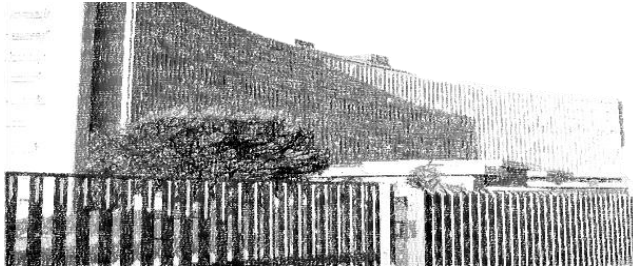


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# **BMAC and ADCSs for osteoarthritis of the knee**

**Nicola Maffulli**  
**Michele Pepino**



Barts and The London  
School of Medicine and Dentistry



Keele  
University

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**Knee osteoarthritis (OA): common degenerative joint disease**

**Pain and disability, often ultimately requiring knee arthroplasty**

**WHAT CAN WE DO?**

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## WHAT CAN WE DO?

**We are not equipped for miracles (yet) ...**

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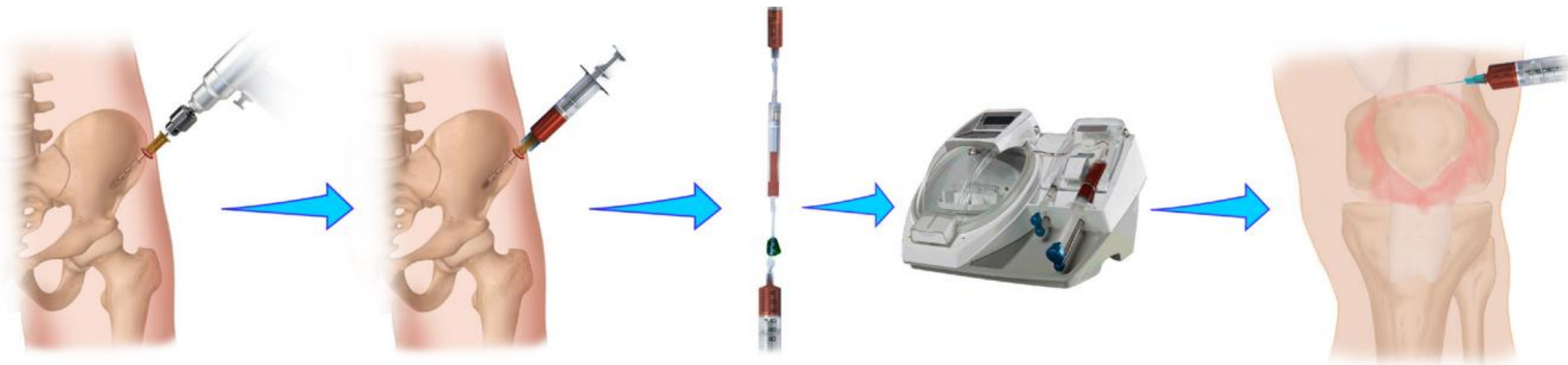


# WHAT CAN WE OFFER?

Orthobiologics → Final Common Pathway

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8<sup>th</sup>  
International  
Symposium  
Intra  
Articular  
Treatment



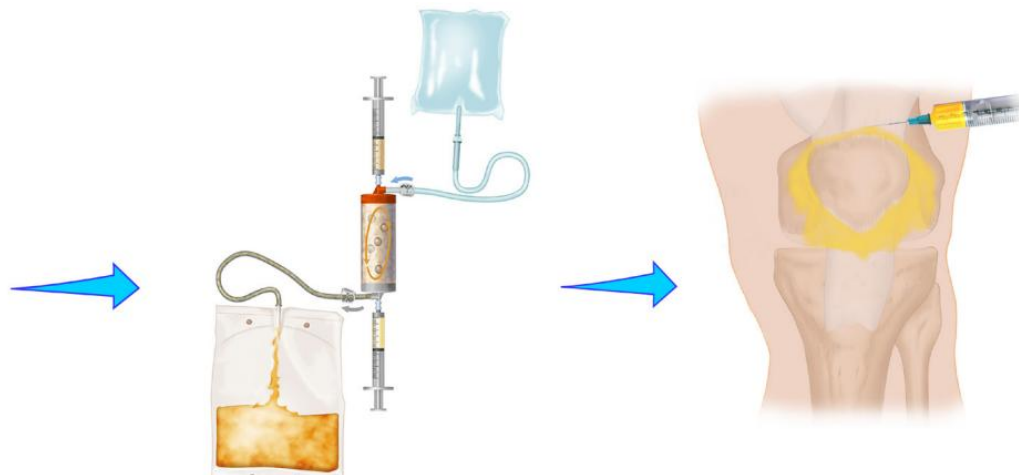
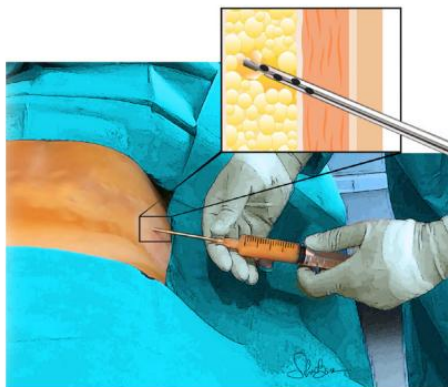
**BMAC**

Adipose tissue-derived versus bone marrow-derived cell concentrates for the injective treatment of knee osteoarthritis: protocol of a prospective randomised controlled trial

Luca Andriolo,<sup>1</sup> Francesca Veronesi,<sup>2</sup> Lorenzo Zanasi,<sup>1</sup> Viviana Costa,<sup>2</sup> Marco Franceschini,<sup>1</sup> Marco Miceli,<sup>3</sup> Paolo Spinnato,<sup>3</sup> Stefano Zaffagnini,<sup>1</sup> Gianluca Giavaresi,<sup>2</sup> Giuseppe Filardo<sup>4</sup>

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Articular  
Treatment



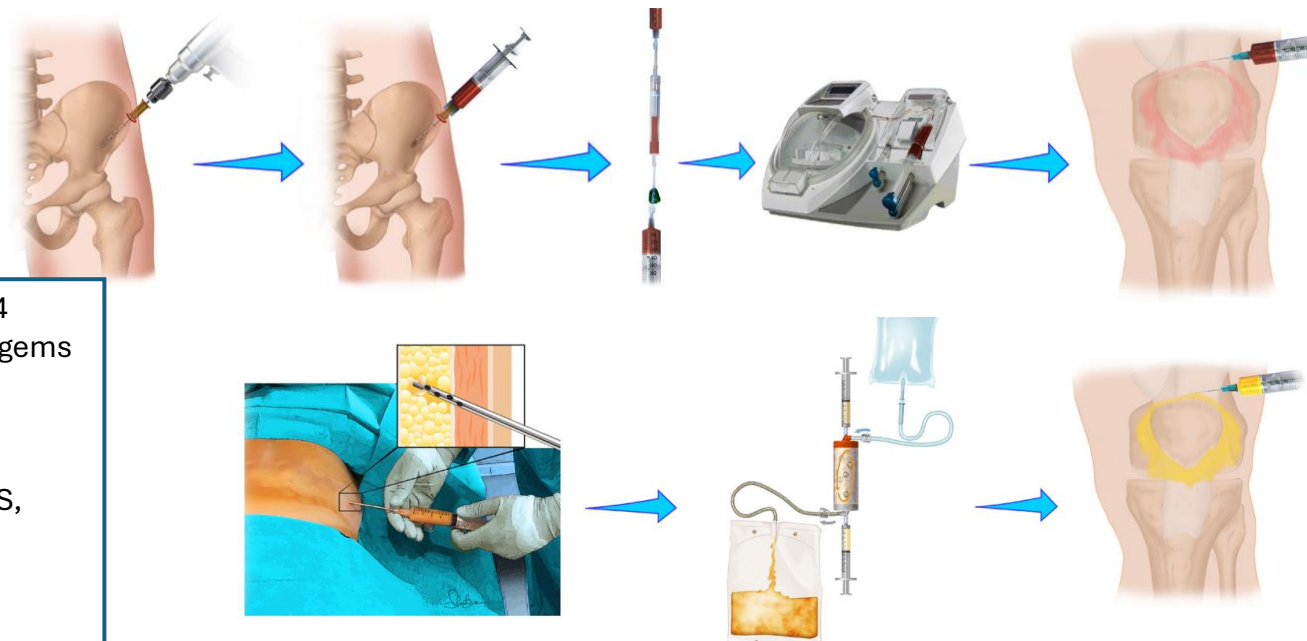
**ADSC**

Adipose tissue-derived versus bone marrow-derived cell concentrates for the injective treatment of knee osteoarthritis: protocol of a prospective randomised controlled trial

Luca Andriolo,<sup>1</sup> Francesca Veronesi,<sup>2</sup> Lorenzo Zanasi,<sup>1</sup> Viviana Costa,<sup>2</sup> Marco Franceschini,<sup>1</sup> Marco Miceli,<sup>3</sup> Paolo Spinnato,<sup>3</sup> Stefano Zaffagnini,<sup>1</sup> Gianluca Giavaresi,<sup>2</sup> Giuseppe Filardo<sup>4</sup>

# Bucharest 2-4 October 2025

8<sup>th</sup>  
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Treatment



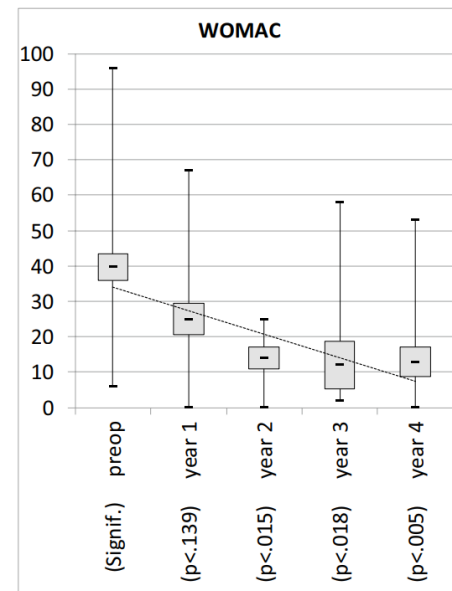
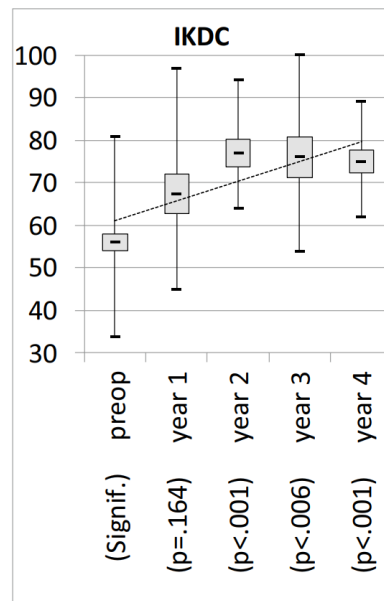
- 204 patients, age 40–75, KL grade 1–4
- Single injection: BMAC vs MFAT (Lipogems system)
- Primary outcome: WOMAC pain @ 6 months
- Secondary: KOOS, IKDC, VAS, EQ-VAS, Tegner (2–12 mo)
- Imaging: X-ray, 3T MRI (WORMS)
- Biomarkers: synovial fluid, miRNAs, osteoclastogenesis
- Will provide Level I evidence (first RCT)

*Ongoing RCT: BMAC vs MFAT for Knee OA  
(Andriolo et al., BMJ Open 2025)*

## Intra-articular injection of bone marrow aspirate concentrate (mesenchymal stem cells) in KL grade III and IV knee osteoarthritis: 4 year results of 37 knees

Christof Pabinger<sup>1,2</sup>, Harald Lothaller<sup>3</sup> & Georg Stefan Kobina<sup>1</sup>

- Prospective cohort, 37 knees, KL grade III-IV
- 4-year follow-up:
  - IKDC ↑ from 56 → 73 ( $p < 0.001$ )
  - WOMAC ↓ from 40 → 18 ( $p < 0.001$ )
  - 95% clinical success rate
- No TKA required during follow-up
- Safe, well-tolerated, only mild transient side effects



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The downside of all these cellular therapies is, that they fall under restrictive legislative constraints, making it almost impossible to offer these therapies to patients in Germany, Austria or Switzerland, except you have a respective license as a hospital, as we do. Some of the cited applications can be viewed as Advanced Therapy Medicinal Products (ATMPs): The use of those requires the knowledge of diverse regulations and an extensive (year long) communication with the national/international authorities, up to the hospital exemption<sup>52</sup>.

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**Best available current evidence: both BMAC and ADCSs produce meaningful improvements in pain and function**

**Most studies: no significant difference between BMAC and adipose cell therapies in PROMS**



## **Head-to-Head Comparative Studies (BMAC vs ADSCs)**

**Mautner et al., 2019 (USA, 106 knees)  
retrospective 1 yr:**

- **BMAC and MFAT → significant improvements (KOOS, VAS, EQOL)**
- **No between-group differences**

**Pintore et al., 2023 (Italy, 102 patients)  
prospective at 6 months:**

**Both groups → KOOS, OKS, VAS improved  
( $p < 0.0001$ )**

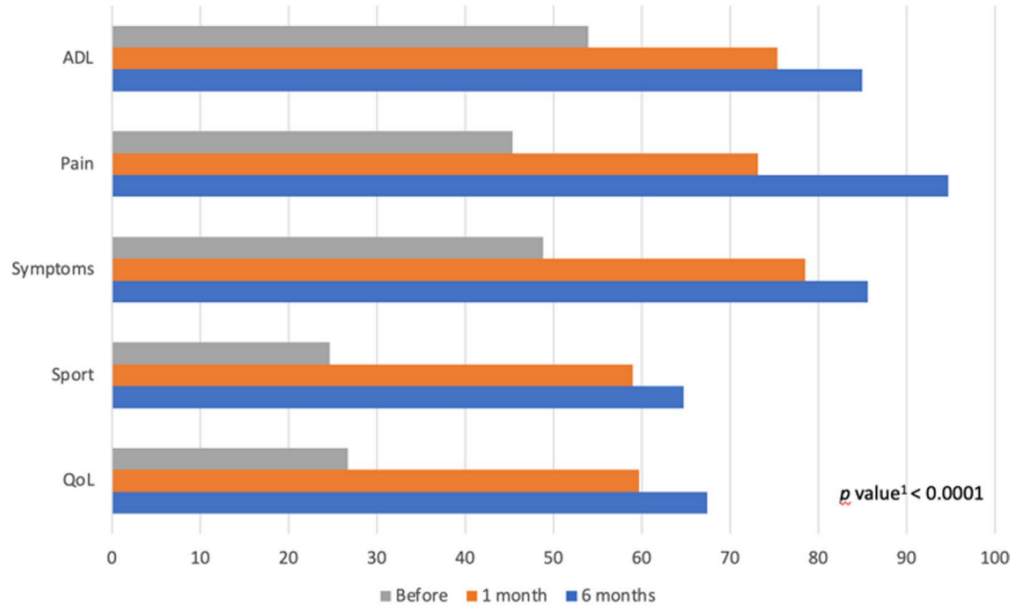
**No significant differences BMAC vs ADSCs  
Better outcomes in KL grade 2 vs KL 3–4**

# Bucharest

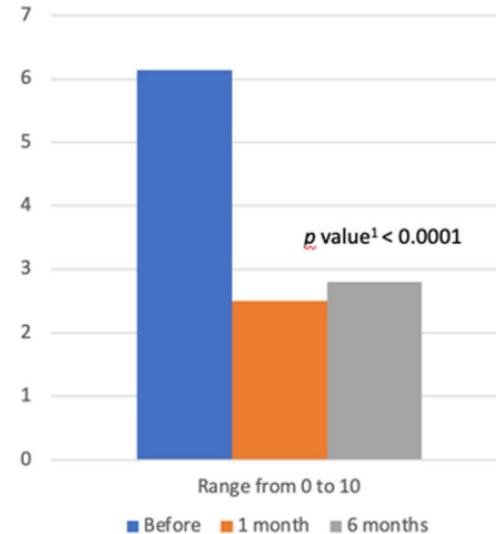
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KOOS score of all patients (N = 102)



VAS score of all patients (N = 102)



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**Table 1.** Univariable repeated-measures analyses: Longitudinal change in functional outcomes by treatment group for symptomatic knee osteoarthritis patients

|                                      | Treatment | Preprocedure |               | Postprocedure |               | p values |      |               | Change (pre-post)       |      |
|--------------------------------------|-----------|--------------|---------------|---------------|---------------|----------|------|---------------|-------------------------|------|
|                                      |           | n            | Mean ± SEM    | n             | Mean ± SEM    | Treat    | Time | Treat by time | Mean change (95% CI)    | p    |
| VAS for pain                         |           |              |               |               |               |          |      |               |                         |      |
| Pain                                 | BMAC      | 41           | 3.9 ± 0.355   | 40            | 2.5 ± 0.351   | .38      | <.01 | .89           | 1.502 (0.780, 2.223)    | <.01 |
|                                      | MFAT      | 35           | 4.3 ± 0.385   | 35            | 2.8 ± 0.376   | –        | –    | –             | 1.411 (0.635, 2.186)    | <.01 |
| Emory quality of life                |           |              |               |               |               |          |      |               |                         |      |
| Mobility                             | BMAC      | 39           | 1.694 ± 0.074 | 39            | 1.407 ± 0.080 | .45      | <.01 | .65           | 0.287 (0.103, 0.470)    | <.01 |
|                                      | MFAT      | 32           | 1.732 ± 0.082 | 32            | 1.508 ± 0.088 | –        | –    | –             | 0.223 (0.019, 0.428)    | .03  |
| Self-care                            | BMAC      | 39           | 1.187 ± 0.057 | 39            | 1.050 ± 0.037 | .50      | .06  | .30           | 0.137 (0.015, 0.259)    | .03  |
|                                      | MFAT      | 32           | 1.102 ± 0.062 | 32            | 1.061 ± 0.041 | –        | –    | –             | 0.041 (–0.094, 0.176)   | .55  |
| Usual activities                     | BMAC      | 39           | 1.646 ± 0.083 | 38            | 1.494 ± 0.094 | .05      | .02  | .65           | 0.152 (–0.071, 0.375)   | .18  |
|                                      | MFAT      | 32           | 1.887 ± 0.091 | 32            | 1.659 ± 0.102 | –        | –    | –             | 0.228 (–0.016, 0.473)   | .07  |
| Pain/discomfort                      | BMAC      | 39           | 2.056 ± 0.079 | 38            | 1.735 ± 0.089 | .28      | <.01 | .51           | 0.321 (0.129, 0.512)    | <.01 |
|                                      | MFAT      | 32           | 2.215 ± 0.087 | 32            | 1.799 ± 0.097 | –        | –    | –             | 0.416 (0.205, 0.627)    | <.01 |
| Anxiety                              | BMAC      | 39           | 1.210 ± 0.070 | 37            | 1.164 ± 0.079 | .24      | .49  | .98           | 0.047 (–0.129, 0.222)   | .60  |
|                                      | MFAT      | 32           | 1.314 ± 0.077 | 32            | 1.271 ± 0.085 | –        | –    | –             | 0.043 (–0.148, 0.235)   | .65  |
| Composite                            | BMAC      | 39           | 0.727 ± 0.027 | 37            | 0.835 ± 0.027 | .09      | <.01 | .98           | –0.108 (–0.162, –0.054) | <.01 |
|                                      | MFAT      | 32           | 0.667 ± 0.030 | 32            | 0.774 ± 0.029 | –        | –    | –             | –0.107 (–0.166, –0.047) | <.01 |
| Knee Injury and Osteoarthritis Score |           |              |               |               |               |          |      |               |                         |      |
| Pain                                 | BMAC      | 39           | 54.6 ± 2.674  | 40            | 70.6 ± 3.313  | .63      | <.01 | .56           | –16.0 (–23.1, –8.9)     | <.01 |
|                                      | MFAT      | 34           | 51.4 ± 2.867  | 32            | 70.4 ± 3.692  | –        | –    | –             | –19.1 (–26.9, –11.2)    | <.01 |
| Symptoms                             | BMAC      | 39           | 53.7 ± 2.992  | 40            | 69.4 ± 3.702  | .94      | <.01 | .61           | –15.7 (–23.2, –8.1)     | <.01 |
|                                      | MFAT      | 34           | 54.9 ± 3.209  | 32            | 67.6 ± 4.120  | –        | –    | –             | –12.7 (–21.1, –4.4)     | <.01 |
| ADL                                  | BMAC      | 39           | 63.6 ± 2.946  | 40            | 79.2 ± 3.053  | .17      | <.01 | .58           | –5.5 (–22.5, –8.6)      | <.01 |
|                                      | MFAT      | 33           | 57.2 ± 3.202  | 32            | 75.6 ± 3.401  | –        | –    | –             | –18.4 (–26.1, –10.7)    | <.01 |
| Sport/recreation                     | BMAC      | 29           | 28.6 ± 4.224  | 26            | 56.1 ± 5.831  | .15      | <.01 | .79           | –27.5 (–40.2, –14.8)    | <.01 |
|                                      | MFAT      | 24           | 21.3 ± 4.634  | 22            | 46.3 ± 6.333  | –        | –    | –             | –25.0 (–39.0, –11.0)    | <.01 |
| QOL                                  | BMAC      | 39           | 28.6 ± 2.995  | 40            | 52.0 ± 3.858  | .70      | <.01 | .45           | –23.4 (–31.7, –15.1)    | <.01 |
|                                      | MFAT      | 32           | 29.4 ± 3.302  | 32            | 48.0 ± 4.303  | –        | –    | –             | –18.6 (–27.9, –9.3)     | <.01 |

Abbreviations: ADL, activities of daily living; BMAC, bone marrow aspirate concentrate; CI, confidence interval; MFAT, microfragmented adipose tissue; QOL, quality of life; VAS, Visual Analog Scale.

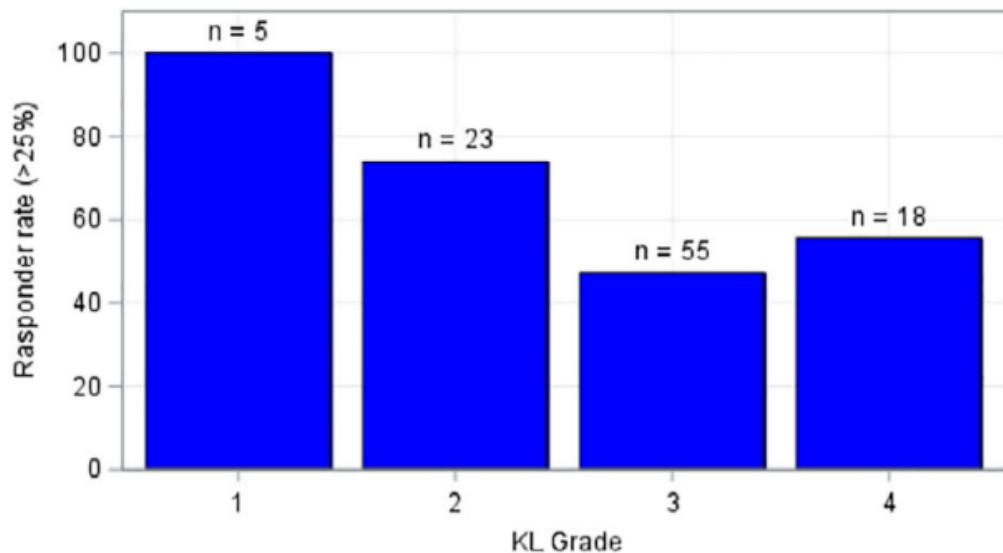
Mautner, Bowers, Easley et al

Responders at least 25% VAS pain reduction

- KL 1: 100% responders
- KL 2: 74% responders
- KL 3: 47% responders
- KL 4: 56% responders

Avg VAS reduction in responders:

- BMAC: 78%
- MFAT: 69%
- Overall: 73%



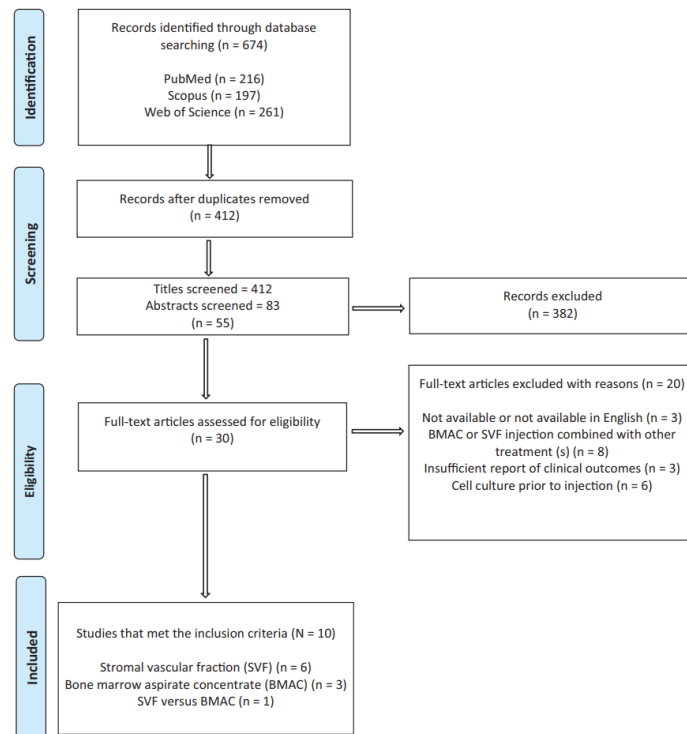
**Figure 1.** Responder rate by Kellgren–Lawrence grade.

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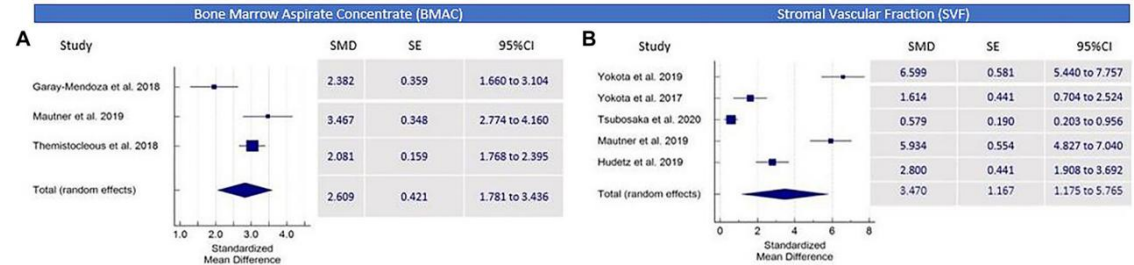
## Clinical Efficacy of Bone Marrow Aspirate Concentrate Versus Stromal Vascular Fraction Injection in Patients With Knee Osteoarthritis

A Systematic Review and Meta-analysis

- 10 studies, 472 patients (233 BMAC, 239 SVF)
- Both groups: significant pain and function improvement
  - BMAC VAS: 5.8 → 2.6
  - SVF VAS: 6.4 → 3.4
  - WOMAC: SMD ~1.3–1.4 (large effect size)
- Both safe, short-term symptomatic benefit



- VAS pain improvement:•  
BMAC:
  - SMD 2.6
  - SVF: SMD 3.4
- Direct comparison: SVF > BMAC
- $p < 0.0001$  (statistically significant)

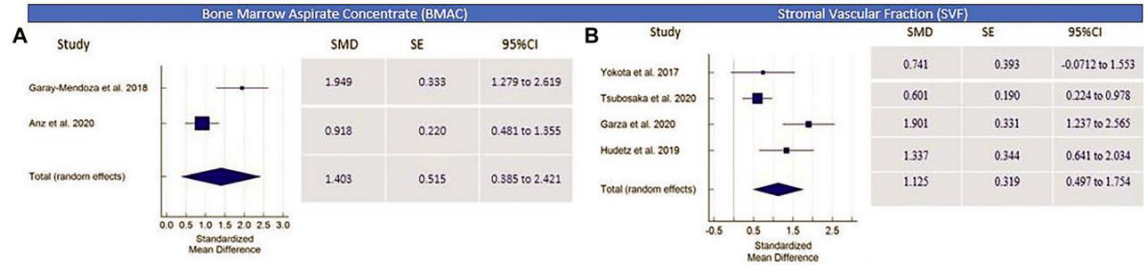


**Figure 2.** Estimated clinical effect of (A) bone marrow aspirate concentrate and (B) adipose-derived stromal vascular fraction injection on the knee pain of patients with osteoarthritis. SMD, standardized mean difference.

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- WOMAC improvement significant in both groups
- BMAC: SMD 1.4
- SVF: SMD 1.1
- No significant difference ( $p = 0.626$ )



**Figure 3.** Estimated clinical effect after (A) bone marrow aspirate concentrate and (B) stromal vascular fraction injection to the knee of patients with osteoarthritis, based on the Western Ontario and McMaster Universities Osteoarthritis index. SMD, standardized mean difference.

*Bolia et al The American Journal of Sports Medicine*

TABLE 4  
Studies Reporting Outcomes After a Single SVF Injection<sup>a</sup>

| Study                                 | Harvest Site      | Patients (M, F) | Age, y     | BMI        | K-L  | Latest Follow-up, mo | Outcome Scores, Pre- vs Postinjection                                                                                          | Rehabilitation                                                                                               | Complications                                                                                                                                                                       |
|---------------------------------------|-------------------|-----------------|------------|------------|------|----------------------|--------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Yokota <sup>49</sup> (2019), LOE 3    | Abdomen           | 38 (7, 31)      | 73 ± 90.1  | 24.8 ± 1.9 | 1-4  | 6                    | VAS: 8 ± 0.6 vs 4 ± 1.2<br>KOOS and OMERACT-OARSI                                                                              | Target: 100 bend-and-stretch exercises of the knees on the day of SVF injection and each day thereafter.     | Mild knee effusion/swelling: 3 cases. Abdominal pain: 6 cases. Internal bleeding at the incision site: 5 cases. Subcutaneous induration at the abdominal area of harvest: 12 cases. |
| Yokota <sup>50</sup> (2017), LOE 2    | Abdomen           | 13 (2, 11)      | 74.5 ± 5.4 | 23 ± 2.2   | 3, 4 | 6                    | VAS: 72.7 ± 18.2 vs 43.5 ± 24.1<br>WOMAC: 49.6 ± 20.4 vs 33.8 ± 20.9<br>JKOM: 55.9 ± 21 vs 43 ± 17.4                           | Target: 100 bend-and-stretch exercises of the knees on the day of SVF injection and each day thereafter.     | Pain/swelling at the injection and fat-harvesting sites that lasted for a few days was observed and all resolved within 2 wk.                                                       |
| Tsubosaka <sup>45</sup> (2020), LOE 3 | Abdomen or breech | 57 (41, 16)     | 69.4 ± 6.9 | 25.1 ± 3.1 | 1-4  | 12                   | VAS: 46.5 ± 23.5 vs 32.8 ± 24.7<br>WOMAC: 33.4 ± 18.2 vs 22.6 ± 17.5<br>KOOS: 48.7 ± 15.8 vs 58.6 ± 16.8<br>JKOM: 34.9 vs 26.8 |                                                                                                              | None                                                                                                                                                                                |
| Mautner <sup>35</sup> (2019), LOE 3   | Abdomen           | 35 (12, 23)     | 63 ± 11    |            | 1-4  | 13                   | VAS: 4.6 ± 0.3 vs 2.8 ± 0.3<br>KOOS: 42.8 ± 16.3 vs 61.6 ± 13.4<br>EMORY: 0.6 ± 0.03 vs 0.7 ± 0.02                             |                                                                                                              |                                                                                                                                                                                     |
| Garza <sup>19</sup> (2020), LOE 1     | Abdomen           | 26 (11, 15)     | 59 ± 9.9   | 27.8 ± 2.9 | 1-3  | 12                   | WOMAC: 51.7 ± 20 vs 17.5 ± 15.1                                                                                                | Minimal weightbearing for 2 d, with full range of motion. Light activity for the first 3 wk after injection. | 1 with knee swelling (negative aspiration), 2 sample cultures were positive for bacteria but patients remained asymptomatic 6-12 mo: no adverse events                              |
| Hudetz <sup>26</sup> (2019), LOE 4    | Abdomen           | 20 (15, 5)      |            |            | 3, 4 | 12                   | VAS: 7.38 ± 1.41 vs 3.38 ± 1.89<br>WOMAC: 55.38 ± 18.83 vs 32.25 ± 14.62<br>KOOS: 35.7 ± 17.9 vs 58.9 ± 17.3                   |                                                                                                              | None                                                                                                                                                                                |
| Lapiente <sup>31</sup> (2020), LOE 4  | Abdomen           | 50 (28, 22)     |            |            | 3, 4 | 12                   | VAS: 7.39 vs 3.04<br>WOMAC: 46.92 vs 14.99<br>Lequesne: 12.9 vs 3.4                                                            |                                                                                                              |                                                                                                                                                                                     |



high concentration in MSCs, but also their ability to respond to an inflammatory environment better than BMAC in preclinical studies.<sup>14</sup> However, as of today, no randomised controlled trial (RCT) directly compared the clinical benefit of BMAC and MFAT orthobiologic approaches, and the current literature provides poor guidance being limited by low level studies, heterogeneity in treatment protocols and overall poor reporting of treatment characteristics and results in terms of both subjective and objective outcomes.

To date, the comparative evidence for BMAC vs adipose-derived cell therapy in knee OA consists mostly of level II/III studies (prospective cohort studies, case series) and meta-analyses. **No completed high-quality randomized controlled trial (RCT) had been published** directly comparing BMAC and adipose cell injections as of the latest literature

*Andriolo L, et al. BMJ Open  
2025;15:e092379.  
doi:10.1136/bmjopen-2024-  
092379*

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**Multicentre RCTs**

**Sound characterisation of the devices used**

**Appropriate PROMS**

**Careful endpoints**

**Meticulous selection of patient**

**Methodical imaging assessment**

**Diligent education of patients and health care providers**

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**We need to understand how to respect biology and nature**



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**Multumesc**

**Thank you**