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Bridging the gap: clinical translation of adipose-derived stem cells - a scoping review of clinical trials

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Abstract

Background Adipose-derived stem cells (ADSCs) have emerged as a promising therapeutic tool in regenerative medicine due to their multipotency, immunomodulatory properties, and ease of procurement. Despite extensive preclinical research, the clinical translation of ADSCs remains fragmented, with challenges in standardization, reproducibility, and evidence synthesis.

Objective This scoping review, complemented by bibliometric analysis, aims to map the landscape of randomized controlled trials (RCTs) evaluating ADSC therapies, identify gaps between basic research and clinical translation, and highlight emerging trends in the field.

Methods A systematic search of Web of Science, PubMed, Embase, ClinicalTrials.gov, EudraCT, and ChiCTR database (2009–2025) identified 82 RCTs. Bibliometric analysis of preclinical studies was conducted using VoSviewer to visualize keyword clusters and temporal trends. Data on trial characteristics, endpoints, and translational challenges were extracted and synthesized.

Results The 82 included RCTs spanned 17 medical specialties, with orthopedics (26.8%), dermatology (14.6%), and neurology (9.7%) being the most studied. Spain (21.95%) and China (18.29%) and the USA (15.85%) led trial numbers, but 97% were single-country studies with a median sample size of 40. Primary endpoints trends from safety to efficacy. Bibliometric analysis revealed three clusters: stem cell sources and basic biology, orthopedic applications, and tissue regeneration mechanisms. Key gaps included protocol heterogeneity (e.g., isolation methods, cryopreservation variability), regulatory fragmentation, limited long-term follow-up, and inconsistent clinical outcomes, particularly in neurology. Emerging trends highlighted the therapeutic potential of stromal vascular fraction (SVF) and ADSC-derived exosomes.

Conclusions While ADSCs demonstrate significant therapeutic potential, clinical translation is hindered by standardization deficits and mechanistic knowledge gaps. Future research should prioritize international collaboration, large-scale trials, and mechanistic studies to optimize ADSC therapies. Innovations in SVF and exosome-based treatments represent promising avenues for advancing regenerative medicine.

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Trial registry This scoping review was preregistered at OSF platform: https://doi.org/10.17605/OSF.IO/YKHW3.

Keywords Randomized controlled trials, Adipose-derived stem cells, Scoping review, Bibliometric analysis, Regenerative medicine

Introduction

Adipose-derived stem cells (ADSCs) have garnered significant attention as a promising therapeutic modality in regenerative medicine, owing to their unique biological properties and relatively straightforward and safe procurement [1, 2]. These multipotent cells, derived from adipose tissue, exhibit remarkable versatility by differentiating into various cell lineages, secreting bioactive molecules, and modulating immune responses [3, 4]. Consequently, they have become attractive candidates for treating a wide range of diseases and conditions, including musculoskeletal disorders [5], cardiovascular diseases [6], and neurodegenerative conditions [7]. However, despite their potential, the efficacy and safety of ADSCs therapy remain subjects of ongoing investigation.

In recent years, there has been a substantial increase in research exploring the therapeutic applications of ADSCs, with numerous studies reporting on their potential benefits and limitations [8]. Randomised controlled trials (RCTs) are considered the gold standard for evaluating the effectiveness of medical interventions, and several RCTs have been conducted to assess the efficacy of ADSCs therapy in various clinical settings [9–11]. These studies have provided valuable insights into the safety and therapeutic potential of ADSCs. Despite the growing preclinical and clinical interest, the translation of ADSCs from bench to bedside remains a significant challenge, with only a few therapies approved for clinical use. Additionally, the evidence base for ADSCs therapies remains fragmented, highlighting the need for a comprehensive and systematic evaluation of existing RCTs to guide future translational research of ADSC.

To address these gaps, this scoping review aims to provide a comprehensive overview, examining the current stage of ADSCs therapy, synthesizing the findings and identifying gaps in the current research landscape. However, traditional scoping review alone may struggle to capture the overall landscape of ADSC research, which has grown exponentially in volume and complexity in recent years. To address this, we integrated bibliometric analysis-a quantitative and visualized method for evaluating research landscape and trend-within the scoping review [12]. This hybrid approach enables a dual perspective: the bibliometric analysis serves as an indicator, mapping the basic research landscape for scoping review to dig into, while the scoping reviews digs deeper into synthesizing qualitative and quantitative insights on ADSC's bench to bedside translation. Together, the hybrid approach provides a holistic view of the state of research regarding to ADSCs therapy. Therefore, complemented by a bibliometric clustering, we broke the large research question into three smaller subjects, each representing a stage in the translational study of ADSC:

- RQ.01- Current stage of RCT: What is the current landscape of RCT on ADSC?
- RQ.02- Connections between clinical trials and basic research: Have the findings from basic research been effectively translated into clinical trials? How has basic research guided the design and implementation of clinical studies?
- RQ.03- Future directions: What are the emerging trends in ADSC's clinical use and where will be the possible research focus in the future?

By combining a scoping review with bibliometric analysis, this study aims to provide a comprehensive overview of the existing RCTs on ADSCs therapy, offering valuable insights into the current state of ADSCs therapy research and guiding future directions for clinical applications and investigations.

Method

This scoping review was conducted according to the JBI Manual for evidence synthesis and adheres to the PRISMA extension for scoping reviews (PRISMA-ScR) [13]. This scoping review was preregistered at OSF platform: https://doi.org/10.17605/OSF.IO/YKHW3.

Search strategy and study selection

Web of Science Core Collection, PubMed, Embase, the Clinicaltrial.gov, EudraCT, and ChiCTR database were searched as the source of relevant literature. The search was first conducted in January 29, 2025, and lasted searched on April 8, 2025. A combination of following search terms was used: ("adipose-derived stem cell" OR "adipose mesenchymal stem cell") AND ("randomized control trials"). The detailed search strategy can be found in the Supplementary Material 1. Two authors (SHK & CHS) screened for potentially relevant articles. Duplicates were first removed, followed by a screening of browsing titles and abstracts. Remaining articles will be screened for the second time to evaluate the full text of all eligible articles. At any point in the process, disagreements were resolved by a joint discussion with a third author (LQL). The eligible criteria were listed in Sect. 2.4.

Bibliometric analysis

Bibliometric analysis was performed to examine gaps between basic research and clinical translation. The Web of Science Core Collection database was searched with the following terms ("adipose-derived stem cell" OR "adipose mesenchymal stem cell") without any filtering. VoSviewer (Leiden University, Leiden, Netherlands) was used to conduct a keyword clustering analysis and development frontiers analysis of the results. The threshold for keyword occurrence was set at 45.

Data extraction

The extracted data includes: NCT number, date of registry, sponsor, speciality, country, centers, sample size, primary outcome, primary result, source of ADSC, and references. Two authors (SHK & CHS) screened relevant included articles and extracted data collectively. Due to the expected heterogeneity in tasks and endpoints, we did not conduct formal meta-analyses. Instead, we present simple descriptive statistics to provide an overview of the features of the eligible RCTs.

Inclusion and exclusion criteria

Inclusion criteria:

1. Randomized controlled trials that examines the therapeutic efficacy of adipose stem cells' treatment.
2. Randomized controlled trials that examines the other aspect of adipose stem cells' treatment.

Exclusion criteria:

1. Not randomized controlled trials.
2. In order to obtain necessary data, we excluded articles that are conference abstract or abstract only.
3. Comments, retracted article are excluded.

Results

RCT selection and characteristics

Figure 1 displays the RCT selection process. Our electronic search retrieved 63,331 study records from Web of Science, Pubmed, Embase, Clinicaltrial.gov, EudraCT, and ChiCTR platform database. Duplicates were first removed and after title and abstract screening, 80 RCTs were retained for full-text review. An additional 2 RCTs were identified through secondary reference screening from other systematic reviews, resulting in a total of 82 unique RCTs included in our scoping review. The references and characteristics for all the included studies are available in the Supplementary Material 2.

Of 82 RCTs, 17 medical specialties were involved. Twenty-two RCTs (26.8%) were related to orthopedics, 12 (14.6%) to dermatology, 8 (9.7%) to neurology, and 6 (7.3%) to vascular surgery. Andalusian Initiative for Advanced Therapies led trials across multiple domains, initiating a total of 9 RCTs (13.4%), primarily focused on vascular surgery (3 RCTs), infectious diseases (2 RCTs) and dermatology (2 RCTs).

Eighty (97%) of 82 RCTs were conducted in a single country, with Spain conducting the most trials (18 [21.95%]), followed by China (15[18.29%]) and the USA (13[19.40%]). The three countries differ significantly in RCT specialities. Trials conducted in the Spain predominantly related to vascular surgery [4 (22.2%) of 18 trials] and infectious diseases [3 (16.6%) of 18 trials], whereas trials conducted in the USA predominantly related to orthopedics [4 (30.7%) of the 13 trials] and Neurology [3 (23%) of the 13 trials] trials and China mainly related to orthopedics [6 (40%) of the 15 trials] and dermatology [5 (33.3%) of the 15 trials]. RCTs were predominantly conducted in a single center [49 (59.7%) of 82) and included a median of 40 patients (IQR 23–84) in their final analysis. And most of the multi-centered trials are still limited into only one country. Trials conducted in multiple countries mainly involved European nations. Figure 2 highlights the distribution of trials across countries and specialties.

As demonstrated in Fig. 3, we examined the number of registered RCTs by year, with the earliest relevant registration being published in 2009. Between 2009 and 2014, publication numbers exhibited a gradual upward trend, signifying an emerging interest in the clinical translation of ADSC. There was a burst in registration in 2020, which seems to be attributed to the outbreak of COVID-19 pandemic [8]. In summary, the field has exhibit constant momentum in worldwide registration since 2009, with new registry of RCT every year, and it is expected to keep the momentum in the years to come.

Out of 82 RCTs, 50 (60.9%) are in Phase 2. 29 (35.3%) are in Phase 1. There are 7 RCTs in Phase 3 trials (8.5%), which is the last phase before commercial distribution. Additionally, 7 RCTs (8.5%) are in Phase 0, a stage introduced following the FDA's 2006 exploratory Investigational New Drug (IND) guidance, which help accelerate drug development by allowing early evaluation of drug-target interactions and pharmacokinetic–pharmacodynamic relationships in humans, potentially reducing attrition rates in later stages. The phase of RCTs revealed that most of the clinical translated therapies of ADSC are still in the early stage of safety confirmation and therapeutic evaluation, with only a few entering Phase 3.

Of the 82 trials published since the start of 2009, 25 (30.4%) of 82 of the trials had primary endpoints relating to safety yield. Other primary endpoints were relating to efficacy (47 [57.3%]), both safety and efficacy (10 [12.1%]). It can be obtained that RCTs have experience two stages: preliminary stage primarily addresses the safety concern of ADSCs treatment. Secondary stage has focused more on the therapeutic efficacy of ADSC (Safety outcomes

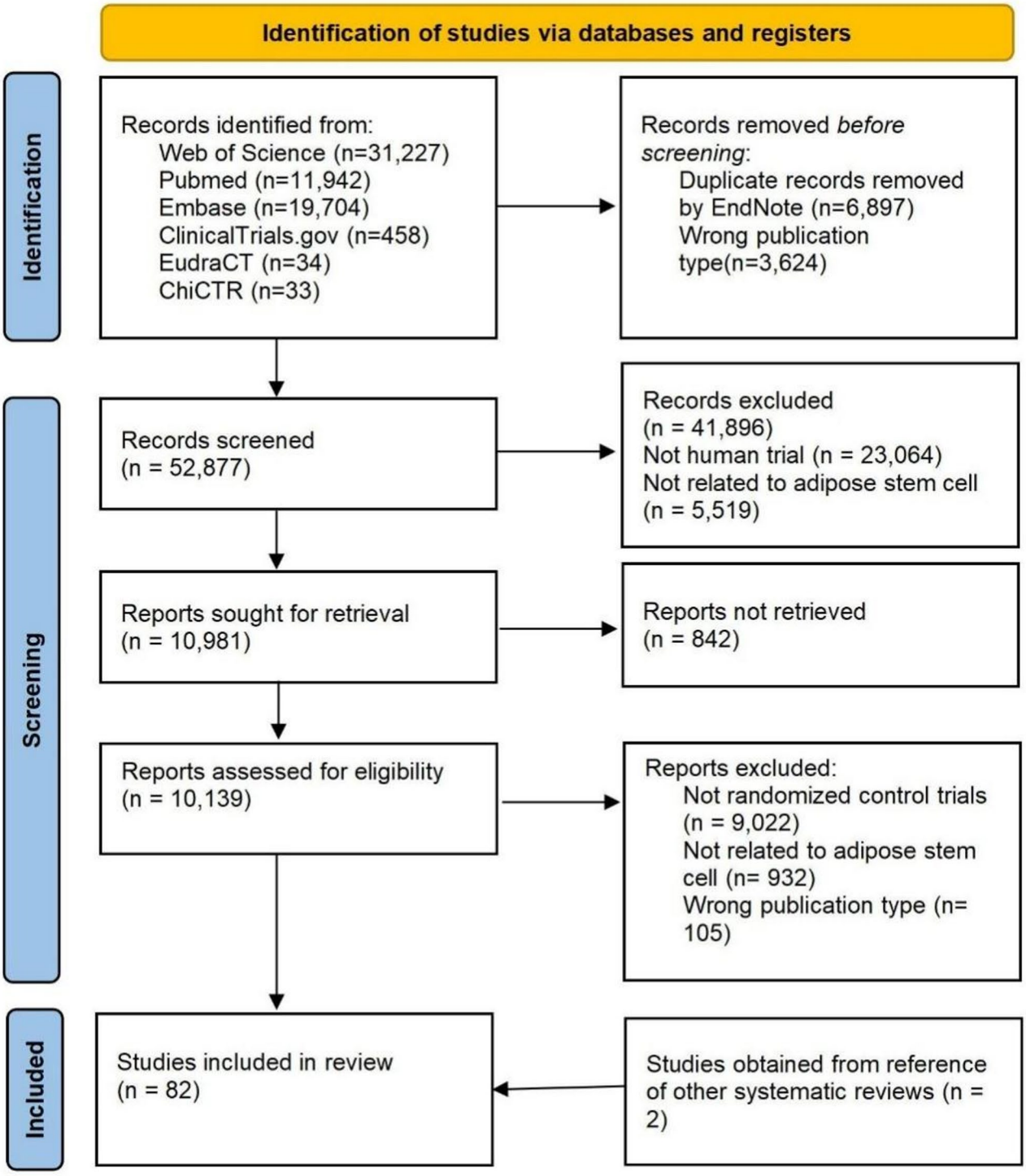

Fig. 1 Illustration of study selection process

accounts for 66.6% RCT in 2014, and 34.2% RCTs in 2024). According to the efficacy result of current RCT, ADSC has shown significant therapeutic potential in vascular surgery, diabetes, orthopedics, and rheumatology [14]. No significant negative effect was observed in areas such as infectious diseases, gastroenterology, and dermatology [15]. It is worth noting that a potential risk of negative side effects was observed in neurology. Such an inconsistency in research results suggest further

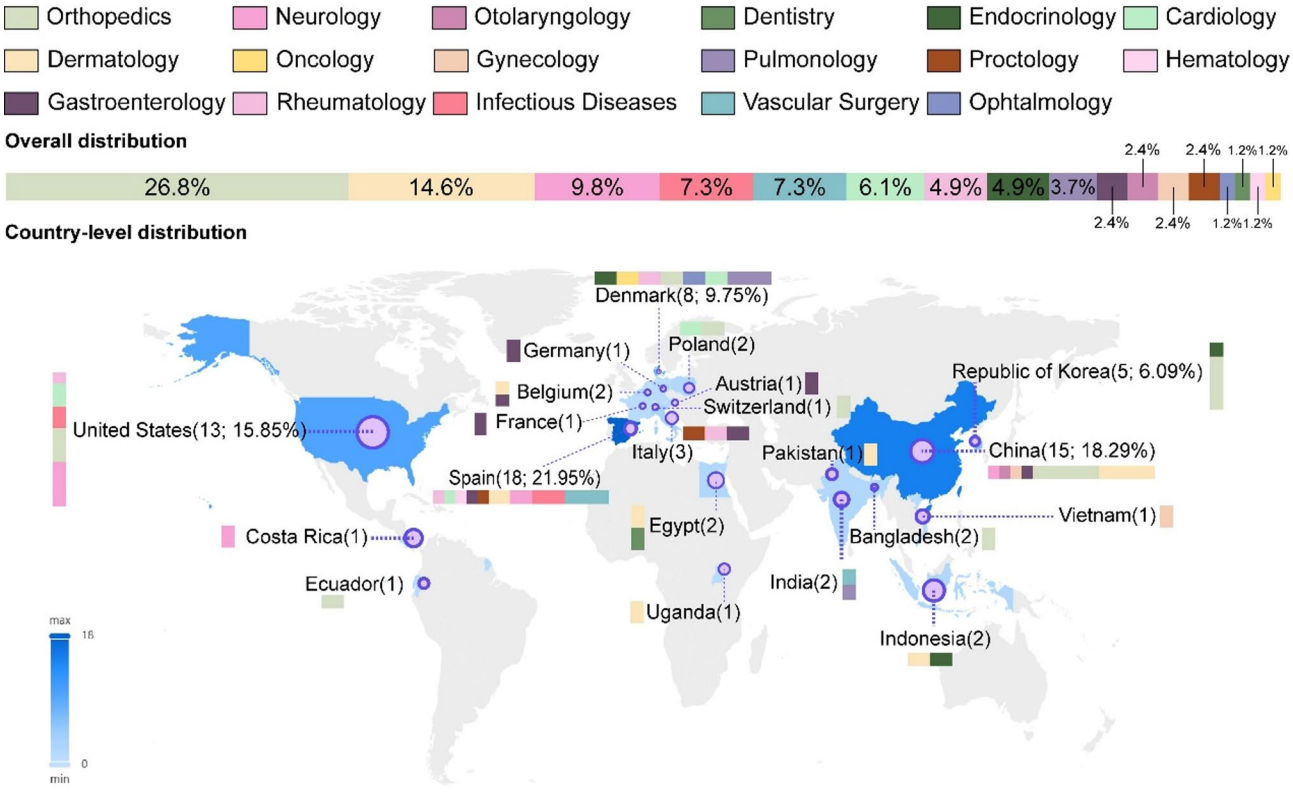

Fig. 2 Randomised controlled trials of adipose-derived stem cell in clinical practice across countries and specialties

refinement of RCT protocol and the need of further study in to the mechanism of treatment in ADSC therapy.

Clinical applications of autologous and allogeneic ADSC have been debated for decades, both exhibiting advantages and drawbacks. Autologous MSCs are easy to obtain without ethical concerns and have a lower chance of exhibiting immune rejection after infusion. However, the process of isolating, expanding in vitro, and releasing autologous MSCs causes damage to patient and is time-consuming. Meanwhile, allogeneic MSCs can offer several advantages such as multiple sourcing options, and off-the-shelf availability. But they also carry risks, such as potential immune rejection, donor-donor heterogeneity, and rapid clearance after infusion [16–18]. Compared to autologous transplantation, the use of allogeneic transplantation has increased in recent years. [In the past decades, the use of allogenic ADSCs as the material increased by 7%, from 33.3% in 2014 to 40% in 2024]. The potential reason for the rise of allogeneic transplantation in recent years could possibly be contributed to the reason that it does not require extraction from the patient's own body and can be stored and used on demand, which is beneficial for commercial application.

Gaps and bridges for bench to bedside translation

We utilized VoSviewer software for visualized bibliometric analysis of ADSC's basic research status, and a total of 3 clusters were obtained (see Fig. 4A). Cluster 1: "Stem cell sources and basic research" is noted in green, with keywords including 'adipose tissue," "mesenchymal stem cells," 'stromal cells," "endothelial cell," "fat grafting" etc. This cluster focuses on the derivation of ADSC and research into its application, highlighting the wide source and usage of ADSC. Cluster 2: "Orthopedics and bone regeneration" is represented blue, keywords including, "bone," "osteogenesis," "osteogenic differentiation," etc. This cluster highlights the application of ADSCs in bone regeneration and bone injuries. Cluster 3"Tissue Regeneration and Repair" is indicative of red, with key words including "stromal vascular fraction," "inflammation," "wound healing," etc. This cluster focuses on the regenerative mechanism of ADSC and the use in tissue repair.

Combining the description of basic research above and the data of current clinical trials, the gaps and bridges between basic research and clinical trials of ADSCs can be described through the keyword clusters.

Gaps

As highlighted by both bibliometric analysis of Cluster 1 ("Stem Cell Sources and Basic Research") and clinical trial data, a critical barrier to the clinical translation of ADSCs is the absence of standardized protocols for their isolation, preservation, and quality control. Key terms such as "adipose tissue," "mesenchymal stem cells,"

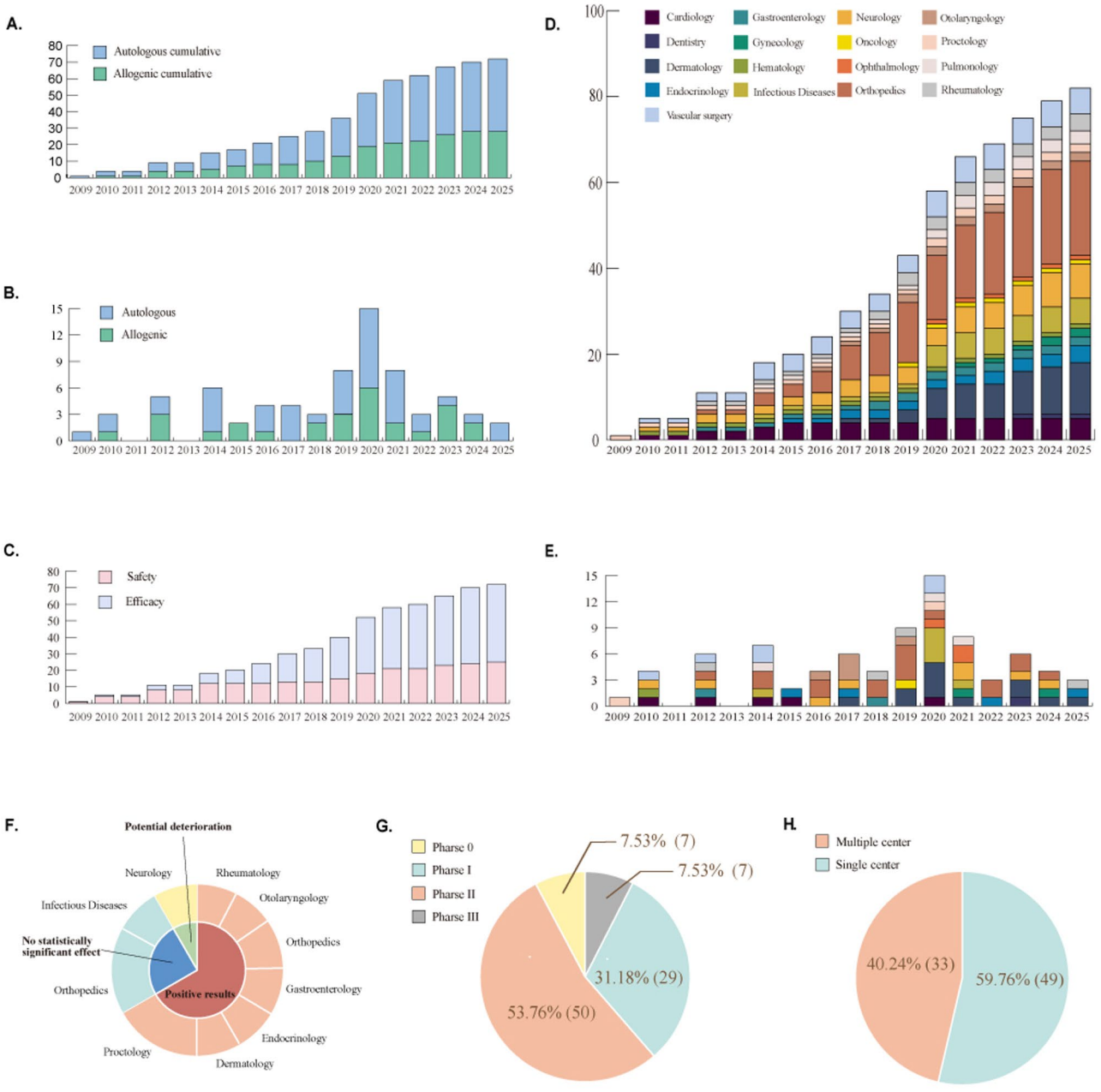

Fig. 3 Overview of ADSC related RCTs. **A**. Cumulative number of initiated ADSC-related RCTs from 2009–2025, color coded for cell source. **B**. Number of RCTs initiated per year, color coded for cell source. **C**. Cumulative number of initiated ADSC-related RCTs from 2009–2025, color coded for outcome type. **D**. Cumulative number of initiated ADSC-related RCTs from 2009–2025, color coded for medical speciality. **E**, Number of RCTs initiated per year, color coded for medical speciality. **F**. Pie chart showing RCTs results and related medical speciality. **G**. Pie chart showing clinical phase of RCTs. H. Pie chart showing center design of RCTs

and "stromal cells," highlights that the basic research focuses on cell heterogeneity and biological characteristics. However, the heterogeneity of ADSCs that is widely discussed in basic research has not been fully translated into standardized operating procedures in clinical trials. Current isolation methods vary widely [19–21], including enzymatic digestion (e.g., collagenase) (NCT02298023, NCT03818737), mechanical dissociation (NCT04553159, NCT03379168), and automated closed systems (e.g., Cytori® Celution® or GID SVF-2®), leading to significant heterogeneity in cell purity, viability, and subpopulation composition [22–24]. This inconsistency is exacerbated by preservation practices: while some trials use freshly isolated autologous ADSCs, others rely on expanded ADSC (NCT05017298) or cryopreserved ADSC (NCT05933434) with poorly explained parameters, such

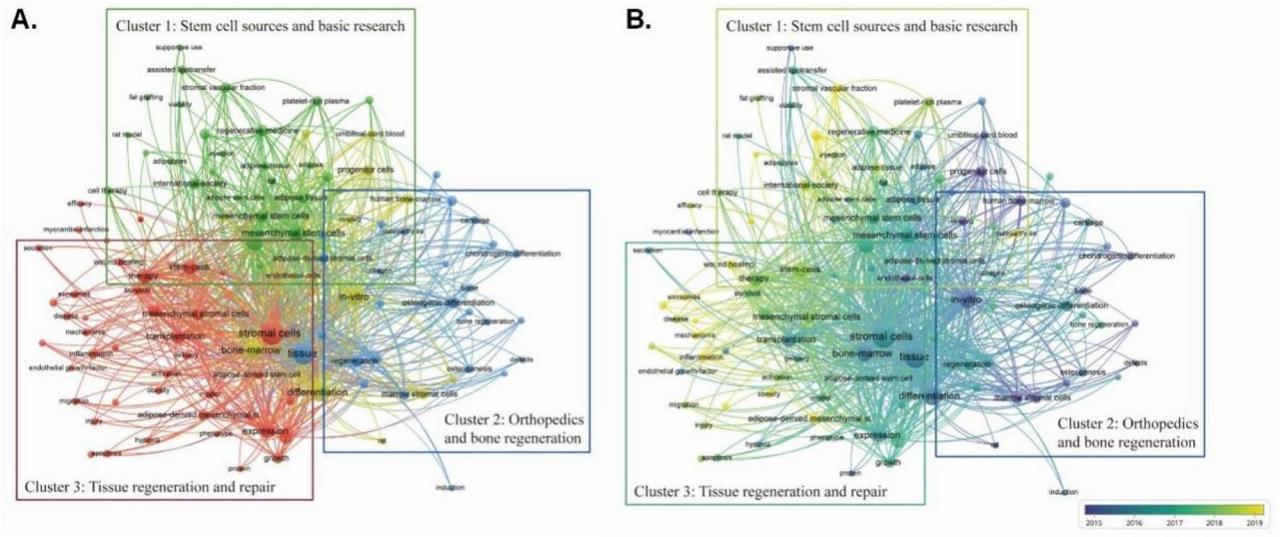

Fig. 4 Keyword co-occurrence network and keyword evolution over time. **A**. Keyword co-occurrence network is divided into 3 clusters of different colors according to the evolution of the research hotspots. **B**. The color of a keyword indicates the average publication time of articles containing that keyword

as divergent dimethyl sulfoxide (DMSO) concentrations or thawing protocols, resulting in unpredictable post-thaw recovery and functional variability. Furthermore, only 2 of the 82 trials reported on the phenotypic markers of ADSC (NCT01222039, NCT06726538). While, it is true that certain trials are conducted using commercially available ADSC sources, such a difference in isolation, preservation, and quality control of ADSC hinders cross-trial comparability and reproducibility, causing inconsistent clinical trial results. For instance, certain neurology-focused clinical trials did not demonstrate significant improvements. It should also be noted that most of current RCTs (68/82) focus on short-term safety and efficacy, with only a few studies conducting long-term follow up on the effects and potential side effects of ADSC treatments [15](NCT01056471, NCT06570291, NCT05934825, NCT04466007).

To bridge this gap, international consensus guidelines must harmonize isolation workflows (e.g., adopting ISO-certified automated systems) and cryopreservation strategies (e.g., serum-free, low-DMSO media like CryoStor®) as was noted as keyword "international society" in cluster 1. Simultaneously, enforcing rigorous quality control—mandating phenotypic profiling, secretome analysis (e.g., VEGF, HGF levels), and functional assays—is essential [25]. Innovations such as microfluidic sorting for CD146 + subpopulations with enhanced paracrine activity, coupled with real-time IoT-monitored cold-chain logistics, could further standardize processes. Regulatory bodies (e.g., FDA, EMA) must also mandate Good Manufacturing Practice (GMP) compliance for ADSC therapies, while collaborative platforms should be built to validate these protocols across multicentric settings. Addressing these challenges holistically will enhance reproducibility, reduce inter-trial variability, and accelerate the translation of ADSC therapies from bench to bedside.

Apart from the technical inconsistencies, most RCTs suffer from small sample sizes and participants who come from specific geographic areas or share similar backgrounds, limiting the generalizability of the findings. This is evident as the median number of participants is 40, and most RCTs (80/82) are performed in a single country without international cooperation. This gap is partially stratified by regulatory reasons in different country. In some countries, for example, the USA or European Union, regulatory rules are flexible, offering rules such as '361 products' (minimally manipulated, homologous use products not requiring premarket approval) or 'conditional market approval' that enable patients to access to stem cell therapies without having a complete trial investigation. These approaches prioritize speed over large-scale evidence, reducing incentives for robust RCTs [26]. Meanwhile, in other countries, for example China, established strict rules over stem cell therapies, confining studies to qualified domestic institutions. The 'Administrative Measures on Stem Cell Clinical Research' for stem cell clinical research requires all hospital-prepared stem cell research to be conducted in qualified class 3 A medical institutions and mandating the establishment of quality control systems and ethical review committees to oversee stem cell research, which in some cases limited international collaboration for RCTs [27].

Bridges

1. Application of basic research findings: Numerous clinical trials are grounded in prior basic research that demonstrated the potential therapeutic effects of ADSCs in vitro and in animal models. The therapeutic efficacy of ADSCs is closely related to their ability to mediate tissue repair through multifaceted molecular mechanisms, including differentiation ability, paracrine signaling of growth factors (e.g., VEGF, HGF), immunomodulation via cytokine-driven macrophage polarization and T-cell suppression, mitochondrial transfer to rescue damaged cells, and hypoxia-triggered angiogenesis. Building on preclinical insights, strategies to utilized ADSC's functionality have transitioned into clinical research. For example, orthopedics has emerged as the most extensively studied specialty in ADSC-related RCTs, largely due to robust preclinical evidence, which can be seen from cluster 2. In vitro studies revealed that ADSCs differentiate into osteogenic and chondrogenic lineages under specific culture conditions, while animal models demonstrated their capacity to accelerate bone regeneration, cartilage repair and modulate microenvironment [28]. For example, a landmark study by Mei et al. showed that intra-articular ADSC administration reduced cartilage degeneration in a rat osteoarthritis model by suppressing inflammatory cytokines (e.g., IL-1β, TNF-α) [29]. These results catalyzed clinical trials such as NCT03818737, a multicenter RCT testing autologous ADSCs against corticosteroid injections for knee osteoarthritis. The trial's primary endpoints (pain reduction via VAS, functional improvement via WOMAC scores) were directly informed by preclinical metrics of cartilage repair and inflammation modulation.
2. Apart from providing a theoretical basis for designing clinical trials, basic research also offers solutions in enhancing therapeutic effect for clinical translation. For instance, "hypoxia" in cluster 3 refers to a commonly adopted pretreatment method for enhancing the therapeutic effect of ADSC. Hypoxia pretreatment of ADSCs enhances their therapeutic potential by improving angiogenesis, cell survival, and differentiation capabilities, which is particularly beneficial in regenerative medicine applications [30]. There was already a register trial studying the effect of hypoxic conditioned ADSC (NCT04889963), but it was only a study on rabbit. Apart from hypoxia pretreatment, drug pre-conditioning has been a heated research topic over the years, offering a valuable strategy for enhancing therapeutic effect of ADSC. For example, we discover researchers from University of the Punjab first discover the regenerative potential of curcumin pretreatment on ADSC [31]. And the results from preclinical studies informed the design of clinical trial such as NCT05610878 by the same researcher group, representing a bench to bedside translation. In the trial, researchers use P2-P3 stage ADSC and incubated with curcumin preconditioned medium for 24 h for the treatment of facial contour deformities.Support from technological advancements: Advances in cell processing technologies and bioengineering, like the development of automated fat tissue processing systems, have made the isolation, expansion, and application of ADSCs more efficient and standardized, facilitating the translation from lab to clinic [32].

In summary, while basic research provides a solid foundation for the clinical application of ADSCs, translating these findings into effective treatments faces numerous challenges. Future efforts need broader collaboration, define protocols for trial, larger sample sizes, and deeper insights into treatment mechanisms to overcome existing gaps.

Future trend of ADSC's clinical trials

Apart from displaying the co-occurrence status of keywords, a time sequence analysis was performed to illustrate changes in keyword prominence and trend. It shows that interests of researchers' investigation gradually shift from Cluster 2 to Cluster 3, and then Cluster 1 (Fig 4B). This reflects an evolving focus as understanding deepens, moving towards more fundamental biological characteristics and broader applications of ADSCs. Additionally, the time sequence analysis also provides new research foci emerging in each cluster, providing guidance for future research trend.

For cluster 1, keywords such as "regenerative medicine," "Stromal Vascular Fraction," are emerging as new keywords in research, highlighting an increasing emphasis on the research into finding novel source of ADSC that could exhibit higher regenerative potential. For example, Stromal Vascular Fraction (SVF) is a heterogeneous mixture of cells derived from adipose tissue, known for its regenerative potential in various medical applications [33]. It includes a variety of cell types such as mesenchymal stem cells, endothelial precursor cells, macrophages, and more. It is a versatile and promising tool in regenerative medicine, with applications across various medical fields [34]. Its ability to promote healing, enhance tissue regeneration, and modulate immune responses makes it a valuable therapeutic option. Research have shown that the mixture of cells in SVF offers unprecedented

therapeutic effect compared with ADSC alone. For example, Onio et al. found that M2 macrophages within SVF promotes cartilage anabolism and inhibiting catabolism, thereby slowing osteoarthritis (OA) progression. The findings suggest that SVF could be an effective regenerative therapy option for OA, with mechanisms distinct from those of ADSCs alone [35]. Currently, there were few RCTs assessing the regenerative potential of SVF, future clinical trials could focus more on exploring the application of SVF in other disease conditions with differentiate mechanisms [10].

Cluster 2 is a relatively old cluster with most of its research already been translated into clinical trials. Nevertheless, we can still obtain a emerging research focus into "osteoarthritis", which is a common, complex, and multifactorial disease with limited effective treatments. ADSCs show promise as a treatment for OA due to their regenerative and anti-inflammatory properties [29, 36]. Research indicates that ADSCs can potentially alleviate symptoms and modify disease progression in OA patients [37]. Future RCTs could focus on evaluating ADSCs therapeutic potential in treating OA.

Cluster 3, with new keywords such as "wound healing," "exosomes" and "secretion", demonstrate the emerging role of ADSC's derivatives in treating diseases. One of the major therapeutic mechanisms of ADSC relies on its paracrine effect [38]. Therefore, the secretion of ADSC holds great promise in treating diseases [39]. There was one RCT already investigating the therapeutic potential of ADSC's secretome in dermatology. One of its secretome is exosome, which are small extracellular vesicles that have shown significant potential in regenerative medicine due to their ability to mediate intercellular communication and influence various biological processes [40]. These exosomes carry proteins, nucleic acids, and other bioactive molecules that can alter the behavior of recipient cells, making them a promising tool for therapeutic applications. Their ability to promote chondrocyte proliferation, modulate immune responses, and enhance ECM synthesis makes them a valuable tool in regenerative medicine [41]. However, while ADSC-derived exosomes hold great promise, challenges remain in their clinical application, including the need for standardized isolation and characterization methods, optimizing delivery methods, understanding their long-term effects, and ensuring their safety and efficacy in diverse patient populations [42]. Future research should focus on overcoming these challenges. Future RCTs could focus on ensuring the safety and measuring the therapeutic potential of ADSC exosomes in regenerative medicine and other clinical applications.

Discussion

This scoping review, complemented by bibliometric analysis, aims to provide a comprehensive overview of the existing RCTs on ADSCs therapy and explores the bridges and gaps in translating findings from basic research to clinical application. While significant progress has been made in this field, several challenges remain in advancing ADSC therapies from bench to bedside.

Firstly, our study shows that the number of RCTs related to ADSCs has steadily increased since 2009, with a notable surge in registrations in 2020, likely due to the outbreak of the COVID-19 pandemic. This trend underscores the recognized potential of ADSCs in treating various diseases. However, despite these advancements, the results of different clinical trials have shown considerable variability. For instance, some neurology-related clinical trials did not demonstrate expected outcomes or meet primary endpoints. These inconsistencies could be attributed to factors such as trial design, sample size, participant diversity, and an incomplete understanding of the mechanisms underlying ADSC action.

Secondly, while most clinical trials focus on assessing short-term safety and efficacy, studies examining long-term effects and potential side effects are relatively scarce. This limitation hinders a full understanding of ADSC therapies and highlights the need for more extended follow-up data to address these knowledge gaps.

Moreover, although basic research provides a solid foundation for clinical applications, effectively translating these findings into practical treatments remains challenging. Technological advances, such as developments in cell processing technologies and bioengineering, have facilitated the isolation, expansion, and application of ADSCs, aiding their transition from lab to clinic. However, challenges persist due to certain ethical concerns, the lack of large-scale, diverse clinical trials and a deeper insight into the specific mechanisms of ADSC action, which limits the optimization of treatment strategies.

It is also worth noticing that we performed a bibliometric analysis coupling our scoping review. This was partly inspired by a "Bibliometric-Systematic Literature Review" approach proposed by Marzi et al. [43]. Such a novel approach provides visualized quantitative evidence supporting our conclusions. By employing this technique, we are able to quickly determine the gaps and bridges between basic research and clinical trials, and are able to indicate potential future research focus for researchers.

Future prospect

Looking ahead, the research trends in ADSCs are shifting towards exploring more fundamental biological characteristics and broader medical applications. Specifically, there is growing interest in Stromal Vascular Fraction (SVF) as a new source of ADSCs with higher regenerative

potential, particularly in dermatology and wound healing. Additionally, osteoarthritis (OA) continues to be a promising area for ADSCs due to their regenerative and anti-inflammatory properties. Furthermore, the role of ADSC derivatives, such as exosomes, in disease treatment is gaining attention. Exosomes, small extracellular vesicles carrying proteins, nucleic acids, and other bioactive molecules, show significant potential in regenerative medicine but face challenges related to standardized isolation methods, understanding long-term effects, and ensuring safety and efficacy across diverse patient populations.

Apart from the result by bibliometric analysis, additional efforts should be paid to address the current challenges in protocol heterogeneity. Future research should prioritize the establishment of standardized guidelines for ADSC isolation, cryopreservation, and quality control. Specific recommendations include recommending the use of automated closed systems for isolation of ADSC or following internationally standardized protocols in manual isolation (There is an absence of such standardized protocol currently). Freshly obtained ADSC should be specifically reported if it is used, otherwise cryopreserved ADSC should have a standardized preservation temperature and report on the preservation time, cryoprotectant, and thawing temperature. We encourage mandatory reporting of CD marker profiling and secretome analysis in clinical trials to ensure batch-to-batch consistency and functional reproducibility across different clinical settings. International collaborative efforts, supported by regulatory bodies such as the FDA and EMA, are essential to harmonize these protocols and facilitate cross-trial comparability. thereby enhancing the reliability of ADSC-based therapies. These measures will bridge the gap between preclinical findings and clinical applications, fostering confidence in ADSC therapies among researchers and clinicians.

Equally critical is the need for RCTs with extended follow-up periods exceeding two years to comprehensively evaluate the durability of therapeutic effects and potential late-onset adverse events. Current studies predominantly focus on short-term outcomes, leaving a significant knowledge gap regarding long-term safety and efficacy. Designing trials with prolonged observation periods will not only elucidate the sustained benefits of ADSC interventions but also identify delayed complications, such as immune reactions or unintended differentiation. Such longitudinal data are indispensable for regulatory approvals and clinical adoption, ensuring that ADSC therapies meet both efficacy and safety benchmarks over the entire patient lifespan. Collaborative multicenter studies, leveraging international registries and diverse patient cohorts, could provide the necessary statistical power to validate these outcomes across populations and specialties, ultimately guiding evidence-based therapeutic strategies.

Limitations of the scoping review process

The scoping review process, though comprehensive, has inherent limitations. Many of the trials listed remain incomplete at the time of writing, so our reporting draws not only on scientific publications but also on clinical trial updates and interim results disseminated via press releases and abstracts from sponsors. It should be noted that data from press releases and abstracts have not undergone scientific peer review and should therefore be interpreted with caution. Further, many RCTs do not have related publications rendering difficulties in acknowledging the author or sponsor of RCTs. Additionally, we only included English language-based trials registration, certain trials been initiated in other countries may be omitted.

Conclusion

In conclusion, while the potential of ADSCs in therapeutic applications is evident, bridging the gap between basic research and clinical practice requires broader collaboration, larger sample sizes, and a deeper understanding of the mechanisms involved. Addressing these challenges will be crucial in harnessing the full potential of ADSC therapies for treating a wide range of complex diseases. Despite the inherent limitations of the scoping review process, this study provides valuable insights and guidance for future research directions in ADSC therapy.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13287-025-04405-3.

Supplementary Material 1

Supplementary Material 2

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The authors declare that they have not use AI-generated work in this manuscript.

Author contributions

SHK: conceptualization and writing– original draft, software, data curation, CHS: writing– original draft, writing– review & editing and methodology, LQL: visualization, XF: writing– review & editing, SYY: writing– review & editing and methodology, CJJ: writing– review & editing and methodology, HYY: visualization, NJY: writing– review & editing, HQ: writing– review & editing, XYJ: writing– review & editing, LCW: writing– review & editing, HBX: writing– review & editing, ZJ: writing– review & editing, LYP: resources, LH: funding acquisition, project administration supervision and validation. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from supplementary material.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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