



Osteoarthritis: Past, Present and the Future

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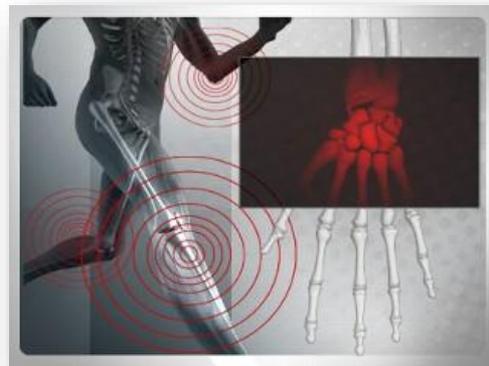
 @ProfDavidHunter



Declaration of interest

I declare that in the past three years I have:

- received royalties from: DJO for a patellofemoral brace patent
- Consulted for Flexion, Tissuegene, Merck Serono
- Supported by an NHMRC Health Practitioner Fellowship.





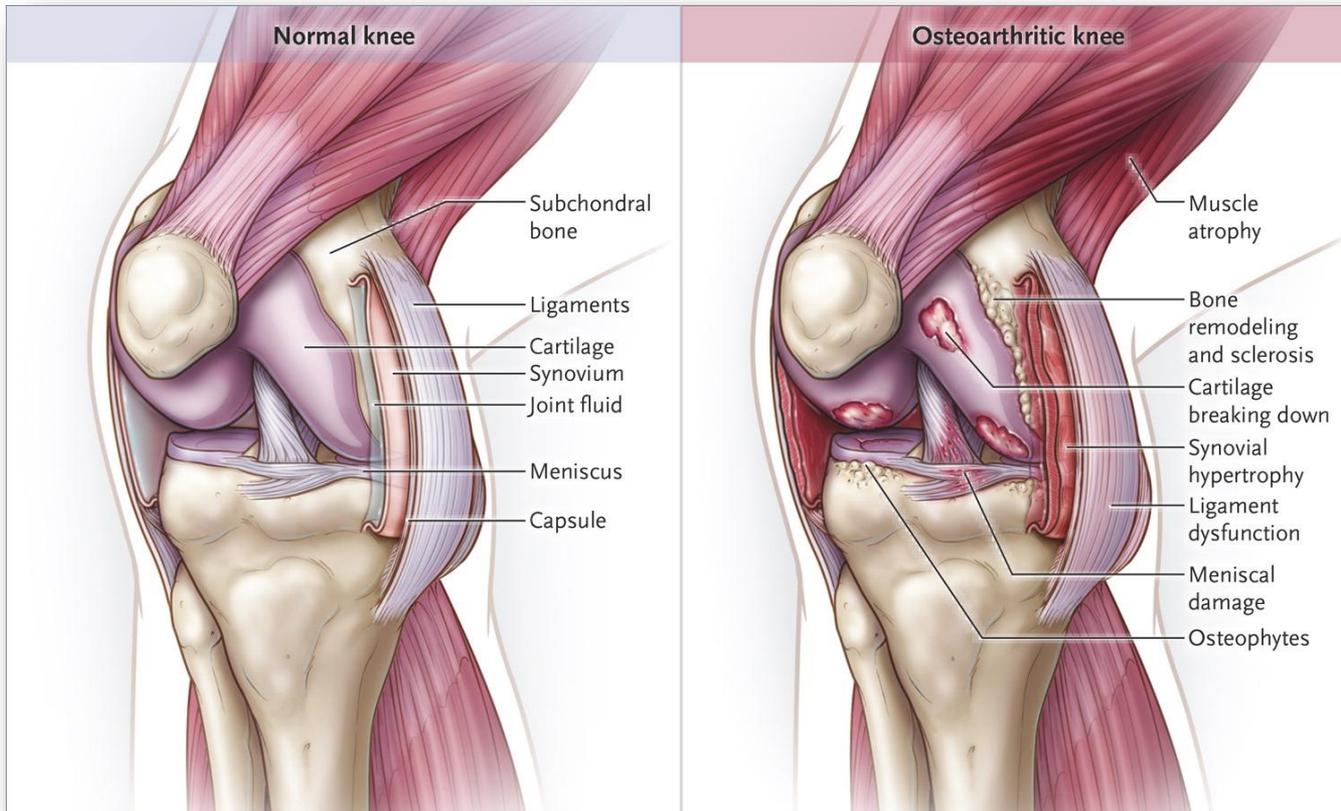
Evidence-based Medicine

- Lower extremity osteoarthritis management needs a paradigm shift. **Br J Sports Med.** 2011 Apr;45(4):283-8.
- OARSI guidelines for the non-surgical management of knee osteoarthritis. **Osteoarthritis Cartilage.** 2014 Mar;22(3):363-88.
- Clinical algorithms to aid osteoarthritis guideline dissemination. **Osteoarthritis Cartilage.** 2016 Sep;24(9):1487-99.
- Osteoarthritis: Models for appropriate care across the disease continuum. **Best Pract Res Clin Rheumatol.** 2016 Jun;30(3):503-535.



What is osteoarthritis?

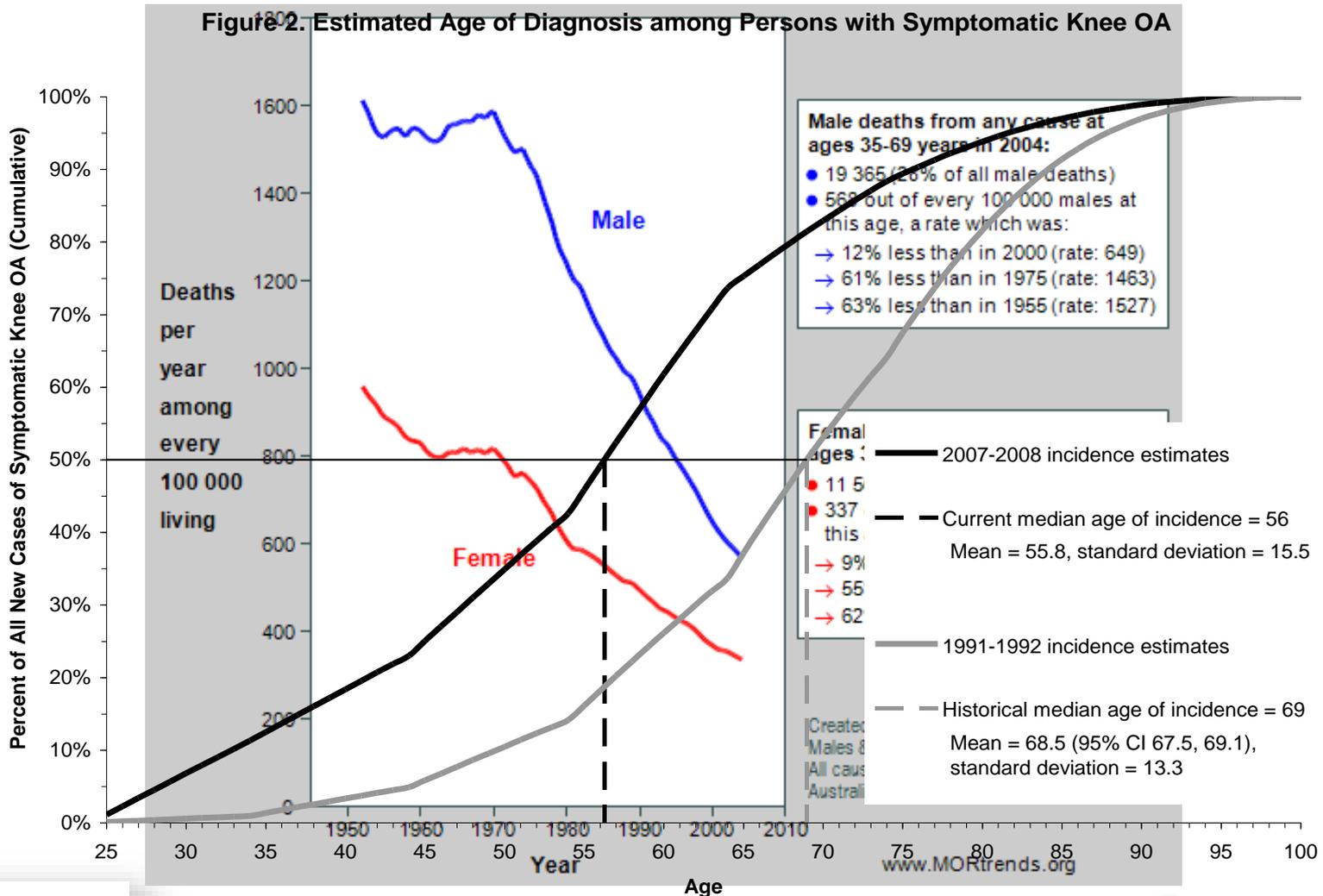
Disease of the whole joint







Declining mortality meet increasing morbidity





Health Care Costs Related to OA Represent about 38% of the Overall Economic Cost with a Total of \$3.8B

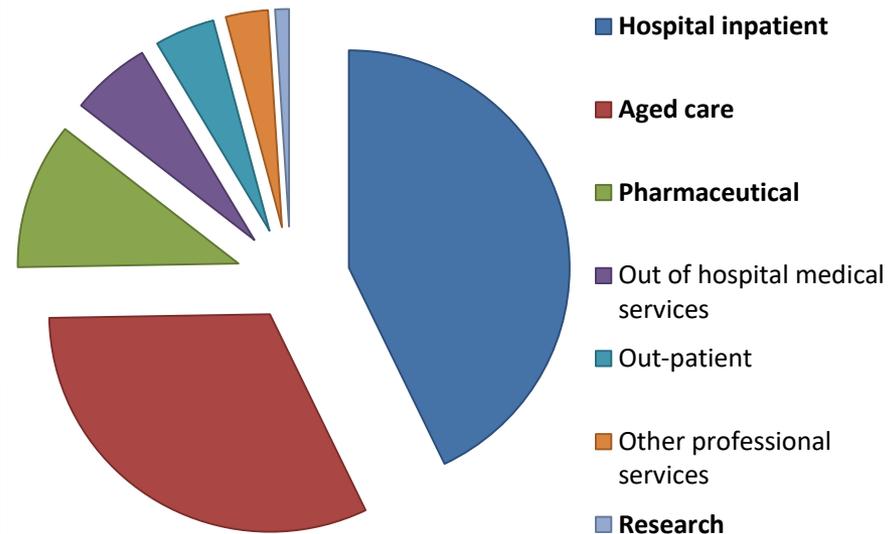
- \$3.8 billion in 2012
- 4X increase since 2000
- Most expensive type of arthritis in direct costs
- \$ 1,684 per patient per year (2012 data)

Source: Access Economics, 2013

- OA represents 41% of the total health cost of musculoskeletal conditions

Source: Access Economics, 2007

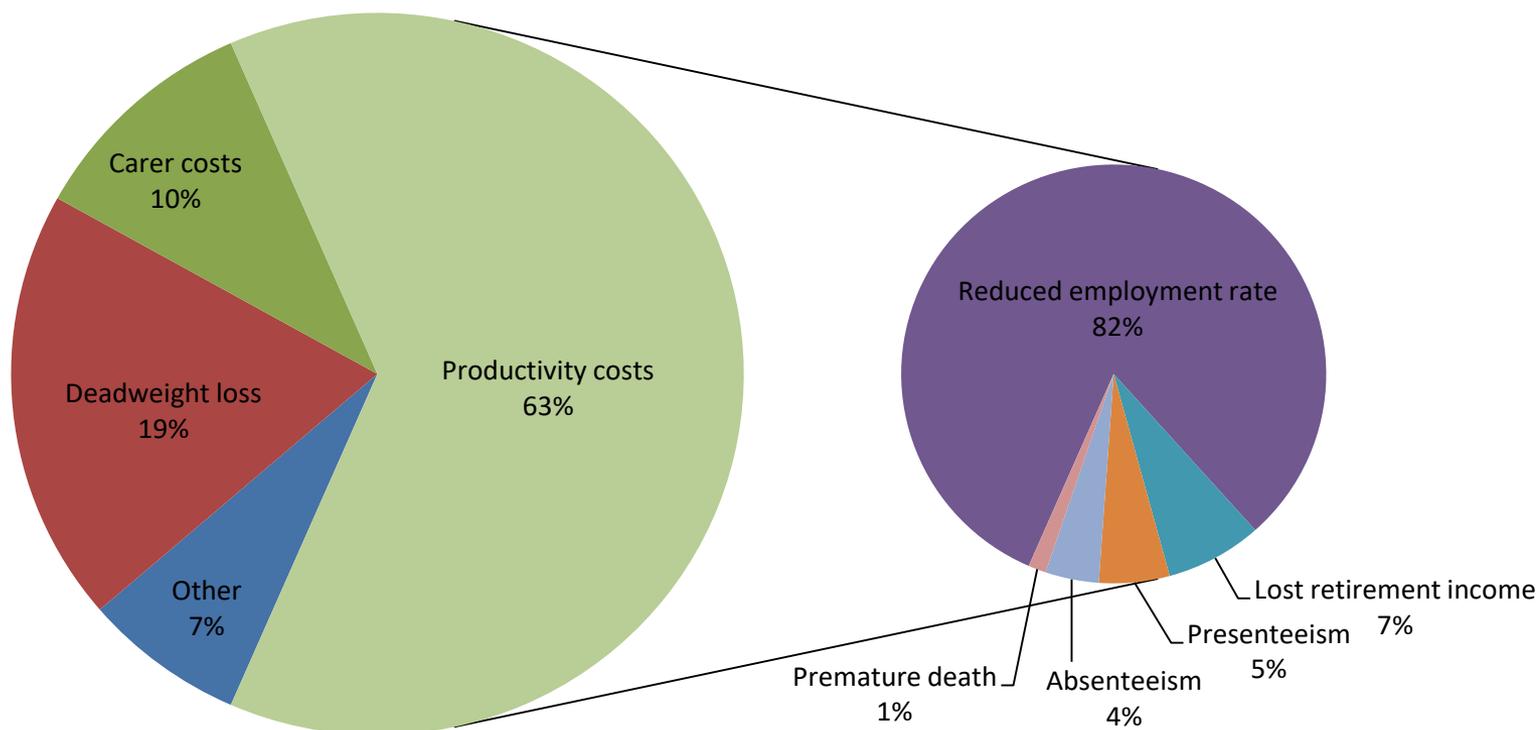
Distribution of OA health care costs



Source: Access Economics, 2013



Distribution of indirect costs for osteoarthritis by kind



Hunter DJ et al. Nature Reviews Rh. 2014 Jul;10(7):437-41.

The individual and socioeconomic impact of osteoarthritis.



Outline



Past- Inappropriate Management



Present- Evidence Based Management



Coordinated Chronic Disease Management
and Identifying Non-responders to TJR



Future- Prevention, Disease Modification



Hard Yards

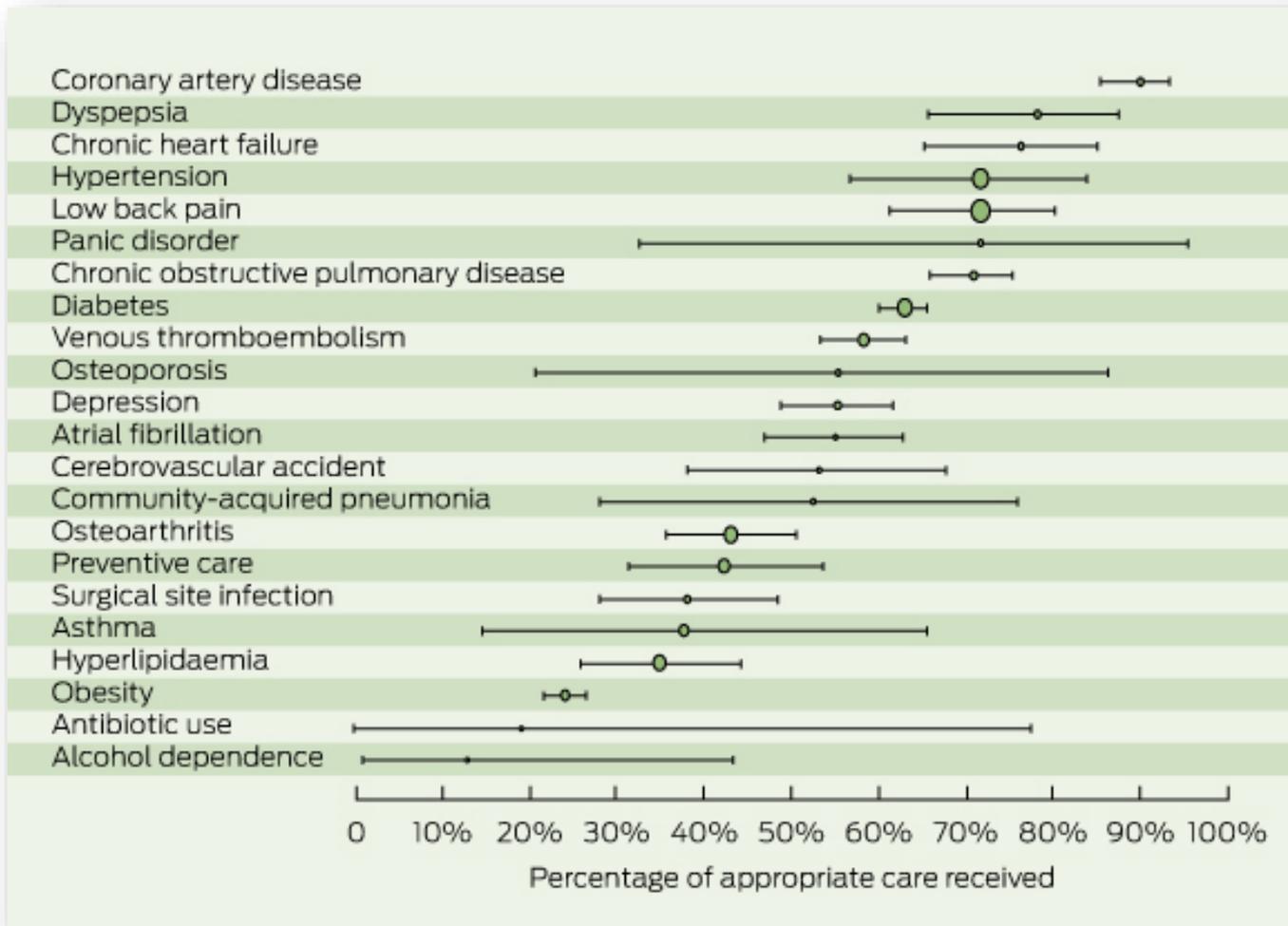
- “osteoarthritis is an easy disease to take care of-when the patient walks in the front door, I walk out the back door”
 - Sir William Osler



Here ... Take this ... I have to go back for my wife



Appropriate care



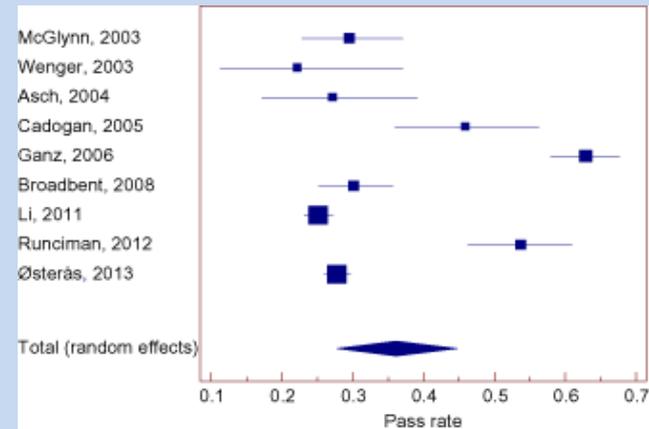
Caretrack. Med J Aust 2012; 197 (2): 100-105.



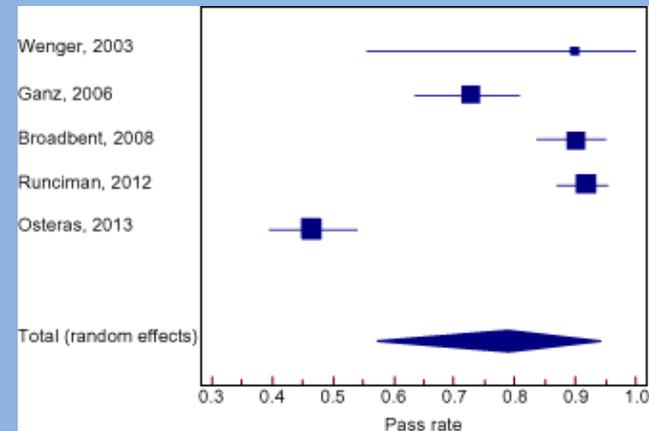
Where are we failing?

- The quality of OA care as assessed by a meta-analysis of Quality indicator pass rates across studies was suboptimal for all treatment domains
- Pass rates:
 - pain and functional status assessment – 48.5% (95% CI 32.6-64.6);
 - non-drug treatment – 36.1%, (95% CI 27.8-44.7);
 - drug treatment – 37.5% (95% CI 30.8-44.5);
 - surgical referral – 78.9% (95% CI 57.4-94.2).

• Non drug treatment



• Surgical referral





Patients are Extremely Unsatisfied: High Unmet Medical Need

Today's treatment paradigm is trapping patients in a vicious cycle of OA knee pain



19%

Knee OA patients are highly satisfied with their current treatment

91%

Not ready for total knee replacement

59%

Will try almost anything prior to surgery





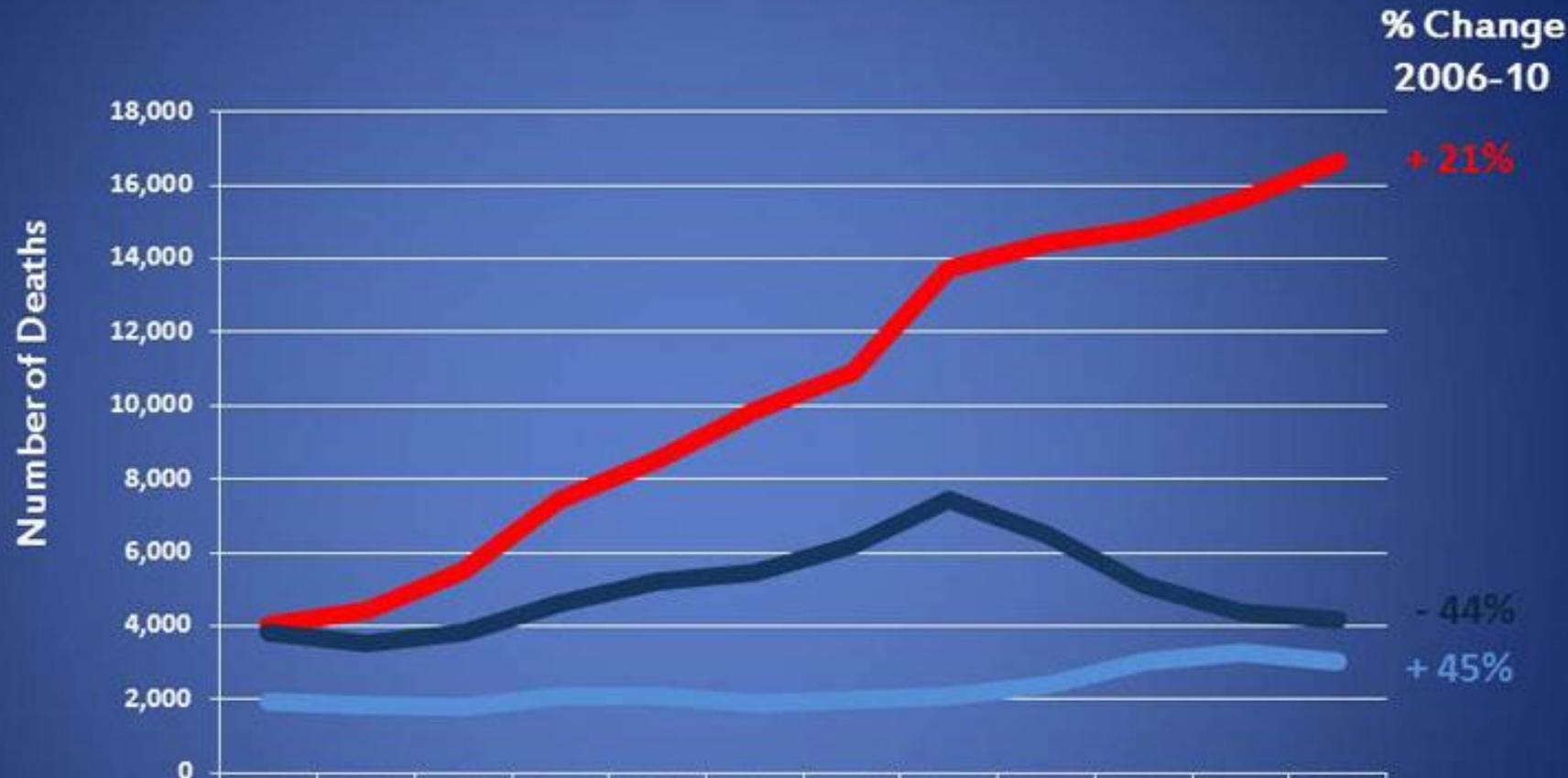


Paracetamol – no longer first line analgesic

- Increased risk of mortality, cardiovascular, GI and renal AEs
 - [Ann Rheum Dis.](#) 2015 Mar 2. pii: annrheumdis-2014-206914.
- Paracetamol is ineffective in the treatment of low back pain and provides minimal short term benefit (not clinically relevant) for people with osteoarthritis.
 - [BMJ.](#) 2015 Mar 31;350:h1225.



Overdose Deaths Involving Opioids, Cocaine and Heroin: United States, 1999–2010



	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
opioid analgesic	4030	4400	5528	7456	8517	9857	10928	13723	14408	14800	15597	16651
cocaine	3822	3544	3833	4599	5199	5443	6208	7448	6512	5129	4350	4183
heroin*	1963	1843	1784	2092	2084	1879	2010	2089	2402	3041	3279	3038



DRUG OVERDOSES

KILL MORE

THAN CARS, GUNS, AND FALLING.



Falling **26,852** deaths



Guns **31,672** deaths



Traffic accidents **33,687** deaths



Drug overdoses **38,329** deaths*

*30,006 of which were unintentional.

Source: CDC Wide-ranging OnLine Data for Epidemiologic Research (WONDER) on Mortality: <http://wonder.cdc.gov/mortsql.html> (2010)



IN OA KNEE PAIN...
**RELIEVE THE PAIN
RESTORE THE MOBILITY**

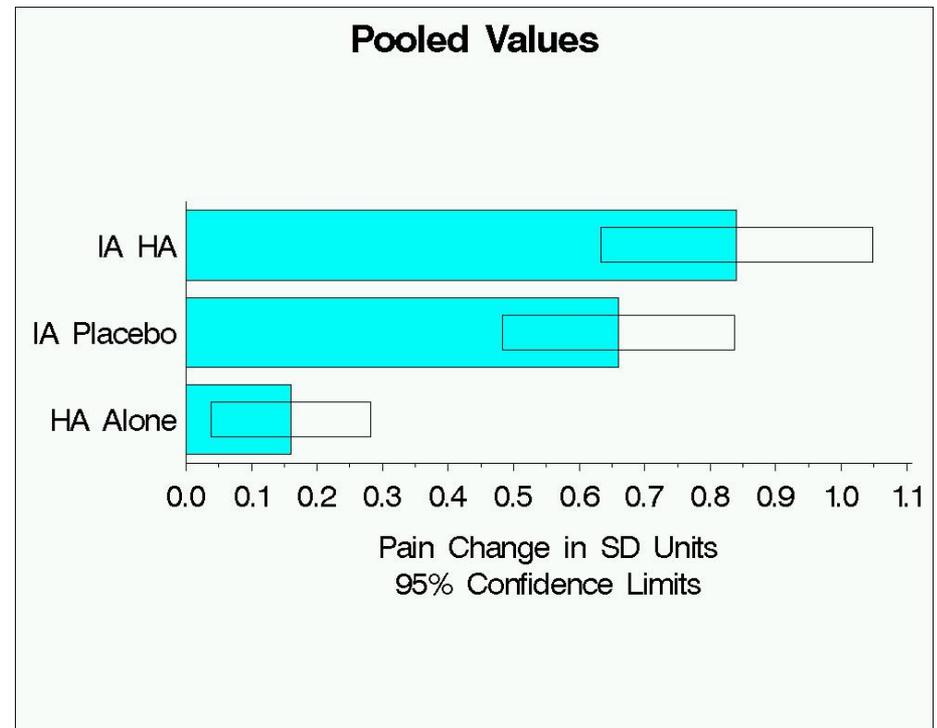
- Drug-free OA knee pain relief that can last for months
- Improvement in mobility nearly twice that of diclofenac¹
- Just 3 injections

SYNVISC®
HYLAN G-F 20
MOVE CLOSER TO HEALTHY
SYNOVIAL FLUID



Viscosupplementation

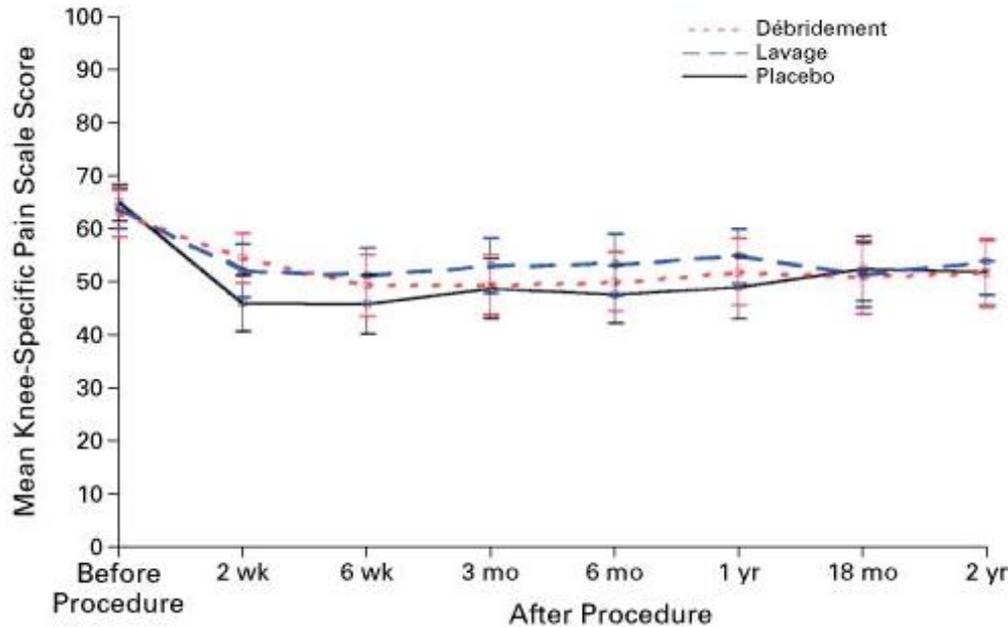
- Systematic review
- Significant heterogeneity, funnel plot markedly asymmetric.
- Pooled effect size of ITT studies was 0.34 (95%CI -0.3- 0.97).



JAMA. 2003 Dec 17;290(23):3115-21



Arthroscopy



No. AT RISK

Placebo	60	59	57	56	57	53	52	55
Lavage	61	59	57	59	59	57	56	55
Débridement	58	59	59	58	56	50	51	53

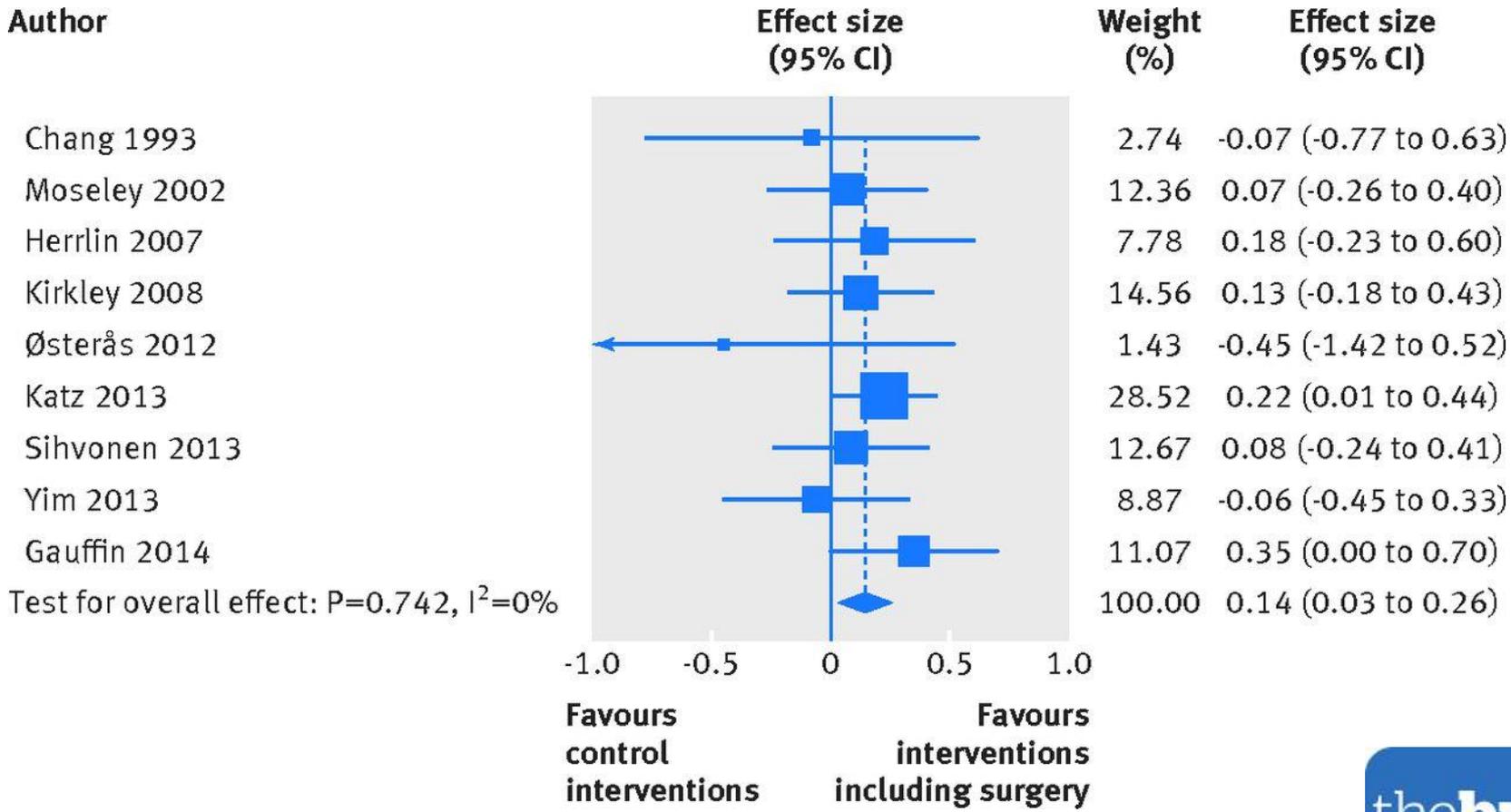
- 100,000/year
- \$500 million
- 2-3* higher in wealthy (fee for service)



Moseley JB, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *NEJM*



Results of primary analysis on benefit on patient reported pain of interventions including arthroscopic knee surgery compared with control interventions (follow-up time range: 3-24 months).



J B Thorlund et al. BMJ 2015;350:bmj.h2747





If you don't believe the evidence what are some other reasons not to do arthroscopy in this setting?

- Adverse outcomes-DVT (0.4%), PE (0.1%), death (0.03%)
 - Bohensky M et al. Arthroscopy: The Journal of Arthroscopic and Related Surgery, Vol 29, No 4 (April), 2013: pp 716-725.
- Increases rate of progression of osteoarthritis.
 - Arthritis Rheum 2004;50:2811-2819
- Shortens time to joint replacement.
 - J Bone Joint Surg Am. 2008 Nov;90(11):2337-45.

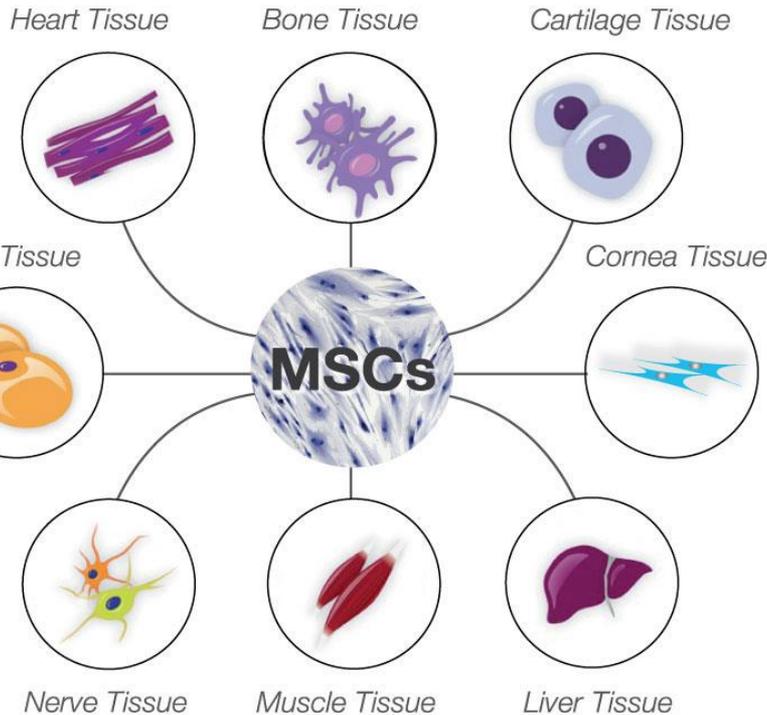


Clinical trials of MSCs for the treatment of OA and related joint defects

Table 3 | Current clinical trials* of MSCs for the treatment of OA and related joint defects

Trial	Sponsor	Phase; current stage*	Indication	Intervention	Comparator
Treatment of Knee Osteoarthritis With Allogenic Mesenchymal Stem Cells (MSV_ allo); NCT01586312 ¹⁰⁴	Red de Terapia Celular	Phase I/II; recruiting	Knee OA	Intra-articular injection of 40×10^6 allogeneic MSCs	Intra-articular injection of 60 mg hyaluronan
Treatment of Knee Osteoarthritis With Autologous Mesenchymal Stem Cells (KDD&MSV); NCT01183728 ¹⁰⁵	Red de Terapia Celular	Phase I/II; active, not recruiting	Knee OA, Kellgren and Lawrence grade II-IV	Intra-articular injection of 40×10^6 autologous MSCs	None (open-label, single-group safety study)
Intra-Articular Autologous Bone Marrow Mesenchymal Stem Cells Transplantation to Treat Mild to Moderate Osteoarthritis; NCT01459640 ¹⁰⁶	National University of Malaysia	Phase II; recruiting	Knee OA, mild to moderate	Single intra-articular implantation of autologous bone marrow-derived MSCs in hyaluronan	None (open-label, single-group safety study)
The Effects of Intra-articular Injection of Mesenchymal Stem Cells in Knee Joint Osteoarthritis; NCT01504464 ¹⁰⁷	Royan Institute	Phase II; completed, no results posted	Knee OA	Intra-articular injection of MSCs	Placebo injection
Mesenchymal Stem Cell Transplantation in Osteoarthritis of Hip Joint; NCT01499056 ¹⁰⁸	Royan Institute	Phase I; completed, no results posted	Hip OA	MSC injection	None (open-label, single-group safety study)
Allogeneic Mesenchymal Stem Cells in Osteoarthritis; NCT01453738 ¹⁰⁹	Stempeutics Research Pvt Ltd	Phase II; active, not recruiting	Knee OA	Intra-articular dose of allogeneic MSCs in 2-4 ml Plasmalyte-A [†] followed by 2 ml hyaluronan	Single intra-articular dose of 2 ml Plasmalyte-A [†]
Side Effects of Autologous Mesenchymal Stem Cell Transplantation in Ankle Joint Osteoarthritis; NCT01436058 ¹¹⁰	Royan Institute	Phase I; completed, no results posted	Ankle joint OA	Intra-articular injection of MSCs	None (open-label, single-group safety study)
Adult Stem Cell Therapy for Repairing Articular Cartilage in Gonarthrosis; NCT01227694 ¹¹⁴	Banc de Sang i Teixits	Phase I/II; active, not recruiting	Knee OA	Intra-articular injection of 40×10^6 autologous MSCs	None (open-label, single-group safety study)
Autologous Adipose Tissue Derived Mesenchymal Stem Cells Transplantation in Patients With Degenerative Arthritis; NCT01300598 ¹¹²	RNL Bio Company Ltd	Phase I/II; completed, no results posted	Knee OA	Intra-articular injection of autologous adipose tissue-derived MSCs. Doses (in 3 ml) listed as: 1×10^7 cells, 5×10^7 cells, 1×10^8 cells	None (open-label, single-group safety study)
Study to Compare the Efficacy and Safety of Cartistem® and Microfracture in Patients With Knee Articular Cartilage Injury or Defect; NCT01041001 ¹¹³	Medipost Co Ltd	Phase III; completed, no results posted (Follow-up study, NCT01626677, ¹¹⁴ now recruiting)	Knee cartilage defect or injury	Intra-articular injection of allogeneic umbilical cord blood-derived MSCs	Microfracture treatment
ADIPOA—Clinical Study; NCT01585857 ¹¹⁵	University Hospital, Montpellier	Phase I; recruiting	Knee OA, moderate or severe	Intra-articular injection of autologous adipose-tissue-derived MSCs. Doses (in 5 ml of human albumin); 2×10^6 , 10×10^6 , 50×10^6 cells	None (open-label, dose-escalating safety study)
Safety and Efficacy Study of MSB-CAR001 in Subjects 6 Weeks Post an Anterior Cruciate Ligament Reconstruction; NCT01088191 ¹¹⁶	Mesoblast, Ltd	Phase I/II; recruiting	Anterior cruciate ligament injury	Single intra-articular injection (into the knee) of MSB-CAR001 [‡] (2 different doses) combined with hyaluronan	Intra-articular injection of hyaluronan
Transplantation of Bone Marrow Stem Cells Stimulated by Proteins Scaffold to Heal Defects Articular Cartilage of the Knee; NCT01159899 ¹¹⁷	University of Marseille	Phase 0; recruiting	Knee cartilage defects	Fresh non-culture-expanded autologous bone marrow-derived MSCs, mixed and activated with protein scaffold	None (open-label, single-group pilot study)

*As of April 2013. [†]Plasmalyte-A is a sterile isotonic buffered salt solution. [‡]MSB-CAR001 is a preparation of MSCs. Abbreviations: MSC, mesenchymal stem cell; OA, osteoarthritis.





Stem Cells and ACSEP

- “hallmarks of ‘quack’ medicine: desperate patients, pseudoscience and large amounts of money being charged for unproven therapies”
 - NSW Coroner
- Recommendation-restrict the use of mesenchymal stem cells to rigorous clinical research trials only.
- Board of the Australasian College of Sport and Exercise Physicians



Need more evidence Put patients before profits





When worlds collide.....

Professional dominance

Profession of medicine is noble; it has special knowledge, inaccessible to laity; it is beneficent; and it will self-regulate.

Exponents believe in professional trust and prerogative.



Accountability and market theory

Exponents believe in accountability, scrutiny, measurement, incentives, and markets.

The machinery is the manipulation of contingencies: rewards, punishments, and pay for performance.

Healthy Era. We need to reject greed

Fundamentally better care, better health, and lower cost. The best route to these goals is the continual design and redesign of health care as a system



**If one does not know to which port
one is sailing, no wind is favorable.**

Lucius Annaeus Seneca





OARSI Guidelines for the Non-surgical Management of Knee OA

Core Treatments
Appropriate for all individuals

Land-based exercise (61.6) Water-based exercise (56.5)
Weight management (60.0) Self-mgmt and education (49.1)
Strength training (59.5)



Knee-only OA without co-morbidities

- Biomechanical interventions (57.0)
- Intra-articular Corticosteroids (53.8)
- Topical NSAIDs (49.9)
- Walking Cane (46.9)
- Oral COX-2 Inhibitors (selective NSAIDs) (43.1)
- Capsaicin (42.6)
- Oral Non-selective NSAIDs (37.6)
- Duloxetine (37.2)
- Acetaminophen/Paracetamol (34.0)

Knee-only OA with co-morbidities

- Biomechanical interventions (50.4)
- Walking Cane (46.9)
- Intra-articular Corticosteroids (47.2)
- Topical NSAIDs (44.7)

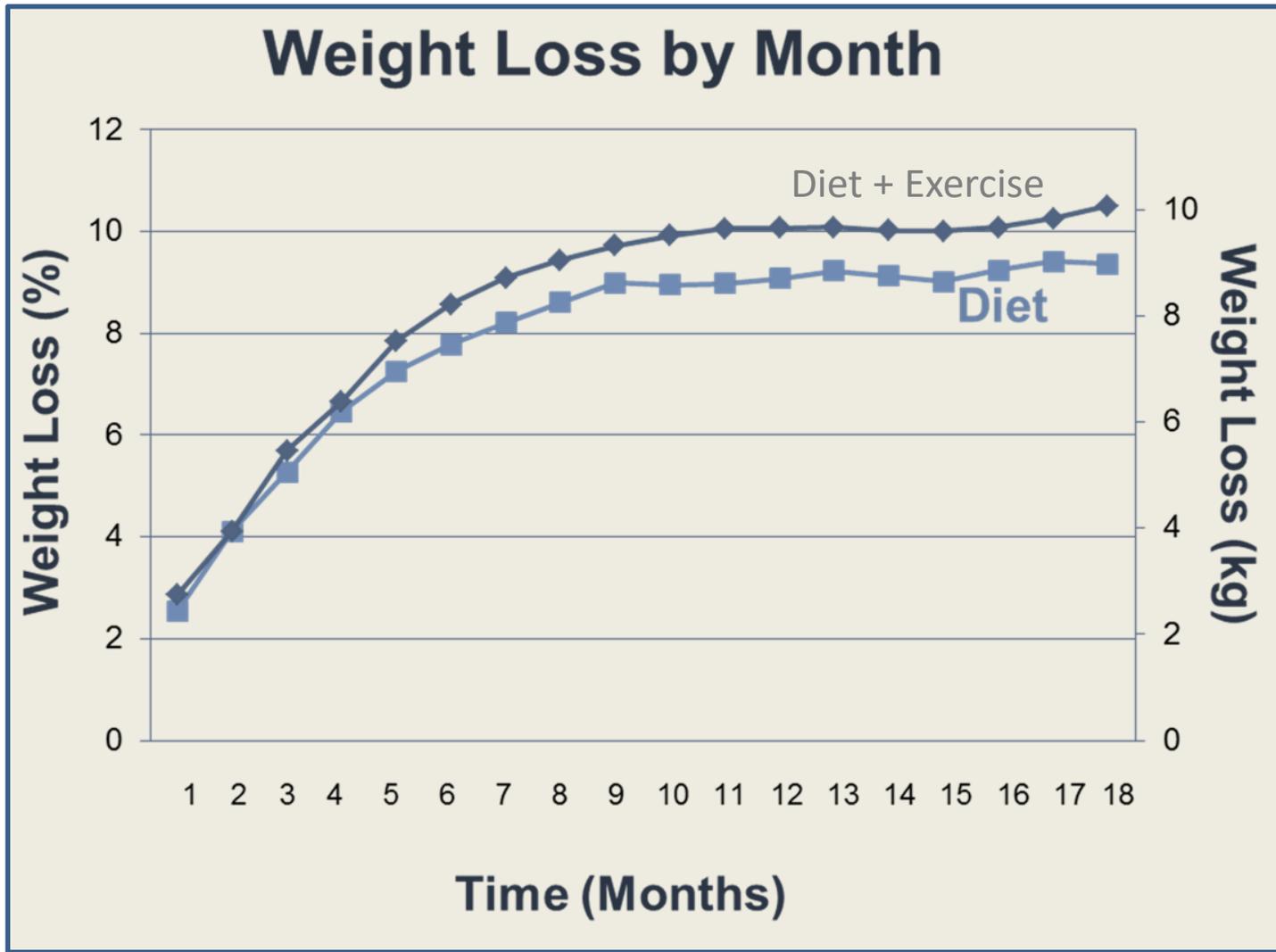
Multi-joint OA without co-morbidities

- Oral COX-2 Inhibitors (selective NSAIDs) (44.0)
- Intra-articular Corticosteroids (42.7)
- Oral Non-selective NSAIDs (39.3)
- Duloxetine (39.3)
- Biomechanical interventions (37.6)
- Acetaminophen/Paracetamol (34.8)

Multi-joint OA with co-morbidities

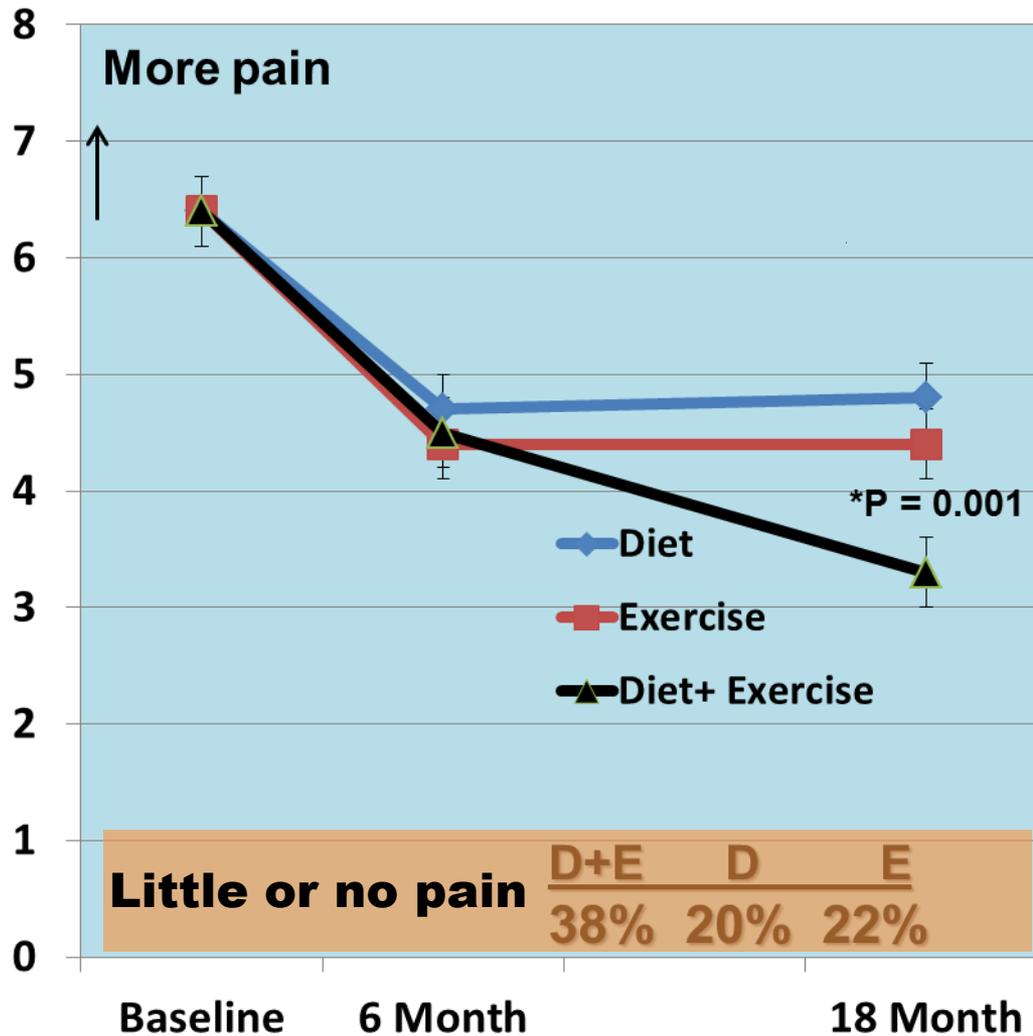
- Balneotherapy (41.9)
- Biomechanical interventions (41.8)
- Intra-articular Corticosteroids (39.2)
- Oral COX-2 Inhibitors (selective NSAIDs) (37.1)
- Duloxetine (35.4)

*OARSI also recommends referral for consideration of open orthopedic surgery if more conservative treatment modalities are found ineffective.
The composite risk-benefit score was calculated as the product of the benefit score (1-10) and the transposed risk score (where 1=highest risk and 10=safest) yielding a composite score from 1 (worst) to 100 (best).





WOMAC Pain
(range 0-20)



*Adjusted for gender, BMI, baseline values

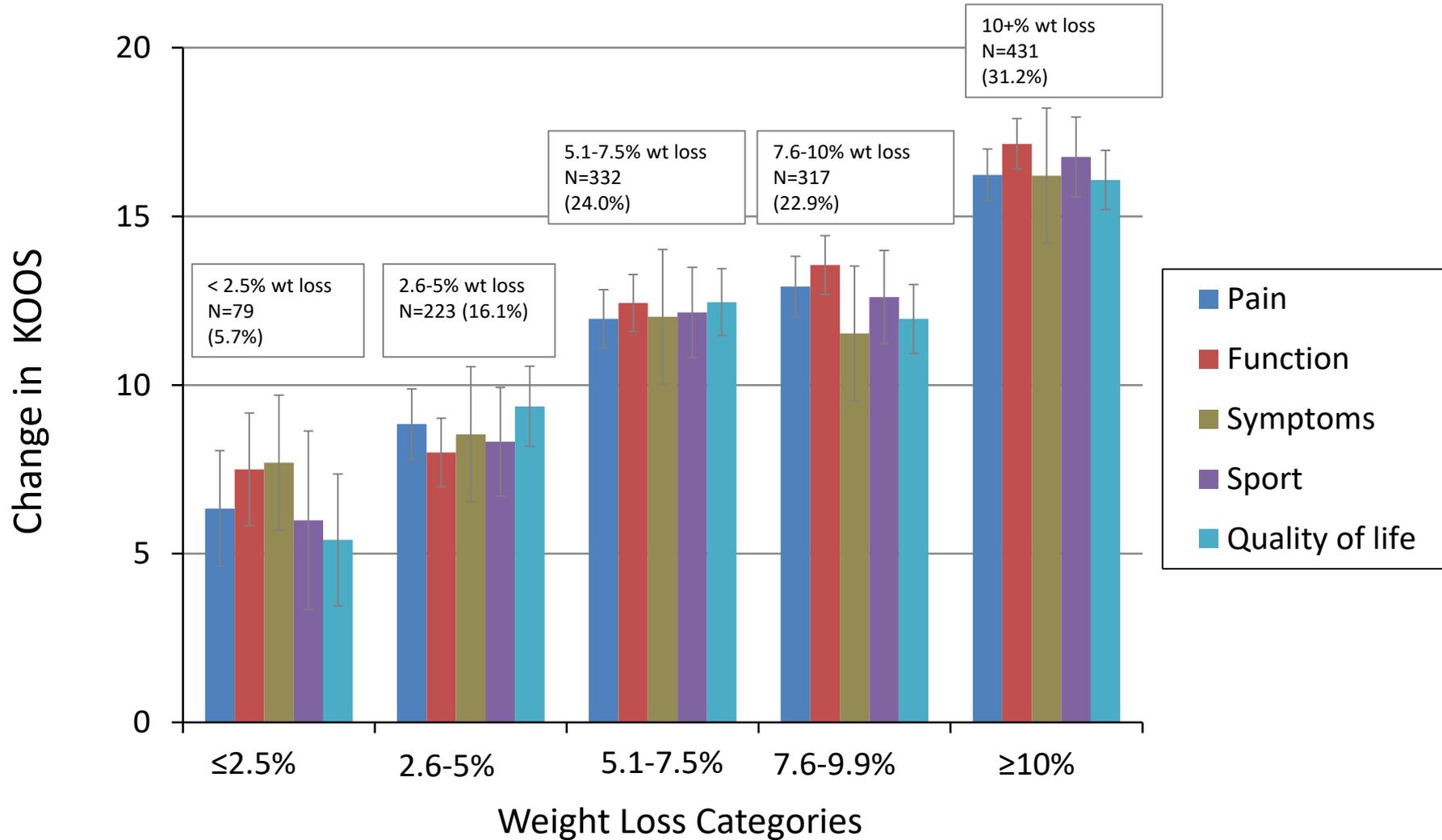
Messier S et al. JAMA. 2013 Sep 25;310(12):1263-73

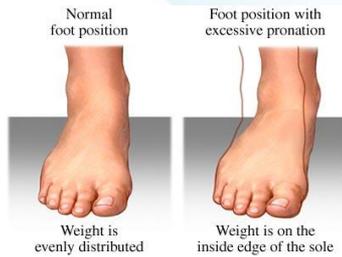


Baseline characteristics (n=1,383)

Age (years) (SD)	64.0 (8.7)
Females	981 (70.9%)
Weight (kg) (SD)	95.1 (17.2)
Height (m) (SD)	1.66 (0.09)
BMI (kg/m ²) (SD)	34.3 (5.17)
Obesity (BMI \geq 30 kg/m ²) BSL	1130 (81.7%)
Obesity (BMI \geq 30 kg/m ²) Final	772 (56.3%)
KOOS pain	56.3 (16.8)
KOOS function	59.5 (18.3)

Difference in KOOS subscales after weight loss intervention





Family Supports

Normal foot position

Foot position with excessive pronation

Weight is evenly distributed

Weight is on the inside edge of the sole



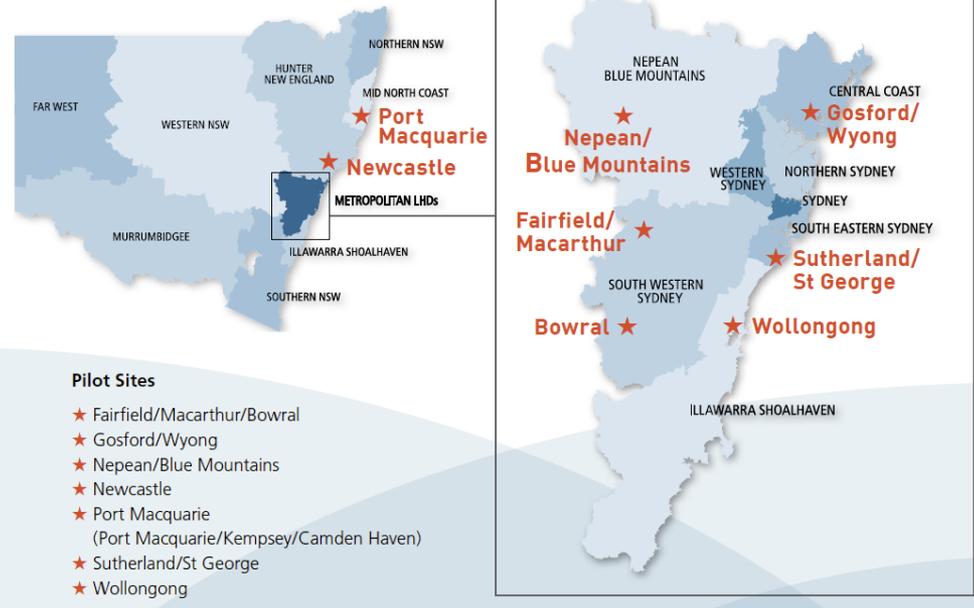
OACCP

Name of Program	Number of persons enrolled/ seen in the program	Website for further information	Health care system, funding model
Osteoarthritis Chronic Care program (OACCP)	~10,000 since 2011	http://www.aci.health.nsw.gov.au/models-of-care/musculoskeletal/osteoarthritis-chronic-care-program	Funded through public hospital system, currently running in 14 public hospitals



ACI NSW Agency for Clinical Innovation

OACCP Pilot Sites





Total Joint Replacement

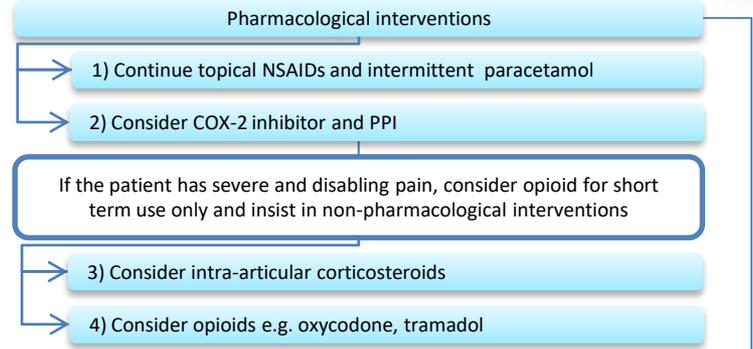
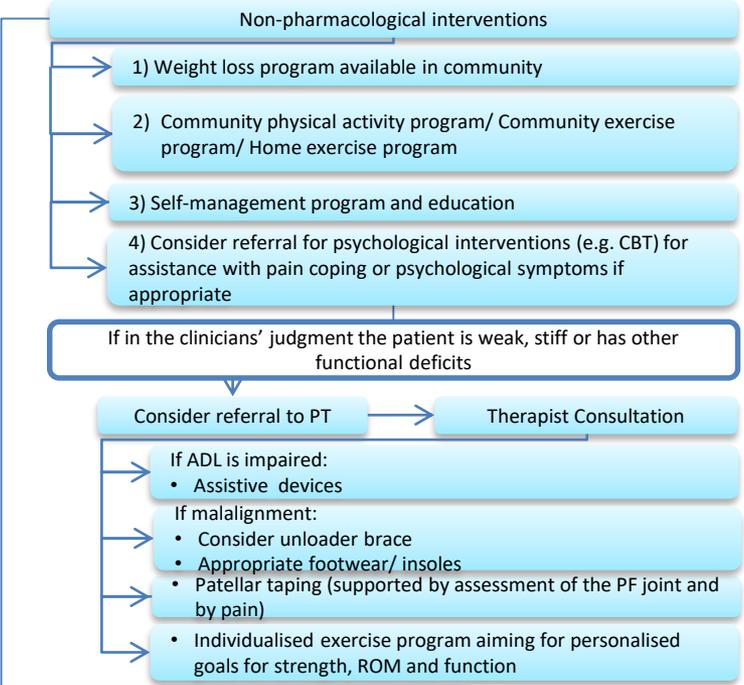
- Right person, right time.
- Up to 25% of persons having a TKR have a bad outcome.
- Importance of shared decision making and screening out non-responders (depressed, BMI>40, KLG<4 and low pain score).





Knee 1 – Case 3

Clinical diagnosis of OA based on history and examination*
Check for co-morbidities e.g. cardiac diseases; hypertension; type 2 diabetes; obesity; COPD; low back pain; chronic pain; depression; and visual or hearing impairments.



If disabling symptoms and if already exhausted all other options including pharmacological and non-pharmacological interventions

Consider referral to specialist knee surgeon for surgical opinion → If necessary: Surgical intervention

Post-operative program

• Long term: Individualised exercise program aiming for personalised goals for strength, ROM and function regarding the replaced joint and other joints at risk

*Signs and symptoms

- Joint pain
- Impaired activities of daily living, such as difficulty climbing stairs, squatting, kneeling and collecting objects from the floor.
- 'Giving way' and locking of the knee are common complaints.
- Small-to-moderate effusions
- Reduced range of motion
- Stiffness
- Crepitus and tenderness along the joint line or with pressure on the patella
- Weakness and wasting of quadriceps muscle





PARTNER OA Model

All people with knee OA



GP

Enhanced consultation

- Assessment
- Diagnosis
- Information provision
- Education about Shared Care and referral to Care Support Team

People with:

- BMI ≥25
- Pain ≥4/10

Centralised Service Remotely-delivered

Care Support Team



- Assessment
- Information/Education
- Collaborative care plan
- Care co-ordination
- Self management support

- Other Health Professionals
- Other services
- Community resources and programs

• Interventions will be directed at GP, care support team and patient behaviours.

↔ Referral and feedback pathway

Remotely-delivered Care Support Team:

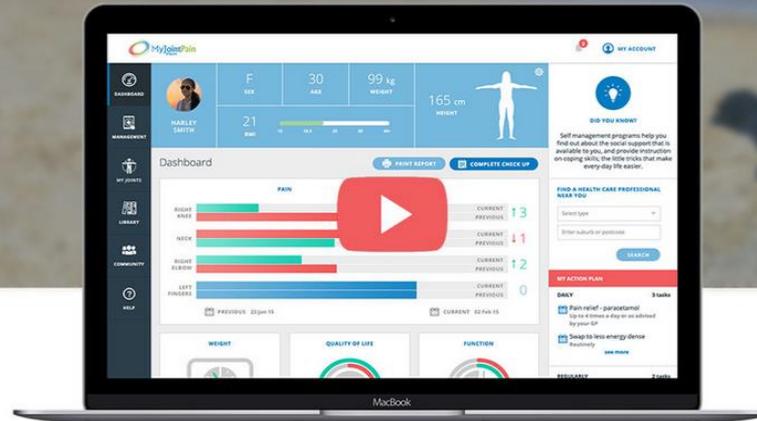
- Allied health professionals (such as pharmacists, physiotherapists, nurses, psychologists) with team skills covering:
 - OA treatments including exercise, weight loss, mood management, medications and other self management strategies
 - Behaviour change support
- IT infrastructure that facilitates communication, patient monitoring and collection of outcome data





Got joint pain? Get long term relief.
Let MyJointPain.org.au show you how.

SIGN UP FOR FREE NOW!



DO A RISK ASSESSMENT



Do you have osteoarthritis (OA)? This joint disease that can lead to ongoing pain and disability. Answer a few questions to learn your risk.

GET A MANAGEMENT PLAN



Answer questions to get relevant treatment options and a management plan tailor-made for you. Weekly check-ups will help you stay on track.

FIND UP-TO-DATE INFORMATION



Learn about new treatments, what works, and what you should avoid. See interviews with experts and connect with healthcare providers who can help you.

CONNECT WITH OUR COMMUNITY



Talk to other people with joint pain as well as experts. Ask questions, get answers and share your experience. Find out who can help you best.

<http://www.youtube.com/watch?v=h6UIZWIB9CA>

<http://www.youtube.com/watch?v=lvRVmay-u24>

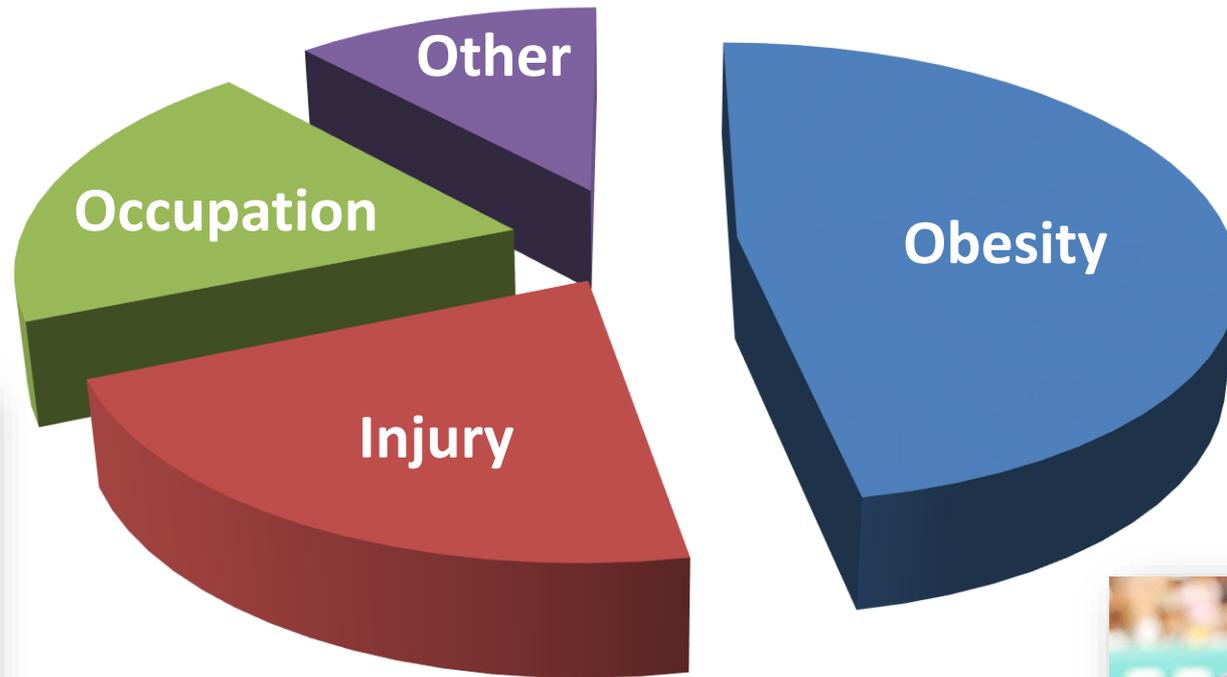


LIMITATIONS

UNTIL YOU SPREAD YOUR WINGS,
YOU'LL HAVE NO IDEA HOW FAR YOU CAN WALK.



Risk for Knee OA

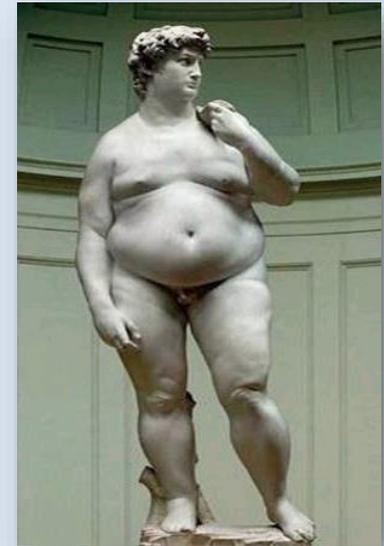
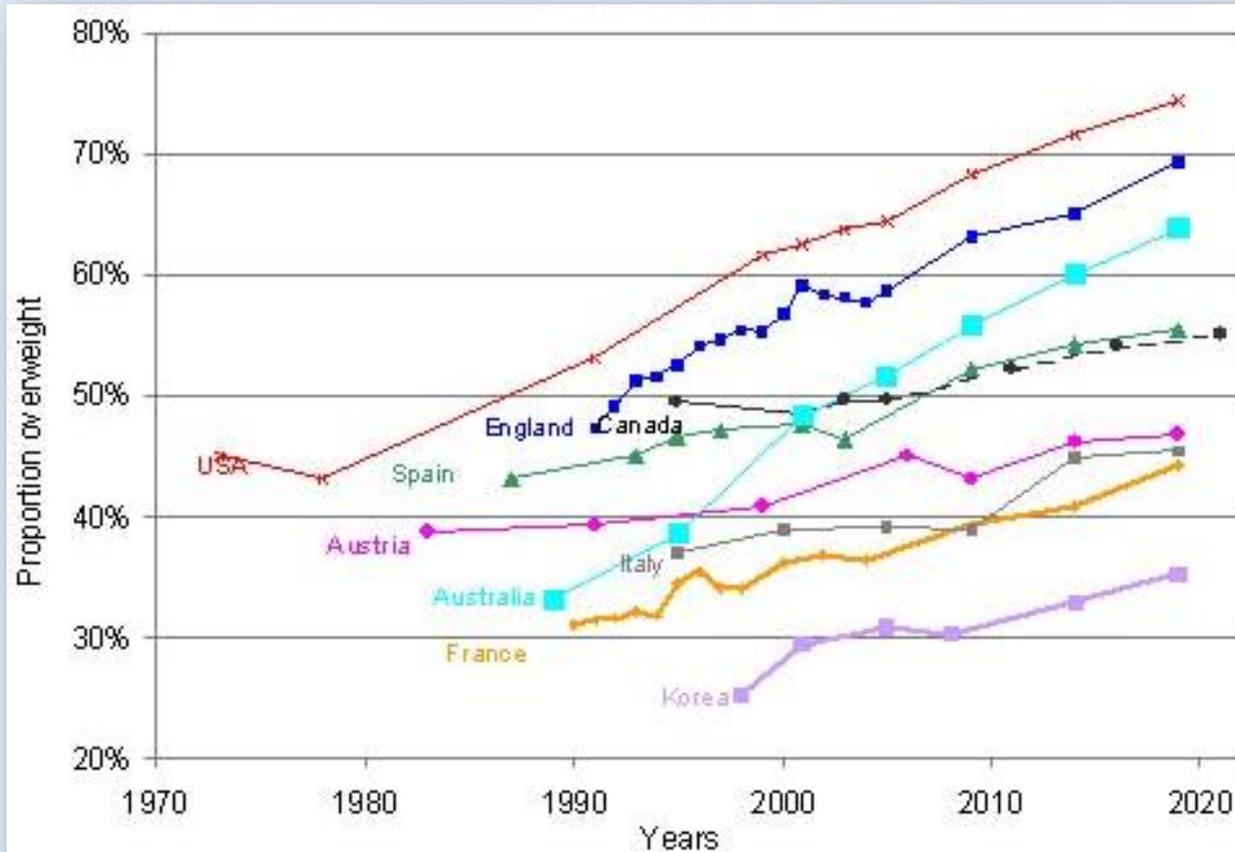


Arthritis Rheum. 1998, Aug;41(8):1343-55.
Osteoarthritis Cartilage. 2009; Sep 2.





Past and projected future overweight rates in selected O.E.C.D countries







Before and After

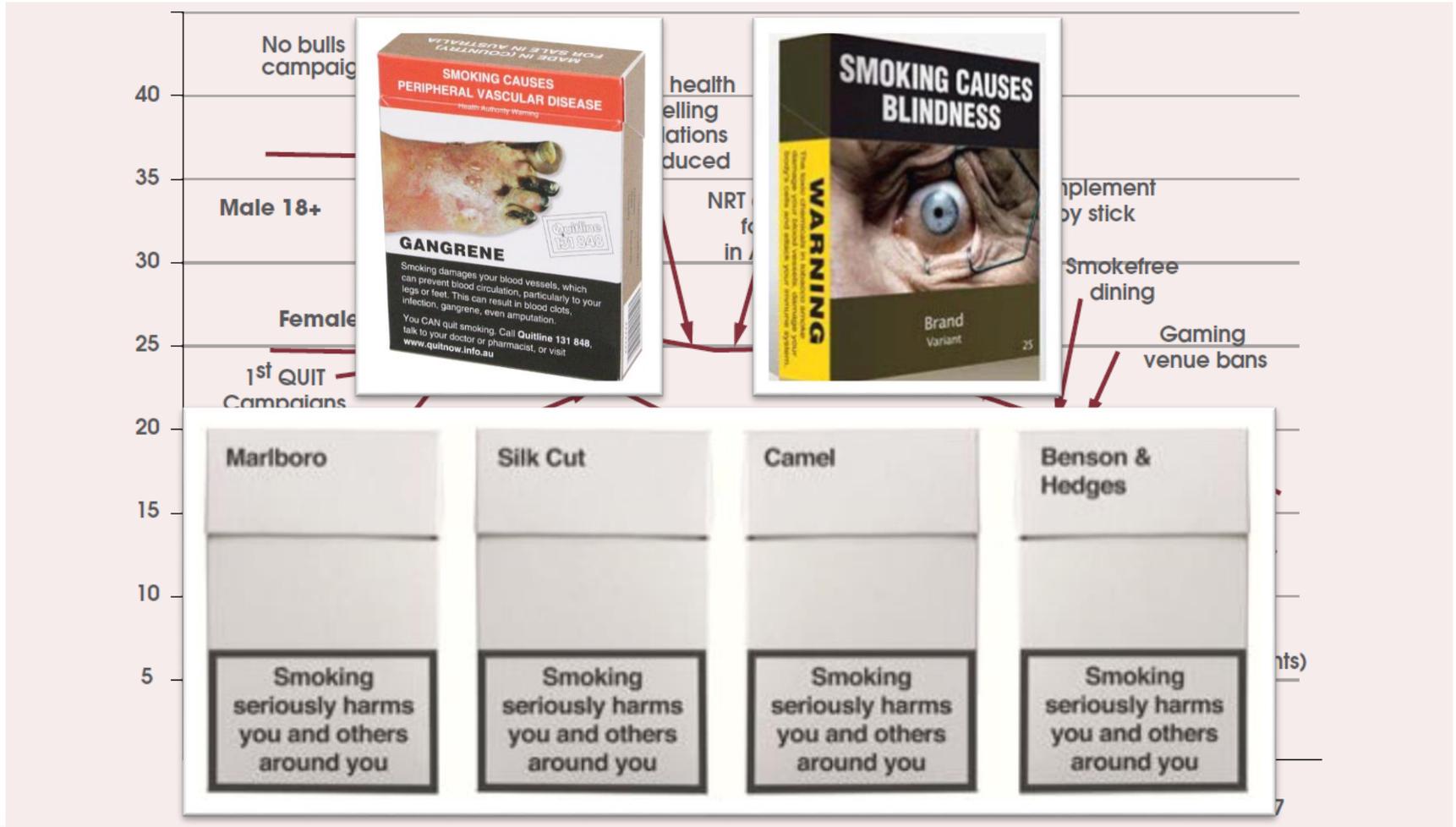


Proudly supported by





Milestones in reducing smoking in Australia 1980–2007





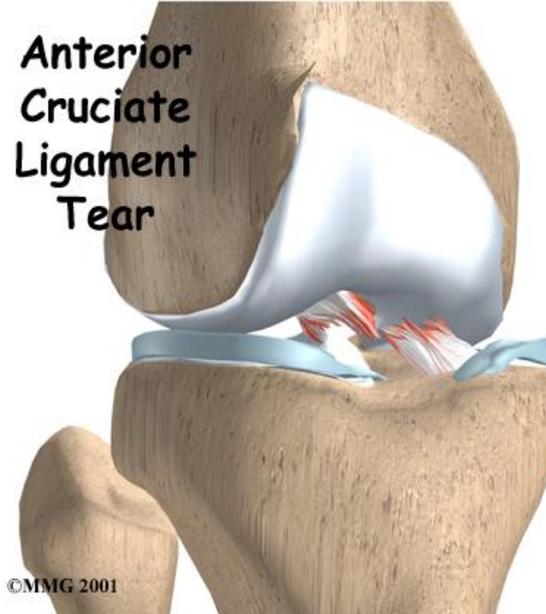
What should we do?

Cost-effectiveness results for selected interventions evaluated in Australia





Injury Prevention



INTERNATIONAL
OLYMPIC
COMMITTEE



THE UNIVERSITY OF
SYDNEY



Natural History of OA

Symptoms



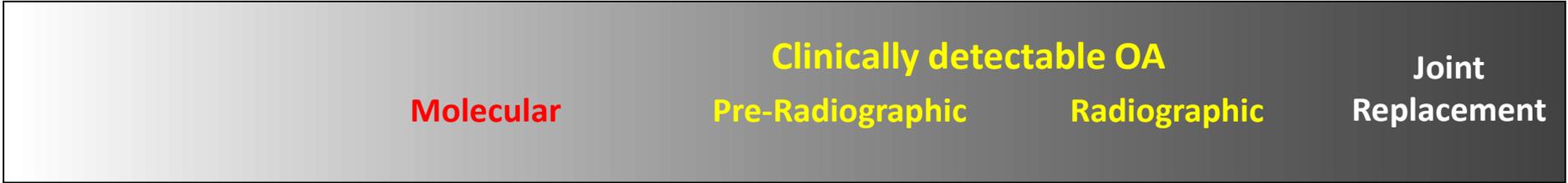
Initiation of
Disease
Process

MRI/Biomarkers
Changes in the
composition of bone,
cartilage,
other soft tissues

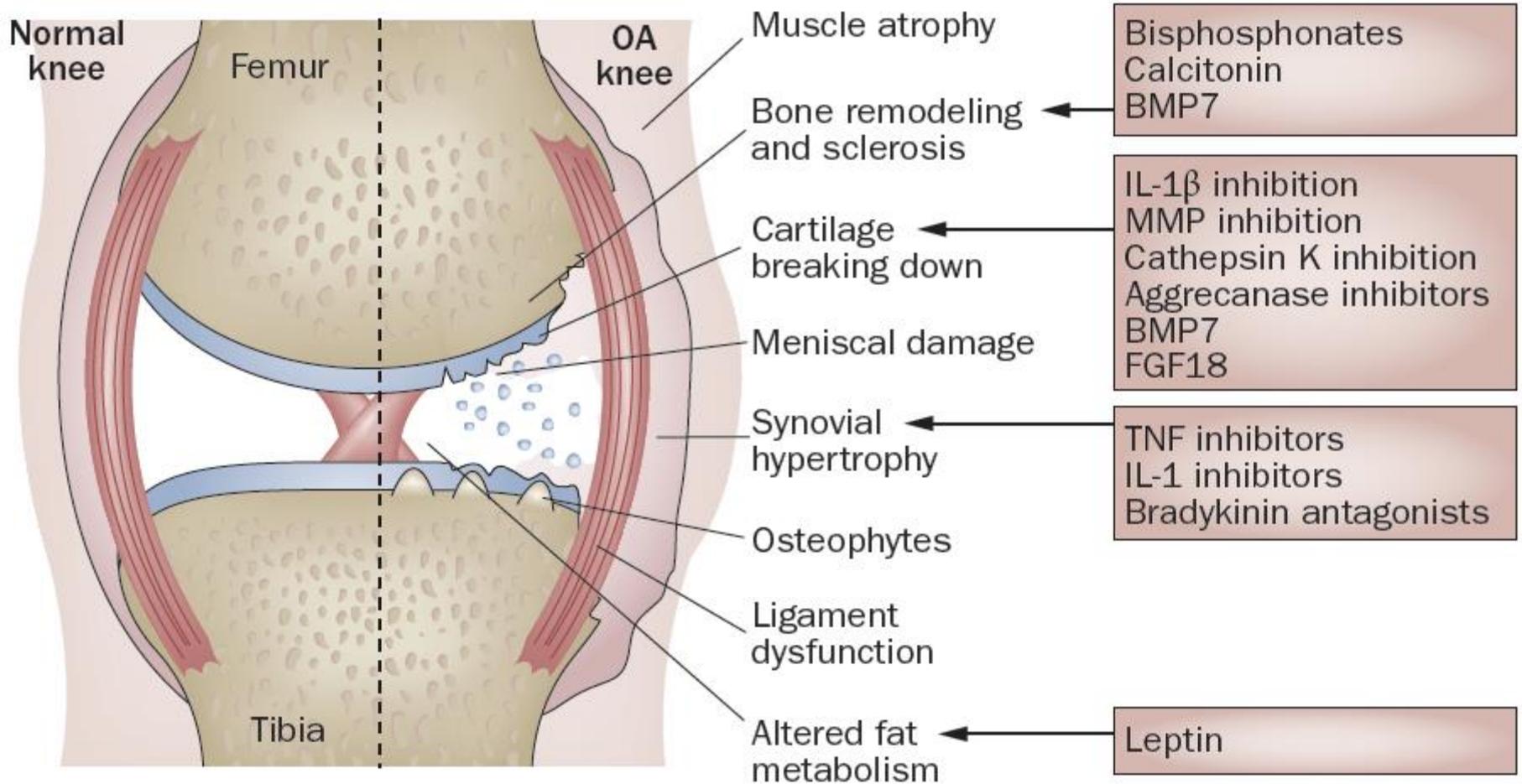
MRI /US
Structural changes
in bone, cartilage,
other soft tissues

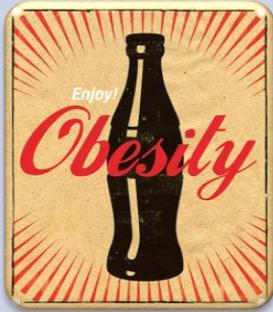
X-ray
Structural
changes in
bone
(i.e., joint
failure)

End-stage
Disease
(i.e., joint
death)



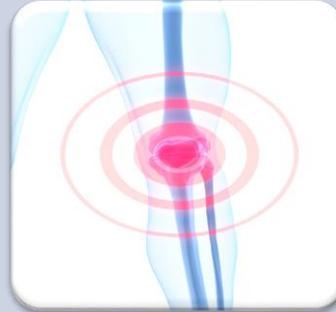
Defining Disease State of Osteoarthritis





Prevention

Obesity
Joint injury



Progression

Reduce load
Disease
modification



Palliation

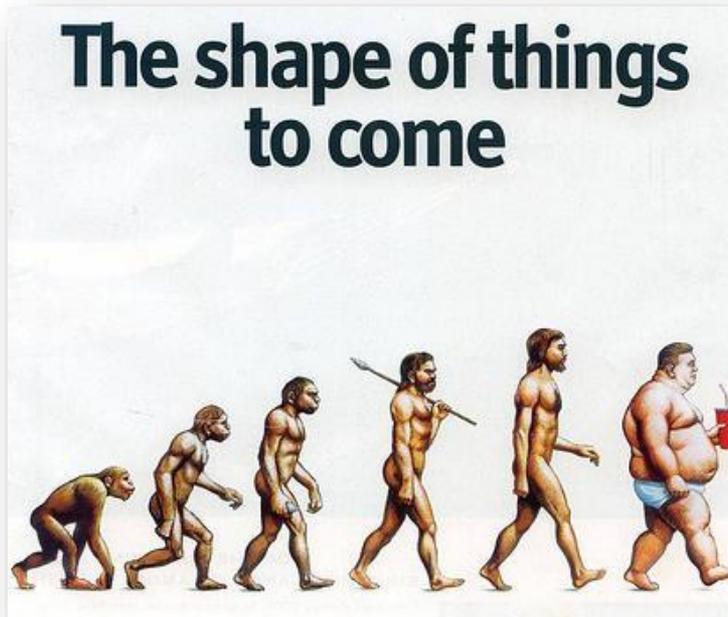
Analgesia
Joint replacement

Hunter DJ. Br J Sports Med. 2011 Apr;45(4):283-8.

Hunter DJ. Nat Rev Rheumatol. 2011 Jan;7(1):13-22.



Conclusion

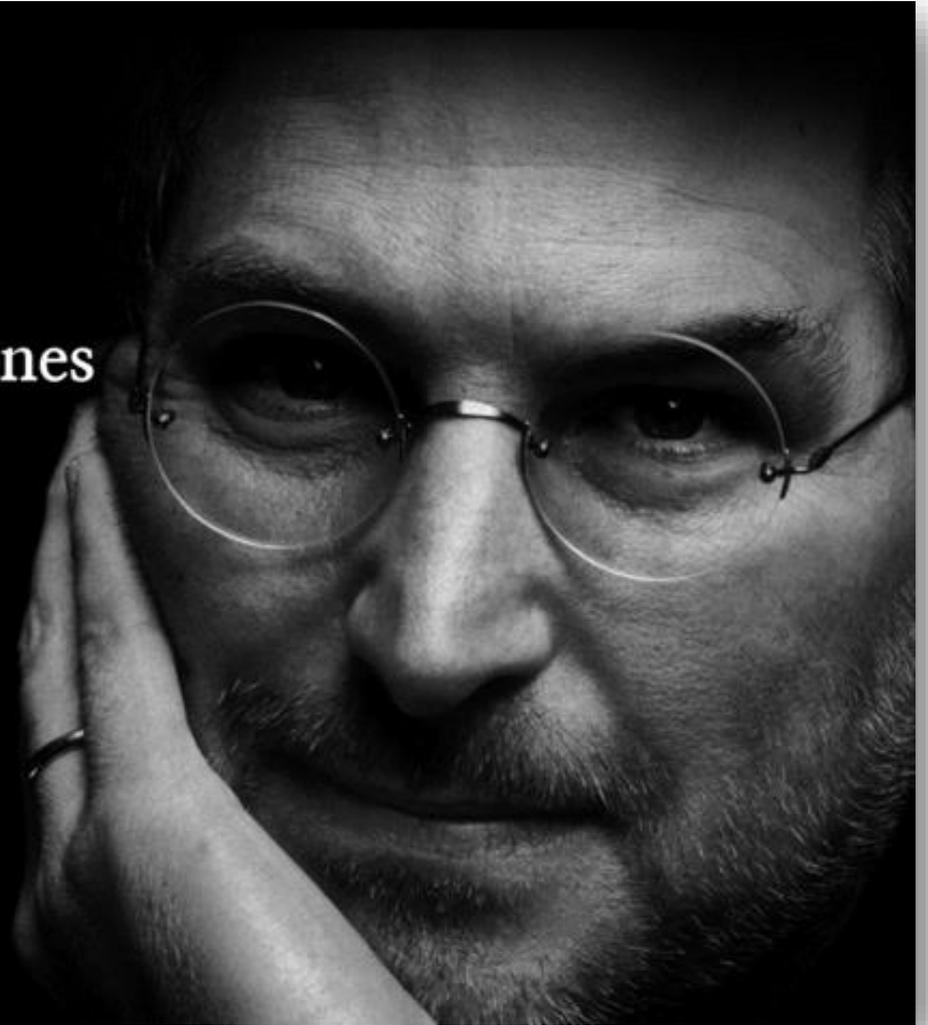


- We can all improve the appropriateness of our OA management.
- Disease management can be improved by moving towards chronic disease management focused in particular on exercise and weight loss.



"The people who are crazy
enough to think they can
change the world are the ones
who do."

– Steve Jobs



#PatienceToPerfection





Osteoarthritis Summit 2017

May 30th, 2017

*The Royal North Shore Hospital
Sydney, Australia*



Discussions on:

Establishing osteoarthritis research
priorities for the next 5 years

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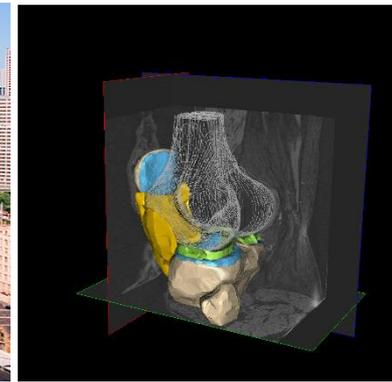
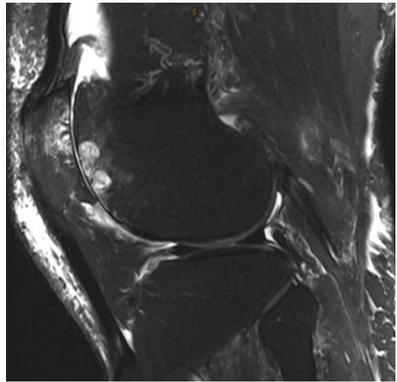
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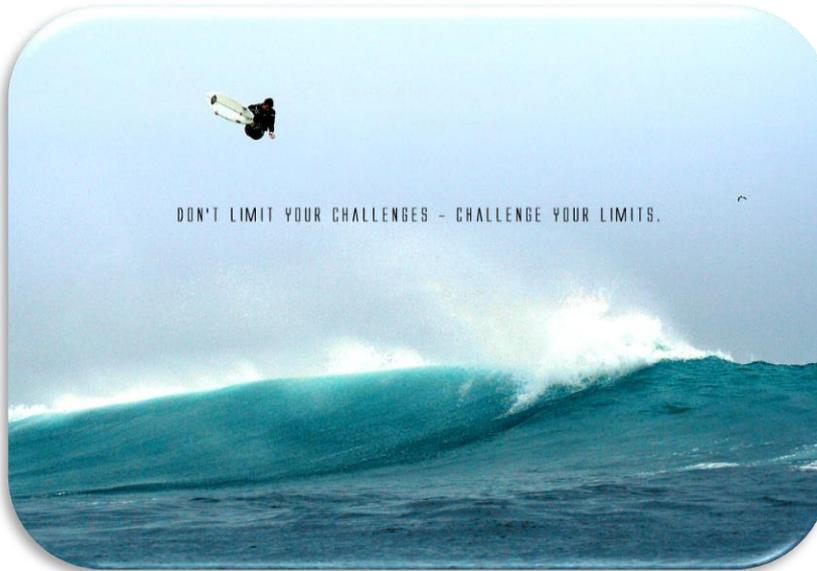
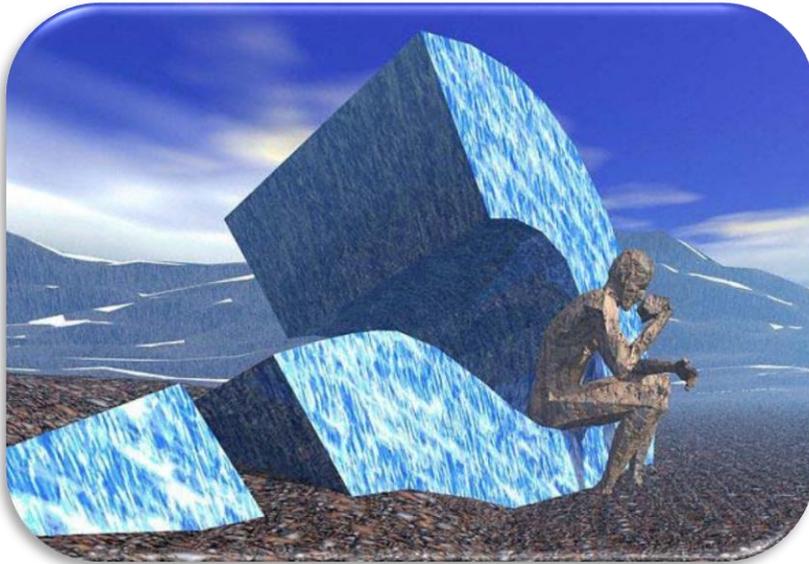


11th International Osteoarthritis Imaging Workshop, Sydney June 1-4th 2017



Register at: <http://www.ismrm.org/workshops/Osteo17/>





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