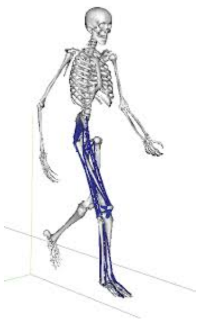

Load modifying interventions for knee osteoarthritis

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Campbell Fellow

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Stream Co-leader – Musculoskeletal
NHMRC Senior Research Fellow

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Sir Randal Heymanson Research Fellow
NHMRC Emerging Leadership Fellow
Dame Kate Campbell Fellow

What is osteoarthritis?

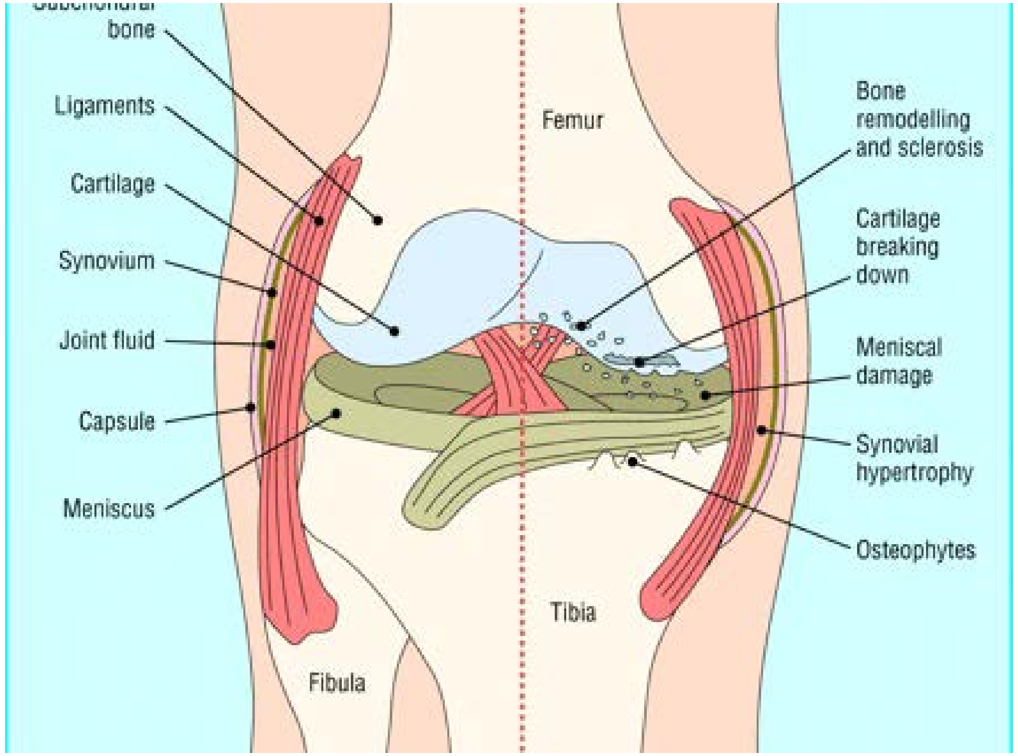
- Most common disorder of moveable joints
- Involves the entire joint organ, not just the articular cartilage

Complex pathological process:

- Micro and macro injury
- Cell stress and extracellular matrix degradation
- Maladaptive repair process/ abnormal joint tissue metabolism
- Anatomic and/or physiologic derangements

Hunter and Felson, *BMJ* 2006 639-642

Normal knee | Osteoarthritic knee



Knee osteoarthritis

- 5-10 times more common in medial than lateral compartment
- Diagnosis based on clinical presentation, supported by radiography
- Knee pain with 3 or more (sensitivity 95%, specificity 69%)
  - Age>50
  - Morning stiffness <30 mins
  - Crepitus on active motion
  - Bony tenderness
  - Bony enlargement
  - No palpable warmth of synovium

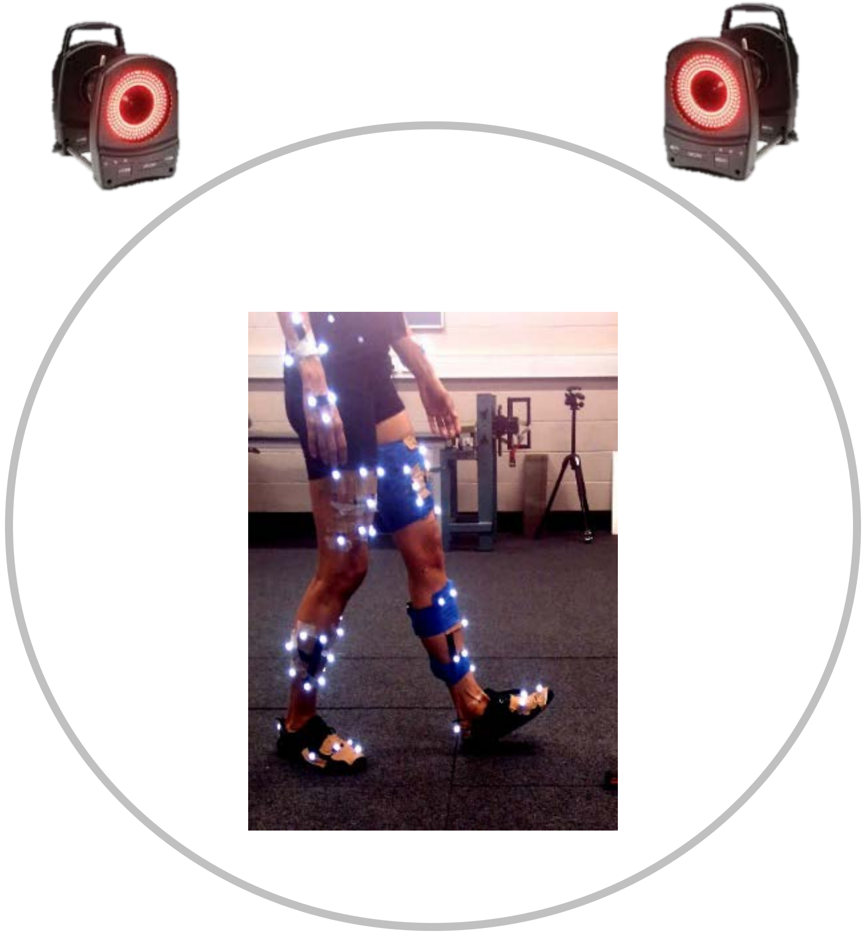
ACR Diagnostic guidelines

The 2.1 billion dollar problem

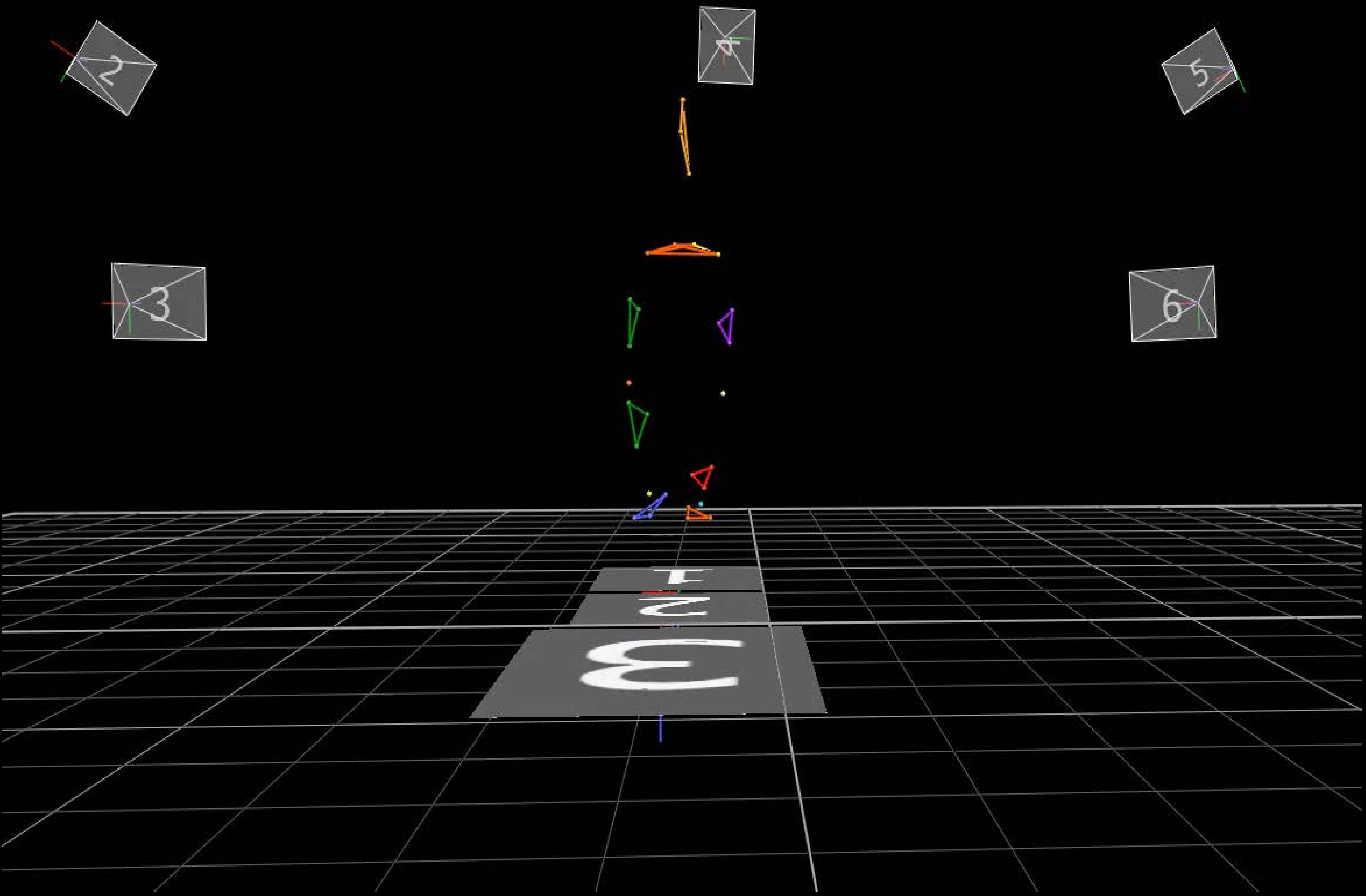
Arth Aust, *Counting the costs (2016)*

Osteoarthritis is in part a mechanical condition

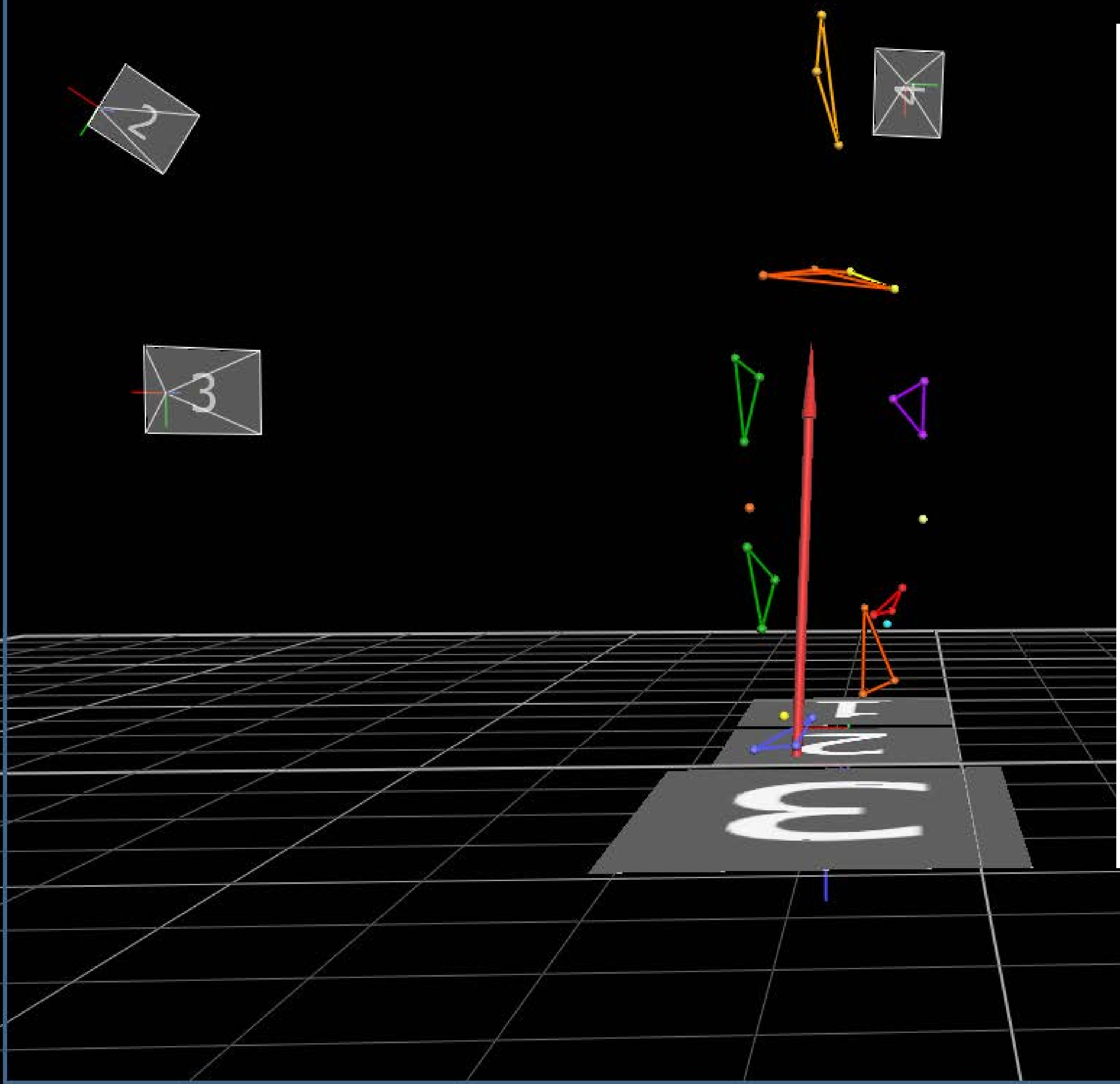
Joint moments often used to infer joint loading

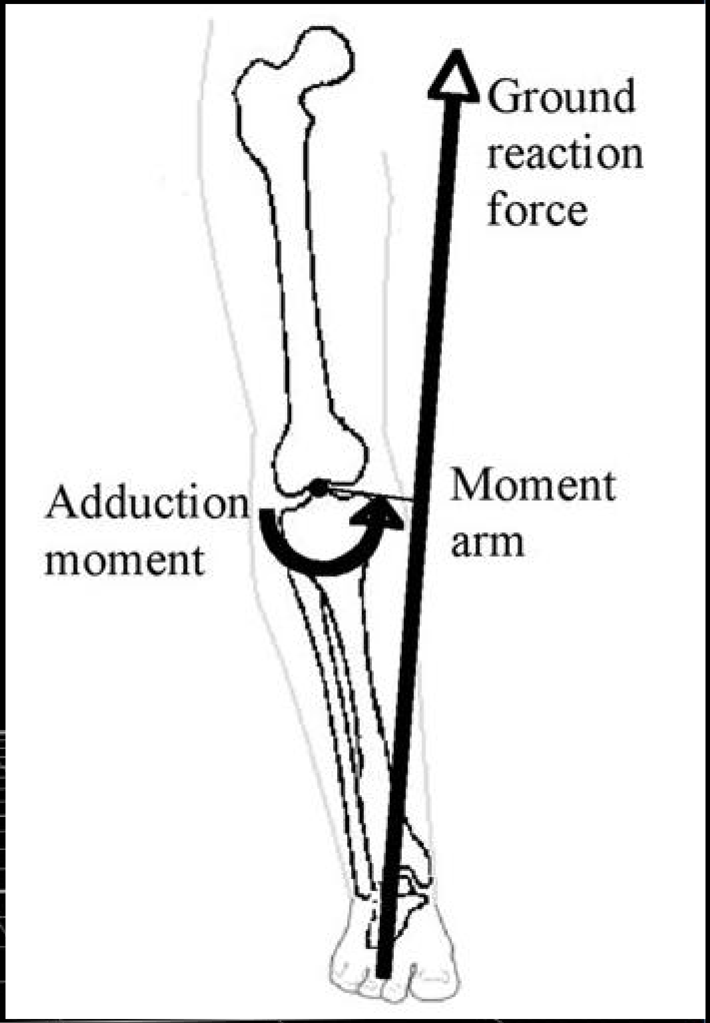


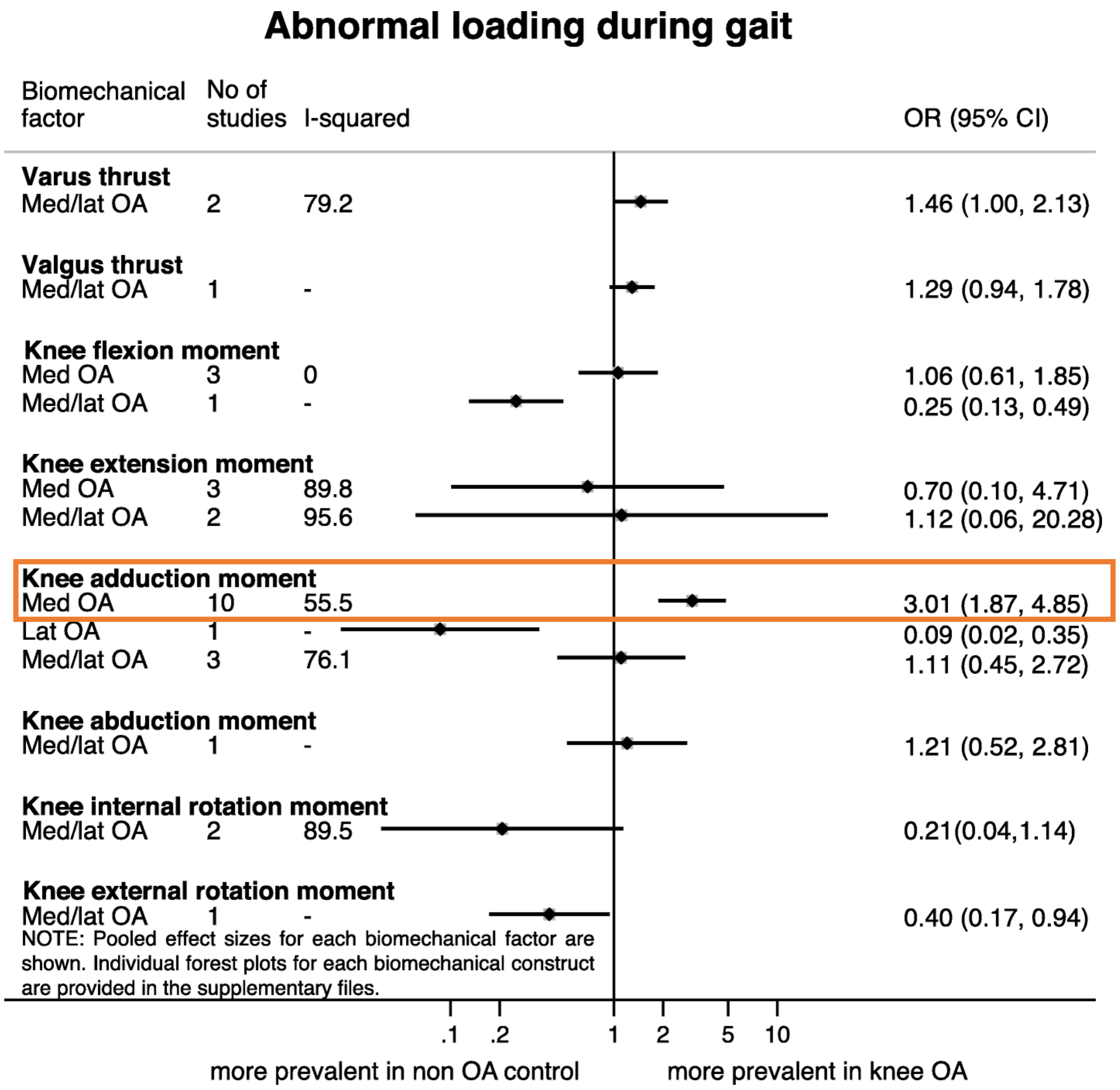
Knee adduction moment (KAM)



Knee adduction moment (KAM)







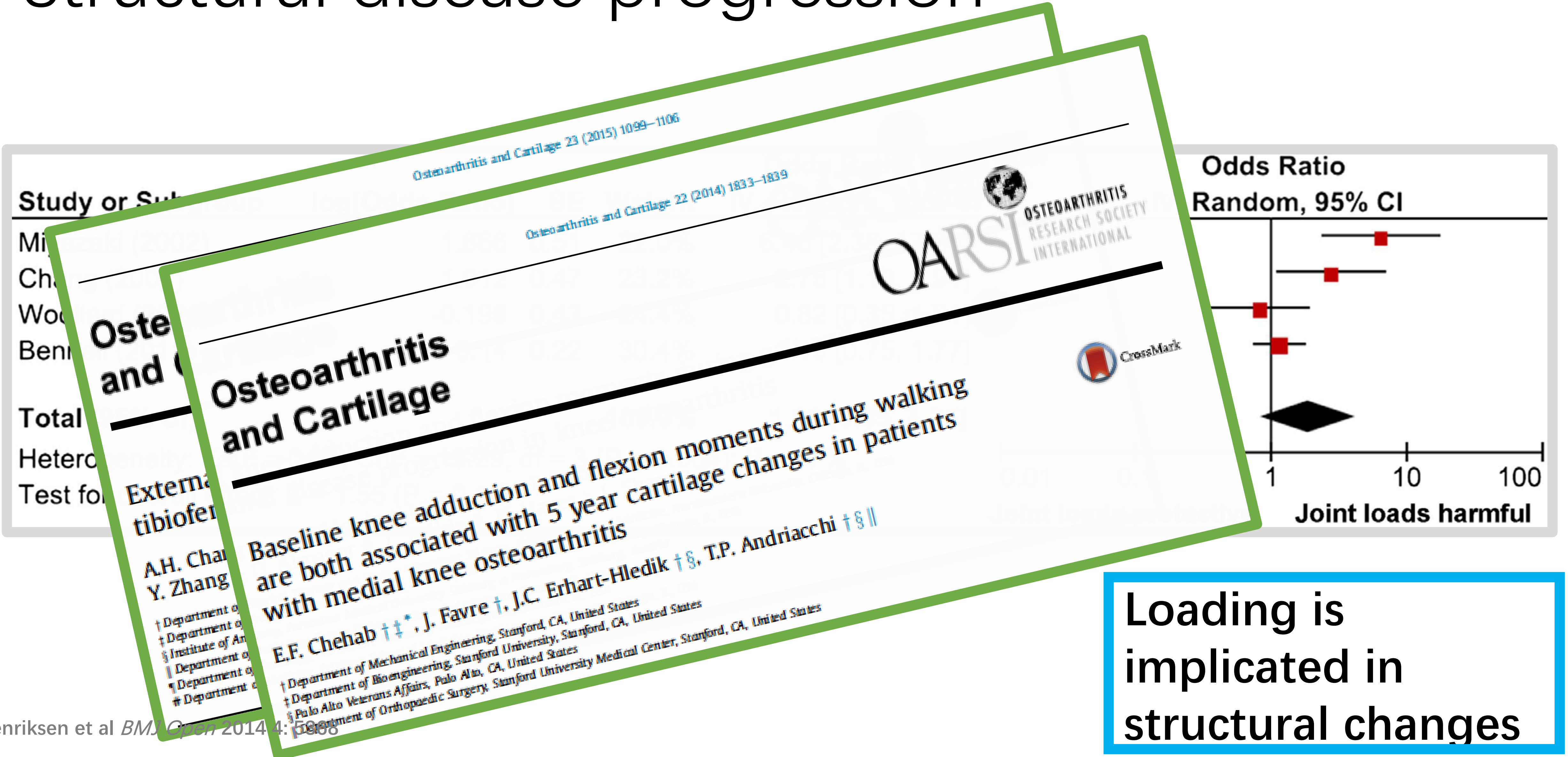
van Tunen et al *BMC Musculoskeletal Disorders* 2018 19: 273

3 Medial knee osteoarthritis higher odds of have a larger knee adduction moment

No evidence of alterations in joint moments according to disease severity

Mills et al *BMC Musculoskeletal Disorders* 2018 19: 273

Structural disease progression

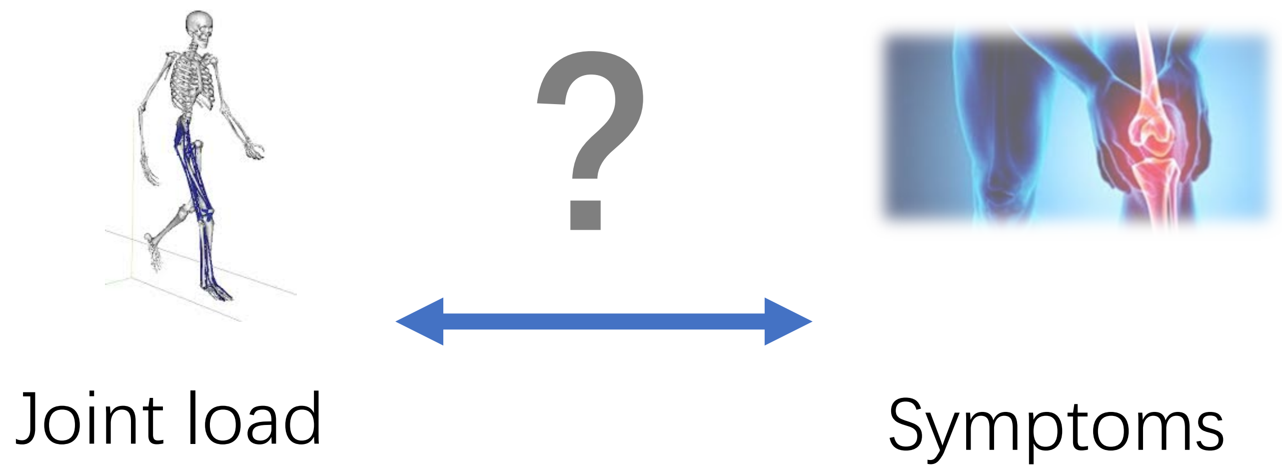


Loading is implicated in structural changes

Henriksen et al *BMJ Open* 2014 4: 5368

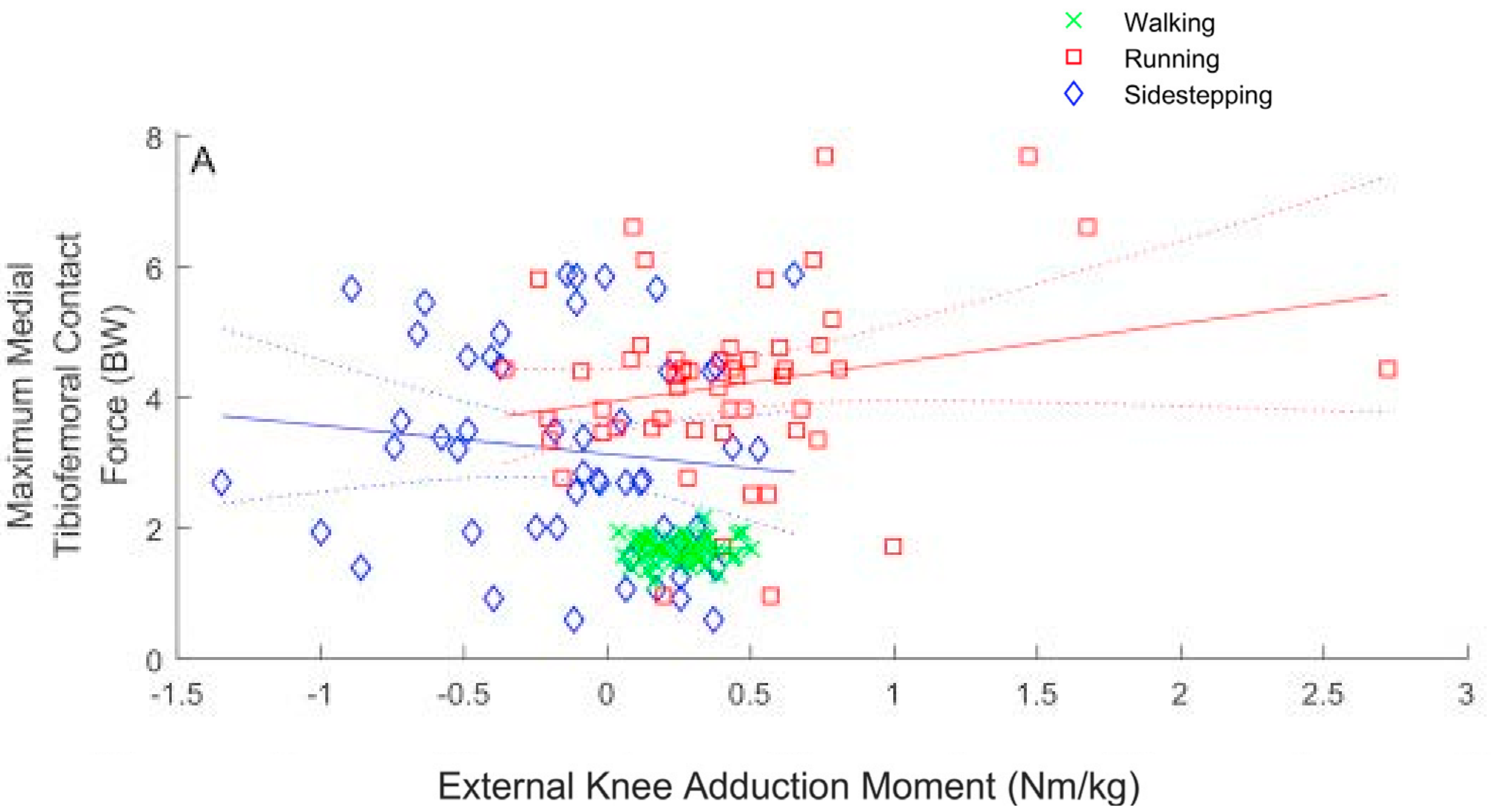
Knee moments and symptoms

Very low, questionable associations between knee joint moments and osteoarthritis symptoms



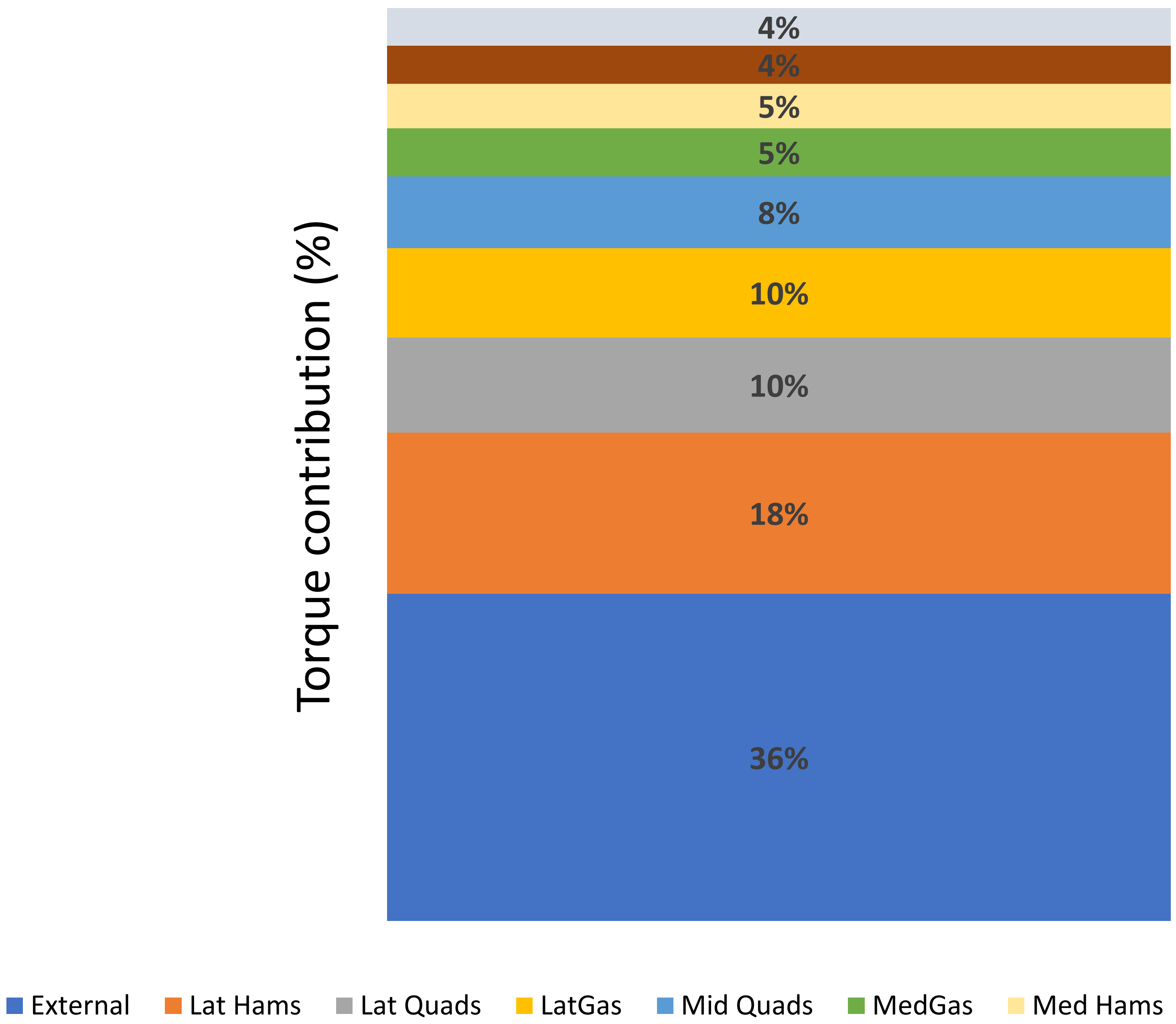
Maly et al *Clin Biomech* 2008 23:796-805; Henriksen et al *Knee* 2012 19:392; Hall et al *Osteoarthritis Cartilage* 2017 25:34

External ≠ internal estimates of joint loading



Saxby DJ et al. *Gait & Posture.* 2016.

Percent peak torque contribution to medial tibiofemoral joint contact force

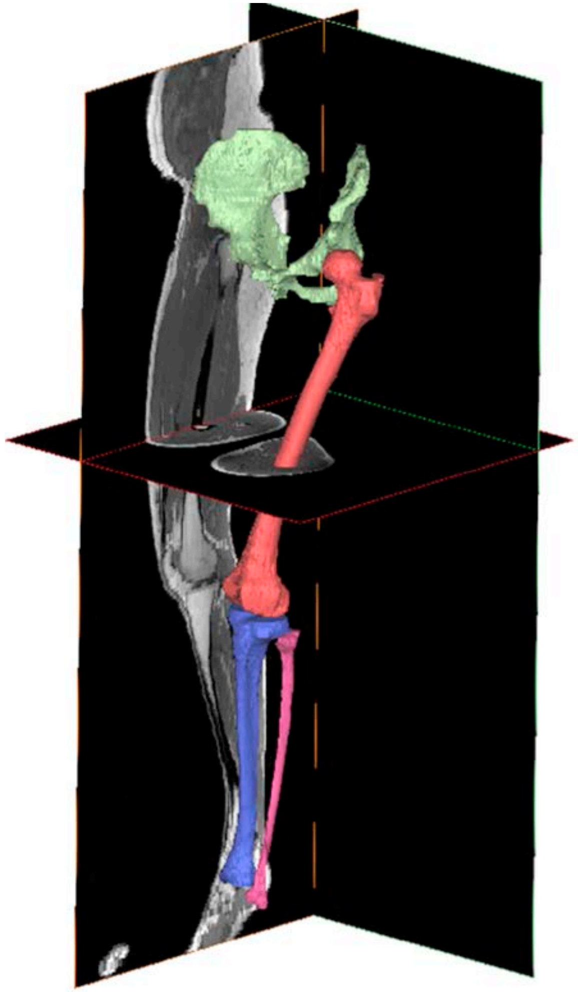


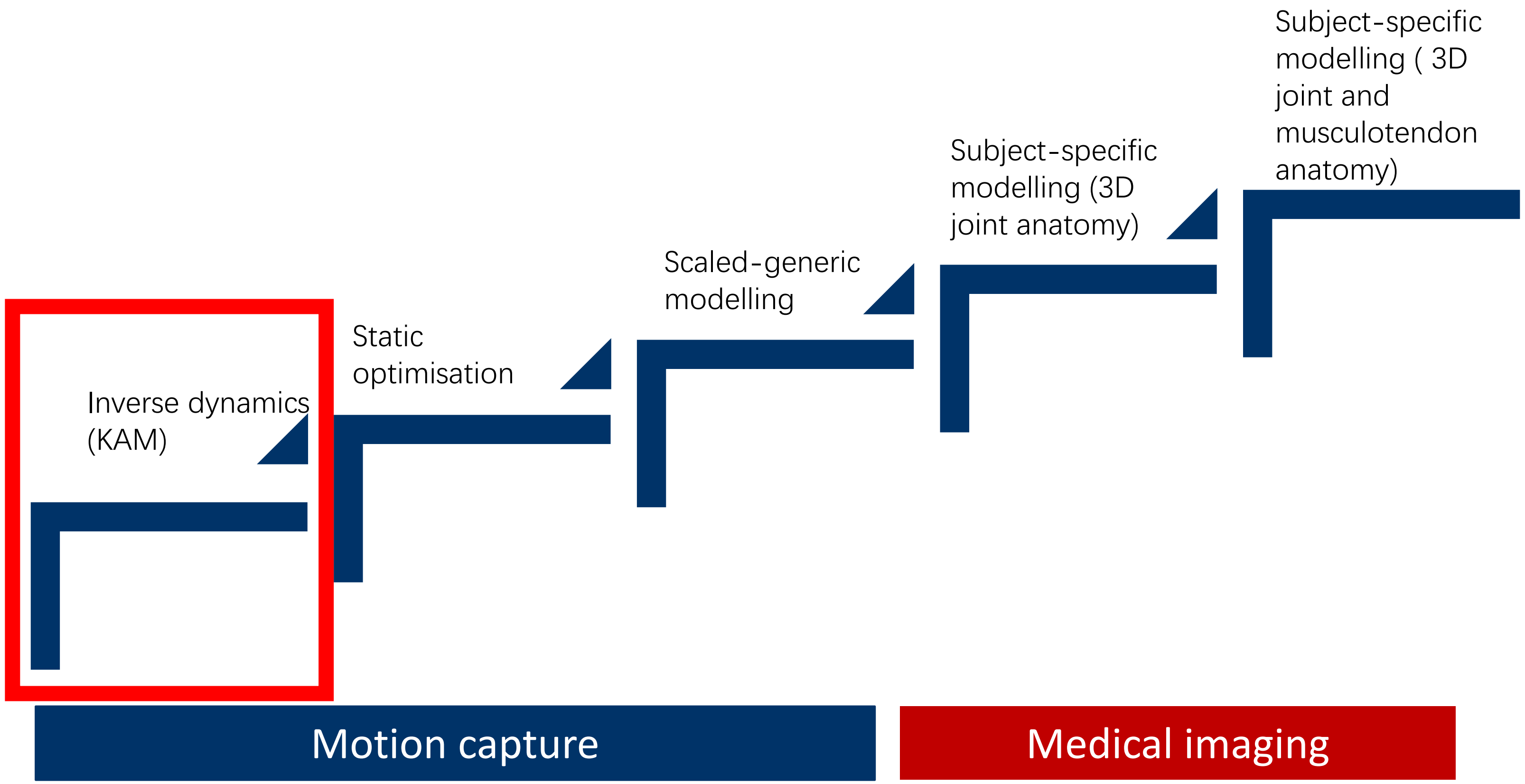
*Mean from 30 participants with knee OA and varus malalignment

A Solution?

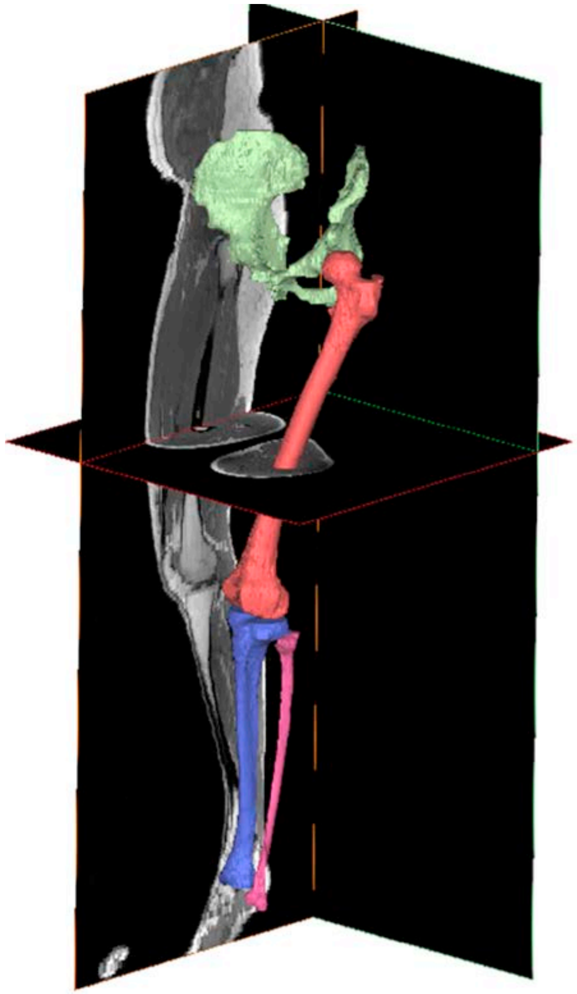
External load + Muscle forces = Medial tibiofemoral joint contact force (MTCF)

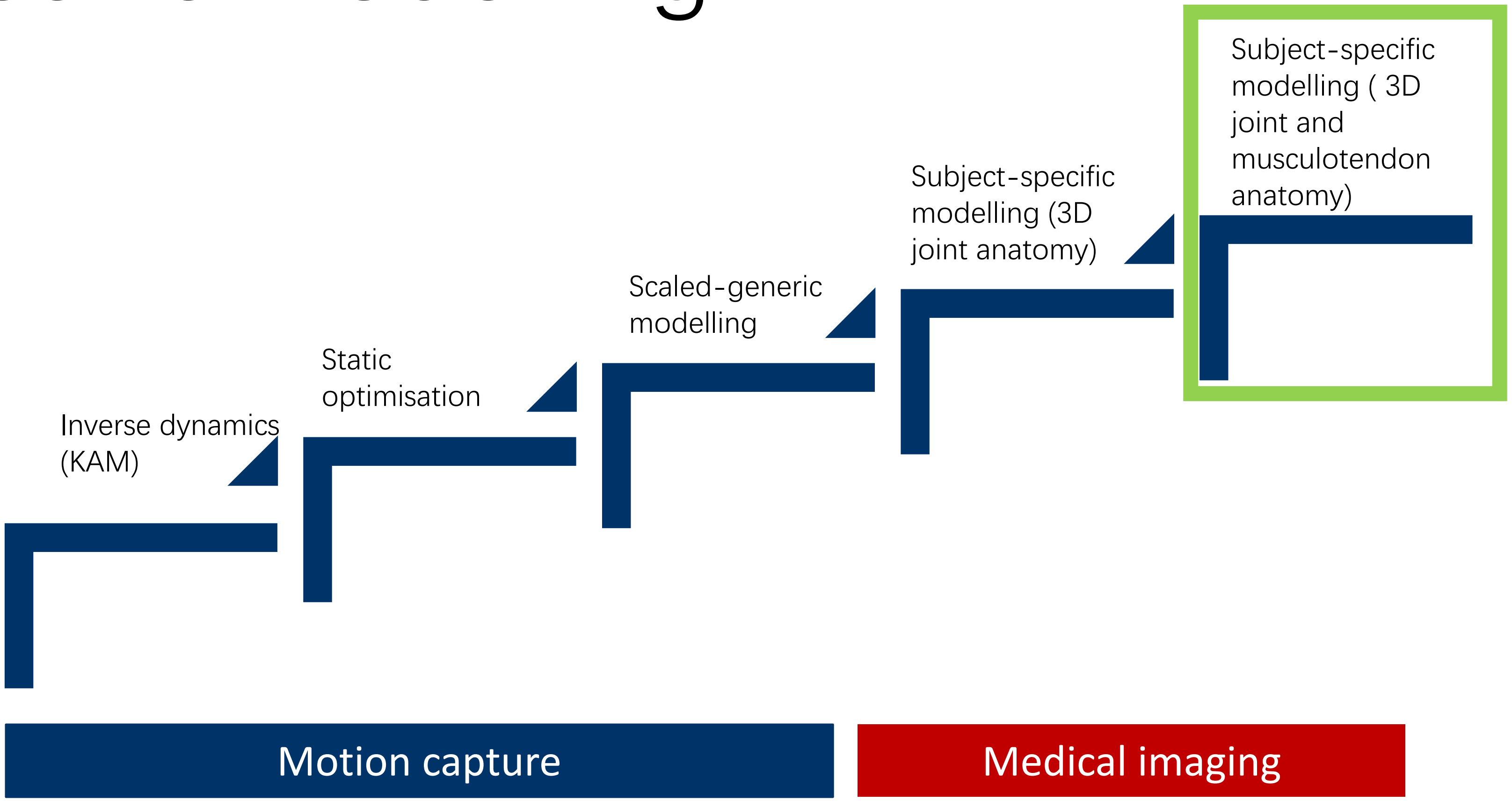
Patient specific modelling



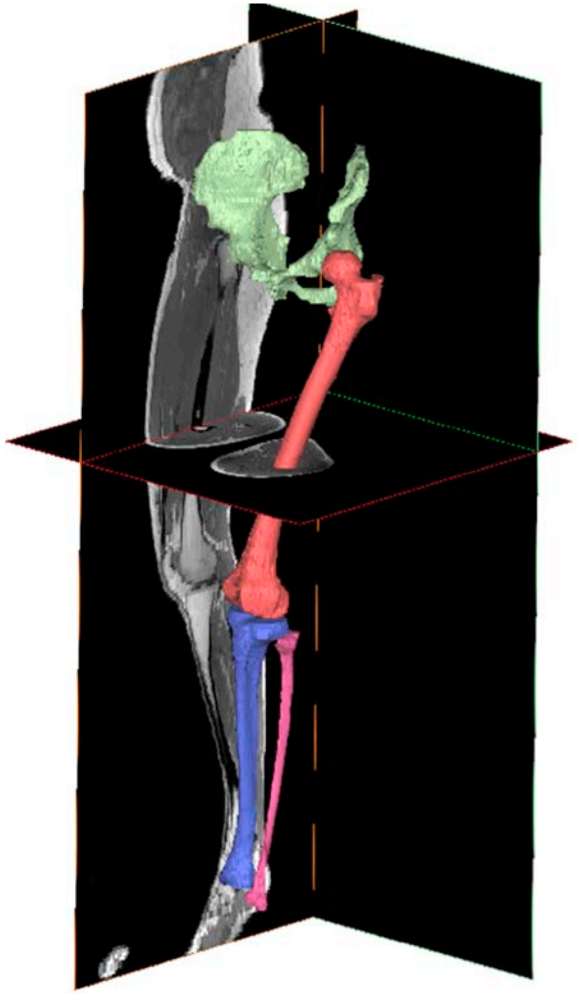


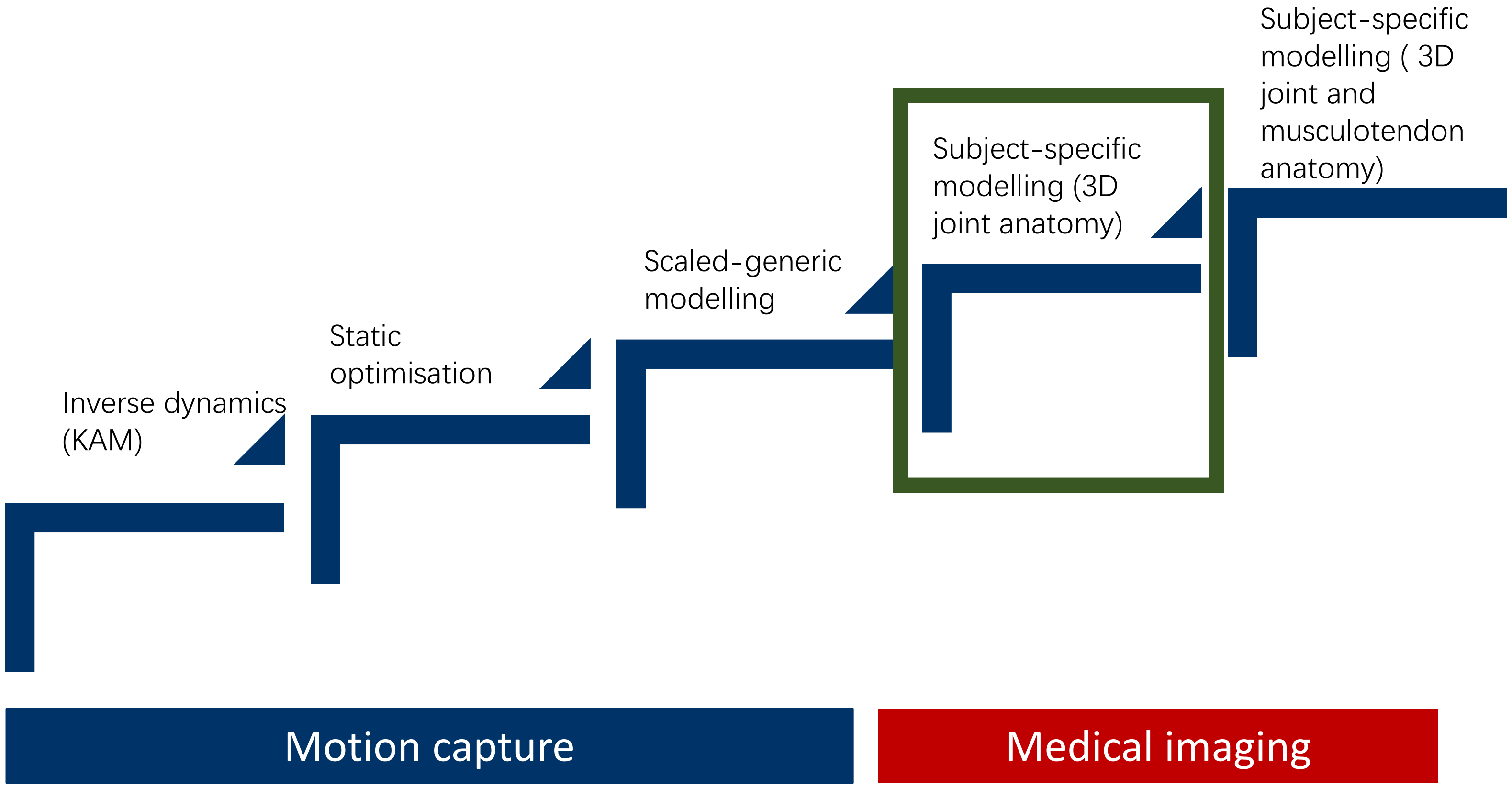
Patient specific modelling

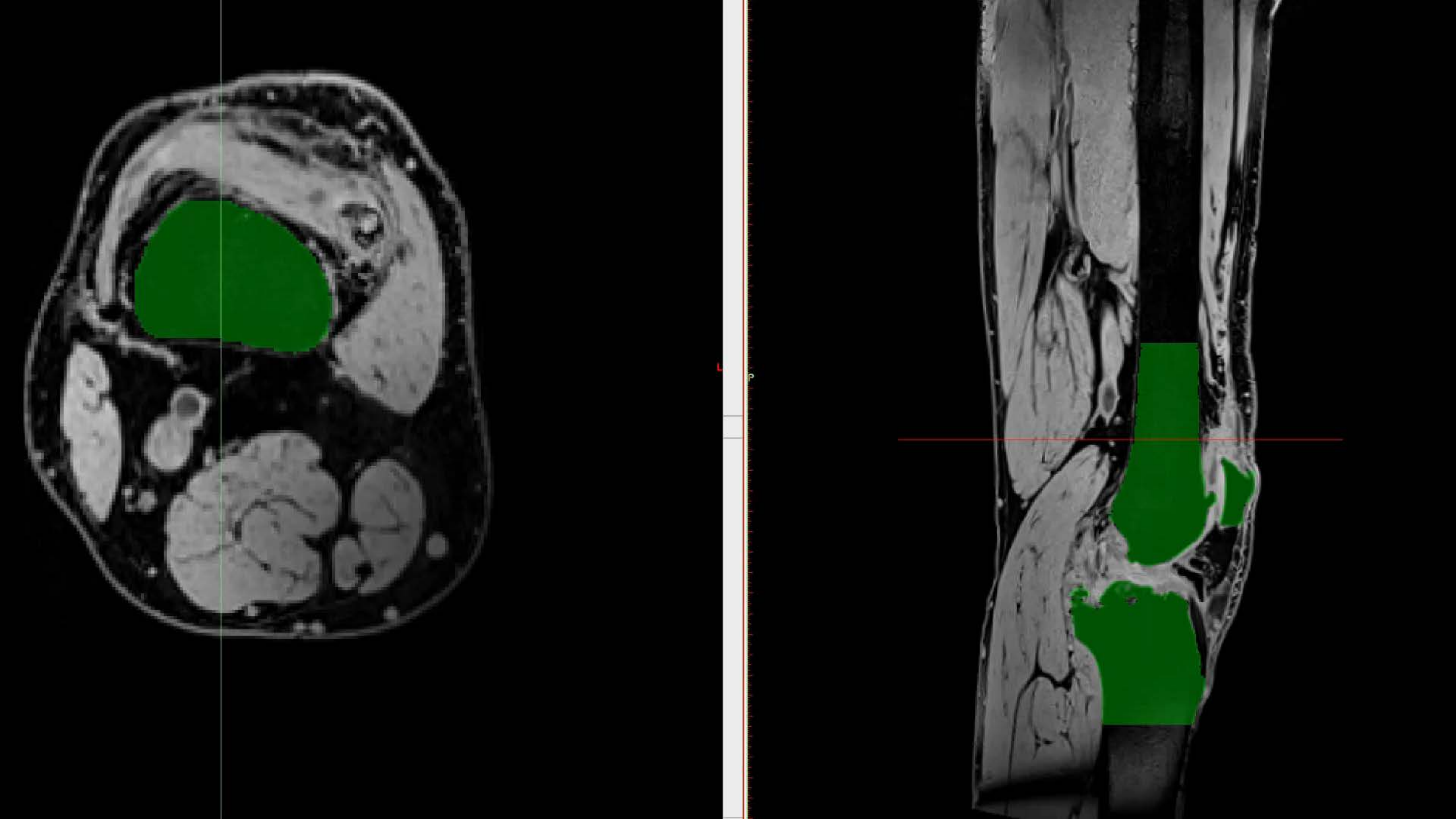




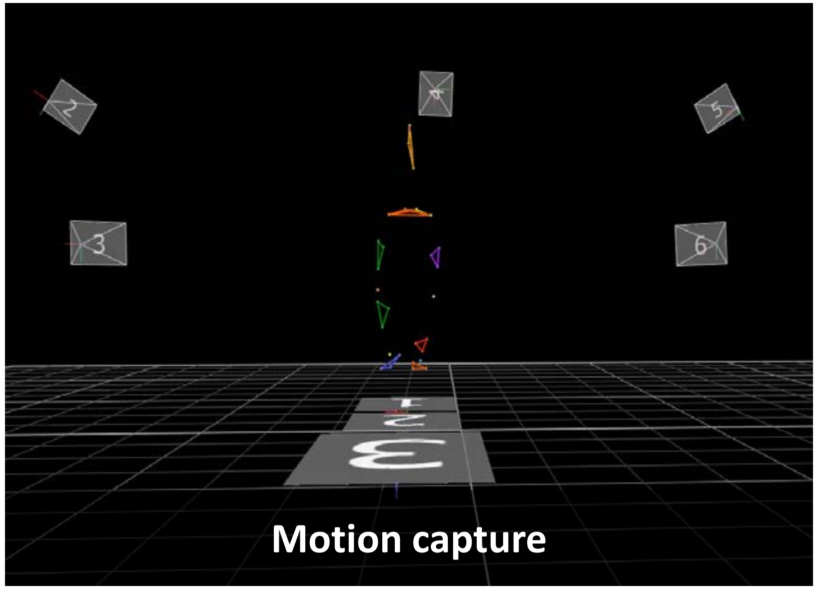
Patient specific modelling

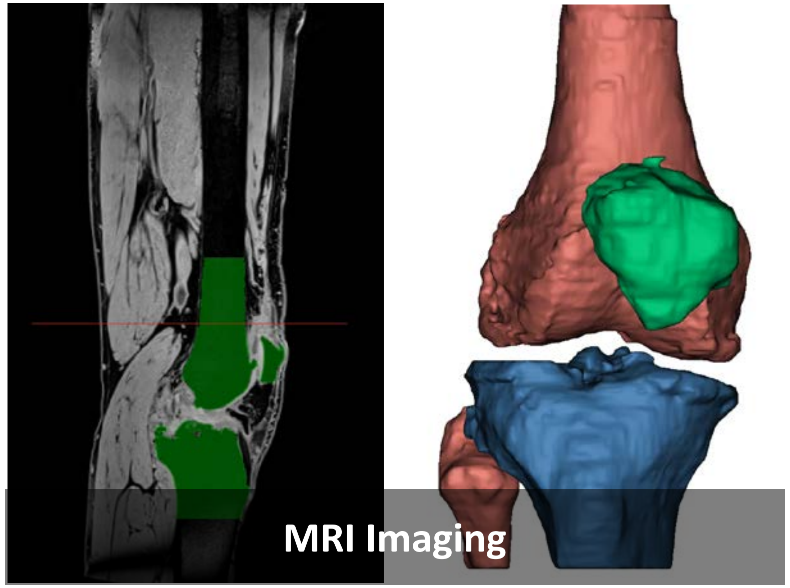


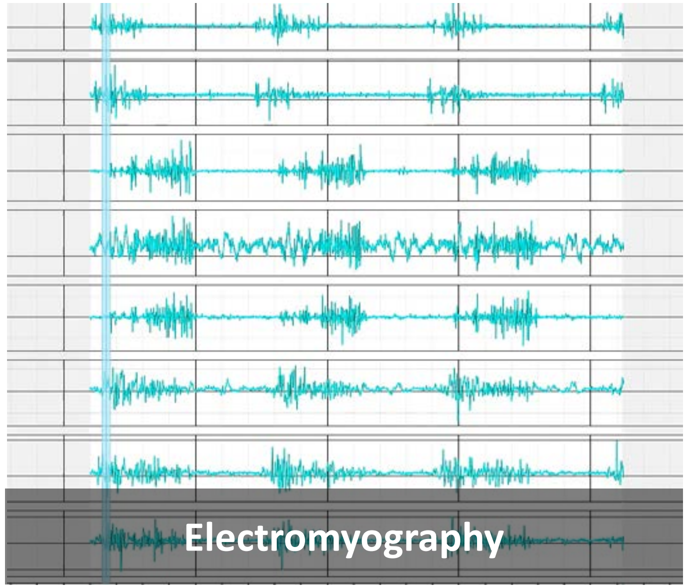


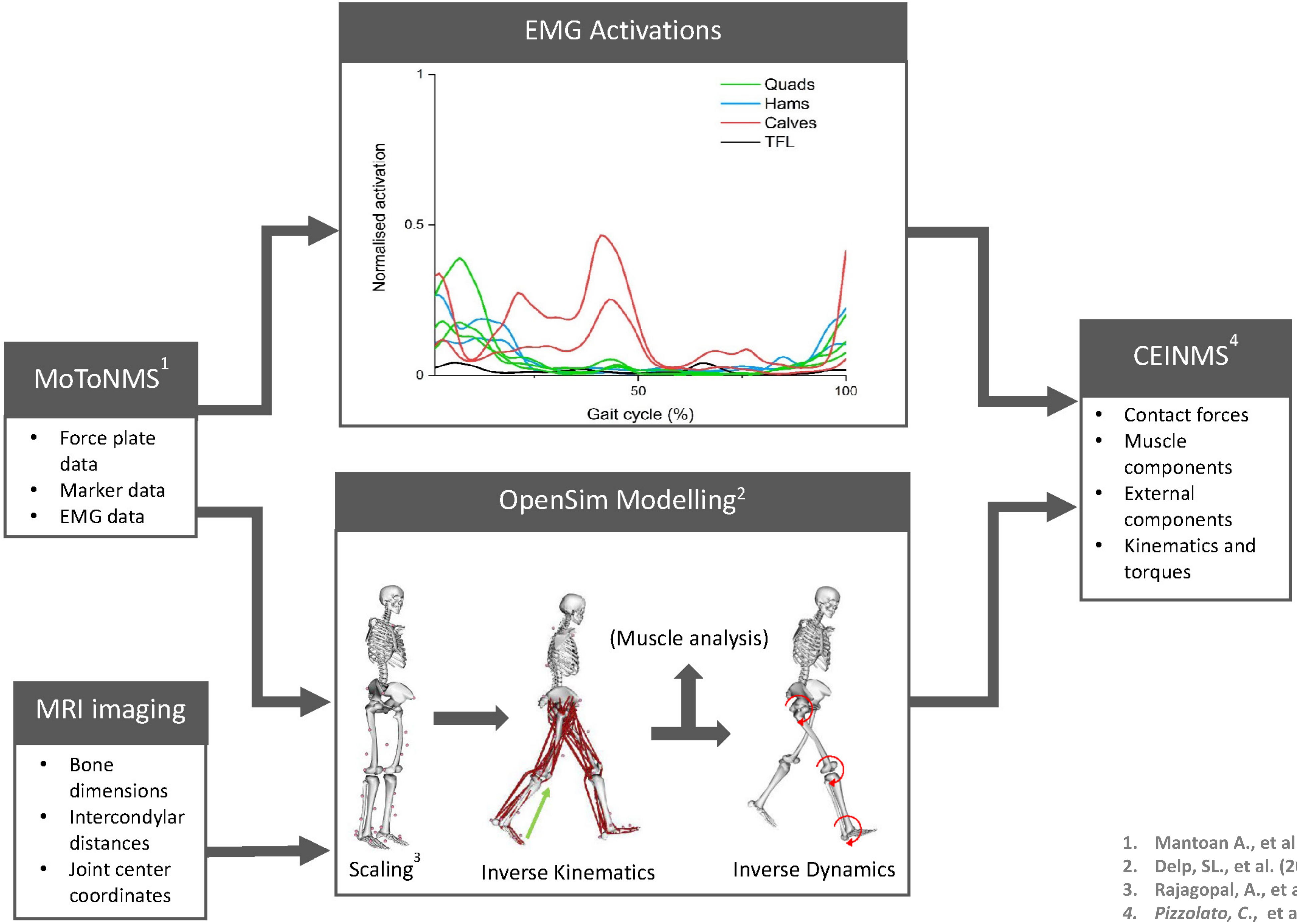


Neuromusculoskeletal modelling


Motion capture

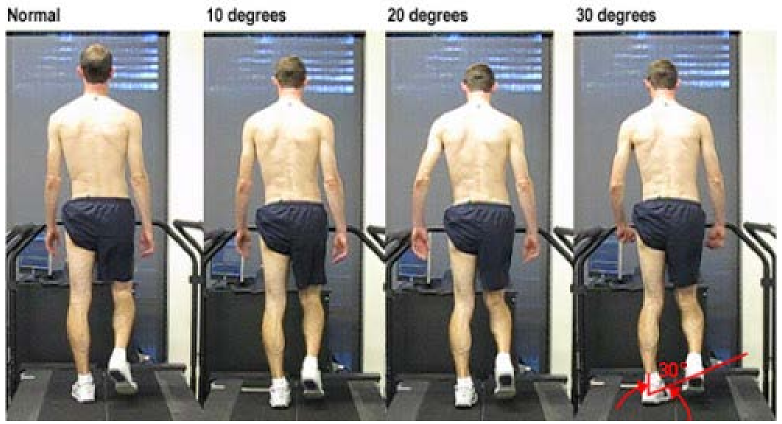

MRI Imaging

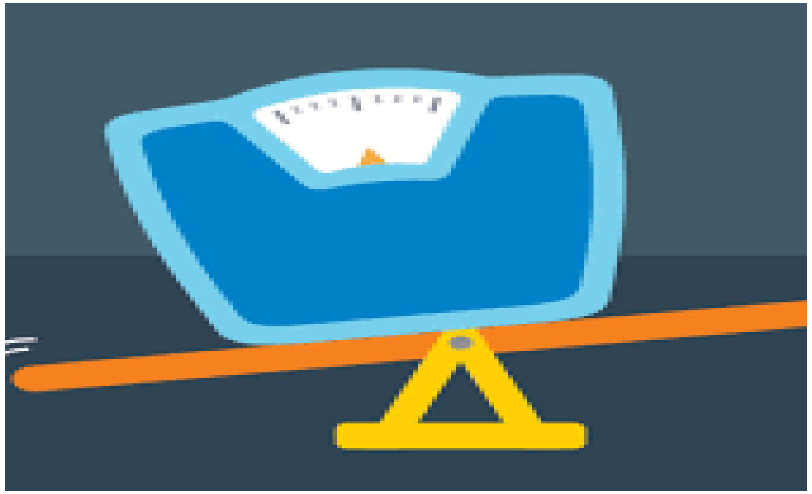

Electromyography



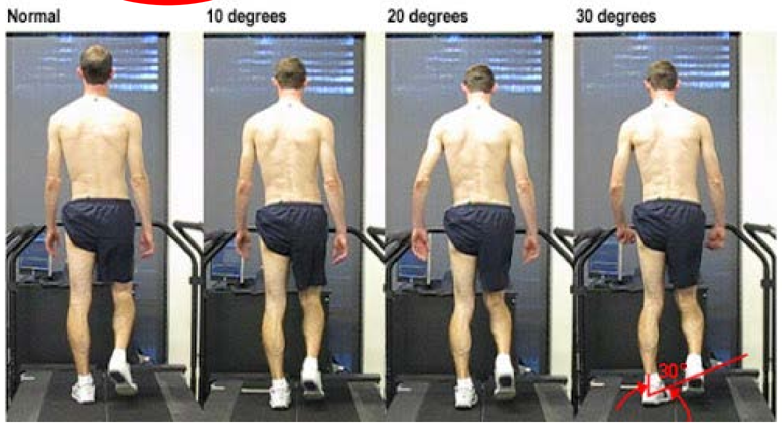
1. Mantoan A., et al. (2015) *Source Code Biol Med.*
2. Delp, SL., et al. (2007) *IEEE Trans Biomed Eng.*
3. Rajagopal, A., et al. (2016) *IEEE Trans Biomed Eng.*
4. *Pizzolato, C.,* et al. (2015) *J Biomech*

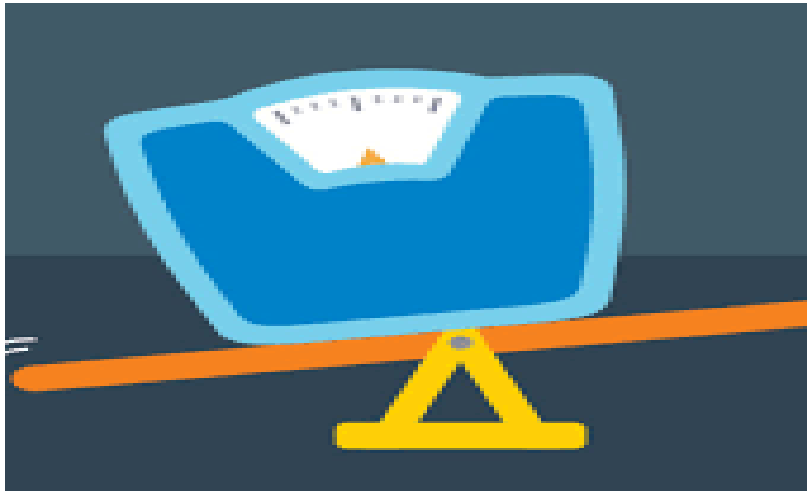
Load modification interventions?





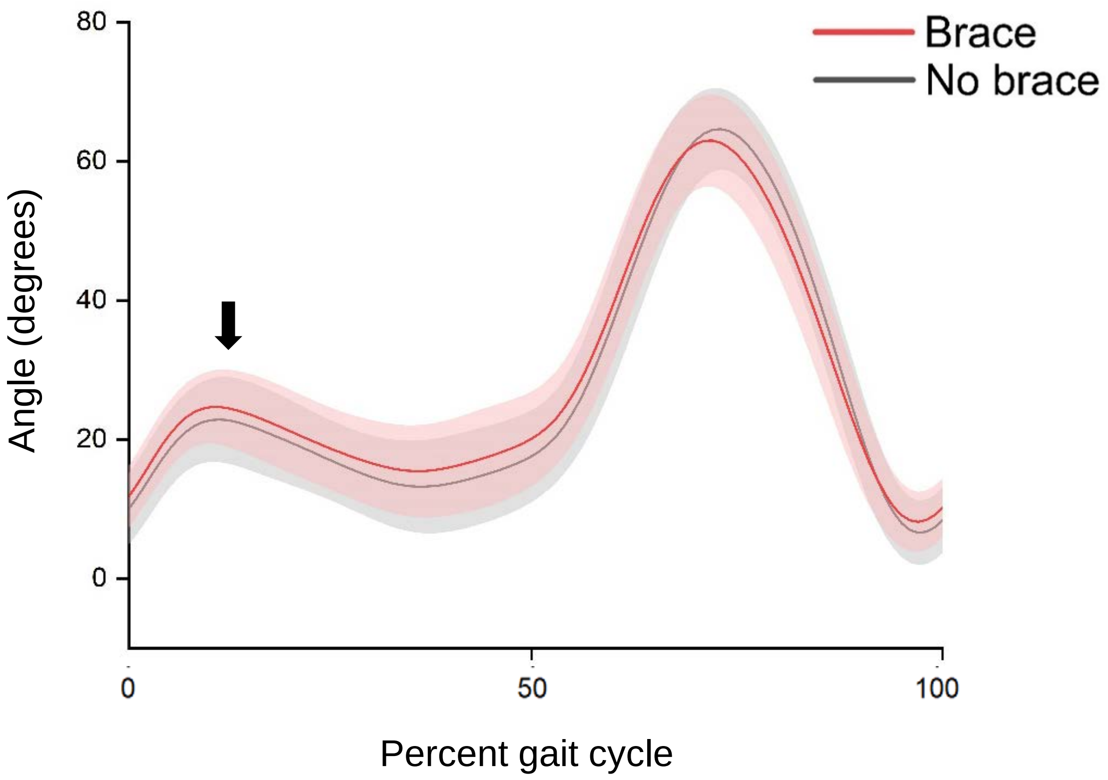
KNEE BRACING





OSSUR Unloader Study

Knee flexion angle during walking

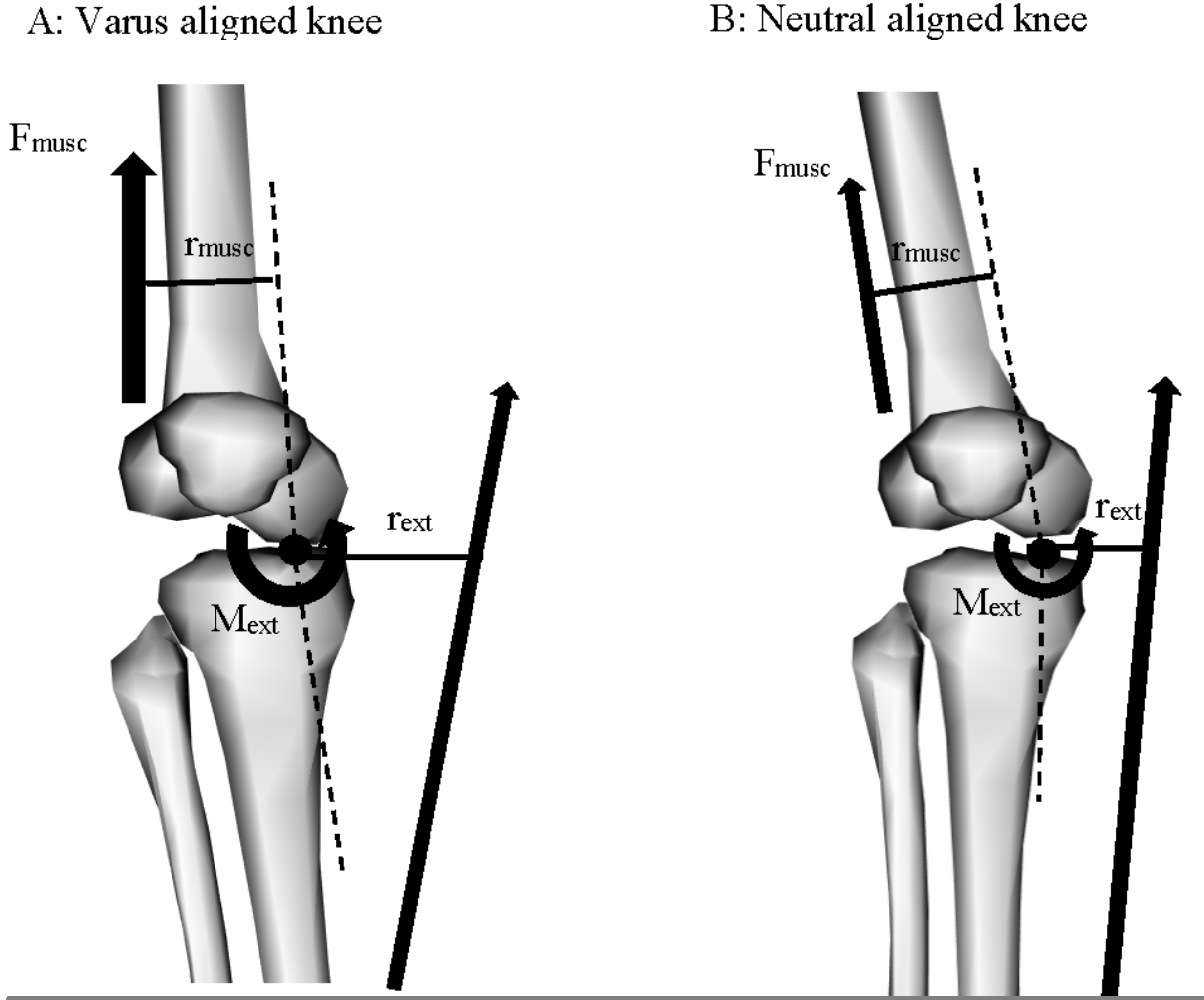


Ossür Unloader One©

- 30 participants with moderate to severe **medial** knee OA, with **varus malalignment**
- 8 weeks of wearing a valgus knee brace (Ossür Unloader One©)
- Immediate and 8 week **cross-sectional effects** of braced compared to no-braced walking on knee joint contact force **impulse**
- **Self reported** pain, function, sports and recreation, quality of life (KOOS)[1], walking pain (NRS) [2], self-efficacy (ASES) [3].

1. Roos, EM. (2003) *Health Qual; 2*. Bellamy, N. (1997), *J Rheumatol; 3; Lorig, K., et al. (1989), Arthritis Rheum*.

Varus malalignment



Greater **functional** and **structural decline** than those with more neutrally aligned knees

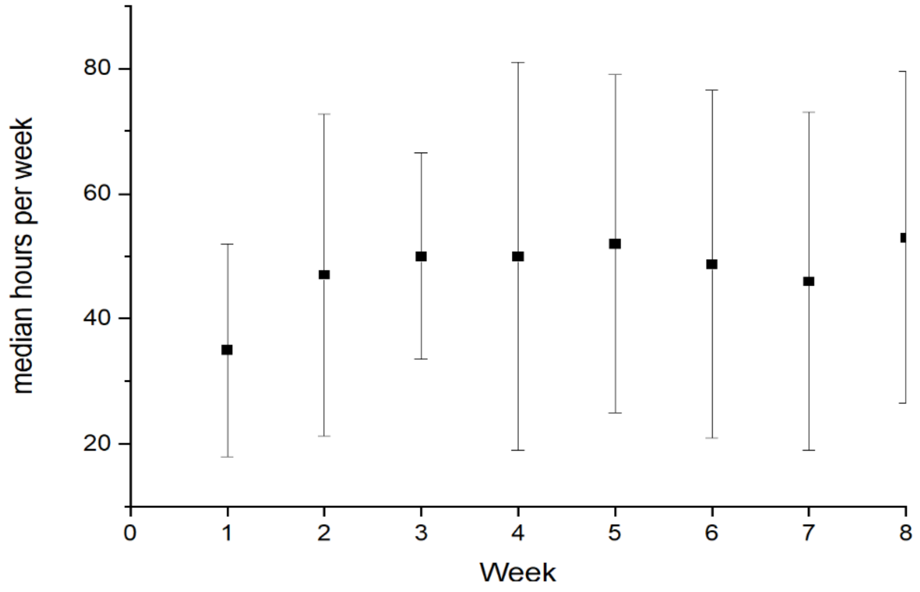
Sharma L, et al. (2001;2010) *JAMA; Ann Rheum Dis*

Participant characteristics

Characteristics	**n=30**
Age, yr	64.1 (4.7)
Male, n(%)	18 (60%)
Height, m	1.69 (0.10)
Weight, kg	85.0 (13.7)
Body mass index, kg/m^2	29.7 (3.3)
Unilateral symptoms, n(%)	16 (53%)
Duration of symptoms, yr	5.2 (4.5)
Average pain over the past week	6.14 (1.56)
Test leg dominant, yes(%)	26 (87%)
Knee alignment, degrees	
Females	178.2 (2.6)
Males	177.9 (3.1)
Radiographic disease severity grade, n(%)	
Grade 2	9 (30%)
Grade 3	12 (40%)
Grade 4	9 (30%)

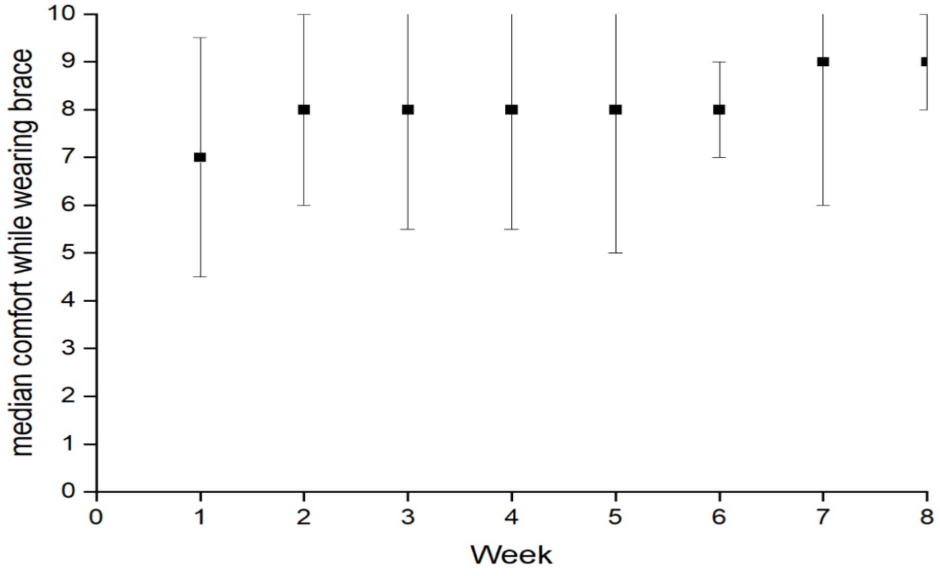
Adherence

Median hours per week wearing brace

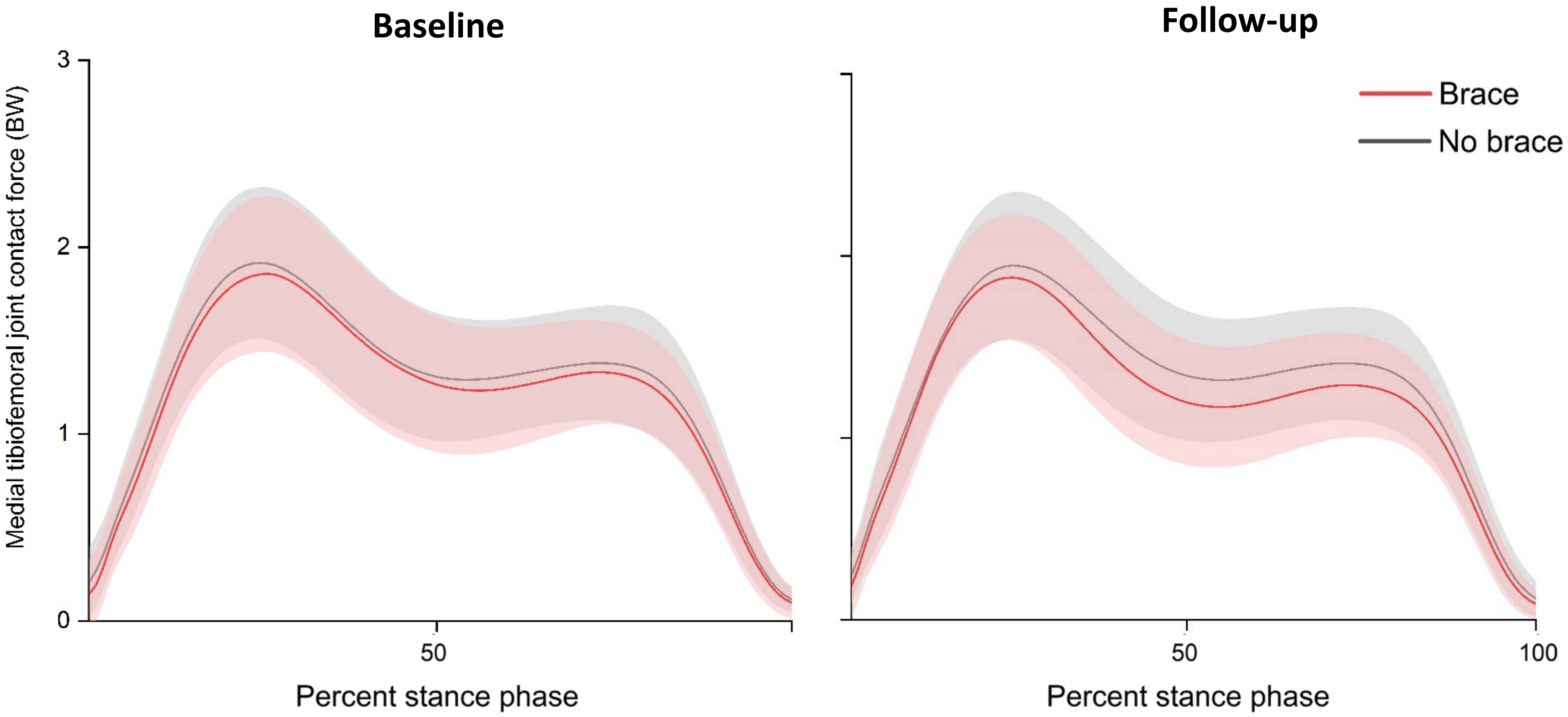


Median: 48 hours per week

Median comfort levels while wearing brace



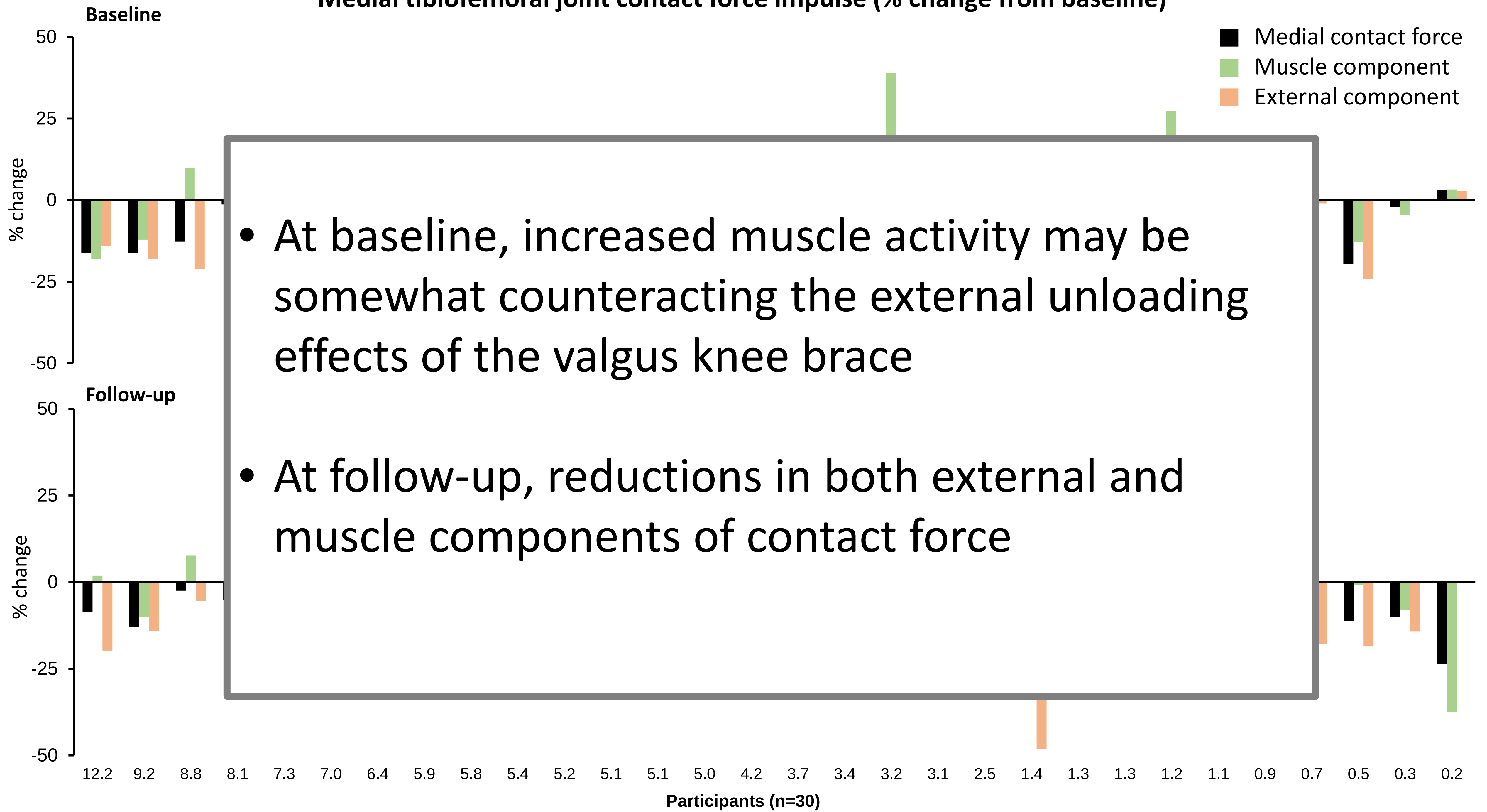
Median: 8 out of 10 comfort level



- 6% reduction in MTCF impulse at baseline
- 10% reduction in MTCF impulse at follow-up
- Improvement in all domains of KOOS and NRS pain while walking (all exceeded MDC scores).
- 20% improvement in self-efficacy (ASES)

Collins, NJ., et al. (2011). *Arthritis Care Res*

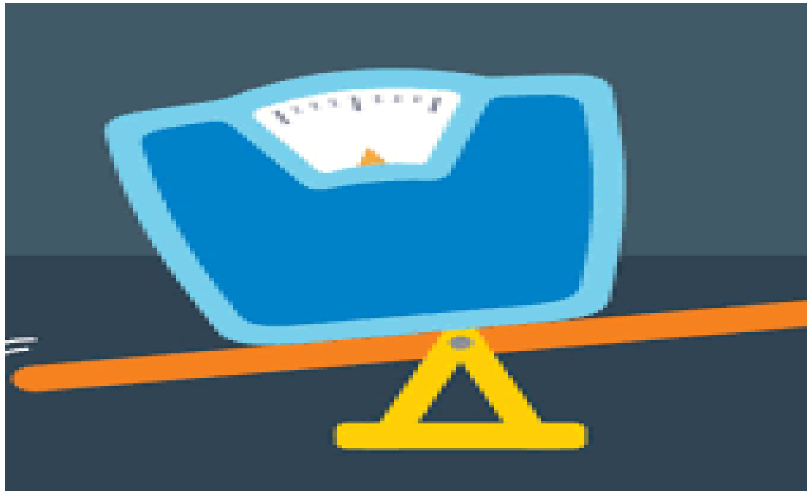
Medial tibiofemoral joint contact force impulse (% change from baseline)

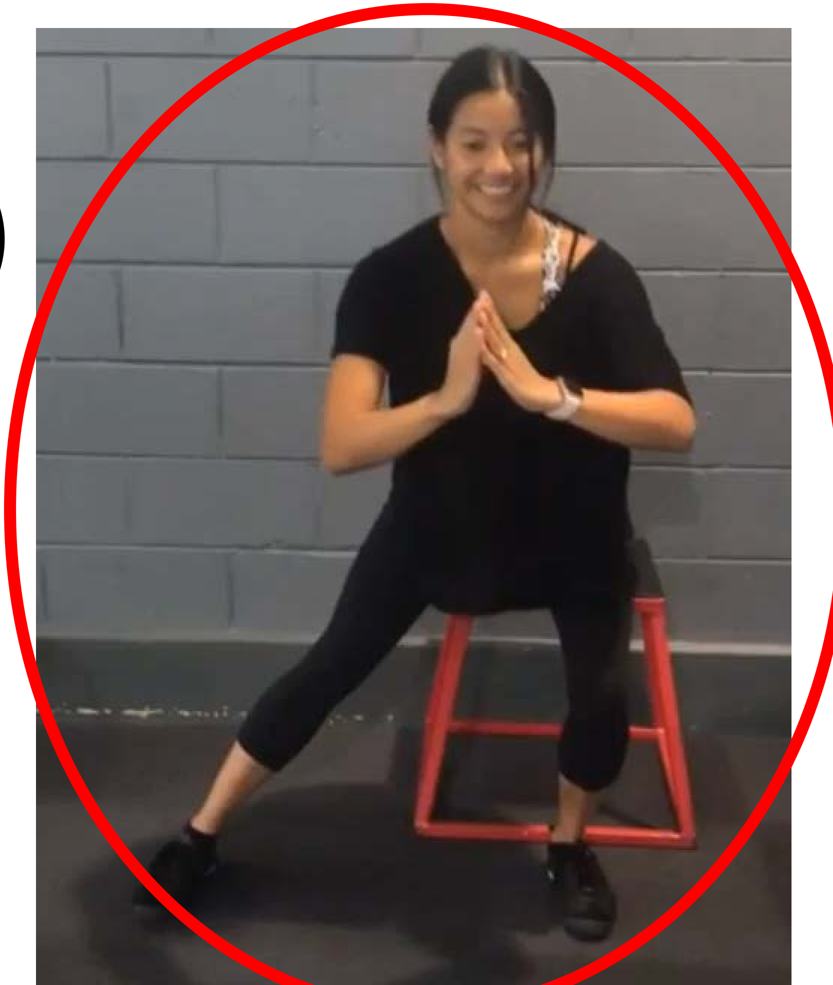


- At baseline, increased muscle activity may be somewhat counteracting the external unloading effects of the valgus knee brace

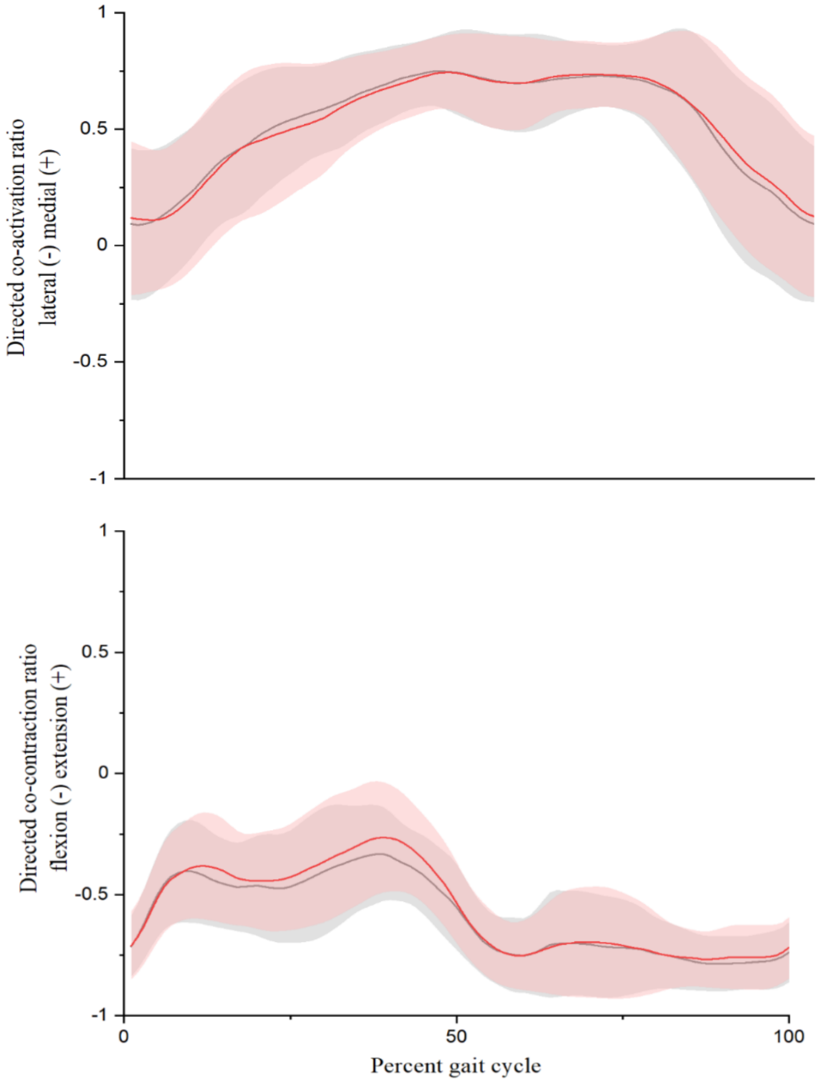
- At follow-up, reductions in both external and muscle components of contact force

EXERCISE





Does ↑ muscle = ↑ knee loads?



EMG co-contraction

- Simultaneous activation of the quads/hams/gastrocs
- ↑ co-contraction is a determinant for ↑ MTCF in-vivo instrumented knee prostheses[1]

Trepczynski, A, et al., (2018) *JNER*

Doe
m

IT DEPENDS
(we think)

At risk / unestablished populations

- 2-years post ACLR the MTCF are lower during walking, running, and side stepping compared to healthy controls[1]
- EMG from vastus muscles and lower vatus torque in ACLR leg compared to uninvolved leg[2]

YES*

Knee Osteoarthritis

- Preliminary evidence that people with knee OA walk with increased co-contraction[3]
- Functional, weightbearing exercise may reduce co-contraction[4]

NO

1. Saxby, DJ et al. (2016) *MSSE*
2. Bryant, AL et al. (2008) *J Orthop Res*
3. Heiden, TL et al. (2009) *Clin Biomech*
4. Preece et al. 2016 *BMC Musc. Disord.*

- 100 participants randomised with moderate to severe knee **medial** OA and **varus malalignment**
- 12 weeks of NWB quadriceps strengthening vs 12 weeks of WB "neuromuscular exercise"
- No change in KAM despite comparable symptom improvement

Osteoarthritis | Free Access

Neuromuscular Versus Quadriceps Strengthening Exercise in Patients With Medial Knee Osteoarthritis and Varus Malalignment: A Randomized Controlled Trial†

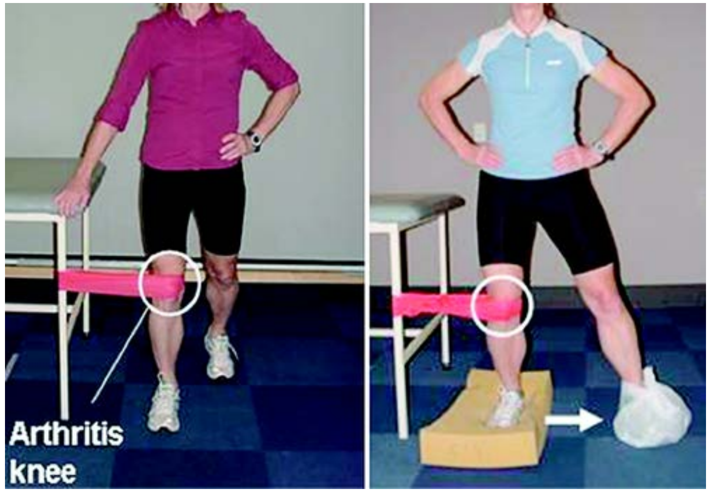
Kim L. Bennell, Mary Kyriakides, Ben Metcalf, Thorlene Egerton, Tim V. Wrigley, Paul W. Hodges, Michael A. Hunt, Ewa M. Roos, Andrew Forbes, Eva Ageberg, Rana S. Hinman

Outcome	Week 0		Week 13		Within-group difference, week 13 minus week 0, mean (95% CI)		Between-group difference, mean (95% CI)
	NEXA (n = 50)	QS (n = 50)	NEXA (n = 38)	QS (n = 44)	NEXA (n = 38)	QS (n = 44)	
Peak KAM, Nm/(BW × Ht)%	3.05 ± 0.90	3.21 ± 0.88	3.26 ± 0.95	3.30 ± 0.79	0.12 (−0.04, 0.29)	−0.04 (−0.18, 0.10)	0.13 (−0.08, 0.33)
Overall VAS score for pain (mm)	54.0 ±13.3	54.2 ± 16.8	34.1 ± 23.6	31.4 ± 19.3	−19.9 (−26.9, −12.9)	−22.0 (−27.9, −16.1)	2.4 (−6.0, 10.8)

Exercise program overview

Neuromuscular exercise (functional WB exercise):
- Forward and backward sliding or stepping
- Sideways exercises
- Functional hip muscle strengthening
- Functional knee muscle strengthening
- Step up and downs
- Balance

Quadriceps strengthening exercise (NWB exercise):
- Quads over roll
- Knee extension sitting
- Knee extension with hold at 30 degrees knee flexion
- Straight leg raise
- Outer range knee extension



Bennell, KL., et al. (2014). *Arthritis Rheumatol*

A case for functional exercise

Compared with healthy controls, people with knee OA have:

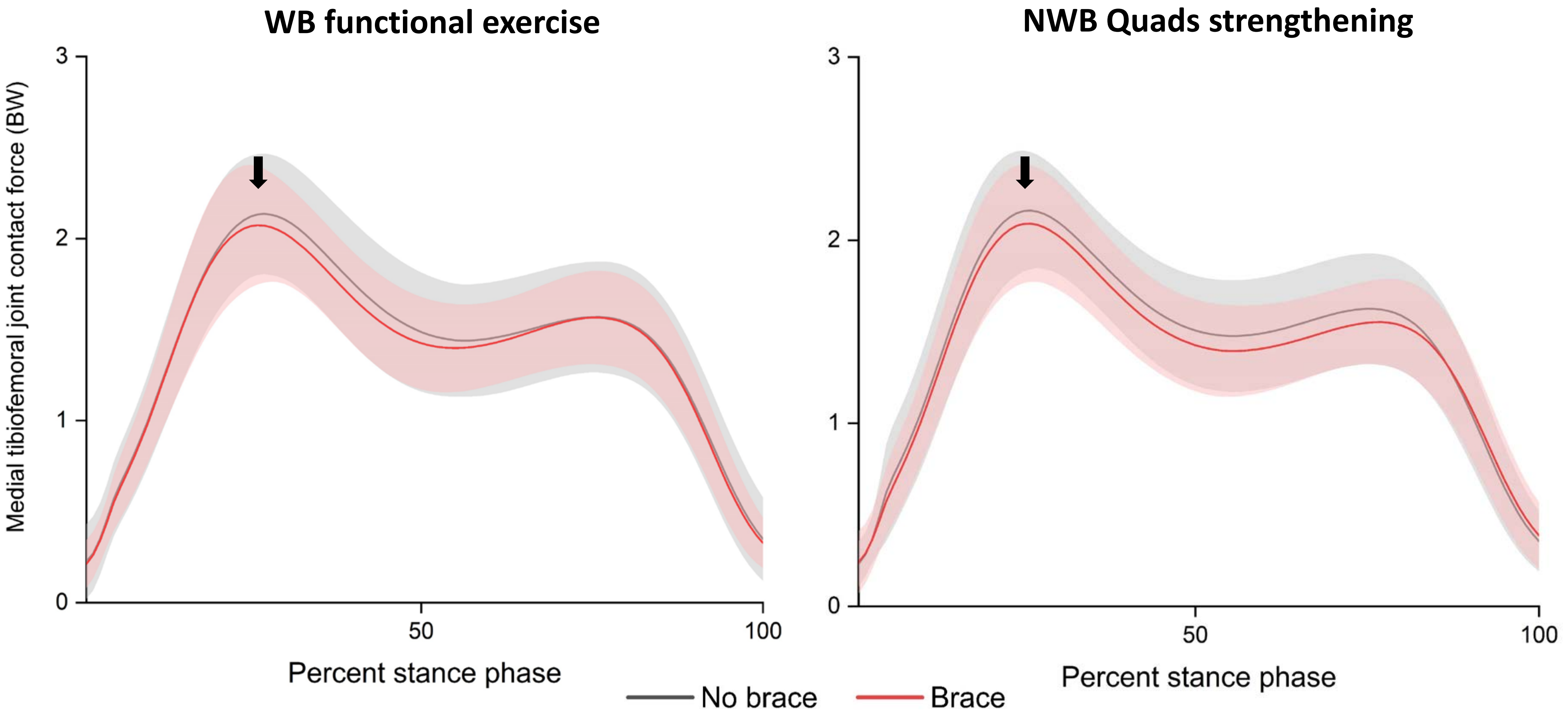
- Higher odds of having lower muscle strength
- Proprioceptive deficits
- More medial varus-valgus laxity
- Less lateral varus-valgus laxity

van Tunen, J.A.C., et al. (2018) *BMC Musc Disord*

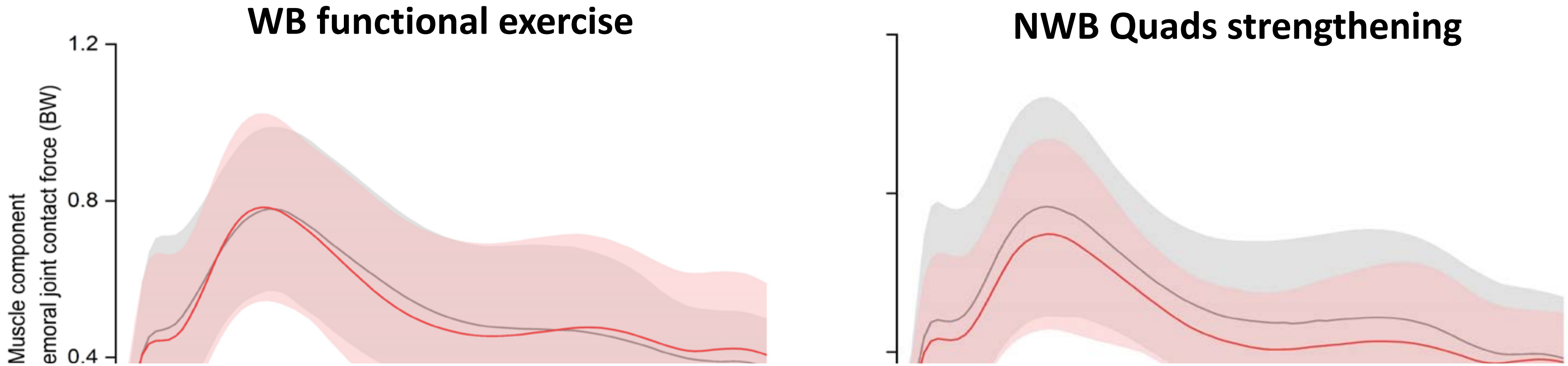
Participant characteristics - secondary analysis

Characteristics	**WB group (n=31)**	**NWB group (n = 36)**
Age, yr	61.0 (6.8)	62.0 (7.0)
Males, %	13 (42%)	19 (53%)
Height, m	1.68 (0.09)	1.66 (0.11)
Body mass, kg	83.2 (14.2)	81.7 (16.0)
Body mass index, kg·m^{-2}	29.4 (3.5)	29.4 (4.5)
Dominant side affected	17 (57%)	19 (50%)
Symptom duration, median (IQR) months	60 (102)	84 (93)
Average knee pain over the past week[a]	53.5 (11.8)	52.9 (17.1)
Knee alignment[b] (°)	177.1 (3.0)	176.5 (3.8)
Males	177.5 (2.8)	176.4 (4.3)
Females	176.8 (3.2)	176.6 (3.2)
Radiographic disease severity[c]		
Grade 2	5 (16%)	10 (28%)
Grade 3	12 (39%)	16 (44%)
Grade 4	14 (45%)	10 (28%)

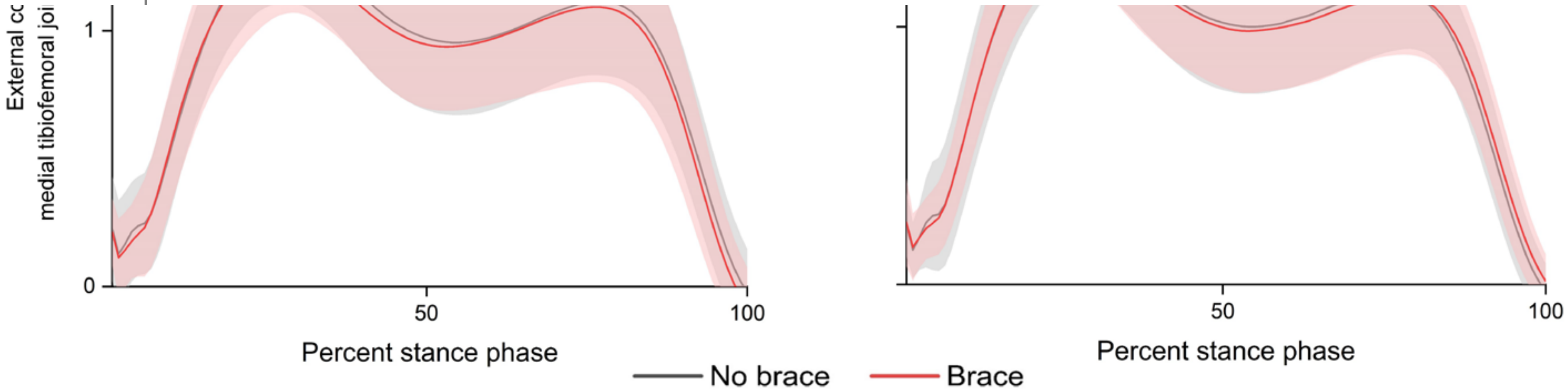
Results - secondary analysis



Starkey, SC., et al. (under peer review)



Outcome	Groups				Within Group Change		Difference in Change	
	Baseline		Follow-up		Follow-up minus Baseline		Between-group	
	WB (n=31)	NWB (n=36)	WB (n-31)	NWB (n=36)	WB (n=31)	NWB (n=36)	NWB minus WB	P Value
Joint contact forces (BW)								
Peak medial	2.19 (0.32)	2.22 (0.31)	2.12 (0.31)	2.14 (0.30)	-0.06 (-0.15, 0.02)	-0.08 (-0.18, 0.02)	-0.02 (-0.12, 0.09)	0.77
(muscle component)	0.79 (0.22)	0.77 (0.27)	0.79 (0.25)	0.71 (0.25)	0.00 (-0.06, 0.06)	-0.06 (-0.13, -0.00)	-0.08 (-0.15, -0.00)	0.04
(external component)	1.39 (0.25)	1.44 (0.22)	1.33 (0.24)	1.43 (0.19)	-0.06 (-0.15, 0.00)	-0.01 (-0.09, 0.07)	0.09 (0.01, 0.18)	0.04



Starkey, SC., et al. (under peer review)

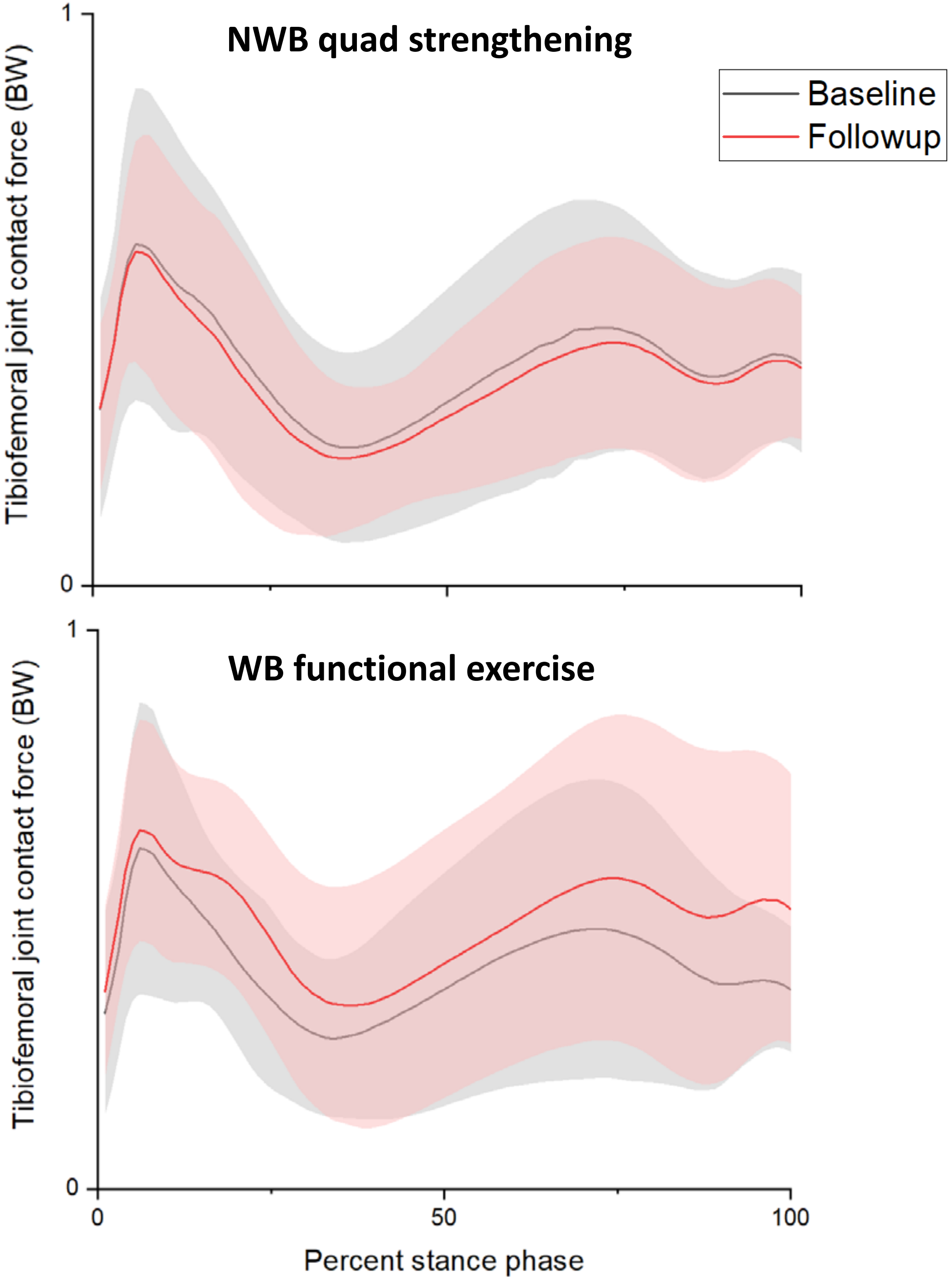
Mechanistic variation

NWB quad strengthening
Muscle component ↓
External component ↔

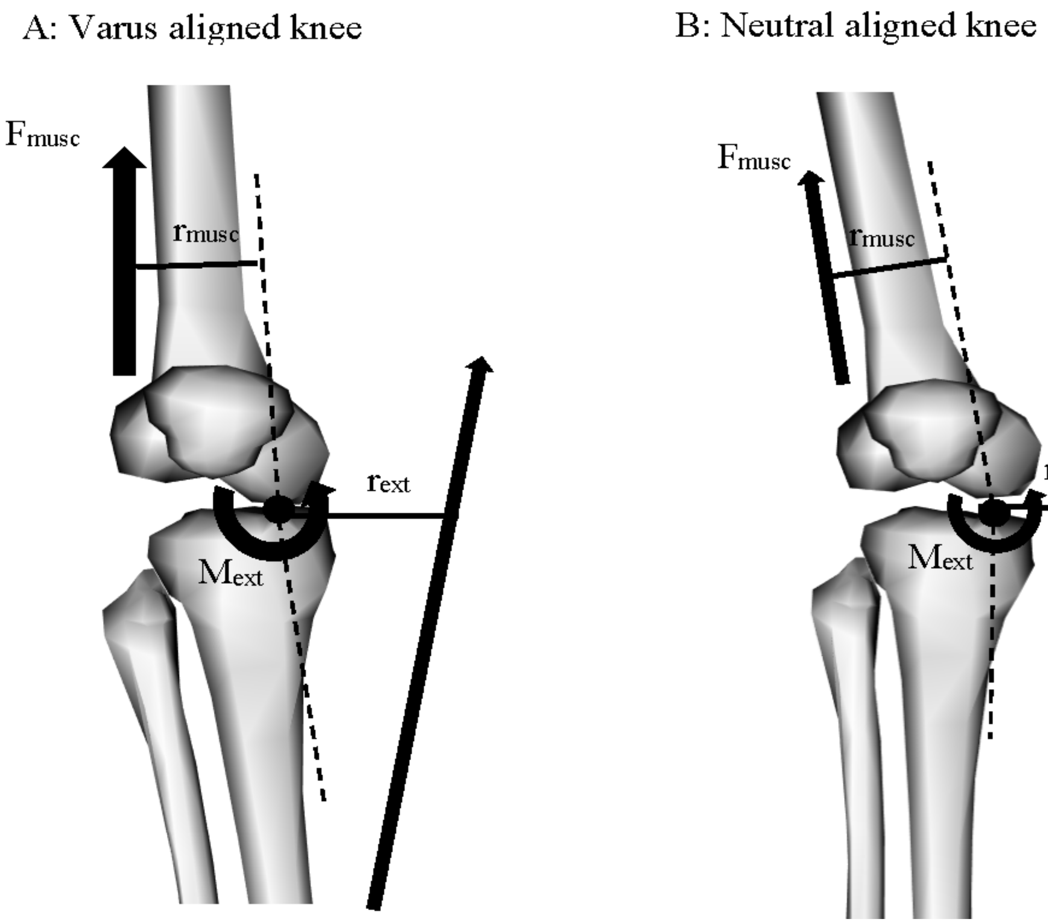
WB functional exercise
Muscle component ↔
External component ↓

→

Outcome
Similar ↓ peak MTCF via differing mechanisms



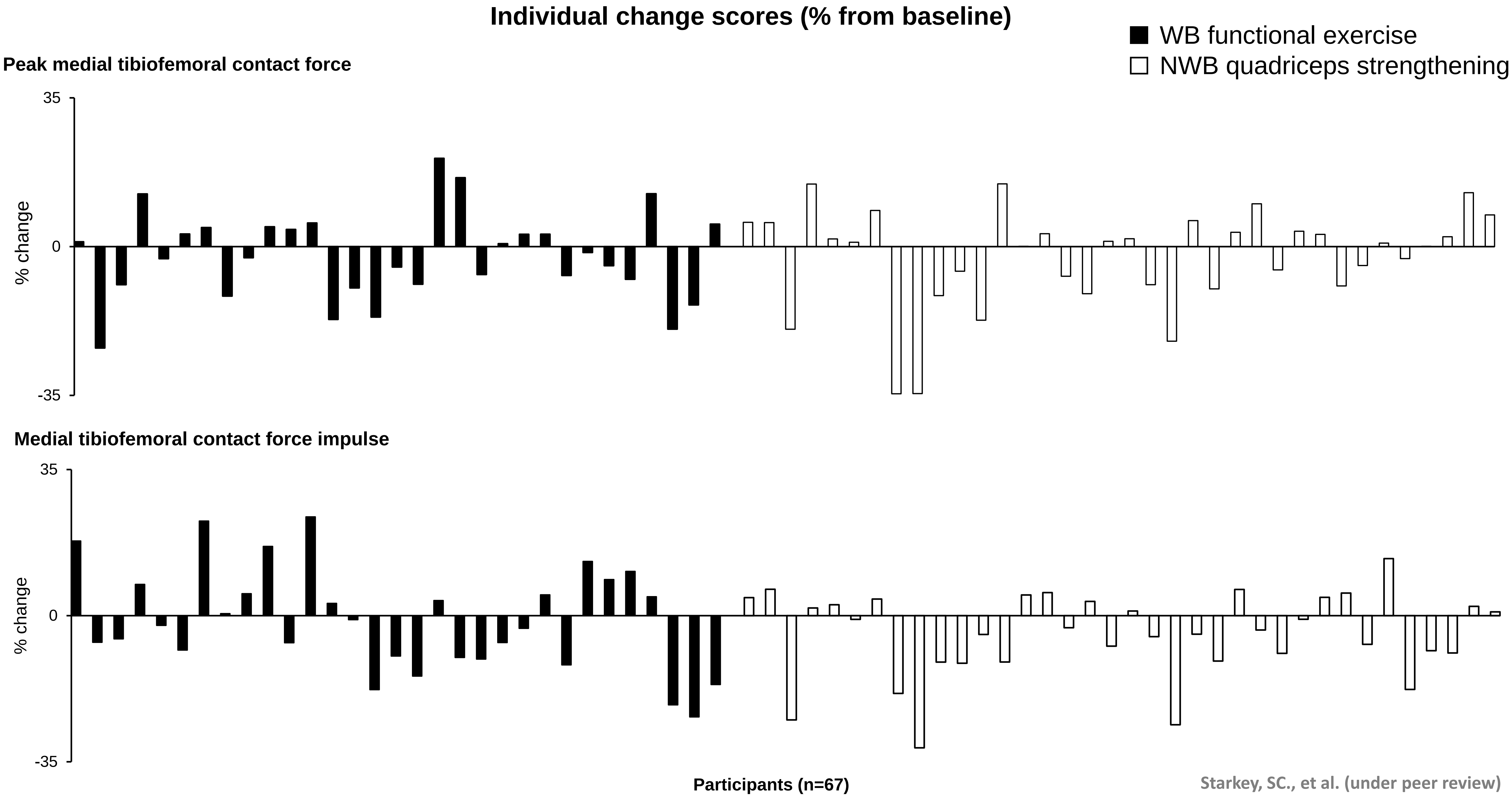
Where did the load go?



Starkey, SC., et al. (under peer review)

Clinical considerations

- NWB quadriceps strengthening may translate to muscular unloading of the medial compartment during walking
- Should we prescribe a combination of quadriceps strengthening and functional exercises to “maximise” reductions?
- Do we avoid functional exercise in bi-compartmental osteoarthritis to prevent increased lateral compartmental loads?


Individual change scores (% from baseline)
WB functional exercise
NWB quadriceps strengthening
Peak medial tibiofemoral contact force
35
0
-35
% change
Medial tibiofemoral contact force impulse
35
0
-35
% change
Participants (n=67)
Starkey, SC., et al. (under peer review)

An issue of heterogeneity

Full length article

Effect of exercise on knee joint contact forces in people following medial partial meniscectomy: A secondary analysis of a randomised controlled trial

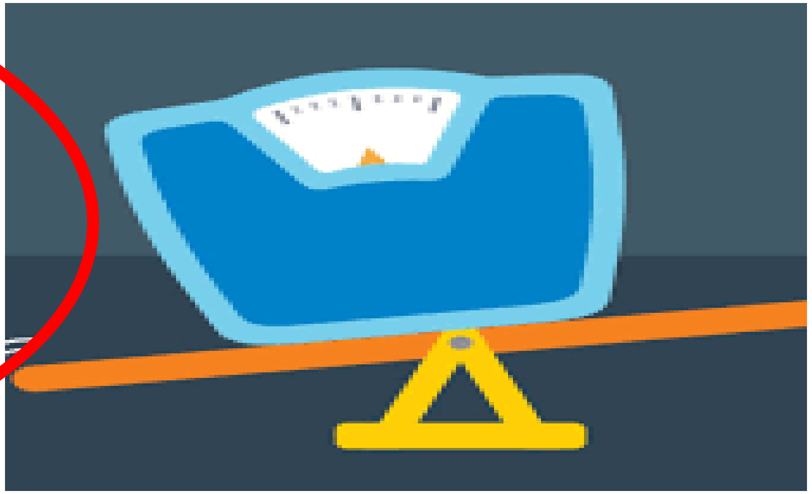
Scott C. Starkey [a], Gavin K. Lenton [b], David J. Saxby [b], Rana S. Hinman [a], Kim L. Bennell [a], Tim Wrigley [a], David Lloyd [b], Michelle Hall [a]

- "It is likely that participants are using subject-specific gait strategies or muscle activation patterns to influence MTCF during their walking task"
- ?Intra-subject variability
- ?Intra-session variability

Gait modification strategies?

- Walking speed
- Toes pointing in/out
- Side-to-side trunk sway
- Internal hip rotation
- Stride length
- Increased step width
- Loading outside of foot
- Changing knee alignment / medial thrust

Gait retraining / biofeedback



1612 IEEE TRANSACTIONS ON NEURAL SYSTEMS AND REHABILITATION ENGINEERING, VOL. 25, NO. 9, SEPTEMBER 2017 EMB

Biofeedback for Gait Retraining Based on Real-Time Estimation of Tibiofemoral Joint Contact Forces

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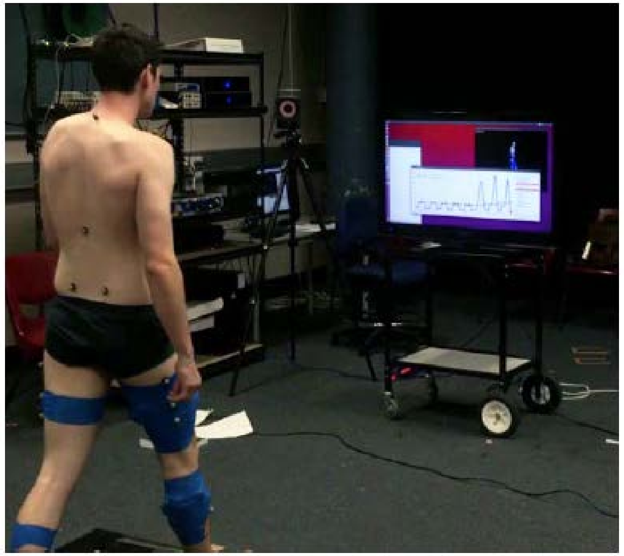
Elena Ceseracciu, Luca Modenese, and David G. Lloyd



- 5 healthy subjects walking on an instrumented treadmill with visual biofeedback of their MTCF
- All subjects were able to increase their MTCF
- Only 3 subjects could decrease it, and only after receiving verbal suggestions about possible gait modification strategies
- ALL subjects utilised different strategies to achieve this

Walking speed

Gait
mod
strat

- Many of these may result in an increase in muscle contraction and no change, or increases to MTCF depending on the participant
- Individually identify possible compensatory mechanisms that your patient is using and whether they are beneficial or detrimental
- Utilise gait-retraining methods with caution and prepare to be flexible

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Challenges

Change in load associated with clinically relevant improvements is still uncertain

- Cost
- Imaging
- Equipment
- Expertise
- Feasibility

Take home messages

- OA is in part a mechanical condition
- Past use of external loads (KAM) to infer internal contact forces may explain the poor associations between knee loads and clinically relevant outcomes
- Neuromusculoskeletal modelling provides a novel means to evaluate knee joint loads, however current research is largely exploratory (hypothesis generating, not conclusive).
- A reduction in knee loads while wearing a valgus knee brace was more prominent after 8 weeks, likely due to muscle adaptations. Self reported benefits (pain + function) well exceeded MDC scores.
- A combination of quadriceps strengthening, functional exercise and gait-retraining may be required to achieve clinically important reductions in knee loads
- Tailored programs are essential given the substantial intra-participant heterogeneity in gait and muscle strategies