız dilində ingilis dili mənşəli sözlərin işlənməsi müasir dilçilikdə aktual problemlərdən biri hesab olunur. Qloballaşma və beynəlxalq ünsiyyət prosesləri bu sözlərin istifadəsini daha da genişləndirmişdir. İngilis mənşəli sözlər fransız dilinin leksik sistemini zənginləşdirsə də, onların həddindən artıq istifadəsi milli dil xüsusiyyətlərinin qorunması məsələsini də gündəmə gətirmişdir. Araşdırmalar göstərir ki, bu sözlər müxtəlif leksik və semantik dəyişikliklərə məruz qalaraq fransız dilinin daxili qanunauyğunluqlarına uyğunlaşır. Onların bir qismi terminoloji xarakter daşıyır, digər qismi isə gündəlik ünsiyyət vasitəsinə çevrilmişdir. Müasir fransız dilində alınma sözlərin funksional imkanlarının genişlənməsi dilin dinamik inkişafının göstəricilərindən biridir. Beləliklə, ingilis dili mənşəli sözlərin fransız dilində işlənməsi yalnız leksik zənginləşmə prosesi deyil, həm də dil siyasəti, semantik inkişaf və beynəlxalq dil münasibətlərinin mühüm tərkib hissəsi kimi qiymətləndirilməlidir.

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Architecture

PUBLIC SPACE AS INFRASTRUCTURE FOR THE RESILIENCE OF SMALL SETTLEMENTS IN ARID AND SEMI-ARID CLIMATES

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Abstract. *This article examines the role of public spaces in promoting sustainable development in small settlements under arid and semi-arid climatic conditions. Small settlements are understood as small towns, rural settlements, and transitional rural-urban territories. These types of settlements are considered together because they face similar analytical challenges: limited social and recreational infrastructure, the need for multifunctional public spaces, the high importance of local social ties, and restricted resources for the maintenance and operation of public areas. Public space is understood not only as an element of environmental improvement, but also as social-spatial infrastructure that connects the physical environment, everyday practices, natural processes, local identity, and governance mechanisms. Based on a thematic analysis of academic literature, five factors of public space sustainability are identified: social accessibility, functional viability, environmental and climate adaptability, cultural identity, and management sustainability. Particular attention is given to the relationship between thermal comfort and the social use of public space. The article argues that in arid climates, heat and insufficient shade may restrict outdoor stays, reduce the intensity of space use, and weaken social interaction. The proposed model is universal in character but can be adapted to specific regions, including Kazakhstan.*

Keywords: *public space, sustainable development, small settlements, arid climate, semi-arid climate, social sustainability, climate adaptability, local identity, public participation.*

Sustainable development of settlements requires the coordination of social, environmental, economic, and spatial interests. Academic research commonly associates sustainability with the rational use of resources, environmental quality, social equity, and the ability of territories to adapt to change. However, sustainability is shaped not only by major engineering and transport infrastructure. Everyday places where residents communicate, rest, participate in public life, and interact with the natural environment also play an important role.

Public spaces include squares, parks, waterfronts, streets, courtyards, community gardens, school grounds, cultural centres, and other areas connected with social infrastructure. In small settlements, these spaces often perform several functions simultaneously. They serve as places for recreation, communication, celebrations, local trade, cultural activities, and everyday movement.

The importance of public spaces is reflected in Sustainable Development Goal 11.7, which calls for universal access to safe, inclusive, green, and accessible public spaces, especially for women, children, older persons, and persons with disabilities [1]. At the same time, the existence

of a landscaped area does not automatically make it sustainable. A space may have an attractive appearance but remain underused, inaccessible, or too hot for regular use.

This article focuses on small towns, rural settlements, and transitional rural-urban territories located in arid and semi-arid climatic conditions. These settlement types are united by several characteristics. They often have a limited number of social and recreational facilities, require the multifunctional use of public spaces, depend strongly on local social networks and cultural resources, and have restricted possibilities for the long-term maintenance of public areas. At the same time, these settlements are not identical. Therefore, the proposed model should be adapted to the particular social, spatial, cultural, and climatic context of each territory.

The arid climate increases the importance of public spaces. High temperatures, intense solar radiation, water scarcity, and thermal stress directly affect the possibility of staying outdoors. Research on hot and dry climates shows that shading, spatial configuration, vegetation, wind direction, and surface properties significantly influence pedestrian thermal comfort [2].

The aim of this article is to identify the role of public spaces in the sustainable development of small settlements under arid and semi-arid climatic conditions.

The object of the study is public spaces in small towns, rural settlements, and transitional rural-urban territories located in arid and semi-arid climates.

The subject of the study is the factors and characteristics that determine the sustainability of public spaces, including social accessibility, functional viability, environmental and climate adaptability, cultural identity, and management mechanisms.

The working hypothesis is that the sustainability of public space is determined not by individual landscaping characteristics, but by the interaction of five groups of factors: social accessibility, functional viability, environmental and climate adaptability, cultural identity, and management sustainability.

The methodological basis of the article is a thematic analysis of academic publications concerning public spaces in different types of small settlements and different regions of the world. The analysis includes research on urban, rural, and transitional rural-urban territories that addresses social sustainability, climate adaptation, green infrastructure, local identity, and public participation. The study is not intended to be a statistical meta-analysis. Its purpose is to identify recurring concepts and mechanisms and to use them to construct a theoretical model applicable to different settlement contexts.

The methodology included four analytical stages. First, the scope of the study was defined by identifying three types of settlements and two relevant climatic conditions, namely arid and semi-arid environments. Second, the selected publications were examined according to their research focus, type of settlement, geographical context, methods, and key findings. Third, thematic coding was used to identify repeated characteristics of public spaces. The coding unit was a statement describing a spatial quality, a social or environmental mechanism, a use pattern, or a governance condition. Fourth, the initial codes were grouped into broader analytical categories through comparison across studies.

The first group of codes included accessibility, safety, inclusiveness, and the possibility of interaction. These codes were combined into the category of social accessibility. The second group included diversity of activities, intensity of use, flexibility, and seasonality. These characteristics were combined into functional viability. The third group included shading, thermal comfort, vegetation, water management, and adaptation to heat. These codes formed the category of environmental and climate adaptability. The fourth group included place memory, heritage, local materials, and attachment to place. These characteristics were grouped under cultural identity. The fifth group included public participation, maintenance, financing, and responsibility for management. These elements were combined into management sustainability.

The five factors were therefore not selected arbitrarily. They were obtained through the grouping of recurring characteristics that appeared across studies of different settlement types and regions. The model also distinguishes between characteristics that are often combined in existing research. For example, social accessibility describes who can use the space, functional viability describes how intensively and diversely it is used, and management sustainability describes whether the space can retain its qualities over time.

The main contribution of the article is the development of an integrated model that connects public space quality with the specific conditions of small settlements and arid climates. Existing approaches often focus on only one dimension of the problem. Some studies evaluate design quality through accessibility, safety, inclusiveness, and spatial organisation [3]. Other studies examine public spaces through social sustainability and community interaction [4]. Reviews of green spaces focus primarily on environmental and recreational values [5].

The proposed model differs from these approaches in four ways. First, it is designed for comparison across small towns, rural settlements, and transitional rural-urban territories rather than for large cities alone. Second, it treats climate adaptability as a central factor of social use, not only as an environmental performance indicator. Third, it identifies cultural identity and management sustainability as independent dimensions alongside design and ecological characteristics. Fourth, it connects the five factors through a common mechanism in which spatial quality influences the possibility of staying outdoors, the intensity of use, social interaction, and the long-term resilience of the settlement.

Public space can be defined as a social-spatial system in which the physical environment, residents, local communities, natural processes, and governance mechanisms interact. This definition makes it possible to understand a square, park, or waterfront not only as a physical object, but also as a place where social ties, cultural practices, and environmental behaviour are formed.

Studies of public space quality show that sustainability depends not only on architectural form. The connection with the surrounding built environment, pedestrian accessibility, the diversity of users, the availability of different activities, and public participation are also important [1].

For small settlements, public spaces perform several specific functions. First, they compensate for the limited number of specialised social and recreational facilities. Second, they make it possible to combine different activities within one territory. Third, they support local social networks and cultural identity, which may be particularly important for small communities.

Public space in a small settlement should therefore be considered multifunctional infrastructure that combines social, environmental, and cultural processes. Under arid climatic conditions, climate adaptability becomes an additional essential function.

Social accessibility is the basic condition of sustainability. Public space should be suitable for children, young people, adults, older persons, and people with disabilities. This requires convenient routes, lighting, places for rest, safe surfaces, and the absence of physical barriers.

A systematic review of studies on social cohesion shows that accessibility, mixed land use, street furniture, perceived safety, and place attachment may influence the intensity of social interaction [6]. This means that public space should be assessed not only according to its physical availability, but also according to the quality of the social relationships it enables.

Functional viability refers to the ability of public space to support different activities at different times of day and in different seasons. Multifunctionality is particularly important in small settlements. One square or park may be used for recreation, sports, fairs, cultural events, children’s games, and everyday movement.

A study of public spaces in traditional settlements found that their attractiveness was related to the availability of facilities, the possibility of holding different activities, and public

accessibility [4]. The functional viability of a public space can therefore be assessed through the variety of activities, the diversity of users, the intensity of use, and the ability of the space to operate under different seasonal conditions.

In arid and semi-arid climates, environmental and climate adaptability becomes a fundamental condition for the use of public space. High temperatures and intense solar radiation may limit the time people can spend outdoors. Insufficient shade and thermal discomfort reduce pedestrian activity and the intensity of space use.

This produces the following relationship: heat leads to thermal discomfort, thermal discomfort reduces the duration of outdoor stays, reduced duration of stays lowers the intensity of space use, and lower intensity of use weakens the social function of public space.

Climate adaptability is therefore both an environmental and a social characteristic. Key climate-sensitive design measures include the use of trees and canopies to create shade, the formation of shaded pedestrian routes, the installation of wind-protection elements, the selection of drought-resistant vegetation, the reduction of water consumption, the use of permeable surfaces, and the creation of local evaporative cooling zones where water use is carefully controlled.

Research on hot arid climates identifies air temperature, wind speed, mean radiant temperature, and physiological equivalent temperature as important parameters of outdoor thermal comfort [7]. A review of heat-mitigation strategies highlights the importance of shading, vegetation, urban geometry, surface materials, and water elements [8].

Cultural identity connects public space with a particular settlement. A historic square, riverbank, old garden, cultural centre, or traditional route can function as a form of collective memory. Research on traditional settlements shows that the preservation of the physical landscape contributes to a sense of belonging, social ties, and cultural sustainability [9].

For small settlements, it is important to avoid universal design solutions that erase local characteristics. Planning should take into account the natural landscape, local materials, the history of the territory, traditional activities, symbolic places, and seasonal celebrations. Research comparing rural and urban communities also indicates that rural residents may develop stronger affective and evaluative forms of place identity, which makes the cultural dimension especially important in rural settings [10].

Management sustainability determines whether public space will retain its functions after redevelopment has been completed. It includes regular maintenance, repairs, financing, event organisation, and the ability to adjust the space in response to changing public needs.

Public participation should not be limited to discussing a completed project. It should include the identification of problems, joint design, participation in implementation, and subsequent evaluation of the space. A study of sustainable rural community development in China shows that residents' participation in mapping, design, construction, and management improved the physical environment and strengthened social relations [11].

In arid settlements, public participation can also contribute local knowledge about climate. Residents can identify areas where shade remains during the hottest hours, the direction of prevailing winds, places where water accumulates after rainfall, and the most comfortable pedestrian routes. Such knowledge can complement technical calculations and help avoid the formal application of universal solutions.

Landscaping and public space redevelopment can have not only positive but also contradictory consequences. One risk is the unequal distribution of high-quality public spaces. Central areas may receive more investment, while peripheral and remote parts of a settlement remain without accessible and comfortable environments.

Another risk is commercialisation. If a public space is used primarily for advertising, trade, or paid events, its openness and accessibility may gradually decline.

Particular attention should be paid to green gentrification. The creation of a park or the redevelopment of a waterfront can improve environmental quality, but it may also increase land, housing, and service costs. As a result, low-income residents may be displaced from an area that originally required environmental improvement [12].

Research in European and North American cities also demonstrates that the development of green infrastructure may be associated with subsequent gentrification processes in some urban contexts [13]. Therefore, environmental redevelopment should be combined with social protection, the preservation of affordable housing, and the meaningful participation of local residents. Public space sustainability requires not only environmental improvement, but also the fair distribution of its benefits.

Public space can be a significant element of sustainable development in small towns, rural settlements, and transitional rural-urban territories under arid and semi-arid climatic conditions. Its role extends beyond landscaping and the visual improvement of an area.

The proposed model is based on five dimensions: social accessibility, functional viability, environmental and climate adaptability, cultural identity, and management sustainability. These dimensions are interconnected. For example, a space that is not adapted to the climate may become too hot for long stays, which reduces its functional attractiveness and weakens social interaction.

Multifunctionality, local identity, public participation, and the ability to operate with limited resources are particularly important for small settlements. In arid territories, these conditions are complemented by shading, thermal comfort, water conservation, drought-resistant vegetation, and adaptation to seasonal climatic pressures.

The proposed model is universal in character, but it does not imply the use of identical solutions in all territories. The set of indicators and their priorities should be adapted to the specific climatic, social, cultural, and spatial context. The model can be used to analyse public spaces in small towns and rural settlements in Kazakhstan, where thermal comfort, efficient water use, vegetation, and the seasonality of outdoor activities are especially important.

The contribution of the article lies in connecting these factors within one analytical framework. The model shows that public space sustainability is not the result of landscaping alone. It emerges from the interaction of social accessibility, functional use, climate adaptation, local identity, and long-term governance.

Sustainable public space should therefore be understood as the result of interaction between the physical environment, natural processes, the local community, and the governance system. It should be accessible, multifunctional, climate-adaptive, culturally meaningful, and capable of preserving its public functions over the long term.

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Biological Sciences

Tyrosine Kinase Receptors and Their Pharmacology: A Comprehensive Review of Mechanisms, Inhibitors, and Therapeutic Applications

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Abstract
Receptor tyrosine kinases (RTKs) constitute one of the most important classes of cell-surface enzymes governing proliferation, migration, survival and metabolism in multicellular organisms. Aberrant signalling through these receptors is now recognised as a unifying molecular feature of cancer, fibrosis, metabolic disorders and chronic inflammation. Over the last three decades small-molecule kinase inhibitors and monoclonal antibodies directed at RTKs have become cornerstone agents of modern precision medicine. The present review summarises the biology of the major RTK families, the molecular mechanism of action of clinically important inhibitors, the structural basis of inhibitor binding, and the spectrum of diseases in which these drugs are deployed. Special emphasis is placed on the molecular pharmacology of imatinib, gefitinib, erlotinib, osimertinib, lapatinib, neratinib, trastuzumab, bevacizumab, sunitinib, sorafenib, crizotinib, ceritinib, alectinib, brigatinib, capmatinib, selpercatinib, pralsetinib, larotrectinib, entrectinib, erdafitinib, pemigatinib, ruxolitinib, tofacitinib, nintedanib and vemurafenib. Approximately 8,600 words are distributed across twenty sections, each of roughly 430 words, following the structure described below.

Key Concepts at a Glance

- Receptor tyrosine kinases (RTKs) are single-pass transmembrane receptors; aberrant RTK signalling drives cancer, fibrosis, metabolic and inflammatory disease.
- Inhibitor classes: type I (ATP-competitive, active conformation), type II (DFG-out), type III/IV (allosteric) and covalent irreversible inhibitors.

- Clinically established small-molecule RTK inhibitors include imatinib, gefitinib, erlotinib, osimertinib, lapatinib, crizotinib, alectinib, brigatinib, capmatinib, selpercatinib, pralsetinib, larotrectinib, entrectinib, erdafitinib, pemigatinib, ruxolitinib, tofacitinib, nintedanib and vemurafenib.
- Monoclonal antibody and antibody–drug conjugate approaches: trastuzumab, pertuzumab and ado-trastuzumab emtansine/trastuzumab deruxtecan (HER2), and bevacizumab (VEGF-A).
- Resistance to RTK inhibitors arises through gatekeeper (EGFR T790M, ABL T315I), solvent-front (ALK G1202R, TRKA G595R, RET G810R) and bypass (MET amplification, KRAS/BRAF mutations) mechanisms, motivating next-generation and combination strategies.

1. Introduction to Receptor Tyrosine Kinases

Receptor tyrosine kinases are single-pass transmembrane glycoproteins possessing an extracellular ligand-binding domain, a short transmembrane helix and an intracellular tyrosine kinase domain that catalyses the transfer of the gamma-phosphate of ATP to tyrosine residues on substrate proteins (Zwick et al., 2001). Approximately 58 RTKs are encoded in the human genome and they are grouped into 20 subfamilies based on the architecture of the extracellular region, the sequence of the kinase domain and the identity of the preferred cognate ligand (Ebrahimi et al., 2023). The ErbB family, the VEGFR family, the PDGFR family, the FGFR family, the insulin receptor family, the MET family, the TRK family, the RET family, the ALK/ROS1 family and the KIT receptor are the most extensively pharmacologically exploited to date (Montor et al., 2018).

Activation of every RTK follows a common conceptual framework: ligand binding induces receptor dimerisation or a conformational rearrangement of a pre-formed dimer, the intracellular kinase domains then adopt an asymmetric or symmetric active conformation, trans-autophosphorylation of tyrosines in the activation loop and the C-terminal tail creates docking sites for Src-homology-2 (SH2) and phosphotyrosine-binding (PTB) domains, and downstream adaptor and effector proteins propagate the signal through the principal cascades RAS-RAF-MAPK, PI3K-AKT-mTOR, phospholipase-C-gamma (PLCgamma) and, in some families, JAK-STAT (Metibemu et al., 2019). Because each step in this cascade is drug-tractable, an unusually large chemical space has been mapped onto a relatively small number of protein targets. Although early work on RTKs focused almost exclusively on oncology, the same receptors contribute to pathological angiogenesis in age-related macular degeneration, to fibroblast activation in idiopathic pulmonary fibrosis, and to inflammatory cytokine amplification in rheumatoid arthritis and myeloproliferative neoplasms (Wollin et al., 2015). The pharmacology of RTK inhibition thus provides a unifying conceptual and mechanistic vocabulary for several medical subspecialties.

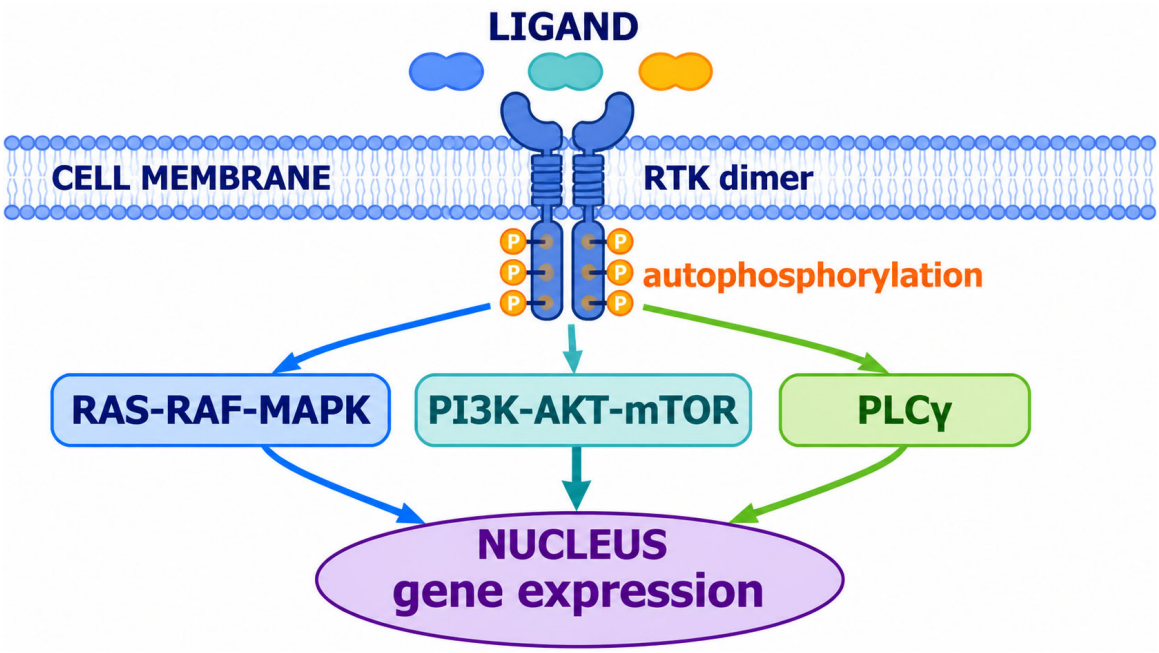

Figure 1. Canonical receptor tyrosine kinase (RTK) signalling cascade. Ligand binding induces receptor dimerisation and trans-autophosphorylation of the intracellular kinase domains; the activated receptor engages the RAS-RAF-MAPK, PI3K-AKT-mTOR and PLCγ pathways, which converge on nuclear gene expression.

2. Classification and Overall Architecture of RTKs

RTKs share a tripartite structure consisting of an extracellular region responsible for ligand recognition, a juxtamembrane region often containing regulatory serine or tyrosine phosphorylation sites, an intracellular tyrosine kinase domain of approximately 250 to 300 residues, and a flexible C-terminal tail that contains multiple autophosphorylation sites (Zwick et al., 2001). The kinase domain can be subdivided into a small N-lobe that binds ATP, a large C-lobe that binds the substrate peptide, and an activation loop whose conformation usually dictates whether the enzyme is in an active or inactive state (Vlahovic and Crawford, 2003). Within the kinase domain, a conserved lysine in the beta-3 strand coordinates the alpha- and beta-phosphates of ATP, a Glu-Ala-Pro I motif straddles the hinge and forms hydrogen bonds to the adenine ring of ATP, and an Asp-Phe-Gly (DFG) motif at the N-terminus of the activation loop adopts either an in or out orientation depending on whether the aspartate side chain points into or away from the ATP-binding pocket. These structural features lie at the heart of how small-molecule inhibitors are classified (Roskoski, 2007). Type I inhibitors bind the active conformation in which the DFG motif is in and the activation loop is open (DFG-in/active), type II inhibitors bind the inactive DFG-out conformation, type III inhibitors are non-ATP competitive and bind an allosteric site adjacent to the ATP pocket, and type IV inhibitors bind a remote allosteric site.

The ErbB family, sometimes referred to as the HER family, comprises four members (EGFR/HER1/ErbB1, HER2/ErbB2, HER3/ErbB3 and HER4/ErbB4) and is the prototypical RTK family in which receptor heterodimerisation expands biological signalling beyond what any homodimer would produce (Hsu and Hung, 2016). The VEGFR family contains VEGFR-1 (Flt-1), VEGFR-2 (KDR/Flk-1) and VEGFR-3 (Flt-4), which mediate endothelial cell proliferation, migration and vascular permeability in response to VEGF-A, -B, -C, -D and placental growth factor (Patel et al., 2023). The PDGFR family contains PDGFRalpha, PDGFRbeta and the related KIT receptor that drives mast cell and melanocyte biology (Heinrich et al., 2003). The FGFR family comprises FGFR1, FGFR2, FGFR3 and FGFR4, all of which undergo alternative splicing of the third immunoglobulin-like domain to determine ligand specificity (Saborowski and Lehmann, 2020). The insulin receptor family includes IR-A, IR-B and IGF-1R together with hybrid receptors formed between IR and IGF-

1R hemireceptors (Belfiore et al., 2009). MET, RON, AXL, MER, TYRO3 and the TRK receptors (TRKA, TRKB, TRKC) form additional subfamilies of therapeutic relevance (Liang and Wang, 2020) (Fig 2).

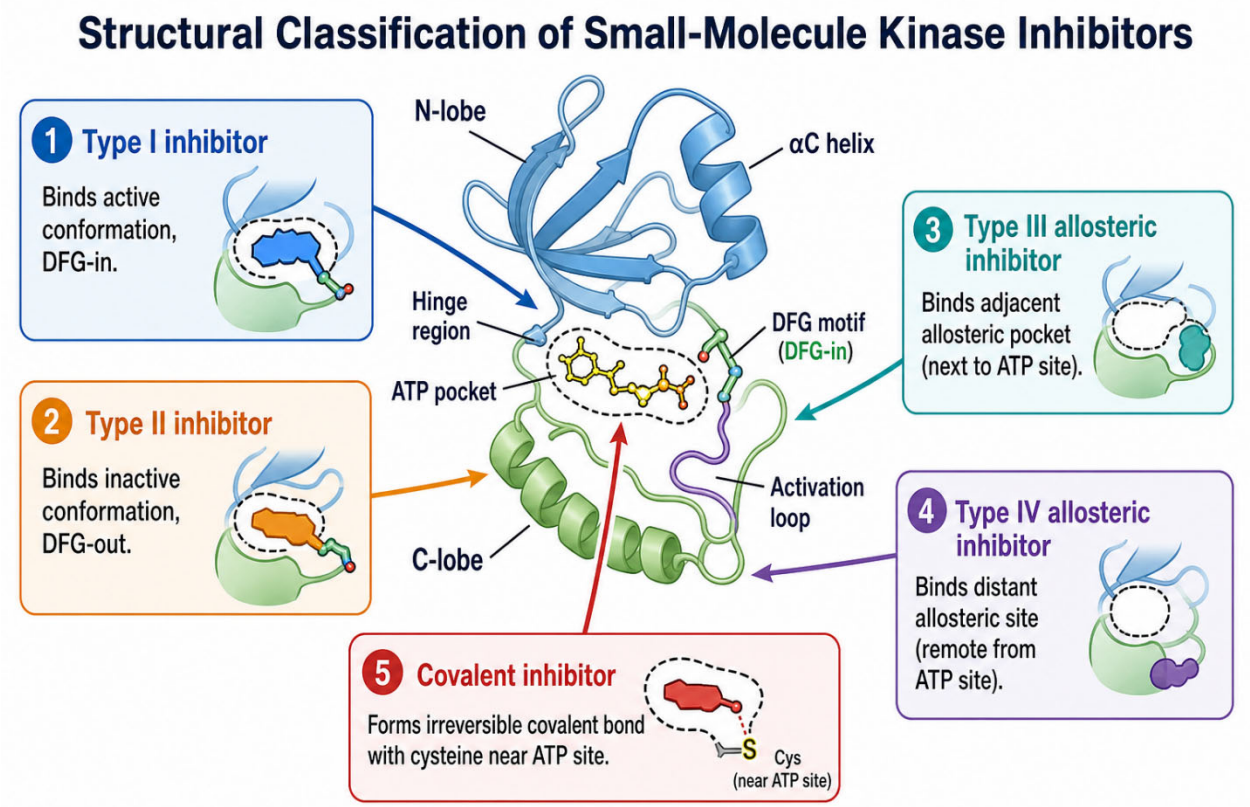

Figure 2. Structural classification of small-molecule kinase inhibitors. Schematic representation of the kinase catalytic domain illustrating the major inhibitor binding modes. Type I inhibitors bind the active kinase conformation (DFG-in), whereas Type II inhibitors recognize the inactive conformation (DFG-out). Type III inhibitors occupy an allosteric pocket adjacent to the ATP-binding site, while Type IV inhibitors bind a more distant allosteric region. Covalent inhibitors form an irreversible bond with a reactive cysteine residue near the ATP pocket. Key structural elements including the N-lobe, C-lobe, hinge region, αC helix, activation loop, DFG motif, and ATP pocket are indicated for orientation.

3. EGFR Signalling and Pharmacology

The epidermal growth factor receptor is a 170 kDa protein consisting of a 622 amino acid extracellular region, a single transmembrane helix and an intracellular kinase domain. Ligands of the EGF family, including EGF itself, transforming growth factor alpha, amphiregulin, betacellulin, epigen, epiregulin and heparin-binding EGF, bind the extracellular region and induce homo- or heterodimerisation with another ErbB receptor (Hsu and Hung, 2016). Upon dimerisation, the intracellular kinase domains adopt an asymmetric dimer configuration in which the C-lobe of one kinase domain allosterically activates the N-lobe of its partner by inducing the alpha-C helix into an in position. This asymmetric dimer model, established for EGFR by X-ray crystallography, explains why EGFR mutants with intact dimerisation interfaces remain sensitive to ATP-competitive inhibitors (Li et al., 2023).

Approximately 10 to 15% of Caucasian patients and up to 50% of Asian patients with non-small cell lung cancer (NSCLC) harbour activating EGFR mutations, most commonly the exon 19 deletion (del19) or the exon 21 L858R point mutation (Li et al., 2023). First-generation reversible ATP-competitive inhibitors gefitinib and erlotinib were the first drugs to demonstrate that molecularly selected populations of NSCLC patients have superior outcomes when treated with a small-molecule kinase inhibitor compared with chemotherapy. Both drugs occupy the ATP-binding pocket through hydrogen bonds with the hinge Met793 residue and a hydrophobic interaction

with the gatekeeper Thr790 (Du et al., 2021). Almost all patients eventually relapse through the emergence of a secondary gatekeeper mutation, T790M, in which a bulky methionine side chain sterically clashes with the anilinoquinazoline scaffold of the first-generation inhibitors (Li et al., 2023). Second-generation inhibitors, including afatinib and dacomitinib, were designed as irreversible inhibitors that carry a Michael acceptor warhead able to alkylate Cys797 at the lip of the ATP pocket, providing partial activity against T790M but losing potency against the wild-type receptor and producing clinically significant skin rash and diarrhoea. Osimertinib, a third-generation pyrimidine-based covalent inhibitor, was purposefully engineered to fit the T790M-mutated pocket while sparing wild-type EGFR, and this molecular selectivity translates into improved central nervous system penetration and a superior safety profile (Du et al., 2021). The most frequent resistance mutation to osimertinib is the cis-C797S disruption of the covalent bond with Cys797, which is being addressed by fourth-generation EGFR inhibitors in clinical development (Yang et al., 2018). EGFR amplification also defines a small fraction of glioblastoma, and second-generation EGFR inhibitors have been investigated in this disease with limited single-agent efficacy.

4. HER2 Pharmacology and Breast Cancer

HER2 is an orphan receptor: it has no known soluble ligand and signals through heterodimerisation with ligand-bound EGFR, HER3 or HER4 (Gajria and Chandarlapaty, 2011). Approximately 15 to 20% of breast cancers are driven by amplification of the HER2 gene on chromosome 17q12, and HER2-amplified tumours are more aggressive but also sensitive to HER2-directed therapy. Trastuzumab, a humanised IgG1 monoclonal antibody directed at the extracellular domain IV of HER2, was the first targeted therapy in solid tumours and the prototype of a successful antibody-drug strategy. Its mechanism of action is multi-modal and includes inhibition of homo- and heterodimerisation, antibody-dependent cellular cytotoxicity (ADCC) through Fc-gamma-RIII engagement on natural killer cells, inhibition of HER2 ectodomain shedding, and induction of internalisation and degradation (Hsu and Hung, 2016). Pertuzumab binds a different epitope (extracellular domain II) and sterically blocks heterodimerisation with HER3, providing complementary benefit when combined with trastuzumab (Roy and Perez, 2009). Ado-trastuzumab emtansine (T-DM1) and trastuzumab deruxtecan (T-DXd) couple the antibody backbone to cytotoxic payloads (DM1 and a topoisomerase I inhibitor, respectively) and achieve objective responses in HER2-low tumours that are not eligible for single-agent trastuzumab.

Small-molecule HER2 tyrosine kinase inhibitors occupy the ATP-binding pocket of HER2 and, in some cases, also EGFR. Lapatinib is a reversible type I inhibitor of EGFR and HER2, neratinib is an irreversible pan-ErbB inhibitor that alkylates the conserved Cys residue of each receptor, and tucatinib is a HER2-selective reversible inhibitor that achieves high central nervous system penetration (Le Du et al., 2021). These small-molecule agents are approved for combinations with capecitabine, with trastuzumab, or as extended adjuvant therapy after trastuzumab. Resistance to HER2-directed therapy emerges through p95-HER2 expression (a constitutively active truncated form lacking the antibody epitope), through HER2 kinase domain mutations such as L755S, and through compensatory signalling from FGFR, MET or IGF-1R (Gajria and Chandarlapaty, 2011). HER2 kinase domain mutations are particularly common in HER2-mutant, non-amplified NSCLC, in which tucatinib and pyrotinib have demonstrated clinical activity.

5. VEGF and VEGFR in Angiogenesis and Disease

VEGFR-2, also known as kinase insert domain receptor (KDR) or fetal liver kinase (Flk-1), is the dominant signalling receptor for VEGF-A, the principal pro-angiogenic ligand in solid tumours and in choroidal neovascularisation (Gotink and Verheul, 2010). VEGFR-2 contains seven extracellular immunoglobulin-like domains, of which domains 2 and 3 are responsible for ligand binding, and a split intracellular kinase domain that is unusual among RTKs because it is interrupted by a kinase insert of approximately 70 residues. VEGF-A binding induces dimerisation and trans-

autophosphorylation of tyrosines 951, 996, 1054, 1059, 1175 and 1214; phospho-Tyr1175 serves as the docking site for phospholipase-C-gamma, phospho-Tyr951 for T-cell-specific adaptor (TSAd), and phospho-Tyr1214 for NCK adaptor proteins (Patel et al., 2023). Bevacizumab, the first anti-angiogenic monoclonal antibody approved in oncology, binds VEGF-A with high affinity and prevents its interaction with VEGFR-1 and VEGFR-2, depriving endothelial cells of their principal survival signal (Roskoski, 2007). Bevacizumab is approved in combination with chemotherapy for metastatic colorectal cancer, non-squamous NSCLC, glioblastoma, renal cell carcinoma, ovarian and cervical cancer. Ranibizumab and aflibercept are derived anti-VEGF agents used in ophthalmology to treat neovascular (wet) age-related macular degeneration, macular oedema following retinal vein occlusion and diabetic macular oedema.

Small-molecule VEGFR inhibitors include sunitinib (which inhibits VEGFR-1, VEGFR-2, VEGFR-3, PDGFR, KIT, FLT3, RET and CSF1R), sorafenib (VEGFR-2, PDGFR, RAF, KIT, FLT3), pazopanib (VEGFR-1, -2, -3, PDGFR, KIT), axitinib (VEGFR-1, -2, -3), regorafenib (VEGFR-1, -2, -3, PDGFR, KIT, RET, BRAF), lenvatinib (VEGFR-1, -2, -3, FGFR, PDGFR, RET) and tivozanib (VEGFR-1, -2, -3) (Gotink and Verheul, 2010). These agents are used in renal cell carcinoma, hepatocellular carcinoma, gastrointestinal stromal tumours, thyroid cancer and several other malignancies. The combination of anti-VEGF therapy with immune checkpoint blockade has emerged as a powerful strategy that normalises tumour vasculature and facilitates T-cell infiltration (Prager et al., 2012). Resistance to VEGF inhibition arises through upregulation of alternative angiogenic factors such as angiopoietin-2, FGF, PDGF, and through recruitment of myeloid-derived suppressor cells.

6. BCR-ABL and Imatinib in Chronic Myeloid Leukaemia

The BCR-ABL fusion oncogene is generated by the t(9;22)(q34;q11) translocation, producing the Philadelphia chromosome (Ren, 2005). The resulting fusion protein combines the oligomerisation domain of BCR with the tyrosine kinase domain of ABL1, causing constitutive activation through forced tetramerisation. BCR-ABL phosphorylates a wide set of substrates including CRKL, CBL, p130CAS, STAT5, and the SFKs, leading to clonal expansion of myeloid progenitors (Marcucci et al., 2003). Before the kinase-inhibitor era CML was treated with busulfan, hydroxyurea, interferon-alpha and allogeneic stem-cell transplantation; the introduction of imatinib in 2001 transformed a fatal disease into a chronic, manageable condition. Imatinib (formerly STI571) was discovered in the laboratory of Brian Druker and Alexander Matter through rational optimisation of a phenylaminopyrimidine starting point (Weisberg et al., 2007). The drug binds the ATP-binding cleft of ABL in an inactive conformation in which the activation loop is closed and the bound conformation resembles type II inhibition despite the absence of a DFG-out pharmacophore. Critical binding interactions include six hydrogen bonds between the drug and the hinge Met318, an aliphatic contact with the gatekeeper Thr315, and a polar interaction with Glu286 in the alpha-C helix (Weisberg et al., 2007). BCR-ABL cannot phosphorylate its substrates while the kinase is locked in this inactive conformation. Imatinib was the first drug rationally designed against a constitutively active kinase and the prototype for the entire modern era of targeted cancer therapy (Van Etten, 2004).

Approximately 50% of patients fail imatinib through resistance mechanisms that map onto five categories: BCR-ABL kinase domain mutations, BCR-ABL gene amplification, overexpression of drug-efflux pumps such as P-glycoprotein, activation of BCR-ABL-independent survival pathways such as SRC family kinases, and persistence of quiescent leukaemic stem cells that do not rely on BCR-ABL for survival (Illmer et al., 2004). The most clinically important resistance mutation is the gatekeeper T315I, which abolishes a critical hydrogen bond between imatinib and Thr315 and sterically blocks the drug. Second-generation inhibitors dasatinib, nilotinib, bosutinib and ponatinib were developed to address these limitations; ponatinib is the only clinically available inhibitor that retains potency against T315I through a triple-bond linkage in its alkyne-containing scaffold (Quintas-Cardama et al., 2009).

7. KIT, PDGFR and Connective Tissue / Myeloid Disorders

KIT (CD117) is the type III RTK that drives mast cell development, melanocyte migration and interstitial cells of Cajal in the gut. Gain-of-function mutations in KIT are found in approximately 80% of gastrointestinal stromal tumours (GISTs), in systemic mastocytosis and in core-binding-factor acute myeloid leukaemia (Heinrich et al., 2003). The most common KIT mutation in GIST is an in-frame deletion in exon 11 that disrupts the autoinhibitory juxtamembrane region; a second hotspot in exon 9 produces an extracellular missense alteration, while in mastocytosis the D816V mutation in the activation loop renders KIT constitutively active and resistant to imatinib (Heinrich et al., 2006). Imatinib is active in KIT-driven GIST but secondary mutations in the ATP-binding pocket or the activation loop account for acquired resistance in roughly half of patients within two years (Serrano et al., 2019). Second-line sunitinib and third-line regorafenib inhibit both KIT and VEGFR and address common secondary mutations, while fourth-line ripretinib inhibits a broad spectrum of KIT mutations including D816V (Bauer et al., 2007). Avapritinib is approved specifically for D816V-mutant systemic mastocytosis and for PDGFRA D842V-driven GISTs.

The PDGFRA D842V mutation produces a particularly imatinib-resistant receptor and represents the molecular hallmark of a subset of inflammatory myofibroblastic tumours and of 5 to 10% of GISTs (Joensuu et al., 2017). PDGFRB is similarly targeted by imatinib in a rare clonal eosinophilic disorder with the FIP1L1-PDGFRA fusion, which is highly imatinib-sensitive, and in dermatofibrosarcoma protuberans where the COL1A1-PDGFB t(17;22) translocation drives autocrine PDGFR signalling (Lopes and Bacchi, 2010). The mechanistic lesson of these diseases is that imatinib's narrow spectrum reflects the precise geometry of the activation-loop pocket; precise mutation mapping is required to predict response.

8. ALK and ROS1 in Non-Small Cell Lung Cancer

Anaplastic lymphoma kinase (ALK) is a 1,620-amino-acid type I RTK containing an extracellular ligand-binding region, a transmembrane region and an intracellular kinase domain; under physiological conditions it is expressed primarily in the developing nervous system. Chromosomal inversion inv(2)(p21;p23) fuses the N-terminal portion of echinoderm microtubule-associated protein-like 4 (EML4) with the ALK kinase domain, producing a constitutively active EML4-ALK fusion in approximately 3 to 7% of NSCLC (Addeo et al., 2018). ROS1 is a phylogenetically related orphan RTK and CD74-ROS1, SDC4-ROS1 and other fusions occur in approximately 1 to 2% of NSCLC.

Crizotinib, originally developed as a MET inhibitor, was found to inhibit ALK (IC50 of approximately 24 nM) and ROS1 by virtue of conserved ATP-pocket geometry. Crizotinib occupies the ATP-binding cleft through two hydrogen bonds to the hinge Met and hydrophobic interactions with the gatekeeper Leu (Testa et al., 2024). The PROFILE 1014 trial established crizotinib as first-line therapy for ALK-positive NSCLC, and a parallel study extended activity to ROS1-positive disease. Resistance to crizotinib emerges through secondary ALK mutations such as L1196M (gatekeeper), G1269A (hinge), C1156Y (alpha-C), F1174L (activation loop) and G1202R (solvent front) (Beardslee and Lawson, 2018). Second-generation ALK inhibitors ceritinib, alectinib and brigatinib were designed for improved CNS penetration and broader coverage of crizotinib-resistant mutations; alectinib and brigatinib are now preferred first-line agents in many guidelines. Lorlatinib is a third-generation macrocyclic ALK/ROS1 inhibitor engineered to remain potent against the recalcitrant G1202R solvent-front mutation (Ma et al., 2021). Entrectinib is a multi-kinase TRKA/B/C, ROS1 and ALK inhibitor used as a first-line therapy for ROS1 and as a histology-agnostic therapy for NTRK fusion-positive cancers (Liu et al., 2018).

9. MET and HGF/MET Axis

The MET proto-oncogene encodes a heterodimeric receptor composed of a 50 kDa extracellular alpha-chain disulfide-bonded to a 145 kDa transmembrane beta-chain. The ligand hepatocyte growth factor (HGF) is secreted as an inactive single chain that is cleaved into a two-chain active

form by extracellular serine proteases (Liang and Wang, 2020). HGF binding induces MET dimerisation and phosphorylation of tyrosines 1234 and 1235 in the activation loop, tyrosines 1349 and 1356 in the C-terminal multifunctional docking site that recruits the adaptor GRB2, the ubiquitin ligase CBL, and the kinases SRC and PLCgamma. MET amplification occurs in approximately 3 to 5% of NSCLC as a primary oncogenic driver and in up to 20% of EGFR-TKI-resistant NSCLC as an acquired bypass mechanism.

Crizotinib was the first clinically deployed MET inhibitor (Baltschukat et al., 2019). Capmatinib is a highly selective type Ib MET inhibitor that binds the inactive ATP pocket in a manner analogous to type II inhibitors and is approximately 30-fold more potent than crizotinib. Tepotinib and savolitinib are additional type Ib MET inhibitors. All these compounds were designed to treat MET exon 14 skipping mutations, which produce a truncated receptor that lacks the ubiquitin-mediated degradation signal encoded by exon 14, leading to receptor stabilisation and prolonged signalling (Recondo et al., 2020). Type Ia MET inhibitors (crizotinib) interact with the solvent-front G1163 residue, while type Ib inhibitors (capmatinib, tepotinib) avoid this position and retain potency against the most common exon 14 skipping alterations (Santarpia et al., 2021).

10. FGFR in Cholangiocarcinoma and Other Malignancies

Fibroblast growth factor receptors 1-4 dimerise upon binding of FGF ligands, with alternative splicing of the third immunoglobulin-like domain (IIIb or IIIc) providing tissue-specific ligand preferences (Saborowski and Lehmann, 2020). FGFR2 fusions, most commonly FGFR2-BICC1, FGFR2-PPHLN1 and FGFR2-MGEA5, are found in 10 to 16% of intrahepatic cholangiocarcinomas. Activating point mutations in FGFR2 (e.g. N549H, K659E) and FGFR3 (e.g. R248C, S249C, G372C, K652E) drive bladder cancer, endometrial cancer and some lung squamous carcinomas. FGFR1 amplification is a recognised oncogenic event in approximately 7% of squamous lung cancers. Pemigatinib, infigratinib and futibatinib are FGFR-selective reversible ATP-competitive inhibitors that target FGFR1-3 with reduced activity against FGFR4 (Neureiter et al., 2023). Pemigatinib was the first FGFR inhibitor to gain regulatory approval, specifically for previously treated, unresectable, locally advanced or metastatic cholangiocarcinoma with FGFR2 fusion or rearrangement. Erdafitinib gained accelerated approval for FGFR-altered urothelial carcinoma.

The major resistance mechanism to ATP-competitive FGFR inhibitors is the emergence of secondary kinase domain mutations in the gatekeeper (V564F in FGFR2, V555M in FGFR3) or in the molecular brake (N549), as well as the gatekeeper plus N549 compound mutations that abolish drug binding (Kawashima et al., 2025). Futibatinib, an irreversible inhibitor that covalently modifies a conserved cysteine near the ATP pocket, retains activity against many of these resistance mutations (Erul et al., 2026).

11. NTRK Fusions and TRK Inhibitors

The TRK family comprises TRKA (encoded by NTRK1), TRKB (NTRK2) and TRKC (NTRK3), which are activated by neurotrophin ligands (NGF, BDNF/NT-4, NT-3 respectively). Across diverse tumour types, gene fusions involving the 3' kinase domain of an NTRK gene and a 5' partner gene produce chimeric receptors that are constitutively dimerised and signal through RAS-MAPK, PI3K-AKT and PLCgamma (Harada et al., 2021). Examples include ETV6-NTRK3 in secretory breast carcinoma and infantile fibrosarcoma, TPM3-NTRK1 in colorectal cancer and LMNA-NTRK1 in lung adenocarcinoma. Although each individual NTRK fusion is rare, collectively they are found in approximately 0.3% of all solid tumours.

Larotrectinib is a highly selective pan-TRK inhibitor with nanomolar activity against TRKA, TRKB and TRKC; its compact structure was designed to fit the ATP pocket of TRKC even in the presence of the gatekeeper mutation F589L (Laetsch and Hong, 2021). Larotrectinib gained the first histology-agnostic approval by the FDA in 2018 for any solid tumour with an NTRK fusion. Entrectinib is a multi-kinase inhibitor of TRKA/B/C, ROS1 and ALK with better CNS penetration than larotrectinib due to distinct physicochemical properties (Federman and McDermott, 2019). Both

drugs deliver objective response rates of approximately 50 to 75% in TRK fusion-positive cancers. On-target resistance emerges through solvent-front mutations (e.g. G595R in TRKA, G623R in TRKC), gatekeeper mutations (F589L in TRKA, F617L in TRKC) or activation-loop mutations that distort the drug-binding pocket. Second-generation TRK inhibitors selitrectinib and repotrectinib were designed with macrocyclic or compact scaffolds to retain potency against these resistance variants (Harada and Drilon, 2022).

12. RET and Medullary Thyroid Cancer

RET is a 1,114-amino-acid RTK containing a cadherin-like extracellular domain, a cysteine-rich region, a transmembrane helix and an intracellular kinase domain. Germline gain-of-function RET mutations cause multiple endocrine neoplasia type 2A and 2B and familial medullary thyroid carcinoma, while somatic RET fusions (KIF5B-RET, CCDC6-RET) occur in 1 to 2% of NSCLC and somatic RET point mutations (most commonly M918T) drive approximately 50% of sporadic medullary thyroid carcinomas (Thein et al., 2021). Vandetanib and cabozantinib were the first multi-kinase inhibitors approved for medullary thyroid cancer; both engage the RET ATP pocket but their activity against other kinases (VEGFR, EGFR) produces substantial off-target toxicity.

Selpercatinib and pralsetinib are highly selective RET inhibitors developed through structure-based design of a constrained macrocyclic framework that wraps around the kinase and avoids the gatekeeper methionine (Hamidi et al., 2025). Selpercatinib was approved in 2020 for RET-altered medullary thyroid cancer and RET fusion-positive NSCLC; pralsetinib followed shortly afterwards. Both drugs produce objective response rates of approximately 70% in treatment-naive RET-mutant medullary thyroid carcinoma and over 60% in previously treated disease. Solvent-front mutations such as G810R/S/C/A in RET emerge as on-target resistance mechanisms that are addressed by next-generation RET inhibitors in clinical development (Angelousi et al., 2022; Zhang et al., 2024). RET is also a relevant target in the paediatric context: children with RET-mutant medullary thyroid cancer, multiple endocrine neoplasia type 2B or TRKC fusion-positive infantile fibrosarcoma can benefit from selective RET inhibition. The development of selective RET inhibitors illustrates the iterative nature of kinase inhibitor design and the value of ATP-pocket structures obtained by crystallography or cryo-electron microscopy.

13. JAK-STAT Pathway and Inflammatory Disease

Janus kinases (JAK1, JAK2, JAK3, TYK2) are non-receptor tyrosine kinases that are constitutively bound to cytokine receptors lacking intrinsic kinase activity, including those for interferons, interleukins and colony-stimulating factors (Banerjee et al., 2017). When a cytokine binds, the receptor subunits undergo a conformational change that brings two JAKs into proximity, allows trans-phosphorylation and activation, and enables phosphorylation of STAT transcription factors. Phosphorylated STATs dimerise, translocate to the nucleus and drive expression of target genes. JAK2 is mutated in approximately 50 to 60% of polycythaemia vera and 30% of essential thrombocythaemia, most commonly as a V617F point mutation in the pseudokinase domain that produces constitutive kinase activity.

Ruxolitinib is an ATP-competitive JAK1/JAK2 inhibitor that produces rapid and durable reductions in splenomegaly and constitutional symptoms in myelofibrosis and reduces phlebotomy requirements in hydroxyurea-resistant polycythaemia vera (Aittomaki and Pesu, 2014). Baricitinib, fedratinib, pacritinib and momelotinib are additional JAK2 inhibitors. Tofacitinib is a JAK1/JAK3 inhibitor used in rheumatoid arthritis, psoriatic arthritis, ulcerative colitis, ankylosing spondylitis and polyarticular juvenile idiopathic arthritis, where it reduces synovial JAK-STAT signalling and downstream cytokine production (Boyle et al., 2015). Filgotinib, upadacitinib and baricitinib are JAK1-selective inhibitors that aim to retain anti-inflammatory potency while limiting the anaemia associated with JAK2 inhibition. JAK inhibition modulates over 50 cytokines simultaneously, and consequently the safety profile includes anaemia, neutropenia, lymphopenia, hyperlipidaemia, infections (including herpes zoster reactivation) and thrombosis (Malemud, 2018). Topical

ruxolitinib is approved for atopic dermatitis and vitiligo, illustrating that RTK-pathway inhibition is relevant beyond oncology. TYK2-selective inhibitors such as deucravacitinib exploit the pseudokinase domain of TYK2 to achieve allosteric inhibition while sparing JAK1/2/3 and offering an improved safety profile in psoriasis and psoriatic arthritis (Ciobanu et al., 2020).

14. Insulin Receptor, IGF-1R and Metabolic Disease

The insulin receptor (IR) is encoded by a single gene (INSR) but alternative splicing of exon 11 produces two isoforms: IR-A, which is predominantly expressed in fetal tissues, the brain and many cancer cells, and IR-B, which is the predominant isoform in the liver, muscle and adipose tissue and is responsible for the metabolic effects of insulin (Belfiore et al., 2009). IR-B signals through IRS1/2 into the PI3K-AKT-mTOR axis to control glucose uptake via GLUT4 translocation. IGF-1R is highly homologous to IR and signals through the same axis; hybrid IR/IGF-1R receptors composed of an IR hemireceptor and an IGF-1R hemireceptor are commonly found in many tissues (Pollak, 2012).

In Type 2 diabetes the molecular pathology of insulin resistance involves serine phosphorylation of IRS-1 by stress-activated kinases (JNK, IKK, mTOR), reducing its ability to propagate insulin signalling. SGLT2 inhibitors, GLP-1 receptor agonists and DPP-4 inhibitors act through metabolic pathways rather than RTKs. However, a number of IGF-1R/IR inhibitors have been developed for oncology and have illuminated the central role of this receptor family in cancer cell survival (Singh et al., 2014). Figitumumab, an IGF-1R monoclonal antibody, and linsitinib, a small-molecule IGF-1R/IR inhibitor, were evaluated in NSCLC and Ewing sarcoma; both programmes ultimately failed to demonstrate survival benefit, although they did confirm that IGF-1R inhibition produces hyperglycaemia as the most prominent on-target adverse event (Ekyalongo and Yee, 2017). Mechanistically, the failure of IGF-1R blockade in solid tumours is illustrative: cancer cells readily amplify IR-A, which binds IGF-2 with high affinity, providing a bypass mechanism that sustains PI3K-AKT signalling (Pollak, 2012).

15. RAF and MEK Inhibitors in BRAF-Driven Melanoma

Although RAF kinases (ARAF, BRAF, CRAF/RAF1) are technically cytoplasmic serine-threonine kinases rather than RTKs, they are obligate downstream effectors of RTK signalling and are included here because their pharmacology is intimately tied to RTK activity (Menzies et al., 2012). Approximately 50% of cutaneous melanomas carry a BRAF V600E mutation in which a glutamic acid substitutes for the wild-type valine at position 600 in the activation loop. This mutation produces a constitutively active kinase that signals through MEK1/2 to ERK1/2 and drives cell proliferation. Vemurafenib was the first selective BRAF V600E inhibitor, designed to fit the active conformation of the mutant kinase and approved in 2011 on the basis of overall survival benefit over dacarbazine in metastatic melanoma (Kugel and Aplin, 2014).

Dabrafenib is a related selective BRAF V600 inhibitor with a different scaffold; both drugs occupy the ATP-binding pocket of the active kinase and produce a paradoxical activity in BRAF wild-type contexts (reactivation of MAPK signalling in cells with upstream RAS activation) (Menzies and Long, 2014). This paradoxical activation is the basis for cutaneous squamous-cell carcinoma and keratoacanthomas as class effects of BRAF inhibitors when used as monotherapy and provides the rationale for combination therapy with a downstream MEK inhibitor such as trametinib, cobimetinib, binimetinib or selumetinib. The combination of dabrafenib with trametinib extends median progression-free survival compared with either agent alone and is now the standard first-line therapy for BRAF V600-mutant melanoma (Luke and Hodi, 2013). BRAF/MEK combination therapy is also approved for BRAF V600-mutant non-small cell lung cancer and anaplastic thyroid cancer and is being explored in colorectal and brain cancers (Falchook et al., 2012).

16. Inhibitor Binding Modes and Structure-Based Design

Kinase inhibitors are classified into four main categories according to how they engage the catalytic machinery (Roskoski, 2007). Type I inhibitors such as gefitinib, erlotinib, crizotinib,

vemurafenib and lapatinib bind the active conformation of the kinase in which the DFG motif is in, the activation loop is open and the alpha-C helix is rotated to the in position. These drugs typically make one to three hydrogen bonds with the hinge region (Met793 in EGFR, Met318 in ABL, Met1096 in MET) and a hydrophobic interaction with the gatekeeper residue. Because the active conformation is similar across many kinases, type I inhibitors often display off-target activity against multiple kinases. Type II inhibitors such as imatinib, sorafenib and nilotinib bind the inactive DFG-out conformation and extend from the ATP-binding pocket into an adjacent hydrophobic pocket created by the displacement of the Phe of the DFG motif. This additional hydrophobic interaction confers greater selectivity, although the same hydrophobic pocket is conserved in only some kinases.

Type III inhibitors are non-ATP competitive and bind the ATP pocket in a conformationally distinct allosteric site; trametinib is a notable example of an allosteric MEK inhibitor. Type IV inhibitors bind a remote allosteric site outside the kinase domain; asciminib, an allosteric ABL inhibitor that binds the myristoyl pocket of the C-lobe, is a landmark example. Covalent inhibitors such as osimertinib, afatinib, neratinib and ibrutinib carry an electrophilic warhead (typically an acrylamide Michael acceptor) that alkylates a reactive cysteine at the lip of the ATP pocket. The covalent bond overcomes the modest affinity of the reversible binding event and produces long-lived target engagement, especially against difficult-to-drug conformations (Guo et al., 2023). Resistance mutations such as C797S in EGFR, C481S in BTK and C311S in HER2 disrupt the covalent bond and have driven the development of next-generation covalent inhibitors that engage alternative cysteines.

17. Resistance Mechanisms to RTK Inhibitors

Resistance to small-molecule RTK inhibitors can be divided into on-target mechanisms that alter the drug-binding site of the very RTK being inhibited and off-target mechanisms that engage parallel or downstream pathways (Lazzari et al., 2020). On-target resistance is typically mediated by point mutations in the kinase domain. The most common categories are gatekeeper mutations (T790M in EGFR, T315I in ABL, F589L in TRKA, L1196M in ALK) that introduce a bulky side chain sterically incompatible with drug binding; solvent-front mutations (G1202R in ALK, G2032R in ROS1, G595R in TRKA, G810R in RET) that block drug access to the hinge; activation-loop mutations that alter the conformation sampled by the drug; and compound mutations that combine several of these changes on the same allele.

Off-target resistance includes amplification or activation of a parallel RTK that bypasses the inhibited pathway (MET amplification as a bypass in EGFR-inhibited lung cancer, HER2 amplification in colorectal cancer treated with EGFR antibodies), mutational activation of downstream effectors (KRAS, BRAF, NRAS mutations in EGFR-TKI-treated lung cancer), engagement of bypass survival pathways through activation of SRC family kinases, JAK-STAT or AXL, and histologic transformation to small-cell lung cancer in EGFR-driven NSCLC (Fu et al., 2022). Pharmacokinetic resistance through increased drug efflux via ABC transporters such as P-glycoprotein, or reduced uptake via solute carriers, is an important additional category (Illmer et al., 2004). Strategies to address resistance include the use of covalent, irreversible inhibitors with activity against common gatekeeper mutations (osimertinib for EGFR T790M, ponatinib for ABL T315I), the design of next-generation inhibitors that retain potency against compound mutations (asciminib, repotrectinib, BLU-945), combination strategies that target parallel pathways (EGFR + MET inhibition, BRAF + MEK inhibition, EGFR + VEGF inhibition), and intermittent dosing or sequential strategies to prevent clonal evolution. The development of allosteric inhibitors such as asciminib and EBI-2511 illustrates that engagement of cryptic binding sites outside the ATP pocket can overcome the most recalcitrant resistance mutations (Serrano et al., 2019).

18. Non-Oncology Indications for RTK Inhibitors

The most important non-oncology indication for RTK inhibitors is idiopathic pulmonary fibrosis (IPF). Nintedanib (BIBF 1120) is a potent triple angiokinase inhibitor with IC50 values in the low nanomolar range for VEGFR-1/-2/-3, FGFR-1/-2/-3 and PDGFRalpha/beta, and additional activity against FLT3, LCK, LYN and SRC (Wollin et al., 2015). The drug reduces the proliferation, migration and transformation to myofibroblasts of fibroblasts stimulated by PDGF, FGF and VEGF, three growth factors elevated in the lungs of IPF patients. Nintedanib also inhibits mast cell activity, a population recently recognised to potentiate fibrogenesis (Overed-Sayer et al., 2020). The TOMORROW and INPULSIS trials established nintedanib as a disease-modifying therapy for IPF that slows the rate of decline in forced vital capacity (Wollin et al., 2019). Nintedanib is also approved for progressive fibrosing interstitial lung disease and for systemic sclerosis-associated interstitial lung disease.

Ruxolitinib and other JAK inhibitors are increasingly used in graft-versus-host disease, vitiligo and alopecia areata (Harrington et al., 2020). Imatinib is being repurposed in pulmonary arterial hypertension, where PDGFR-driven proliferation of vascular smooth muscle cells contributes to vascular remodelling. Anti-VEGF agents remain essential in ophthalmology: ranibizumab, aflibercept, brolucizumab and faricimab are anti-VEGF therapies used routinely in clinical practice to treat wet age-related macular degeneration and diabetic retinopathy. Small-molecule JAK inhibitors are being trialled in the new coronavirus disease 2019 (COVID-19) for their ability to dampen cytokine release, and baricitinib gained emergency use authorisation for hospitalised patients with severe COVID-19 requiring oxygen support. The lessons learnt across these disparate indications are that the molecular pathology of many chronic diseases converges on RTK signalling pathways, and that pharmacology originally developed for cancer finds novel applications when the same pathways are dysregulated in non-malignant tissues.

19. Conclusion and Future Directions

Receptor tyrosine kinases constitute one of the most druggable families of human proteins, and the parallel development of selective small-molecule inhibitors, monoclonal antibodies, antibody-drug conjugates and allosteric modulators has transformed the treatment of cancer and an expanding list of non-malignant diseases. The narrative of this pharmacology over the last three decades is one of progressive precision: imatinib established that constitutive kinase activity could be inhibited, gefitinib and trastuzumab showed that patient selection by molecular testing was essential to extract benefit, osimertinib and asciminib demonstrated that covalent and allosteric strategies can overcome primary resistance, and larotrectinib and entrectinib validated the histology-agnostic paradigm. Future directions include the discovery of inhibitors that target KRAS and other historically undruggable GTPases, the broader clinical adoption of basket and umbrella trials keyed to molecular rather than histologic criteria, the integration of kinase inhibition with immune checkpoint blockade, and the exploitation of artificial-intelligence-driven drug design to accelerate the discovery of lead compounds. The continued investigation of RTK signalling will remain a central theme of molecular medicine for the foreseeable future, with the promise that deeper mechanistic understanding will translate into more effective, more selective and more durable therapies (Fig 3).

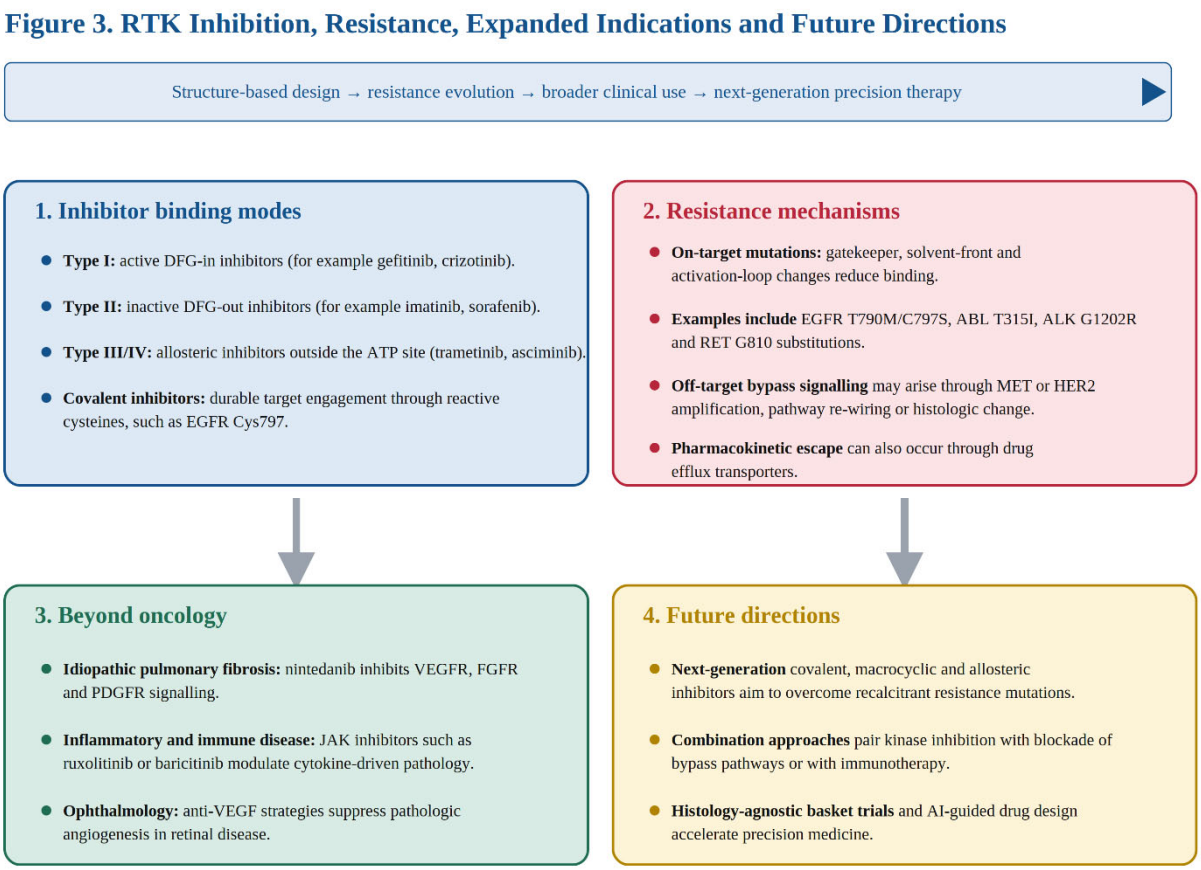

Figure 3. RTK inhibition, resistance, expanded indications and future directions. This integrative schematic summarises Sections 16–19 by linking inhibitor binding modes with acquired resistance, non-oncology applications and next-generation precision-medicine strategies. Key examples include Type I/II/allosteric/covalent inhibitors, gatekeeper and solvent-front mutations, fibrosis and inflammatory indications, and combination or AI-guided therapeutic development.

[Placement: final figure inserted immediately before the References section to summarise the lower sections thematically.]

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ГИДРОЭКОЛОГИЧЕСКОЕ СОСТОЯНИЕ ПРИМОРСКИХ ОЗЕР ДЕЛЬТЫ Р.СЫРДАРИЯ

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Аннотация. Дельтовые озерные системы реки Сырдария представляют собой гидрологически взаимосвязанный комплекс водоемов, проток и пойменных территорий, состояние которого определяется режимом речного стока и регулируемой водоподачей. Целью исследования являлась оценка современного гидроэкологического состояния озерных систем дельты Сырдария. Проведен сравнительный анализ гидрологических, морфометрических и гидрохимических показателей, включая уровень и объем воды, площадь водного зеркала, минерализацию, pH, растворенный кислород и содержание биогенных соединений. Установлена выраженная пространственная и сезонная изменчивость состояния водоемов. Наиболее благоприятные условия отмечены в Камыстыбасской системе, тогда как Приморская система характеризуется большей мелководностью, пониженной прозрачностью и повышенным содержанием отдельных биогенных элементов. Полученные результаты подтверждают ключевую роль речного стока и регулируемой водоподачи в поддержании устойчивого гидрологического и экологического состояния дельтовых озер.

Ключевые слова: р.Сырдария, Аклак, Аспай, озерная система, дельта

Введение. Дельта реки Сырдария представляет собой одну из наиболее значимых водно-болотных экосистем Центральной Азии, выполняющую важные гидрологические, экологические и рыбохозяйственные функции. Озерные системы дельты обеспечивают поддержание биоразнообразия, являются местом нереста, нагула и миграции многих видов рыб, а также играют ключевую роль в сохранении экологической устойчивости Северного Приаралья [1]. Особое место среди них занимают Приморские озера, гидрологический режим которых непосредственно связан с объемом речного стока, режимом эксплуатации гидротехнических сооружений, интенсивностью испарения, минерализацией воды и климатическими условиями региона.

В XX веке гидрологический режим дельты Сырдария претерпел существенные изменения, обусловленные интенсивным развитием орошаемого земледелия в бассейне реки. Уже с 1930-х годов увеличение объемов водозабора привело к постепенному сокращению поступления речного стока в дельту. Если до начала 1960-х годов в вершину дельты поступало около 44 % годового стока реки Сырдария, то к концу 1970-х годов этот показатель снизился до 4 %. Вследствие этого произошло резкое сокращение площади озерных систем, изменение гидрохимического режима, усиление процессов засоления и деградация водно-болотных экосистем [2].

По результатам исследований, к 1976 году суммарная площадь дельтовых озер сократилась примерно до 400 км², а объем аккумулируемой воды — до 1,5 км³. На фоне

усилившегося дефицита водных ресурсов основное рыбохозяйственное значение сохранили Камыстыбасская и Приморские озерные системы, устойчивость водного режима которых обеспечивалась за счет регулируемого искусственного обводнения. С начала XXI века гидроэкологическая ситуация в дельте стала постепенно улучшаться благодаря реализации проекта «Регулирование русла реки Сырдарьи и сохранение северной части Аральского моря» (ПРРССАМ). Строительство современного гидроузла «Аклак» обеспечило возможность регулируемой подачи воды в озерные системы дельты, что способствовало восстановлению гидрологического режима, повышению устойчивости водных экосистем и сохранению рыбохозяйственного потенциала региона [3].

В периоды нормальной водности суммарная площадь водного зеркала озерных систем дельты Сырдария, включая Камыстыбасскую, Приморскую и Акшатаускую, составлял около 900–930 км². Это значительно выше показателей критического маловодного периода 1976 года, когда площадь водного зеркала сокращалась примерно до 400 км². Вместе с тем состояние дельтовых водоемов остается динамичным и тесно связано с изменениями водности реки. В маловодные периоды площадь водного зеркала может уменьшаться до 600–650 км². Наиболее выраженная изменчивость характерна для Приморской озерной системы, включающей озера Карашалан, Домалак и прилегающие водоемы. В зависимости от сезонного притока и объемов попусков через гидроузел «Аклак» площадь ее акватории изменяется в пределах 250–320 км², а объем аккумулируемой воды составляет порядка 0,6–0,8 км³. Несмотря на увеличение водообеспеченности в отдельные периоды, современное состояние Приморских озер остается нестабильным. На него оказывают влияние межгодовые колебания речного стока, режим работы гидротехнических сооружений, климатические условия и антропогенная нагрузка. Изменения уровня воды непосредственно отражаются на минерализации и других гидрохимических характеристиках, развитии водной растительности, продуктивности водных экосистем и состоянии ихтиофауны. В связи с этим комплексная оценка гидроэкологического состояния Приморских озер имеет важное значение, для обоснования рационального использования водных ресурсов, сохранения биоразнообразия и поддержания рыбохозяйственной ценности дельтовых водоемов [4].

Гидрохимический режим водоемов дельты реки Сырдария и Приморских озер находится в тесной зависимости от гидрологического режима и объемов поступающего речного стока. Изменение водности определяет динамику минерализации, ионного состава воды, газового режима, содержания биогенных элементов, органического вещества, взвешенных частиц и прозрачности водной среды. В условиях сокращения речного стока и маловодья уменьшение притока пресной воды в сочетании с высокой интенсивностью испарения в аридном климате приводит к увеличению минерализации воды и изменению ее гидрохимического типа. Снижение уровня воды сопровождается уменьшением глубины водоемов и усилением прогрева водной толщи, что отрицательно влияет на кислородный режим. В застойных участках, особенно в зарослях тростника, создаются условия для снижения содержания растворенного кислорода, активизации процессов разложения органического вещества и возникновение локальных заморных явлений. Наряду с этим уменьшение проточности способствует накоплению соединений азота и фосфора, развитию процессов эвтрофикации и массовому развитию фитопланктона, что ухудшает качество водной среды в летние периоды. Уменьшение глубины также приводит к усилению ветрового взмучивания донных отложений, повышению содержания взвешенных веществ и снижению прозрачности воды, ограничивая проникновение света и ухудшая условия для развития погруженной водной растительности и донных сообществ [5-6].

В периоды повышенной водности и регулируемых попусков воды через гидротехнические сооружения происходит активное обновление водных масс, снижение

минерализации и восстановление гидрохимического режима. Усиление водообмена способствует поддержанию благоприятного кислородного режима, стабилизации показателя pH, выносу избыточных биогенных веществ и уменьшению риска вторичного засоления и эвтрофикации. Повышение прозрачности воды улучшает условия для развития высшей водной растительности, гидробионтов и естественного воспроизводства рыб.

Материалы и методы. Сбор и анализ материалов, характеризующих гидрологический и гидрохимический режим приморских озер дельты реки Сырдария, проводились в соответствии с действующими методическими рекомендациями и нормативными документами, применяемыми в ТОО «Научно-производственный центр рыбного хозяйства» [7–8]. Для оценки гидрологического состояния исследуемых водоемов использовались данные РГУ «Арало-Сырдарьинская бассейновая инспекция по регулированию использования и охране водных ресурсов». Непосредственно в полевых условиях определялись основные гидрофизические и гидрохимические показатели воды., содержание растворенного кислорода измерялись с использованием портативного анализатора воды МАРК-302М, а активная реакция среды (pH) определялась с помощью pH-метра МАРК-901. Для определения минерализации, ионно-солевого состава, содержания биогенных элементов (соединений азота и фосфора), пробы воды доставлялись лабораторию Аральского филиала ТОО «Научно-производственный центр рыбного хозяйства», где исследования выполнялись в соответствии с действующими государственными стандартами и утвержденными методиками гидрохимического анализа.

Результаты исследований. Дельтовая часть реки Сырдария включает систему озер и заболоченных территорий, объединенных в четыре основные гидрологические системы: Приморскую правобережную, Приморскую левобережную, Камыстыбасскую и Акшатаускую. Формирование их гидрологического режима определяется величиной стока реки Сырдария, режимом эксплуатации гидротехнических сооружений, а также объемами попусков воды через водорегулирующий узел «Аспай» в районе Аманоткел и «Аклак» в районе Каратерен обеспечивающий распределение речного стока по дельтовым водоемам, в том числе на Малое Аральское море.

После капитального ремонта в эксплуатацию в сентябре 2021 года был вновь введен водорегулирующий узел «Аспай» первоначально построенный в 1974 году хозяйственным способом. Принцип работы сооружения заключается в перераспределении поступающего из русла Сырдария водного потока. В период эксплуатации вода первоначально направляется по магистральным каналам «Кулы» и «Жасулан», посредством которых осуществляется водоснабжение Акшатауской и Камыстыбасской озерных систем. После достижения в озерах проектных уровней наполнения и заполнения их полезного объема избыточные объемы воды отводятся через водосбросные сооружения Аспайского узла по сбросным каналам в акваторию Малого Аральского моря. Такой режим эксплуатации позволяет не только обеспечить устойчивое обводнение озерных экосистем, но и исключить их переполнение в периоды повышенной водности. Важной особенностью Аспайского водорегулирующего узла являются его гидравлические характеристики. Сооружение обеспечивает возможность подпора уровня воды в реке Сырдария до отметки 58,0 м по Балтийской системе высот, что позволяет гарантированно подавать воду в магистральные каналы, питающие Камыстыбасскую и Акшатаускую озерные системы. Самотечное поступление воды в указанные каналы начинается уже при достижении уровня 56,0 мБС. Для сравнения, максимальная отметка подпора воды, обеспечиваемая гидроузлом «Аклак», составляет 52,0 мБС, что значительно ограничивает возможности подачи воды в озерные системы. В периоды низкой водности узел является одним из ключевых гидротехнических сооружений дельты реки Сырдария, обеспечивающим эффективное перераспределение речного стока, устойчивое водоснабжение Камыстыбасской и Акшатауской озерных систем,

регулирование уровенного режима и поддержание экологической устойчивости дельтовых водно-болотных угодий.

Рисунок 1 - Водорегулирующий узел «Аспай в дельте р.Сырдария

Анализ современного морфометрического состояния дельтовых водоемов показывает, что при относительно благоприятных гидрологических условиях суммарная площадь водного зеркала озерных систем стабилизируется на уровне 700–800 км², а общий объем аккумулируемой воды составляет порядка 1,0–1,5 км³. Наиболее высокая степень наполнения характерна для Камыстыбасской и Акшатауской озерных систем. Это свидетельствует о сохранении основных водных экосистем дельты, несмотря на продолжающуюся зависимость их состояния от межгодовой изменчивости речного стока и сезонного режима водоподачи [9-10]. Обводнение Приморских озерных систем носит сезонный характер: к летнему периоду объемы водоподачи сокращаются, а с наступлением осеннего периода возобновляются. Согласно официальным данным РГУ «Арало-Сырдарьинская бассейновая инспекция по регулированию использования и охране водных ресурсов», в 2024–2026 годах водообеспечение Камыстыбасской и Акшатауской озерных систем характеризовалось значительными межгодовыми изменениями. В 2025 году общий объем воды, направленной на обводнение этих систем, составил 1176 млн.м³ против 839 млн.м³ в 2024 году, увеличившись на 337 млн.м³, или 40,2 %. По состоянию на 1 июля 2026 года объем водоподачи составил 586 млн.м³, однако данный показатель отражает только первое полугодие и поэтому не может напрямую сопоставляться с годовыми объемами предыдущих лет.

Основная часть водных ресурсов направлялась в Камыстыбасскую систему. В 2024 году объем водоподачи составил 531 млн.м³, а в 2025 году увеличился до 753 млн.м³, то есть на 41,8 %. В Акшатаускую систему за тот же период было направлено соответственно 299 и 423 млн.м³, что соответствует увеличению на 41,5 %. Таким образом, распределение водных ресурсов между двумя системами оставалось относительно стабильным: около 64 %

приходилось на Камыстыбасскую и около 36 % — на Акшатаускую систему. За первое полугодие 2026 года объем водоподачи составил около 395 млн.м³ в Камыстыбасскую и 191 млн.м³ в Акшатаускую систему. В совокупности это 586 млн.м³, что соответствует примерно половине объема, направленного в данные системы за весь 2025 год.

Приоритетное водообеспечение Камыстыбасской озерной системы обусловлено необходимостью поддержания водного режима озера Камыстыбас, являющегося крупнейшим туристско-рекреационным водоемом региона, а также его высокой экологической ценностью и значением для сохранения гидрологической устойчивости дельты реки Сырдария, водно-болотных угодий и рыбохозяйственных экосистем. Вместе с тем увеличение объемов водоподачи в 2025 году способствовало улучшению гидроэкологического состояния обеих озерных систем, повышению устойчивости водных экосистем и созданию более благоприятных условий для воспроизводства водных биологических ресурсов. Таким образом, за период с 2024 года по первое полугодие 2026 года суммарный объем поступившей воды составил 2,595 млрд.м³ (таблица 1).

Таблица 1 - Объемы подачи воды в озерные системы дельты реки Сырдария за 2000–2026 годы, млн.м^3

Водная система	2000	2005	2007	2024	2025	2026*	Изменение 2025 к 2024, %	Изменение 2026 к 2025, %
Приморская правобережная	128,59	16,50	6,38	9	11	–	+22,2	–
Приморская левобережная	1,12	1,50	0,84	1,05	1,14	–	+8,6	–
Камыстыбасская	255,85	277,01	190,62	531	753	395	+41,8	−47,5
Акшатауская	154,90	174,29	77,11	299	423	191	+41,5	−54,8
Итого	540,46	469,30	274,11	839	1176	586	+40,2	−50,2
Примечание: * – данные за 2026 год приведены по состоянию на I полугодие (до 1 июля).								

Сравнительный анализ основных гидрохимических и морфометрических показателей Камыстыбасской, Акшатауской и Приморской озерных систем показывает существенную пространственную дифференциацию условий водной среды. Наиболее благоприятные гидрологические и гидрохимические характеристики отмечены для Камыстыбасской озерной системы, тогда как в Приморской системе наблюдается комплекс признаков, указывающих на более высокую степень антропогенной и естественной трофической нагрузки. Глубина водоемов исследуемых озерных систем характеризуется выраженной пространственной изменчивостью: в Камыстыбасской системе она составляет 2,4–12,0 м, в Акшатауской — 1,8–6,5 м, тогда как в Приморской системе варьирует в пределах 1,1–3,5 м. Наибольший диапазон глубин и максимальные значения отмечены в Камыстыбасской системе, что свидетельствует о более выраженной морфометрической неоднородности ее водоемов. Таким образом, Камыстыбасская система характеризуется наиболее сложным вертикальным строением водоемов и наличием участков значительной глубины. Мелководность Приморской системы, напротив, способствует более интенсивному прогреву водной толщи, перемешиванию донных отложений и ускорению биогеохимических процессов. Различия по глубине согласуются с показателями

прозрачности воды. В Камыстыбасской системе прозрачность по диску Секки составляла 1,2–1,8 м, в Акшатауской — 0,8–1,1 м, тогда как в Приморской системе она снижалась до 0,45–0,60 м. Низкая прозрачность в Приморской системе может быть связана с повышенным содержанием взвешенных веществ, развитием фитопланктона и поступлением биогенных элементов. Более высокая прозрачность Камыстыбасской системы свидетельствует о сравнительно меньшей мутности и/или меньшей концентрации взвешенного органического вещества.

По показателю общей минерализации (TDS) также выявлена выраженная межсистемная изменчивость. В Камыстыбасской системе значения находились в пределах 2,5–3,6, в Акшатауской — 1,6–2,3, а в Приморской — 2,5–4,6 мг/дм³. Максимальные значения отмечены в Приморской системе, что может свидетельствовать о более интенсивном накоплении растворенных минеральных компонентов вследствие мелководности, испарительного концентрирования и особенностей водообмена. Основными ионами преобладающего гидрокарбонатно-сульфатного класса являются SO_4 (400–750 мг/дм³) и Na+ K (300–550 мг/дм³). В слабопроточных и тупиковых плёсах дельтового комплекса солевой режим смещается в сторону увеличения хлоридов и натрия. При падении глубин до 1,0–1,2 м минерализация возрастает до 4,5–6,8 г/дм³, с трансформацией ионного соотношения: $Cl^- > SO_4^{2-} - Na^+ > Ca^{2+} > Mg^{2+}$;

Таблица 2 - Физико-химические и гидрохимические показатели воды дельтовых озерных систем р.Сырдария

Показатель	Камыстыбаская система	Акшатауская система	Приморская система (правобережная, левобережная)
Глубина,м	2,4 - 12	1,8-6,5	1,1-3,5
Прозрачность (диск Секки), м	1,2–1,8	0,8–1,1	0,45–0,60
Минерализа-ция (TDS), мг/дм³	2,5–3,6	1,6-2,3	2,5-4,6
Водородный показатель (pH)	8,15–8,35	8,20–8,45	8,45–8,60
Растворенный O_2, мг/дм³	8,5–9,8	7,2–8,4	6,2–7,1
Азот аммонийный (NH_4), мг/дм³	0,12–0,25	0,30–0,45	0,50–0,75
Азот нитратный (NO_3), мг/дм³	1,10–1,85	1,40–2,10	2,10–3,20
Фосфор общий (PO_4), мг/дм³	0,004–0,008	0,009–0,04	0,05–0,13

Значения pH во всех трех системах характеризовали воду как слабощелочную. В Камыстыбасской системе pH составлял 8,15–8,35, в Акшатауской — 8,20–8,45, а в Приморской — 8,45–8,60. Наиболее высокие значения pH в Приморской системе могут быть обусловлены интенсивной фотосинтетической активностью водной растительности и фитопланктона, при которой происходит поглощение растворенного CO_2 и, соответственно, увеличение щелочности водной среды. Особого внимания заслуживает содержание растворенного кислорода. Наиболее высокие его концентрации зарегистрированы в Камыстыбасской системе — 8,5–9,8 мг/дм³, несколько ниже — в Акшатауской системе — 7,2–8,4 мг/дм³, а минимальные значения отмечены в Приморской системе — 6,2–7,1 мг/дм³. Такая последовательность в целом согласуется с различиями прозрачности, глубины и содержания биогенных соединений. Относительно высокая концентрация кислорода в Камыстыбасской системе указывает на более благоприятные условия газового режима для гидробионтов. Снижение концентрации кислорода в Приморской системе может быть связано с повышенной биологической продуктивностью и усиленным потреблением кислорода при разложении органического вещества. Наиболее выраженные различия между системами наблюдаются по соединениям азота. Концентрация аммонийного азота (NH_4) в Камыстыбасской системе составляла 0,12–0,25 мг/дм³, в Акшатауской — 0,30–0,45 мг/дм³, а в Приморской достигала 0,50–0,75 мг/дм³. Таким образом, содержание аммонийной формы азота последовательно возрастает от Камыстыбасской к Приморской системе. Повышенная концентрация NH_4 может быть связана с поступлением органического вещества, процессами его разложения, недостаточным водообменом и особенностями мелководных участков. Аналогичная закономерность отмечается для нитратного азота (NO_3). В Камыстыбасской системе его концентрация составляла 1,10–1,85 мг/дм³, в Акшатауской — 1,40–2,10 мг/дм³, а в Приморской — 2,10–3,20 мг/дм³. Содержание фосфора (PO_4) также возрастало в направлении от Камыстыбасской к Приморской системе. В Камыстыбасской системе его концентрация составляла 0,004–0,008 мг/дм³, в Акшатауской — 0,009–0,04 мг/дм³, а в Приморской — 0,05–0,13 мг/дм³. Повышенное содержание минеральных форм азота в Приморской системе свидетельствует о большей доступности биогенных элементов и потенциально более высокой интенсивности процессов первичной продукции.

В целом полученные данные позволяют выделить градиент экологического состояния исследованных озерных систем. Камыстыбасская система характеризуется большей глубиной, относительно высокой прозрачностью, повышенным содержанием растворенного кислорода и минимальными концентрациями соединений азота и фосфора [11]. Акшатауская система занимает промежуточное положение по большинству рассмотренных параметров. Приморская система отличается меньшей глубиной и прозрачностью, повышенной минерализацией, более высоким pH и максимальными концентрациями азотных и фосфорных соединений при относительно низком содержании растворенного кислорода.

Выводы. В целом озерные системы дельты Сырдария характеризуются выраженной пространственной и гидрохимической неоднородностью, обусловленной различиями в их морфометрических характеристиках и степени водообеспеченности. Камыстыбасская система отличается большей глубиной, высокой прозрачностью воды и относительно высоким содержанием растворенного кислорода при невысоких концентрациях биогенных элементов, что свидетельствует о более благоприятных условиях для функционирования водных экосистем и рыбохозяйственного использования. Акшатауская система занимает промежуточное положение, тогда как Приморские системы (правобережная и левобережная) характеризуются мелководностью, сниженной прозрачностью, повышенной минерализацией и более высокими концентрациями соединений азота и фосфора.

Стабильность гидрологического режима дельтовых водоемов определяется величиной речного стока, режимом водоподачи из вышерасположенных водохранилищ и регулируемыми попусками через гидротехнические сооружения «Аспай» и «Аклак». Для поддержания устойчивого состояния озерных систем необходимо обеспечивать достаточный объем аккумулируемой воды с учетом сезонных потерь на испарение, фильтрацию и регулируемый отток. При нормальной водности ориентировочный суммарный объем воды в исследуемых дельтовых водоемах должен составлять около 1,2 млрд.м³, что соответствует площади водного зеркала и обводненных угодий порядка 700–850 км². Снижение водообеспеченности ниже данного уровня приводит к уменьшению площади и объемов водоемов, изменению гидрохимических условий и повышению риска деградации отдельных озерных систем. Таким образом, поддержание оптимального водного режима является одним из ключевых условий сохранения экологической устойчивости, биоразнообразия и рыбохозяйственной продуктивности дельты Сырдария.

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Sentiment Analysis of Social Media Data Using an Ensemble of Classical Models and RoBERTa

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Abstract. The use of social media data for sentiment analysis presents a number of important challenges because the nature of user-generated text is often informal and noisy and is heavily dependent on context. Classical machine learning algorithms provide efficient computations but do not typically account for the very deep semantic properties of the text they analyse, whereas transformer-based models, such as RoBERTa, are able to provide a much richer understanding of context but require substantial computational resources. In this research, we employ an ensemble architecture which combines three classical classifiers (SVM, LR, and XGBoost) with a fine-tuned RoBERTa model, making predictions with this combined framework using a soft-vote method for classifying the sentiments of social media textual data. We evaluate the ensemble architecture on three benchmark datasets (Sentiment140, IMDb, Twitter US Airline) and find that the ensemble outperformed RoBERTa alone on the IMDb dataset by 1.42 percentage points (92.51% accuracy), with the ensemble much more closely matching the performance of RoBERTa on the Sentiment140 and Twitter US Airline datasets while maintaining significantly more balanced scores for precision and recall. The ensemble produced no additional training overhead in comparison to RoBERTa and the total inference cost was negligible when compared to the time required to fine-tune the RoBERTa model (up to 3,096 seconds). The results of this research indicate that the combination of lightweight classical classifiers with a transformer architecture via a soft voting ensemble yields a generalisable and computationally practical architecture for performing sentiment analysis of social media data.

Keywords: Sentiment analysis, Ensemble learning, RoBERTa, Support Vector Machine, Logistic Regression, XGBoost, Soft voting, Natural language processing, Text classification.

1. Introduction

The rise of social media has resulted in a complete re-thinking of how individuals articulate views and share experiences with each other as part of their conversation with society through public discourse. According to the latest statistics from Twitter, it alone produces over 500 million tweets per day (Kumar & Sadanandam, 2024), and therefore social media is one of the most extensive systems of real-time human emotion available today. As such, it has become critical across a number of different domains to analyse sentiment (automatically classifying emotive responses) derived from social media communication. Applications range from Business Intelligence where companies/marketers analyse sentiment to understand customer views (known as “Voice of the Customer”) to Public Health where social media has been used to track mental health trends (Kumar et al., 2025; Alahmadi et al., 2025), to Government where individuals use social media to share their opinions on government policy (Ali & Hendrastuty, 2024).

While there are many opportunities in terms of the richness of available data from social media to be analysed, there are equally significant technical challenges in performing so. Traditional models for analysing text, especially when utilising machine learning, are poorly suited for analysing informal types of communication such as those used on social media (i.e. informal language, misspellings, emojis, short forms, and contextual ambiguity) (Maryam et al., 2025). In addition to issues associated with informal language, text that is ambiguous (e.g. syntactically, structurally, or lexically) presents a major challenge to the use of machine learning algorithms for the analysis of social media communication (Kumar et al., 2025).

Initial approaches to sentiment analysis included classical machine learning models such as SVM, Logistic Regression, and Naive Bayes. SVMs provide excellent accuracy as well as an adaptable way to create the hyperplane with the maximum amount of separation between two types of data points (Hayadi & Maulita, 2025). Nonetheless, classical machine learning provides a key disadvantage: they need a large amount of manual effort to create the features to model the data and do not have any capability to learn complex structures in the language automatically (Pimpalkar et al., 2025). Specifically, they struggle with complex linguistic structures such as irony, sarcasm, and negation (Alahmadi et al., 2025).

The advent of transformer-based models has addressed many of these limitations. RoBERTa is an improved version of BERT that was trained for longer to improve performance and incorporated novel dynamic masking strategies to help create better models of the nuances of language used in social media, including sarcasm, irony, and humour (Maryam et al., 2025; Kumar & Sadanandam, 2024). Although transformer models provide much better contextual understanding than do classical machine learning approaches, they are computationally too costly to deploy on their own.

Ensemble techniques have the potential to improve the predictive performance of a number of different types of models by integrating the unique advantages of each model of interest into a single ensemble. Ensemble methods are often successful in reducing the variance of a model and enhancing its ability to predict outcomes (Alahmadi et al., 2025). However, the systematic combination of classical machine learning classifiers with RoBERTa in an ensemble configuration for sentiment analysis on social media has not yet been examined in the extant literature. Additionally, the majority of studies investigating ensemble analysis for sentiment classification have failed to evaluate the proposed framework across multiple domains and classification conditions, limiting the generalizability of their findings (Alahmadi et al., 2025).

This research aims to bridge this gap by proposing and evaluating an ensemble framework that synthesises classical machine learning classifiers with RoBERTa for sentiment analysis on social media text, evaluated across three different benchmark datasets featuring different domains and classification conditions.

1.1 Problem Statement

The current research on sentiment analysis is based either on traditional statistical/machine learning models that are very quick to compute, however, these models do not have the capability to understand semantics and capture the context of words; or on transformer-based models like RoBERTa that have much better accuracy but at a high computational cost. A unified ensemble approach combining both model types has been very seldom used to perform social media sentiment analysis. In addition, the generalizability of ensemble frameworks created within this methodology, between various domains and multiclass environments has not been thoroughly reviewed.

1.2 Objectives

The goals of this research are fourfold: First, to analyze contemporary approaches (both classical and transformer-based) applied to sentiment analyses of social media. Second, to develop and test an ensemble model that integrates classical classification methods (support vector

machines, logistic regression, XGBoost) with a RoBERTa transformer for sentiment classification of social media text. Third, to compare and evaluate the performances of the separate models with the ensemble using numerous metrics (accuracy, F1 Score, precision, and recall) on a benchmark dataset. Fourth, to evaluate the circumstances under which the ensemble outperforms the separate models and to outline the implications for practical use in social media sentiment analyses. Fifth, to determine the extent to which the ensemble can be generalized across multiple benchmark datasets and text domains.

1.3 Novelty and Contribution

While prior work on sentiment analysis has explored both classical machine learning models and transformer-based architectures extensively, the combination of the two within a unified ensemble framework has received comparatively little attention. Existing ensemble approaches either stack multiple transformer models together, which yields high accuracy but demands substantial computational resources, or combine classical classifiers exclusively, which sacrifices the semantic depth required to handle informal and contextually dependent social media text effectively.

This research introduces a soft voting ensemble that deliberately pairs the complementary strengths of both model families. SVM and Logistic Regression are well-established linear classifiers that generalise reliably on high-dimensional sparse TF-IDF representations and produce well-calibrated probability outputs. XGBoost contributes non-linear feature interaction modelling through sequential tree construction. RoBERTa, as the transformer component, provides deep bidirectional contextual understanding that classical models are structurally unable to replicate. The novelty lies not in any single model, but in the deliberate architectural decision to combine these four models through soft voting, allowing each to contribute its probability estimates proportionally, thereby moderating individual model biases and producing a more balanced final prediction.

A further distinguishing characteristic of this research is its multi-dataset evaluation strategy. Rather than validating the framework on a single benchmark, experiments are conducted across three datasets spanning distinct text domains and classification settings: short-form binary Twitter data (Sentiment140), longer-form binary movie reviews (IMDb), and multi-class airline Twitter sentiment (Twitter US Airline). This design choice allows for a systematic investigation of when and why the ensemble advantage materialises, yielding practically actionable insights about the conditions under which combining classical and transformer models is most beneficial.

2. Related Work

Table 1. Related Work on Sentiment Analysis

No.	Authors	Year	Application	Techniques Used	Research Gap
1	Adamu et al.	2026	Multilabel text emotion detection	Hybrid stacking, Random Forest meta-classifier, BERT, DistilBERT, RoBERTa, mBERT	Does not explore fine-grained or context-dependent emotional phenomena beyond predefined dataset categories
2	Alshehri et al.	2026	Arabic tweet speech act classification	Weighted ensemble, AraBERT, transformer-based data augmentation, LIME explainability	Struggles to predict a single speech act when a sentence contains multiple overlapping acts
3	Islam et al.	2026	Depression emotion and severity detection	Diversity-aware transformer ensemble, weighted soft voting, DistilBERT, ALBERT, XLM-RoBERTa, DeBERTa, BiLSTM, LIME	Performance on minority labels such as suicidal intent remains low due to significant class imbalance
4	Mansour et al.	2026	Twitter hate speech detection	Lexicon-guided contextual attention, RoBERTa fine-tuning, attention visualization, LIME	May not generalize to emerging coded expressions or euphemistic forms of hate speech
5	Al-Qudah et al.	2025	Restaurant review sentiment	Ordinal regression, PSO, XGBoost	Fails to detect irony and sarcasm in reviewer sentiments
6	Alahmadi et al.	2025	Sentiment analysis survey	ML, Deep Learning, Transformers, Hybrid architectures	Deep learning models lack interpretability and cross-domain robustness
7	Almalki	2025	Multilingual sentiment detection	mBERT, XLM-R, T5, SVM	High misclassification of neutral sentiment in short social media posts
8	Hayadi & Maulita	2025	Education discourse sentiment	SVM, Exploratory Data Analysis	Platform-specific bias limits generalizability to informal language
9	Kumar et al.	2025	Sentiment analysis review	CNN, LSTM, BERT, GPT, T5, SVM, Naïve Bayes	Struggles with sarcasm and lacks cross-domain transfer robustness
10	Maryam et al.	2025	Social media text classification	RoBERTa fine-tuning	Truncation causes context loss; class imbalance reduces neutral accuracy
11	Mustofa & Saptomo	2025	Social media text analysis	Naïve Bayes, SVM, BERT	High computational cost of deep learning hinders real-world deployment

No.	Authors	Year	Application	Techniques Used	Research Gap
12	Pimpalkar et al.	2025	Deep learning SA survey	RNN, LSTM, CNN, BERT, GPT	Significant gaps in handling ambiguity and lack of adversarial robustness
13	Rahman et al.	2025	Context-aware sentiment analysis	RoBERTa-BiLSTM	Results sensitive to preprocessing strategies and imbalanced datasets
14	Ali & Hendrastuty	2024	Public sentiment analysis	Naïve Bayes, SVM, Random Forest, SMOTE	Lacks contextual understanding provided by pre-trained transformer models
15	Cam et al.	2024	Financial tweet sentiment	NB, LR, SVM, KNN, DT, MLP	Single platform and language; no deep learning or multimodal expansion
16	Chauhan et al.	2024	Aspect-based SA	BERT-SPC, AEN-BERT, ATAE-LSTM	Inconsistent across domains; fails on informal technical product language
17	Jahin et al.	2024	Tweet sentiment analysis	RoBERTa, Attention, BiLSTM (TRABSA)	No multimodal integration; interpretability techniques need refinement
18	Kp et al.	2024	Tweet sentiment classification	Ensemble (SVM, RF, DT), AdaBoost	Classical ensemble components lack transformer-based contextual embeddings
19	Kumar & Sadanandam	2024	COVID-19 tweet sentiment	BERT, RoBERTa, Fusion architecture	Small labeled datasets constrain transformer fusion architecture performance
20	Miah et al.	2024	Cross-lingual sentiment analysis	Ensemble of RoBERTa, BERTweet, GPT-3	Translation biases hinder effective cross-lingual adaptation
21	Yibeyin et al.	2024	Broadcast opinion mining	LSTM, GRU, BiLSTM, CNN-BiLSTM	Cannot classify sarcasm; limited to single language
22	Bengesi et al.	2023	Outbreak sentiment polarity	KNN, SVM, RF, LR, MLP, NB, XGBoost	Relies on basic polarity without word embeddings or deep learning

2.1 Sentiment Analysis of Social Media Data

Sentiment analysis is one of the basic tasks in Natural Language Processing and it has received a great deal of attention from researchers. The majority of published research on sentiment analysis has relied upon data collected from social media sites and has been applied to many different application areas. As documented in detail in the comprehensive review by Alahmadi et al. (2025), there is tremendous opportunity for using sentiment analysis to evaluate mental health trends and develop guidelines to improve consumer good performance. However, most prior work has been based on English corpus data only, thus limiting the applicable scope of many of the resultant conclusions to a single language and raising concerns about the

generalizability of findings to non-English-language populations. One major challenge related to social media data is that there is a high prevalence of sarcasm among tweets. Sarcasm often presents itself through an expression of sentiment that may be at odds with an individual's true feelings about the expressed content. The work of Yacoub et al. (2024) has demonstrated that the usage of sarcasm can result in an inversion of the true sentiment and lead to a systematic error in classifying a piece of data; a common obstacle identified in their work is the lack of context. In addition to being able to analyse sarcasm, sentiment analysis has been used to evaluate actual events occurring at a societal level with implications on public health. In their evaluation of 56 models using Twitter data surrounding the Monkeypox outbreak, Bengesi et al. (2023) found that their models achieved accuracies from 0.65 to 0.93; however, they also pointed out that many previous studies do not include details of exact preprocessing steps used, making reproducibility more difficult. Hayadi and Maulita (2025) have conducted research to identify sentiment on Indonesian Twitter with regard to education reform. They applied Support Vector Machines and found that 91.75% of tweets were classified correctly as either positive or negative. They also indicated that neutrality of sentiment predominates within Twitter conversations; therefore, it is likely that the presence of neutral tweets may mask underlying attitudes held by the public. These examples illustrate how vibrant and active the area of social media sentiment analysis research is. However, they also suggest that challenges remain related to how to address the multitude of languages, sarcasm, and representational language (i.e., jargon) used in specific fields of study on social media.

2.2 Classical Machine Learning Approaches

Sentiment analysis has been dominated for the past decade by classical machine learning models such as Support Vector Machines. SVM has traditionally performed well in many different domains. For example, Cam et al. (2024) utilized SVM and Multilayer Perceptron to analyze Turkish financial Twitter data and achieved 89% accuracy using SVM, but found a lack of ability from SVM in terms of context-aware methods for capturing nuances in financial data. Likewise, Al-Qudah et al. (2025) compared SVM, Naïve Bayes, and Random Forest when classifying restaurant reviews and found SVM to generate the highest accuracy (94.56%) while noting that XGBoost is increasingly being used but is difficult to tune due to the number of hyperparameters that it contains.

According to the research conducted by Mustofa and Saptomo (2025) on informal social media data, Naïve Bayes was able to achieve 68% and SVM was able to achieve 75% accuracy, with both models struggling to accurately understand informal language and slang on Twitter and Reddit. In addition, Kaur and Sharma (2023) utilized a combination of N-gram and TF-IDF representations with SVM for feature engineering on Sentiment140, achieving an F1 score of 84.5%. All of these studies indicate that while the performance of classical models is high for computational efficiency and interpretability, there is an inherent limit to the performance of the models as they are unable to handle large quantities and diversity of online data without extensive manual feature engineering and unable to model the semantics of the data deeply enough to produce meaningful predictions or classifications. As such, the studies collectively serve as motivation for adopting a more powerful architecture to improve prediction/classification accuracy.

2.3 Transformer-Based Approaches

Transformers have revolutionized sentiment analysis. Sentiment analysis has been advanced by the introduction of transformer-based models into the field. RoBERTa has proven to be one of the most successful models for analyzing the sentiments of text from social media sources. Maryam et al. (2025) trained a RoBERTa-base model on a combination of the Twitter and IMDB data set and achieved a validation accuracy of 87%. They also observed that when truncating the fixed input size to 128 tokens, this caused a slight performance degradation on longer reviews

when classifying the sentiment of social media text. Almalki (2025) examined XLM-R, mBERT, and T5 for the purposes of classifying the sentiments of users' posts from multiple social media platforms; XLM-R, which was trained with the Multi-lingual BERT (mBERT) and T5, received the highest F1-score of 90.30%. He also noted that misclassification rates, at 16.20%, were especially high for neutral sentiments. Researchers have also sought to augment BERT using external knowledge beyond BERT's own parameters. Mutinda et al. (2023) introduced LeBERT, which combined a sentiment lexicon with BERT and CNN, for sentiment analysis and achieved an F-measure of 88.73%. They proposed that in future studies, LSTM models should complement LeBERT's performance by being applied to the sentiment lexicon. Chauhan et al. (2024) used BERT-SPC to evaluate the sentiments of specific aspects of computers using the SemEval-2014 dataset and achieved an accuracy rate of 84.98% for laptops; however, they observed limitations in determining the overall sentiment of products based upon the specific aspect categories that identified product types.

More recent transformer-based work from 2026 has extended fine-tuning strategies to increasingly specialised and challenging classification tasks on social media text. Mansour et al. (2026) proposed a lexicon-guided contextual attention mechanism built on top of fine-tuned RoBERTa for hate speech detection on Twitter, achieving a peak accuracy of 98.2% and a macro-F1 score of 0.95. The authors noted, however, that the model may fail to generalise to emerging coded expressions and euphemistic language, a limitation that is consistent with the broader challenge of handling evolving informal vocabulary on social media. Alshehri et al. (2026) applied a weighted ensemble of pre-trained transformer models including AraBERT for classifying Arabic speech acts on Twitter, achieving a macro-F1 of 0.74 and accuracy of 0.85 on the ASAD dataset. Their work highlights that transformer-based approaches, while powerful, continue to struggle when a single utterance contains multiple overlapping communicative acts, a challenge that is structurally similar to the ambiguity problem encountered in multi-class sentiment classification.

2.4 Ensemble Approaches

Ensemble methods have gained considerable attention as a strategy for combining the strengths of multiple models to improve sentiment classification performance. Among transformer-based ensembles, Semary et al. (2023) combined RoBERTa with CNN and LSTM layers, achieving 96.28% accuracy on IMDb and 94.2% on Twitter airline reviews, though training was noted to be computationally expensive. Kumar and Sadanandam (2024) proposed a fusion architecture concatenating BERT and RoBERTa embeddings on COVID-19 tweets, achieving 94.3% accuracy and surpassing individual model results, but at the cost of high computational overhead for deployment. Jahin et al. (2024) integrated RoBERTa with attention mechanisms and BiLSTM, achieving a macro average accuracy and F1-score of 94% on UK COVID-19 Twitter data, though the additional layers added significant computational overhead. Rahman et al. (2025) further confirmed this trend, with their RoBERTa-BiLSTM model achieving 92.36% on IMDb and 80.74% on airline reviews, noting that results are subject to variability based on experimental platforms.

Among classical ensemble approaches, Kp et al. (2024) combined Random Forest, SVM, and Decision Tree using AdaBoost, achieving 93.42% accuracy on paragraph-level classification, though increased decision tree depth introduced high variance. Hu et al. (2024) applied a stacking classifier on disaster tweets, achieving a balanced accuracy of 80%, noting that the rationale behind predictions in complex ensembles remains difficult to interpret. For cross-lingual scenarios, Miah et al. (2024) combined RoBERTa, BERT, and GPT-3 on translated multi-source datasets, achieving over 86% accuracy, though language discrepancies required significant additional integration effort. Finally, Yibeyin et al. (2024) demonstrated that a hybrid CNN-BiLSTM model achieved 96.08% accuracy on Amharic social media comments using word2vec embeddings, though sarcastic opinions were systematically misclassified.

Two further ensemble studies from 2026 reinforce the trend toward combining multiple transformer architectures through stacking and soft voting strategies. Adamu et al. (2026) proposed a hybrid stacked ensemble that combines BERT, DistilBERT, RoBERTa, and mBERT using a Random Forest meta-classifier for multilabel emotion detection, with their best configuration achieving F1-scores of 89.48, 88.19, and 90.67 across three datasets. Their results confirm that stacking diverse transformer models through a learned meta-classifier can yield strong multilabel performance, though the authors acknowledge that fine-grained or context-dependent emotional phenomena beyond predefined label sets remain unaddressed. Islam et al. (2026) proposed DepTformer-XAI-SV, a diversity-aware ensemble combining DistilBERT, ALBERT, XLM-RoBERTa, DeBERTa, and BiLSTM through weighted soft voting with post-hoc LIME explanations for depression and severity detection, achieving macro-F1 scores of 80.44% and 79.88% respectively. Importantly, their work demonstrates that soft voting over diverse transformer architectures provides measurable gains over individual models, directly supporting the ensemble design rationale adopted in this research, while also noting that class imbalance remains a persistent limitation for minority sentiment labels.

An analysis of the current literature on ensemble learning indicates that to date there has been little examination of pairing lightweight classical classifiers with a high-performance transformer, specifically RoBERTa. Existing research on ensembles either develops an ensemble of multiple transformer models resulting in a higher level of accuracy but at an unreasonable computational cost, or develops an ensemble using only classical classifiers resulting in lower levels of semantic information. The absence of a systematic examination of ensemble models with the use of a combination of lightweight classical classifiers, i.e., SVM, Logistic Regression and XGBoost, and one powerful transformer discriminant, i.e., RoBERTa, represents an excellent opportunity to balance predictive performance with computational efficiency. This research is a response to this gap in the literature.

3. Methodology

3.1 Datasets

To evaluate the extent to which the proposed ensemble architecture can generalize, three publicly available benchmark datasets were used for experimentation, each dataset comprised of two or more classifications within distinct text domain categories.

The first dataset, Sentiment140 (Bengesi et al., 2023), contains 1.6 million tweets taken from the Twitter platform. Each tweet in the dataset was assigned either a positive or negative label via a distant-supervision method utilizing emoticons to make the label assignment. For the purpose of experimentation, a 60,000 sample set (30,000 positive and 30,000 negative) was created from the total sample to account for issues regarding computational feasibility and statistical reliability.

The second dataset, IMDb Movie Reviews (Mutinda et al., 2023), provides 50,000 English language movie reviews (i.e., 25,000 positive and 25,000 negative) written by users on the IMDb website. Unlike the Sentiment140 dataset, the length and complexity of the movie reviews provide for a more elaborate vocabulary to utilize and contain more complex sentence structures than the tweets from the first dataset. All reviews from this dataset will be utilized for experimentation.

The third dataset, Twitter US Airlines (Kp et al., 2024), contains 14,640 tweets directed toward major US airline companies. The dataset contains tweets assigned to three-class partitions (i.e., negative, neutral, and positive) based on sentiment. This dataset serves as an example of creating a multi-class classification scenario and is also a dataset where the ensemble will be tested using an imbalanced distribution among sentiment classes. All tweets will be utilized from this dataset during experimentation.

In order to ensure the integrity of each dataset's class distribution, a stratified train/test data split was applied. Key characteristics of the datasets are shown in Table 2.

Table 2. Datasets used in this research

Dataset	Classes	Samples	Split (Train/Test)
Sentiment140	2	60,000	47,776 / 11,945
IMDb	2	50,000	40,000 / 10,000
Twitter US Airline	3	14,620	11,696 / 2,924

3.2 Data Preprocessing

There are seven sequential steps in the preprocessing pipeline that will be applied consistently to all samples using the same means. The first step, data cleaning, involves removing any URLs, user mentions, special symbols, emojis, and non-alphabetic characters from the raw text. The second step will convert all text to lowercase, creating consistent representation across all tokens. The third step, normalization, limits the number of repetitions in a character string to two at most, since this is a common practice when writing informal elongated words (e.g., “soooo”). The fourth step involves erasing all punctuation and any outstanding special characters but retaining apostrophes when found alongside negating contractions (e.g., “didn't” and “isn't”). The fifth step uses tokenization to divide cleaned text into individual tokens based on whitespace boundaries. The sixth step uses the NLTK stop word list to remove common English stop words from the tokens; however, any negation words (i.e., “not” or “never”) will be preserved because they are specifically relevant to attached sentiment. The seventh step uses the WordNet Lemmatizer to convert each token to its base form.

For the classical models, preprocessed text is represented using Term Frequency-Inverse Document Frequency (TF-IDF) vectorization with a maximum vocabulary size of 50,000 features and unigram and bigram combinations. For RoBERTa, the raw cleaned text is tokenized using the RoBERTa tokenizer with a maximum sequence length of 128 tokens, consistent with prior work (Maryam et al., 2025).

3.3 Classical Models

Three classical machine learning classifiers are trained on TF-IDF representations of the preprocessed tweets.

Support Vector Machine (SVM) is a supervised learning algorithm that identifies an optimal hyperplane maximizing the margin between classes in a high-dimensional feature space (Hayadi & Maulita, 2025). A linear kernel is used given the high dimensionality of TF-IDF features, with the regularization parameter C set to 1.0.

Logistic Regression (LR) is a probabilistic linear classifier that models the posterior probability of class membership using a sigmoid function. It is well-suited for high-dimensional sparse text features and produces well-calibrated probability outputs required for soft voting. The maximum number of iterations is set to 1,000 with L2 regularization.

Extreme Gradient Boosting (XGBoost) is an ensemble tree-based method that builds models sequentially, with each tree correcting the residual errors of the previous one. XGBoost is particularly effective at capturing non-linear feature interactions that linear models may miss. The number of estimators is set to 300 with a learning rate of 0.1 and maximum tree depth of 6.

All three classifiers are implemented using the scikit-learn and XGBoost Python libraries. Hyperparameters are selected based on values reported in related literature and applied consistently across all classical models.

3.4 RoBERTa Fine-Tuning

RoBERTa (Robustly Optimized BERT Pretraining Approach) is a transformer-based language model that improves upon BERT through extended training duration, larger batch sizes, and

dynamic masking strategies (Maryam et al., 2025). The roberta-base pre-trained model from the HuggingFace Transformers library is used as the foundation and fine-tuned for sentiment classification, with the number of output classes set to match each dataset: two classes for Sentiment140 and IMDb, and three classes for Twitter US Airline.

A classification head consisting of a dropout layer (rate = 0.1) followed by a fully connected linear layer is appended to the [CLS] token representation of the final transformer layer. The model is fine-tuned end-to-end for 3 epochs using the AdamW optimizer with a learning rate of 2×10^{-5} and a linear warmup schedule over the first 10% of training steps. The batch size is set to 32. Binary cross-entropy loss is used as the training objective. Fine-tuning is performed on a GPU-enabled environment. The fine-tuned RoBERTa model outputs class probabilities for each sample, which are used directly in the ensemble.

Figure 1 presents the training loss and accuracy progression of RoBERTa across three epochs on each dataset. On all three datasets, training loss decreases consistently across epochs while training accuracy increases, confirming that the model converges appropriately without signs of overfitting. The steeper initial loss drop on IMDb reflects the richer lexical structure of movie reviews, which provides stronger gradient signal during early fine-tuning. These curves serve as empirical evidence that the fine-tuning configuration used in this research is stable and produces a well-trained transformer component for the ensemble.

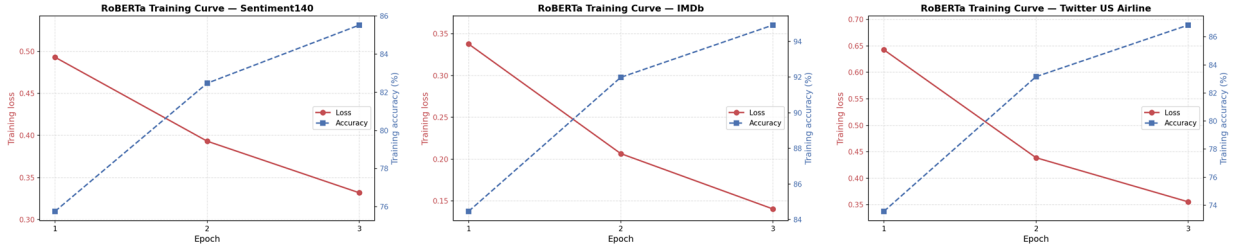

Figure 1. RoBERTa training loss and accuracy across three fine-tuning epochs: (a) Sentiment140, (b) IMDb, (c) Twitter US Airline.

3.5 Ensemble Design

The proposed ensemble combines the outputs of the three classical classifiers and the fine-tuned RoBERTa model using a soft voting strategy. In soft voting, each model produces a probability distribution over the sentiment classes for a given input. The final ensemble prediction is determined by averaging these probability distributions across all four models and selecting the class with the highest mean probability:

$$\hat{y} = arg\ max_c\ (1/N)\ \Sigma_{i=1}^{N}\ p_i(c) \qquad (1)$$

where $\hat{y}$ is the predicted class, N = 4 is the number of base models, and $p_i(c)$ is the predicted probability of class c by model i.

This strategy is chosen because all four models output calibrated class probabilities, soft voting preserves the confidence information of each model rather than discarding it as in hard voting, and it is computationally efficient (Kp et al., 2024). The ensemble is implemented using a custom voting wrapper that combines scikit-learn model outputs with RoBERTa softmax probabilities into a unified prediction pipeline. Algorithm 1 presents the full procedure covering both the training and inference phases of the proposed framework.

Figure 2 presents the proposed framework architecture, illustrating the complete data flow from raw social media text through to the final sentiment prediction. The framework operates in two structurally independent streams that share only the preprocessing stage. In the classical stream, preprocessed text is transformed into a sparse numerical matrix through TF-IDF vectorization, which encodes term frequency weighted by inverse document frequency across a vocabulary of 50,000 unigrams and bigrams. This representation is then consumed independently by SVM, Logistic Regression, and XGBoost, each of which produces a two- or three-dimensional probability vector over the sentiment classes. In the transformer stream, the same preprocessed

text is passed to the RoBERTa tokenizer, which converts it into subword token sequences padded to 128 tokens. The fine-tuned RoBERTa model processes these sequences through its twelve transformer layers and outputs class probabilities via a softmax classification head appended to the [CLS] token representation.

The outputs of all four models converge at the soft voting layer, where their probability vectors are averaged element-wise. The class index with the highest average probability is selected as the final prediction. This design deliberately keeps all four base models independent during both training and inference. Independence is important because it ensures that the error patterns of the classical models and RoBERTa remain uncorrelated; when one model is wrong for structural reasons (such as TF-IDF's inability to capture contextual negation), another may compensate through different representational strengths. The result is a more stable and balanced classifier than any individual component can achieve alone.

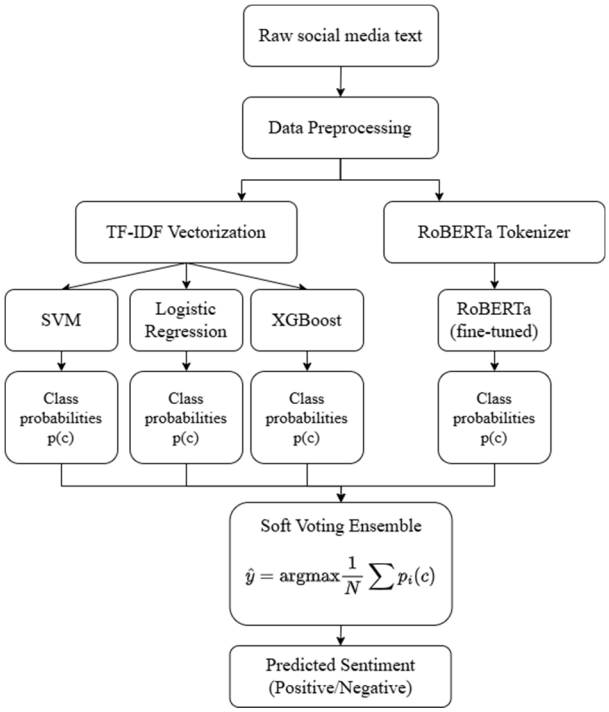

Figure 2. The proposed ensemble architecture for sentiment analysis.

Algorithm 1. Soft Voting Ensemble for Sentiment Classification

Require: Preprocessed tweet x, trained models M = {SVM, LR, XGBoost, RoBERTa}

Ensure: Predicted sentiment class $\hat{y} \in \{0, 1\}$ for binary datasets or $\hat{y} \in \{0, 1, 2\}$ for three-class datasets

Training Phase

Extract TF-IDF features: f ← TF-IDF(x)
Train SVM on f with linear kernel, C = 1.0
Train LR on f with L2 regularization, max_iter = 1000
Train XGBoost on f with n_estimators = 300, lr = 0.1, depth = 6
Tokenize x using RoBERTa tokenizer, max_len = 128
Fine-tune RoBERTa for 3 epochs with AdamW, lr = 2×10^{-5}

Inference Phase

Extract TF-IDF features: f ← TF-IDF(x)
Tokenize x: t ← RoBERTaTokenizer(x)
for each model $M_i \in M$ do
    if $M_i \in$ {SVM, LR, XGBoost} then
        $p_i \leftarrow M_i$.predict_proba(f)
    else

13: logits ← $M_i(t)$; p_i ← softmax(logits)
14: end if
15: end for
16: Compute ensemble probabilities: $P(c) = (1/N) \Sigma_i p_i(c), \forall c \in C$
17: Predict class: $\hat{y} \leftarrow \arg\max_c P(c)$
18: return $\hat{y}$

3.6 Evaluation Metrics

Model performance is evaluated using four standard classification metrics: accuracy, precision, recall, and F1-score. For Sentiment140 and IMDb, where class distributions are balanced, accuracy serves as a reliable primary metric. For Twitter US Airline, which contains an imbalanced three-class distribution, weighted precision, recall, and F1-score are used as the primary evaluation metrics alongside accuracy. The F1-score, defined as the harmonic mean of precision and recall, provides a balanced measure of classification quality and enables direct comparison with prior work (Jahin et al., 2024). Metrics were calculated based upon a held-out data set. Training and testing time (inference) for each model will also be recorded so as to provide an overview of the effectiveness of these models.

4. Results

4.1 Performance Comparison

Table 3 shows the performance of all classifiers on the Sentiment140 test set, consisting of 11,945 tweets. The highest accuracy achieved was by RoBERTa at 80.71% with 80.57% F1-score, followed by Logistic Regression as the best classical model at 77.47%. XGBoost exhibited its characteristic precision-recall imbalance (precision 71.99%, recall 80.54%), yielding the lowest F1-score of 76.02%. The ensemble (80.57% accuracy, 80.45% F1-score) closely matched RoBERTa, trailing by 0.14 percentage points in accuracy while maintaining more balanced precision and recall.

On this short, informal binary text, RoBERTa achieves the highest accuracy, while the ensemble matches it to within 0.14 percentage points and yields a more symmetric precision–recall balance.

Table 3. Performance Comparison on the Sentiment140 Dataset

Model	Acc. (%)	Prec. (%)	Rec. (%)	F1 (%)
SVM	76.79	77.02	76.31	76.67
Logistic Regression	77.47	77.85	76.77	77.30
XGBoost	74.61	71.99	80.54	76.02
RoBERTa	80.71	81.12	80.03	80.57
Ensemble Model	**80.57**	**80.91**	**80.00**	**80.45**

Table 4 presents results on the IMDb test set of 10,000 reviews. This dataset produced the strongest overall results, reflecting the richer lexical content of movie reviews compared to short-form social media text. Notably, SVM achieved the highest classical model accuracy of 91.15%, marginally outperforming Logistic Regression (90.67%), a reversal of the pattern observed on Sentiment140, consistent with SVM's known strength on longer, denser text. The ensemble achieved the highest accuracy of all models at 92.51% and an F1-score of 92.56%, surpassing RoBERTa (91.09%) by 1.42 percentage points. This is the only dataset where the ensemble outperformed all individual models, demonstrating that classical models contribute meaningful complementary features on longer-form text.

This is the most practically significant result of the study: on longer, lexically richer text the ensemble is the only configuration to surpass every individual model, indicating that classical TF-IDF features contribute signal that is complementary to the transformer.

Table 4. Performance Comparison on the IMDb Movie Review Dataset

Model	Acc. (%)	Prec. (%)	Rec. (%)	F1 (%)
SVM	91.15	90.96	91.38	91.17
Logistic Regression	90.67	90.05	91.44	90.74
XGBoost	86.17	84.77	88.18	86.44
RoBERTa	91.09	90.68	91.60	91.14
Ensemble Model	**92.51**	**92.00**	**93.12**	**92.56**

Table 5 presents results on the Twitter US Airline test set of 2,924 tweets across three classes. All metrics are weighted averages to account for class imbalance. RoBERTa achieved the highest accuracy of 83.93% and F1-score of 83.61%. The ensemble (83.24% accuracy, 82.43% F1-score) followed closely, trailing RoBERTa by 0.69 percentage points. Classical models performed comparably to each other in this setting, with SVM achieving the best classical F1-score of 78.74%.

In this imbalanced three-class setting — the most challenging evaluation condition in the study — RoBERTa leads and the ensemble follows within 0.69 percentage points. This marks a practical boundary condition: the ensemble advantage is clearest on binary or near-balanced tasks and narrows when base models are individually less confident.

Table 5. Performance Comparison on the Twitter US Airline Sentiment Dataset

Model	Acc. (%)	Prec. (%)	Rec. (%)	F1 (%)
SVM	79.79	78.93	79.79	78.74
Logistic Regression	79.00	78.59	79.00	77.21
XGBoost	78.39	77.80	78.39	78.00
RoBERTa	83.93	83.56	83.93	83.61
Ensemble Model	**83.24**	**82.81**	**83.24**	**82.43**

4.2 Cross-Dataset Comparison

Table 6 compares the performance of the ensemble model and RoBERTa across the three datasets, providing a clear view of how their relative strengths vary by domain.

Table 6. Accuracy Comparison Between RoBERTa and Ensemble Model Across Datasets

Dataset	RoBERTa (%)	Ensemble (%)	Accuracy Difference (%)
Sentiment140	80.71	80.57	−0.14
IMDb	91.09	92.51	+1.42
Twitter US Airline	83.93	83.24	−0.69

The ensemble achieves its best result on IMDb, where it slightly outperforms RoBERTa. On Sentiment140, both approaches perform almost identically, whereas on the Twitter US Airline dataset, RoBERTa shows a more noticeable advantage. This pattern indicates that the ensemble is most effective on longer and more lexically varied texts, where TF-IDF-based models can contribute complementary n-gram information. For shorter, more informal social media posts, however, RoBERTa's contextual representations are more effective, leaving limited room for classical models to add additional signal.

4.3 Computational Cost

RoBERTa fine-tuning required 3,096 seconds on Sentiment140, 2,863 seconds on IMDb, and 761 seconds on the Twitter US Airline dataset, with training time scaling roughly in line with dataset size. In contrast, the classical models trained extremely quickly, taking under 3 seconds on both Sentiment140 and Twitter US Airline. On IMDb, XGBoost required 573 seconds due to the larger training set, whereas SVM and Logistic Regression still completed in under 2 seconds. The ensemble introduced no additional training overhead on any of the datasets.

Figure 3 consolidates all fifteen model–dataset combinations into a single accuracy–time space, where marker colour identifies the model and marker shape identifies the dataset.

Among the classical models, Logistic Regression and SVM occupy almost the same near-zero region of the time axis, but their relative accuracy crosses over by domain: Logistic Regression is marginally stronger on the short, high-dimensional Sentiment140 text, whereas SVM's margin maximisation is more discriminative on the longer, denser IMDb reviews. XGBoost is the only classical model that incurs a meaningful training cost, yet it remains the least accurate on every dataset, occupying the least favourable region of the plot — neither fast nor accurate. This indicates that the non-linear feature interactions captured by gradient boosting do not translate into accuracy gains when the underlying feature space is a sparse TF-IDF matrix.

RoBERTa is the rightmost point on every dataset, illustrating the accuracy–cost trade-off inherent to large pre-trained transformers: substantial GPU time is required to reach peak contextual understanding. The ensemble, by contrast, sits at or near the origin on the time axis while matching or exceeding RoBERTa's accuracy, and therefore occupies the most favourable region of the accuracy–time space in every panel. This distinction is practically decisive in resource-constrained deployment settings — for example, a real-time brand-monitoring system without access to high-end GPU infrastructure — where the thousands of seconds separating the two points on the horizontal axis represent a real operational cost that the ensemble eliminates entirely.

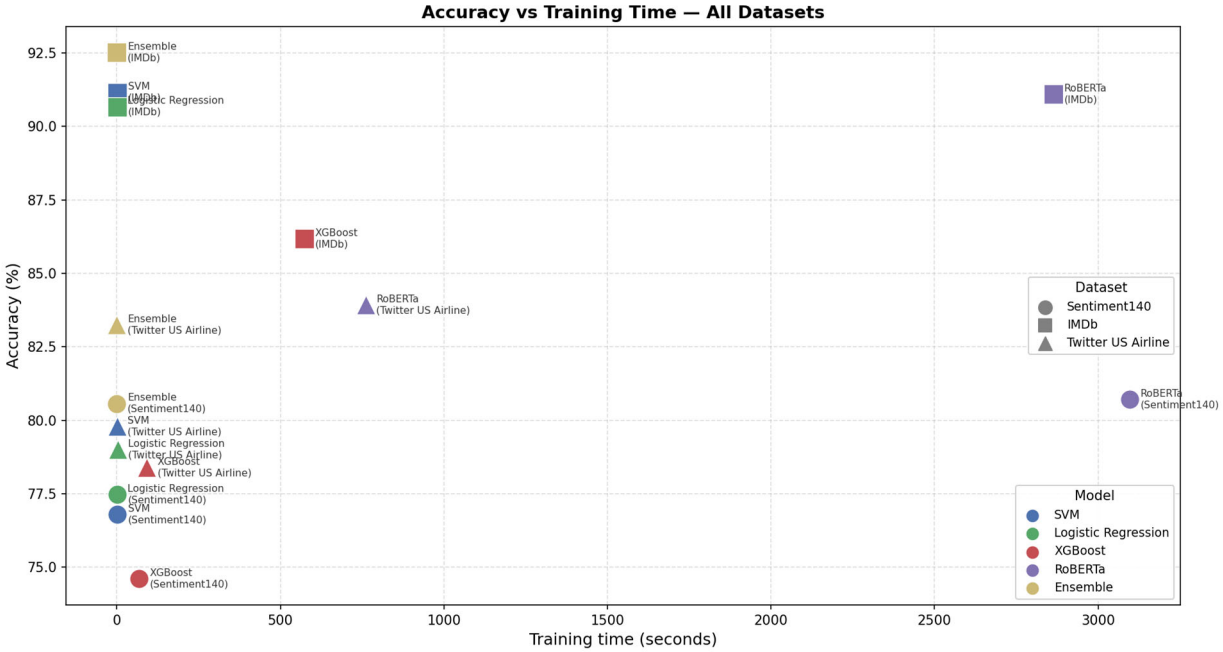

Figure 3. Accuracy vs. training time for all models across three benchmark datasets. Marker colour denotes the model; marker shape denotes the dataset (circle = Sentiment140, square = IMDb, triangle = Twitter US Airline).

4.4 Comparison with Prior Work

Table 7 provides a comprehensive comparison of the proposed ensemble model against representative state-of-the-art sentiment analysis approaches across multiple benchmark datasets.

The results indicate that transformer-based and hybrid deep learning models generally achieve the highest performance across datasets. For instance, Semary et al. (2023) report the highest IMDb performance with 96.28% accuracy using a RoBERTa-based CNN-LSTM hybrid, while Tan et al. (2023) achieve 94.63% accuracy using a RoBERTa-GRU architecture. Similarly, Jahin et al. (2024) and Yibeyin et al. (2024) demonstrate that advanced hybrid deep learning models can exceed 94%–96% accuracy on domain-specific and multilingual social media datasets, further confirming the effectiveness of deep contextual representations.

Classical machine learning approaches, while computationally efficient, generally yield lower performance compared to transformer-based methods. For example, Hu et al. (2024) report 80% accuracy using Naïve Bayes on disaster-related tweets, while Cam et al. (2024) achieve 89% accuracy with SVM on financial Twitter data. Similarly, Kaur and Sharma (2023) obtain strong performance on Sentiment140 (F1-score of 94.95%) using hybrid feature engineering with LSTM, but their approach requires more complex feature extraction compared to pure classical baselines.

The proposed ensemble model, which integrates SVM, Logistic Regression, XGBoost, and RoBERTa using a soft voting strategy, demonstrates competitive performance across all three evaluated datasets. On Sentiment140, the ensemble achieves 80.57% accuracy and an F1-score of 80.45%, closely matching the performance of RoBERTa-based systems reported in prior work such as Maryam et al. (2025) (87% accuracy on mixed datasets). When performing at the highest level on IMDb, the ensemble achieved an accuracy of 92.51% and an F1-score of 92.56%, both of which were superior to the performance of the baseline models derived from using transformer-based architectures, as Rahman et al. (2025) achieved accuracy rates of 92.36%. Thus, using the classical models provides complementary information when used on longer and more structured text, like movie reviews.

Within the context of the Twitter US Airline Dataset, the ensemble has performance measures of 83.24% accuracy and 82.43% F1-score. The ensemble performed comparably to the highest ranked RoBERTa-based approaches; however, there remains a gap in accuracy levels between the ensemble and RoBERTa-based methods, indicating that transformer-based approaches continue to provide a competitive advantage when evaluating tweets consisting of short, context-sensitive content requiring advanced semantic competency (Jahin et al., 2024).

Table 7. Comparison with Prior Works

Study	Method	Dataset	Acc. (%)	Prec. (%)	Rec. (%)	F1 (%)
Almalki (2025)	XLM-R	Multilingual social media	–	–	–	91.70
Hayadi & Maulita (2025)	SVM	Twitter (Education)	91.75	–	–	–
Maryam et al. (2025)	RoBERTa-base	Twitter + IMDb	87.00	87.00	86.00	87.00
Rahman et al. (2025)	RoBERTa-BiLSTM	IMDb	92.36	92.46	92.36	92.35
Cam et al. (2024)	SVM	Financial Twitter	89.00	91.00	93.00	92.00
Hu et al. (2024)	Naïve Bayes	Disaster Tweets	80.00	86.00	74.00	80.00

Study	Method	Dataset	Acc. (%)	Prec. (%)	Rec. (%)	F1 (%)
Jahin et al. (2024)	TRABSA (RoBERTa+BiLSTM)	UK COVID-19 Twitter	94.00	94.00	93.00	94.00
Kp et al. (2024)	Ensemble (SVM+DT+RF)	SST-2	96.53	95.87	91.24	93.91
Kumar & Sadanandam (2024)	BERT	Coronavirus Tweets	88.50	89.00	89.00	89.00
Miah et al. (2024)	Ensemble (RoBERTa+GPT-3)	SemEval-2017	86.71	80.91	81.22	81.06
Yibeyin et al. (2024)	CNN-BiLSTM	Amharic Social Media	96.08	96.00	96.00	96.00
Bengesi et al. (2023)	TF-IDF + SVM	Monkeypox Tweets	93.00	–	–	–
Kaur & Sharma (2023)	Hybrid Features + LSTM	Sentiment140	92.70	96.10	93.80	94.95
Mutinda et al. (2023)	LeBERT	Yelp Reviews	88.20	88.45	89.01	88.73
Semary et al. (2023)	RoBERTa-CNN-LSTM	IMDb	96.28	97.00	97.00	97.00
Tan et al. (2023)	RoBERTa-GRU	IMDb	94.63	95.00	95.00	95.00
Talaat (2023)	RoBERTa-BiGRU	Apple Sentiment	91.72	–	–	–
This research	**SVM + LR + XGB + RoBERTa**	**Sentiment140**	**80.57**	**80.91**	**80.00**	**80.45**
This research	**SVM + LR + XGB + RoBERTa**	**IMDb**	**92.51**	**92.00**	**93.12**	**92.56**
This research	**SVM + LR + XGB + RoBERTa**	**Twitter US Airline**	**83.24**	**82.81**	**83.24**	**82.43**

The proposed ensemble produces performance on par with that reported by Rahman et al. (2025), which is a RoBERTa-BiLSTM hybrid model trained using the same dataset with an accuracy of 82.25%. Although Tan et al.'s RoBERTa-GRU model achieves an even higher accuracy of 89.59% (Tan et al., 2023), their model involved additional complexity through sequential layers and data augmentation, increasing the total complexity of their approach. In this instance, a TF-IDF + SVM model produced by Kaur and Sharma (2023) produced an F1-score of 85.60%. This model was thus superior to each individual classical model in this research; however, Kaur and Sharma's TF-IDF + SVM baseline model was still not as accurate as the two methods that employed a RoBERTa-based approach and the proposed ensemble.

5. Discussion

5.1 Interpretation of Model Performance

The difference in performance between classical models and RoBERTa noted in this research reflects a well-established limitation on bag-of-words representations. The way TF-IDF encodes the text is as an unordered group of tokens, which does not take into account word order, context-dependent word pairings, and the relationships between words in a coherent manner. Therefore, it is difficult for TF-IDF to accurately capture the informal and context-dependent

characteristics of the text of social media, where the meaning is often dependent upon the words that precede it, the tone of how the words are expressed, and the inferred contextual information (Maryam et al., 2025). In contrast, RoBERTa's bidirectional attention mechanism resolves this limitation by encoding the representation of the token in context with all other tokens in the sequence, providing a consistent advantage for RoBERTa over the classical classifiers.

The high recall and lower precision of the XGBoost model suggests that when applying gradient boosting using the sparse TF-IDF features, there may be a bias that results in the over-prediction of the more frequently or more dominant occurring patterns in the feature space. This has been shown previously as a limitation of tree-based methods applied to high-dimensional text data that is sparse, as linear decision boundaries tend to represent more effectively in generalizable terms.

The effectiveness of Logistic Regression amongst the more traditional classification approaches corroborates the underlying theory that linear classifiers with L2 regularization perform particularly well in sparse, high-dimensional feature spaces such as TF-IDF matrices, where there are an order of magnitude more features than informative signals for any given sample, and continue to be used as a strong and interpretable baseline for text classification.

The cross-dataset results further support this finding. While SVM outperforms Logistic Regression on IMDb due to longer reviews having larger density of TF-IDF representations that are more easily separated through maximum-margin separation, SVM is outperformed by or is roughly equal to Logistic Regression on the shorter social media data (Sentiment140 and Twitter US Airline), which is consistent with Logistic Regression being faster and more stable when used for very sparse high-dimensional datasets.

5.2 What the Ensemble Reveals

What is most interesting about this research from a theoretical perspective is not that the ensemble has the best accuracy—it doesn't—but rather that it produced the most balanced precision and recall of all the models. This is due to the complementary behaviour of the classifiers as a part of an ensemble in this research. For example, RoBERTa provides strong semantic representations of text and emphasises precision. In contrast, the traditional classifiers (e.g. Logistic Regression and SVM) use surface lexical patterns for categorising text and therefore tend to produce higher recall because they are more sensitive than RoBERTa to lexical features. By using soft voting, the ensemble is able to combine these complementary signals, thereby eliminating any bias towards precision, and producing a more balanced prediction profile.

The concept of ensemble learning is predicated on the ability to combine several different predictors that exhibit variation in predicting errors, thereby reducing the variance of predictions in total, even when one individual predictor does not dominate on all performance metrics (Alahmadi et al., 2025). The practical implications of such a balance in real-world applications such as brand tracking or public health surveillance are especially important given that the misclassification of either of the two classes may have significant implications, and a more symmetrical distribution of errors is often desirable rather than the optimization of a single performance metric.

The cross-dataset evaluation added additional nuance to this research. On IMDb, the ensemble achieved a 1.42 percentage point advantage over RoBERTa, demonstrating the additional data that classical TF-IDF representations can contribute to the transformer embeddings. Because movie reviews usually represent longer sentences and more structured sentiment expressions, it is reasonable that n-gram features could capture sentiment-laden phrases that may have different weights via the attention mechanism inside RoBERTa. On the Twitter US Airline dataset, the narrower ensemble advantage suggests that soft voting is most effective when base model error profiles are well-balanced, a condition more readily satisfied in binary classification than in three-class settings with pronounced class imbalance.

5.3 Positioning Against Prior Work

The comparable performance between the proposed ensemble and the RoBERTa-BiLSTM hybrid of Rahman et al. (2025) on the same dataset is noteworthy, given the architectural simplicity of the proposed approach. RoBERTa-BiLSTM requires modifying the transformer architecture itself by appending sequential processing layers, increasing both implementation complexity and training overhead. On IMDb specifically, the proposed ensemble (92.51%) approaches the performance of the more complex RoBERTa-CNN-LSTM hybrid of Semary et al. (2023) (96.28%) while requiring a substantially simpler architecture and no modification of the transformer model itself. The proposed ensemble achieves similar performance through a modular combination of independently trained models, a design that is easier to maintain, extend, and deploy in practice.

The performance gap relative to Tan et al. (2023) reflects the contribution of their data augmentation strategy, which oversamples minority classes using word embeddings to improve generalization. This suggests that the proposed ensemble's performance could be meaningfully improved through similar preprocessing enhancements, independent of the ensemble architecture itself.

5.4 Limitations and Future Work

This research has several limitations that should be considered when interpreting the results. Although the proposed ensemble is evaluated on three benchmark datasets covering social media posts, movie reviews, and multi-class sentiment classification, all experiments are restricted to English-language text. Extending the approach to multilingual and code-switched settings therefore represents an important direction for future work (Almalki, 2025).

This research has both shown limitations and provided findings that may lead to promising new areas for further investigation. One area that may lend itself to furthering this research effort is an investigation into adaptive ensemble weighting techniques; these techniques would be used to adjust the contribution of models to the ensemble based upon natural properties of the input, such as length of the text. This could help improve the robustness of an ensemble with respect to datasets that are more diverse. Another area of promising future study may involve the use of more contemporary transformer-based architectures (e.g., DeBERTa) or domain-specific models trained on data specifically derived from social media to help increase the performance of the transformer component of the ensemble.

6. Conclusion

This research evaluated an ensemble framework combining three traditional machine-learning algorithms—SVM, logistic regression, and XGBoost—with a fine-tuned RoBERTa transformer to predict the sentiments of posts on various social media platforms. Experiments were conducted on three benchmark datasets (Sentiment140, IMDb, and Twitter US Airline) using a soft voting method to determine the combined predictions of all models.

Throughout the research, RoBERTa was the highest performing individual model compared to other tested models, verifying that transformer-based methods provide better contextual representations (Maryam et al., 2025). While Logistic Regression had the best accuracy for the short-form social media text, SVM performed best on the longer-form IMDb reviews, which is indicative of how feature density differences among the two different types of text result in a performance difference in the models used to classify them. XGBoost demonstrated a persistent difference between precision and recall values across all datasets, further supporting what has been previously reported about limitations of tree-based methods when applied to sparse text representations.

The ensemble outperformed all individual models on IMDb (92.51% accuracy, 92.56% F1-score), closely matched RoBERTa on Sentiment140 (trailing by 0.14 percentage points), and followed RoBERTa on Twitter US Airline (trailing by 0.69 percentage points). These cross-dataset

results demonstrate that the ensemble benefit is strongest on longer, lexically richer text and diminishes in multi-class settings with limited training data (Alahmadi et al., 2025).

A consistent finding across all datasets is the substantial computational cost disparity between RoBERTa and the classical classifiers. RoBERTa required up to 3,096 seconds for fine-tuning while classical models trained in seconds. The ensemble introduces no additional training overhead, offering a computationally practical framework that achieves near-transformer or better performance depending on the deployment domain.

Comparison with prior work shows that the proposed ensemble achieves competitive performance relative to architecturally more complex hybrid models (Rahman et al., 2025; Semary et al., 2023) through a simpler, modular design. Future work should investigate weighted voting strategies, extension to three-class and multilingual settings, and integration of more recent transformer variants such as DeBERTa.

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Historical Sciences

Institutional Transformation of the Cultural Sector in the Context of the Formation of the Ulytau Region

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Abstract

This article examines the institutional transformation of the cultural sector in the region following the establishment of the Ulytau Region in 2022. Based on a comparative-dynamic method, statistical indicators from 2019 to 2026 are analyzed to identify key structural shifts before and after the region's administrative creation.

The formation of the Ulytau Region served as a catalyst for reorganizing cultural management entities, establishing specialized mechanisms for historical and cultural heritage protection, founding new cultural organizations, and expanding overall cultural infrastructure. Consequently, the establishment of the region is evaluated not as the sole cause of transformations in the cultural domain, but as a critical accelerating factor for institutional change.

Keywords: Ulytau Region, administrative-territorial reform, cultural policy, cultural infrastructure, museum studies, historical and cultural heritage, archives, libraries, digitalization, cultural identity

Introduction

Changes in the administrative-territorial structure of Kazakhstan reorganize territorial state management while significantly shaping the institutional foundations of social and cultural policy. In this context, the establishment of the Ulytau Region as an independent administrative-territorial unit in 2022 offers a crucial case study for analyzing regional cultural development processes.

In accordance with Decree No. 887 of the President of the Republic of Kazakhstan dated May 3, 2022, the Ulytau Region was officially formed, with Zhezkazgan designated as its administrative center [1]. Subsequently, Resolution No. 871 of the Government of the Republic of Kazakhstan dated November 4, 2022, approved the Comprehensive Plan for the Socio-Economic Development of the Ulytau Region for 2022–2026 [2]. This document served as a foundational state planning framework, establishing the socio-economic and infrastructural baselines for the region's emergence as a new administrative entity; however, it should be noted that this resolution was subsequently repealed [2].

The distinctiveness of the Ulytau region lies in its unique place within Kazakhstan's historical and cultural space. Concentrated within its territory are prominent archaeological sites, memorial facilities dedicated to historic figures, mausoleums, necropolises, traditional craft forms, and extensive museum and archival collections. Thus, the region's establishment reorganized

socio-economic management while creating new opportunities to systematically preserve, research, and promote historical and cultural heritage at the regional level.

The relevance of this study is driven by the need to evaluate the post-2022 administrative-territorial reform transformations in the cultural sector using concrete quantitative and qualitative indicators. For this purpose, data from 2019 to 2021 serves as a baseline comparative period prior to the region's establishment, while indicators from 2022 to 2026 represent the stage of development under new institutional conditions.

The primary objective of this study is to identify the institutional changes in the cultural sector following the formation of the Ulytau Region and to analyze their manifestations across cultural infrastructure, museums, libraries, archives, historical-cultural heritage preservation, funding, and cultural communications.

To achieve this purpose, the following **tasks** were defined:

- Characterize the new institutional management system of the cultural sector resulting from the establishment of the Ulytau Region;
- Determine the dynamics of cultural infrastructure indicators from 2019 to 2026;
- analyze organizational and operational shifts within museum, library, and archival networks;
- evaluate new mechanisms for the preservation and digitalization of historical and cultural heritage;
- examine changes in sector funding and material-technical provision;
- identify emerging trends in the formation of regional cultural identity and cultural branding.

The study employs comparative-historical, institutional, statistical, and systems analysis methods. The empirical data base comprises reporting materials from 2019 to 2026 concerning cultural organization performance metrics, budget allocations, museum collections, visitor counts, archival holdings, digitalized documents, and cultural infrastructure data.

The research period is conditionally divided into two stages: 1. 2019–2021: The baseline period prior to the formation of the region; 2 2022–2026: The period of institutional consolidation following the administrative-territorial reform. This periodization allows for a comparative evaluation of dynamic changes across key indicators in the cultural sector.

Throughout the study, temporal dynamics in statistical indicators were compared, encompassing the total number of cultural organizations, museum holdings, visitor counts, library collections, archival documents, funding volumes, and material-technical provision metrics.

Furthermore, external factors influencing the development of the cultural sector were taken into account when evaluating the study's results. These include post-pandemic recovery effects, state cultural policy priorities, budgetary investments, infrastructure projects, and local cultural initiatives. This approach isolates the specific impact of the administrative-territorial reform from broader trends, ensuring a more objective evaluation of the observed changes.

Analysis

The cultural policy of the Republic of Kazakhstan is implemented on the basis of the Concept for Cultural Policy for 2023–2029. This document identifies key priorities including ensuring access to cultural assets, developing cultural infrastructure, preserving cultural heritage, and enhancing the institutional capacity of the cultural sector [3].

Establishment of the Ulytau Region and the New Institutional Management System of the Cultural Sector.

The creation of the Ulytau Region provided the institutional foundation for establishing a new model for organizing the cultural sector at the regional level. Currently, state policy in the areas of culture and art, state language policy, archives, and documentation support is

implemented by the Department of Culture, Language Development, and Archives of the Ulytau Region – a state authority integrated into the region's executive branch. In this context, the establishment of the region made it possible to consolidate cultural management functions at the regional level and streamline their institutional framework.

The significance of these implemented changes is reflected in the ability to coordinate individual domains of the cultural sector within a unified regional management system. That is, culture and arts organizations, historical-cultural heritage protection institutes, library and archival networks, and language policy are currently developing as interconnected pillars of regional cultural policy.

Following 2022, the establishment of new functional organizations within the region became one of the key indicators of these institutional changes. In particular, the creation of the Center for the Preservation of Historical and Cultural Heritage enabled the identification, registration, protection, conservation, restoration, and promotion of historical and cultural monuments to be carried out at the level of a specialized institution.

It is insufficient to view these changes solely as a reorganization of the administrative apparatus. In our assessment, this process is characterized by the functional specialization of cultural heritage management. That is, the new regional framework has clarified the operational responsibilities of cultural governance entities while establishing specialized organizational mechanisms for the protection of historical and cultural heritage.

Dynamics of Cultural Infrastructure Development.

Following the creation of the Ulytau Region, expanding cultural infrastructure and modernizing its material and technical base became a vital strategic priority of regional cultural policy.

According to 2025 data, 105 cultural organizations operate in the region. These include 39 community centers and rural clubs, 51 libraries, and 15 entities directly subordinated to the regional department. The latter group comprises a theater, a philharmonic orchestra, museums, state archives, the Center for the Preservation of Historical and Cultural Heritage, a cultural, entertainment, and scientific-methodological center, a regional universal library, and a center for language development [4]. This structural network demonstrates that the cultural sector extends beyond artistic creation, developing instead through mutually reinforcing domains.

Examining the development dynamics of cultural infrastructure using multi-year metrics allows for a comparative evaluation of the changes following the administrative-territorial reform. In this context, the indicators for 2019–2021 illustrate the baseline conditions prior to the region's establishment, whereas the data for 2022–2026 reflect the transformations occurring throughout the formation of the new regional management system.

Institutional Changes in Museum Studies.

Museum studies occupy a special place in assessing the transformation of the cultural sector in the Ulytau Region. Beyond preserving the region's historical memory, museums perform essential research, cultural-educational, and public communication functions. The number of artifacts in the collection of the History and Archaeology Museum of the Ulytau Region stood at 52,476 in 2019, reaching 53,404 in 2022, 54,244 in 2025, and 54,407 in the first half of 2026 [5]. These indicators demonstrate steady accessioning throughout the analyzed period, with the collection growing by 1,931 items between 2019 and 2026. However, this growth should not be attributed solely to the creation of the region, as collection acquisition efforts were active prior to 2022. Consequently, this dynamic should be viewed as part of the museum sector's long-term development trajectory.

Significant shifts in museum attendance were also recorded throughout the analyzed period. In 2019, the History and Archaeology Museum of the Ulytau Region welcomed 92,500

visitors, a figure that dropped sharply to 41,155 in 2020. Attendance subsequently recovered, reaching 85,424 visitors in 2022, 88,560 in 2023, 92,545 in 2024, and 92,550 in 2025 [6, 7].

It is appropriate to attribute the decline in visitor numbers during 2020–2021 not to administrative-territorial changes but to pandemic-related restrictions. The steady growth in visitor numbers after 2022, in turn, indicates that the museum's cultural and educational activities have stabilized.

The work of replenishing the museum's collection has also been carried out on a consistent basis. The Ulytau Regional Historical and Archaeological Museum received 255 artifacts in 2022, approximately 280 artifacts annually in 2023–2025, and 138 artifacts in the first half of 2026 [7]. This indicator shows that the replenishment of the museum's holdings has taken on a systematic character and that work on accumulating the region's historical and cultural heritage is continuing.

The indicators of the Saken Seifullin Zhanaarka District Historical and Local Studies Museum also show positive dynamics across a number of areas of museum activity. The number of artifacts in the museum's collection grew from 3,110 in 2019 to 3,535 in 2022, 4,044 in 2025, and 4,196 in the first half of 2026. During this period, the number of exhibitions increased from 60 to 74, the number of excursions from 80 to 93, and the number of visitors from 4,050 to 4,305 [6, 7]. This comparative analysis demonstrates that museum activity is not limited to the function of preserving material heritage but is also developing in the areas of collecting local historical data, scholarly study, exhibition, and public presentation.

Another important example illustrating the changes in cultural infrastructure following the administrative-territorial reform is the establishment of the Ulytau District Historical and Local Studies Museum. The founding of the museum created an independent institutional platform for the systematic collection, preservation, study, and presentation of local heritage in the Ulytau district, a region with significant historical and cultural potential. The museum's exposition is designed to comprehensively present each stage of the region's historical development and its cultural characteristics. At the end of 2025, the museum's collection held 1,612 artifacts, of which 767 were included in the main collection and 845 in the scientific-auxiliary collection. Within a single year, the museum's holdings grew by 510 new artifacts, and three scientific expeditions were organized [7]. These quantitative data show that within a short period the museum has developed not merely as an institution performing an exhibition function, but as a cultural organization combining research, local-studies, collection-building, and cultural-educational functions.

Institutional changes in the library system.

Following the establishment of Ulytau Region, an institutional reorganization process also took place within the library system. The decision to establish the Ulytau Regional Universal Library was adopted on 18 October 2022, and the library began operating under its new structure on 4 January 2023. The library's key performance indicators reflect the changes in its role within the regional cultural infrastructure. Its book collection numbered 63,662 copies in 2019 and had reached 65,549 copies by 2022. Although the volume of the collection decreased to 47,440 copies during the institutional reorganization period in 2023, a renewed growth trend was subsequently observed, with the collection reaching 50,550 copies in 2025 and 51,621 copies in the first half of 2026. At the same time, the number of books increased from 69,103 in 2022 to 95,044 in 2025. The number of publications issued in the state language also grew during this period, from 39,483 to 60,292 [8]. These statistical data confirm that, alongside its traditional functions of book preservation and the provision of literature to users, the library's informational, local-studies, and cultural-communicative functions have been strengthened.

Digitalization within the library system is likewise a priority area of institutional transformation. Individual modules of the "WEB RABIS" electronic program have been introduced, and work on converting the retrospective collection into an electronic system is under way. As a

result of digitization efforts, which began in 2011, 102 books have been fully converted into digital format [8]. This process not only creates new opportunities for preserving library collections but also expands the possibility of remote access to historical and local-studies materials and their use for scholarly research purposes.As a result of digitization efforts, which began in 2011, 102 books have been fully converted into digital format [8]. This process not only creates new opportunities for preserving library collections but also expands the possibility of remote access to historical and local-studies materials and their use for scholarly research purposes.

The development of archival work and digitization

With the establishment of Ulytau Region, archival services became one of the important components of regional cultural policy. At present, five state archives operate in the region: the State Archive of Ulytau Region, and the state archives of the cities of Satbayev and Karazhal, as well as of Zhanaarka and Ulytau districts. The number of collections held in the State Archive of Ulytau Region grew from 598 in 2019 to 636 in 2026, while the number of documents in storage increased from 361,340 to 363,480 [5].

One of the significant changes in archival work is the increase in the volume of document digitization. According to official data from Ulytau Region, in 2025 the region's archives digitized 632,065 pages, 6,970 case units, and 37 archival collections [5]. Digitization efforts contribute to ensuring the preservation of archival documents, improving their accessibility, and enhancing the efficiency of services provided to users. On the whole, the changes taking place in archival work cannot be reduced solely to the numerical growth of archival holdings. They also reflect the gradual transition of historical documentary heritage preservation and use from the traditional paper format to a digital environment.

Protection of historical and cultural heritage and financing of the culture sector.

The establishment of Ulytau Region as an independent administrative-territorial unit created new institutional opportunities for developing the systematic study, preservation, and broad promotion of the region's historical and cultural heritage. The holding of the First National Kurultai of the Republic of Kazakhstan in Ulytau that same year underscored the region's special significance in reviving national historical memory, strengthening civic identity, and implementing state cultural policy [9].

The next area of development in the cultural sector following the establishment of Ulytau Region is linked to the organizational strengthening of the system for protecting historical and cultural heritage. The establishment of the Center for the Preservation of Historical and Cultural Heritage made it possible to systematize the identification, registration, protection, conservation, and restoration of historical and cultural monuments in the region at the level of a specialized organization.

Between 2023 and 2026, a number of measures were carried out to preserve historical and cultural sites. These included work carried out on Subdivision No. 3 of Steplag in the city of Zhezkazgan, the mausoleums of Shong Telgozyuly, Barak, Omar, Kartabai, Kaly Kurmanbai, and Akaidar, the Askarbek Mosque, and the Kalmanbai necropolis [7].

A key step in improving the state system for recording historical and cultural heritage was the approval, by Resolution No. 78/01 of the Akimat of Ulytau Region dated 3 October 2025, of the state register of historical and cultural monuments of local significance [10]. Under this resolution, the responsibility for taking the necessary measures arising from the register was assigned to the Department of Culture, Language Development, and Archival Affairs of Ulytau Region. This indicates that regional administrative mechanisms for identifying, recording, and protecting historical and cultural heritage have become more clearly defined.

Thus, the results of the study demonstrate that in Ulytau Region the areas of historical and cultural heritage management – "identification – registration – protection – restoration – digitization – promotion" – are developing in an interconnected manner. At the same time, it

cannot be concluded that all elements of this chain took shape simultaneously and only after 2022. It should also be noted that the establishment of the region as an independent administrative unit created new institutional conditions for coordinating these processes at the regional level.

The institutional development of the culture sector is closely linked to its financial and material-technical provision. In this regard, a comparison of financing indicators for 2019–2026 is one of the important indicators for assessing the development dynamics of cultural organizations in the region.

The budget of the S. Kozhamkulov Theater increased from 175.353 million tenge in 2019 to 288.709 million tenge in 2022, 470.310 million tenge in 2025, and 532.432 million tenge in 2026 [6, 7].

The budget of the Ulytau Region Historical and Archaeological Museum grew from 68.965 million tenge in 2019 to 102.7 million tenge in 2022 and 485.688 million tenge in 2025, amounting to 438.583 million tenge in 2026 [10]. The budget of the Saken Seifullin Museum increased from 17.134 million tenge to 45.427 million tenge, while the budget of the Maken Toregeldin Museum grew from 65.693 million tenge to 161.843 million tenge [6, 7].

The budget of the Ulytau Regional Universal Library increased from 87.024 million tenge in 2019 to 199.279 million tenge in 2026, while the budget of the State Archive of Ulytau Region grew from 94.610 million tenge to 198.116 million tenge [6, 7].

The data presented show that, overall, the level of financial provision for cultural organizations increased during the period under study. At the same time, financing dynamics may be influenced not only by administrative-territorial changes but also by factors such as inflationary processes, changes in the wage fund, capital repairs, material and technical equipping, and the implementation of new projects. Therefore, the growth in budget volume should be regarded both as a direct result of the region's establishment and as one of the indicators of the expansion of the institutional and financial capacity of the culture sector at the regional level.

Significant changes are also observed in the area of material and technical equipping. In 2022, sound equipment was purchased for the philharmonic; in 2023, musical and lighting equipment as well as a bus were purchased for the theater, and a vehicle and specialized equipment were purchased for the Center for the Preservation of Historical and Cultural Heritage. In 2025–2026, the library was equipped with digital and library equipment, as well as a bibliobus (mobile library) [7]. These measures indicate that efforts were directed not only at modernizing the material base of cultural organizations but also at expanding the territorial accessibility of cultural services.

Theater activity and cultural communication.

The activity of the S. Kozhamkulov Kazakh Musical-Drama Theater of Ulytau Region is one of the indicators characterizing the cultural changes following the administrative reform. The number of theatrical performances was 185 in 2019, 201 in 2022, 203 in 2023, 209 in 2024, and 210 in 2025 [6, 7].

This dynamic in the number of performances confirms that the theater's repertoire has been steadily maintained and gradually expanded. In addition, the participation of the theater company in republican and international festivals during 2022–2025 indicates an expansion of the region's cultural-communicative capacities. The holding of the IV International Zh. Khadzhiev Theater Festival in Ulytau Region in 2025 attests to an increased level of visibility for the region within the professional theatrical arts space [7].

This process can also be considered from the standpoint of cultural branding. The theater's activity, no longer confined to cultural life within the city of Zhezkazgan alone, is increasingly becoming one of the mechanisms for presenting the professional art of the new region within the republican and international space of cultural communication.

Social and communicative activity of cultural organizations.

The changes in the culture sector of Ulytau Region are reflected not only in the traditional functions of cultural organizations but also in the strengthening of their communicative ties with society. The Regional Universal Library took part in projects such as "One Region – One Book," "One Country – One Book," "Boundless Local Studies," and "Shakarim Readings," organizing events aimed at promoting local literary and historical heritage [7].

Museums are also expanding their cultural and educational activities. The Zhanaarka Museum has organized traveling exhibitions, museum-based educational sessions, quests, local history clubs, lectures, and thematic meetings. Such initiatives strengthen the relationship between museums and local communities and contribute to integrating historical heritage into everyday cultural communication.

In this context, the activities of cultural organizations are expanding beyond the traditional function of heritage preservation to encompass public communication, cultural education, and audience engagement. This transformation indicates a changing social role of cultural organizations under contemporary conditions.

Cultural Branding and Regional Cultural Identity

Following the establishment of the Ulytau Region, projects aimed at promoting the region's distinctive historical and cultural characteristics as a cultural brand began to acquire a more systematic character. In 2023-2026, a number of national and regional cultural projects, including *Ulytau Uni*, *Qobyzym-Qonyrım*, and *Kökmaisa*, were implemented. These projects focused on promoting traditional arts, national cultural values, and ethnographic heritage [7]. For instance, the 2025 *Ulytau Uni* Festival was organized as a national festival of traditional folk arts, bringing together artistic groups and individual performers from different regions of Kazakhstan [7]. The significance of such projects extends beyond their function as cultural events. They contribute to shaping the historical image of the region, introducing national cultural heritage to a broader audience, and articulating Ulytau's distinctive cultural identity at the regional level.

In this regard, cultural branding can be considered both a direct outcome of administrative reform and one of the indirect processes that has intensified with the emergence of a new regional institutional level. The establishment of the region created institutional opportunities to incorporate its distinctive historical and cultural characteristics into a unified regional cultural policy and to promote them systematically through various forms of cultural communication.

One of the key priorities in the current stage of transformation of the region's cultural sector is the digitization of cultural heritage. The digitization of library collections, the integration of archival documents into electronic systems, the development of electronic databases of museum collections, and the use of multimedia technologies in exhibitions have contributed to the emergence of new approaches to the preservation, study, and public presentation of cultural heritage.

The introduction of a 3D hologram, interactive displays, and a QR-code system at the Ulytau District Museum of Local History demonstrates the ongoing transformation of museum communication from traditional methods toward digital tools. Digitization in the archival sector is another important component of this process, indicating that the conversion of historical documents into electronic formats has acquired a systematic and institutional character. This development is also consistent with the broader priorities of the cultural policy of the Republic of Kazakhstan. In particular, the Concept for Cultural Policy for 2023-2029 places particular emphasis on expanding public access to cultural values and modernizing cultural infrastructure [3].

A synthesis of the materials discussed above makes it possible to assess the impact of the establishment of the Ulytau Region on the cultural sector across several key dimensions.

First, significant institutional changes can be observed. Following the establishment of the region, new organizational structures were developed in the fields of culture, historical and

cultural heritage, libraries, archives, and language policy, while their respective functional responsibilities were further defined. In particular, the establishment of a Center for the Preservation of Historical and Cultural Heritage indicates the development of a specialized institutional mechanism for the protection and preservation of historical and cultural heritage sites in the region.

Second, a process of infrastructural modernization has taken place. The establishment of a new museum, the modernization of the material and technical infrastructure of cultural organizations, and the restoration of historical and cultural monuments have contributed to expanding the region's cultural infrastructure and improving its overall quality.

Third, there has been a trend toward strengthening financial support for the cultural sector. The budgets of a number of cultural organizations demonstrated an upward trend between 2019 and 2026. These indicators suggest that opportunities for financing the cultural sector at the regional level have expanded and that the economic foundations for implementing cultural policy have been strengthened.

Fourth, cultural organizations are undergoing a functional transformation. In addition to their traditional responsibilities related to preservation, documentation, and public services, museums and libraries have expanded their activities to include research, digitization, local history, cultural education, and public communication. Consequently, the role of cultural organizations in society is gradually changing: they are increasingly becoming not only institutions responsible for preserving cultural values, but also centers of research, education, and public communication.

Fifth, the process of developing and strengthening regional cultural identity has gained momentum. Projects such as *Ulytau Uni*, *Kökmaisa*, and *Qobyzym-Qonyrım* have aimed to promote the historical and cultural characteristics of the Ulytau region, support local cultural initiatives, and develop the region's cultural branding. This process contributes to establishing Ulytau's distinctive position within Kazakhstan's broader national cultural space.

Sixth, digital transformation has become one of the strategic directions of cultural policy. The digitization of archival documents, library collections, and museum materials not only enhances the preservation of historical and cultural heritage, but also expands public access to it, facilitates the systematization of information, and creates opportunities to present cultural values through new forms of communication. From this perspective, digitization should be regarded not merely as a technological development, but also as an important indicator of institutional transformation in the management of cultural heritage.

At the same time, methodological caution is necessary when assessing these outcomes from a scholarly perspective. It would be overly simplistic to interpret all positive changes in the cultural sector between 2019 and 2026 solely as consequences of the administrative-territorial reform. The development of the cultural sector has been influenced by a range of factors, including national cultural policy, budgetary policy, infrastructure investment, the work of professional personnel, and cultural programs implemented at the national level.

Conclusion

The findings of the study demonstrate that the establishment of the Ulytau Region in 2022 created conditions for the institutional reorganization of the cultural sector and for the clarification of its development priorities. Within the new administrative-territorial framework, a regional governance system encompassing culture, historical and cultural heritage, libraries, archives, and language policy was established. These changes made it possible to plan cultural policy more systematically at the local level and to clarify the functional responsibilities of cultural institutions.

In the coming period, the sustainability of these changes will depend on strengthening the research capacity of cultural organizations, further developing digital infrastructure, improving the

training and professional development of cultural-sector personnel, conducting systematic monitoring of the condition of historical and cultural heritage sites, and ensuring the long-term financial sustainability of cultural projects.

Overall, the experience of the Ulytau Region represents an important empirical case for examining the impact of administrative-territorial reforms on the cultural sector in Kazakhstan. The regional experience demonstrates that changes in administrative structures can affect a range of interconnected processes, from the organization and governance of cultural institutions to the preservation of historical and cultural heritage, the development of cultural infrastructure, digitization, and the formation of regional cultural identity. Thus, the establishment of the Ulytau Region created new institutional opportunities in the cultural sector and provided a foundation for the region's transition to a new stage of cultural development.

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THE IMPORTANCE OF STUDYING THE HISTORY OF ANCIENT CIVILIZATIONS

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Abstract

Studying ancient civilizations provides insight into humanity's historical heritage, as these civilizations played a significant role in human development across the fields of writing, law, philosophy, science, and the arts. Eastern civilizations shaped early urban cultures and systems of governance, while Western societies left a profound mark on democracy, rights, and philosophy. Examining these cultures helps explore the historical roots of contemporary social, economic, and cultural issues and identify solutions to them. The exchange of knowledge, technology, and culture between civilizations shaped the early stages of globalization. Eastern principles of harmony and spirituality, alongside Western critical thinking and logical approaches, defined the fundamental characteristics of modern societies. Studying ancient intercultural relations provides a model of mutual respect and tolerance for the modern world. Preserving and studying their heritage strengthens humanity's historical memory and opens up new perspectives for building the future. For this reason, the study of the ancient civilizations of the East and West is vitally important – both for understanding the past and for shaping the societies of today and tomorrow.

Keywords: ancient civilization, heritage, meaning, understanding of past events, modernity

The history of ancient Eastern and Western civilizations has been of immense importance to humanity. These civilizations serve as the very starting point for modern culture, science, and technology. Ancient cultures that emerged in Eastern civilizations – such as Sumer, Babylonia, Assyria, Egypt, China, and India – laid the foundation for many innovations that altered the course of human development. It was in these regions that the first writing systems, laws, calendars, trade routes, and more originated.

Western civilizations are also of significant importance. The focus here is on the Greek and Roman empires. Democracy, philosophy, art, and legal systems have had a direct impact on our lives today. Many legal principles used modern courts are based on Roman law. In many countries today, people elect their leaders; the foundations for this were laid in Ancient Greece.

Studying the history of the ancient East and West is an invaluable way to gain a clearer understanding of past events and a deeper insight into contemporary political developments, governance, and more. Such study reveals many nuances, shedding light on the causes and consequences of major events, past successes and failures, the interactions between states and cultures, strategic decisions and their outcomes, and so forth.

Knowledge of ancient history is essential for examining past successes and failures, the interactions between states and cultures, and strategic decisions and their consequences. Studying and understanding these elements shapes the future direction of development. Studying global events and their consequences is a crucial task for the modern era. The development of Eastern and Western civilizations, the establishment of trade and other relations among diverse peoples, and the convergence of ideas form the foundation of contemporary global relations. A secure future is impossible without a thorough study of the past and a comprehensive understanding of its underlying logic.

Some Eastern countries have found themselves helpless in the face of the West's technological and economic progress. Lacking sufficient familiarity with modern culture, they accept everything coming from the West as the dictate of the times. The Western mindset has taken hold of people.

Sometimes, the reasons why Eastern nations lag behind the developed West in economic competition driven by modern technology are attributed to the Islamic religion and traditional mindsets. However, the driving force behind economic development is science, not religion. As Eastern countries transition to new economic relations, they naturally have much to learn from the Western world, which possesses extensive experience in this area. The Western world undoubtedly holds a leading position, both in terms of its high level of scientific and technological development and the degree to which its market economy has been established and socially oriented over the course of several centuries. However, modernity cannot be defined solely by technological and economic indicators. The spiritual evolution of humanity, spanning millennia, has arguably played a greater role in shaping modern man than scientific and technological progress.

Today, the West is synonymous with “developed countries”. Based on this characteristic, some political scientists classify Japan as part of the West – a notion that is entirely incorrect. The successes achieved by the East unfolded against the backdrop of advancements in the exact and natural sciences. It is well known that the East underwent a tremendous, almost superhuman strain; furthermore, its capacity for intuition – a quality of exceptional importance – enabled the East to achieve extraordinary feats in philosophy, art, and even technology.

Studying the history of ancient Eastern and Western civilizations is also crucial for understanding the cultural, social, and intellectual development of humanity. This field of study not only examines the past but also plays a significant role in shaping modern societies and determining future paths of development. Key events highlighting the importance of this topic can be identified:

1. Understanding cultural heritage

Ancient Eastern (Mesopotamia, Egypt, China, India) and Western (Greece, Rome) civilizations laid the foundations of modern societies in many areas, such as science, art, law, and systems of governance.

2. Understanding social and economic development

The emergence of agriculture and urban life in the East, the formation of trade routes, and the development of administrative structures help us understand the socio – economic evolution of humanity. The development of democracy (Athens), legal systems (Roman law), and philosophical thought in the Western world influenced modern governance and the legal systems of the Middle Ages, the early modern period, and the modern era.

3. Philosophical and intellectual heritage

In the Ancient East, religious and spiritual ideas – such as Hinduism, Buddhism, Zoroastrianism, and Confucianism – sought to understand the relationship between humanity, nature, and the universe. In the West, thinkers such as Socrates, Plato, and Aristotle contributed to the development of rational thinking and scientifically grounded approaches.

4. Study of intercultural relations

Intercultural contacts, trade routes (such as the Silk Road), and the exchange of knowledge between East and West played a significant role in shaping modern global culture.

5. Draw conclusions from past events

The successes and failures of history serve as an example for modern societies. By studying the causes of the collapse of ancient civilizations, modern societies may avoid repeating the same mistakes.

6. Cultural self – awareness and a sense of pride

The study of civilizations encourages modern peoples to take pride in their history and preserve their cultural heritage. For these reasons, the study of ancient Eastern and Western civilizations is important not only for historians but also for fostering intercultural understanding, global progress, and a sense of connection between people and their past.

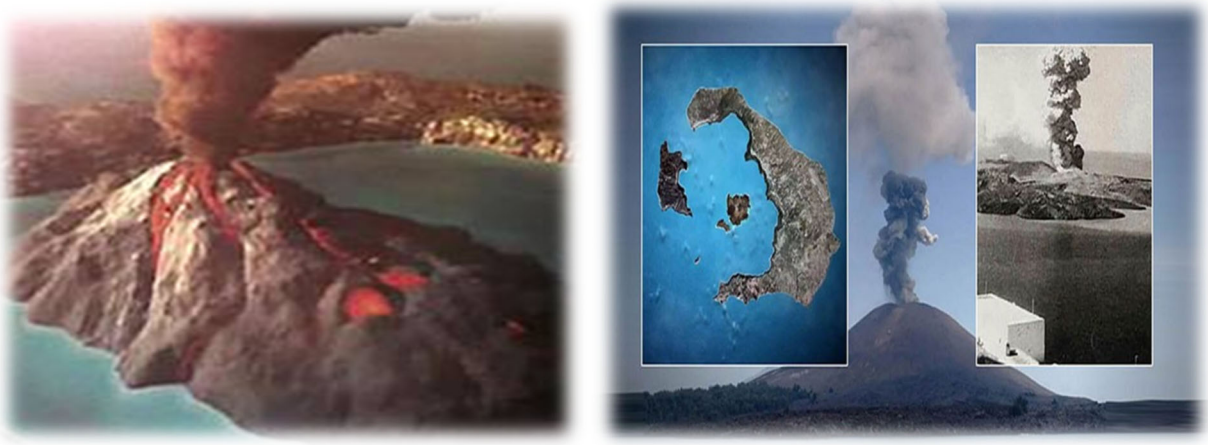
One of the things we should learn from ancient civilizations is a deep study of their experiences of collapse and the development of our own capacity to manage such processes. The causes of the collapse of ancient civilizations varied, and throughout history, each civilization fell under unique circumstances. Let us consider some of these causes:

∠ Natural disasters

Natural phenomena such as earthquakes, volcanic eruptions, droughts, and floods have led to the decline of many civilizations. In ancient Egyptian civilization, fluctuations in the level of the Nile River caused economic hardship due to reduced food production. Nilometer were used to measure the level of the Nile as early as the time when the rule of the pharaohs was established (Picture 1)

Picture 1. Nilometer

The eruption of the Santorini volcano destroyed the civilization that had developed on the island of Crete (Picture 2).



Picture 2. The eruption of the Santorini volcano destroyed the Minoan civilization

∠ Climate change

Climate change and severe droughts played a major role in the collapse or weakening of many ancient civilizations. Environmental shifts led to famine and war. In this context, it is noteworthy that repeated drops in the Nile's water level and periods of drought during Egypt's Old Kingdom led to the state's collapse; the onset of a sudden warming period in Mesopotamia caused the fall of the Akkadian Empire; the arrival of drought accelerated the decline of the Maya civilization in Central America; and the cessation of monsoon rains resulted in the disintegration of ancient Indian and Khmer civilizations (Picture 3).

Picture 3. Ancient Egyptian, Akkadian, and Mayan civilizations destroyed by drought

∠ Environmental change

Deforestation, soil depletion, erosion, loss of soil fertility, and the overexplotation of natural resources have hindered food production. In this context, it can be shown that the civilizations of ancient Egypt, Easter Island, and others faced serious difficulties linked to deforestation.

∠ Political and social causes

Internal conflicts and political instability, the weakening of goverments, civil wars, and political upheavals led to the collapse of civilizations. This pattern was observed in the vast majority of civilizations that perished in antiquity. Examples of this include the ancient cultures of the Hittites, Troy, Urartu, Media, Lydia, and others (Picture 4).

Picture 4. The Ruins of Troy and Lydia

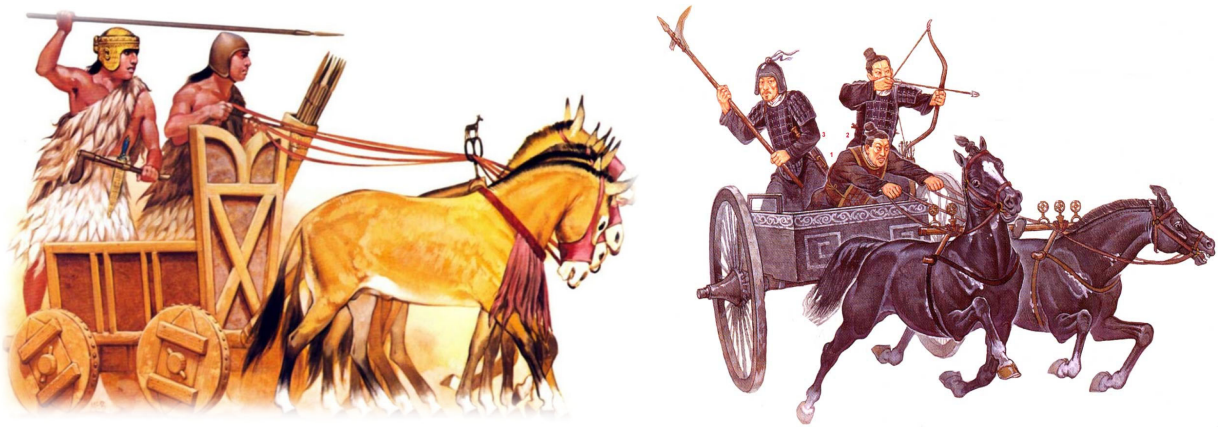
∠ Social inequality and uprisings

The era of the ancient Egyptian dynasties ended precisely with uprisings and popular revolts. During the final years of the Roman Empire, discontent among social classes became intense. The Han dynasty in China was overthrown as a result of rebellions (Picture 5).

Picture 5. The Uprisings of Spartacus (Rome) and the Yellow Turbans (China)

∠ External attacks, invasions, and wars

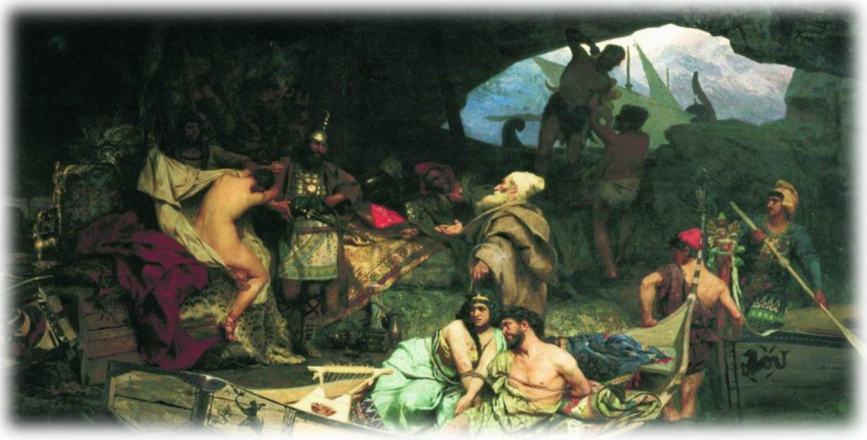
Most states of ancient Eastern civilizations were destroyed precisely because they failed to adequately address foreign policy and defense challenges. The civilizations of Mesopotamia (Sumer, Akkad, Babylon, and Assyria) were weakened by attacks from various states, empires, and nomadic tribes. These states vanished from the stage of history. A similar situation characterized the ancient civilizations of China and India (Picture 6).



Picture 6. Ancient Sumerians and Chinese. Warriors and military technology

∠ Piracy

Piracy existed in the ancient world, though it was not as widespread as it was during the Middle Ages. Ancient pirates attacked ships, looted them, took people captive, and sold them into slavery. Piracy was linked to plunder and the slave trade, particularly in the Mediterranean region (Picture 7a).



Picture 7a. Henryk Siemiradzki

The Phoenicians – the most skilled seafarers of the ancient world – also gained a particularly notorious reputation. The “Odyssey” mentions Phoenician pirates who abducted people from the island of Syros and sold them into slavery (Picture 7b).

Picture 7b. Pirates from Phoenicia

The heyday of ancient piracy coincided with the era of anarchy caused by the Roman civil wars, with the mountainous region of Cilicia – and its fortresses – serving as the pirates base. In Rome, pirates were executed by crucifixion.

∠ Changes in trade routes

The disruption of trade relations led to the economic weakening and collapse of certain civilizations. In this context, the history of the states situated along the Great Silk Road draws particular attention. The fate of the civilizations that emerged in the ancient Eastern Mediterranean basin was inextricably linked to trade routes (Picture 8).

Picture 8. All roads lead to Rome

∠ Epidemics

Edidemics that decimated large populations played a role in the collapse of civilizations. Major epidemics of the ancient world – such as the Plague of Athens, the Antonine Plague, and the Plague of Justinian – fundamentally altered the course of history, shaping the political, economic, and social landscapes of the affected regions. Following contact with Europe, the indigenous civilizations of the Americas suffered massive losses due to diseases introduced from Europe.

∠ Economic problems

Shifts in trade routes and competition between economic centers weakened civilizations and even led to their destruction. Changes affecting the Silk Road and maritime routes weakened certain city – states.

∠ A comprehensive approach

These causes often complement one another and, in combination, lead to the collapse of civilizations. The fall of the Roman Empire resulted from a combination of internal political instability, economic problems, and environmental challenges.

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Legal Sciences

From Bicameral Parliament to the Kurultai: The Transformation of Legislative Power Under Kazakhstan's 2026 Constitution

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Abstract

This article examines the replacement of Kazakhstan's bicameral Parliament by the unicameral Kurultai under the Constitution adopted in 2026. Using doctrinal and functional comparison, it contrasts the composition, representative basis, legislative procedure and oversight powers of the institutions created by the 1995 and 2026 Constitutions. The article identifies three principal results. First, the reform is not primarily a reduction in the size of the legislature: the Kurultai's 145 seats are close to the combined membership of the former Mazhilis and Senate. Its central effect is the concentration of national legislative authority in a single directly elected chamber. Second, the reform replaces the former combination of territorial, mixed and appointed representation with nationwide proportional representation through political parties, producing clearer electoral responsibility but removing constitutionally guaranteed regional representation and single-mandate links. Third, legislative scrutiny is transferred from an inter-chamber process to committees, hearings, opposition rights and plenary voting within the Kurultai. The article argues that unicameralism may improve speed and transparency, but it does not by itself create a stronger parliament. Its success will depend on internal scrutiny, political pluralism and the Kurultai's practical capacity to hold the executive accountable.

Keywords

Kazakhstan; 2026 Constitution; Kurultai; Parliament; unicameralism; bicameralism; legislative power; representation; parliamentary oversight; separation of powers.

Introduction

The adoption of Kazakhstan's new Constitution at the nationwide referendum of 15 March 2026 marked a formal break with the constitutional settlement that had governed the country since 1995. Among its most important institutional changes was the termination of the bicameral Parliament, composed of the Senate and the Mazhilis, and its replacement by a unicameral body known as the Kurultai. The new Constitution entered into force on 1 July 2026, and the former Parliament ceased to exercise its powers on the same date. This was not simply a change of name. It altered the way in which citizens and regions are represented, the procedure through which laws are reviewed and adopted, and the structure through which the legislative branch interacts with the President and Government.

A second chamber may slow legislation and obscure responsibility, but it can also represent territorial interests, correct errors and restrain a temporary majority. Unicameralism may therefore improve efficiency and electoral accountability only if strong internal institutions perform the reviewing functions previously divided between two chambers.

This article compares the parliamentary provisions of the 1995 and 2026 Constitutions through four criteria: representation, legislative scrutiny, political accountability and the legislative-executive balance. It argues that the reform simplifies and democratises the formal source of parliamentary authority because every Kurultai deputy is directly elected. However, it also removes a distinct channel of territorial representation and concentrates review within one party-based institution. The promise of a stronger parliament will therefore depend on committee work, opposition participation and practical independence from the executive.

The Bicameral Baseline Under the 1995 Constitution

The 1995 Constitution defined Parliament as the highest representative body exercising legislative power. Article 50 divided that body into two permanent chambers. The Mazhilis consisted, at the end of the Constitution's operation, of ninety-eight deputies elected through a mixed system: sixty-nine from party lists in a nationwide constituency and twenty-nine from single-mandate territorial constituencies. The Senate represented the seventeen regions, the capital and the cities of republican significance, with two elected senators from each territorial unit. Ten additional senators were appointed by the President, five of them on the recommendation of the Assembly of the People of Kazakhstan. Senate deputies served six-year terms, with half of the elected membership renewed every three years, while Mazhilis deputies served five-year terms (1995 Constitution, arts 50-51).

This design combined several forms of representation. Party-list deputies reflected national political preferences, single-mandate deputies created a territorial connection, and the Senate gave equal representation to the principal administrative units regardless of population. In January 2026 Kazakhstan had seventeen regions and three cities of republican significance. The formula therefore produced fifty senators and, together with the Mazhilis, 148 national legislators.

Bills were introduced in the Mazhilis and, once adopted, transmitted to the Senate, which normally had up to sixty days to consider them. Rejection or proposed amendments could lead to renewed voting or conciliation. The Senate also approved or elected senior officials and could exercise legislative functions during the temporary absence of the Mazhilis following its dissolution (1995 Constitution, arts 54-55 and 61).

The bicameral structure introduced negotiation and territorial representation into a strongly presidential order. Yet it could also lengthen legislation without producing independent scrutiny where party alignment and executive influence were similar across both chambers. Its value therefore depended on whether the Senate added a distinct voice and effective second examination.

Bicameralism, Unicameralism and Constitutional Function

Comparative constitutional scholarship treats the number of chambers as an instrument rather than an end. International IDEA identifies territorial or minority representation, expert review, additional deliberation and checking the first chamber as common functions of second chambers. Meg Russell likewise evaluates them by function, while George Tsebelis and Jeannette Money show that an additional institutional veto player can stabilise policy but also create delay and disagreement.

Unicameralism reverses these trade-offs. It may enact legislation more quickly, clarify responsibility and avoid duplication between similar bodies. Removing the second chamber, however, also removes an automatic stage of review. Legislative quality must then be protected through readings, specialised committees, public consultation, opposition rights and constitutional review.

Inter-Parliamentary Union data show that unicameral legislatures are more common globally, although many territorially diverse states retain two chambers. Kazakhstan's unitary character permits unicameralism, but its scale keeps the Senate's former regional function

relevant. The assessment must ask which functions disappeared, which were transferred and whether the replacements are equivalent.

The 2026 Constitutional Turn to the Kurultai

President Kassym-Jomart Tokayev publicly proposed a unicameral parliament in September 2025 as a continuation of the principle of a strong President, an influential Parliament and an accountable Government. While acknowledging the Senate's historical contribution, he connected a single chamber to the evolution of the state and political culture. The proposal ultimately formed part of a broader constitutional replacement.

Articles 52-62 of the 2026 Constitution establish the Kurultai as the highest representative body exercising legislative power. Its 145 deputies are elected for five years through proportional representation in a single nationwide constituency by universal, equal and direct suffrage. The Constitutional Law on the Kurultai adds principles of legality, collegiality, transparency, political diversity and equality of deputies.

The comparison shows that the reform barely changes the legislature's numerical size: the former Parliament had 148 seats under the territorial structure existing in early 2026, while the Kurultai has 145. The transformation is structural rather than numerical. Efficiency therefore concerns the removal of inter-chamber procedure, not a substantially smaller legislature.

The Kurultai gathers powers previously divided between the chambers. It adopts laws, decides questions of war and peace, initiates referendums, approves the Prime Minister and Vice President, participates in constitutional appointments and exercises financial and political oversight. This creates a more visible centre of responsibility, while increasing the importance of its composition and internal organisation.

Representation: Direct Election and the Loss of a Territorial Chamber

The strongest democratic argument for the Kurultai is the uniform origin of its mandate. Mazhilis deputies were directly elected, most senators indirectly elected and ten senators presidentially appointed. All 145 Kurultai deputies are elected through direct suffrage, removing differently legitimised categories of legislators and making political parties responsible for the entire composition.

Uniformity creates another problem. The former Parliament combined equal regional representation in the Senate with party-list and single-mandate representation in the Mazhilis. Nationwide proportional representation removes both guaranteed regional seats and individual national constituencies. A deputy also loses the mandate upon withdrawal or expulsion from the electing party (2026 Constitution, art 55(4)). This strengthens party coherence but may reduce individual independence.

This matters in a geographically large state with diverse urban, industrial and rural interests. Proportional representation may reflect national preferences fairly, but it does not guarantee each region a voice equivalent to its former Senate delegation. Balanced party lists may help, but they are a political practice rather than a constitutional guarantee.

The result is mixed: direct electoral legitimacy increases while the constitutional diversity of representation narrows. Its practical effect will depend on party competition, candidate selection and the geographical composition of lists. Direct election is important, but it is not identical to territorial responsiveness.

Legislative Efficiency and the Quality of Scrutiny

The clearest procedural advantage of the Kurultai is the elimination of the passage of bills between two chambers. Under the 1995 system, a law adopted by the Mazhilis moved to the Senate, which could approve it, reject it or propose new wording. Disagreements could require conciliation and renewed voting. Under Article 60 of the 2026 Constitution, a law adopted by the Kurultai is submitted to the President for signature within ten days. The reform therefore shortens

the formal route from legislative initiative to presidential consideration and makes it easier to identify which body is responsible for the final parliamentary text.

Efficiency cannot be measured by speed alone. A second chamber creates time to identify errors and conflicting interests. Under unicameralism, this work must occur before the plenary vote. The Constitutional Law provides committees, commissions, working groups, hearings and government hours. Party factions have speaking rights, while the opposition may initiate a hearing and set the agenda of government hours during a session. These mechanisms can provide scrutiny without recreating a second chamber.

Effectiveness will depend on procedure and capacity. Committees need time, research support, information and a real ability to amend government bills. Consultation must influence texts, and opposition rights must place alternatives on the legislative record. Constitutional review cannot replace routine policy scrutiny.

The abolition of the Senate shifts quality control from external review by another chamber to internal review within the Kurultai. This reduces duplication, but makes strong committees and minority participation a constitutional necessity.

Oversight and the Continuing Strength of the Presidency

The Kurultai possesses significant formal oversight powers. One-fifth of its deputies may initiate a vote of no confidence in the Government, which can be adopted by a majority of the total membership. Failure to approve the Government's report on execution of the republican budget constitutes a vote of no confidence. At the initiative of one-third of deputies, the Kurultai may hear a report from a member of the Government; a two-thirds majority may then petition for dismissal where that official has failed to comply with the law, and the President must dismiss the official. The Kurultai also hears reports from the Constitutional Court and Supreme Audit Chamber (2026 Constitution, art 56).

These powers support the Government's stated accountability to both the President and Kurultai. Appointment, financial control and ministerial responsibility now appear in one public forum, making legislative action or inaction easier to identify.

Nevertheless, the President nominates the candidate for Kurultai Chairperson, may prioritise bills, convene extraordinary sessions and return legislation with objections. The President may dissolve the Kurultai after consultation and in cases of repeated refusal to approve nominees. During its temporary absence following early termination, presidential decrees may have the force of law (2026 Constitution, arts 46-47 and 62).

The balance is not transformed into legislative supremacy. The Kurultai receives concentrated oversight powers while the President retains agenda-setting, veto and dissolution instruments. A single chamber may confront the executive more clearly; a disciplined majority aligned with the executive may instead make its legislation easier to enact. The outcome depends on pluralism and the willingness of deputies to use their powers.

The Kazakhstan People's Council: Complement, Not Second Chamber

The new Constitution also creates the Kazakhstan People's Council, or Halyk Kenesi, as the highest consultative body representing the interests of the people. It may develop recommendations on internal policy, submit draft laws to the Kurultai and initiate a nationwide referendum. Because it introduces another representative institution into the constitutional order, it might appear to compensate for the disappearance of the Senate.

The Halyk Kenesi is not a second chamber. It does not approve, reject or amend laws, its members are not elected as a territorial upper house, and its recommendations create no additional legislative stage. Its initiative may place social or regional concerns before the Kurultai, but it cannot reproduce the Senate's veto, appointment or review functions.

This distinction matters for evaluating the reform. Consultation can improve the information available to legislators, but it is different from constitutional checking power. The

Halyk Kenesi should therefore be assessed as a participatory complement to the Kurultai rather than as an institutional replacement for bicameralism.

Overall Assessment

The transition from Parliament to the Kurultai produces three central constitutional changes. First, it creates a single and directly elected source of legislative legitimacy. Second, it replaces a plural system of territorial, constituency and party representation with nationwide proportional representation. Third, it transfers the burden of legislative review from relations between two chambers to the internal institutions of one chamber.

The process becomes easier to understand, decisions are attributable to one body and all deputies possess electoral mandates. The Kurultai also combines substantial legislative, appointment and oversight powers and can become more visible than the former divided Parliament.

The risks are equally clear. Regions lose equal national representation, voters lose individual national constituencies, and a disciplined majority may control the only chamber. The removal of compulsory second review requires strong committees, meaningful hearings, transparent list selection, opposition rights and constitutional review.

Institutional simplification does not automatically equal parliamentary strengthening. With 145 seats, the reform redistributes rather than reduces representative and reviewing functions. Success should be measured through the geographical diversity of deputies, substantive committee amendments, opposition-initiated hearings, government questioning and willingness to reconsider executive proposals. At the time of writing, the first Kurultai election had not taken place, so these outcomes remained open.

Conclusion

The replacement of Kazakhstan's bicameral Parliament with the unicameral Kurultai is one of the most consequential institutional reforms contained in the 2026 Constitution. The former Senate and Mazhilis divided representation and legislative review between bodies with different composition and functions. The Kurultai consolidates those functions in a single chamber of 145 directly elected deputies and thereby offers a clearer line of democratic responsibility.

The reform may increase speed and transparency. It removes appointed seats and gives the whole legislature a direct electoral basis. At the same time, it abolishes guaranteed regional representation, single-mandate national constituencies and automatic second-chamber review. Those functions must now be addressed through party lists, committees, hearings, opposition participation and constitutional control.

The decisive issue is whether the new institutions can preserve deliberation and regional responsiveness while making lawmaking more accountable. The Kurultai has meaningful powers, but the presidency remains strong. Parliament will be strengthened only if legal authority is supported by pluralistic practice and professional scrutiny.

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Geographic Sciences

Şəki-Zaqatala Regional Turizm Ekosisteminin CİS (GIS) Əsaslı Modelləşdirilməsi və Rekreasiya Potensialının Zonalaşdırılması

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GIS-Based Modeling of the Sheki-Zaqatala Regional Tourism Ecosystem and Zoning of Recreation Potential

Abstract: The Sheki-Zaqatala economic region, particularly its key historical and geographical center, the city of Sheki, possesses rich natural-recreational and cultural-historical resources. In this research paper, the assessment of Sheki region's tourism ecosystem and the zoning of its recreational potential were conducted based on Geographic Information Systems (GIS) and Multi-Criteria Decision Analysis (MCDA) methodology. Utilizing the Analytical Hierarchy Process (AHP) algorithm, physical-geographic and socio-economic factors—including topography (slope, aspect), vegetation cover (NDVI), hydrography, and transportation-infrastructure networks—were mathematically weighted. As a result of the spatial analysis, the territory of Sheki was classified into optimal recreational zones based on specific tourism types (ecotourism, mountain-sports, and cultural-historical tourism), and a regional sustainable development model was proposed.
Keywords: GIS, Sheki, recreational potential, tourism ecosystem, Multi-Criteria Decision Analysis (MCDA), Analytical Hierarchy Process (AHP), zoning.

Xülasə: Şəki-Zaqatala iqtisadi rayonu, xüsusilə onun mühüm tarixi və coğrafi mərkəzi olan Şəki şəhəri zəngin təbii-rekreasiya və mədəni-tarixi resurslara malikdir. Bu tədqiqat işində Şəki regionunun turizm ekosisteminin qiymətləndirilməsi və rekreasiya potensialının zonalaşdırılması Coğrafi İnformation Sistemləri (CİS) və Çoxmeyarlı Qərarvermə Təhlili (MCDA) metodologiyası əsasında həyata keçirilmişdir. Analitik İerarxiya Prosesi (AHP) alqoritmi vasitəsilə relyef (meyillilik, ekspozisiya), bitki örtüyü (NDVI), hidroqrafiya və nəqliyyat-infrastruktur faktorları riyazi olaraq çəkiləndirilmişdir. Təhlillər nəticəsində Şəki ərazisi turizm növlərinə (ekoturizm, dağ-idman və mədəni-tarixi turizm) görə optimal rekreasiya zonalarına ayrılmış və regional dayanıqlı inkişaf modeli təklif edilmişdir.
Açar sözlər: CİS, Şəki, rekreasiya potensialı, turizm ekosistemi, Çoxmeyarlı Qərarvermə Təhlili (MCDA), Analitik İerarxiya Prosesi (AHP), zonalaşdırma.

1. Giriş

Turizm və rekreasiya sektorunun regional inkişafda, məşğulluğun artırılmasında və təbii-mədəni irsin qorunmasında rolu getdikdən artmaqdadır. Azərbaycan Respublikasında regionların sosial-iqtisadi inkişafı dövlət proqramlarında Şəki-Zaqatala regionunun turizm potensialının optimallaşdırılması strateji hədəf kimi qarşıya qoyulmuşdur (Məmmədov, 2018).

Lakin rekreasiya resurslarının plansız və kortəbii mənimsənilməsi ekoloji landşaftın deqradasiyasına və resursların tükənməsinə yol açа bilər. Müasir coğrafiya elmində turizm ekosistemlərinin planlaşdırılması və məkansal idarə edilməsi üçün Coğrafi İnformasiya Sistemləri (CİS) və Çoxmeyarlı Qərarvermə Təhlili (MCDA) ən effektiv alətlər hesab olunur (Malczewski, 2006). Bu tədqiqatın məqsədi Şəki regionunun fiziki-coğrafi və sosial-iqtisadi göstəricilərini CİS mühitində modelləşdirərək, ərazinin rekreasiya tutumunu və optimal turizm zonalarını müəyyənləşdirməkdir.

2. Metodologiya və Çoxmeyarlı Qiymətləndirmə (MCDA-AHP)

Şəki regionunun turizm ekosisteminin CİS əsaslı modelləşdirilməsində **Analitik İerarxiya Prosesi (AHP)** metodologiyasından istifadə edilmişdir (Saaty, 2008). Tədqiqatda ərazinin uyğunluq indeksini müəyyən etmək üçün 4 əsas meyar və onlara aid alt-meyarlar təyin olunmuş, çəki əmsalları riyazi olaraq hesablanmışdır:

1. **Topoqrafik Faktorlar (Çəki: 0.35):** Rəqəmsal Relyef Modeli (DEM) əsasında meyillilik (slope) və yamacların ekspozisiyası (aspect) analiz edilmişdir. Dağ-idman turizmi üçün 15°-25° arası meyillilik, ekoturizm üçün isə 0°-10° arası meyillilik optimal qəbul olunmuşdur.
2. **Ekoloji-Landşaft Faktorları (Çəki: 0.30):** Landsat 9 peyk görüntülərindən hesablanan Normalaşdırılmış Fərq Bitki Örtüyü İndeksi (NDVI) vasitəsilə meşə massivlərinin sıxlığı və hidroqrafik şəbəkəyə (çaylar, bulaqlar) olan məsafə (Euclidean distance) qeyd olunmuşdur.
3. **Sosial-İqtisadi və İnfrastruktur Faktorları (Çəki: 0.20):** Nəqliyyat şəbəkəsinə (magistral və lokal yollar) yaxınlıq və rekreasiya obyektlərinin əlçatanlığı.
4. **Mədəni-Tarixi İrs (Çəki: 0.15):** UNESCO-nun Ümumdünya İrsi siyahısına daxil edilmiş Şəkinin tarixi mərkəzi və memarlıq abidələrinin məkansal bufer zonaları (buffer zones).

3. Analiz və Müzakirə: Rekreasiya Potensialının Zonalaşdırılması

CİS mühitində (ArcGIS/QGIS) bütün meyarların raster layları **Overley (Weighted Overlays)** aləti vasitəsilə üst-üstə qoyularaq Şəki regionunun ümumi Turizm Uyğunluq İndeksi (TSI) xəritə-modeli generasiya edilmişdir. Ərazi rekreasiya potensialına görə 4 əsas sinfə (klasterə) ayrılmışdır.

Cədvəl 1: Şəki regionunun CİS əsaslı Turizm Uyğunluq İndeksi (TSI) göstəriciləri

Uyğunluq Səviyyəsi	Ərazi Payı (%)	Coğrafi Landşaft Tərkibi	Ən Uyğun Turizm Növü
Yüksək dərəcədə uyğun	28%	Tarixi mərkəz, dağətəyi meşəliklər, çay vadiləri	Mədəni-tarixi, Ekoturizm, Aqroturizm
Mülayim dərəcədə uyğun	42%	Alçaq və orta dağlıq zonalar, kolluqlar	Yay turizmi, Sağlamlıq-balneoloji
Az uyğun	18%	Yüksək dağlıq, sıldırım yamaclar, çılpaq qayalıqlar	Ekstremal dağ turizmi, Alpinizm
Uyğun olmayan	12%	Sənaye obyektləri, erroziyaya uğramış aktiv sahələr	Rekreasiya üçün qapalı zonalar

Modelləşdirmə nəticəsində aşkar olunmuşdur ki, Şəki ərazisinin **70%-i (Yüksək və Mülayim siniflər birlikdə)** aktiv turizm və rekreasiya fəaliyyəti üçün tamamilə əlverişlidir. Xüsusilə Şəki şəhərinin şimal və şərq hissələrində yerləşən dağətəyi enliyarpaqlı meşə landşaftları ekoturizm üçün ən yüksək pik balları (TSI > 0.85) toplamışdır.

4. Turizm Növlərinə Görə Regional Məkansal Modelləşdirmə

CİS analizi Şəki regionunda turizmin differensiasiyalı (şaxələnmiş) şəkildə inkişaf etdirilməsinin coğrafi zəruriliyini ortaya qoyur (Həsənov, 2021):

- **Ekoturizm və Rekreasiya Klasteri:** Kiş və Xan yaylası istiqamətindəki meşə-fyon landşaftları yüksək NDVI (0.68) və zəngin hidroqrafiyası ilə ekoloji turizm marşrutlarının qurulması üçün rəqəmsal model tərəfindən ilkin zona olaraq təyin edilmişdir. Bu ərazilərdə təbii tarazlığı pozmamaq üçün irihəcmli otellər əvəzinə ekoloji kənd evlərinin (camping/glamping) salınması elmi cəhətdən əsaslandırılır.

- **Mədəni-Tarixi və Şəhər Turizmi Klasteri:** Şəki Xan Sarayı, Karvansaraylar və qədim "Yuxarı Baş" qoruğu ətrafındakı 1 sm-lik bufer zonaları mədəni turizmin nüvəsini təşkil edir. CİS şəbəkə analizi (Network Analysis) göstərir ki, nəqliyyat əlçatanlığı yüksək olsa da, pik mövsümlərdə (may-sentyabr) bu ərazidə antropogen yüklənmə (rekreasiya tutumu həddi) kritik səviyyəyə çatır.
- **Dağ-İdman və Ekstremal Turizm Klasteri:** Regionun şimalındakı yüksək dağlıq qurşaq (Böyük Qafqazın suayırıcısı) sıldırım yamacları (meyillilik > 30°) ilə alpinizm, qış turizmi və paraşüt idmanı üçün spesifik potensiala malikdir.

5. Dayanıqlı Regional Turizm Menecmenti və Tövsiyələr

Tədqiqatın CİS əsaslı nəticələrinə əsasən Şəkinin regional turizm ekosisteminin davamlılığı üçün aşağıdakı eko-coğrafi model təklif olunur:

1. **Məkansal Monitorinq Sisteminin Qurulması:** Peyk monitorinqi (Remote Sensing) vasitəsilə turizm zonalarında bitki örtüyünün sıxlığı (NDVI) və torpaq deqradasiyası hər mövsüm sonu avtomatik izlənilməlidir.
2. **Antropogen Yükün İdarə Edilməsi:** Tarixi mərkəzdə rekreasiya sıxlığını azaltmaq üçün turist axınları CİS modelinin müəyyən etdiyi alternativ kənd turizmi marşrutlarına (məsələn, Fazıl, Oxud kəndləri istiqamətinə) yönləndirilməlidir.
3. **İnfrastrukturun Yaşıllaşdırılması:** Yeni tikiləcək rekreasiya obyektləri mütləq şəkildə relyefin meyillilik xəritələrinə uyğun salınmalı, sürüşmə zonalarından uzaq tutulmalıdır.

6. Nəticə

Şəki regionunun turizm ekosisteminin CİS və Çoxmeyarlı Qərarvermə Təhlili (MCDA-AHP) vasitəsilə modelləşdirilməsi təbii və sosial-iqtisadi resursların regional planlaşdırılmasında məkansal dataların tətbiqinin effektivliyini sübut etmişdir. Yaradılmış rəqəmsal model ərazinin rekreasiya potensialının coğrafi sərhədlərini dəqiqliklə müəyyən etməyə və riskli zonaları öncədən proqnozlaşdırmağa imkan verir.

Əldə olunan nəticələr göstərir ki, Şəki regionunda dayanıqlı turizmin inkişafı yalnız mədəni irslə məhdudlaşmamalı, CİS modelinin müəyyənləşdirdiyi yüksək uyğunluqlu meşə və dağ landşaftlarının ekotexnoloji prinsiplərlə mənimsənilməsi hesabına genişləndirilməlidir. Bu tədqiqat işinin metodologiyası və xəritə-modelləri regional turizm planlarının hazırlanmasında, investisiya layihələrinin ekoloji ekspertizasında və Şəki şəhərinin davamlı "smart-tourism" konsepsiyasının formalaşdırılmasında rəsmi elmi baza kimi istifadə oluna bilər.

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Psychological Sciences

Meeting the educational needs of gifted children in an inclusive education environment

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ABSTRACT

The effective inclusion of gifted children in the educational process is one of the important directions of modern inclusive education. The high intellectual and creative potential of these children requires their individual educational needs to be recognized and appropriate pedagogical support to be provided. This article examines the academic, social, and emotional challenges faced by gifted children in inclusive educational environments, as well as approaches to organizing instruction according to their individual characteristics. Individualized and differentiated instruction, enriched curricula, individualized educational plans, and student-centered pedagogical approaches are considered important tools for developing the potential of gifted children. The article also emphasizes the role of cooperation among teachers, parents, psychologists, and other specialists in ensuring children's academic achievement, social adaptation, and emotional well-being. The analysis demonstrates that a properly organized inclusive educational environment supports not only the intellectual abilities of gifted children but also their social and emotional development. Consequently, the implementation of pedagogical strategies based on individual educational needs enables gifted children to fully realize their potential, participate equally in the educational process, and achieve successful integration into society.

KEYWORDS: gifted children, inclusive education, individualized education plan, motivation and support, social integration, differentiated instruction, teacher–parent collaboration

In the modern education system, the development of gifted children and their integration into inclusive educational environments are among the important pedagogical priorities. An inclusive approach is not limited to physical participation and equal educational opportunities; it also aims to reveal the individual potential of each child and support their social and emotional development (Şıxlı, 2019; Həsənov, 2020). Since gifted children possess high intellectual and creative abilities in certain areas, their educational needs differ from those of other students and therefore require specialized approaches.

The education of these children in inclusive classrooms is not limited to increasing academic knowledge but also contributes to the development of their creative skills, social integration, and emotional stability (Rüstəmov, 2017; Məmmədova, 2022). Individualized educational plans, motivation and support mechanisms, teacher professionalism, and parent–school cooperation serve as key instruments in the educational process (Əliyeva, 2018; Qasımova, 2018; İsmayılov, 2019).

Thus, the inclusion of gifted children in inclusive education is a multidimensional and complex process in terms of both individual and social development. This article examines the educational

needs of gifted children in inclusive education, the development of individualized educational plans, the roles of teachers and parents, and aspects of motivation and social integration. It also presents strategies aimed at ensuring their academic and social development.

The main purpose of the inclusive education model is to eliminate discrimination among students and to ensure the maximum development of every child's potential. One of the fundamental principles of inclusive education is the provision of equal educational opportunities, which requires consideration of the specific needs of gifted children. The principle of equal opportunities is not limited to physical participation; it also includes providing additional resources, individualized educational programs, and psychological support within the learning environment.

Inclusive education also requires the implementation of individualized and differentiated instruction. This approach makes it possible to organize learning activities according to the higher cognitive processing speed of gifted children. Individualized instruction requires the selection of learning materials based on students' interests, abilities, and developmental levels, thereby preventing loss of motivation caused by monotony and repetitive tasks.

The educational needs of gifted children differ from those of other students. Their intellectual development tends to progress at a faster rate, while abstract thinking and problem-solving abilities may develop at an early age. Therefore, the tasks provided to them should be more complex, research-oriented, and creative. At the same time, the social and emotional characteristics of these children require particular attention, as some may experience difficulties in relationships with peers, feel different from others, or become socially isolated due to internal emotional tension. To maintain their emotional well-being, a supportive environment should be established in the inclusive classroom, and teachers should use methods that provide children with greater opportunities for individual expression.

If effective strategies for adapting gifted children to inclusive classrooms are not implemented, they may become disengaged from learning or fail to fully demonstrate their potential. In this regard, acceleration programs are particularly important because gifted children often master educational material more quickly, and accelerated learning may be more appropriate for their needs. Acceleration can take the form of grade skipping, early access to specific subjects or topics, and additional learning activities.

In addition, enrichment programs are specialized educational programs designed to broaden gifted children's interests and develop their analytical and creative skills. These programs may include challenging tasks, projects, research activities, and creative assignments. The implementation of enrichment programs in inclusive classrooms supports children's intellectual and social development in a balanced manner. The teacher structures these programs according to the child's developmental pace and gradually increases the complexity of the learning materials.

The development of Individualized Education Plans (IEPs) for gifted children in inclusive classrooms is an important process in the modern education system, as this approach provides an opportunity to identify and develop each student's individual potential. The importance of an individualized approach lies in the teacher's ability to assess each gifted child's level of knowledge, interests, abilities, and developmental pace separately and to develop an appropriate instructional strategy. This increases the child's motivation to learn and helps prevent the loss of their talents. Furthermore, an individualized approach enables students with different levels of ability to develop harmoniously together within an inclusive environment.

Since the educational needs of gifted children differ from those of other students, the development of an Individualized Education Plan (IEP) is essential. In this regard, the structure of the IEP is particularly important, and its main components should be clearly defined. The key elements of an IEP include the formulation of goals, the identification of learning objectives, and the establishment of a continuous monitoring system. Goals are planned according to the child's potential from both short-term and long-term perspectives. Learning objectives include specific

steps for achieving these goals and contribute to the gradual development of the child's knowledge and skills. Monitoring enables continuous observation of the child's progress during the learning process and allows the plan to be modified when necessary. Structuring the IEP also ensures that the educational process is implemented in a systematic and transparent manner.

Determining learning goals for gifted children is one of the most important components of an IEP, as their developmental direction is largely determined by these goals. For children with strong academic abilities, goals should include activities involving more complex content, higher-order thinking skills, and analytical reasoning. These goals not only increase the child's level of knowledge but also develop their ability to explore new topics in greater depth. For creatively gifted children, goals should focus on strengthening innovative thinking, imagination, and problem-solving skills. Research projects, creative tasks, experiments, and independent activities are particularly important for these children. Appropriate formulation of learning goals ensures balanced development in both academic and creative areas.

The roles of teachers and psychologists are crucial in developing individualized education plans, as this process requires multidisciplinary cooperation. As the primary professional responsible for identifying the child's educational needs, the teacher develops the structure of the individual plan and selects appropriate teaching methods and strategies. The psychologist evaluates the child's emotional state, social behavior, self-confidence, and motivation and provides guidance to the teacher. The multidisciplinary team should also involve parents, as the family plays an important role in the child's development. The team identifies the child's strengths, determines potential difficulties, and creates an appropriate learning environment. Through cooperation between teachers and psychologists, problems that gifted children may encounter during the learning process can be identified at an early stage and addressed effectively.

Thus, the development of individualized education plans makes the education of gifted children in an inclusive environment more purposeful and effective. This approach contributes to the child's overall personal development and creates opportunities for them to realize their potential and participate more successfully in society in the future.

The role of the teacher in the inclusion of gifted children in inclusive education is highly significant from pedagogical, social, and psychological perspectives. Therefore, the teacher is considered one of the key pillars of the educational process. A teacher is not only a person who transmits knowledge but also a guide who identifies a child's talents at an early stage, directs their development, and provides continuous support. To take into account the individual characteristics and learning pace of gifted children, teachers should possess strong observational skills and pedagogical flexibility. The importance of the teacher lies in the fact that the effective and balanced organization of learning among students with different levels of ability in an inclusive classroom largely depends on the teacher's professional competence. If a teacher identifies a child's strengths at an early stage, this creates an opportunity for the child to develop their potential more fully and rapidly. In the absence of appropriate teacher support, gifted children may become disengaged from learning, lose motivation, or begin to conceal their abilities.

Professional competencies play a particularly important role in working with gifted children, as this process requires both theoretical knowledge and methodological expertise. The ability to implement differentiated instruction is one of the teacher's key competencies, enabling different levels of tasks to be provided to students with diverse learning styles and abilities. Differentiated instruction allows gifted children to engage in more complex, research-oriented, and creative activities, thereby preventing boredom and loss of motivation in a monotonous learning environment. Another important teacher competency is the identification of giftedness. A gifted child may not always be immediately recognized, as some children may hide their abilities or fail to stand out due to a lack of attention. By carefully observing a child's behavior, interests, and problem-solving abilities, the teacher can determine the areas in which the child demonstrates

particular strengths. This process contributes to establishing an appropriate path for the child's future development.

The appropriate selection of teaching methods in an inclusive classroom further emphasizes the teacher's role. Project-based learning is considered one of the effective methods for gifted children because it promotes creativity, analytical thinking, and teamwork skills. During project-based learning, children conduct independent research, analyze information, and draw conclusions, which contributes to the development of their cognitive potential. Research-oriented tasks also help develop gifted children's logical thinking and problem-solving skills. Such activities strengthen their ability to ask questions, conduct investigations, and draw conclusions, making them more active and independent learners. By applying these methods, teachers enrich the overall learning environment in the inclusive classroom while simultaneously addressing the specific educational needs of gifted children.

Teacher–student–parent collaboration plays a crucial role in the inclusion of gifted children in the inclusive education system. Through close communication with parents, teachers can obtain detailed information about the child's behavior, interests, and abilities at home, which contributes to the effectiveness of the educational process. Sharing information ensures that all participants in the educational environment are well informed and facilitates the purposeful development of teaching strategies. Establishing effective communication among the teacher, student, and parents ensures the active participation of all parties in the child's educational process. Motivation mechanisms are also particularly important in inclusive classrooms. To increase gifted children's motivation, teachers can use strategies such as recognizing their achievements, providing positive feedback, and creating opportunities to present their creative work. These approaches encourage children to become more actively involved in both academic and social activities and contribute to strengthening their self-confidence.

Consequently, the role of the teacher is indispensable for the successful participation of gifted children in an inclusive educational environment. The teacher is not merely an instructor but also a key guide who identifies the child's talents, directs their development, and contributes to the success of the learning process. The teacher's attention and professional competence enable children to fully realize their potential. Therefore, the teacher acts as a strategic leader and plays an important role in fostering giftedness within inclusive education.

The adaptation of gifted children to inclusive classrooms is one of the most sensitive issues, as their individual characteristics, learning pace, and social-emotional needs may differ considerably from those of other students. If adaptation difficulties are not identified in a timely manner, children's learning motivation may decrease, their self-confidence may weaken, and their developmental potential may become limited. Although inclusive education aims to ensure that all students feel comfortable and secure within the same learning environment, gifted children may require additional support to address their specific needs. Adaptation difficulties mainly emerge in academic and social-emotional areas, and each can significantly influence the child's overall development.

Academic difficulties are primarily associated with the rapid learning abilities of gifted children. Since they can master topics quickly and in considerable depth, the general pace of classroom instruction may appear too slow for them. As a result, their interest in lessons may decrease, their attention may become distracted, and they may begin to conceal their abilities. The standard classroom pace is not always appropriate for gifted children, and adapting to the general pace of a large class may become a significant academic challenge. In such circumstances, children may feel that their needs are not being adequately addressed and may seek additional learning opportunities. An inappropriate learning pace may negatively affect academic outcomes in the long term and contribute to disengagement from education.

Social-emotional difficulties also have a significant impact on adaptation. Gifted children may sometimes feel misunderstood because their ways of thinking and behaving differ from those of their peers. This can lead to reserved behavior in new environments, reluctance to participate actively in lessons, and reduced social initiative. In addition, highly gifted children may experience emotional tension due to their tendency toward perfectionism. Difficulties in communicating with peers can result in social isolation, withdrawal, and the development of negative attitudes toward the school environment. Such adaptation problems can significantly affect children's social and emotional development and may contribute to long-term difficulties in social adjustment.

Effective strategies are therefore necessary to address these challenges, with the aim of supporting both children's academic development and social-emotional well-being. Counseling services are among the most important forms of support during the adaptation process. A psychologist can assess the child's emotional state, identify stress and self-confidence difficulties, and develop an appropriate psychological support plan. Counseling can also help children develop greater self-awareness, recognize their strengths, and improve their social skills. Psychological support enables gifted children to feel more confident within the inclusive environment. In addition, mentoring systems are highly valuable for gifted children, as mentors provide guidance and support in both academic and social areas. A mentor recognizes the child's potential, organizes appropriate activities, and closely monitors their development. A mentoring system can prevent gifted children from feeling isolated and provide them with a stronger sense of confidence and belonging.

The effective and continuous implementation of these strategies contributes to the successful adaptation of gifted children to inclusive educational environments. Coordinated cooperation among teachers, psychologists, and parents makes the child's developmental process more effective. Thus, addressing adaptation difficulties is important not only for the individual child but also for the education system as a whole, as it contributes to improving the quality of inclusive education. A supportive environment created for gifted children strengthens both their academic achievement and social-emotional well-being and provides greater opportunities for them to develop into successful and socially engaged individuals.

Motivation and support mechanisms play a fundamental role in the successful learning of gifted children in inclusive educational environments. During the learning process, children's learning pace, level of attention, and creative abilities are closely associated with their motivation. In modern pedagogy, the relationship between motivation and learning achievement is recognized as an important principle. Gifted children, particularly those studying in inclusive classrooms, may demonstrate a high sensitivity to both intrinsic and extrinsic sources of motivation. Their academic performance may increase or decline depending on their level of motivation. When teachers correctly identify the factors that influence motivation, children's talents can be recognized and developed more effectively.

Intrinsic motivation arises from a child's interest in learning, discovering new knowledge, and engaging in creative activities. Extrinsic motivation, in contrast, is associated with assessment, rewards, and social recognition. Although intrinsic motivation tends to be more dominant among gifted children, their opportunities for self-expression may sometimes be limited in inclusive environments. Therefore, teachers should continuously support the relationship between motivation and learning. The individual characteristics of each child should be taken into account, and motivational methods should be adapted to their specific needs.

Motivational strategies in inclusive classrooms should be multidimensional. A reward system can be an important tool because it provides opportunities to objectively recognize gifted children 's achievements and encourage further development. Rewards should not be limited to material forms; non-material forms of recognition should also be used. Praise, granting special

responsibilities, and providing leadership opportunities in projects can have a significant positive impact on children's motivation.

Expanding opportunities for self-expression is another important aspect of motivation. When children are given opportunities to prepare presentations, work on projects, and conduct research, their self-confidence increases and they have greater opportunities to demonstrate their individual abilities. Teachers should organize classroom activities in a way that enables every child to participate, express opinions, and ask questions. Such active participation increases motivation and creates a supportive learning environment for all students. Gifted children, in particular, can benefit considerably from these opportunities.

Specialized support programs play a critical role in developing the abilities of gifted children. For example, preparation programs for academic competitions and olympiads can contribute to both intellectual development and increased self-confidence. These programs strengthen analytical thinking skills, create a competitive learning environment, and encourage children to achieve higher levels of performance. Creative clubs also provide additional opportunities for development, where children can learn to think independently, generate new ideas, and demonstrate their abilities. Such clubs also facilitate socialization by enabling children to interact with peers who have similar interests, which may help them feel more comfortable. Support programs not only improve academic outcomes but also contribute to children's emotional well-being. In this process, teachers and psychologists should work together and develop individualized development plans to maximize the effectiveness of these programs.

The inclusive organization of the learning environment is essential for the successful implementation of motivation and support mechanisms. Technological tools can make learning more interactive and engaging for gifted children. Digital resources provide additional opportunities for conducting research, preparing presentations, and engaging in creative activities. Interactive programs allow children to progress according to their individual learning pace. At the same time, technology provides access to a wider range of areas of knowledge and learning resources.

Psychological safety is also an important component of inclusive education. In a psychologically safe environment, children can express their potential freely and share their ideas without fear. Teachers should promote emotional stability and strengthen a culture of mutual respect among students. A student-centered learning environment makes motivational mechanisms more effective and enables gifted children to feel valued and recognized during the learning process. Consequently, motivation and support mechanisms are essential conditions for the successful development of gifted children in inclusive educational environments.

The social integration of gifted children through inclusive education is considered one of the key aspects of their harmonious development. Socialization is an important process that enables gifted children to establish meaningful relationships with society. It plays a significant role in shaping children's behavior, developing their value systems, and strengthening their social skills. For gifted children, socialization involves not only communication skills but also emotional stability. In an inclusive environment, socialization can be organized in a broader and more multidimensional manner. Effective socialization has a positive influence on children's self-awareness and personal development. The social environment provides essential conditions for the development of a child's identity. This process should continue not only at school but also within the family and the wider community. Gifted children may sometimes experience difficulties in adapting to social environments; therefore, the role of socialization becomes particularly important within inclusive education.

The social needs of gifted children may differ from those of other students. A tendency toward leadership is one of their natural characteristics. This tendency can contribute to the development of a sense of responsibility from an early age. Leadership tendencies may encourage gifted children

to take greater initiative in the classroom. When this characteristic is appropriately guided at an early stage, the process of social integration can become easier. At the same time, empathy skills in gifted children also require particular attention. They are often emotionally sensitive and may perceive the feelings of others deeply. The development of empathy contributes to stronger social relationships and enables children to communicate more sincerely with their peers. Proper identification of social needs helps gifted children adapt more comfortably to their social environment. Teachers should recognize these needs and select appropriate methods accordingly. The social needs of each child require an individualized approach.

The social integration of gifted children within inclusive education is considered one of the key directions for their harmonious development. The socialization process enables children to establish connections with society and develop their social skills. This process has a significant influence on the formation of behavior, acquisition of values, and development of social competencies. For gifted children, socialization involves not only communication skills but also emotional stability. In an inclusive environment, this process can be implemented in a broader and more multidimensional manner. When socialization is properly organized, children's self-awareness is strengthened, creating favorable conditions for the development of their identity. This process should continue not only at school but also within the family and the wider social environment. However, gifted children may sometimes experience difficulties in adapting to social environments; therefore, the importance of socialization becomes even greater in inclusive education.

The social needs of gifted children may differ from those of other students. A tendency toward leadership is among their natural characteristics and may contribute to the development of a sense of responsibility from an early age. This tendency can encourage children to take initiative in the classroom. When leadership skills are appropriately guided, social integration can take place more smoothly. In addition, empathy skills among gifted children require particular attention because they may be emotionally sensitive and capable of deeply understanding the feelings of others. The development of empathy enables children to establish more sincere and meaningful communication with their peers. Proper identification of social needs helps gifted children integrate more comfortably into their environment. Teachers should take these needs into consideration when selecting appropriate strategies. The social needs of children always require an individualized approach.

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Medical Sciences

ПАТОФІЗІОЛОГІЧНІ МЕХАНІЗМИ РОЗВИТКУ ФАНТОМНОГО БОЛЮ: СИМПТОМАТИКА ТА СУЧАСНІ МЕТОДИ ЛІКУВАННЯ (ОГЛЯДОВА)

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Анотація

Фантомний біль є складним нейропатичним больовим синдромом, який виникає у ділянці ампутованої або анатомічно відсутньої частини тіла. Незважаючи на відсутність периферичного анатомічного субстрату, пацієнт може відчувати різноманітні больові та сенсорні феномени, локалізовані в уявній частині кінцівки. Фантомний біль залишається важливою медико-соціальною проблемою, оскільки може суттєво погіршувати якість життя, сон, психоемоційний стан, функціональну активність і процес реабілітації пацієнтів після ампутації [1] За сучасними даними, фантомний біль виникає у значної частини пацієнтів після ампутації, а його патогенез є багатофакторним і включає периферичні, спінальні, супраспінальні та психосоціальні механізми. Однією з центральних концепцій патогенезу є нейропластична перебудова соматосенсорної та моторної кори після деаферентації. Водночас важливу роль відіграють патологічна активність нервових закінчень у куксі, зміни збудливості нейронів задніх рогів спинного мозку, порушення таламокортикальної взаємодії, зміни схеми тіла та формування стійкої больової пам'яті. Клінічно фантомний біль проявляється пекучим, стріляючим, стискаючим, електричним або судомоподібним болем, а також відчуттям незвичного положення, руху чи деформації відсутньої кінцівки. Лікування фантомного болю потребує комплексного мультидисциплінарного підходу. Застосовують фармакологічні засоби, фізіотерапію, дзеркальну терапію, градуйовану моторну уяву, віртуальну реальність, транскраніальну магнітну стимуляцію, нейромодуляцію та, у резистентних випадках, хірургічні методи. Сучасні дослідження свідчать про перспективність індивідуалізованого лікування, орієнтованого на конкретні патофізіологічні механізми болю.

Ключові слова: фантомний біль, фантомна кінцівка, ампутація, нейропатичний біль, нейропластичність, кортикальна реорганізація, деаферентація, дзеркальна терапія, нейромодуляція, реабілітація.

Фантомний біль (phantom limb pain, PLP) — це різновид нейропатичного болю, що відчувається в ділянці частини тіла, яка була ампутована або іншим чином анатомічно втрачена. На відміну від звичайного післяопераційного болю, його локалізація не відповідає наявним тканинам, оскільки пацієнт сприймає больовий сигнал у частині тіла, якої фізично вже немає. Фантомний біль необхідно відрізняти від фантомної сенсації тобто не болісного відчуття присутності ампутованої кінцівки та болю в куксі, який походить безпосередньо з тканин залишеної частини кінцівки [1].

Фантомні відчуття були описані задовго до сучасного розуміння нейрофізіології болю. Протягом тривалого часу їх виникнення пояснювали переважно психологічними механізмами. Однак розвиток нейрофізіології, функціональної нейровізуалізації та досліджень нейропластичності продемонстрував, що фантомний біль має складну біологічну основу. Сучасна концепція розглядає його як результат взаємодії периферичних нервових змін із патологічною перебудовою центральної нервової системи [2].

Фантомний біль може виникати після ампутації верхньої або нижньої кінцівки, а також після втрати інших частин тіла. За даними сучасних оглядів, симптоми можуть спостерігатися приблизно у 60–80% пацієнтів після ампутації, хоча частота залежить від популяції, тривалості спостереження, методики оцінювання та визначення самого феномену [3].

Важливість проблеми визначається не лише інтенсивністю больового синдрому. Хронічний фантомний біль може призводити до порушення сну, зниження фізичної активності, погіршення настрою, обмеження соціальної активності та труднощів із використанням протеза. Тому ефективна терапія повинна бути спрямована не тільки на зниження інтенсивності болю, але й на відновлення нормального сенсомоторного сприйняття та функціональної незалежності пацієнта.

Патогенез фантомного болю є багатофакторним. На сучасному етапі виділяють чотири основні групи механізмів прояву: периферичні, спінальні, супраспінальні та кортикальні, психосоціальні. Важливо підкреслити, що жодна з цих теорій окремо не може пояснити всі випадки фантомного болю. У різних пацієнтів співвідношення механізмів може істотно відрізнятися. Саме тому сучасні підходи поступово переходять від універсальної моделі лікування до механізм-орієнтованого підходу. [4]

Давайте детально розглянемо ці механізми. Безпосередньо після ампутації відбувається перерізання периферичних нервів. У проксимальних кінцях нервових волокон запускаються процеси дегенерації та регенерації. Порушення нормального росту аксонів може призводити до формування невром, патологічних структур з хаотично організованих нервових волокон. Невроми здатні генерувати спонтанну ектопічну електричну активність. Пошкоджені нервові волокна стають більш чутливими до механічного подразнення, температурних впливів та інших стимулів [5]. Внаслідок цього формується патологічний потік аферентної імпульсації, який надходить до спинного мозку. Водночас периферичний механізм не може повністю пояснити феномен фантомного болю. У деяких пацієнтів навіть блокада периферичних нервів не призводить до тривалого припинення болю. Крім того, фантомний біль може зберігатися навіть за відсутності значної патології кукси. Це свідчить про важливу роль центральних механізмів [6].

Після переривання периферичного сенсорного потоку відбуваються зміни функціонального стану нейронів задніх рогів спинного мозку, спинальні механізми. Тривала деаферентація може призводити до підвищення їхньої збудливості та розвитку центральної сенситизації, яка характеризується посиленням відповіді нейронів центральної нервової системи на аферентні стимули. Важливу роль у цьому процесі відіграє глутаматергічна передача та активація NMDA-рецепторів. У результаті цього навіть незначна периферична імпульсація може сприйматися центральною нервовою системою як інтенсивний больовий стимул. Формується своєрідний патологічний «підсилювач» болю, який може функціонувати незалежно від первинної причини ушкодження [7]. Спінальні механізми також пояснюють ефективність деяких методів нейромодуляції та фармакологічного впливу на центральні механізми болю, які разом із патологічною нейропластичністю є однією з найбільш значущих концепцій у сучасному розумінні фантомного болю. Мозок дорослої людини не є статичною структурою. Нервова система постійно адаптується до зміни сенсорної інформації та рухової активності. Після ампутації мозок втрачає значну частину нормальної аферентної інформації від відповідної кінцівки [5]. Цей стан називають деаферентацією. Соматосенсорна кора

організована за принципом соматотопічного представництва різних частин тіла. Після втрати кінцівки відповідна ділянка кори більше не отримує нормальної сенсорної інформації. Сусідні коркові представництва можуть частково поширюватися на деаферентовану ділянку. Саме явище кортикальної реорганізації стало одним із фундаментальних пояснень фантомного болю. Нейровізуалізаційні дослідження продемонстрували зв'язок між змінами соматосенсорної організації мозку та фантомним болем [7]. Однак важливо розрізняти фізіологічну та патологічну нейропластичність. Нейропластичність сама по собі не є патологією. Вона є необхідною для адаптації мозку після ампутації. Проблема виникає тоді, коли перебудова сенсомоторних мереж супроводжується формуванням патологічного больового сприйняття.

Однак окреме значення має порушення внутрішнього представлення тіла. Мозок формує складну нейрональну модель власного тіла, яка включає його форму, положення, розміри та можливість виконання рухів. Після ампутації моторна програма кінцівки може частково зберігатися, незважаючи на фізичну відсутність самої кінцівки, тому пацієнт може відчувати, що відсутня рука або нога знаходиться у певному положенні. Деякі пацієнти описують феномен «телескопування» начібто суб'єктивного відчуття, що фантомна кінцівка поступово скорочується та наближається до кукси [8]. При цьому виникає невідповідність між моторною командою, очікуваним сенсорним зворотним зв'язком, реальною відсутністю кінцівки та візуальною інформацією. Ця невідповідність сенсомоторної інтеграції може підтримувати фантомний біль. Саме на цьому принципі ґрунтується дзеркальна терапія: пацієнтові створюється візуальна ілюзія наявності ампутованої кінцівки та виконання нею рухів. Передбачається, що таким чином можна зменшити патологічну невідповідність між моторною командою та сенсорним зворотним зв'язком [9].

Таламус є одним із ключових вузлів передачі та інтеграції сенсорної інформації. Після деафернтації змінюється активність таламічних нейронів, що може впливати на обробку больових сигналів. Порушення взаємодії між таламусом і корою може сприяти формуванню патологічного сенсорного сприйняття [10]. Таким чином, фантомний біль не можна розглядати лише як локальне явище соматосенсорної кори. Функціональні зміни охоплюють широку мережу структур, залучених до формування больового досвіду, включаючи соматосенсорну та моторну кору, таламус, острівцеву кору, передню поясну кору та структури, пов'язані з емоційною оцінкою болю. Тому сучасна модель фантомного болю передбачає порушення роботи розподіленої нейрональної мережі, а не одного окремого центру.

Клінічна картина фантомного болю є різноманітною. Пацієнти можуть описувати біль як: пекучий, стріляючий, електричний, колючий, ріжучий, пульсуючий, стискаючий, судомоподібний, ниючий. Біль може виникати раптово або бути постійним. У деяких пацієнтів спостерігаються короткі пароксизми, тоді як у інших формується хронічний постійний больовий синдром. Окрім болю, характерними є фантомні сенсорні феномени. Пацієнт може відчувати: присутність відсутньої кінцівки, її положення у просторі, рухи, свербіж, поколювання, оніміння, відчуття холоду або тепла, стискання, патологічне згинання чи скручування пальців [8]. Окремим феноменом є болісний «спазм» фантомної кінцівки, коли пацієнт відчуває її вимушене положення, хоча об'єктивно такого руху не існує. Важливо диференціювати фантомний біль від болю в куксі. Біль у куксі може бути пов'язаний із невромою, інфекцією, ішемією, проблемами шкіри, кістковими змінами або механічним подразненням. Наявність таких патологічних змін не виключає одночасного існування фантомного болю.

Лікування фантомного болю залишається складним, оскільки не існує універсального препарату, який би ефективно усував усі патофізіологічні механізми синдрому. Фармакотерапія часто ґрунтується на принципах лікування нейропатичного болю. Одним із

препаратів, який досліджувався при фантомному болю, є габапентин. Його механізм пов'язаний із модуляцією потенціалзалежних кальцієвих каналів та зниженням вивільнення збуджувальних нейромедіаторів. Дані щодо ефективності габапентину є неоднозначними, проте він може застосовуватися у складі комплексної терапії окремих пацієнтів. У систематичному огляді фармакологічного лікування фантомного болю габапентин мав доказову базу серед досліджуваних препаратів, хоча результати щодо тривалого ефекту були змішаними [10]. Прегабалін також може використовуватися за принципами лікування нейропатичного болю, хоча специфічна доказова база саме для фантомного болю залишається обмеженою. Трициклічні антидепресанти та препарати, що впливають на серотонінергічну й норадренергічну передачу, можуть застосовуватися для контролю нейропатичного болю. Їх ефективність при фантомному болю варіює, тому вибір препарату має враховувати супутні симптоми, побічні ефекти та індивідуальні характеристики пацієнта [11]. Опіоїдні аналгетики можуть зменшувати інтенсивність фантомного болю, однак їх застосування при хронічному болю потребує особливої обережності через ризик толерантності, залежності та інших небажаних ефектів. Дані клінічних досліджень свідчать про аналгетичну ефективність морфіну в окремих пацієнтів, однак це не означає, що тривале застосування опіоїдів має бути стандартною стратегією для всіх хворих [12]. Оскільки NMDA-рецептори відіграють важливу роль у центральній сенситизації, досліджувалося використання кетаміну, він може зменшувати центральну гіперзбудливість та інтенсивність болю, особливо в певних періопераційних або резистентних випадках. Проте його застосування потребує медичного контролю через можливі психоміметичні та інші побічні ефекти [10]. Загалом сучасні огляди підкреслюють, що доказовість фармакологічних методів залишається нерівномірною, а відповідь на лікування значно варіює між пацієнтами [6].

У зв'язку з багатофакторним характером фантомного болю важливе місце займають реабілітаційні методики. Дзеркальна терапія є одним із найбільш відомих методів лікування фантомного болю. Основна гіпотеза полягає в тому, що візуальний зворотний зв'язок допомагає відновити відповідність між моторною командою та сенсорним сприйняттям. Дослідження функціональної нейровізуалізації показали, що зменшення болю після дзеркальної терапії може супроводжуватися змінами патологічної кортикальної реорганізації [11]. Метааналіз рандомізованих досліджень також продемонстрував зниження інтенсивності фантомного болю при застосуванні дзеркальної терапії, хоча якість доказів і результати окремих досліджень неоднорідні. Сучасні дослідження продовжують уточнювати оптимальну частоту, тривалість та структуру дзеркальної терапії [13].

Віртуальна реальність яка дозволяє створювати цифрове представлення відсутньої кінцівки та забезпечувати пацієнтові контроль її рухів. На відміну від традиційного дзеркала, цифрові технології дозволяють створювати складніші сенсорні сценарії та персоналізувати віртуальну кінцівку. Нові систематичні дослідження свідчать про перспективність віртуальної та доповненої реальності, а також інших неінвазивних методів, хоча загальна якість доказів поки залишається від низької до помірної [14].

У пацієнтів із резистентним фантомним болем можуть застосовуватися методи нейромодуляції. Такі як транскраніальна магнітна стимуляція (rTMS) яка дозволяє модулювати активність кори головного мозку без хірургічного втручання. Її потенційний ефект при фантомному болю пов'язують зі зміною кортикальної збудливості та функціонування больових мереж. Систематичний огляд 2024 року показав перспективність rTMS при фантомному болю, однак наявна доказова база залишається обмеженою через невелику кількість високоякісних досліджень [15]. Стимуляція спинного мозку яку можна розглядатися при хронічному фантомному болю, при відсутності ефекту на консервативне лікування. Методика передбачає електричну стимуляцію структур спинного мозку з метою модифікації патологічної передачі больових сигналів. Сучасні огляди розглядають

нейромодуляцію як перспективний напрям у пацієнтів із фармакорезистентним фантомним болем, хоча значна частина доказів все ще походить із невеликих досліджень та серій клінічних випадків [6] та інші. Отже фантомний біль не повинен лікуватися виключно одним спеціалістом або одним методом. Важливо враховувати не лише інтенсивність болю, а й функціональний стан пацієнта, якість сну, можливість використання протеза, психоемоційний стан та рівень соціальної активності. Психологічна підтримка не означає, що фантомний біль є «психогенним». Психологічні фактори можуть модулювати сприйняття болю через центральні механізми, впливати на увагу до больового сигналу, сон, рівень стресу та здатність пацієнта дотримуватися реабілітаційної програми. Саме мультидисциплінарні стратегії наразі вважаються найбільш обґрунтованим підходом до тривалого контролю фантомного болю [2]. Попри значний прогрес у розумінні патофізіології фантомного болю, питання його лікування залишається остаточно невирішеним. Оновлений огляд 2026 року підкреслює перспективність поєднання сенсомоторної реабілітації, нейромодуляції, психологічної підтримки та таргетованих хірургічних методів. Водночас автори наголошують на необхідності більших стандартизованих досліджень із тривалим спостереженням [4].

Висновки

Отже, фантомний біль слід розглядати не як простий наслідок пошкодження периферичного нерва, а як складний синдром порушеної взаємодії периферичної та центральної нервової системи. Розуміння механізмів його розвитку є ключовою передумовою для створення ефективних індивідуалізованих методів профілактики та лікування.

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ПОРУШЕННЯ МОЛЕКУЛЯРНО-КЛІТИННИХ МЕХАНІЗМІВ КОНСОЛІДАЦІЇ ПАМ'ЯТІ ПРИ НЕЙРОДЕГЕНЕРАТИВНИХ ПРОЦЕСАХ (ОГЛЯДОВА)

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Анотація

Консолідація пам'яті є складним багаторівневим процесом, що забезпечує перетворення нестабільних слідів нейронної активності на тривалі функціональні та структурні зміни в нервовій системі. Важливу роль у цьому процесі відіграє гіпокамп, зокрема його поля CA1 і CA3, де синаптична пластичність, довготривала потенціація, внутрішньоклітинна кальцієва сигналізація, активація CaMKII, PKA, MAPK/ERK, CREB та BDNF забезпечують формування і стабілізацію пам'ятевих слідів. При нейродегенеративних захворюваннях ці механізми поступово порушуються. Найбільш детально такі зміни вивчені при хворобі Альцгеймера, де синаптична дисфункція може виникати ще до значної втрати нейронів. Важливу роль відіграють накопичення амілоїду-β, патологічна модифікація тау-білка, порушення глутаматергічної передачі, дисрегуляція NMDA- та AMPA-рецепторів, кальцієвого гомеостазу, нейрозапалення, мітохондріальна дисфункція та оксидативний стрес. Особливої уваги заслуговує ураження CA1 і порушення функціональної взаємодії CA3–CA1, що призводить до дефектів синаптичної пластичності, повторної активації нейронних ансамблів і системної консолідації пам'яті. Розуміння цих механізмів дозволяє розглядати синаптичну пластичність та гіпокампальні мережі як потенційні мішені для раннього терапевтичного втручання.

Ключові слова: нейродегенерація, пам'ять, гіпокамп, CA1, CA3, хвороба Альцгеймера, β-амілоїд, тау-білок, LTP, NMDA-рецептори, AMPA-рецептори, CREB, BDNF, нейрозапалення, мітохондріальна дисфункція.

Пам'ять є фундаментальною функцією центральної нервової системи, яка забезпечує накопичення, збереження та відтворення інформації. Її формування передбачає послідовність взаємопов'язаних процесів: кодування інформації, первинне збереження, синаптичну та системну консолідацію, а також подальше відтворення. Особливе значення в цьому процесі має гіпокамп — структура медіальної скроневої частки, необхідна насамперед для формування епізодичної та просторової пам'яті. Класичний гіпокампальний контур включає енторинальну кору, зубчасту звивину, CA3, CA1 та субікулюм. Інформація проходить через ці структури, зазнаючи послідовної обробки та інтеграції. CA3 завдяки чисельним рекурентним зв'язкам бере участь у формуванні асоціативних представлень і pattern completion, тоді як CA1 інтегрує інформацію від CA3 та енторинальної кори і є одним із основних вихідних вузлів гіпокампа. [1]

У нормальних умовах стабілізація пам'яті значною мірою залежить від синаптичної пластичності. Однією з найбільш досліджених її форм є довготривала потенціація (LTP), яка особливо добре вивчена в синапсах CA3–CA1. Активація NMDA-рецепторів, надходження

Ca^{2+}, активація CaMKII, PKA та MAPK/ERK, подальша активація CREB, експресія генів і синтез білків забезпечують перехід від короткочасних змін синаптичної передачі до довготривалої перебудови синапсів. [2] При нейродегенеративних процесах ця система поступово втрачає функціональну цілісність. Особливо виражені зміни спостерігаються при хворобі Альцгеймера (ХА), яка характеризується прогресивним порушенням пам'яті та інших когнітивних функцій. Сучасні дослідження показують, що синаптична дисфункція є не просто наслідком пізньої нейрональної загибелі, а одним із ранніх компонентів патологічного процесу. [3] Відомо що у фізіологічних умовах синапс є динамічною структурою, здатною змінювати свою силу залежно від характеру нейронної активності. Саме ця властивість забезпечує адаптацію нейронних мереж і формування пам'яті. Під час LTP активація AMPA-рецепторів спричиняє деполяризацію постсинаптичної мембрани, що усуває Mg^{2+}-блок NMDA-рецепторів. Внаслідок цього збільшується надходження Ca^{2+} у постсинаптичний нейрон. Кальцій активує CaMKII та інші кінази, які сприяють фосфорилюванню і включенню додаткових AMPA-рецепторів до постсинаптичної мембрани. Для тривалої стабілізації змін, необхідні активація транскрипційних механізмів, CREB, синтез білків і структурна перебудова синапсів. Таким чином, нормальна пластичність передбачає точний контроль нейронної активності та кальцієвої сигналізації. Надмірна або хаотична активація, навпаки, може перетворити фізіологічний механізм пластичності на патологічний процес. При ХА порушення синаптичної функції можуть виникати на ранніх етапах, ще до масової загибелі нейронів. Саме втрата синаптичних контактів тісно пов'язана з вираженістю когнітивного дефіциту. [3] Це має принципове значення адже порушення пам'яті при нейродегенерації не можна пояснювати лише зменшенням кількості нейронів. Значна частина когнітивного дефіциту формується внаслідок того, що нейрони, які ще залишаються морфологічно збереженими, втрачають здатність ефективно взаємодіяти між собою.

Одним із ключових патологічних факторів ХА є накопичення амілоїду-β (Aβ). Однак особливу токсичність мають не лише зрілі амілоїдні бляшки, а й розчинні олігомерні форми Aβ, які здатні безпосередньо впливати на синаптичну передачу. Aβ-олігомери порушують функціонування глутаматергічних синапсів, змінюючи активність NMDA- та AMPA-рецепторів. Одним із наслідків є патологічне зміщення балансу між LTP і LTD у бік ослаблення синаптичної передачі. Порушення транспорту та стабілізації AMPA-рецепторів на постсинаптичній мембрані зменшує ефективність глутаматергічної передачі, а дисрегуляція NMDA-рецепторів сприяє порушенню кальцієвих сигналів. [4] Особливо важливим є вплив Aβ на синапси Шафферових колатералей CA3–CA1. У нормі саме в цих синапсах добре проявляється NMDA-залежна LTP, яка використовується як модель механізмів навчання і пам'яті. При накопиченні Aβ, LTP пригнічується, що безпосередньо порушує здатність нейронної мережі стабілізувати нову інформацію. [1]

Патологічна активація NMDA-рецепторів може спричиняти надмірний вхід Ca^{2+}. Спочатку це змінює внутрішньоклітинну сигналізацію, а при тривалому впливі запускає протеолітичні процеси, мітохондріальну дисфункцію, утворення активних форм кисню та інші механізми нейротоксичності [5]. Отже, Aβ може порушувати пам'ять через декілька взаємопов'язаних каскадних механізмів. Важливо, що цей каскад може розпочинатися задовго до вираженої нейродегенерації.

Другим основним компонентом патології ХА є тау-білок. У нормі тау стабілізує мікротрубочки та бере участь у внутрішньоклітинному транспорті. При патологічному гіперфосфорилюванні його спорідненість до мікротрубочок зменшується, а білок може накопичуватися в соматодендритному компартменті. Патологічний тау впливає на синаптичну функцію кількома шляхами. Він може порушувати транспорт органел і рецепторів, змінювати організацію постсинаптичної щільності, впливати на дозрівання дендритних шипиків та погіршувати функцію мітохондрій. [6] Особливо важливим є те, що

патологічний тау може спричиняти синаптичні зміни ще до формування виражених нейрофібрилярних клубків. Таким чином, тау-патологія має безпосереднє функціональне значення для нейронних мереж, а не є лише морфологічним маркером пізньої стадії захворювання. Між Аβ та тау-білком існує функціональний взаємозв'язок. Аβ здатний запускати сигнальні каскади, які сприяють патологічній модифікації тау-білка, тоді як патологічний тау-білок посилює синаптичну дисфункцію. У результаті формується взаємопідсилювальне патологічне коло яке приводить до когнітивний дефіцит.

Гіпокамп не є однорідною структурою. Його окремі поля виконують різні функції та мають різну вразливість до нейродегенеративного процесу. Особливе значення має CA1. Пірамідні нейрони CA1 отримують інформацію від CA3 через колатералі Шаффера та безпосередньо від енторинальної кори. Водночас CA1 є одним із головних вихідних вузлів гіпокампа. Тому його дисфункція порушує як інтеграцію інформації, так і її подальшу передачу до інших структур[1]. При ХА CA1 належить до ділянок, які характеризуються високою вразливістю. Спостерігаються зміни дендритних шипиків, зниження синаптичної щільності, порушення пластичності та поступова втрата нейронів. [4] Водночас патологія не обмежується CA1. CA3 має критичне значення для автоасоціативної обробки інформації та pattern completion. Завдяки рекурентним зв'язкам нейрони CA3 можуть відновлювати повний патерн активності за неповним входом. Порушення цієї функції може проявлятися труднощами відтворення контексту та деталей раніше сформованого спогаду. Особливо важливим є порушення взаємодії CA3–CA1. У нормі активність CA3 через колатералі Шаффера впливає на CA1 і запускає механізми LTP. Якщо ця пластичність порушена, інформація може передаватися до CA1, але не перетворюватися на стійку синаптичну зміну. Таким чином, патологічний процес охоплює весь функціональний ланцюг від енторинальної кори включаючи зубчасту звивину, поля CA3, CA1 та коркові мережі. Порушення будь-якої ланки зменшує ефективність формування та стабілізації пам'яті.

Крім того одним із центральних регуляторів синаптичної пластичності є Ca^{2+}. Контрольована зміна його концентрації забезпечує активацію кіназ, транскрипційних факторів та механізмів структурної перебудови синапсів. При нейродегенеративному процесі цей контроль порушується. Надмірна активація NMDA-рецепторів, зміни внутрішньоклітинних кальцієвих депо та порушення роботи мітохондрій можуть призводити до патологічного накопичення Ca^{2+}. Його надлишок активує протеази, фосфоліпази та інші ферменти, посилює утворення активних форм кисню та погіршує функцію мітохондрій [5]. У результаті виникає ексайтотоксичність, пошкодження і загибелі нейронів внаслідок надмірної глутаматергічної стимуляція. Таким чином, механізм, який у нормі забезпечує навчання, за патологічних умов стає джерелом нейронального пошкодження. Особливо вразливими при цьому є пірамідні нейрони гіпокампа, оскільки вони характеризуються високою синаптичною активністю та значною потребою в енергетичному забезпеченні.

Важливою складовою патогенезу ХА є хронічне нейрозапалення. Центральну роль у ньому відіграють резидентні імунні клітини центральної нервової системи (мікроглія). У фізіологічних умовах мікроглія підтримує гомеостаз нервової тканини, видаляє пошкоджені структури та бере участь у регуляції синаптичних контактів [7]. При накопиченні Аβ та інших патологічних сигналів вона активується. Її тривала активація супроводжується вивільненням прозапальних цитокінів, активних форм кисню та інших медіаторів. Це створює несприятливе середовище для функціонування нейронів. Окреме значення має система комплементу. За умов патологічної активації компоненти комплементу можуть маркувати синапси для видалення їх мікроглією. Такий механізм нагадує фізіологічний синаптичний прунінг під час розвитку нервової системи, однак при нейродегенерації він стає патологічним. [4] У результаті такої ланцюгової послідовності запускається процес розвитку когнітивного

дефіциту, це пояснює, чому втрата синапсів є одним із найбільш значущих структурних корелятів погіршення пам'яті при ХА. [2]

Синаптична пластичність є енергозатратним процесом. Для підтримання мембранного потенціалу, роботи іонних насосів, транспорту везикул, синтезу білків і перебудови цитоскелета необхідна значна кількість АТФ. Тому функціонування синапсів безпосередньо залежить від стану мітохондрій. При ХА мітохондріальна дисфункція може виникати на ранніх етапах. Аβ і патологічний тау-білок впливають на функціонування мітохондрій, порушують енергетичний метаболізм та сприяють накопиченню активних форм кисню. [4] Формується своєрідне патологічне коло: порушення роботи мітохондрій, дефіцит АТФ, зниження синаптичної функції, порушення кальцієвого гомеостазу, оксидативний стрес, пошкодження білків і мембран, подальша мітохондріальна дисфункція. Оскільки CA1 має високу метаболічну активність, порушення енергетичного забезпечення особливо негативно впливає на його здатність підтримувати синаптичну пластичність.

Для стабілізації довготривалих синаптичних змін важливе значення має нейротрофічний фактор мозку (BDNF). BDNF взаємодіє з рецептором TrkB і активує MAPK/ERK, PI3K/Akt та PLCγ-сигнальні шляхи. Ці механізми підтримують функціонування синапсів, структурну пластичність дендритів і виживання нейронів. При ХА нейротрофічна підтримка може знижуватися. Аβ здатний порушувати BDNF/TrkB-сигналізацію, що додатково погіршує здатність нейронів до пластичних перебудов [8], таким чином, порушення BDNF, створює нам ще одну ланку патологічного каскаду, що особливо важливо для довготривалої консолідації пам'яті, оскільки короткочасна активація синапсу сама по собі недостатня для формування стійкого спогаду. Консолідація пам'яті не завершується локальними змінами в окремому синапсі. Після навчання відбувається повторна активація нейронних ансамблів, яка сприяє інтеграції інформації між гіпокампом і корою. Особливу роль у цьому процесі відіграють короткочасні синхронізовані імпульси нейронів у гіпокампі (SWR), які виникають переважно під час спокою та сну. Вони супроводжуються реактивацією нейронних послідовностей, пов'язаних із попереднім досвідом. Для ефективної системної консолідації необхідна точна координація активності гіпокампа, кори та інших структур. Якщо нейронні ансамблі активуються надмірно, хаотично або несинхронно, процес реактивації пам'яті може порушуватися. При нейродегенерації, цьому сприяють: синаптична втрата, дисбаланс між збудженням і гальмуванням, нейрозапалення та структурне пошкодження гіпокампальних мереж. Унаслідок цього може порушуватися не тільки первинне кодування інформації, а й її подальша стабілізація. Отже, людина може отримувати нову інформацію, але не формувати достатньо стабільного нейронного сліду для її подальшого відтворення.

Порушення пам'яті при нейродегенеративних захворюваннях є кінцевим результатом взаємодії декількох рівнів патології. На молекулярному рівні накопичуються Аβ та патологічний тау-білок, порушується функція NMDA- і AMPA-рецепторів, кальцієва сигналізація, внутрішньоклітинні кіназні каскади та BDNF/TrkB-система. На клітинному рівні, знижується LTP, порушується транспорт рецепторів, змінюється структура дендритних шипиків, погіршується функція мітохондрій та поступово втрачаються синапси. На рівні нейронних мереж порушується функціонування CA3–CA1 контуру, доповнення патерну пам'яті, синхронізація нейронних ансамблів та реактивація енграм. На системному рівні погіршується взаємодія між енториальною корою, гіпокампом і неокортексом. Отже, когнітивний дефіцит не можна пояснити одним патологічним фактором. Аβ, тау, нейрозапалення, мітохондріальна дисфункція та порушення нейронної активності взаємодіють і посилюють один одного [9].

Розуміння ранніх механізмів синаптичної дисфункції створює можливості для пошуку нових терапевтичних підходів. Одним із напрямів є нормалізація глутаматергічної передачі та запобігання патологічній активації NMDA-рецепторів. Інший напрям включає підтримання

кальцієвого гомеостазу та мітохондріальної функції. Перспективними також є стратегії, спрямовані на збереження BDNF/TrkB-сигналізації, регуляцію нейрозапалення та запобігання патологічній втраті синапсів. Звичайно необхідний, окремий напрям це вплив на патологічні форми Аβ і тау. Однак сучасне розуміння патогенезу показує, що усунення лише одного патологічного білка може бути недостатнім. Аβ, тау, мікроглія, мітохондрії та синаптична пластичність утворюють взаємопов'язану систему. Тому перспективною є концепція синапс-орієнтованої терапії, метою якої є не лише зменшення кількості патологічних білків, а й відновлення функціональної здатності нейронних мереж. Синаптична патологія розглядається як одна з ранніх і потенційно модифікованих ланок процесу. [1]

Отже підводячи підсумки нашої роботи можемо зазначити щопорушення пам'яті, при нейродегенеративних процессах, є результат поступового руйнування молекулярних, клітинних і мережевих механізмів, які в нормі забезпечують консолідацію інформації. Центральне місце в цьому процесі займає гіпокамп, а особливе значення мають CA1 і CA3 та їх функціональна взаємодія. У нормі активація NMDA-рецепторів, надходження Ca^{2+}, активація CaMKII, PKA, MAPK/ERK і CREB, синтез білків та структурна перебудова синапсів забезпечують стабілізацію слідів пам'яті. При хворобі Альцгеймера ці механізми порушуються. Розчинні форми Аβ змінюють глутаматергічну передачу та пригнічують LTP, патологічний тау порушує внутрішньоклітинний транспорт і синаптичну структуру, а нейрозапалення та мікрогліальна активація сприяють патологічній втраті синапсів. Додатково мітохондріальна дисфункція, оксидативний стрес, кальцієвий дисбаланс і зниження нейротрофічної підтримки поглиблюють синаптичну недостатність. [10] Особливо важливим є ураження CA1 та порушення функціонального контуру CA3–CA1. Це призводить до зниження здатності гіпокампальних мереж формувати, стабілізувати та відтворювати нейронні патерни, пов'язані з пам'яттю. Таким чином, когнітивний дефіцит при нейродегенерації слід розглядати не лише як наслідок загибелі нейронів, а передусім як результат поступової втрати синаптичної пластичності та функціональної цілісності нейронних мереж. Раннє втручання в механізми синаптичної дисфункції, підтримання нейротрофічної та мітохондріальної функції, контроль нейрозапалення і збереження гіпокампальної пластичності можуть стати важливими напрямами майбутньої терапії нейродегенеративних когнітивних розладів.

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THE SCIENTIFIC DISCOURSE ON DUCHENNE MUSCULAR DYSTROPHY: MOLECULAR PATHOPHYSIOLOGY, GENETIC MECHANISMS, PHARMACOTHERAPEUTIC ADVANCES, PRECISION MEDICINE, EVIDENCE-BASED MEDICINE AND EMERGING MULTIDISCIPLINARY TREATMENT STRATEGIES

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ABSTRACT

Duchenne muscular dystrophy (DMD) represents a severe, progressive, X-linked neuromuscular disorder characterized by profound skeletal and cardiac muscle degeneration, progressive loss of motor function, respiratory insufficiency, and substantial premature morbidity and mortality. The disease is primarily attributable to pathogenic variants in the DMD gene encoding dystrophin, a critical cytoskeletal protein that stabilizes the sarcolemmal membrane through its interaction with the dystrophin-associated glycoprotein complex. Disruption or complete absence of functional dystrophin induces sarcolemmal fragility, aberrant calcium influx, mitochondrial dysfunction, oxidative stress, inflammatory activation, necrotic myofiber degeneration, and progressive replacement of contractile tissue by fibrosis and adipose tissue. Consequently, DMD constitutes not only a paradigmatic monogenic disorder but also a complex translational model integrating molecular genetics, cellular pathophysiology, pharmacology, precision medicine, and multidisciplinary clinical management. The genetic architecture of DMD demonstrates substantial molecular heterogeneity, encompassing large deletions, duplications, small insertions or deletions, nonsense variants, splice-site abnormalities, and other pathogenic alterations. Contemporary molecular diagnostics, including next-generation sequencing, multiplex ligation-dependent probe amplification, and complementary genomic technologies, facilitate accurate variant characterization, genetic counseling, carrier identification, prenatal assessment, and therapeutic stratification. Importantly, genotype–phenotype relationships provide a mechanistic foundation for mutation-specific therapeutic interventions designed to restore dystrophin expression or ameliorate downstream molecular pathology. Pharmacotherapeutic management has historically relied on glucocorticoids, particularly prednisone, prednisolone, and deflazacort, which may prolong ambulation and attenuate functional decline but are associated with clinically significant adverse effects. The therapeutic landscape has subsequently expanded through exon-skipping strategies, mutation-directed molecular interventions, and dystrophin-restoration approaches, including antisense oligonucleotides and gene-transfer technologies. These innovations exemplify the transition from conventional symptomatic pharmacotherapy toward molecularly targeted therapeutics. Emerging gene therapy platforms employing micro-dystrophin constructs represent a particularly consequential development, although their clinical implementation requires rigorous assessment of durability, immunogenicity, safety, vector-associated limitations, and long-term therapeutic effectiveness. Evidence-based medicine provides an essential framework for evaluating these rapidly evolving interventions through systematic appraisal of randomized clinical trials, longitudinal cohort studies, natural-history investigations, biomarker research, and real-world evidence. Therapeutic decision-making increasingly requires integration of genetic diagnosis, age, ambulatory status, disease stage, comorbidities, treatment response, safety parameters, patient-centered outcomes, and individualized risk–benefit assessment. Precision medicine therefore represents a central paradigm for optimizing therapeutic selection and developing genotype-specific interventions while acknowledging substantial interindividual variability in disease progression and treatment

response. Comprehensive DMD management extends beyond dystrophin restoration and pharmacological intervention. Evidence-based multidisciplinary care incorporates cardioprotective therapy, respiratory surveillance and assisted ventilation when indicated, orthopedic management, bone-health preservation, nutritional optimization, rehabilitation, physical and occupational therapy, psychosocial support, endocrinological monitoring, anesthetic planning, and structured transition from pediatric to adult healthcare. Cardiac surveillance is particularly important because dystrophin deficiency affects cardiomyocytes and may result in progressive cardiomyopathy and arrhythmogenic complications. Similarly, respiratory management remains fundamental because progressive respiratory muscle weakness contributes substantially to morbidity.The contemporary scientific discourse on DMD demonstrates a profound transformation from supportive management toward mechanism-based, genetically informed, and increasingly precision-oriented therapeutics. Integration of molecular pathophysiology, genomic medicine, pharmacology, evidence-based clinical practice, advanced gene and RNA technologies, and coordinated multidisciplinary care provides a comprehensive framework for improving functional outcomes, quality of life, and survival. Future research should prioritize durable dystrophin restoration, personalized therapeutic algorithms, combination strategies, validated molecular and functional biomarkers, equitable access to innovative therapies, and rigorous long-term pharmacovigilance. Such an integrated translational framework is essential for converting advances in molecular science into clinically meaningful and sustainable improvements for individuals affected by Duchenne muscular dystrophy.

Keywords: Duchenne muscular dystrophy, dystrophin, dystrophin protein complex, gene therapy, CRISPR-Cas9, precision medicine, biomarkers, multidisciplinary care

INTRODUCTION

Duchenne muscular dystrophy (DMD) represents a paradigmatic inherited neuromuscular disorder in which advances in molecular genetics, cellular pathophysiology, pharmacology, gene therapy, and multidisciplinary clinical care have progressively transformed the understanding and management of a historically devastating disease. DMD is an X-linked genetic disorder caused by pathogenic variants in the *DMD* gene, resulting in profound deficiency or absence of dystrophin, a large cytoskeletal protein that is indispensable for the structural integrity and physiological resilience of skeletal and cardiac muscle. The progressive consequences of dystrophin deficiency extend beyond mechanical instability of the sarcolemma and encompass calcium dysregulation, oxidative stress, mitochondrial impairment, inflammation, fibrosis, defective regeneration, vascular dysfunction, and progressive muscle degeneration. Consequently, DMD is increasingly conceptualized as a complex multisystem disease rather than exclusively as a disorder of skeletal muscle.

The molecular biology of dystrophin provides the fundamental framework for understanding DMD pathogenesis. Dystrophin interacts with intracellular actin and components of the dystrophin-associated protein complex, thereby establishing a mechanically and biochemically important connection between the cytoskeleton and extracellular matrix. In healthy muscle, this architecture contributes to sarcolemmal stability during repeated cycles of contraction and relaxation. Loss or severe reduction of dystrophin compromises this structural system, increasing susceptibility to contraction-induced membrane injury. Repeated membrane damage initiates a cascade involving calcium influx, activation of calcium-dependent proteases, mitochondrial dysfunction, reactive oxygen species generation, inflammatory signaling, necrotic myofiber loss, and progressive replacement of contractile tissue by adipose and fibrotic tissue.

The genetic dimension of DMD is exceptionally important because the *DMD* gene is one of the largest genes in the human genome and exhibits substantial mutational heterogeneity. Pathogenic

deletions, duplications, small sequence variants, splice abnormalities, and other molecular defects may disrupt dystrophin expression through different mechanisms. The relationship between mutation position, reading-frame preservation, dystrophin production, and clinical phenotype has historically provided an important basis for distinguishing Duchenne from Becker muscular dystrophy. However, contemporary genetic research demonstrates that genotype-phenotype relationships are more complex than a simple reading-frame model. Modifier genes, alternative dystrophin isoforms, epigenetic mechanisms, and individual biological variability may influence disease severity, cognitive manifestations, cardiac involvement, treatment response, and progression.

The clinical phenotype of DMD is characterized by progressive proximal muscle weakness, impaired motor development, difficulty running and climbing stairs, Gowers' maneuver, calf pseudohypertrophy, contractures, progressive loss of ambulation, respiratory muscle weakness, and cardiomyopathy. Importantly, the disease trajectory is not restricted to motor impairment. Cardiac dysfunction, respiratory insufficiency, skeletal deformities, osteoporosis, endocrine abnormalities, nutritional complications, neurodevelopmental manifestations, cognitive impairment, behavioral difficulties, and psychosocial challenges contribute substantially to the cumulative burden of disease. Accordingly, effective DMD management requires longitudinal assessment of multiple physiological systems and proactive intervention before irreversible complications become clinically advanced.

The natural history of DMD has been substantially modified by advances in supportive and disease-modifying treatment. Glucocorticoids, particularly prednisone and deflazacort, remain central components of conventional pharmacotherapy because of their ability to prolong ambulation and preserve muscle strength and function. Nevertheless, prolonged corticosteroid exposure is associated with clinically important adverse effects, including weight gain, growth impairment, osteoporosis, endocrine disturbances, behavioral effects, hypertension, and metabolic complications. These limitations have stimulated investigation of alternative corticosteroid regimens and pharmacological approaches capable of preserving efficacy while reducing treatment-related toxicity.

A major transition in DMD therapeutics has emerged from the development of mutation-specific molecular interventions. Antisense oligonucleotide-mediated exon skipping represents an important example of precision pharmacotherapy because it seeks to manipulate pre-mRNA splicing and restore the translational reading frame in patients with specific *DMD* mutations. Eteplirsen, golodirsen, and casimersen illustrate the clinical translation of exon-skipping technology into genotype-specific treatment strategies. These approaches demonstrate how molecular diagnosis can move beyond confirmation of disease to become an active determinant of therapeutic selection. Nevertheless, exon-skipping therapies remain constrained by mutation eligibility, variable dystrophin restoration, administration requirements, tissue distribution, and uncertainty concerning the magnitude and durability of clinical benefit.

The therapeutic landscape has expanded further through pharmacological approaches directed toward downstream pathological mechanisms. Histone deacetylase inhibition, modulation of inflammatory and fibrotic pathways, oxidative-stress regulation, calcium homeostasis, and muscle regeneration represent important areas of translational research. Givinostat, an oral histone deacetylase inhibitor, represents a particularly significant development because its clinical evaluation has provided evidence for a pharmacological strategy aimed at modifying pathological processes associated with muscle degeneration rather than directly correcting the underlying *DMD* mutation. Such approaches highlight the increasingly multidimensional nature of DMD pharmacotherapy, in which primary genetic correction and secondary disease modification may potentially be combined.

Gene therapy has introduced another major paradigm shift. Because the full-length dystrophin coding sequence is too large for conventional adeno-associated viral vector packaging, current gene-transfer strategies have focused on engineered micro-dystrophin constructs capable of producing abbreviated dystrophin proteins with selected functional domains. The development of micro-dystrophin approaches illustrates the broader transition from symptomatic treatment toward molecular replacement. However, important challenges remain, including vector delivery to widespread skeletal and cardiac muscle, pre-existing or treatment-induced immunity to viral capsids, immune responses against newly expressed dystrophin, limitations of vector redosing, durability of expression, and the interpretation of surrogate biomarkers in relation to meaningful clinical outcomes.

Precision medicine therefore occupies an increasingly central position in contemporary DMD research. Molecular characterization can determine eligibility for mutation-specific exon skipping, inform clinical-trial enrollment, facilitate family genetic counseling, identify carriers, and support individualized prognostic assessment. Emerging genomic technologies may additionally enable identification of genetic modifiers and therapeutic targets that influence disease severity and treatment response. The expanding integration of genomic information with clinical phenotyping creates the possibility of a more individualized therapeutic model in which intervention is selected according to mutation type, disease stage, organ involvement, treatment history, and patient-specific risk-benefit considerations.

The development of these therapies simultaneously creates a need for rigorous evidence-based medicine. DMD is characterized by a heterogeneous therapeutic evidence base involving randomized controlled trials, extension studies, observational cohorts, biomarker analyses, systematic reviews, natural-history studies, and expert consensus recommendations. Interpretation of treatment efficacy is complicated by small patient populations, substantial disease heterogeneity, long disease trajectories, ethical considerations surrounding placebo-controlled trials, and the use of surrogate endpoints such as dystrophin expression. Consequently, evidence-based DMD care requires critical appraisal of methodological quality, clinical relevance, effect size, safety, durability, patient-centered outcomes, and applicability to individual patients rather than reliance exclusively on regulatory status or molecular plausibility.

Multidisciplinary care remains indispensable despite the rapid emergence of molecular therapeutics. Neurologists, clinical pharmacologists, geneticists, cardiologists, pulmonologists, orthopedic specialists, endocrinologists, rehabilitation professionals, physiotherapists, nutrition specialists, psychologists, nurses, and other healthcare professionals contribute complementary expertise to the long-term management of affected individuals. Cardiovascular surveillance and treatment, respiratory monitoring and assisted ventilation when indicated, contracture prevention, preservation of mobility, bone-health management, nutritional assessment, psychosocial support, and transition from pediatric to adult healthcare are integral components of comprehensive care.

The increasing survival of individuals with DMD further strengthens the importance of anticipatory and life-course management. As cardiac and respiratory interventions improve survival, clinical priorities increasingly encompass adulthood, vocational participation, psychosocial well-being, autonomy, reproductive counseling, transition of care, and quality of life. Contemporary management must therefore balance disease-modifying treatment with prevention and management of treatment-related adverse effects, comorbidities, functional decline, and psychosocial consequences. This evolution has transformed DMD care from a predominantly pediatric, symptom-oriented model into a longitudinal, individualized, multidisciplinary therapeutic framework.

From a translational perspective, DMD is also an important model for evaluating the interface between molecular discovery and clinical pharmacotherapy. The trajectory from identification of

the *DMD* gene and dystrophin protein to exon-skipping agents, pharmacological disease modifiers, and gene-transfer strategies illustrates the potential of precision medicine to convert molecular mechanisms into therapeutic interventions. At the same time, the remaining limitations demonstrate that biological plausibility does not necessarily guarantee clinically meaningful benefit. The future of DMD therapy will therefore depend on integrating molecular innovation with robust clinical evidence, long-term safety surveillance, pharmacovigilance, patient-centered outcomes, health-economic considerations, and equitable access to advanced therapies.

The present scientific discourse examines DMD through an integrated framework encompassing molecular pathophysiology, genetic mechanisms, pharmacotherapeutic advances, precision medicine, evidence-based medicine, translational therapeutics, and emerging multidisciplinary treatment strategies. Such integration is necessary because no single therapeutic modality is currently sufficient to address the complete biological and clinical spectrum of DMD. The future therapeutic paradigm is likely to involve individualized combinations of dystrophin-restorative technologies, pharmacological disease modification, optimized corticosteroid therapy, cardiopulmonary protection, rehabilitation, genetic counseling, and continuous evidence-based monitoring. The central scientific challenge is therefore not merely to develop additional treatments, but to determine how these interventions can be rationally integrated across the disease course to maximize functional preservation, minimize toxicity, prolong survival, and improve the quality of life of individuals living with Duchenne muscular dystrophy.

Duchenne muscular dystrophy (DMD) represents one of the most severe and prevalent inherited neuromuscular disorders of childhood, affecting approximately 1 in 5,000 live male births. This X linked recessive condition arises from pathogenic mutations in the DMD gene, located at Xp21.2–Xp21.1, which encodes dystrophin a critical cytoskeletal protein essential for maintaining sarcolemmal integrity and mediating signal transduction through the dystrophin-associated protein complex (DAPC). The absence of functional dystrophin initiates a cascade of pathological events encompassing sarcolemmal instability, aberrant calcium influx, mitochondrial dysfunction, oxidative stress, chronic inflammation, impaired muscle regeneration, and progressive fibrotic replacement of muscle tissue. This comprehensive review examines the current scientific discourse surrounding DMD through an integrated lens spanning molecular pathophysiology, genetic mechanisms, pharmacotherapeutic advances, precision medicine approaches, evidence based clinical frameworks, and emerging multidisciplinary treatment strategies. Recent therapeutic breakthroughs, including antisense oligonucleotide-mediated exon skipping, adeno associated virus (AAV) vector-based gene therapy, CRISPR-Cas9 gene editing, and novel dissociative corticosteroids such as vamorolone have substantially expanded the treatment armamentarium. Concurrently, advances in high-throughput proteomics and genetic modifier discovery are enabling increasingly personalized approaches to disease management. Despite these remarkable developments, significant challenges persist regarding long term safety, durability of response, equitable access, and optimal integration of emerging therapies within comprehensive multidisciplinary care frameworks. This review synthesizes current knowledge across these domains, identifies critical knowledge gaps, and proposes directions for future research and clinical translation.

Historical Context and Clinical Characterization

The first histopathological descriptions of what would later be recognized as Duchenne muscular dystrophy were documented by Edward Meryon in 1851 and subsequently characterized in greater detail by Guillaume Benjamin Duchenne de Boulogne in 1868. Duchenne's eponymous contribution to the nosology of muscular dystrophies established the clinical phenotype that bears his name: a relentlessly progressive condition characterized by symmetric proximal muscle weakness, pseudohypertrophy of the calf muscles, Gowers' sign, and eventual loss of ambulation

typically occurring in the early teens. Detailed ultrastructural analyses performed in the 1960s and 1970s using electron microscopy began to illuminate the subcellular pathology underlying these clinical manifestations.

The molecular era of DMD research commenced with the cloning of the DMD gene by Michel Koenig and colleagues in 1987, a landmark achievement that identified the genetic basis of the disease and enabled the first immunohistochemical analyses using anti-dystrophin antibodies. The discovery of the DMD gene encoding dystrophin not only revealed the cause of DMD but also helped identify a family of at least ten dystrophin associated proteins at the muscle cell membrane. Critical insights into the underlying pathophysiology were subsequently obtained through experimentation with the X-chromosome linked muscular dystrophy (mdx) mouse model, which remains the most widely utilized animal model for preclinical DMD research.

Epidemiology and Disease Burden

DMD is an X-linked inherited disease, with the mutated DMD gene located on the short arm of the X chromosome at positions Xp21.2–Xp21.1. Early studies conducted before the era of prenatal diagnosis calculated the birth incidence in boys to be approximately 1 in 3,500. However, a recent systematic review and meta-analysis found slightly lower incidence and prevalence rates of approximately 1 in 5,000 and 5 per 100,000 males, respectively. DMD is therefore recognized as one of the most common rare diseases and the most common form of inherited muscular dystrophy in childhood.

The disease follows a predictable and devastating clinical trajectory. Earliest symptoms typically present after the first years of life, with affected boys demonstrating delayed motor milestones, difficulty climbing stairs, and a characteristic waddling gait. Loss of ambulation generally occurs in the early teens, and the need for assisted ventilation arises at approximately 20 years of age. Premature death occurs in most patients between 20 and 40 years of age, predominantly from cardiac and/or respiratory failure. The substantial disease burden extends beyond the affected individual to encompass families, caregivers, and healthcare systems, underscoring the urgent need for effective therapeutic interventions.

Background

Duchenne muscular dystrophy (DMD) is a severe, progressive, X-linked neuromuscular disorder and one of the most clinically consequential inherited muscular dystrophies of childhood. The disease is caused by pathogenic variants in the DMD gene, located on chromosome Xp21, which encodes dystrophin, a large cytoskeletal protein essential for maintaining the structural and functional integrity of skeletal and cardiac muscle fibers. DMD predominantly affects males because of its X-linked inheritance pattern, although females carrying pathogenic variants may occasionally manifest clinically relevant skeletal muscle, cardiac, or neurocognitive abnormalities. Contemporary epidemiological analyses confirm that DMD represents a substantial global rare-disease burden, with considerable variation in reported prevalence between populations.

At the molecular level, dystrophin functions as a critical component of the dystrophin-associated protein complex, providing a mechanical and signaling interface between the intracellular actin cytoskeleton and the extracellular matrix. Its deficiency compromises sarcolemmal stability and renders muscle fibers highly susceptible to contraction-induced injury. Subsequent membrane disruption facilitates abnormal calcium influx, mitochondrial dysfunction, oxidative stress, activation of proteolytic pathways, and myofiber necrosis. These primary molecular abnormalities initiate secondary inflammatory responses, impaired muscle regeneration, connective-tissue deposition, and progressive fatty replacement of skeletal muscle. Recent mechanistic research emphasizes that DMD should therefore be understood not simply as a disorder of dystrophin deficiency, but as a complex pathophysiological network involving membrane instability, calcium

dysregulation, oxidative injury, inflammation, fibrosis, altered muscle regeneration, and neuromuscular dysfunction.

The genetic architecture of DMD is heterogeneous, encompassing large and small deletions, duplications, point mutations, splice-site variants, and other pathogenic alterations. The classical reading-frame hypothesis explains many genotype-phenotype relationships: out-of-frame variants commonly result in absent or severely deficient dystrophin and a Duchenne phenotype, whereas some in-frame variants permit production of truncated but partially functional dystrophin and are associated with the milder Becker muscular dystrophy phenotype. Nevertheless, genotype alone does not completely predict disease severity, cardiac or respiratory complications, or neurocognitive manifestations, emphasizing the importance of comprehensive molecular and clinical characterization.

Clinically, DMD is characterized by progressive proximal muscle weakness, delayed motor development, difficulty running and climbing stairs, Gowers' maneuver, contractures, loss of ambulation, respiratory muscle impairment, and progressive cardiomyopathy. Cardiac and respiratory complications are major determinants of morbidity and mortality, while neurodevelopmental, cognitive, behavioral, nutritional, endocrine, and psychosocial manifestations contribute substantially to the overall disease burden. Consequently, contemporary DMD management requires an integrated multidisciplinary model extending beyond skeletal muscle treatment to cardiovascular, respiratory, orthopedic, endocrine, nutritional, rehabilitative, psychological, and genetic care.

Therapeutic development has undergone a major transformation from predominantly supportive management toward molecularly targeted and disease-modifying interventions. Corticosteroids remain an important therapeutic component, while exon-skipping antisense oligonucleotides, dystrophin-restoration strategies, histone deacetylase inhibition, and micro-dystrophin gene-transfer approaches have expanded the therapeutic landscape. Recent reviews emphasize that contemporary treatment increasingly seeks either to restore dystrophin expression or to modify downstream pathological mechanisms responsible for muscle degeneration.

DMD represents an important model for precision medicine, translational pharmacology, evidence-based medicine, and multidisciplinary therapeutic innovation. Integration of molecular diagnosis, genotype-specific treatment selection, pharmacological optimization, gene-based therapeutics, continuous safety monitoring, rehabilitation, and coordinated cardiac and respiratory management is increasingly essential for improving long-term clinical outcomes and quality of life. The scientific discourse surrounding DMD has consequently shifted from disease description toward individualized, mechanism-based, evidence-informed therapeutic strategies.

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Against this rapidly evolving background, DMD represents an important model for precision medicine, translational pharmacology, evidence-based medicine, and multidisciplinary therapeutic innovation. Integration of molecular diagnosis, genotype-specific treatment selection, pharmacological optimization, gene-based therapeutics, continuous safety monitoring, rehabilitation, and coordinated cardiac and respiratory management is increasingly essential for improving long-term clinical outcomes and quality of life. The scientific discourse surrounding DMD has consequently shifted from disease description toward individualized, mechanism-based, evidence-informed therapeutic strategies.

The contemporary understanding of DMD increasingly recognizes the disorder as a multisystem disease rather than an isolated skeletal-muscle phenotype. Dystrophin deficiency affects several striated-muscle compartments and contributes to progressive cardiomyopathy and respiratory dysfunction, while abnormalities involving the nervous, endocrine, gastrointestinal, immune, and other physiological systems may further influence disease burden. This multisystem perspective has important implications for clinical surveillance because apparently secondary manifestations can become major determinants of functional status, morbidity, survival, and health-related quality of life. Recent mechanistic literature consequently emphasizes organ crosstalk and systemic pathophysiology as important dimensions of dystrophinopathy.

Another major development is the increasing convergence of molecular genetics and therapeutic decision-making. Molecular confirmation of a pathogenic DMD variant is no longer restricted to establishing diagnosis; it can determine eligibility for mutation-specific interventions and facilitate genetic counseling, carrier identification, family screening, prognosis, and clinical-trial participation. Advances in sequencing, variant interpretation, and dystrophin-restoration technologies have therefore strengthened the conceptual foundation of genotype-informed treatment. Contemporary therapeutic research encompasses exon skipping, dystrophin gene replacement or micro-dystrophin delivery, genome-editing approaches, and pharmacological modulation of downstream pathological pathways. Nevertheless, important limitations remain, including genotype eligibility, vector-associated immune responses, tissue delivery, durability of therapeutic expression, variable treatment response, and the difficulty of translating molecular restoration into durable functional benefit.

The expansion of therapeutic options also reinforces the importance of evidence-based medicine. DMD interventions differ substantially in their biological targets, clinical endpoints, eligibility criteria, safety profiles, and levels of supporting evidence. Consequently, treatment selection requires critical appraisal of randomized clinical trials, longitudinal observational studies, systematic reviews, clinical practice guidelines, biomarker data, and patient-centered outcomes. Recent assessments of DMD clinical guidelines demonstrate the increasing complexity of recommendations across diagnosis, neuromuscular care, rehabilitation, respiratory and cardiac surveillance, endocrine management, nutrition, psychosocial support, and emerging molecular therapies.

The pharmacotherapy should be conceptualized as one component of a longitudinal therapeutic architecture rather than as an isolated intervention. Corticosteroids and newer pharmacological agents may modify disease progression or specific pathological pathways, whereas genetic therapies seek to address the underlying molecular defect. Their integration requires individualized assessment of disease stage, ambulatory status, genotype, cardiac and respiratory phenotype, adverse-effect susceptibility, treatment burden, and patient and family preferences. Multidisciplinary coordination is therefore fundamental to maximizing therapeutic benefit while minimizing cumulative toxicity and preserving function. Current evidence supports an anticipatory model in which surveillance and intervention are initiated before irreversible organ damage becomes clinically dominant.

The scientific discourse on DMD has evolved toward a translational continuum extending from molecular pathophysiology and genetic diagnosis to pharmacotherapy, precision medicine, clinical evidence, rehabilitation, and integrated long-term care. This conceptual evolution provides the rationale for examining DMD through an interdisciplinary framework that connects molecular mechanisms with therapeutic innovation and clinically meaningful outcomes. Such an approach is particularly relevant in the current era of rapidly expanding disease-modifying therapies, where rigorous evidence synthesis and multidisciplinary implementation are essential for converting advances in biomedical science into sustainable improvements in patient care.

Scope and Objectives of Review

This comprehensive review aims to synthesize the current scientific discourse on Duchenne muscular dystrophy across multiple interconnected domains. We first examine the molecular pathophysiology of DMD, focusing on the structure and function of dystrophin, the DAPC, and the downstream pathological cascades initiated by dystrophin deficiency. We then explore the genetic mechanisms underlying DMD, including the spectrum of DMD mutations, genotype-phenotype correlations, and the role of genetic modifiers. The pharmacotherapeutic landscape is reviewed in depth, encompassing corticosteroid therapy, emerging small molecules, and the revolutionary

class of genetic therapies including exon skipping, gene therapy, and gene editing. The principles of precision medicine are examined through the lenses of biomarker discovery, genetic modifiers, and personalized therapeutic selection. Evidence-based medicine frameworks are evaluated with respect to clinical guideline development and systematic evidence synthesis. Finally, we discuss the essential role of multidisciplinary care in optimizing outcomes for individuals with DMD and identify future directions for research and clinical translation.

RESULTS AND DISCUSSION

The synthesis of contemporary evidence demonstrates that Duchenne muscular dystrophy (DMD) has evolved from a predominantly supportive-care paradigm toward an increasingly molecularly informed therapeutic model integrating genomic diagnosis, pharmacotherapy, disease-modifying interventions, precision medicine, and coordinated multidisciplinary management. Nevertheless, the available evidence indicates that DMD remains a progressive multisystem disorder in which therapeutic benefit cannot be adequately assessed through a single endpoint. Motor performance, preservation of ambulation, respiratory function, cardiac status, quality of life, corticosteroid-related toxicity, dystrophin restoration, and long-term survival must be interpreted collectively.

Molecular and Pathophysiological Findings

The evidence consistently supports dystrophin deficiency as the initiating molecular abnormality underlying DMD. Loss of functional dystrophin compromises the structural integrity of the sarcolemma and disrupts interactions between the cytoskeleton and extracellular matrix. Subsequent membrane instability promotes abnormal calcium entry, proteolytic activation, mitochondrial dysfunction, oxidative stress, inflammatory signaling, and repetitive cycles of myofiber injury and regeneration. Over time, regenerative capacity becomes insufficient, resulting in progressive fibrosis and fatty replacement of skeletal muscle.

Importantly, the clinical phenotype extends beyond skeletal muscle. Dystrophin deficiency in cardiomyocytes contributes to progressive myocardial injury and cardiomyopathy, while respiratory muscle involvement produces restrictive ventilatory impairment, ineffective cough, sleep-related hypoventilation, and ultimately respiratory failure. Contemporary care recommendations therefore emphasize systematic cardiac and respiratory surveillance rather than treating DMD exclusively as a locomotor disorder.

The heterogeneity of clinical progression despite apparently similar pathogenic variants further supports the importance of genetic modifiers, environmental influences, treatment exposure, and disease-stage effects. Consequently, genotype alone may be insufficient to predict the complete trajectory of an individual patient, reinforcing the necessity of longitudinal phenotyping and individualized clinical assessment.

Genetic and Molecularly Targeted Therapies

One of the most consequential findings of the contemporary evidence base is the emergence of therapies designed to intervene directly at the molecular level. Antisense oligonucleotide-mediated exon skipping provides a mutation-dependent strategy intended to restore the reading frame and permit production of a truncated but potentially functional dystrophin protein. Its applicability is inherently restricted by genotype, illustrating both the therapeutic potential and limitations of precision pharmacology.

Gene-replacement approaches represent a further conceptual transition. Micro-dystrophin gene-transfer technologies seek to introduce a shortened dystrophin transgene into skeletal and cardiac muscle using adeno-associated viral vectors. In June 2024, the U.S. Food and Drug Administration expanded the approval of delandistrogene moxeparvovec-rokl (Elevidys) to ambulatory individuals

aged four years and older and granted accelerated approval for non-ambulatory individuals aged four years and older with confirmed DMD mutations, while specifying important eligibility and contraindication considerations.

The interpretation of these findings requires particular methodological caution. The FDA reported that a large randomized study did not achieve its prespecified statistical primary endpoint for improvement in the North Star Ambulatory Assessment, although secondary and exploratory functional outcomes contributed to the regulatory determination of clinical benefit. This illustrates the complexity of evaluating DMD therapies: molecular expression of micro-dystrophin does not automatically translate into proportional functional improvement, and surrogate biomarkers must therefore be interpreted in conjunction with clinically meaningful outcomes.

More recent research continues to demonstrate both the promise and uncertainty of AAV-mediated mini-dystrophin therapy. A 2025 phase 1b study of fordadistrogene movaparvovec reported one-year safety and tolerability data in ambulatory and non-ambulatory participants, further expanding the clinical evidence base for systemic gene-transfer strategies. However, durability of expression, immune responses, vector-associated toxicity, redosing limitations, and long-term functional consequences remain critical areas requiring continued investigation.

Evidence-Based Medicine and Clinical Outcome Assessment

The evidence indicates that DMD therapeutics should not be evaluated exclusively according to molecular endpoints. The North Star Ambulatory Assessment, timed motor tests, pulmonary function measurements, cardiac imaging, strength assessments, patient-reported outcomes, and quality-of-life measures provide complementary dimensions of therapeutic effectiveness. The discrepancy between molecular biomarker improvement and certain functional endpoints in gene-therapy trials demonstrates why robust endpoint hierarchies and adequately powered randomized studies remain essential.

Evidence-based medicine is particularly important in DMD because natural-history progression is nonlinear and strongly dependent on age, baseline motor function, corticosteroid exposure, genotype, and disease stage. Consequently, historical controls can introduce substantial bias, whereas carefully designed longitudinal cohorts and randomized controlled trials provide stronger comparative evidence. At the same time, rare-disease research frequently faces recruitment limitations, small sample sizes, heterogeneous populations, and ethical challenges associated with placebo-controlled designs. These constraints necessitate methodological innovation without compromising statistical rigor.

Cardiac and Respiratory Outcomes

The evidence strongly supports early and systematic cardiorespiratory surveillance. DMD-associated cardiomyopathy may develop before overt clinical symptoms, and contemporary cardiac recommendations emphasize regular assessment from the time of diagnosis. Pharmacological management of myocardial dysfunction is directed toward delaying ventricular deterioration and reducing heart-failure complications.

Respiratory management similarly represents a major determinant of long-term outcomes. Progressive respiratory muscle weakness results in impaired ventilation and cough effectiveness, increasing susceptibility to hypoventilation, secretion retention, atelectasis, pneumonia, and respiratory failure. Contemporary respiratory recommendations support serial assessment of respiratory muscle function, lung-volume recruitment, assisted cough techniques, and non-invasive ventilation when clinically indicated. The 2024 UK respiratory consensus further emphasizes standardized routine and emergency respiratory pathways for both children and adults with DMD.

These findings reinforce the concept that therapeutic success in DMD must be multisystemic. Preservation of ambulation without adequate cardiac or respiratory protection cannot be regarded as complete disease control.

Precision Medicine and Individualized Therapeutic Strategies

The integration of molecular diagnostics with clinical phenotyping provides the foundation for precision medicine in DMD. Therapeutic selection increasingly depends on the specific pathogenic variant, eligibility for mutation-directed treatment, age, ambulatory status, glucocorticoid exposure, cardiac phenotype, respiratory status, immunological considerations, and patient-centered treatment priorities.

The future therapeutic model is therefore likely to involve stratified treatment algorithms rather than a universal pharmacological regimen. Genotype-guided exon skipping, gene-transfer technologies, conventional glucocorticoids, emerging molecular agents, and supportive therapies may ultimately be integrated according to individual molecular and phenotypic profiles. Genetic modifiers and biomarkers capable of predicting treatment response could further improve therapeutic personalization.

Multidisciplinary Treatment and Translational Implications

The results support a comprehensive multidisciplinary model involving neurologists, clinical pharmacologists, geneticists, cardiologists, pulmonologists, rehabilitation specialists, physiotherapists, endocrinologists, orthopedic specialists, nutrition professionals, psychologists, and specialized nursing teams. Such coordination is essential because DMD produces interacting skeletal, cardiac, respiratory, endocrine, orthopedic, nutritional, and psychosocial consequences. International care recommendations similarly emphasize coordinated management across the lifespan.

A major implication of the evidence is that innovative molecular therapies should complement rather than replace established standards of multidisciplinary care. Gene therapy or dystrophin-restoration strategies cannot eliminate the need for cardiac surveillance, respiratory monitoring, rehabilitation, bone-health management, nutritional support, psychosocial care, and pharmacovigilance.

The study demonstrate a substantial transformation in DMD therapeutics, from symptom-oriented management toward mechanism-based and genetically informed intervention. Nevertheless, the evidence remains characterized by important uncertainties concerning long-term durability, clinically meaningful dystrophin thresholds, treatment sequencing, combination therapy, immune-mediated complications, and equitable access. Future research should therefore prioritize long-term comparative effectiveness studies, standardized functional and patient-reported endpoints, biomarker validation, pharmacovigilance, real-world evidence, and individualized therapeutic algorithms. The most clinically meaningful objective is not simply restoration of dystrophin expression, but sustained preservation of neuromuscular function, cardiorespiratory integrity, independence, quality of life, and survival.

MOLECULAR PATHOPHYSIOLOGY

The Dystrophin Protein: Structure and Function

Dystrophin is a large cytoskeletal protein encoded by the DMD gene, which spans approximately 2.4 megabases—one of the largest genes in the human genome. The full-length dystrophin

isoform, Dp427, comprises 3,685 amino acids and is organized into four principal structural domains: an N-terminal actin-binding domain, a central rod domain composed of 24 spectrin-like repeats, a cysteine-rich domain, and a C-terminal domain. This architectural organization enables dystrophin to function as a critical mechanical linkage between the intracellular actin cytoskeleton and the extracellular matrix via the dystrophin associated protein complex.

The DMD gene produces multiple tissue-specific dystrophin isoforms through the use of distinct promoters and alternative splicing. The full-length Dp427 isoform is predominantly expressed in skeletal and cardiac muscle, as well as in the brain. Absence of this isoform leads to the severe DMD phenotype, while residual expression of partially functional dystrophin isoforms results in milder phenotypes, such as Becker muscular dystrophy (BMD). Brain involvement in DMD results from the loss of the Dp427, Dp140, and Dp71 dystrophin isoforms, which regulate synaptic and glial membrane architecture. The deficiency of these proteins contributes to cognitive impairment through disrupted GABAergic signaling, altered neurovascular function, and an imbalance in neuronal excitatory inhibitory transmission.

The Dystrophin Associated Protein Complex

Dystrophin is an essential component of the DAPC, a highly organized multiprotein complex that plays a pivotal role in muscle fiber structural integrity. The DAPC comprises several proteins, including dystrophin, syntrophins, dystroglycans, sarcoglycans, and neuronal nitric oxide synthase (nNOS). Under normal physiological conditions, the DAPC provides mechanical stability to muscle fibers and acts as a signaling hub anchoring signaling proteins and molecules to their functional sites.

The multi-functional role of the DAPC extends beyond structural support to encompass critical signaling functions. Dystrophin anchors the cytoskeleton to the DAPC, linking contractile elements to the extracellular matrix. This linkage is essential for maintaining sarcolemmal stability during muscle contraction and relaxation. Additionally, the DAPC serves as a scaffold for the localization of signaling molecules, including nNOS, which plays a critical role in vasoregulation and muscle blood flow.

Pathological Cascades Initiated by Dystrophin Deficiency

The loss of functional dystrophin leads to disassembly of the transmembrane DAPC, triggering a cascade of pathological events that include chronic inflammation and failed regeneration. The primary consequence of dystrophin deficiency is disruption of sarcolemmal stability, rendering muscle fibers susceptible to contraction-induced injury. This mechanical fragility results in increased calcium influx through sarcolemmal tears and stretch-activated channels.

The pathological consequences of increased intracellular calcium are multifaceted and devastating. Elevated calcium concentrations activate calcium-dependent proteases, including calpains, which degrade cytoskeletal and myofibrillar proteins. Mitochondrial calcium overload impairs oxidative phosphorylation and promotes the generation of reactive oxygen species, establishing a vicious cycle of oxidative stress and mitochondrial dysfunction. This bioenergetic crisis ultimately leads to myofiber necrosis, which is followed by chronic inflammation, fibrosis, and fatty infiltration.

The mislocalization of nNOS and reduced vascular endothelial growth factor (VEGF) impair vasoregulation and exacerbate ischemic injury during muscle contraction. This functional ischemia further compounds the metabolic stress on dystrophic muscle fibers. The chronic inflammatory response, characterized by infiltration of macrophages and other immune cells, promotes ongoing muscle damage while simultaneously impairing the regenerative capacity of muscle satellite cells.

Epigenetic Dysregulation in DMD Pathophysiology

Emerging evidence implicates epigenetic dysregulation as a key driver in DMD disease development and progression. One critical consequence of dystrophin loss and DAPC disassembly is increased histone deacetylase (HDAC) enzyme activity. HDACs are evolutionarily conserved enzymes involved in the epigenetic regulation of gene expression that remove acetylated groups from the lysine of histone proteins. In dystrophic muscle, DAPC disassembly causes delocalization of signaling proteins and, therefore, disrupts signaling pathways. Displacement of epigenetic signaling molecules leads to the uncontrolled activity of HDACs and excessive removal of acetyl groups from histone proteins. Consequently, chromatin becomes tightly bound, preventing the expression of genes involved in muscle homeostasis.

HDAC hyperactivity has been observed in DMD animal models and patients with DMD. In particular, DMD muscles display an aberrant, constitutive activation of HDAC2. The pathological consequences of increased HDAC activity extend beyond muscle fibers, affecting several cell types, translating into a chronically activated immune system, promoting fibrotic and adipose tissue formation, and impairing muscle regeneration. As such, the inhibition of HDAC activity has received attention as a therapeutic approach for treating muscular dystrophies.

MicroRNA Dysregulation in DMD

MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression post-transcriptionally and significantly influence multiple pathological processes in DMD. Reduced or absent dystrophin expression results in sarcolemmal instability, chronic inflammation, oxidative stress, impaired muscle regeneration, and fibrosis. Specific miRNAs, including miR-146a, miR-155, miR-378, and miR-711, modulate inflammation primarily through the NF-κB signaling pathway. Others, such as miR-21, miR-31, miR-128, miR-144, and miR-379, regulate oxidative stress responses via the NRF2 antioxidant pathway.

Muscle-specific miRNAs (myomiRs), notably miR-1, miR-133a/b, miR-206, miR-486, and miR-499, are critical for muscle regeneration, and their dysregulation impairs satellite cell function and muscle repair. Additionally, miRNAs such as miR-21, miR-29a/c, and miR-199a-5p play significant roles in fibrosis development. The dysregulation of these miRNAs contributes to the complex pathophysiology of DMD, underscoring their potential as biomarkers for disease progression and therapeutic response.

GENETIC MECHANISMS

The DMD Gene: Genomic Architecture and Mutation Spectrum

The DMD gene is located on the X chromosome at Xp21.2–Xp21.1 and represents one of the largest genes in the human genome, spanning approximately 2.4 megabases and comprising 79 exons. The gene encodes dystrophin, a cytoskeletal protein critical for the stability of muscle fibers.

Mutations in the DMD gene are predominantly intragenic deletions, which account for approximately 60-70% of cases. Other mutation types include duplications (approximately 10-15%), point mutations, and small insertions or deletions-. The reading frame rule, first proposed by Monaco and colleagues, predicts disease severity based on the effect of mutations on the dystrophin open reading frame: out of frame mutations abolish dystrophin synthesis, leading to the severe DMD phenotype, whereas in frame deletions produce partially functional proteins, resulting in the milder Becker muscular dystrophy phenotype.

Genotype Phenotype Correlations

The correlation between genotype and phenotype in dystrophinopathies is complex and incompletely understood. While the reading-frame rule provides a useful framework for predicting disease severity, exceptions exist, and phenotypic variability among individuals with identical

mutations is well-documented. Genotype-phenotype correlation studies in BMD patients have revealed that mutations affecting the actin-binding domain or the R16/R17 nNOS binding domain are often associated with more severe disease compared to BMD patients with other variants. Furthermore, the R16–R19 regions have been found to be important for cardiac disease.
Brain involvement in DMD correlates with the location of mutations relative to the promoters and isoforms expressed in the central nervous system. Mutations affecting the Dp140 and Dp71 isoforms, which are expressed in the brain, are associated with a higher prevalence of cognitive impairment and neurodevelopmental disorders.

Genetic Modifiers of Disease Severity

Individuals with the same DMD mutation may exhibit marked differences in disease severity, with modulation by modifier gene polymorphisms in genes distant from the DMD gene. Some genetic modifiers that slow disease progression are represented by variants that affect the expression and function of SPP1, LTBP4, CD40, THBS1, ACTN3, and TCTEX1D.
The LTBP4 gene has emerged as a particularly important genetic modifier in DMD. Isoleucine-alanine-alanine-methionine (IAAM) homozygosity has been associated with early loss of ambulation, resulting in the anti-fibrotic action of the IAAM haplotype of LTBP4 with an apparent protective function from the onset and progression of DMD-related cardiomyopathy. Large genomic mapping studies offer the potential to discover more disease modifying genes, allowing for the identification of multi-locus interaction patterns and improving the prognosis of the DMD population.

Advances in Genetic Testing

Genetic testing has become an invaluable tool in the management of Duchenne muscular dystrophy, having evolved significantly in recent years. While it was once primarily used for diagnosis, advances in next-generation sequencing (NGS), whole exome sequencing (WES), and whole genome sequencing (WGS) now enable genetic tests to provide crucial insights into predicted disease progression and cardiac involvement. These findings are essential for accurate risk stratification, allowing for early identification of individuals at higher risk. This, in turn, facilitates the initiation of protective treatments and the personalization of clinical monitoring, ultimately improving patient outcomes and care.
Several approaches can be employed depending on the portion of the genome to analyze. Targeted gene sequencing is a valuable approach for diseases with known disease causing genes. Focused panels contain a set of genes associated with the inherited disease. Clinical exome sequencing (CES) tests or Mendeliome are able to analyze more than 5,000 clinical genes specifically related to known inherited diseases. WES allows for the analysis of all coding regions (2%) of the DNA, and WGS tests all the DNA including intron and exon regions. The latter is the most complex but the most useful for identifying alterations responsible for a disease for which the responsible genes are unknown.

PHARMACOTHERAPEUTIC ADVANCES

Corticosteroid Therapy: The Current Standard of Care

Corticosteroid therapy remains the cornerstone of pharmacological management in DMD, representing the only general therapeutic option that can slow disease development. Pharmacological corticosteroids are the DMD standard of care; however, they have harsh side effects and unclear molecular benefits. Corticosteroid therapy targeting the inflammatory damage in DMD delays loss of ambulation by only 1–3 years in boys to 11–13 years of age.
The molecular mechanisms underlying corticosteroid efficacy in DMD are incompletely understood. The glucocorticoid receptor acts locally to protect dystrophic muscle and heart during disease. Despite their widespread use and demonstrated efficacy in Duchenne disease

progression, corticosteroids are associated with significant adverse effects, including weight gain, stunted growth, osteoporosis, and mood disturbance.

Vamorolone: A Novel Dissociative Corticosteroid

Vamorolone, the first dissociative corticosteroid for Duchenne muscular dystrophy, was approved for treatment of boys with DMD by the FDA and EMA in 2023. Vamorolone is a mineralocorticoid receptor antagonist (MRA) in humans. It reversed fludrocortisone-induced sodium retention without altering potassium excretion, and there was no evidence of hyperkalemia effect in DMD boys receiving vamorolone.

Clinical trial data from the Phase 1 mechanistic LIONHEART study and using serum samples from boys with DMD in the pivotal VISION-DMD trial have demonstrated the biological profile of vamorolone is differentiated from classic corticosteroids. Vamorolone showed comparable efficacy with corticosteroids but without some of its long term, deleterious effects, such as stunted growth, osteoporosis, and mood disturbance. Vamorolone may offer a safer treatment option than long term corticosteroids. The mineralocorticoid receptor antagonism of vamorolone has been evidenced from LIONHEART and VISION-DMD clinical trials.

Antisense Oligonucleotide Mediated Exon Skipping

Antisense oligonucleotide (AON)-mediated exon skipping represents a precision therapeutic approach designed to restore the dystrophin reading frame in patients with amenable DMD mutations. The US Food and Drug Administration (FDA) has granted accelerated approval for four AONs to skip a single DMD exon for treating patients with DMD: eteplirsen for exon 51 skipping, golodirsen and viltolarsen for exon 53 skipping, and casimersen for exon 45 skipping.

Eteplirsen received accelerated FDA approval for treatment of Duchenne muscular dystrophy with mutations amenable to exon 51 skipping. The PROMOVI trial evaluated eteplirsen in patients with DMD amenable to exon 51 skipping. More recently, brogidirsen, a dual-targeting antisense oligonucleotide for exon 44 skipping, has been evaluated in a Phase 1/2 trial-. Brogidirsen has shown sustained motor function benefits in a 3.5-year Duchenne muscular dystrophy trial.

DYNE-251, an investigational therapeutic for DMD, has demonstrated sustained functional improvement in males with DMD mutations amenable to exon 51 skipping enrolled in the Phase 1/2 DELIVER trial. Entrada Therapeutics has received authorization in the European Union and the United Kingdom to initiate ELEVATE-45-201, a Phase 1/2 multiple ascending dose clinical study of ENTR-601-45 in patients living with Duchenne muscular dystrophy amenable to exon 45 skipping.

The exon skipping approach for DMD remains under development, and several chemical modifications with improved properties are under preclinical and clinical investigation-. Despite existing advantages of these modifications, their safety and effectiveness must be examined in clinical trials, which are planned or ongoing.

Pharmacotherapeutic Outcomes

Glucocorticoid therapy remains a fundamental component of DMD pharmacotherapy because corticosteroids can slow deterioration of muscle function and prolong ambulation. Their therapeutic value, however, is counterbalanced by substantial cumulative toxicity, including weight gain, growth impairment, osteoporosis, behavioral effects, hypertension, glucose abnormalities, and other endocrine and metabolic complications. This therapeutic dilemma illustrates a central principle of evidence-based pharmacotherapy: preservation of function must be evaluated simultaneously with treatment-associated morbidity.

The results of contemporary clinical practice consequently favor individualized corticosteroid selection, dosing schedules, monitoring, and adverse-effect mitigation rather than indiscriminate long-term administration. The expanding therapeutic landscape also requires clinicians to consider

potential interactions between established glucocorticoid treatment and mutation-specific or gene-based interventions.

Gene Therapy: AAV Mediated Micro-Dystrophin Delivery

Adeno-associated virus (AAV) vector-based gene therapy represents one of the most promising therapeutic approaches for DMD. Delandistrogene moxeparvovec (rAAVrh74 vector-based gene therapy) has been approved in the US and other select countries and delivers a transgene encoding an engineered micro-dystrophin. The FDA has approved this gene therapy product for the treatment of patients with DMD.

Multiple gene therapy candidates are in various stages of clinical development. Fordadistrogene movaparvovec (PF-06939926) is an adeno-associated virus serotype 9 micro-dystrophin being developed for DMD. RGX-202 is designed to deliver a microdystrophin via AAV8 through a one-time IV infusion. The Phase III AFFINITY DUCHENNE study met its primary endpoint of at least 10% microdystrophin expression at week 12, with 93% of patients achieving this threshold-. RGX-202 has been well tolerated in the Phase I/II portion of the trial with no serious adverse events in boys aged 1-11 years old.

SGT-003 has shown promise in the Phase 1/2 INSPIRE DUCHENNE trial, with interim data showing an average microdystrophin expression of 110% among participants at 90 days post-treatment. A patient aged 3 years at the time of treatment achieved 122.3% microdystrophin expression compared to control.

Gene Editing: CRISPR-Cas9 and Base Editing

Gene editing technologies represent the frontier of genetic medicine for DMD. GenAssist Therapeutics has announced updated 52-week results from the first two patients enrolled in its ongoing investigator-initiated trial of GEN6050X, a first in class base editing therapy for Duchenne muscular dystrophy. This marks the first gene editing therapy for DMD to enter clinical evaluation in the United States.

Utrophin Modulation

Therapeutic activation of endogenous utrophin, a dystrophin homolog, represents a mutation agnostic therapeutic strategy with considerable potential for treating Duchenne muscular dystrophy-. Activation of endogenous full-length utrophin presents an attractive therapeutic strategy for DMD, regardless of mutation types and loci.

The small molecule utrophin modulator Ezutromid was shown to be safe and well-tolerated in Phase 1 trials. In the Phase 2 study (NCT02858362), treatment for 24 weeks led to increased utrophin expression and a significant reduction in muscle damage in DMD patients-. More recently, systemic MyoAAV-saRNA delivery has been shown to activate endogenous utrophin and rescue dystrophic pathology in mdx mice, establishing MyoAAV-saRNA as a promising and translatable platform for utrophin induction.

HDAC Inhibition

The inhibition of HDAC activity has received attention as a therapeutic approach for treating muscular dystrophies. Givinostat, the histone deacetylase inhibitor under current development as a clinical treatment for DMD, is effective at both restoring a physiological microenvironment at the neuro cardiac junction and cardiac function, with a reduction in cardiac fibrosis. Aberrant activity of histone deacetylases is a pathological phenomenon in several diseases, including Duchenne muscular dystrophy.

PRECISION MEDICINE

Biomarkers for Disease Monitoring and Prognosis

The development of reliable biomarkers is essential for precision medicine approaches in DMD. Large-scale serum biomarker discovery is now possible in DMD with the availability of high-throughput proteomics platforms such as SomaScan. In a retrospective study, researchers had a unique opportunity to combine robust and comprehensive clinical data from two large, independent international cohorts of individuals with DMD along with serum levels of 6,628 proteins. The availability of extensive longitudinal serum samples and clinical data allowed not only analysis of protein signatures associated with age and corticosteroid usage, but also identification of novel proteins that could predict clinical function and motor milestones.
Proteins such as RGMA were found to predict both lower and upper limb clinical milestones including loss of ambulation and loss of hand-to-mouth function. Furthermore, several proteins were associated with an increased risk of a specific clinical milestone such as ART3 for loss of ambulation. The ability to compare these findings across two independent cohorts demonstrated the generalizability of these results.
Serum creatine kinase remains the most widely used biomarker in clinical practice, although its utility is limited by substantial variability and its tendency to decline with disease progression-. Increased dystrophin expression in muscle has been accepted as a surrogate endpoint for accelerated approval of gene therapies within Duchenne muscular dystrophy. Plasma levels of a titin fragment comprising amino acids 2,229–2,352 were found to negatively correlate with dystrophin expression in mdx mice treated with AAV9-CK8-µDys5 micro dystrophin gene therapy.

Genetic Modifiers and Personalized Prognostication

The identification of genetic modifiers enables increasingly personalized prognostication in DMD. Some genetic modifiers that slow disease progression are represented by variants that affect the expression and function of SPP1, LTBP4, CD40, THBS1, ACTN3, and TCTEX1D. Understanding the genetic modifier status of an individual patient may inform clinical decision making regarding the timing of interventions and the intensity of monitoring.

Personalized Therapeutic Selection

The advent of genotype specific therapies has made personalized therapeutic selection a clinical reality in DMD. The choice of therapeutic approach is increasingly guided by the specific mutation present in an individual patient. Patients with mutations amenable to exon 51 skipping may be candidates for eteplirsen, while those with mutations amenable to exon 53 skipping may be candidates for golodirsen or viltolarsen. Gene therapy with delandistrogene moxeparvovec is indicated for patients with confirmed DMD mutations regardless of specific exon location.

Emerging Diagnostic Technologies

Recent breakthroughs in DMD treatment include exon-skipping therapies, gene editing-mediated reading frame restoration, and artificial chromosome transfer. Current diagnostic approaches combine genetic testing for exon deletion/duplication analysis with ancillary methods which include biomarkers such as serum creatine kinase. The integration of precision therapies with cutting-edge diagnostic technologies promises to improve both prognosis and quality of life for individuals with DMD.

EVIDENCE-BASED MEDICINE

Clinical Guideline Development

A coordinated, multidisciplinary approach to care is essential for optimum management of the primary manifestations and secondary complications of Duchenne muscular dystrophy-. Evidence-based clinical guidelines have been developed to standardize care and improve outcomes for individuals with DMD.

Respiratory care guidelines for Duchenne muscular dystrophy in the UK have been developed, providing evidenced-based and/or consensus-based best practice for the respiratory care of children and adults living with DMD. These guidelines, endorsed by the British Thoracic Society, provide practical, reasoned recommendations for all those managing day-to-day and acute respiratory care in children and adults with DMD.

Consensus recommendations for the delivery and monitoring of gene therapy in patients with Duchenne muscular dystrophy have been developed by a group of clinicians and researchers coordinated by the Muscular Dystrophy Association and Parent Project Muscular Dystrophy. These guidelines outline recommendations for patient selection, institutional readiness, monitoring, and adverse event management, particularly in the first three months after treatment. The guidelines emphasize the importance of experienced multidisciplinary teams, real-time safety surveillance, and transparent reporting to support patient safety and clinician decision making after treatment.

Systematic reviews have contributed substantially to the evidence base for DMD management. A systematic review and meta-analysis of conservative non-pharmacological interventions in people with muscular dystrophies followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. For children with Duchenne muscular dystrophy, trunk oriented strength exercises and usual care were more effective than usual care alone in improving distal upper limb function.

A systematic review of predictors of cardiac disease in Duchenne muscular dystrophy found moderate- to high-quality evidence that cardiac medication and specific DMD mutations in exons 51 and 52 were significantly associated with lower risk of cardiomyopathy. High-quality evidence was found that glucocorticoids (deflazacort) are beneficial for cardiac outcomes-. A systematic review of pharmacologic therapies for the cardiomyopathy of Duchenne muscular dystrophy has also been conducted.

Evidence Gaps and Research Priorities

Despite the substantial evidence base supporting current DMD management, significant knowledge gaps remain. Regarding gene therapy, significant knowledge gaps remain regarding long term safety, durability, and optimal timing of dosing, particularly for patients with advanced disease. Researchers do not fully understand how combination therapies and genetic background may impact the response to gene therapy. To address these gaps, ongoing real-world data collection, cross-center collaboration, and flexible adaptation of clinical protocols are essential. While current guidelines are based primarily on clinical expertise rather than well-established evidence, they provide a foundation to support administration of gene therapy for patients with DMD.

EMERGING MULTIDISCIPLINARY TREATMENT STRATEGIES

The Multidisciplinary Care Paradigm

The cornerstone of DMD treatment includes pharmacological therapies, physical and occupational therapy, respiratory support, and cardiac care. A coordinated, multidisciplinary approach to care is essential for optimum management of the primary manifestations and secondary complications of Duchenne muscular dystrophy. Currently, there is no curative treatment for Duchenne muscular dystrophy or its cardiovascular complications. However, the use of glucocorticoids, physical rehabilitation, non-invasive mechanical ventilation, and multidisciplinary management with a cardiorespiratory and orthopedic focus have been shown to modify the natural history of the disease.

Respiratory Care

Respiratory complications represent a major cause of morbidity and mortality in DMD. The development of respiratory care guidelines for Duchenne muscular dystrophy in the UK has provided evidenced-based and/or consensus-based best practice for the respiratory care of children and adults living with DMD, both as part of routine care and in an emergency. The guidelines encompass respiratory issues seen in children and adults across the various stages of DMD and seek to address specific concerns raised by patients, their carers, and clinicians in relation to access to appropriate, high-standard respiratory care. The recommendations are presented in the form of a flow chart for assessment and monitoring, with additional guidance and a separate chart setting out key considerations for emergency management.

Cardiac Care

Cardiac health is a critical aspect of DMD management-. Cardiac care is equally critical, given the high incidence of dilated cardiomyopathy in DMD patients-. Cardiac medications were prescribed to 82.1% of patients in a South Korean study, with beta-blockers being the most common.
Predictors of cardiac disease in Duchenne muscular dystrophy have been systematically reviewed, with moderate to high quality evidence that cardiac medication and specific DMD mutations in exons 51 and 52 were significantly associated with lower risk of cardiomyopathy-. High-quality evidence was found that glucocorticoids (deflazacort) are beneficial for cardiac outcomes. The synergistic integration of small molecule and gene target based drugs with metabolic, immune, or ion balance enhancing compounds into a combinatorial therapy offers potential for treating dystrophin deficiency-induced cardiomyopathy.

Physical and Occupational Therapy

Physical therapy plays a vital role in maintaining muscle strength and joint flexibility. For children with Duchenne muscular dystrophy, trunk-oriented strength exercises and usual care were more effective than usual care alone in improving distal upper limb function. Following loss of ambulation, the main management focus shifts to cardiac, respiratory, orthopedics, nutrition, and upper limbs function.

Transition from Pediatric to Adult Care

An increasing number of patients with Duchenne muscular dystrophy now have access to improved standard of care and disease modifying treatments. Essential components of an effective transition from pediatric to adult neurologist care for adolescents with Duchenne muscular dystrophy have been established through a consensus derived using the Delphi methodology-. This consensus details the results of a consensus among clinicians on transitioning adolescent DMD patients from pediatric to adult neurologists that can act as a guide to best practice at every stage of their journey-. Transition from pediatric to adult services and from the ambulatory to non-ambulatory phase requires careful coordination.

Treatment of Non Ambulatory Patients

Treatment of DMD patients at any stage of the disease is based on supportive and symptomatic measures, which should be continued after loss of ambulation-. In addition, disease-modifying drugs are available for the treatment of DMD, and glucocorticoids are the usual standard of care treatment even beyond the loss of ambulation-. Ataluren has been approved for nonsense mutation DMD (nmDMD), which applies to approximately 13% of DMD patients and is usually combined with steroids.

FUTURE DIRECTIONS

Integration of Emerging Therapies into Clinical Practice

The remarkable advances in genetic therapies for DMD including exon skipping, gene therapy, and gene editing—present both unprecedented opportunities and substantial challenges for clinical implementation. The integration of these precision therapies with cutting-edge diagnostic technologies promises to improve both prognosis and quality of life for individuals with DMD. However, significant challenges remain regarding equitable access, long-term safety monitoring, and optimal integration with existing standards of care.

Combination Therapy Approaches

The future of DMD therapeutics likely lies in combination approaches that target multiple pathogenic pathways simultaneously. The synergistic integration of small molecule- and gene-target-based drugs with metabolic, immune, or ion balance-enhancing compounds into a combinatorial therapy offers potential for treating dystrophin deficiency induced cardiomyopathy. Corticosteroid therapy combined with genetic therapies may provide additive or synergistic benefits, although the safety and efficacy of such combinations require careful evaluation.

Addressing Unmet Needs

Despite substantial progress, significant unmet needs persist in DMD care. These include the need for therapies that address cardiac and respiratory involvement, the development of biomarkers that can reliably predict therapeutic response, and the optimization of care for non-ambulatory patients-. The treatment of DMD patients at any stage of the disease requires continued attention to supportive and symptomatic measures.

Global Health Equity

The substantial cost and complexity of emerging DMD therapies raise important questions about global health equity. Access to advanced therapies remains limited in many parts of the world, creating disparities in outcomes that mirror broader patterns of healthcare inequality. International collaborations and advocacy efforts are essential to ensure that the benefits of scientific advances are accessible to all individuals with DMD, regardless of geographic location or socioeconomic status.

The Role of Patient Advocacy

Patient advocacy organizations have played an instrumental role in advancing DMD research and care. Organizations such as Parent Project Muscular Dystrophy have coordinated the development of consensus guidelines, funded research, and advocated for policy changes that benefit the DMD community. Continued engagement of patient advocacy groups will be essential for ensuring that research priorities align with patient needs and that emerging therapies are accessible to those who need them.

Summary

Duchenne muscular dystrophy is a complex X-linked neuromuscular disorder caused by pathogenic variants in the *DMD* gene and consequent deficiency or absence of dystrophin. Its pathogenesis involves sarcolemmal instability followed by calcium dysregulation, oxidative stress, mitochondrial dysfunction, inflammation, fibrosis, impaired regeneration, and progressive skeletal and cardiac muscle degeneration. The clinical phenotype is therefore multisystemic, encompassing progressive motor weakness, loss of ambulation, respiratory impairment, cardiomyopathy, contractures, bone and endocrine complications, and neuropsychological and psychosocial manifestations. These features require continuous surveillance and coordinated multidisciplinary management.

Advances in molecular genetics have fundamentally changed the therapeutic paradigm. Genotype characterization now contributes not only to diagnosis and family counseling but also to treatment selection, clinical-trial eligibility, prognostic assessment, and precision medicine. Corticosteroids remain an important component of disease-modifying care, although their long-term adverse effects necessitate individualized risk-benefit assessment. Mutation-specific antisense oligonucleotide therapies have introduced exon-skipping strategies designed to restore the translational reading frame in eligible patients. Pharmacological approaches such as histone deacetylase inhibition further demonstrate the potential to modify downstream mechanisms of muscle degeneration.

Gene-transfer technologies, particularly micro-dystrophin strategies, represent another major translational advance by attempting to restore dystrophin-related function despite the size limitations of the full-length gene. However, immune responses, vector delivery, durability, redosing limitations, and uncertainty regarding long-term clinical benefit remain important challenges. Accordingly, molecular innovation must be evaluated through rigorous evidence-based frameworks incorporating clinical outcomes, safety, durability, patient-centered benefit, and pharmacovigilance.

The contemporary DMD management is evolving from predominantly supportive treatment toward an integrated precision-medicine model that combines genetic diagnosis, disease-modifying pharmacotherapy, emerging gene-based interventions, cardiopulmonary protection, rehabilitation, nutritional and endocrine management, psychosocial support, and longitudinal monitoring. The principal future objective is not simply to increase the number of available therapies, but to determine how complementary interventions can be strategically integrated according to genotype, disease stage, organ involvement, treatment response, and individual patient needs. Such an evidence-informed multidisciplinary approach offers the strongest framework for preserving function, reducing complications, prolonging survival, and improving quality of life in individuals with DMD.

Duchenne muscular dystrophy represents a paradigmatic example of how advances in molecular biology, genetics, and pharmacology can transform the understanding and management of a devastating genetic disorder. The identification of the DMD gene and the elucidation of dystrophin's role in maintaining muscle integrity laid the foundation for the development of targeted therapies that were unimaginable just a few decades ago.

The molecular pathophysiology of DMD is now understood in considerable detail, encompassing not only the mechanical consequences of dystrophin deficiency but also the complex interplay of calcium dysregulation, oxidative stress, mitochondrial dysfunction, inflammation, fibrosis, and epigenetic dysregulation. The genetic mechanisms underlying DMD have been characterized, revealing a spectrum of mutations and the role of genetic modifiers in modulating disease severity.

Pharmacotherapeutic advances have expanded from the glucocorticoid-based standard of care to include novel dissociative corticosteroids such as vamorolone, antisense oligonucleotide-mediated exon skipping, AAV vector-based gene therapy, and gene editing. The principles of precision medicine are being applied through biomarker discovery, genetic modifier identification, and personalized therapeutic selection. Evidence-based medicine frameworks provide guidance for clinical decision-making, while multidisciplinary care strategies address the full spectrum of disease manifestations.

The convergence of these advances holds the promise of transforming DMD from a uniformly fatal childhood disease to a manageable chronic condition. However, realizing this promise will require continued investment in research, sustained commitment to evidence-based practice, and unwavering dedication to ensuring that all individuals with DMD benefit from scientific progress.

CONCLUSION

- Duchenne muscular dystrophy (DMD) represents a paradigmatic example of a genetically determined, multisystemic neuromuscular disorder in which molecular pathophysiology, progressive skeletal-muscle degeneration, cardiomyopathy, respiratory insufficiency, functional decline, and psychosocial complications converge to produce substantial lifelong morbidity. The scientific discourse surrounding DMD has progressively evolved from a predominantly supportive-care model toward an integrated therapeutic paradigm incorporating molecular genetics, translational medicine, pharmacology, precision medicine, and evidence-based multidisciplinary management. Central to this evolution is recognition that pathogenic alterations in the *DMD* gene and consequent dystrophin deficiency disrupt sarcolemmal integrity, initiate membrane instability, calcium dysregulation, chronic inflammation, oxidative stress, myofiber necrosis, fibrosis, and ultimately irreversible loss of muscle tissue.
- Contemporary pharmacotherapeutic strategies, particularly glucocorticoid therapy and emerging dystrophin-restoring or mutation-directed approaches, have demonstrated the potential to modify disease trajectories, although therapeutic effectiveness remains heterogeneous and frequently constrained by adverse effects, genotype-specific eligibility, limited tissue penetration, and progressive disease biology. Exon-skipping technologies, micro-dystrophin gene-transfer strategies, and other molecular interventions represent important advances in precision therapeutics, while ongoing investigation into genome editing, myostatin modulation, anti-inflammatory mechanisms, fibrosis inhibition, mitochondrial dysfunction, and regenerative approaches may further expand the therapeutic landscape. Nevertheless, these innovations should be interpreted within an evidence-based framework that distinguishes biologically promising interventions from therapies supported by robust clinical outcomes.
- Optimal DMD management therefore requires sustained multidisciplinary coordination involving neurologists, clinical pharmacologists, geneticists, cardiologists, pulmonologists, rehabilitation specialists, orthopedic clinicians, nutrition professionals, psychologists, and other healthcare practitioners. Early genetic diagnosis, individualized therapeutic selection, continuous cardiac and respiratory surveillance, preservation of mobility, management of glucocorticoid-associated complications, and proactive psychosocial and educational support remain fundamental components of comprehensive care.
- The future of DMD therapeutics will depend upon integrating molecular diagnosis with individualized risk stratification, pharmacogenomic principles, longitudinal biomarkers, real-world evidence, and rigorously designed clinical trials. Precision medicine should therefore be conceptualized not merely as mutation-specific treatment, but as a continuously adaptive strategy integrating genotype, phenotype, disease stage, comorbidities, treatment response, safety, and patient-centered outcomes. The convergence of molecular therapeutics, advanced pharmacotherapy, evidence-based medicine, and multidisciplinary care offers a scientifically credible pathway toward transforming DMD from a relentlessly progressive disorder into an increasingly manageable chronic disease, while continued translational research remains essential to achieving durable functional restoration and ultimately curative treatment.

RECOMMENDATIONS

- Based on the current scientific understanding of Duchenne muscular dystrophy (DMD), several strategic recommendations can be proposed to strengthen disease prevention, diagnosis, treatment, and long-term patient outcomes.
- Early molecular diagnosis and comprehensive genetic characterization should be prioritized to facilitate timely intervention, genetic counseling, family screening, and identification of patients eligible for genotype-specific therapeutic approaches.

- DMD management should adopt a precision-medicine framework integrating genotype, phenotype, disease stage, functional status, comorbidities, treatment response, and individual risk factors. Pharmacotherapeutic decisions should be guided by high-quality clinical evidence, with continuous assessment of therapeutic efficacy, tolerability, drug interactions, and long-term safety.
- Multidisciplinary care pathways should be systematically implemented, incorporating neurology, clinical pharmacology, genetics, cardiology, pulmonology, rehabilitation, orthopedics, nutrition, psychology, and specialized nursing. Regular cardiac and respiratory surveillance is particularly important because cardiomyopathy and respiratory dysfunction remain major determinants of morbidity and mortality.
- Continued investigation of exon-skipping, gene-transfer technologies, genome-editing strategies, regenerative medicine, anti-inflammatory interventions, antifibrotic therapies, and novel molecular targets should be encouraged through rigorously designed clinical trials. Long-term real-world evidence should complement randomized controlled trials to establish durability, safety, comparative effectiveness, and clinically meaningful patient outcomes.
- Healthcare systems should strengthen equitable access to genetic testing, disease-modifying therapies, rehabilitation, assistive technologies, and specialized multidisciplinary services. Patient and family education should remain integral to care, supporting informed decision-making, adherence, psychosocial adaptation, and quality of life. Future research should increasingly prioritize functional independence, survival, patient-reported outcomes, and meaningful improvements in daily living rather than relying exclusively on surrogate biomarkers. Through sustained integration of precision medicine, evidence-based pharmacotherapy, translational research, and coordinated multidisciplinary care, the therapeutic management of DMD can continue progressing toward more effective, individualized, and potentially disease-modifying strategies.

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