LEGITIMATE USES OF ORTHOBIOLOGIC INJECTIONS vs ORTHOPEDIC SURGERY

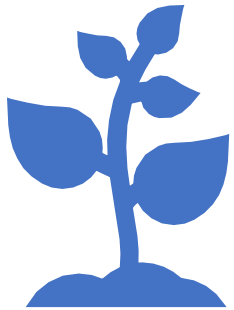
Jonathan E Fenton, DO,
FAAPM&R,
C-AOCPM&R, C-SPOMM, C-AAOM, R-MSK

VERMONT REGENERATIVE MEDICINE
321 MAIN ST
WINOOSKI, VT
VERMONTREGENERATIVEMEDICINE.COM

What we'll discuss:

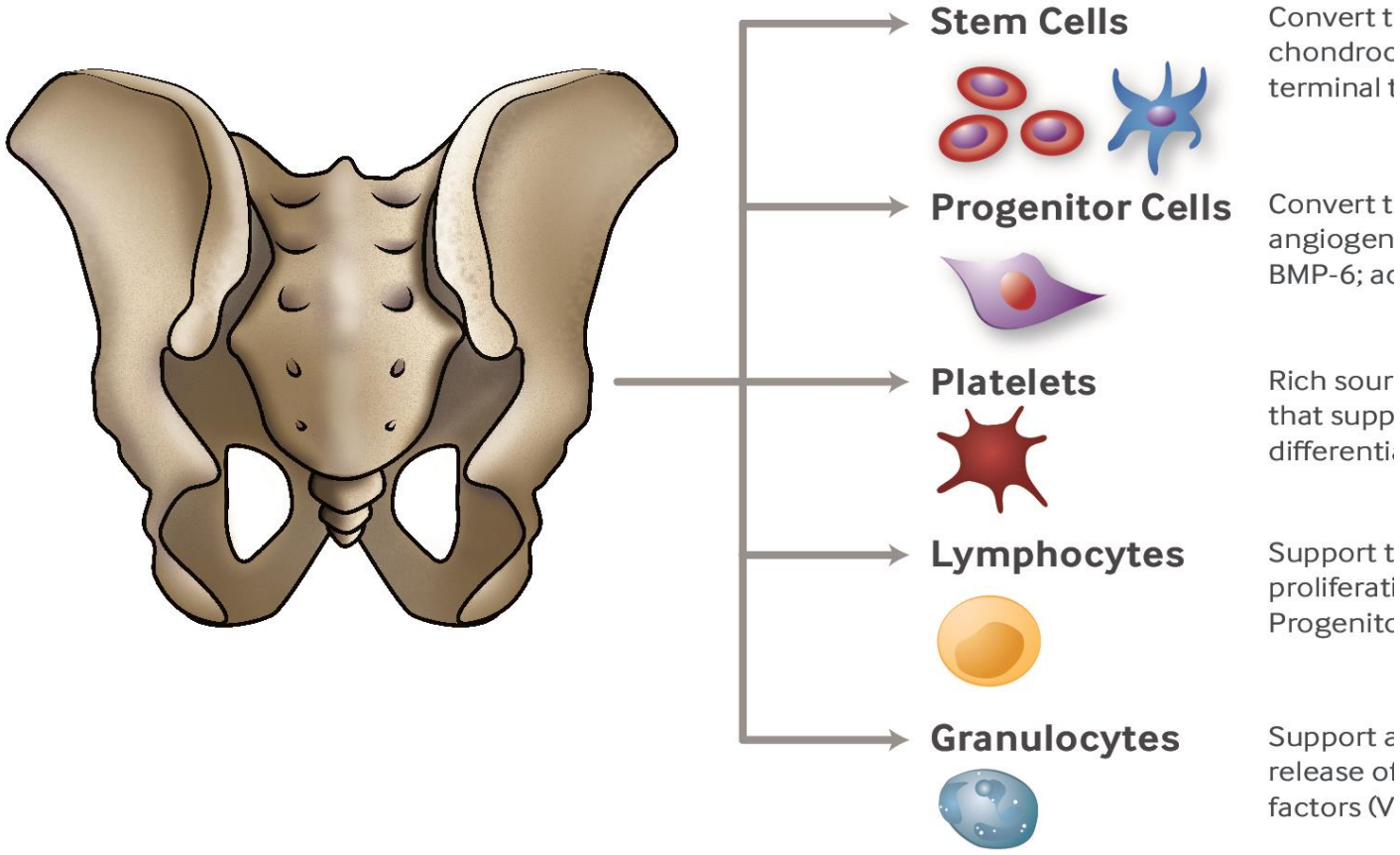
- What are orthobiologics?
- Regulations
- What are problems in the use of orthobiologics?
- How much evidence do we have that common orthopedics surgeries are effective?
- How much evidence do we have that interventional orthopedics is effective?
- detailed cost savings models

Orthobiologics



The use of substances to enhance the healing or maintenance of orthopedic tissues

What are Common Orthobiologics?



- Platelet-rich plasma (PRP)
- Bone marrow concentrate
- M-fat (microfragmented adipose tissue)
- Cytokine enriched plasmas

Orthobiologics Regulation

- 21 CFR 1271
- Same surgical procedure exemption (1271.15(b)) allows for minimally manipulated autologous transplant tissues
- Hence autologous PRP and Bone Marrow Concentrate for orthopedic use are regulated by state medical boards and not federally
- This would be the same category as transplanting a vein from the leg into the heart in a CABG procedure
- Does not apply to allogenic (not from the patient) tissues

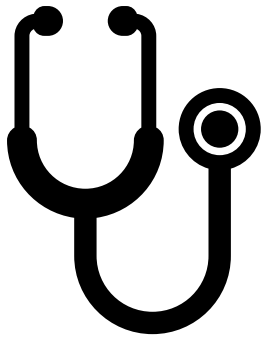
The problem with orthobiologics?

- **The autologous PRP and BMC cell preps vary widely in content and dose**
- **There is rarely measurement of dosing / cell counts**
- **Provider skill varies widely**
- **Protocols used are all over the map**
- **The clinical outcome and complications data is rarely collected**
- **There is no or little candidacy information**
- **There are rarely any treatment guidelines**

The autologous PRP and BMC cell preps vary widely in content and dose

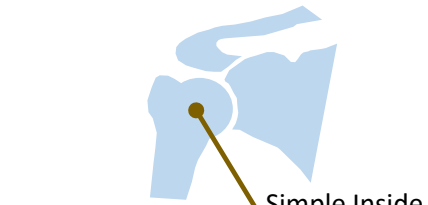
Need to use standardized PRP and bone marrow concentrate preps and doses (in-house cell counting)

Provider skill varies widely



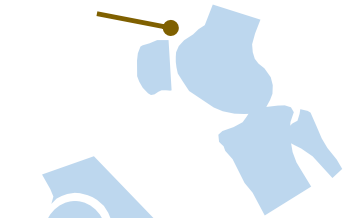
- Ideally only those with advanced MSK/orthopedic knowledge plus advanced fluoroscopy and / or ultrasound guidance skills

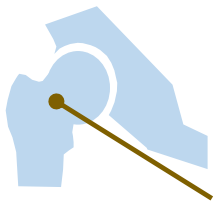
What is Interventional Orthopedics?



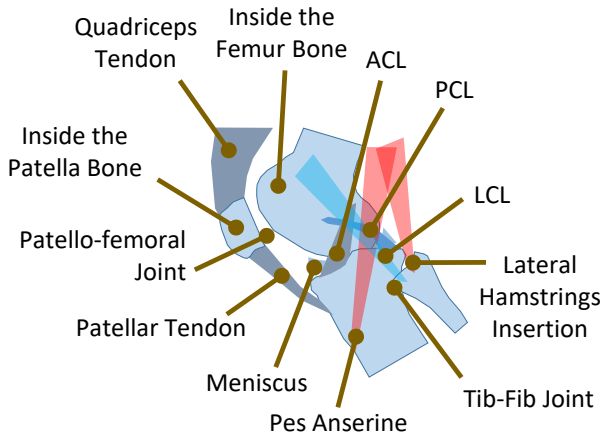
Simple Inside the Joint (Intra-articular) Injection

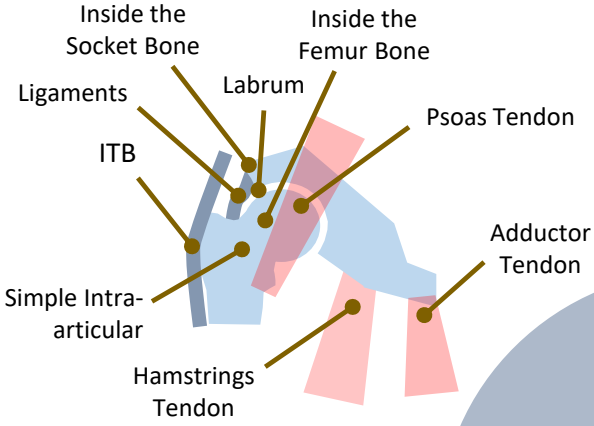
Simple Inside the Joint (Intra-articular) Injection

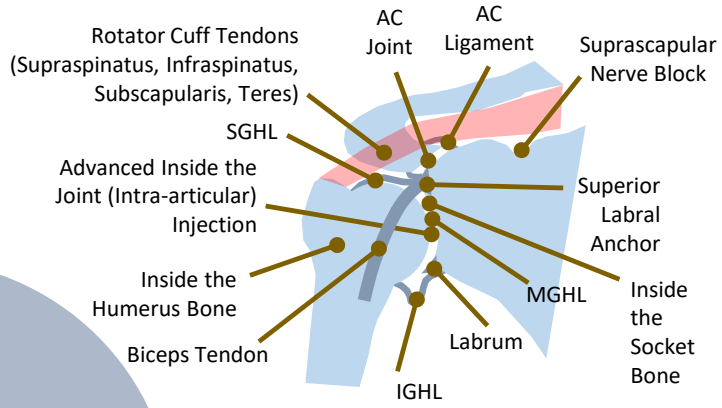




Simple Inside the Joint (Intra-articular) Injection



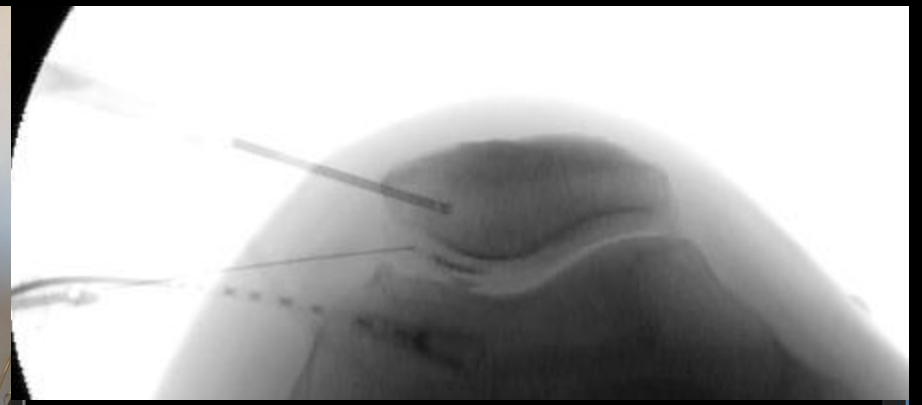


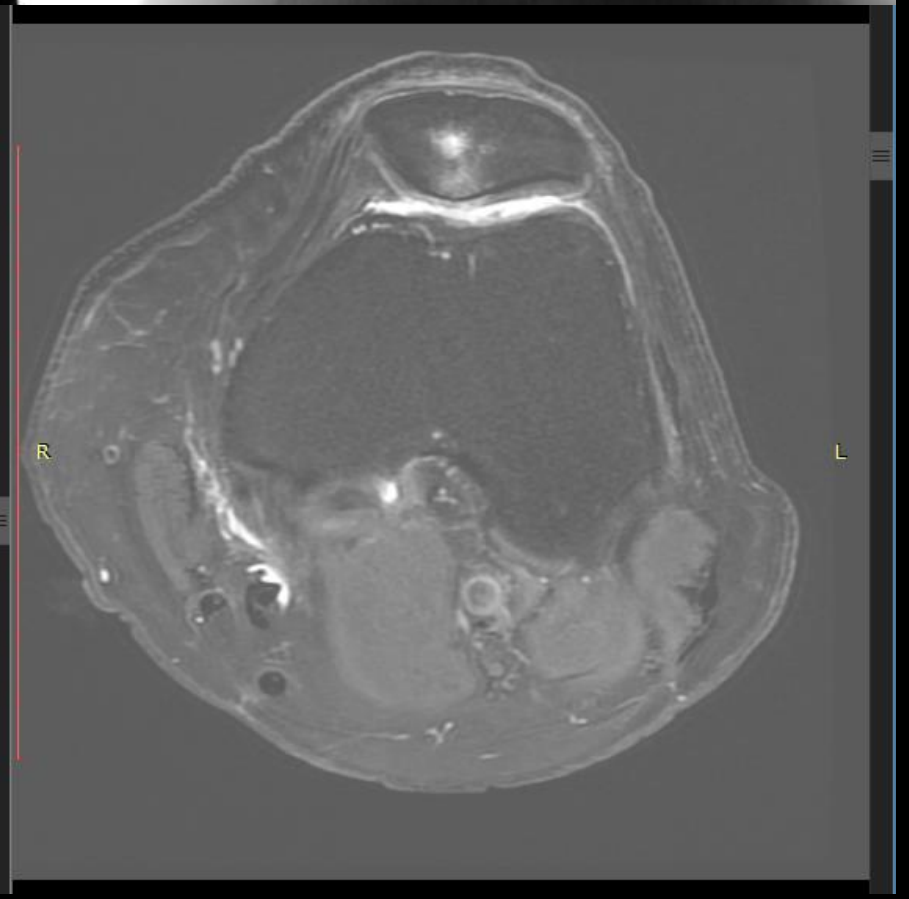


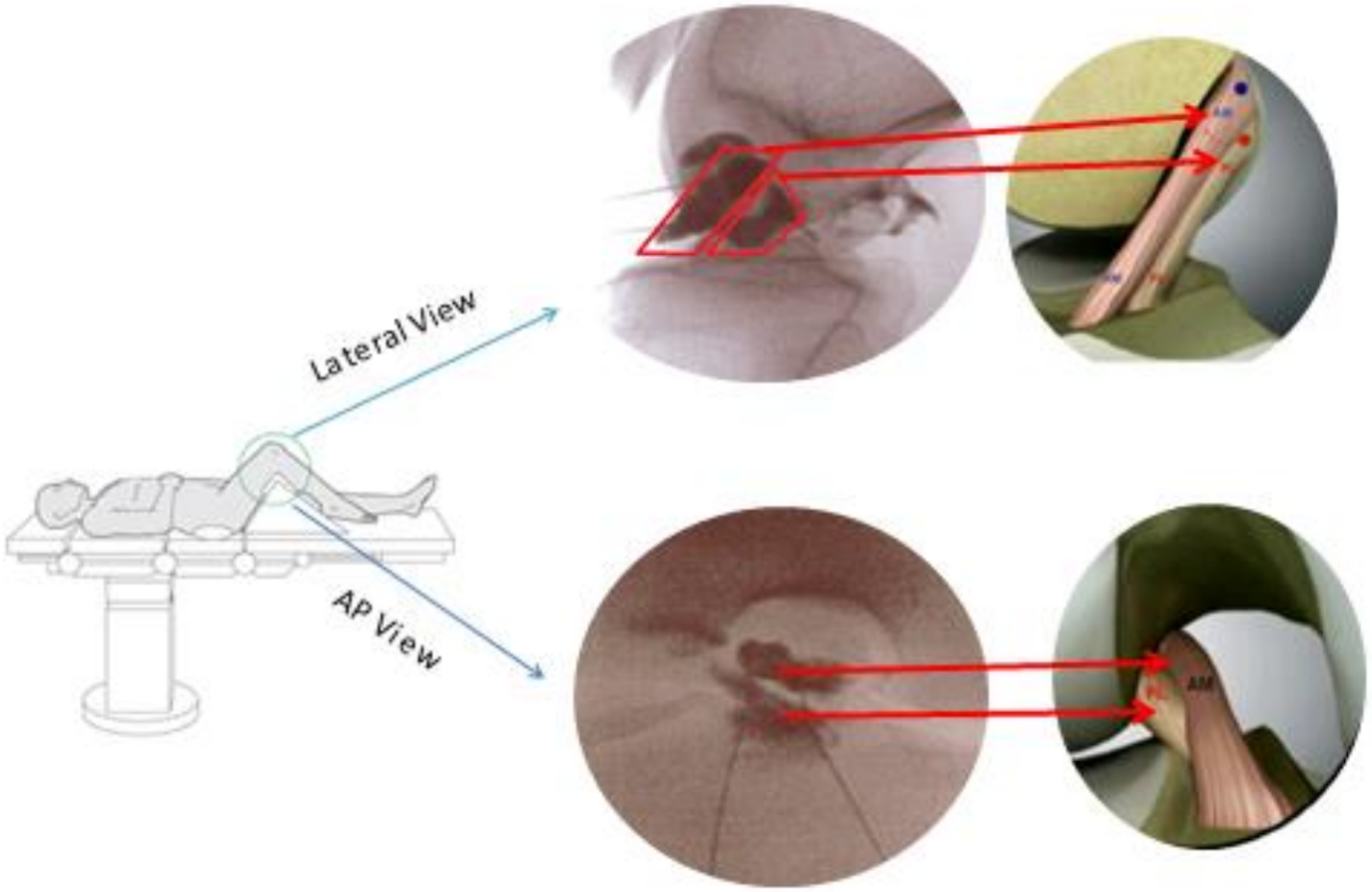
Simple Injections

Interventional Orthopedics

Surgery




R
L



Injecting the ACL bands (AM and PL) under fluoro

Shoulder SLAP tear injection

Protocols used are all over the map

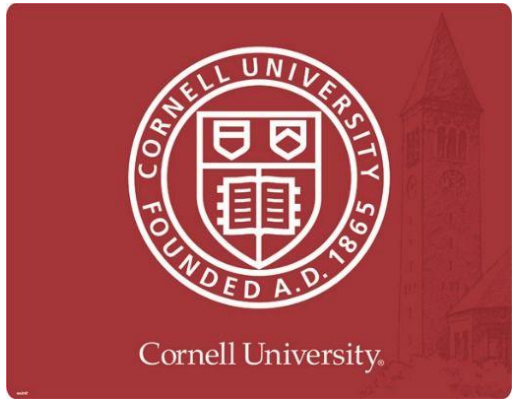
- Treat all the involved structures, not just the joint

The clinical outcome and complications data is rarely collected

- Need registry tracking
- Should publish data regularly

Partner with university physicians to produce Orthobiologic guidelines:

The following academic medical centers (and UVM!) have physicians <u>using</u> PRP and Bone Marrow Concentrate:



Recent Academic Delphi Panel on Bone Marrow Concentrate Use Guidelines…

Academics associated with more than a dozen universities took part

These included physicians from Mayo Clinic, Emory, UCLA, University of Michigan, Univ of Pittsburgh, Stanford, HSS, Rutgers, Univ of British Columbia, Univ of Toledo, Dartmouth, and Cornell

Delphi Panel Recommendation	REGENEXX CLINICS
Treatment Registry	**YES**
Candidacy Grades	**YES**
Expanded Informed Consent	**YES**
Publication of Research	**YES**
Advertising Grounded in Science	**YES**
Use of an IRB for New Applications	**YES**
Use of Imaging Guidance	**YES**
Minimal Level of Clinical Research Evidence Before Use	**Case Series to Comparison Trial**

Comparing Health Evidence: A Self-funded Plan Perspective

Best Evidence Synthesis/Qualitative Evidence Synthesis (QES)

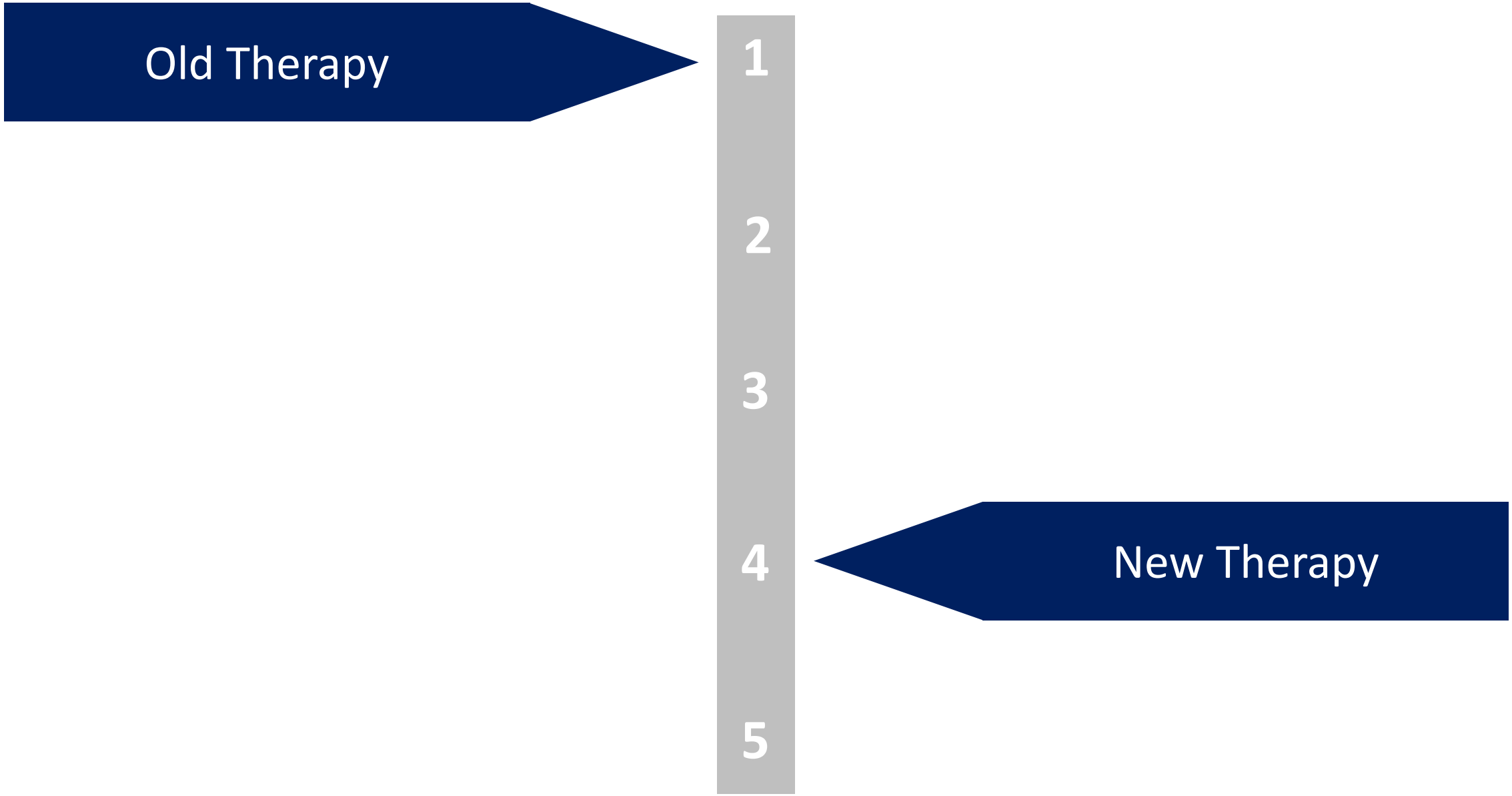
- “Methods for conducting QES have developed against a backdrop of increasing demand from decision makers for evidence that goes beyond ‘what works’; a form of evidence traditionally established through systematic reviews of quantitative evidence, particularly reviews of randomized controlled trials (RCT). It is increasingly recognized that healthcare provision involves complex, multifactorial decisions which may require more than this original ‘rationalist’ model of synthesis can provide.[2]”
- *Flemming K, Booth A, Garside R, et al. Qualitative evidence synthesis for complex interventions and guideline development: clarification of the purpose, designs and relevant methods. BMJ Global Health 2019;**4:**e000882.*

The steps we'll use here:

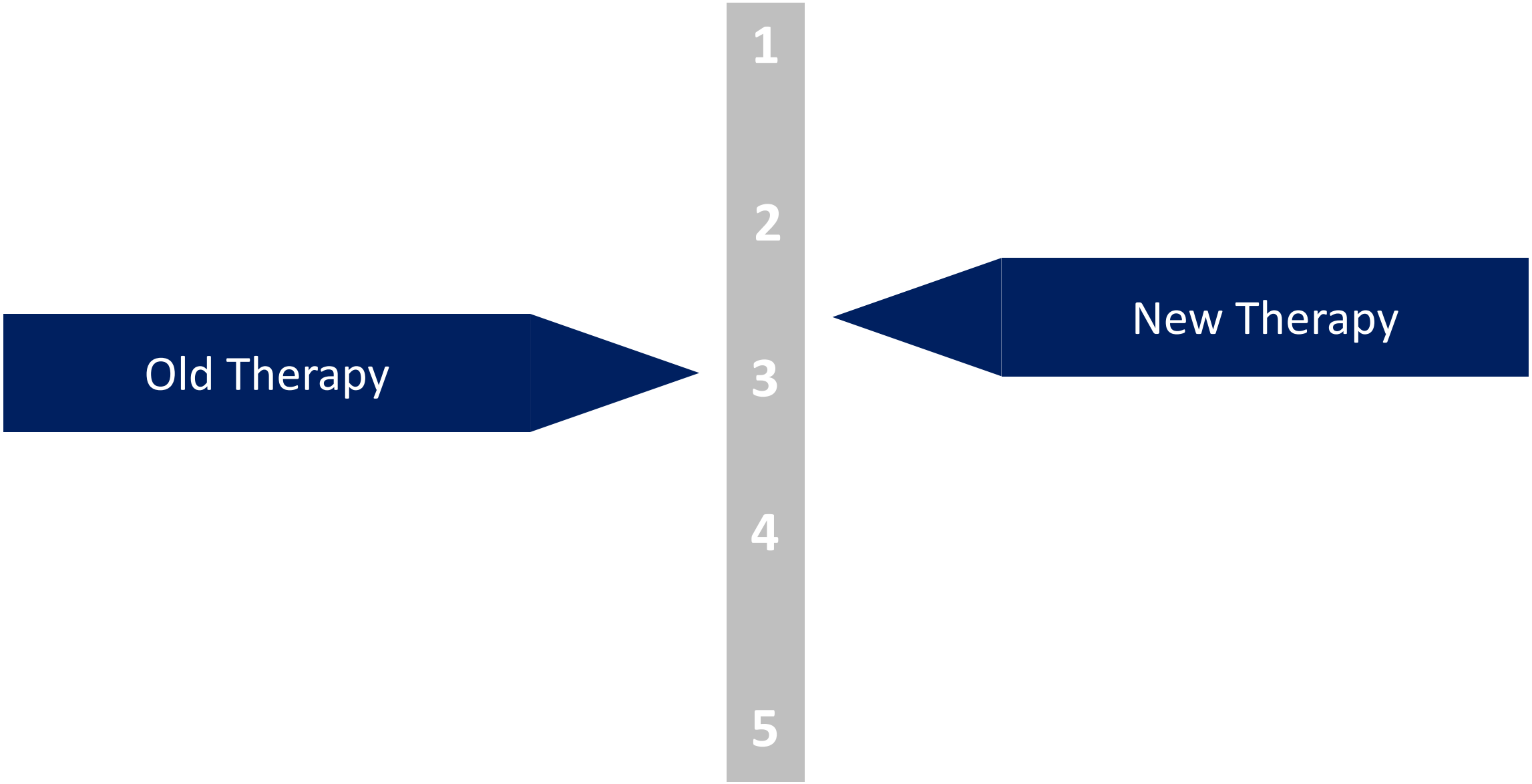
What's the prevailing level of evidence for what you currently cover

What's the prevailing level of evidence for the new therapy

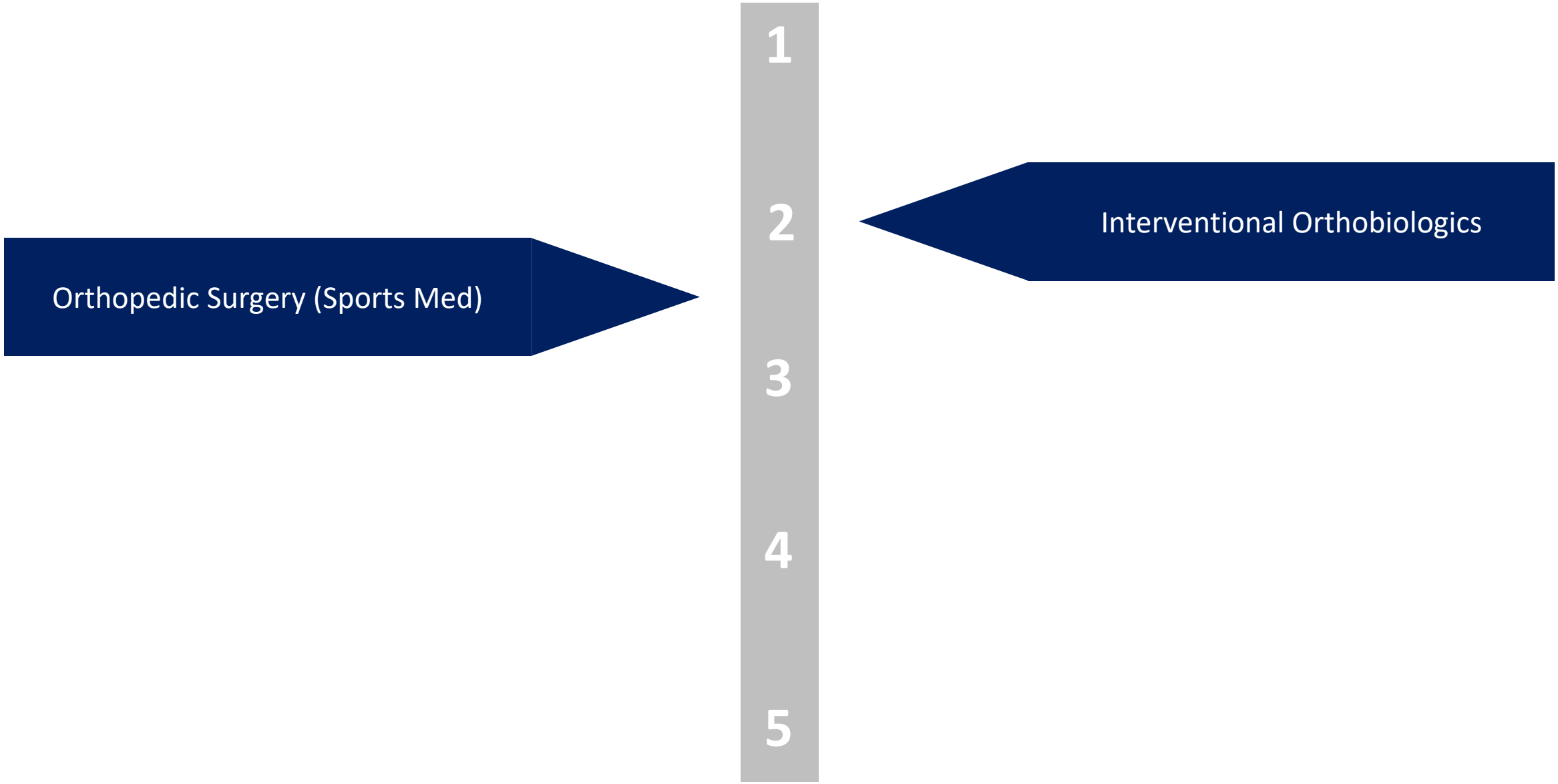
A Poor Health Plan Addition:



A Good Health Plan Addition:



What I will show:



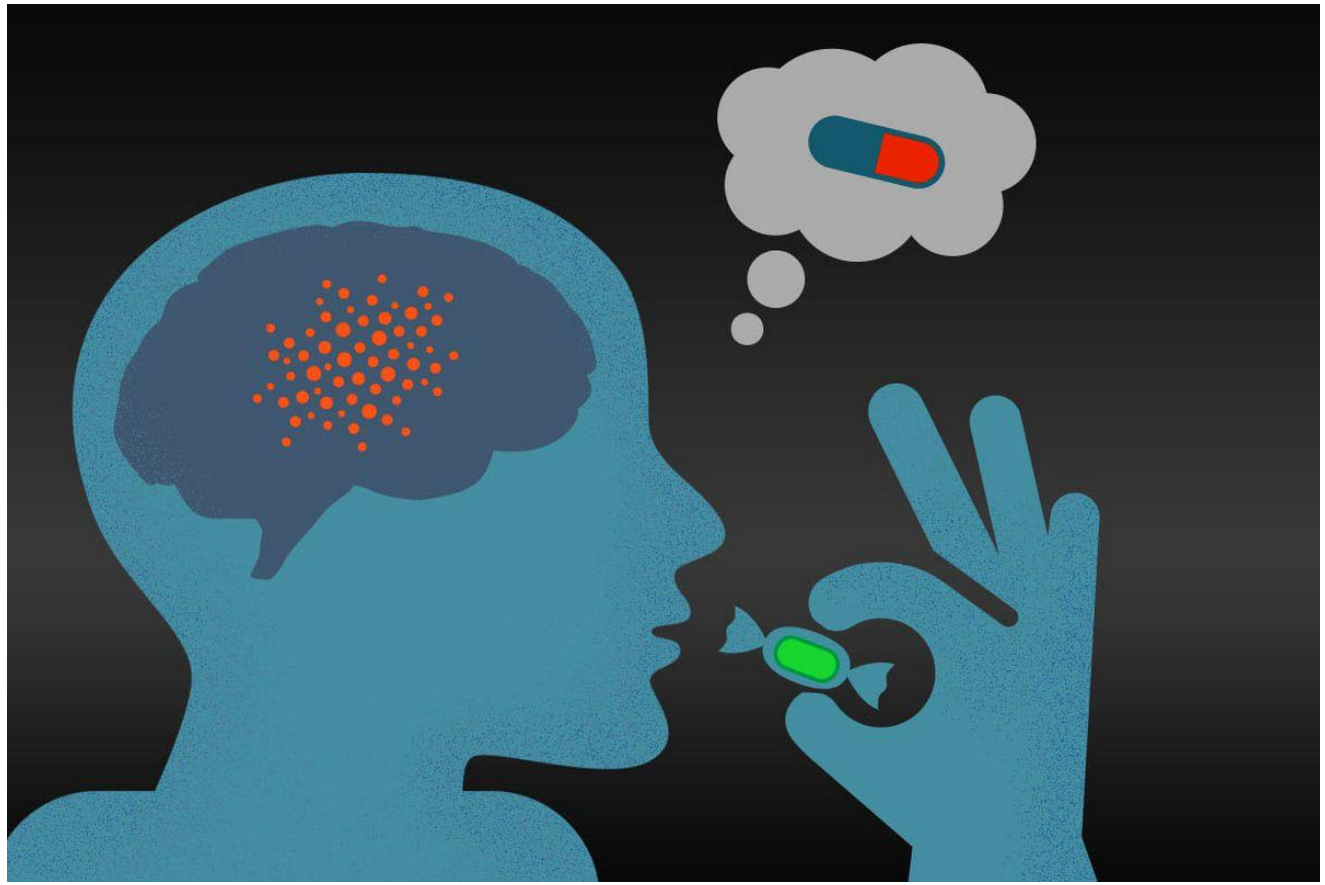
Orthopedic Surgery?

Does orthopedic surgery work?

- For 80% of the elective sports medicine procedures the answer is that we don't know
  - Lohmander L Stefan, Roos Ewa M. The evidence base for orthopaedics and sports medicine *BMJ* 2015; 350 :g7 835
- For the other 20% with high level data, most are not RCTs against sham

A standard in clinical trials has long been a placebo control:

- The problem is that few RCTs in orthopedic surgery have a sham arm
- The most common control arm is physical therapy



Grades Used for the purposes of this presentation)

A-Statistically Robust, well-designed randomized controlled trials

B-Statistically Robust, well-designed cohort studies

C-Multi-site observational studies

D-Single-site observational studies

E-In the absence of strong and compelling scientific evidence, medical policies based upon national consensus statements by recognized authorities

F-Procedure shown in RCTs to be ineffective or no better than conservative care

F- Large, statistically robust RCT showing no efficacy vs. sham.

Arthroscopic Debridement in Knee OA

N Engl J Med 2008; 359:1097-1107

F- 3 large, statistically robust RCTs showing no efficacy vs. PT or sham.

Meniscectomy for all meniscus tear indications-no OA, OA, and locking

N Engl J Med 2013; 368:1675-1684
N Engl J Med 2013; 369:2515-2524
Ann Intern Med. 2016;164(7):449-455.

A or F?

A- 1 RCT showing minimal efficacy (NTT for 15% functional improvement is 5-6) and 3 in 4 patients at 1 year cancelled TKA due to results with PT.

F- Analysis of OAI and MOST datasets shows that TKA is not cost-effective.

Total Knee Arthroplasty for OA

No Sham Control Study Has Ever Been Conducted!

N Engl J Med. 2015 Oct 22;373(17):1597-606

BMJ 2017;356:j1131

F? - Meta-analysis couldn't conclude based on high-level evidence that surgical outcomes were better than conservative outcomes (meaning only low quality evidence supported most metrics in the study).

ACL Reconstruction for ACL Tear

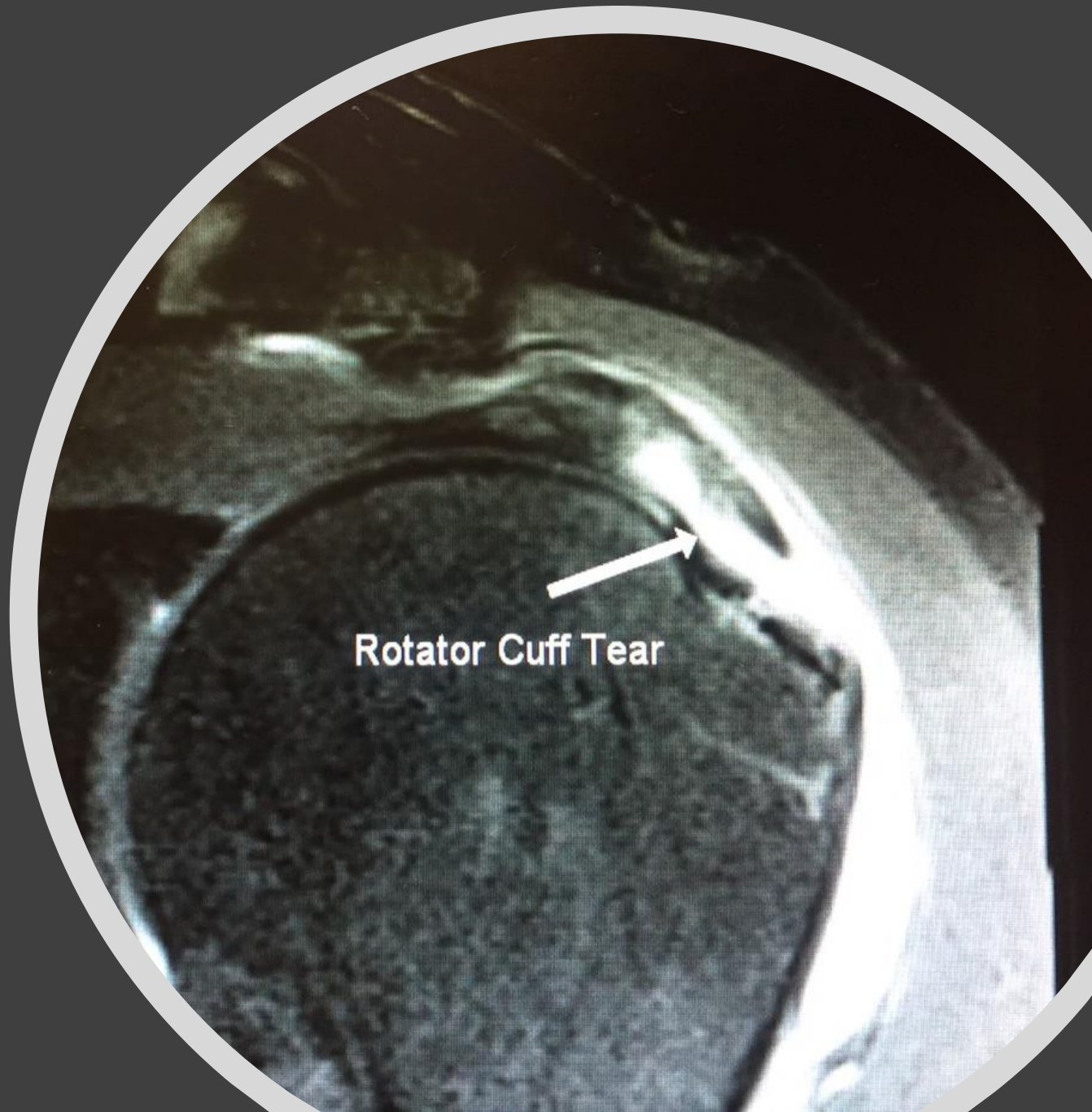
No Sham Control Study Has Ever Been Conducted!

Cochrane Database Syst Rev. 2016 Apr 3;4:

F-Meta-analysis of 5 RCTs indicated no benefit from decompression and the relationship to structural acromion type and outcome was not confirmed. Second meta-anlysis confirmed.

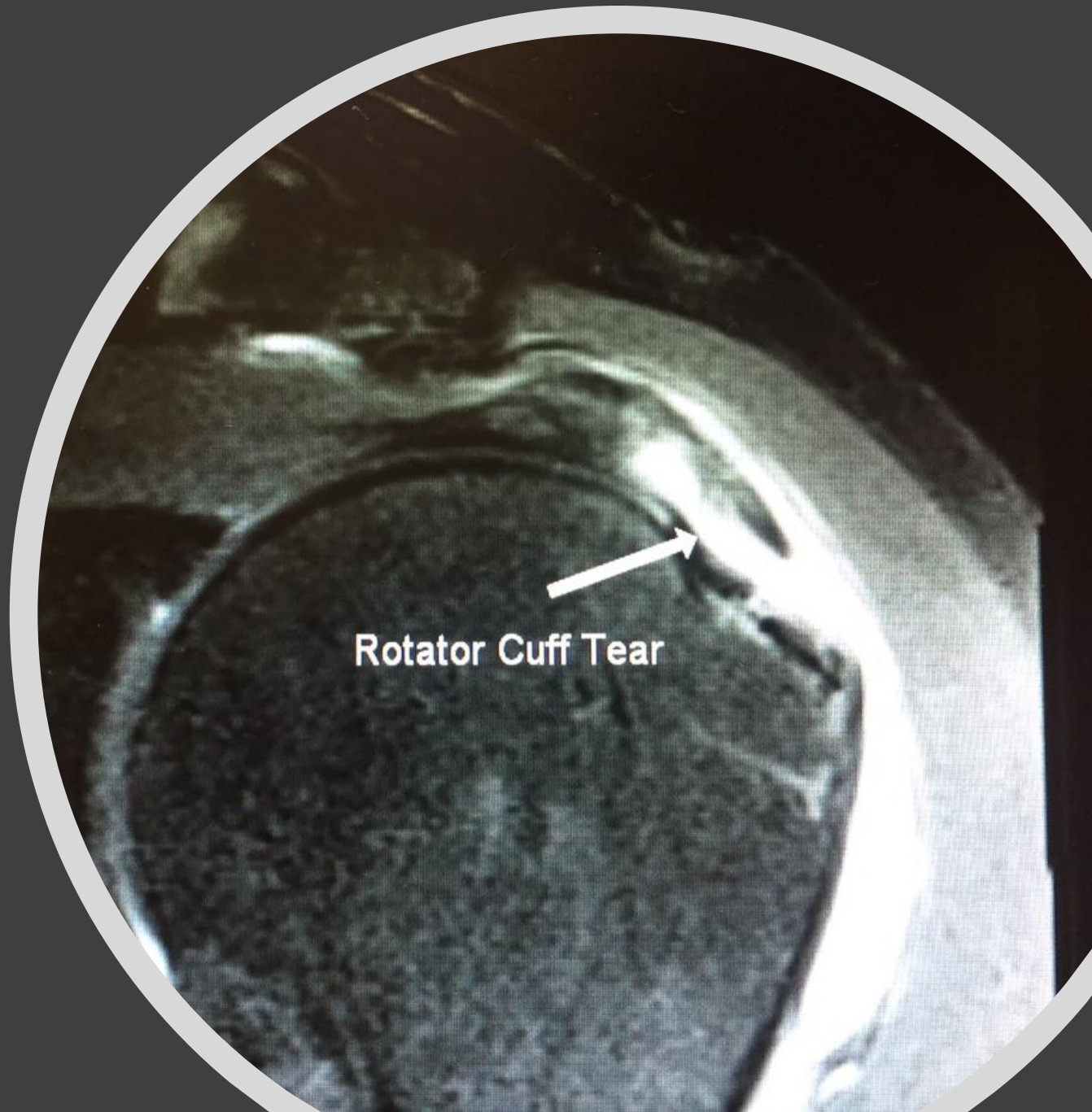
Shoulder Rotator Cuff Repair with Decompression or Shoulder Pain

Springerplus. 2016 May 21;5(1):685.
Br J Sports Med. 2019 Jan 15.



F-Meta-analysis of many RCTs indicated no difference between surgical repair and conservatively treated groups.

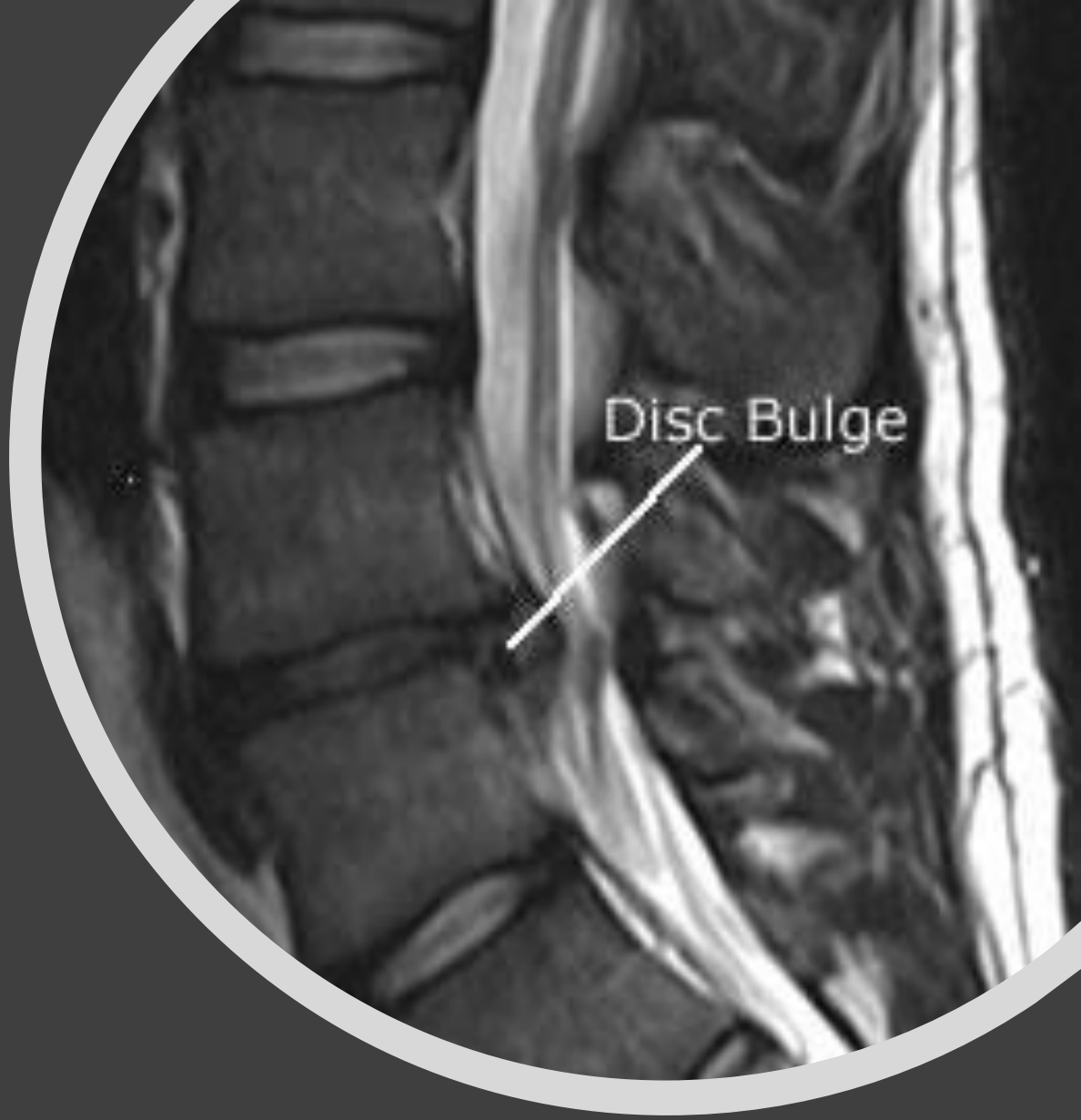
Shoulder Rotator Cuff Repair for Full Thickness Tear



Am J Sports Med. 2018 Jun 1.

F-Meta-analysis on 5 RCTs, fusion no better than conservative care but with a 10-24% complication rate.

Lumbar Fusion for DDD



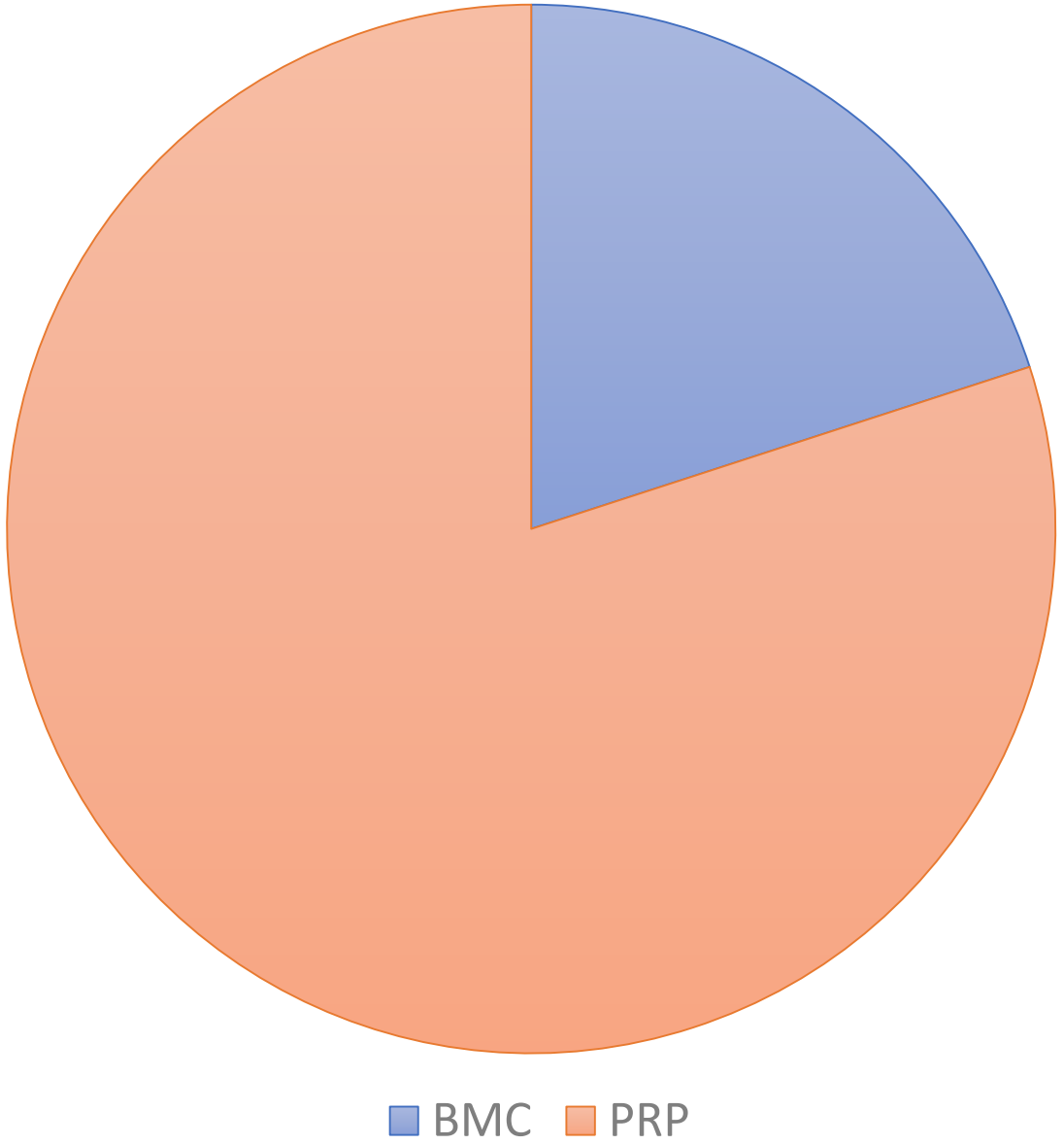
Cochrane Database Syst Rev. 2016 Jan 29;

Interventional Orthopedics

Major Differences in Interventional vs. Surgical Approaches

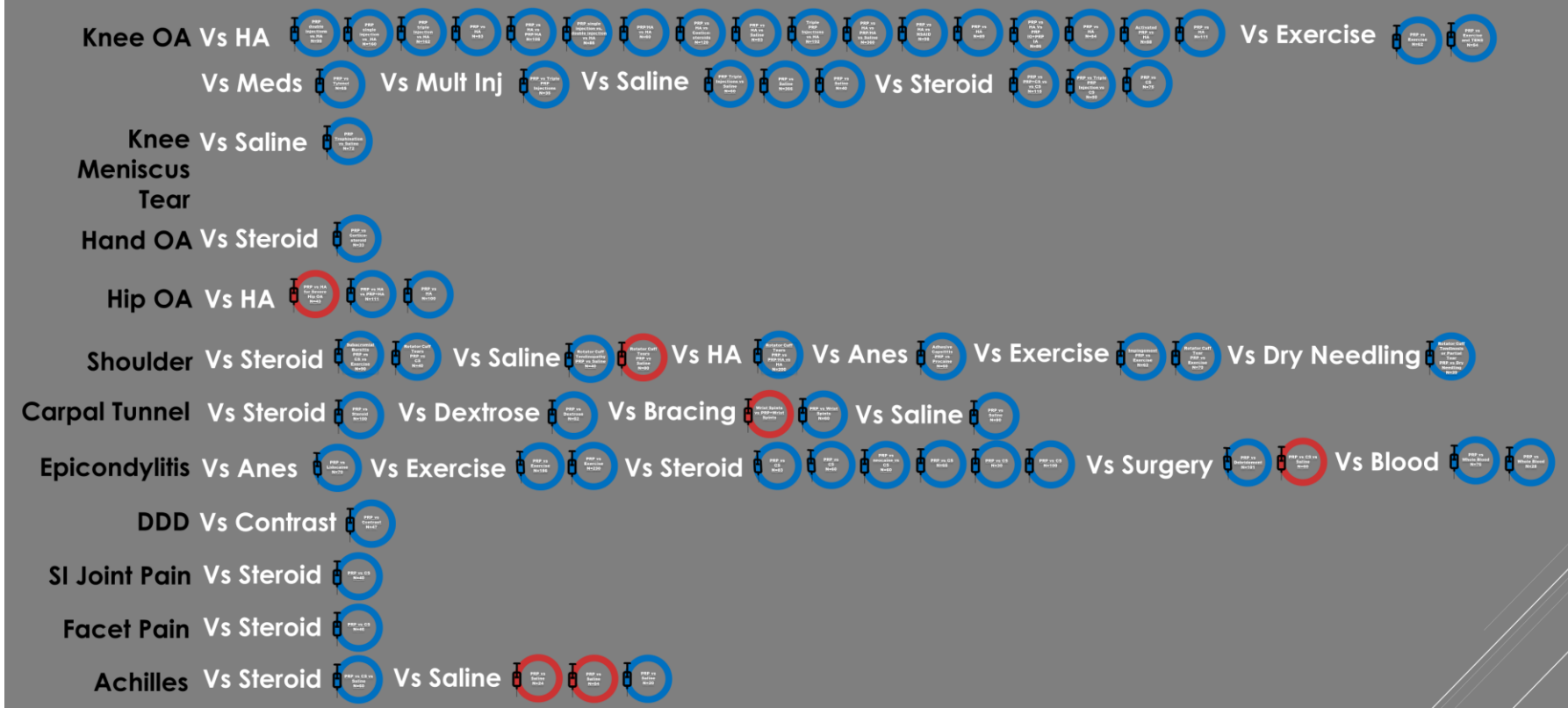
	Orthopedic Surgery	**Interventional Orthopedics**
Invasiveness	More	Less
Need for Rehab	To return the patient back to their pre-op function	To fix biomechanical problems that caused the problem
Complication Rates	Moderate to Low	Low to Minimal
Average Quality of Published Research	3	2
In-Hospital or Surgery Center Facility Fees	Yes-Expensive	No
Add-on Fees for Devices and Implants	Yes-Expensive	No

What should be the frequency of orthobiologics use?



Platelet Rich Plasma Injection Randomized Controlled Trials

If you're interested in using this slide in presentations or for any other purpose, please request permission in writing from Chris Centeno, M.D. at centenooffice@centenoschultz.com.



Each circle represents a randomized controlled trial that used PRP to treat an orthopedic indication. Each circle has the number of patients treated and the comparison group listed. **Click on the text in each circle to be taken to the PubMed link**. Only studies listed in the US National Library of Medicine were included. The blue circles represent studies where PRP was effective, beat the comparison group, or was non-inferior to the standard of care. The red circles mean that PRP was inferior to a known placebo.

PRP effective in 60/66 RCTs

ReGenexx

A-Meta-analysis of 10 studies (describing multiple RCTs) with two used for data aggregation (low risk of bias) concluded that PRP used to treat mild to moderate knee OA was effective.

Knee OA

Int J Rheum Dis. 2017 Nov;20(11):1612-1630

A-Meta-analysis 5 RCTs comparing corticosteroid injections with PRP found that PRP was effective in the long-run and corticosteroids only provided short-term relief.

Elbow Epicondylitis

SICOT J. 2018;4:11.

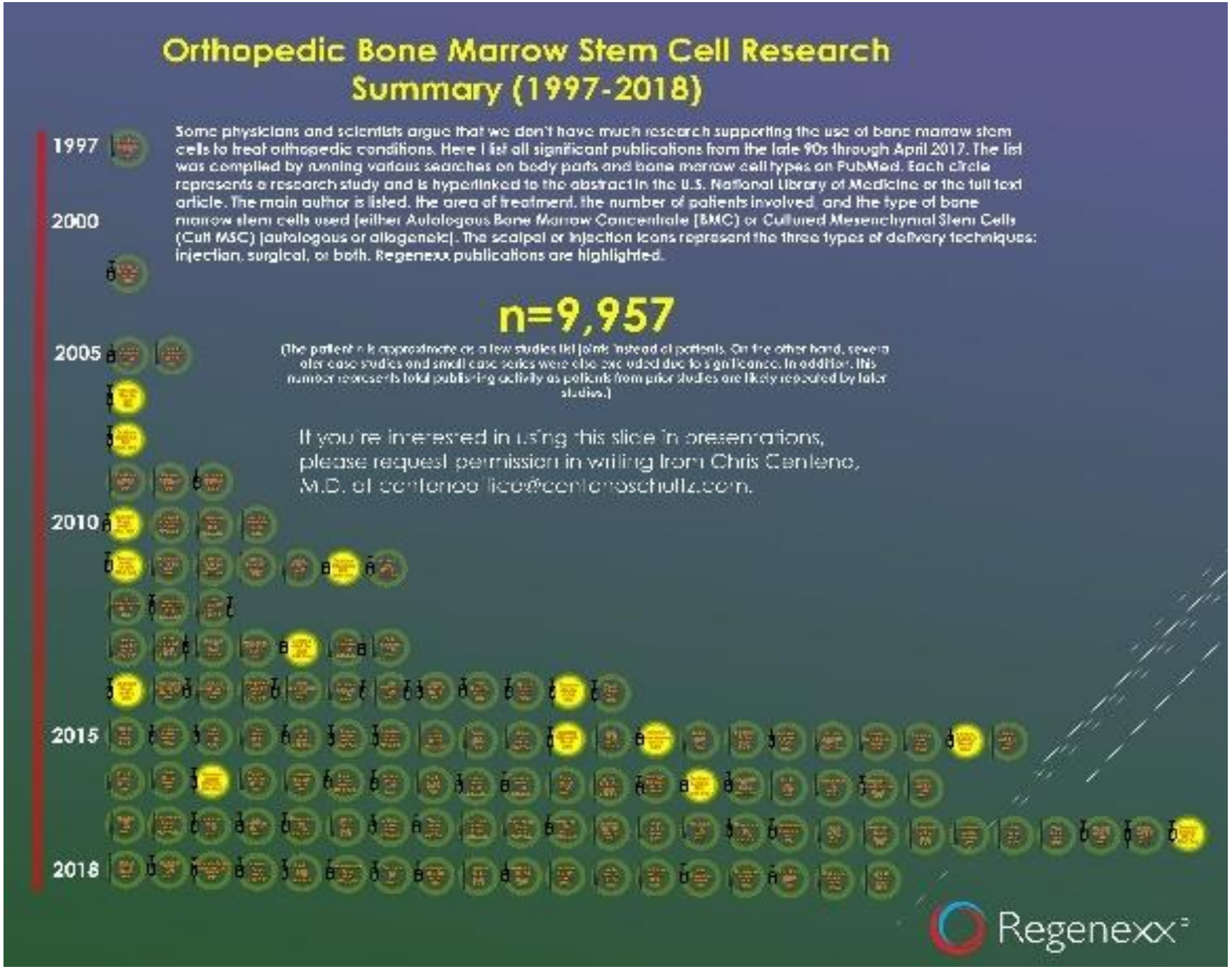
A-Meta-analysis of 14 level 1 studies of both surgical and injection based treatment for shoulder tendinopathy and rotator cuff tears concluded that PRP was effective for tendon healing.

Shoulder Rotator Cuff Injuries

Am J Sports Med. 2018 Jul;46(8):2020-2032.

Regenexx Grades High Dose Bone Marrow Concentrate

Orthopedic Bone Marrow Stem Cell Research Summary (1997-2018)



Some physicians and scientists argue that we don't have much research supporting the use of bone marrow stem cells to treat orthopedic conditions. Here I list all significant publications from the late 90s through April 2017. The list was compiled by running various searches on body parts and bone marrow cell types on PubMed. Each circle represents a research study and is hyperlinked to the abstract in the U.S. National Library of Medicine or the full text article. The main author is listed, the area of treatment, the number of patients involved, and the type of bone marrow stem cells used (either Autologous Bone Marrow Concentrate [BMC] or Cultured Mesenchymal Stem Cells (Cult MSC) [autologous or allogeneic]. The scalpel or injection icons represent the three types of delivery techniques: injection, surgical, or both. Regenexx publications are highlighted.

n=9,957

(The patient n is approximate as a few studies list clinic instead of patients. On the other hand, several older case studies and small case series were also excluded due to significance. In addition, this number represents total publishing activity as patients from prior studies are likely reported by later studies.)

Regenexx

A-RCT. 48 patients in cross-over with physical therapy.

Knee OA

Centeno et al. J Transl Med (2018) 16:355

B-840 procedure case series comparing the efficacy of bone marrow concentrate vs. same with adipose graft.

Knee OA

Biomed Res Int. 2014;2014:370621.

C-373 patient case series where dose versus response was determined and a minimum dose of 400M TNCC was determined.

Knee OA

BMC Musculoskelet Disord. 2015 Sep 18;16:258.

A-Still recruiting-50 patient RCT with cross over to physical therapy. Excellent preliminary results shown in abstract section.

Partial to complete ACL Tears

D-Two single site MRI before/after case series with pain/functional outcome.

Partial to complete ACL Tears

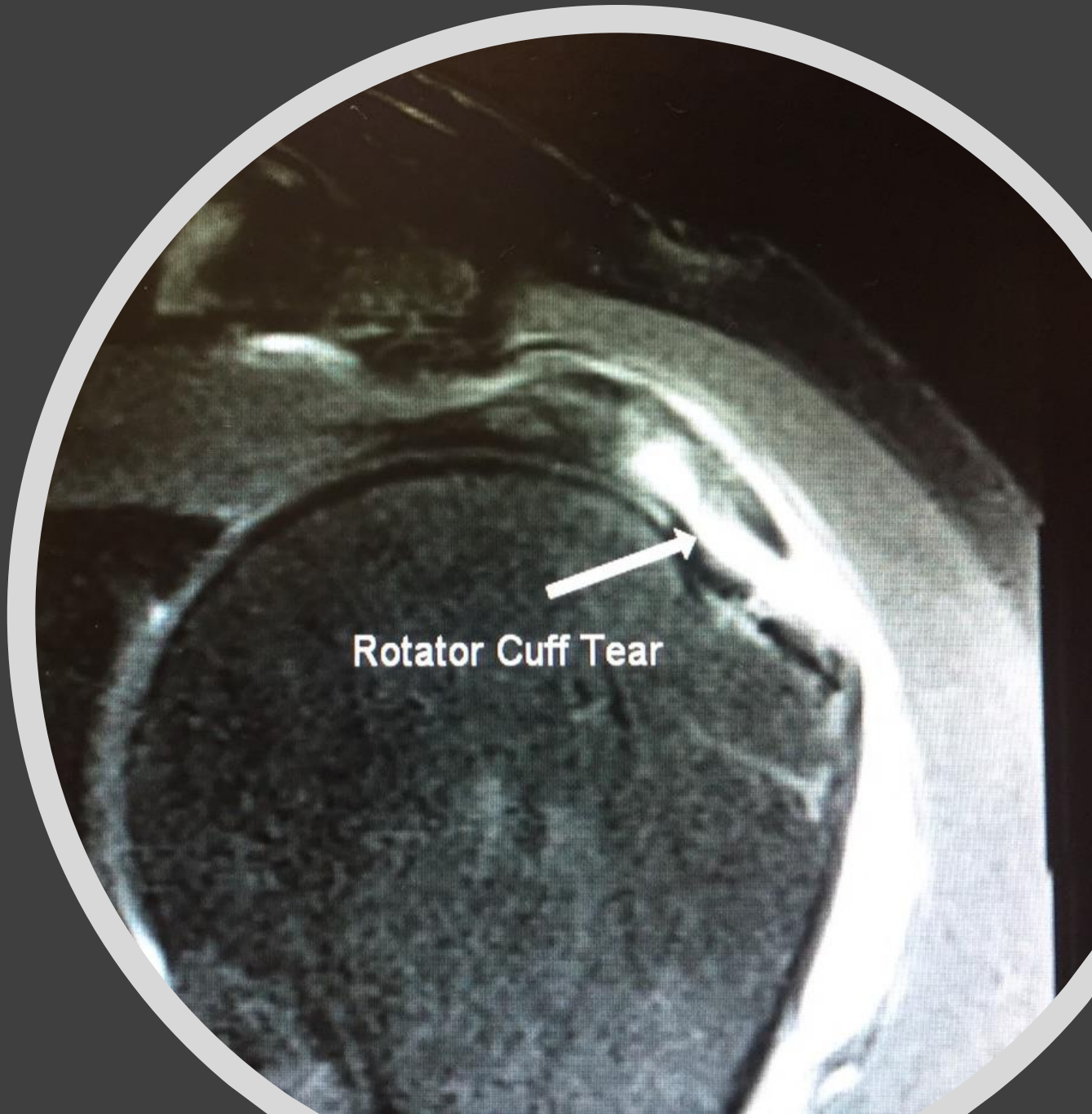
J Pain Res. 2015 Jul 31;8:437-47.

J Transl Med. 2018 Sep 3;16(1):246.

C-case series of 102 patients with outcome collected from multiple sites

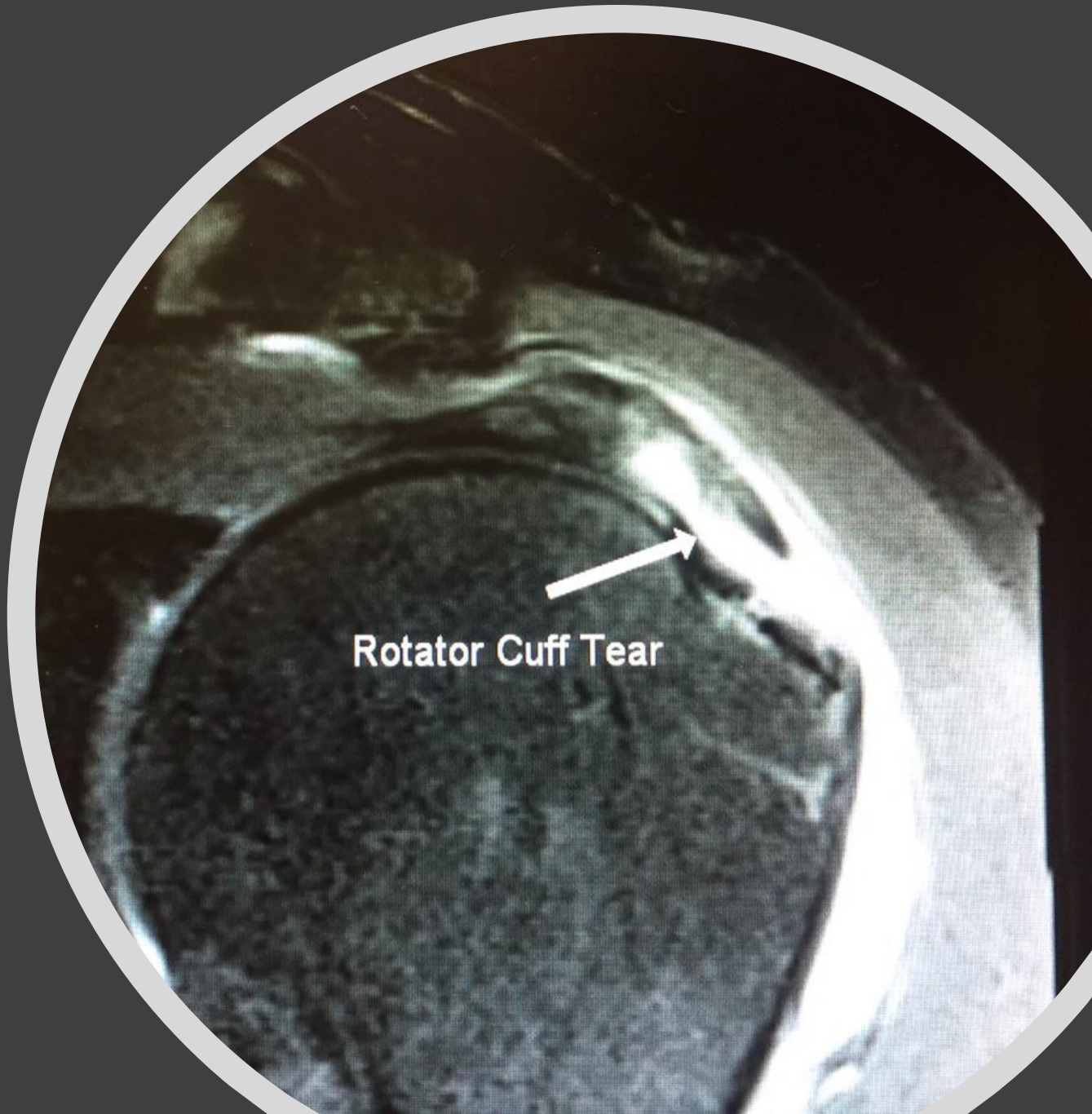
Shoulder OA and Rotator Cuff Tears

J Pain Res. 2015 Jun 5;8:269-76.



A-Still recruiting-50 patient RCT with cross over to physical therapy. Excellent preliminary results shown in abstract section.

Partial to Complete Rotator Cuff Tears



C-case series of 196 patients with hip OA, determined that patients over 55 have less robust results.

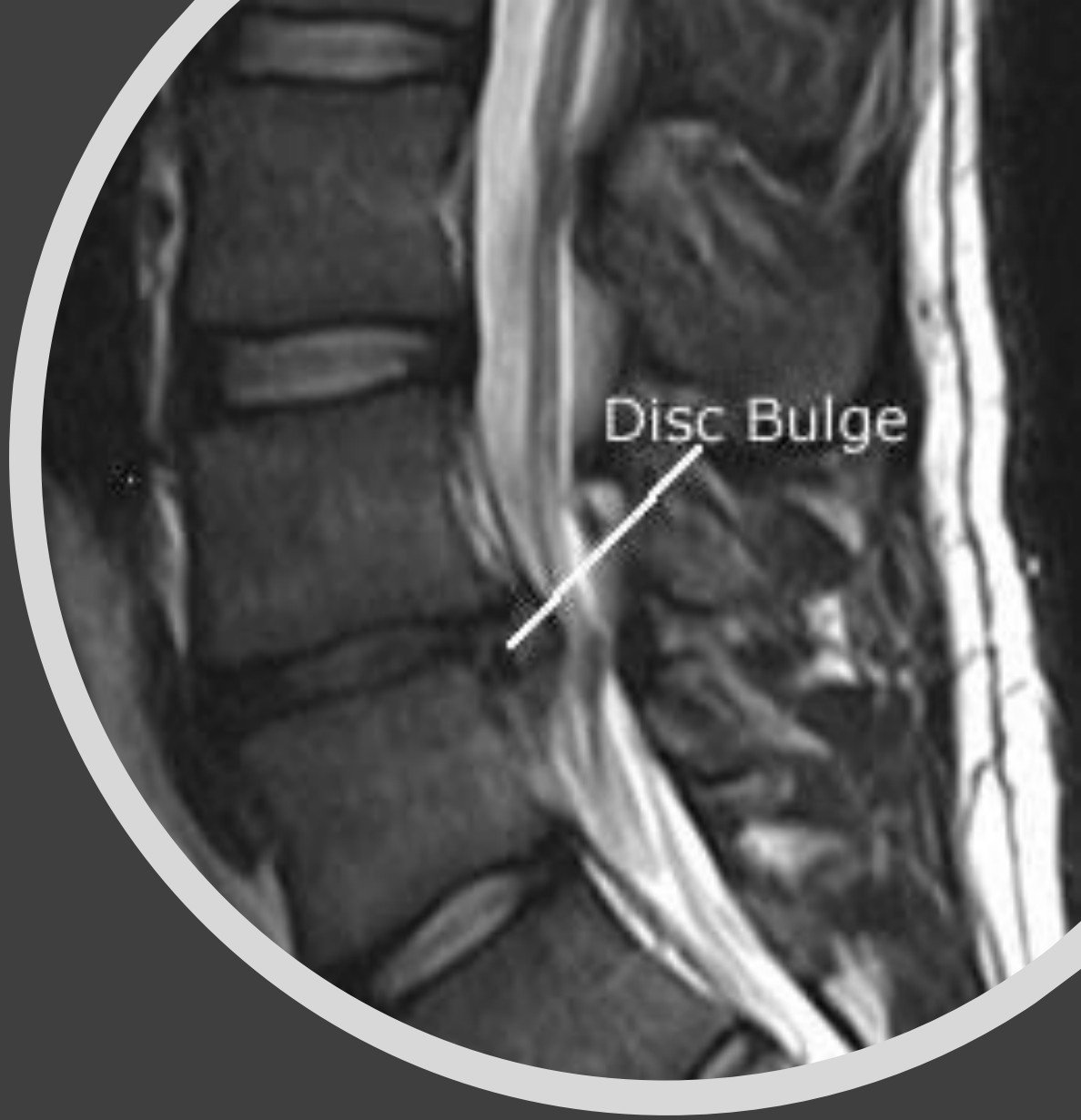
Hip OA

Centeno et al., J Stem Cell Res Ther 2014, 4:10

C-case series of 470 patients with lumbar radiculopathy treated with platelet lysate epidurals

Lumbar Disc Bulge

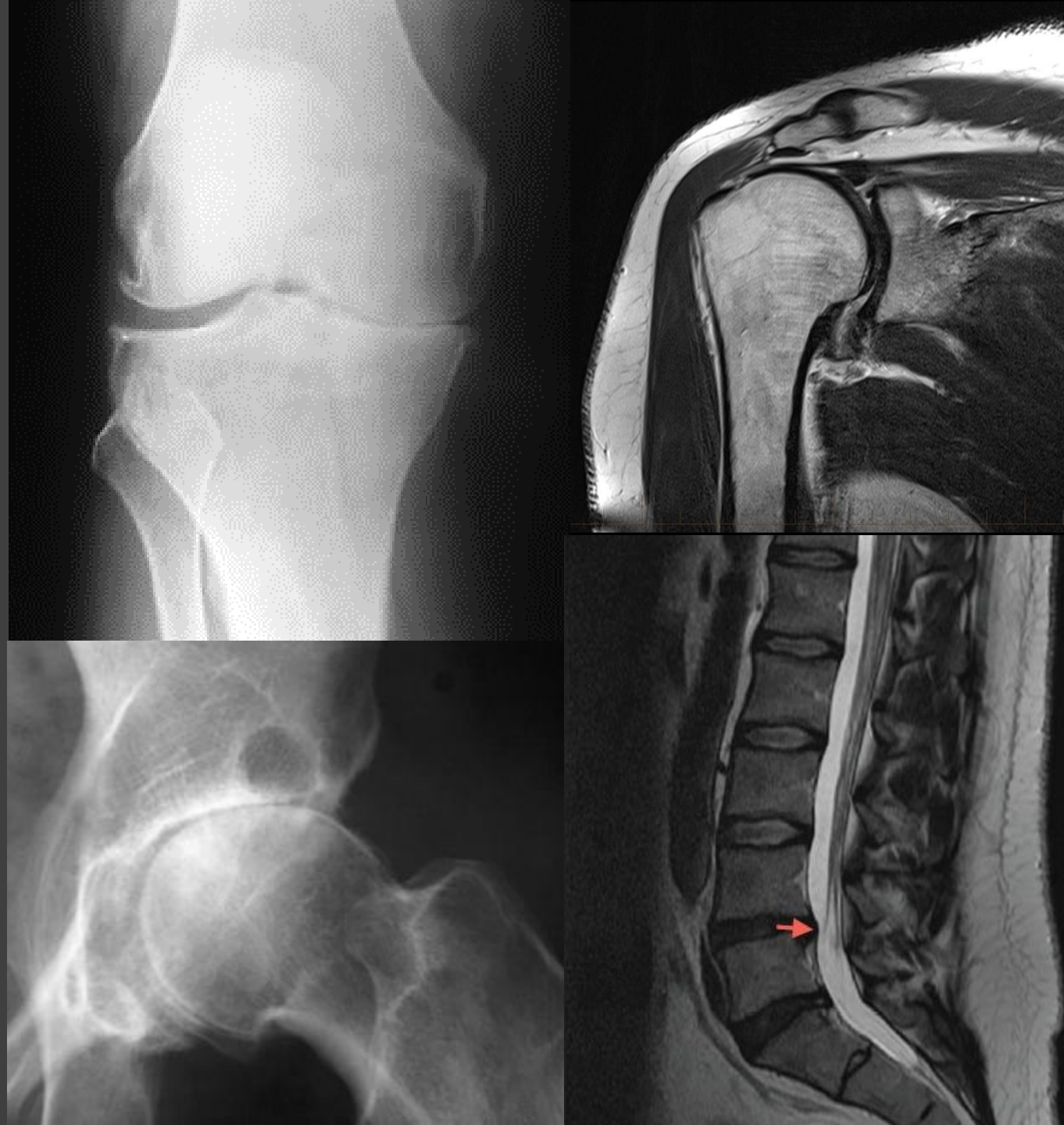
J Exp Orthop. 2017 Nov 25;4(1):38.



C-Multi-site all complications safety paper with independent adjudication of SAEs showing that the safety of BMC and MSC procedures are better than the surgical procedures they replace.

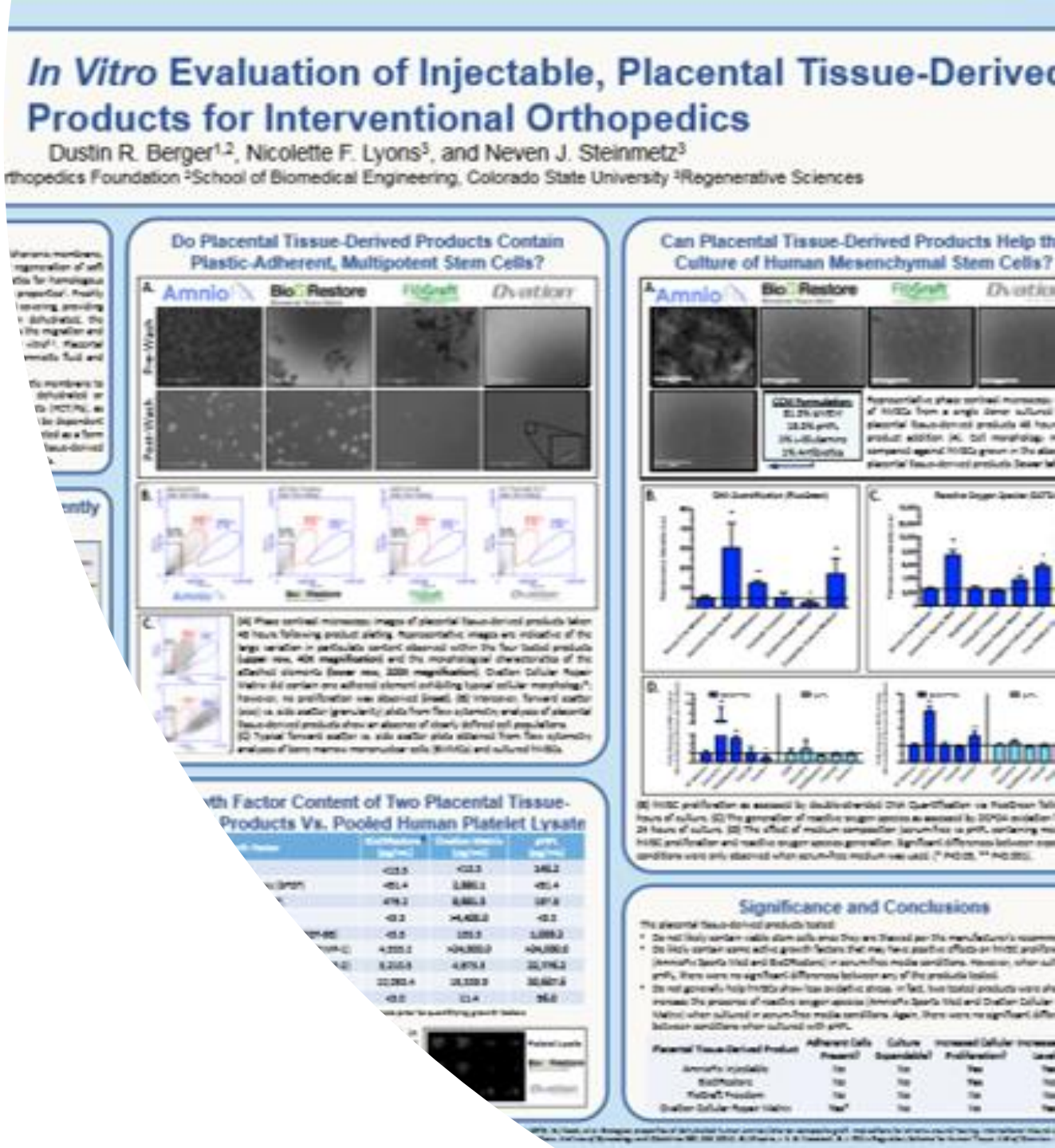
Safety in >3,000 procedures over 9 years in multiple body areas

Int Orthop. 2016 Aug;40(8):1755-1765



The biggest abuse we see is amniotic, placental, or cord “stem cell” injections.

3 national labs (plus our main lab) extensively tested these products and found them to be dead tissue with no viable cells…



They are also regulated by THE FDA
as *dead tissue* products.

How do they work?

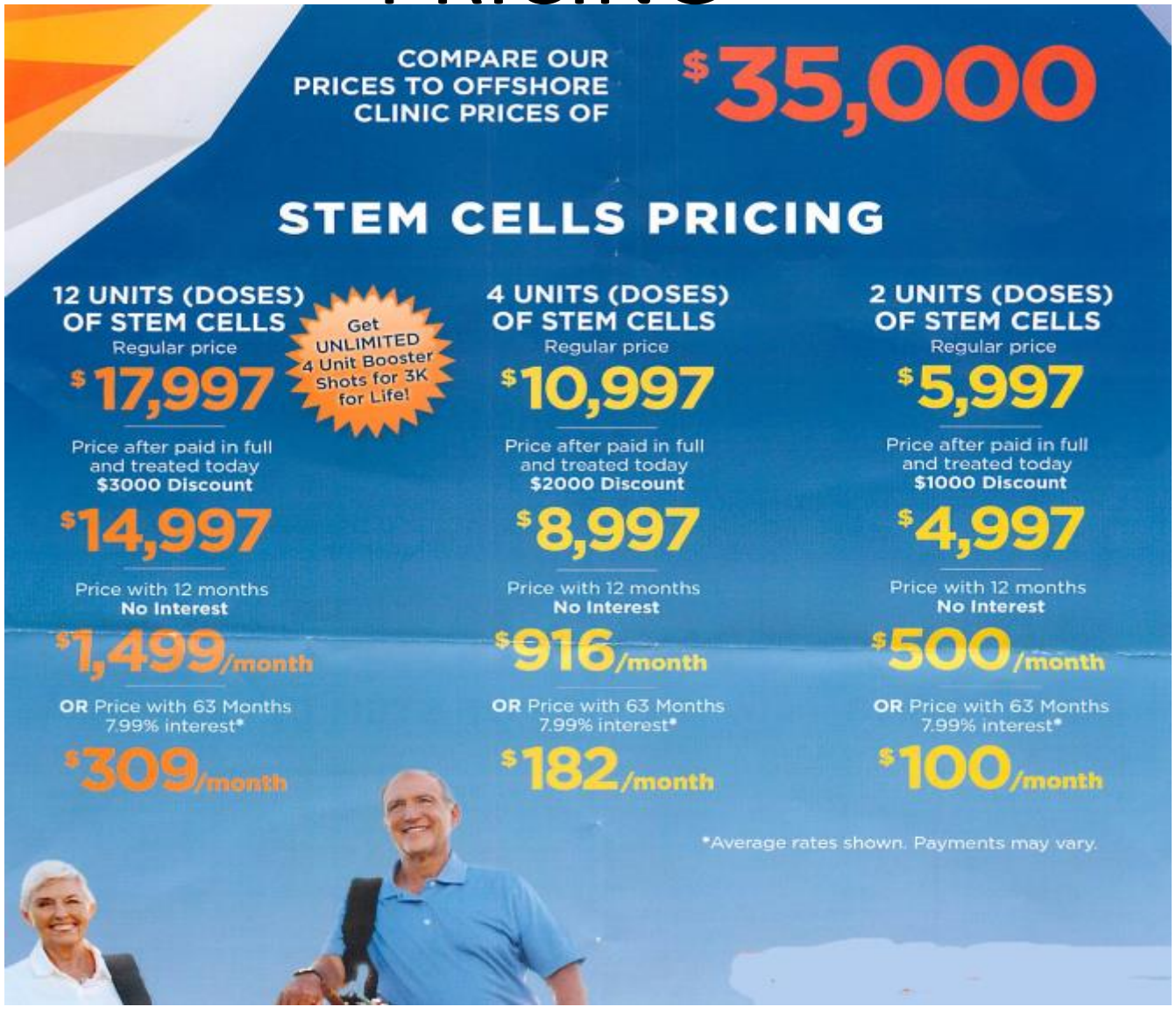
They are a collagen and growth factor shot.

Any claims that these are “stem cell” procedures is consumer fraud.

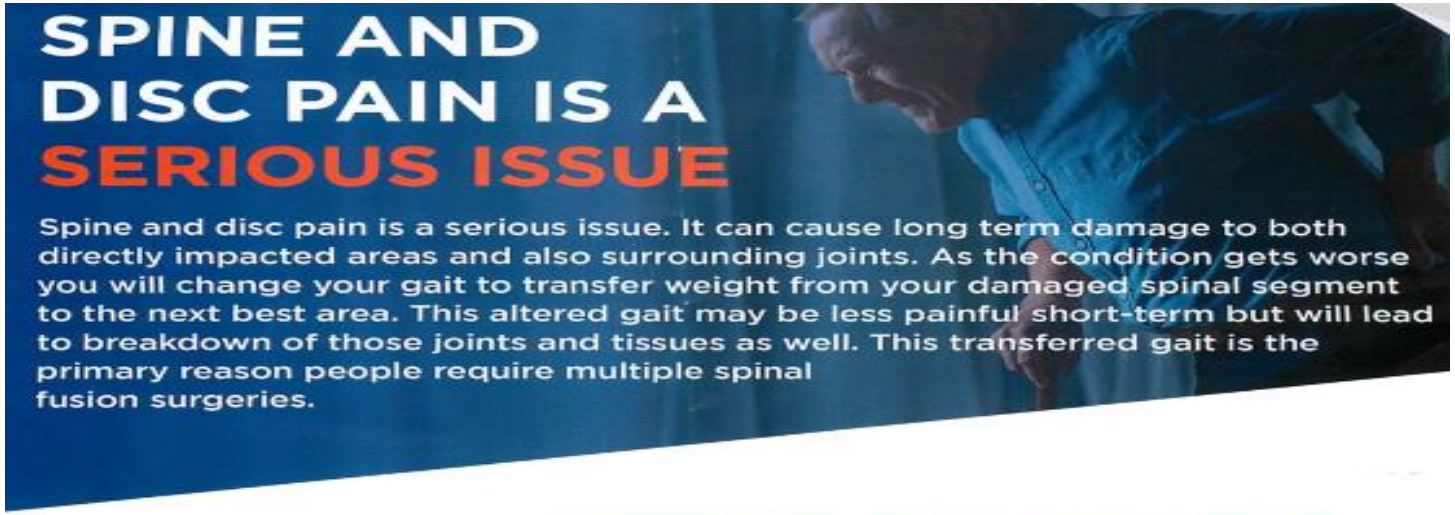
These are often performed by NPs owned by or in a chiropractic office

- Usually no guidance
- By a NP, PA or ND
- Often IV or into muscle, not the joint/tendon needed
- These are dead cell products
- The costs are often higher than having BMC cells injected under image guidance

TYPICAL FRAUD CLINIC'S HARD SELL AND PRICING



TYPICAL FRAUD CLINIC'S HARD SELL



The research bait and switch…

- Clinics list research studies
- The studies have little to do with the procedure they offer
- No research done on what they offer

When you should run…

- Treats every A-Z disease
- Promises extremely high success rates that seem too good to be true
- Claims that a doctor took a “stem cell fellowship” from AAAAM
- The “physician” is not an MD or DO
- The clinic just opened, but claims to have treated thousands of patients
- Claim they will “regrow your knee cartilage”

CONCLUSIONS

- Elective orthopedic surgery should be a last resort
- Well done physical therapy is the mainstay of treatment
- Interventional regenerative orthopedic medicine injections with PRP and BMC are an excellent and researched approach to many musculoskeletal conditions, and are a bridge between PT and surgery
- The use of birth tissue products (amniotic and umbilical cord) as a stem cell source is fraud