OSTEOARTHRITIS
Overview of Current Treatment Options

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THE UNIVERSITY OF THE WEST INDIES
AT CAVE HILL, BARBADOS

Caribbean
SPORTS ORTHOPAEDIC CLINIC

DISCLOSURES

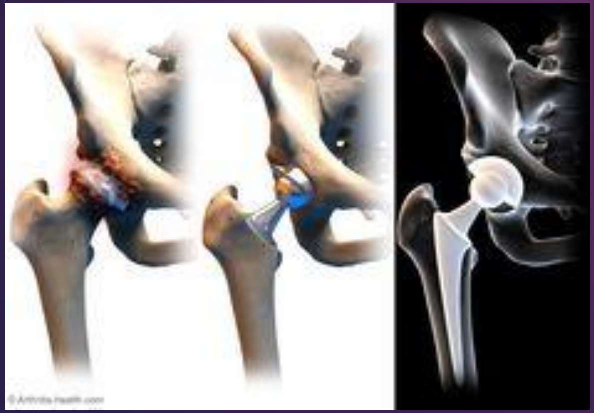
Within the past 12 months, I or my family members have had the following financial interest/arrangement(s) or affiliation(s) below.

- Support for travel................................. NONE
- Honoraria for lectures ....NONE
- Honoraria for advisory board activities ...NONE
- Participation in clinical trials .... NONE
- Research funding .... *Caribbean Sport Orthopaedic Clinic LTD*
- Financial shares and options .... *Caribbean Sport Orthopaedic Clinic LTD*

OVERVIEW

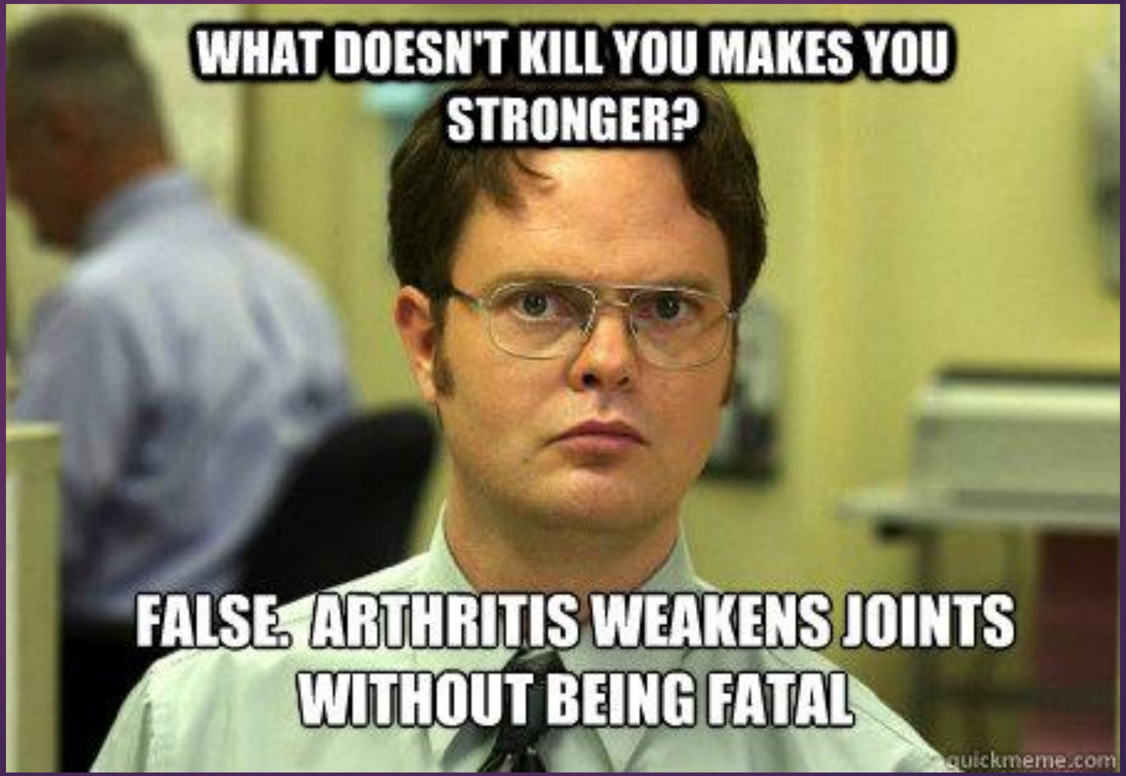
- Multifactorial aetiology & pathogenesis of OA influence treatment options
- Treatments Principles:
  1. *Manage pain*
  2. *Offload the affected joint*
  3. *"Cure" Arthritis*
  4. *(Prevention)*
- Treatment Choices:
  - *Pharmacological*
  - *Non-pharmacological*
  - *Regenerative*
  - *Surgical*
  - *(Adjuvant Therapies)*
- Factors influencing Treatment Strategies:
  - *Disease factors – e.g Location of the OA, Chronicity*
  - *Patient factors – Genetics, Socio-economics, Compliance*
  - *Resources available to physician & to patient*
  - *Health Policy - Guidelines/ Protocols from "powers that be"*
- T-BOP
  - *The Barbados Osteoarthritis Project*

OA: "The Nature of the beast"
What do we know?



What is “Arthur”?

“I don’t want ”Arthur” nah!, Dat go kill mih!”



What is "Arthur"?

- Osteoarthritis (OA) is <u>a heterogeneous group of conditions</u> that have in common:
  - Disturbed integrity of articular cartilage <u>and</u>
  - Changes in the underlying bone
  - (Variable degrees of inflammation depending on aetiology)

- Pathogenesis is multifactorial
  - Genetic (female line)
  - Metabolic (Diabetes - Charcot joints)
  - Biochemical (Inflammation, Acidic diet)
  - Biomechanical (e.g. ↑BMI , Hypermobility, Trauma, Repetitive overuse)
  - Variable components of Inflammation (autoimmune, psoriatic, gout)

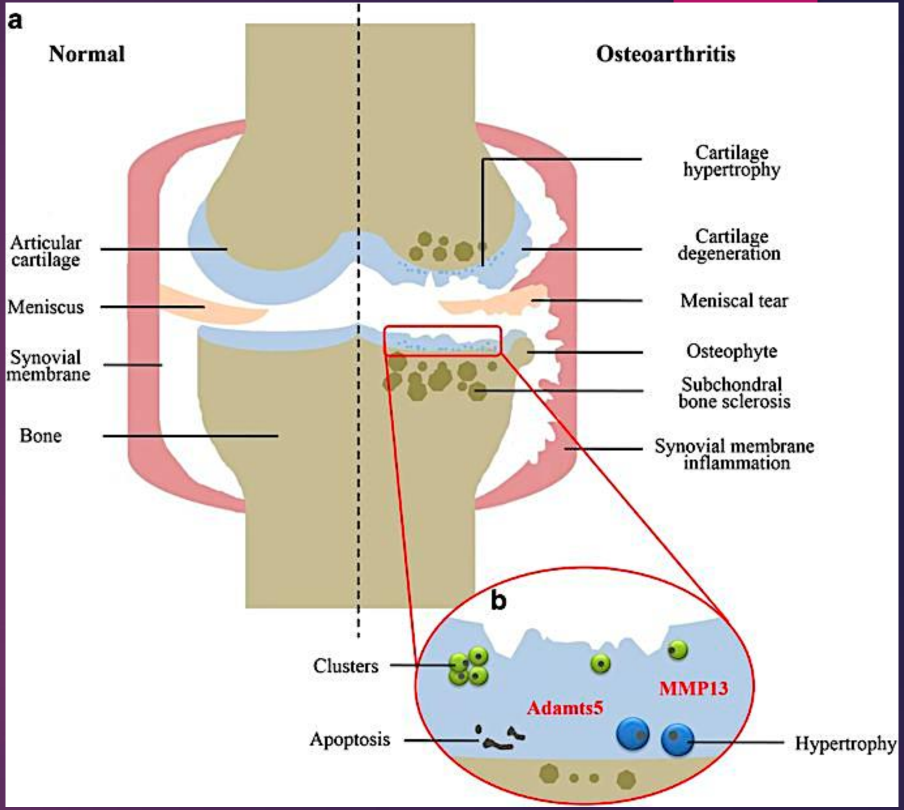


Figure 1. OA cartilage.
(a) The changes of articular structure during OA progression.

(b) Cellular responses in OA cartilage.

OA TREATMENT PRINCIPLES

1. *Manage pain*
2. *Offload the affected joint to slow progression*
3. *"Cure" Arthritis by stimulating cartilage regeneration*
4. *(Prevention – control modifiable risk factors)*

1. Managing OA Pain

1. *Pharmacological*
2. *Non-Pharmacological*
3. *Regenerative Therapies*
4. *Surgery*
5. *(Alternative Therapies)*

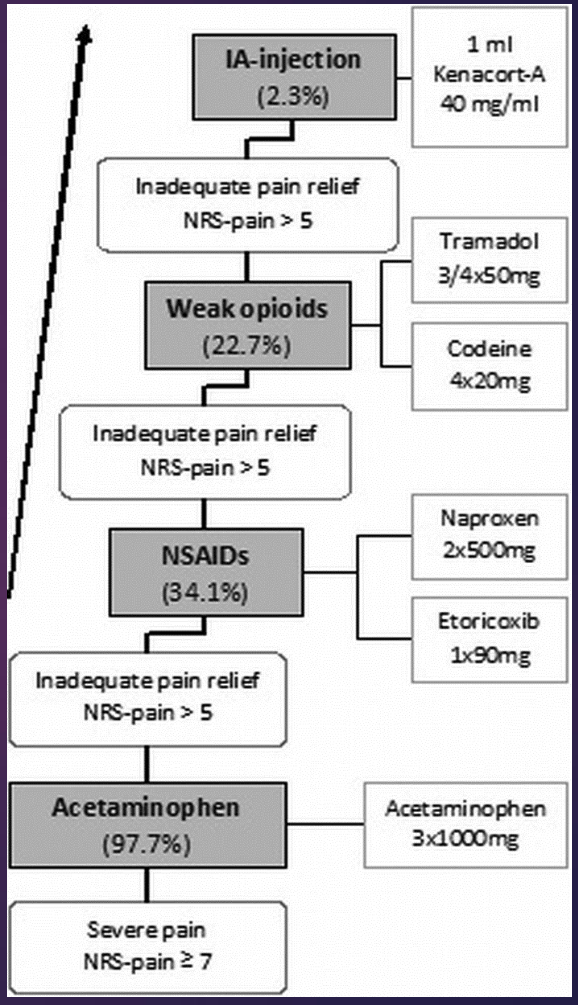
Managing OA Pain
Current Pharmacological Treatments

- ORAL ANALGESICS
  - NSAIDs/ Acetaminophen/ Weak opiods (not strong)
  - Oral Prednisolone --------------- ------- *NO EVIDENCE!!*
- TOPICAL
  - NSAIDs
  - Topical rubefacients (e.g. Deep Heat) - *NO EVIDENCE!!*
  - WD40 !! ------------------------------------ *NO EVIDENCE!!*
- INTRA-ARTICULAR INJECTIONS
  - Glucocorticoid
  - Hyalauronic Acid (e.g. Synvisc One)- -*LIMITED SCIENTIFIC EVIDENCE*

    ……*BUT GOOD ANECDOTAL EVIDENCE!!*

Managing OA Pain
Current Pharmacological Treatments 2

- **NEUTRICIALS** – *Limited Evidence*
  - Glucosamine/ Chondroitin
  - *Fish Oils*
  - *Omega XL*
  - *Tumeric*
  - *Ginger*



Managing OA Pain:
New Pharmacological Treatments 1

- **DMARD's……** trials ongoing
  - Hydroxychloroquinine
  - Methotrexate

- **Antibodies** ..targeting OA Pain biomarkers
  - IL-1 e.g.(Anakinra)
  - IL-17, or -18,
  - TNFa

Table 2. Biomarkers of OA Pain, 2014–2016.

Blood	Synovial Fluid
Increased	***Increased***
2-AG[139]	Autotaxin[140]
Autotaxin[140]	CCL2[141]
BDNF[142]	CD14[143]
CB1R/CB2R (PBL expression)[139]	CGRP[144]
CD14[143]	CX3CL1/fractalkine[145]
CGRP[144]	YKL-40[146,147]
COMP[148]	
CX3CL1/fractalkine [145]	***Decreased***
HMGB-1[149]	IL-17[150]
sHA[148]	sTNFR1, sTNFR2[136]

2-AG, 2-arachidonoylglycerol; BDNF, brain-derived neurotrophic factor; CB1R/CB2R, cannabinoid receptors 1 and 2; PBL, peripheral blood leukocyte; CCL, C-C motif chemokine ligand; CD14, cluster of differentiation 14; CGRP, calcitonin gene-related peptide; COMP, cartilage oligomeric matrix protein; CX3CL1, fractalkine; HMGB, high-mobility group box; IL, interleukin sHA, serum hyaluronic acid; sTNFR, soluble tumor necrosis factor receptor; YKL-40, chitinase-3-like protein 1 (CHI3L1).

Published in: David A. Walsh; Joanne Stocks; SLAS DISCOVERY: Advancing Life Sciences R&D 22, 931-949.
DOI: 10.1177/2472555217716912

Managing OA Pain:
New Pharmacological Treatments 2

- **Osteoclast inhibitors/ Agents affecting bone turnover**
  - Bisphosphonates
  - Strontium Ranelate
  - Osteoprotegerin
  - Cathepsin K inhibitors
- **Peripheral Sensory Nerve blockers**
  - Anti- NGF (eb Tanezumab, Fasinumab)
- **CNS Pain Modulation (for "Chronic" Pain)**
  - Antideppressants e.g. Duloxetine – an SSNRI
  - Anxiolytics/ Mood stabilizers
  - Neuropathic pain meds
    - Pregabalin

Table 2. New OA drugs and emerging therapeutics investigated in clinical studies (*) or preclinical animal studies

Mode of action	*Targets*	*Potential therapeutics*
Chondrogenic differentiation	BMP-7*	rhBMP-7 (OP-1)[70]
	FGF*	rhFGF-18 (sprifermin)[76]
	PRP (containing several kinds of growth factors)*	Autologous PRP[78–80]
Inhibition of hypertrophy and ossification	PTH/PTHrP receptor	rhPTH (1–34) (teriparatide, Forteo),[126] rhPTHrP (1–40)[123]
	Hedgehog signaling	Smo inhibitor (HhAntag, LDE223)[127–128]
Inhibition of matrix degradation	MMP13	MMP13 inhibitor (CL82198)[118]
	Adamts-5	Adamts-5 inhibitor (114810)[119]
	Syndecan-4	Syndecan-4-specific antibody[120]
Inhibition of inflammation	IL-1β*	IL-1β receptor antagonist,[71] IL-1β receptor antibody (AMG108)[7
	HSA*	a < 5-kDa ultrafiltrate of HSA (Ampion)[83–84]
	Methotrexate*	Methotrexate[85–88]
Reduction in pain	β-NGF*	Monoclonal antibody against β-NGF (Tanezumab)[73–75]
Subchondral bone	TGF-β	TGF-β type I receptor inhibitor (SB-505124), TGF-β antibody
	Wnt/b-catenin	Wnt antagonist (Dkk-1)[131]

β-NGF, β-nerve growth factor; BMP-7, bone morphogenetic protein-7; OP-1, osteogenic protein-1; Dkk-1, dickkopf-related protein-1; FGF, fibroblast growth factor; HSA, human se albumin; PTH, parathyroid hormone; PTHrP, parathyroid hormone-related protein; rhBMP-7, recombinant human BMP-7; rhFGF; recombinant human FGF; rhPTHrP; recombi human PTHrP; MMP13, matrix metalloproteinase 13; OA, osteoarthritis; PRP, platelet-rich plasma; TGF-β, transforming growth factor-β.

Published in: NATURE: Bone Research (2016), W Zhang et al

Managing OA Pain:
Non-Pharmacological Treatments 1

- **WEIGHT LOSS**
  - By Regular Exercise (not DIET alone!)
- **PHYSICAL & OCCUPATIONAL THERAPIES**
  - Pain relieving modalities (e.g.Temperature)
  - Functional exercises
  - Muscle strengthening
- **ALTERNATIVE THERAPIES**
  - Accupuncture
  - Osteopath
  - Chiropractor







Managing OA Pain:
Non-Pharmacological Treatments 2

PSYCHOSOCIAL INTERVENTIONS

- Education & Self-management
- Community Group activities e.g. Exercise
- Psychotherapy/ CBT

A. https://www.cdc.gov/arthritis/interventions/index.htm

B. https://arthritishealth.selfmanage.org/

https://health.gov/moveyourway/

Managing OA Pain:
Non-Pharmacological Treatments 3

- Offloading Arthritic Joints
- “Curing “Arthritis by Regenerating Cartilage
- “Curing “Arthritis by Surgery – Cartilage Restoration Procedures
- “Curing “Arthritis by Surgery – Arthroplasty

2. Offloading Arthritic Joints

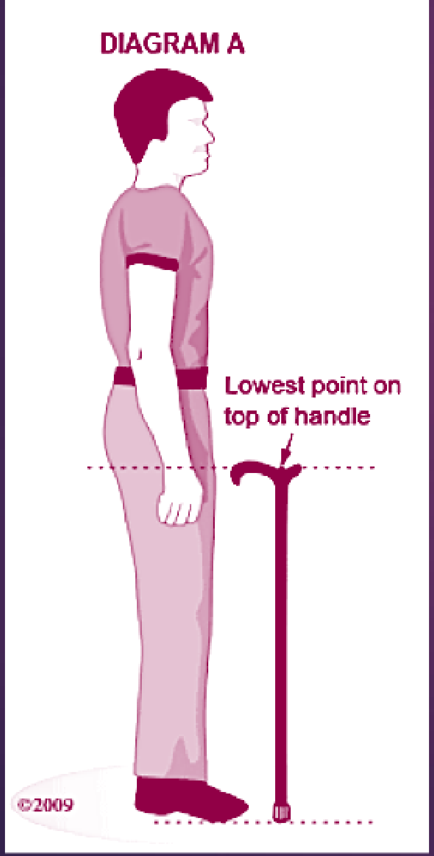
MECHANICAL DEVICES

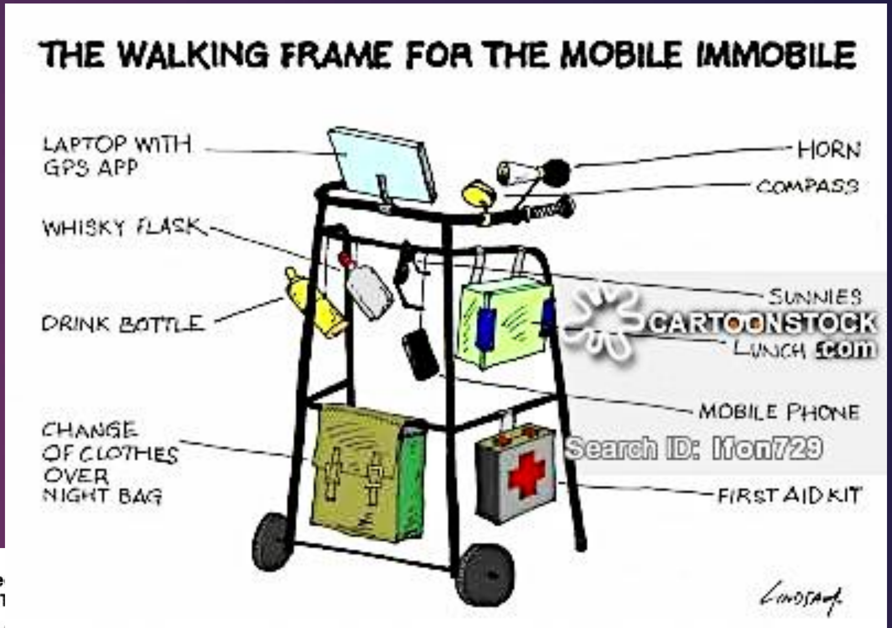
- Walking aids
- Braces
- Orthotics

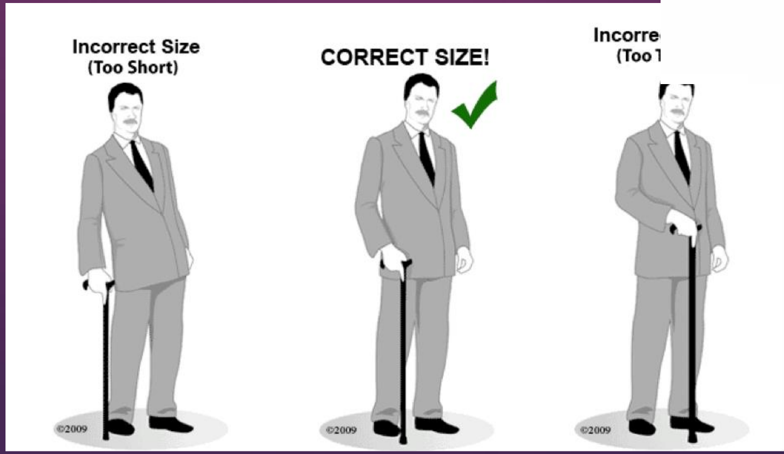
SURGERY

- Osteotomy
- Ligament Reconstruction
- Osteoplasty
- Arthroplasty

"Offloading" Arthritic Joints
Walking Aids







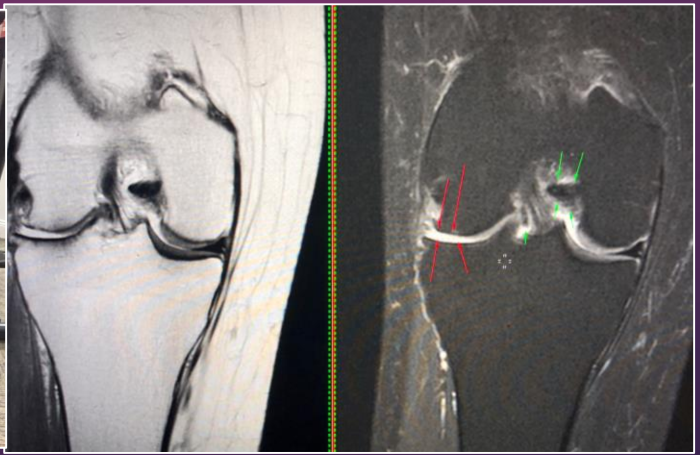
"Offloading" Arthritic Joints
Orthotics and Braces

- Braces
- Orthotics





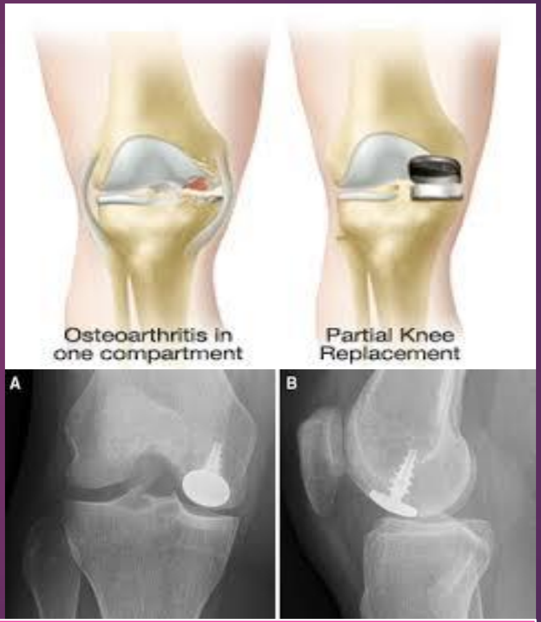





"Offloading" Overloaded-Joints:
Surgical Treatments

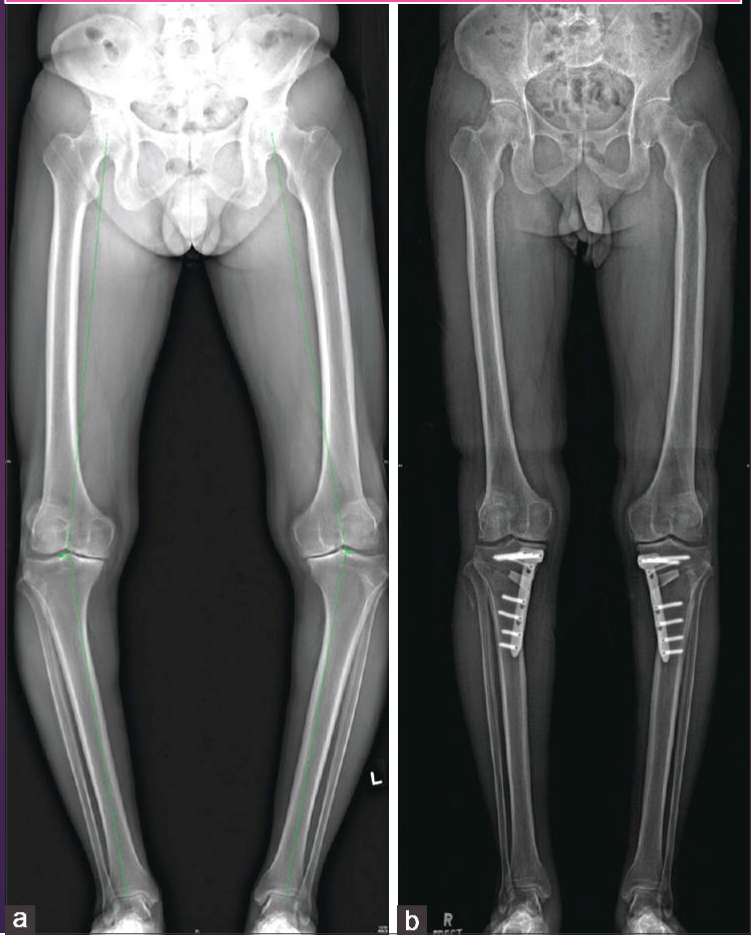
- Osteotomy
- Osteoplasty
- Partial Joint Replacement

Hip Arthroscopy and Osteoplasty for FAI



Partial Joint Replacement

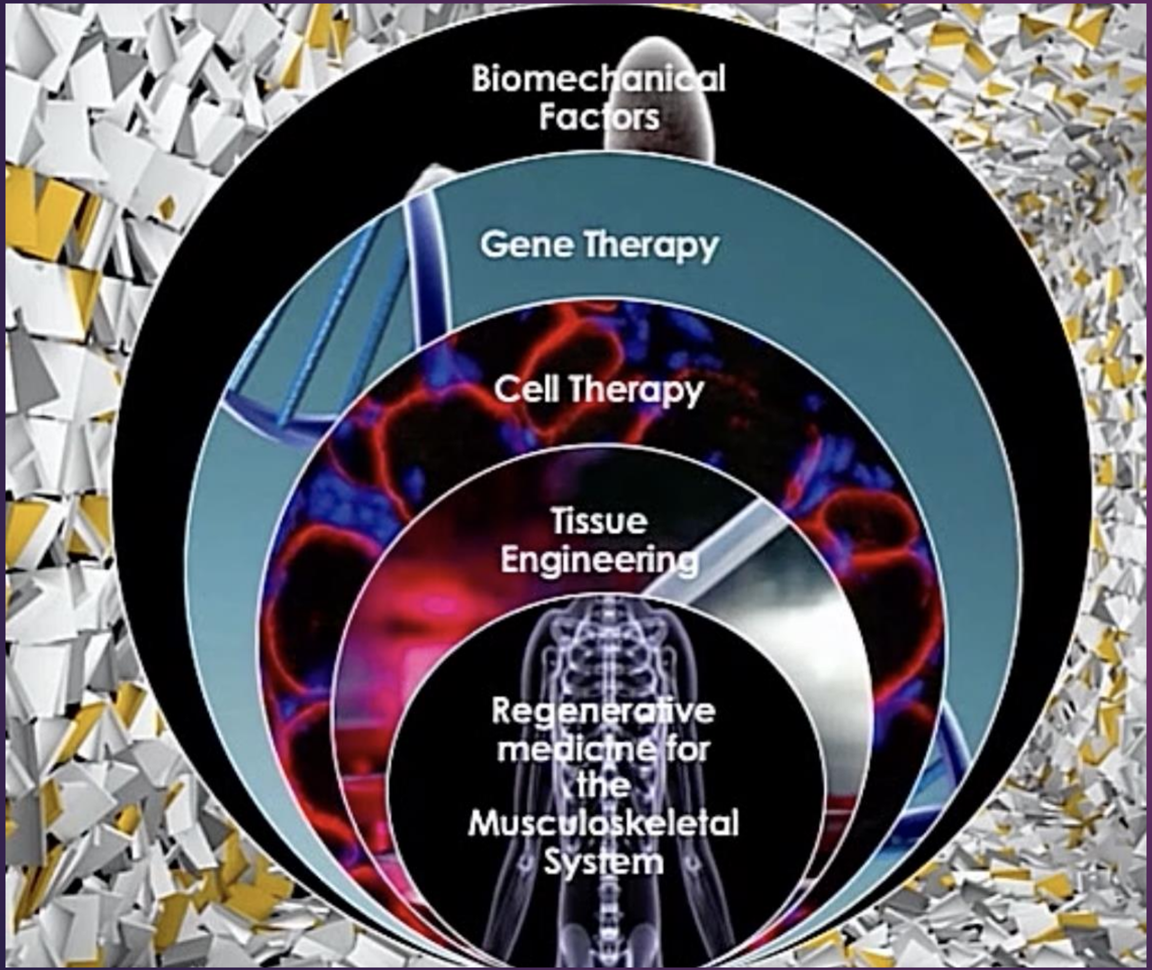
Bilateral Knee Osteotomies for medial compartment OA



3. "Curing" Arthritis

- MEDICAL REGENERATIVE THERAPIES
  - PRP
  - Stem Cells
  - Gene Therapy
- SURGICAL CURES FOR OA
  - Cartilage Restoration Surgical Procedures
  - Arthroplasty

A CURE FOR ARTHRITIS? – Regenerative Therapies



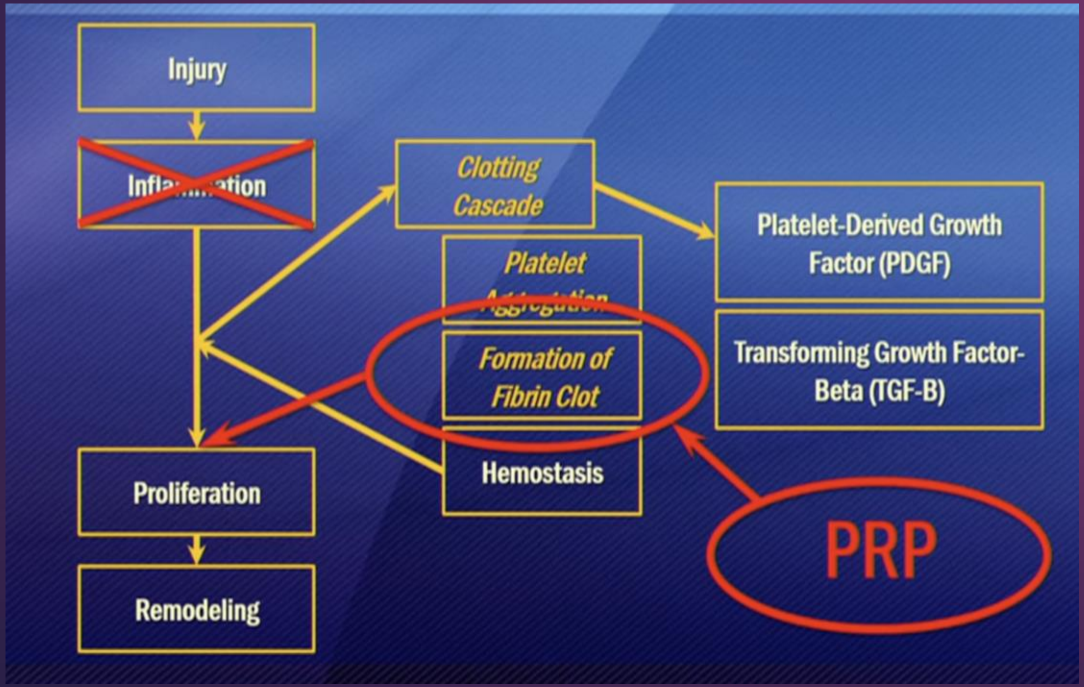
Targets for Biological Treatment of Osteoarthritis

PLATELET RICH PLASMA (PRP)

<u>How does PRP Work?</u>

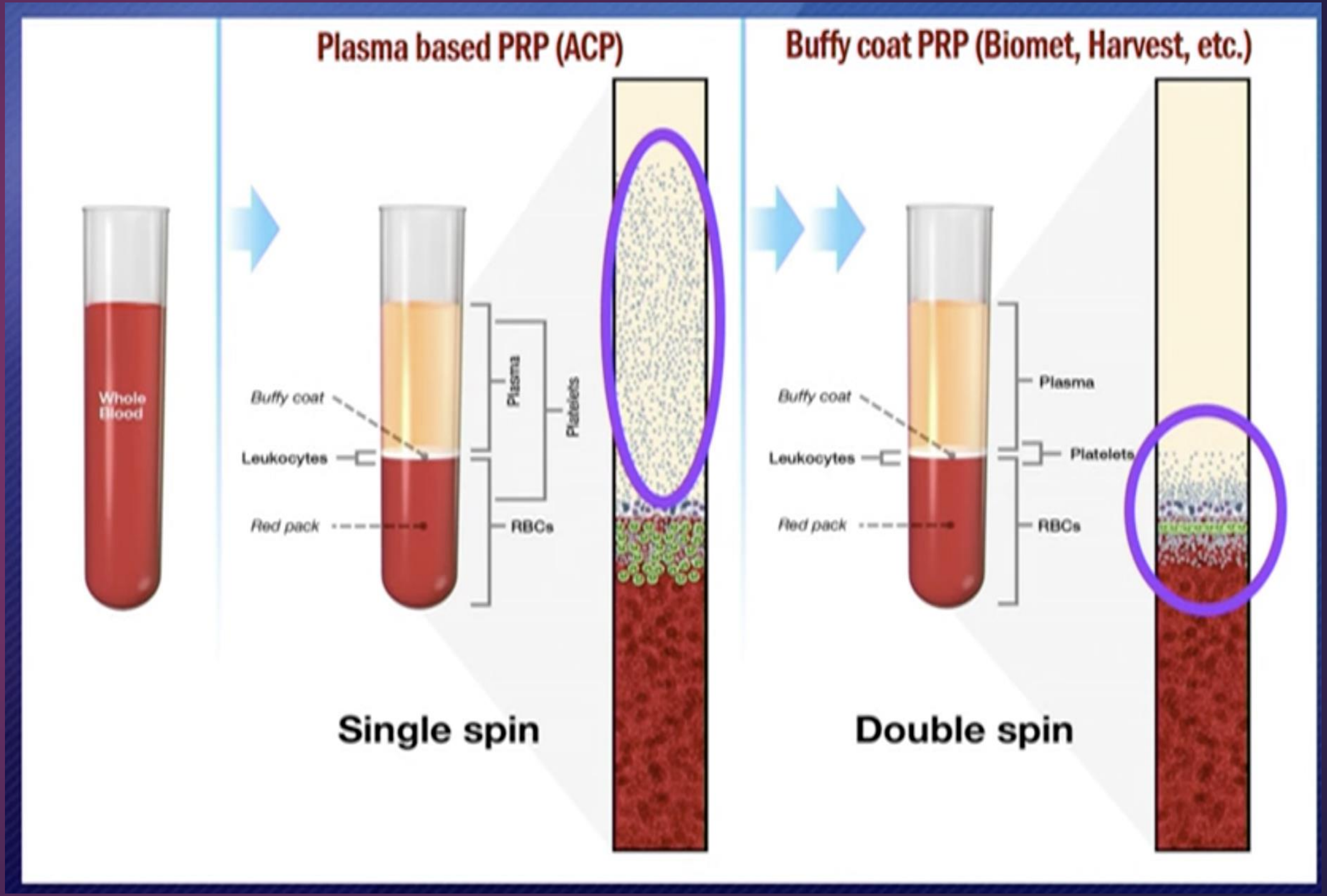
- Attempts to take advantage of the blood's natural healing properties to repair damaged musculoskeletal tissues: cartilage, tendons, ligaments, muscles, and even bone.

- PRP is injected into the affected tissue which *<u>leads to local inflammation</u>* and a *<u>"wound healing cascade":</u>*



Generation 1 PRP – 4 main types

- **Autologous blood injection**
- **Leukocyte-rich PRP (LR-PRP)** produced from the buffy coat layer:
  - a. GPS kit (Biomet Biologistics)
  - b. MyCells kit (Kaylight Ltd)
  - c. Prosys kit (Tozai Holdings Inc):
- **Leukocyte-poor PRP** (LP-PRP)
- **ACP** (minimal leucocytes)

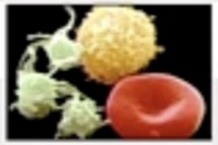


Platelet Rich Plasma (PRP)

- The platelet concentration
- Cytokines
- Growth Factors
- ***STIMULATE STEM CELLS***
- ***Anti-inflammatory properties***
- ***But also can be Pro-inflammatory***

PRP 1507 unique proteins in platelets

GROWTH FACTORS	FUNCTION
PD-EGF platelet-derived epidermal growth factor	Cell growth, recruitment, Differentiation, skin closure, Cytokine secretion
PDGF A + B platelet-derived growth factor	Potent cell growth, recruitment Blood vessel growth, granulation Growth factor secretion; matrix formation with BMPs (collagen and bone)
TGF-β1 transforming growth factor	Blood vessel (±), collagen synthesis, Growth inhibition, apoptosis (cell death), Differentiation, activation
IGF-I, II insulin-like growth factor	Cell growth, differentiation, recruitment, Collagen synthesis with PDGF
VEGF, ECGF vascular endothelial growth factor, endothelial cell growth factor	Angiogenesis, Mitogenesis, Cell growth, migration, new blood vessel growth Anti-apoptosis (anti–cell death)
bFGF basic fibroblast growth factor	Chemotaxis, Cell growth, Cell migration, blood vessel growth



Growth factors positive effect cartilage metabolism and regeneration
Synovium, Meniscus, chondrocytes

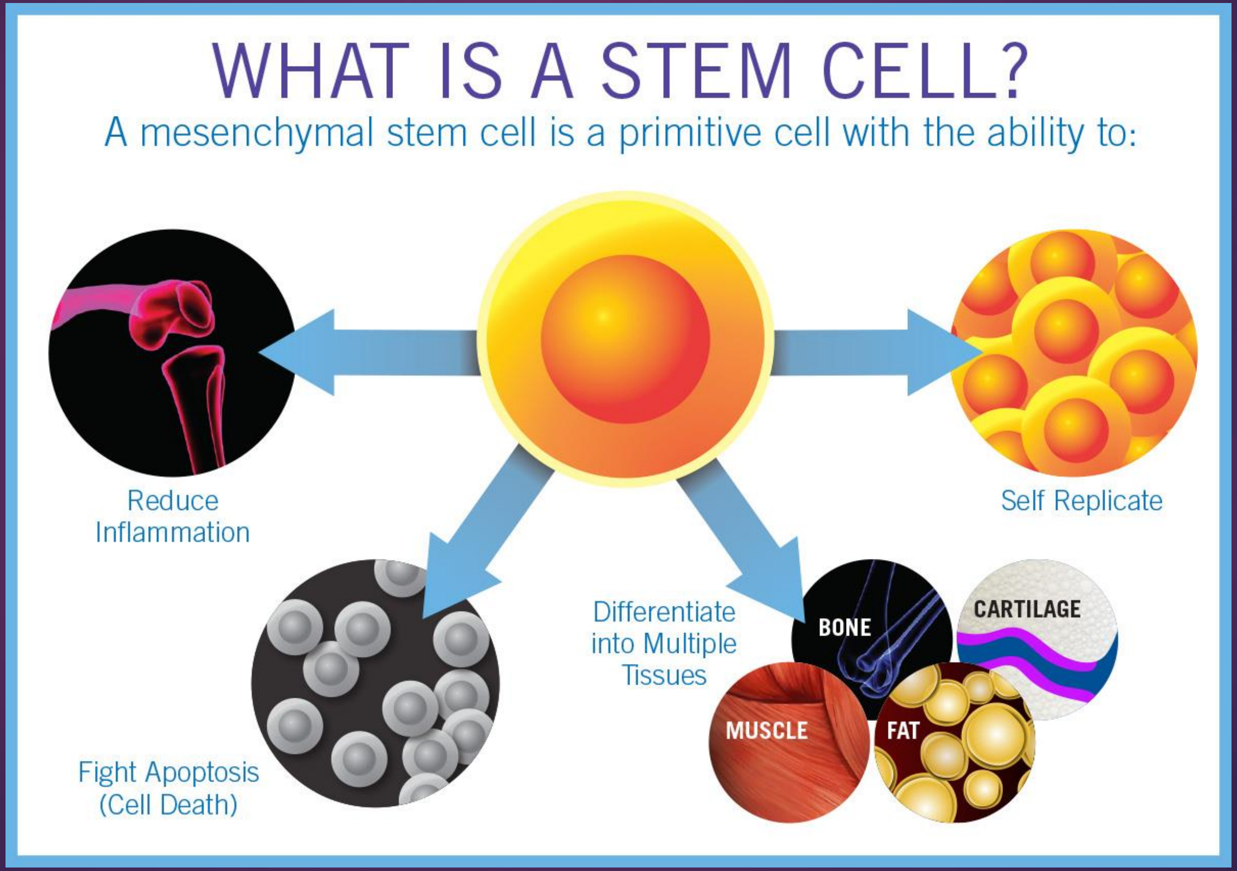
Akeda K et al. Osteoarthritis Cartilage. 2006
Wu W et al. J Oral Maxillofac Surg. 2007
Frisbie D et al. Am J Vet Res. 2007
Saito M et al. Clin Exp Rheumatol. 2009

Uncertainties of PRP Treatment

- PRP encourages cell regeneration – HOW?
- Indications in OA – what stage/ grade?
- What are the optimal concentrations of platelets and white blood cells?
- How much PRP should be injected?
- When and with what frequency? Is one injection enough?
- What is the best rehabilitation protocol to use after PRP injection?
- Do certain additives, such as thrombin, make the PRP more effective?

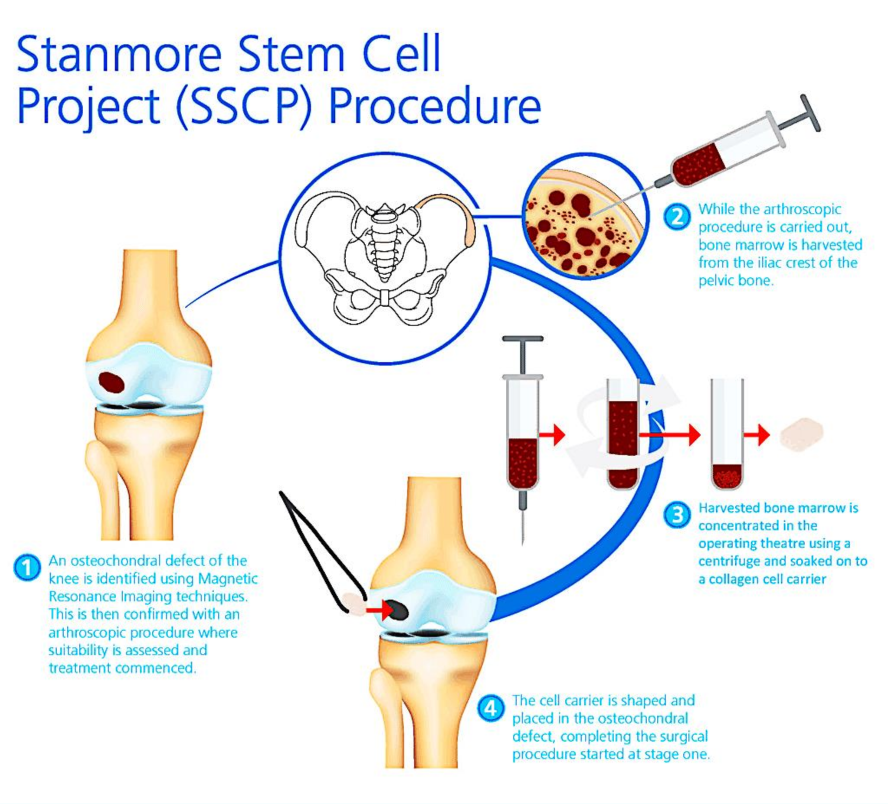
A faulty part from an independent supplier leads to the creation of a multibillion-dollar sports medicine profession.

A CURE FOR ARTHRITIS?
Stem Cell Therapies



Cartilage Regeneration:
Surgical Procedures (Research)

STEM Cell Procedures - UK



MACI PROCEDURE – Cartilage Cells- USA

https://www.maci.com/patients/dara/index.html

Other Surgical Treatment Options

- Arthroscopy and Debridement alone
  - No Evidence in OA & NOT RECOMMENDED!!

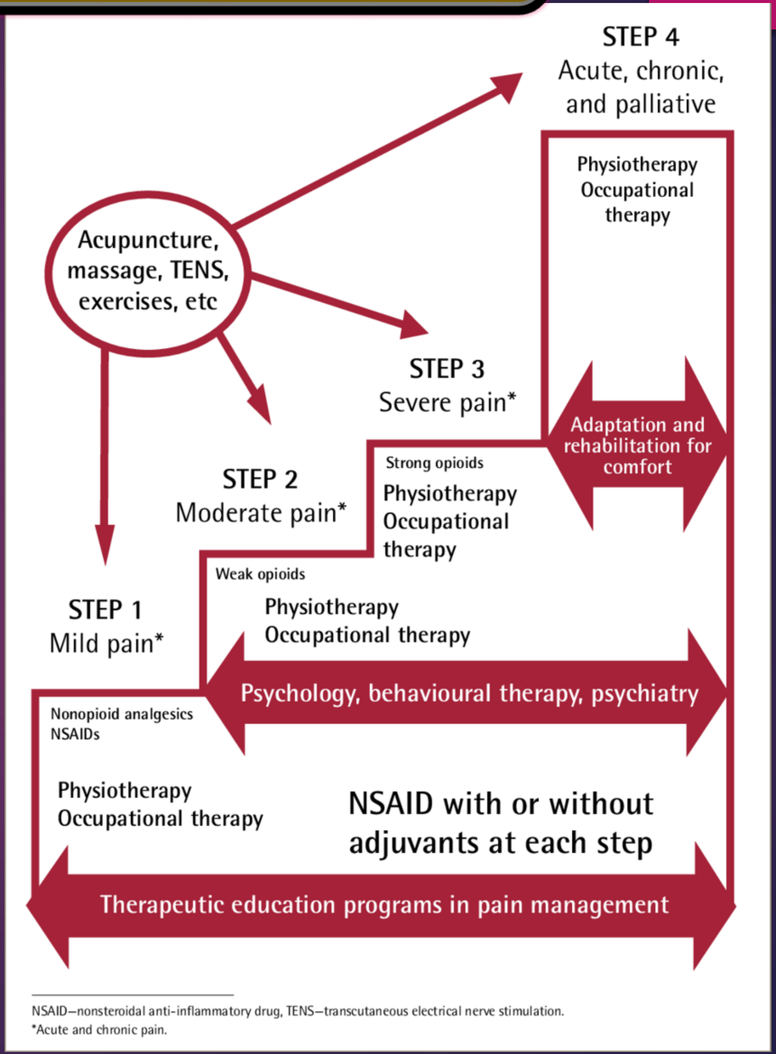
AAOS Recommended Treatments

- Arthroscopy & Marrow Stimulation Procedures e.g Microfracture
- ACI & MACI
- OATS – Autograft and Allograft
- ARTHROPLASTY -----Remains the GOLD STANDARD in Treatment of Severe OA

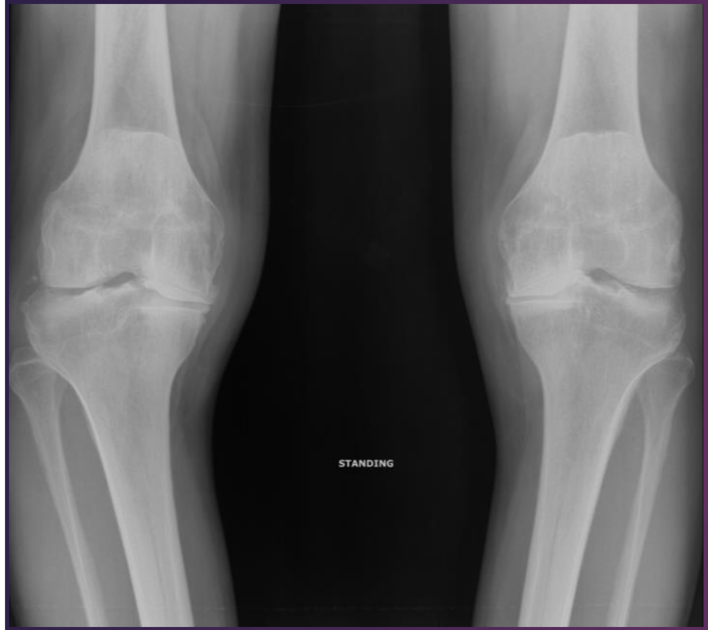
TREATMENT STRATEGIES

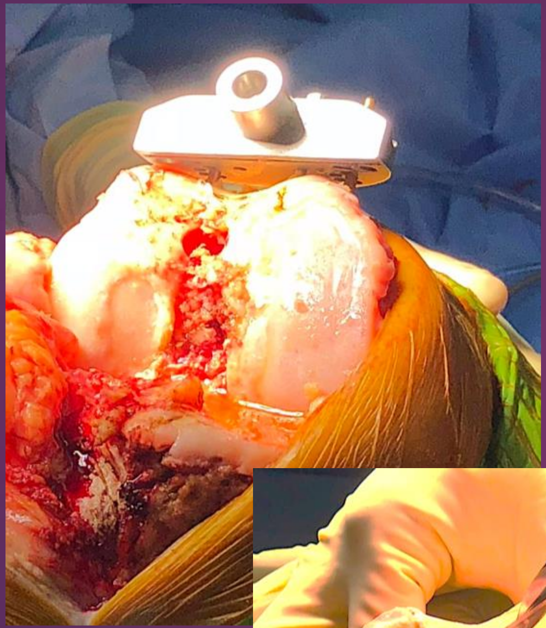
What treatment for OA & and when?

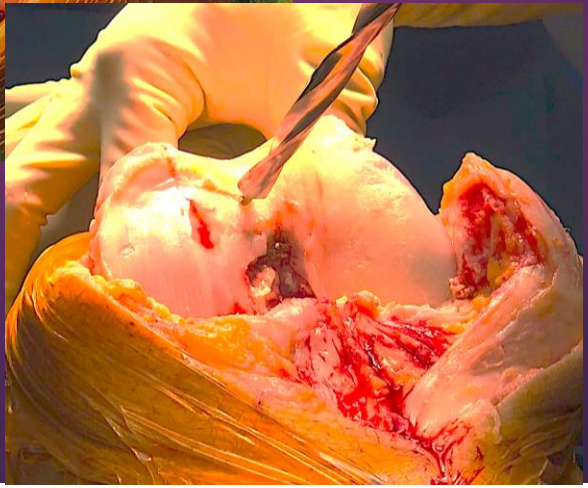
- Combination of pharmacological and non-pharmacological is the first line
- Surgery is last resort …but don't leave it too late
- Many international guidelines –with different recommendations
- What is best for Barbados?

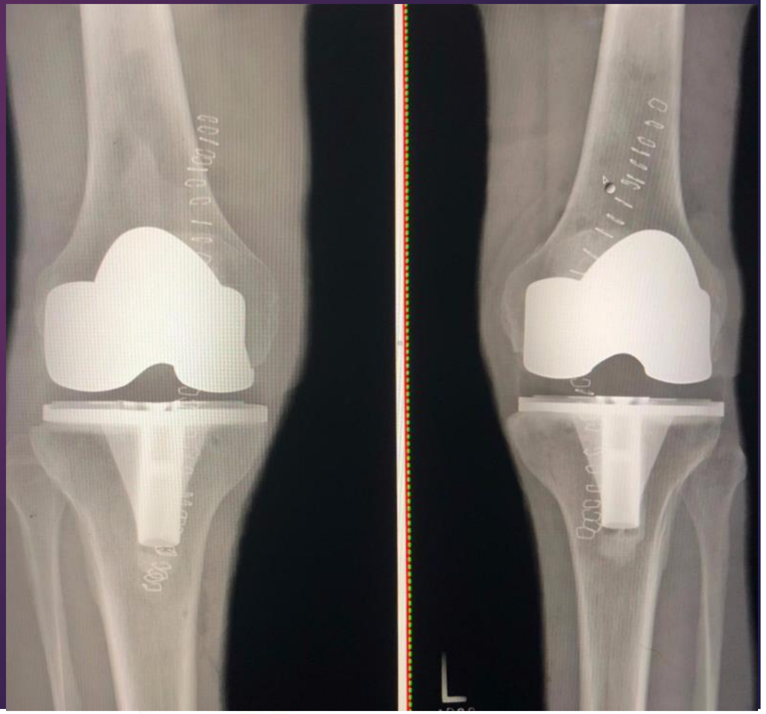


Better The Devil You Know…….

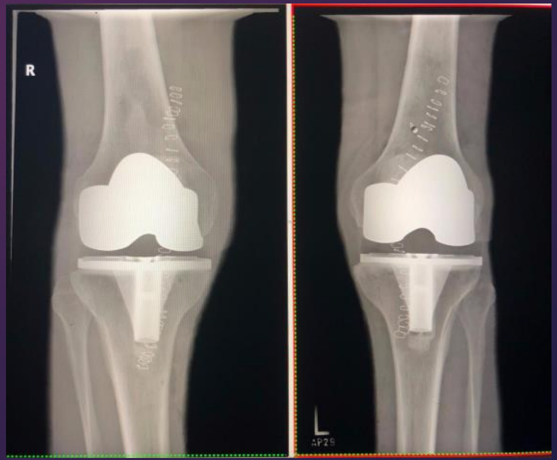








Better The Devil You Know.......



T-BOP
THE BARBADOS OSTEOARTHRITIS PROJECT

- Research Project to:
  - Estimate and highlight the prevalence, patterns and burden of the OA locally
  - Assess current knowledge, attitudes and perceptions of OA
  - Influence Caribbean Health Policy to optimize treatments

What is best for Barbados?

- 1st STAGE: INVITATION TO ONLINE SURVEY TO DOCTORS

CaveHillOrtho@ Gmail.com

T-BOP Stage 1: DOCTORS (K.A.P) SURVEY

INVITATION TO ONLINE SURVEY TO DOCTORS

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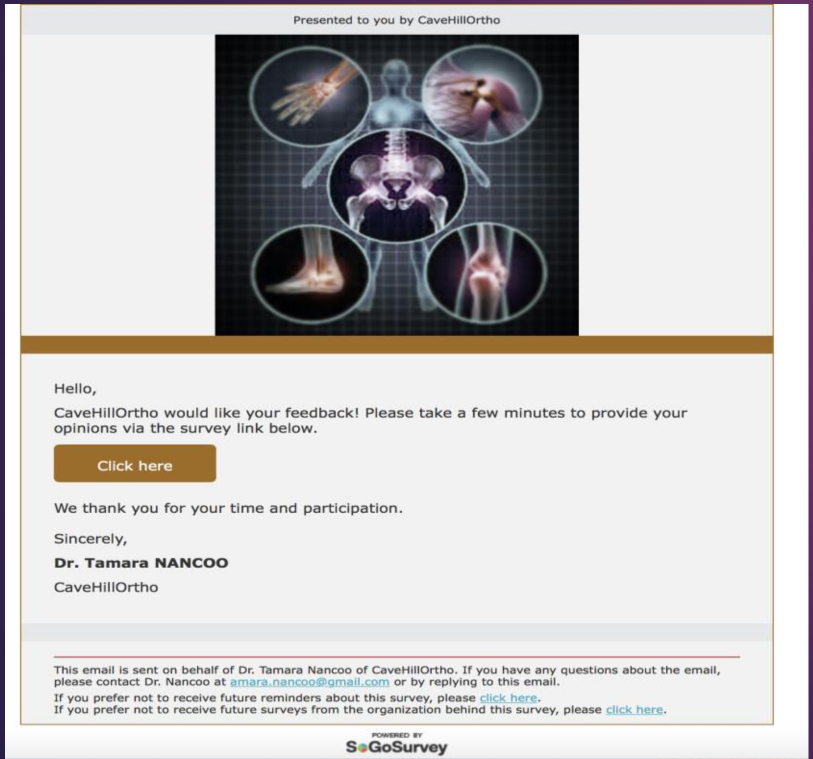
Presented to you by CaveHillOrtho

Hello,

CaveHillOrtho would like your feedback! Please take a few minutes to provide your opinions via the survey link below.

Click here

We thank you for your time and participation.

Sincerely,

Dr. Tamara NANCOO

CaveHillOrtho

This email is sent on behalf of Dr. Tamara Nancoo of CaveHillOrtho. If you have any questions about the email, please contact Dr. Nancoo at amara.nancoo@gmail.com or by replying to this email.

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THE UNIVERSITY OF THE WEST INDIES AT CAVE HILL, BARBADOS

QUEEN ELIZABETH HOSPITAL BARBADOS

Caribbean SPORTS ORTHOPAEDIC CLINIC

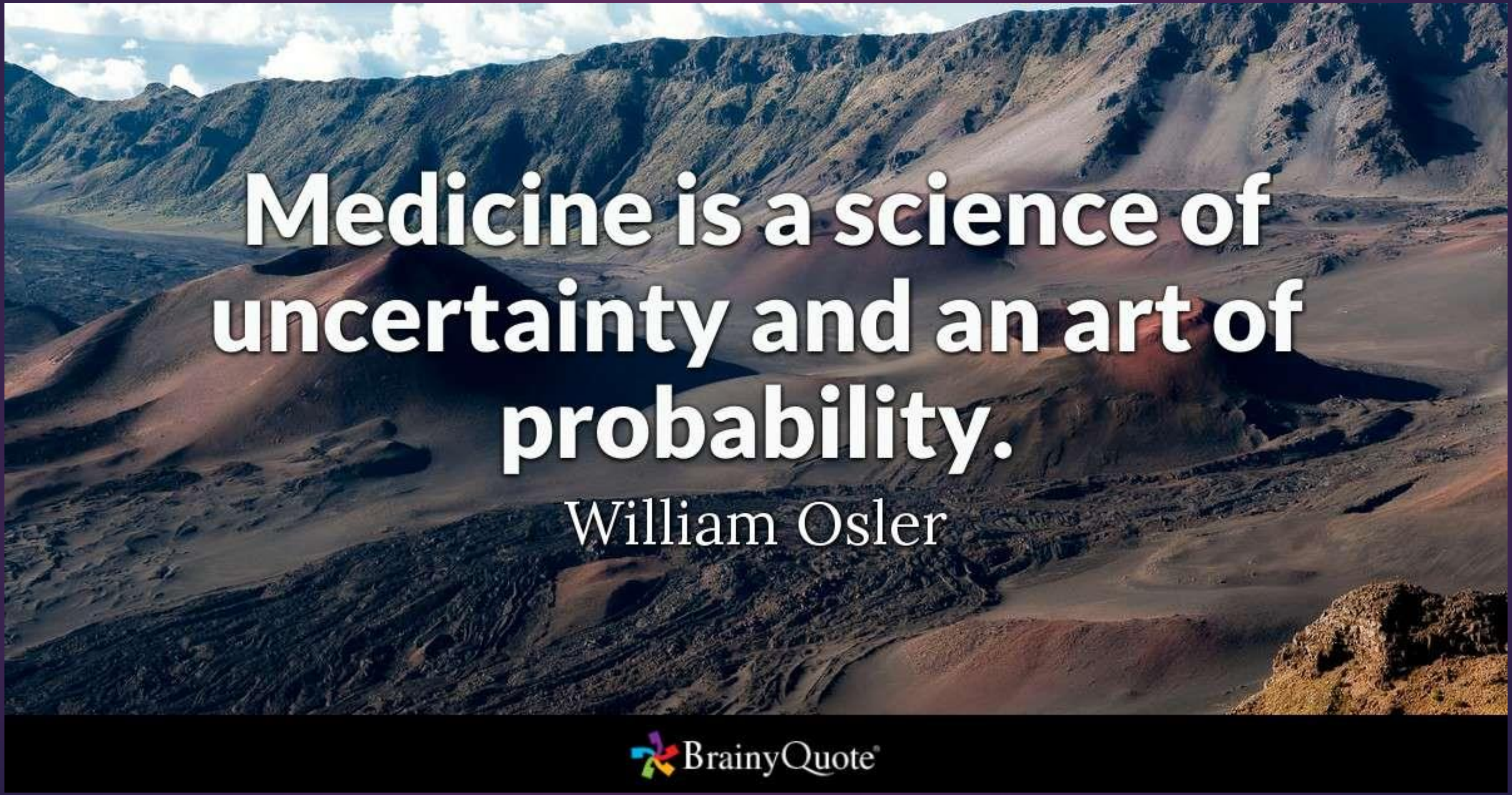
SUMMARY OF AVAILABLE TREATMENTS

TABLE 1: SUMMARY OF THERAPIES

Therapy	Current Use	Available Evidence
Corticosteroid	Injection for osteoarthritis all stages	Level 1
Hyaluronic Acid	Injection for osteoarthritis all stages	Level 1
Platelet-rich Plasma	Injection for mild-moderate osteoarthritis	Level 1
Mesenchymal Stem Cell	Injection for mild osteoarthritis	Level 2-3
Bone Marrow Aspirate Concentrate	Injection mild osteoarthritis, Surgical Augmentation of osteochondral lesion	Level 2-3
Osteochondral Autograft Transplantation	Small osteochondral lesions	Level 1
Autologous Chondrocyte Implantation/Matrix-induced Autologous Chondrocyte Implantation	Large Shallow osteochondral lesions	Level 1
Osteochondral Allograft	Large deep osteochondral lesions, SPONC	Level 1
Partial/Total Joint Allograft	Degenerative joint disease, tumor, severe osteochondral Loss	Experimental

COURTESY OF RIVKA C. IHEJIRIKA, MD

Questions?


Medicine is a science of uncertainty and an art of probability.
William Osler
BrainyQuote

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  - **DOI : 10.2174/1573397113666170829155149**

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  - David A. Walsh, Joanne Stocks
  - First Published July 6, 2017: SLAS DISCOVERY: Advancing Life Sciences R&D 22, 931-949.
  - https://doi.org/10.1177/2472555217716912

- Efficacy of Hydroxychloroquine in Hand Osteoarthritis: A Randomized, Double-Blind, Placebo-Controlled Trial
  - Weiching Lee, Liesbeth Ruijgrok, Bianca Boxma-de Klerk, Marc R. Kok, Margreet Kloppenburg, Andreas Gerards, Margriet Huisman, Mieke Hazes, Peter de Sonnaville, Bart Grillet, Angelique Weel and Natalja Basoski
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