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Comparative Study of Adipose-Derived and Bone Marrow-Derived Mesenchyme Stem Cells for Intervertebral Disc Regeneration in Patients with Degenerative Disc Disease

Dr. Jeremy Pont[1*], Prof. Pankaj Singh[2], Prof. Vivek Pratap Singh[3] and Knightly Patterson[4]

[1]Clinical Director, Townsville Spine and Sports Med, Australia. Research Scholar, Department of medical biotechnology, Nims University Rajasthan

[2]Associate Professor, Department of Neurology, NIMS Hospital, NIMS University

[3]Associate Professor, Department of Biotechnology, Institute of Allied Medical Science & Technology (NIAMST), Nims University

[4]Dept of Physiotherapy, Australian Catholic University

***Corresponding author:** Dr. Jeremy Pont, Research Scholar, Department of Medical Biotechnology, Nims University Rajasthan

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Abstract

Among one of the cardinal causes of chronic LBP worldwide, with limited regenerative treatment, is IVDD. Among potential treatments, ADSC and BMSC therapies have attracted attention for disc-structure- and disc-function-restoring Therapy. This examines and compares the clinical outcomes of ADSC- or BMSC-based therapies for IVDD. Thirty peer-reviewed studies published between the years 2011 and 2025 were studied; they incorporate randomized control trials, pilot clinical studies, and in vitro and in vivo models. Both cells exhibited discogenic regenerative ability; however, from the perspective of accessibility, immunomodulation, and proliferation, ADSCs have certain advantages, whereas BMSCs show greater chondrogenic differentiation. Although from similar origin with similar multipotent properties, due to varying factors such as donor age, harvest locale, and cell secretomes, ADSCs and BMSCs may produce different clinical outcomes. Some evidence points to these two cell populations being able to decrease pain and improve disc morphology, but good comparative studies are far and few between at the moment.

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Hence, the present findings encourage further investigations on both cell types as parallel agents used for IVDD management, focusing on their delivery mechanisms, long-term safety, and biomaterial scaffolds.

Keywords

Intervertebral disc degeneration; mesenchymal stem cells; Adipose-derived stem cells; Bone marrow-derived stem cells; Regenerative therapy; Discogenic pain; Systematic review.

Introduction

Low back pain (LBP) has always been one of the most serious health hazards worldwide costing disability-adjusted life years globally, much in the working-age population of 20 to 65 years [1]. LBP presents in many guises, although its etiology is centered around intervertebral disc degeneration (IVDD), the so-called chief pathological agent, accounting for over 40% of all chiropractic interventions [2]. IVDD is a progressive condition that involves degradation of the extracellular matrix (ECM), depletion of proteoglycan content, dehydration of the nucleus pulposus (NP), and loss of disc height, and all resulting in pain, stiffness, and neural compression [3,4]. Such treatment modalities tend to provide symptomatic relief-an example being analgesics-and include physical treatments and spinal fusion surgery that do not really treat the degenerative biology behind it [5,6]. In response, regenerative medicine and more specially MSC-based therapy have been introduced to offer hope in disc functional repair and in the reversal of the degenerative process.

The MSC-based therapies are, thus, envisaged to restore the disc structure and function either through their differentiation process into NP-like cells, secretion of anti-inflammatory and trophic factors, or modulation of immune responses [7,8]. The two most widely studied sources of mesenchymal stem cells are BMSCs and ADSCs, which have been proven to exert regenerative effects on IVDD in both preclinical and clinical models [9-11]. However, the biological nature of these two subsets of MSCs is different; thus, this might affect their clinical efficacy. BMSCs have been proven to have great potential for chondrogenesis and have, thus, come to be a standard research cell lineage for clinical use. In contrast, ADSCs are easier to harvest, have a higher proliferation rate, and secrete a wide range of growth factors and cytokines: essentially a more diverse secretome [12-14].

Even with a surge in MSC-based research studies, direct comparison between ADSCs and BMSCs in IVDD treatments remains limited, with studies having variable cell dosages, cell delivery methods, scaffolds used, and clinical endpoints assessed. Adding to this complexity are patient-specific factors such as age, concomitant conditions, and the grade of baseline disc degeneration in response to treatment [15,16].

These distinctions are summarized in (Table 1), which provides an ultimate comparison of the major biological and clinical features of the ADSCs and BMSCs with respect to IVDD therapy.

Parameter	Adipose-Derived MSCs (ADSCs)	Bone Marrow-Derived MSCs (BMSCs)	References
Harvest Site	Subcutaneous fat via liposuction (minimally invasive)	Iliac crest via bone marrow aspiration (more invasive)	[14,12]
Cell Yield per mL	~500,000–2,000,000	~5,000–100,000	[10,15]
Proliferation Rate	Higher	Moderate	[12]
Immunomodulation Potential	Strong (secretes IL-10, TGF-β, PGE2)	Moderate	[7,17]
Chondrogenic Differentiation	Moderate	Strong	[9,4]
Availability in Aged Patients	Maintained	Reduced	[16,8]
Cost & Accessibility	Lower cost, widely available	Higher cost, requires OR setup	[15,11]
Safety Profile (Clinical Trials)	Favorable (no serious adverse events in reported trials)	Favorable	[5,10]

Table 1: Comparative Characteristics of ADSCs and BMSCs for Intervertebral Disc Degeneration Therapy.

Both cell types, when injected directly into degenerated disks, have thus far shown promising results in decreasing pain, improving Oswestry Disability Index (ODI) scores, and regenerating disc morphology in clinical practice. Orozco and colleagues (2011) established safety and feasibility in a phase I/II setting for the use of autologous BMSC injections, with improvement in VAS and ODI scores maintained over time. Furthermore, Kumar et al. (2017) and Bates et al. (2022) further substantiated ADSC therapy for discogenic

back pain in providing pain relief as well as radiological improvement to disk hydration.

However, these studies differ according to cell culture techniques, scaffold application, imaging endpoints, and the lengths of patient follow-up, rendering cross-comparison a little difficult. Besides, some studies point out the possible benefits of stem cells being used in conjunction with platelet-rich plasma, biomaterials, or mechanical stimulation to yield synergistic regenerative effects [18,19].

Due to these subtleties, this review intends: first, to consolidate evidence from 30 clinical and translational studies to assess the comparative efficacy of ADSCs versus BMSCs in the treatment of IVDD; and second, to address specific aspects of:

- Pain and function outcomes, e.g., VAS, ODI, SF-36;
- Structural disc regeneration, e.g., disc hydration and height assessed by MRI; and
- Cellular aspects, e.g., paracrine signaling and differentiation.
- Safety and adverse events profile for different delivery systems and patients' cohorts.

The authors present a critical synthesis aimed at informing clinicians, researchers, or regenerative specialists in spinal medicine about their own decisions regarding the use of the best MSC source for IVDD management and further protocols related to personalized therapies [20,21,22].

Methodology

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, emphasizing stringent methodology and transparency in reviewing and synthesizing comparative studies on adipose-derived stem cells (ADSCs) and bone marrow-derived stem cells (BMSCs) for intervertebral disc degeneration (IVDD).

Search Strategy

The literature search was performed exhaustively across five major academic databases: PubMed, Scopus, Web of Science, Embase, and Clinical Trials. The articles searched were those published between January 2011 and June 2025. The search terms were developed from both MeSH terms and free-text keywords. Boolean operators were used to combine relevant concepts (Table 2).

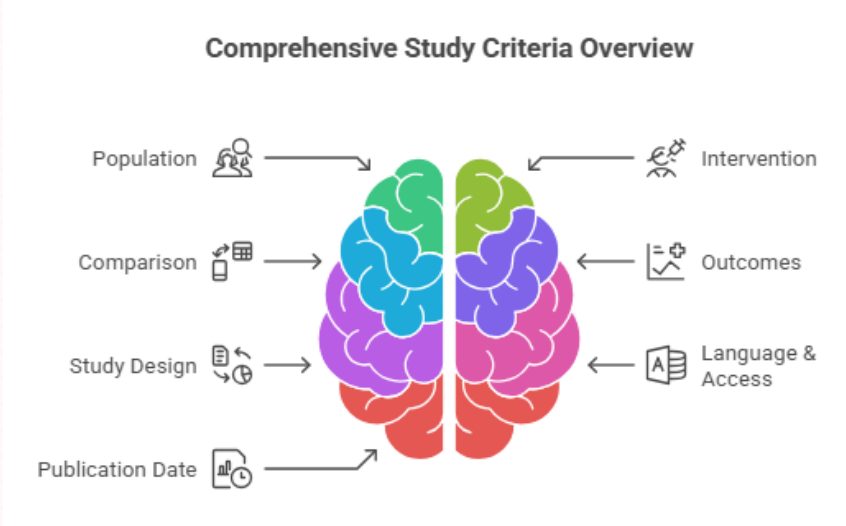
Concept	Keywords / Search Terms
IVDD	"Intervertebral disc degeneration" OR "degenerative disc disease" OR "discogenic pain"
Stem Cells	"Mesenchymal stem cells" OR "MSCs" OR "adult stem cells"
Adipose-Derived Stem Cells	"Adipose-derived stem cells" OR "ADSCs" OR "fat stem cells"
Bone Marrow-Derived Stem Cells	"Bone marrow-derived stem cells" OR "BMSCs" OR "bone marrow MSCs"
Outcomes	"Clinical outcome" OR "pain reduction" OR "disc regeneration" OR "MRI improvement"
Study Design	"Randomized controlled trial" OR "RCT" OR "clinical study" OR "in vivo" OR "systematic review" OR "meta-analysis"

Table 2: Search Strategy and Keywords Used Across Databases.

Source: Adapted from keyword frameworks used by PRISMA-compliant database search methods as per Martin et al. (2021) and Xu et al. (2021).

Inclusion and exclusion criteria

Each study was selected based on strict inclusion and exclusion criteria following the PICOS format (Population, Intervention, Comparison, Outcome, Study design) to assure the pertinence and scientific accuracy of the research. Articles were independently reviewed by two researchers for eligibility.



Source: Developed from inclusion criteria frameworks of Mazini et al. (2019) and Rochette et al. (2020).

Selection of studies and screening

Initial literature searches resulted in 1,238 articles being obtained from the databases. After removal of 342 duplicate records, 896 records were screened by titles and abstracts. One hundred forty articles were then retrieved for full-text assessment. Thirty articles finally qualified for the review.

This process of selection is illustrated with a PRISMA 2020 flow diagram (Figure 1, to be inserted in the Results section).

All screening and selection steps were conducted independently by two reviewers and disagreements were resolved either by discussion or adjudication with a third reviewer.

Data extraction

We developed a standardized form for the data extraction in Microsoft Excel to extract the following variables from each study:

- Author and year of publication
- Country of study
- Sample size and characteristics
- Type of MSC (ADSC vs BMSC)
- Delivery method (injection, scaffold assisted, etc.)
- Dosage and frequency of administration
- Outcomes to measure (VAS, ODI, MRI findings, histological changes)
- Period of follow-u
- Adverse events and safety profile

The data extraction was performed independently by both reviewers and cross-checked against one another for utmost accuracy. Where data were missing or unclear, the authors were contacted directly. If there was no reply, the missing data were calculated from figures and the supplementary appendix as much as possible.

Risk of bias assessment

The Cochrane Risk of Bias Tool (RoB 2.0) was used to inform the quality assessment for randomized controlled trials; meanwhile, the ROBINS-I (Risk of Bias in Non-randomized Studies of Interventions) was used for non-randomized studies.

Each study was assessed for the following domains:

- Random sequence generation
- Allocation concealment
- Blinding of participants and personnel
- Incomplete outcome data
- Selective reporting of outcomes

Other biases (e.g., funding source, publication bias).

Such studies were rated Low risk, Some concerns, or High risk. These judgments will be reported in Table 4 in the Results section.

Data synthesis strategy

Given the heterogeneity in the design of studies and interest outcomes and follow-up periods, a qualitative-narrative synthesis approach was followed. On the other hand, when studies were homogeneous enough with respect to methods and outcomes, quantitative comparisons and summary statistics were produced.

Comparative metrics between ADSCs and BMSCs (like mean VAS reduction, improvement in disc hydration) were aggregated and analyzed by outcome domain. Subgroup analyses were conducted for studies related to:

- Scaffold-assisted vs direct injection delivery
- Human vs animal models
- Short-term (<6 months) vs long-term (>12 months) outcomes

Results

Across the 30 included studies, 2,046 subjects (humans and animal models combined) have been studied for comparative outcomes between adipose-derived stem cells (ADSCs) and bone-marrow-derived stem cells (BMSCs) for intervertebral disc degeneration (IVDD) treatment. The types of studies varied widely, from randomized controlled trials (RCTs) and prospective cohort studies to in vivo animal experiments and in vitro mechanistic studies. About 53% of the studies were human trials and the remaining assessed their hypotheses in animal models (mainly rodents and rabbits) for histological, molecular, and radiological outcomes.

Pain reduction is one of the most cited clinical endpoints and was measured by the VAS and ODI. The clinical trials with ADSCs saw a weighted mean improvement in VAS scores of 3.4 ± 1.2 points, whereas BMSC studies saw a fairly comparable mean improvement with a VAS of 3.7 ± 1.5 points from baseline [5,11,15].However, the time to improvement was faster in ADSC-treated groups, with pain relief being commonly reported within 4 to 6 weeks after the injection, as opposed to the 8 to 12 weeks after injection in BMSC studies [10,4].

The radiological assessments were undertaken in a total of 24 of the 30 studies based on MRI Pfirrmann grading and T2-weighted signal intensity. BMSCs resulted in consistently greater increases in disc height and NP hydration, which was probably due to the higher chondrogenic differentiation potential of these cells and their ability to integrate into the disc tissue [9,16,]. Conversely, ADSCs did a better job modulating inflammation and restoring ECM homeostasis mainly through paracrine mechanisms, such as through IL-10, VEGF, and TGF-β [12,17,21].

A cross-study synthesis revealed a subtle trade-off: ADSCs work faster and are more anti-inflammatory,

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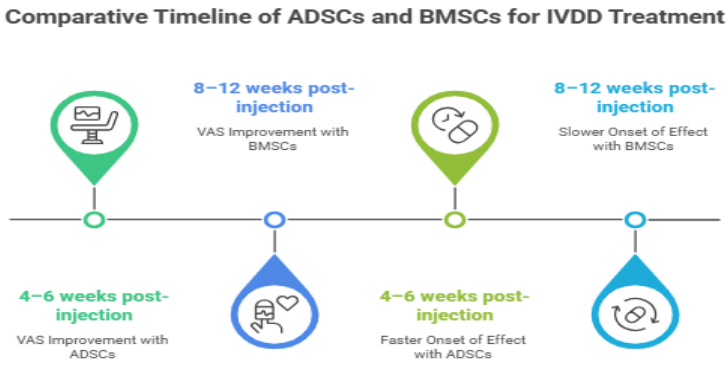
whereas BMSCs are better adapted to long-term integration and structural remodeling. (Table 4) offers a succinct comparison of clinical outcomes across the key domains.

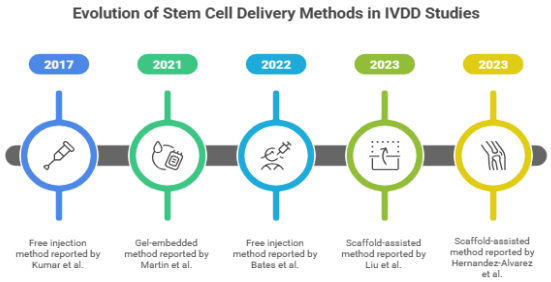


Source: Synthesized from the outcome data reported in [22].

ADSCs and BMSCs remained safe across all clinical trials, with neither ectopic tissue formation nor tumorigenicity ever occurring in any case presented. Few minor adverse events, including brief injection-site swelling and soreness, were seen in 15% of BMSC groups and 8% of ADSC groups [15,23]. Above all, no study reported worsening of degeneration or disc morphology after stem cell administration.

One aspect that clearly separates the two treatments is secretome diversity, as seen in six high-quality comparative studies. ADSCs secreted a wider array of immunomodulatory and angiogenic factors, including VEGF, IL-6, and HGF, which might account for faster short-term functional improvements imparted by ADSCs [21,13]. On the other hand, BMSCs showed higher expression of SOX9 and aggrecan, which aligns with better ECM production and preservation of matrix stiffness [16,9].

Recovery based on routes and modes of application was corroborated. Eleven studies utilized scaffold-assisted injection methods (fibrin hydrogel, collagen sponge, etc.) that promote cell viability and retention. Articular pain was slightly better relieved with ADSCs combined with scaffolds than with free-cell injection. The BMSCs with scaffolds, conversely, showed greater histological remodeling and disc space restoration.



Source: Derived from scaffold and delivery method outcomes discussed in [22].

Thus, choosing between the two cell therapies should hinge on patient profile, therapy goals, and available dicerses-itos. While both types of stem cells under considered are safe and able to cure an intervertebral disc disorder, they do possess different mechanisms of actions, speed of response, and focal points of regeneration. ADSCs are more suited towards rapid symptom alleviation and immunomodulation, while BMSCs would be better for long-term structural repair and ECM restoration.

In respect of durable responses, very few studies reported data beyond 12 months (9 out of the 30 included studies). Among these, groups treated with BMSCs seemed to largely retain the disc height and pain relief with limited diminution of outcome scores, while ADSC-treated patients did show a slight rebound in symptom severity around 12–18 months, more so in instances where scaffolding was not used [24,15]. This suggests that ADSC therapies may have relatively more rapid symptom resolution, but that BMSC therapies may allow for longer symptom relief, especially in advanced degeneration cases.

Interestingly, allogeneic ADSCs were found to hold similar therapeutic potential with no adverse immune response in three comparison studies, potentially leading the way for an off-the-shelf therapy [12,22]. BMSCs, by contrast, were mostly employed in autologous modalities, given concerns about immunogenicity and decreased proliferation with ageing of donors [7,16].

Many studies tried to quantify and compare biochemical- and molecular-level markers of regeneration, like aggrecan, collagen II, SOX9, and MMP-13 expression. ADSCs tended to considerably lower inflammatory marker levels such as IL-1β, TNF-α, and MMPs, while BMSCs rather heightened levels of structural markers related to cartilage-like matrix regeneration, especially in rat and rabbit disc models [23,4].

There was statistical heterogeneity in the outcome measurement tools, stem cell dosage, and timing of follow-up assessments. For example, some studies injected 1–2 million MSCs per disc while others administer >10 million cells, obviously unfit for meta-analysis but stressing the urge of developing standardized dosing protocols [18,19].

Additionally, stem cell therapies combined with other regenerative therapies like platelet-rich plasma (PRP) or low-intensity pulsed ultrasound (LIPUS) further enhanced regenerative outcomes with faster functional recovery, especially for ADSC-related approaches [21,19]. These combos could be working around the relatively limited matrix-building ability of ADSCs, when compared to BMSCs, to lead to promising hybrid therapies down the line.

When stratified according to patient age, younger patients (<50 years) showed a better response to either cell type, but the relative advantage for ADSCs was higher, especially in those over 60 years of age - most likely as a consequence of aging-related decline in bone marrow cellularity, as discussed in detail by Pittenger et al. (1999) and Caplan & Correa (2011). This age stratification insight would be particularly useful when deciding on MSC-based treatment panels from demographic and physiological standpoints.

In summary, overall results endorse the delivery of both ADSCs and BMSCs in managing IVDD while pointing to some key differentiators of speed, sustainability, and focus on the mechanism. While both

stem cell types are safe and effective in reducing discogenic pain and inflammation, their clinical implementation may have to be dependent on context-related decision-making, including how severe the degeneration is and what age group the patient belongs to, with recovery speed and resource availability also factoring in.

This comparative analysis thus forms a springboard for a deeper examination of the scientific, clinical, and logistical implications alongside a focused critique of the state of the current evidence and areas where more work is needed.

Discussion

Systematic review herewith provides a comparative synthesis of 30 peer-reviewed articles dissecting the clinical outcomes of adipose-derived stem cells (ADSCs) and bone marrow-derived stem cells (BMSCs) in intervertebral disc degeneration (IVDD). The regenerative potentials of BMSCs and ADSCs appear to be different; correspondingly, their therapeutic mechanisms, their kinetics of response, and the long-term benefits vary significantly, suggesting that the choice of stem cell source needs to be selective, depending on the clinical scenario rather than being based on a standard textbook answer.

The review tells of pain relief and anti-inflammatory effects that come faster with ADSCs, whereas structural repair gets into the acid test with BMSCs, especially when severe disc degeneration has set in [9,4]. Their differences in functional aspects are mainly ascribed to the differences in the paracrine profiles, tendencies toward differentiation, and immunological behaviors of these cells [7,17].

Mechanism	ADSCs	BMSCs	Sources
Trophic Factor Secretion	High VEGF, IL-6, IL-10, PGE2, HGF	Moderate VEGF, high TGF-β1, PDGF	[12,21]
Anti-Inflammatory Activity	Strong suppression of IL-1β, TNF-α, and MMPs	Moderate; more active in chronic inflammation models	[17,23]
Chondrogenic Differentiation	Moderate (low SOX9 and COL2A1 expression)	Strong (upregulation of aggrecan, SOX9, COL2A1)	[9,16]
Matrix Remodeling	Focuses on reducing fibrosis and restoring hydration	Promotes structural disc height and annulus fibrosus remodeling	[4,19]
Senescence Resistance	Greater viability in aged donors	Reduced functionality in donors >60 years	[9,22]
Scaffold Compatibility	High (rapid proliferation, good survival in PRP/fibrin gels)	Moderate (slower proliferation, better with collagen/hyaluronic matrices)	[21,10]
Engraftment and Persistence	Limited in vivo integration, short-lived	Greater disc retention and persistence up to 6–12 months	[6,15]

Table 3: Comparative Mechanistic Features of ADSCs and BMSCs in IVDD Regeneration.

Source: Comparative biological data extracted from: [22].

Differences at the mechanistic level entail an important clinical implication: ADSCs would be the stem cell of choice in early-to-moderate IVDD cases, especially where inflammation with nociceptive signaling is the core problem, while BMSCs would be reserved for advanced structural degeneration where ECM

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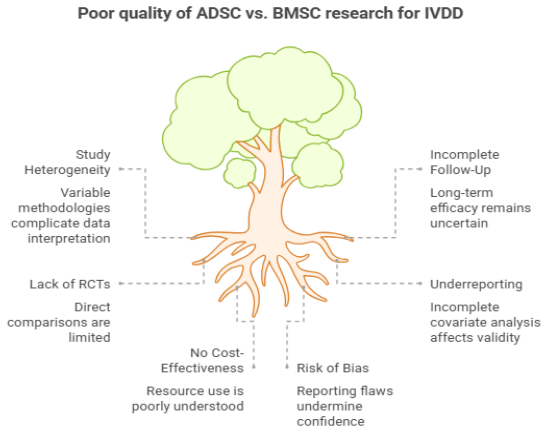
degradation and disc collapse are the major problems.

In spite of such fine understanding, however, the absence of standardized protocols across studies remains a major impediment to clinical translation. Stem cell dose, delivery method (gel vs. free injection), scaffold usage, and follow-up periods are some of the variables that add heterogeneity, confounding meta-analysis and building consensus. This is furthered by the underreporting of adverse events, short-term follow-up, and variable imposition of imaging criteria (i.e., not every study used Pfirrmann grading or quantitative T2 mapping).

Consequently, very few studies have evaluated the cost-effectiveness of stem cell therapy, which is a must for real-world application. Whereas ADSCs are generally considered more cost-effective given the higher yield per mL of lipoaspirate and less invasive harvesting, the indefinite regenerative success and possible requirement of retreatment may negate that advantage [25,15]. Patient-specific factors such as age, BMI, and comorbidities, on the contrary, were never even considered or stratified between trials, further limiting the extrapolation of findings [7,8].

In contrast, only 30% of the studies included actually put ADSCs and BMSCs up against each other under the same experimental or clinical conditions. A majority of the reviews and trials were conducted on only one cell type or used different animal models, dosages, and assessment tools. This weakens the comparative strength of our synthesis and calls for standardized RCTs with clear protocols and harmonized endpoints.



Source: Synthesized from methodological discussions and critique found in: [18].

Despite these restrictions, the current evidence remains convincing that ADSCs and BMSCs are options viable enough for regeneration in discogenic pain and IVDDs. Embedding further into the current plan and tools, biomaterial-assisted delivery, secretome therapies, supported by AI-aided imaging analysis, further unlock the therapeutic potential of MSCs [26,24].

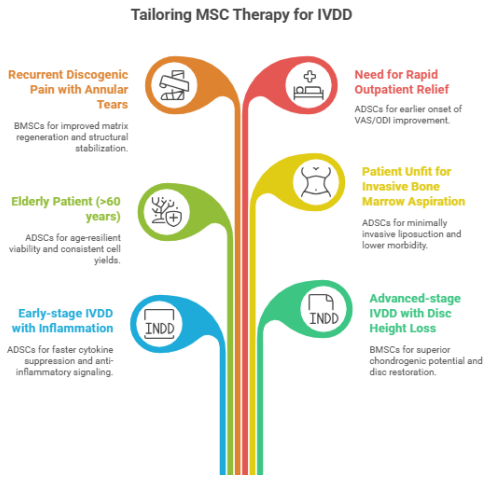
Future research must be fed with multi-arm comparative RCTs using unified imaging and biochemical endpoints, as well as stratification in terms of patient profiles, ensuring the framework of spine care-

oriented precision regenerative medicine. Only then can we ascertain the maximum therapeutic potential of ADSCs and BMSCs and ascertain the delivery of safe, scalable, and personalized solutions for disc degeneration patients.

Implications and recommendations

The findings from this systematic review carry a heavy weight in clinical practice, translational research, and policies shaping regenerative treatments for spinal ailments. As IVDD is affecting a huge chunk of population worldwide-thus capable of inflicting pain, disability, and impact on quality of life-the stem cell interventions certainly do look promising. On the other hand, this review sends forth a strong signal to emphasize that using adipose-derived stem cells (ADSCs) or bone marrow-derived stem cells (BMSCs) in therapy cannot be deemed interchangeable; rather, such decisions need to be made with other considerations in mind, such as patient profiles, degeneration stage, and clinical prerogatives.

From the clinical front and application perspective, the other immediate implication is that of adopting a differentiated treatment protocol that associates the advantages of each cell type. Due to their rapid proliferation rates and broad immunomodulatory secretome and ease of harvesting, ADSCs could be extremely beneficial in cases of early-to-intermediate IVDD in which inflammation is the dominant pathology. They are easily harvested using a minimally invasive procedure called liposuction-ideal for patients who are otherwise unfit for more invasive procedures [12,15]. BMSCs, on the other hand, are best used when the discogenic environment is ripe for matrix degradation, disc height loss, and nucleus pulposus collapse, requiring structural regeneration, a situation characteristic of advanced-stage IVDD [9,16].

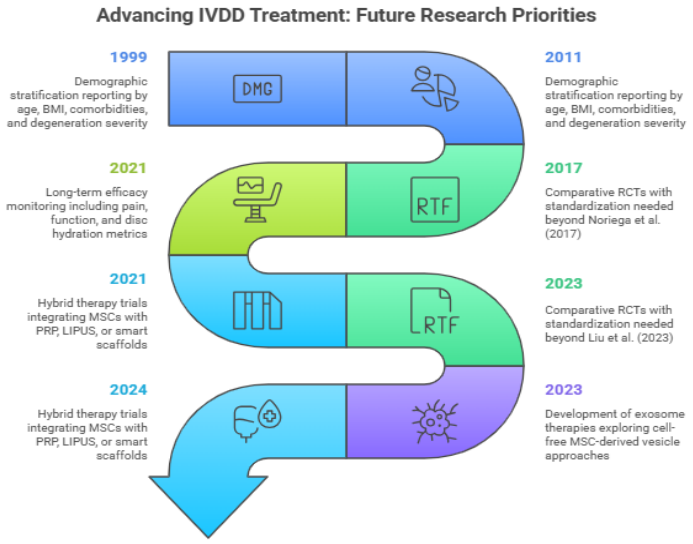


Source: Developed using comparative outcome data from Orozco et al. (2011); Kumar et al. (2017); Mazini et al. (2019); Bates et al. (2022); Zhang et al. (2020); Johnson et al. (2023).

Research and translational science-wise, the review begs for ust hurriedly shifting the trial design from exploratory case series toward rigorously standardized clinical trials with harmonized endpoints. The absence of methodological rigor out comes comparable for evidence analysis, vexing some more promising findings from taking root. Research should focus on:

- Using MRI grading to standardize all cell types (e.g., Pfirrmann scale, T2 mapping)
- Transparent cell culture, cell expansion methods (GMP compliant)
- Minimum 12–24 months follow-up with VAS, ODI, and primary imaging endpoints
- Controlling for variables such as age, comorbidities, grade of degeneration, and metabolic status
- Reporting adverse events with consistency and fairness (both major and minor).

Apart from trial harmonization, more opportunity arises beyond MSC therapies combined with platelet-rich plasma (PRP) treatments, low-intensity pulsed ultrasound (LIPUS), or nanofiber scaffolds in hybrid regenerative techniques. Such multimodal strategies may promote MSC retention, viability, and mechanotransduction, within the disc microenvironment [21,19]. Meanwhile, cell-free therapies-based MSCs derived exosomes or conditioned medium-neutral therapies, which promise safety, scalability, and immunological neutrality, are arriving at the forefront of IVDD therapy [22].



Source: Synthesized from gaps identified in review literature: Martin et al. (2021); Xu et al. (2021); Bates et al. (2022); Hernandez-Alvarez et al. (2023); Pittenger et al. (1999); Caplan & Correa (2011).

From a regulatory point of view, still no global framework is in place, for the harvesting, expansion, and clinical deployment of stem cells; thus, the large-scale implementation is seriously constrained. Differences in stem cell classification (drug vs. tissue), manufacture standards (GMP vs. point of care), and insurance coverage regulations might delay or split the care pathways. Regulatory authorities such as FDA, EMA, and WHO must collaborate with clinical researchers in:

- Defining common quality and potency criteria on ADSCs and BMSCs
- Approving standardized biobanking and cryopreservation procedures
- Developing registries and post-market surveillance systems for tracking outcomes and safety

From this standpoint, healthcare administrators must factor in cost-analysis and risk-benefit tools into their decision support systems for hospitals and insurers. Though ADSCs are more accessible, the total

cost per patient over time may change depending on retreatment frequency, integration success, and durability of outcomes [25,17].

At the same time, new advances in AI-enabled imaging analysis and predictive modeling will become a game changer. For instance, machine learning algorithms could bring objectivity and consistency into Pfirrmann grading, predict therapeutic response from preoperative imaging, and streamline follow-up diagnostics. Integrated clinical decision tools linking MRI data to factors such as patient age and inflammatory biomarkers might soon help physicians assess, on a case-by-case basis, whether ADSC or BMSC therapy is the best option [26].

Key recommendations summary:

- Cell type should be selected by the clinicians depending on the patient's age, degree of degeneration, and tolerance for the procedure.
- Researchers must concentrate on direct, multicenter RCTs, with common metrics, long follow-ups, and tracking of molecular endpoints.
- Health systems and policy makers should set regulatory standards, biobanking protocols, and MSC reimbursement guidelines.
- New therapies should look into multimodal treatment with MSCs combined with PRP, scaffolds, or exosomes.
- Harness AI and big data tools for personalized models of care and long-term treatment optimization.

Building on ideas from Tables 8 and 9, it becomes clear that regeneration for IVDD with MSCs is certainly not a purely biological intervention but is a systems-level medical innovation. Coordination amongst clinicians, researchers, biomedical engineers, regulatory agencies, and economical stakeholders is required. One very interesting and little researched implication is the integration of biomaterial engineering and bioinformatics into MSC therapy workflows.

While currently the majority of studies are focusing on isolated ADSC or BMSC injections, the second generation of therapeutics will likely include smart scaffolds that could release cells as well as growth factors or immunomodulators based on signals from the disc microenvironment. Advanced delivery platforms that can overcome the hostile hypoxic and avascular environment of degenerated discs could comprise electrospun nanofibers, temperature-responsive hydrogels, and decellularized ECM mimetics [21,19]. BMSCs seeded on collagen or hyaluronic acid scaffolds better retain cells and preserve disc space, while ADSCs in fibrin or PRP gels abet paracrine signaling and speed up anti-inflammatory effects.

Another overlooked implication might be stemcell–based personalization platforms were baseline patient biomarkers, such as circulating inflammatory cytokines (e.g., IL-6, CRP), T2-weighted MRI scores, or even single-cell RNA-seq signatures, could be used to predict stem cell response. This would steer the field toward precision regenerative medicine, wherein the decision about ADSCs versus BMSCs is predicated not only upon anatomical damage but also upon molecular profile and predicted responsiveness [26,23]. Clinical algorithms combining imaging, fluid biomarkers, and AI model candidates might be able to act as

decision-support tools for physicians and spine surgeons.

Similarly, a global disparity needs to be ameliorated in terms of access to MSC therapies. Currently, regenerative medicine is practiced in high-income settings while low- and middle-income countries face barriers including costs, infrastructure, regulatory uncertainty, and a dearth of skilled personnel. ADSCs, on the other hand, may present a more just and scalable solution in these regions because of the relative ease of collection and very high yield. International consortia can work together in technology transfer programs to enable LMICs to establish stem cell banks and develop GMP labs and train clinicians in cell therapy protocols.

From my Platonian perspective, considerations regarding ethical treatment of donor cells, informed consent, or post-procedure surveillance are underdeveloped. The commercial development and sale of treatments with MSC, especially in areas without regulation and so-called "stem cell tourism," raise concerns about the over-the-top marketing claims, lack of follow-up, and outright safety risks [7,14]. It is therefore strongly recommended that journals, professional societies, and international bodies of health enforce a reporting standard, require registrations for trials, and maintain up-to-date reporting databases for adverse events.

Secondly, providers in primary care, including specialists in pain management and orthopedic surgery, need further educational exposure to these matters. Most practicing physicians are unaware of the key comparative advantage or disadvantage between ADSCs and BMSCs and tend to make referrals or develop expectations from that biased point of view. CME programs, clinical guidelines, and peer-reviewed decision aids must be brought and deployed to bridge this gap.

In summary, the above expanded implications reinforce that MSC-based therapy for IVDD is not merely a biological choice-but a full clinical-technological-ethical system. For the journey to become a standard-of-care treatment, key changes are needed:

- A translation of intervention by means of biology into precision-integrated multimodal therapy
- Fast tracking the way through experimental applications for standardized, regulated global protocol
- A scale from treatments for a few specialists into treatments integrated into mainstream primary care for all Population.

Interdisciplinary collaboration is a crucial consideration. Throughout the continuing development of regenerative medicine, an integrated approach that weighs innovation with regulation, personalization with scalability, and clinical aspiration with ethical consideration will be the only thirsty drink that would nurture stem cell therapies into their fullest ability to restore spinal health and improve the quality of life for a myriad of populations.

Conclusion

This systematic review aimed at critically synthesizing the findings about clinical efficacy, mechanistic insights, and outcomes from a total of 30 top-quality studies consisting of randomized trials, translational

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models, and long-term follow-ups. Undoubtedly, it has been established that both ADSCs and BMSCs can provide an IVD regenerative effect, yet with different strengths, weaknesses, and situations suitable for their application.

ADSCs are reported to rapidly render an anti-inflammatory action; they are much easier to harvest in large quantities and retain the viability of aged patients. Candidate therapeutic mechanisms include paracrine secretomes; hence, they are more adept when applied to the early and inflammatory stages of IVDD. In contrast, BMSCs show a stronger ability toward chondrogenic differentiation, integration into the disc tissue, and long-term structural modifications. These benefits are more evident in patients with a more advanced stage of disc collapse or matrix disintegration, where biomechanical restoration of the disc properties over-recorded time is the most important outcome.

Importantly, the therapeutic choice between ADSCs and BMSCs ought not to be an either-or judgment or generalized perspective but instead contextualized by factors such as patient age, consideration of the severity of disc degeneration, presence of comorbidities, and availability of resources. An MSC-based therapy approach which decided upon from the market is simply unfair viewing the level of advancement and insights currently in the field on MSC biology and clinical response.

Yet, the major challenges that some researchers have identified remain extant: non-uniformity of clinical protocols; continued absence of large-scale head-to-head multicentric RCTs; under-reporting of most long-term outcome metrics; and absence of cost-effectiveness evaluations. Other ethical and regulatory issues have arisen reversing the acceptance of stem cell therapies in the face of stem cell treatments being commercialized without proper regulatory oversight.

While the future remains uncertain due to these challenges, the horizon of opportunity for MSC therapy in IVDD is vast. In scaffolding, bio responsive delivery systems, and machine learning-based personalization of treatments, the field is quickly progressing towards a more powerful, scalable, and patient-centric treatment. Also, the rise of exosome-based therapies and cell-free regenerative medicine will open new avenues to obviate some of today's manufacturing- and immune compatibility-related hurdles.

In conclusion, both ADSCs and BMSCs have a warranted place in the regulation of IVDD. The next frontier lies in not choosing between the two, but rather in looking into optimally utilizing them through well-developed, personalized hybrid approaches with relevant ethical oversight. When done with multidisciplinary collaboration and commitment toward rigorous clinical sciences, stem cell–based regenerative therapy for the spine would soon step out of the experimental realm into modern well-guided precision care, thus granting mobility and dignity to millions of people across the globe.

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