New insights into the mechanisms of tendon injury

This lecture

1. What other factors affect onset of tendinopathy?

2. What treatments are best for tendinopathy?

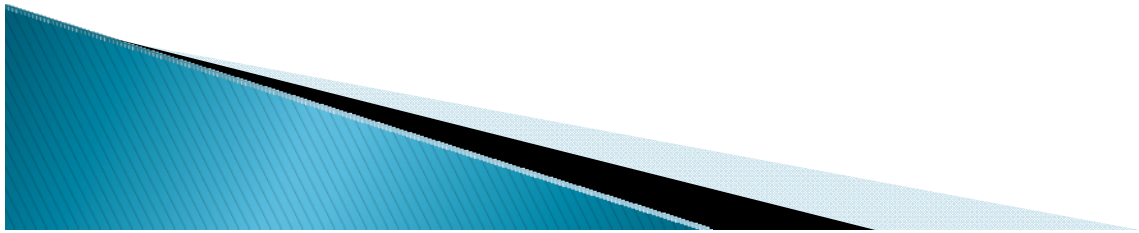
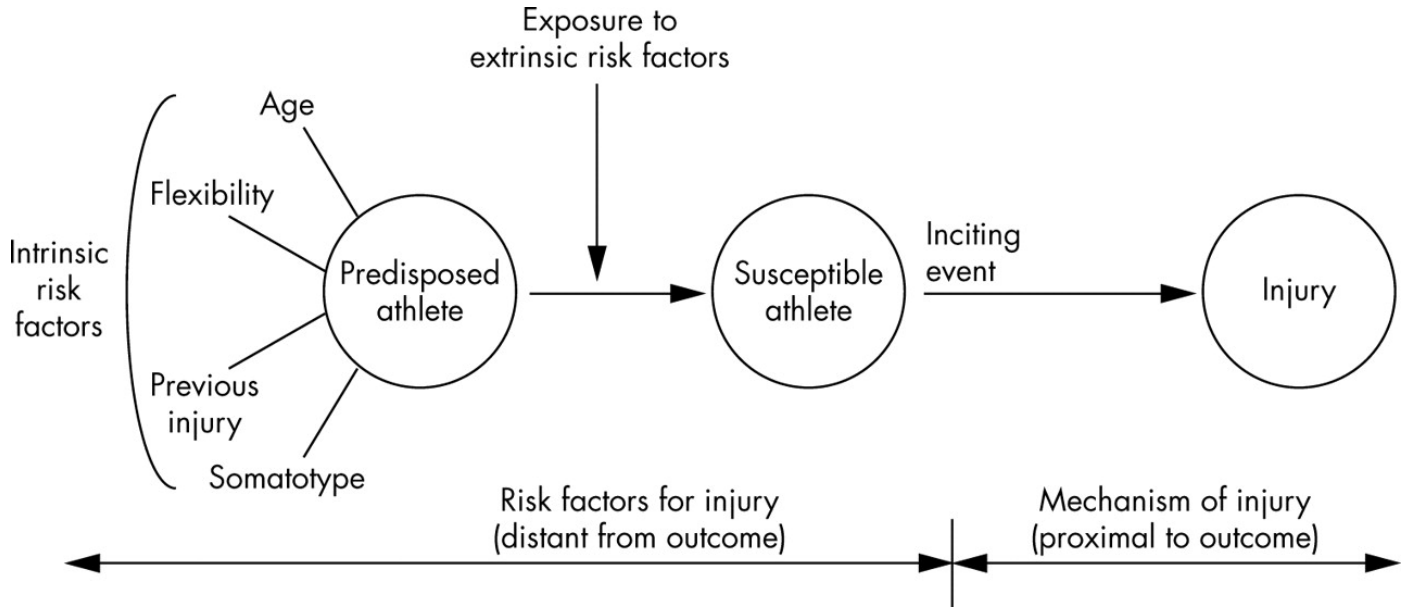


Figure 2 Complex interaction between internal and external risk factors leading to an inciting event and resulting in injury.



Bahr, R et al. Br J Sports Med 2005;39:324-329

What factors predispose a person to tendon injury?

- In some tendons, extrinsic factors (load) make a person susceptible
  - Young active men
    - Patellar tendon in jumping athletes
    - Adductor tendon in kicking athletes
- In some tendons it appears that intrisic factors have a strong influence
  - Older sedentary women
    - Gluteal tendinopathy (? Long term compressive loads)
    - Supraspinatus
      - Both sexes

Tendinopathy

- Achilles tendon is heterogeneous in prevalence and onset
- Intrinsic and extrinsic factors are evident
  - Presents across a range of ages and activity
  - 11% lifetime incidence (Kujala et al 07)
    - Young high load athletes
    - Middle aged moderate load people
    - Older low load post menopausal women (Maffulli et al)
    - Sedentary people

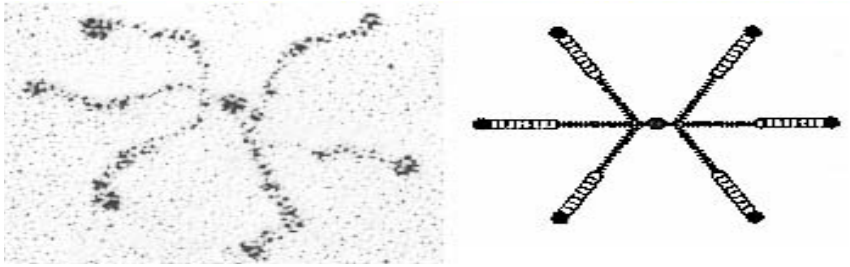
Tendinopathy is a person disease with a load topping

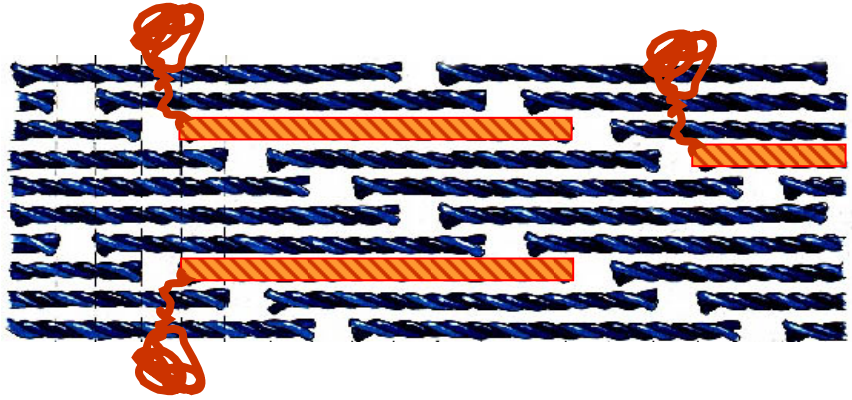
- Tendinopathy in systemic disease
  - Diabetes, arthridites
- Collagen diseases
  - Marfan's, Ehlers-Danlos
- Drug induced tendinopathies
  - Statins, fluroquinolones
- What intrinisic factors have been shown to affect tendons?
  - Genes
  - Age
  - Sex
  - Body composition
  - Biomechanics

Genes

Blood group
- Yes (Kannus et al 91, Jarvinen 92)
- No (Maffulli)

- Specific polymorphisms for type V collagen and tenascin-C gene are more common in those with chronic Achilles tendon pain
  - No difference Type I collagen
    - Mokone et al 05, Collins et al 08





Age

- After the third decade tendinopathy appears to increase dramatically
  - Evidence for this is lacking
  - Compressed tendons under some load seem vulnerable
    - Gluteus medius
    - Rotator cuff
- They do not become pathological just because they are older
- Tendons lose
  - Proteoglycans
  - Water
- Become stiffer
  - Less capable of absorbing load

Young people

Are also at risk in tensile loaded tendons

Number of patellar tendons imaged	US abnormality as relative risk for symptoms
48 female basketball **Khan 1997**	**Same as past symptoms**
54 young athletes **Cook 2000**	**3 times greater risk in 14-18 yr**
40 male athletes **Cook 2001**	**No greater risk**
54 male athletes **Fred berg 2002**	**No greater risk**

Body composition

- BMI in subjects that failed the Achilles eccentric program higher (>28) than in responders (Alfredson et al)
- BMI correlated with pathology score (Mokone et al)
- BMI over 35 increased risk of shoulder tendon surgery by more than 3 times (Wendleboe et al 04)

Body composition

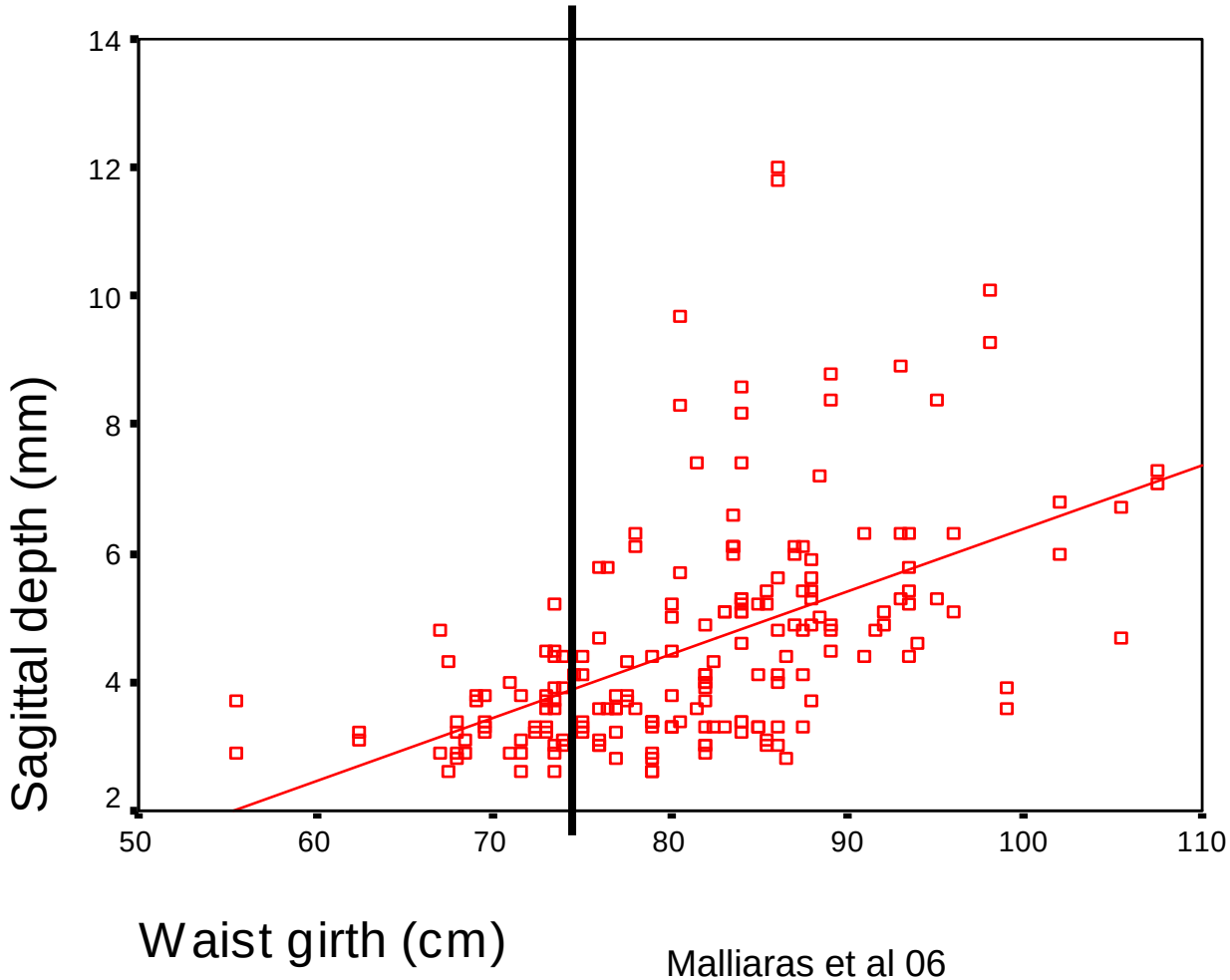
- BMI as a **RISK** factor for upper extremity tendinitis
- Cohort study in 500 workers over 5 years
  - No baseline symptoms
  - Clinical diagnosis of wrist, elbow or shoulder tendinopathy
  - Aside from symptoms and history of other conditions (CTS), BMI was the ONLY significant factor
    - 29.5 UET, 27.7 no UET (no variance reported)
  - Age, sex, job, exercise, smoking, support, stress, disease all not significant
    - Werner et al 05

Body composition

- Systematic review identified 41 studies that examined tendons and body fat
  - 19 found a significant association (Gaida et al, submitted)
  - Trends in same direction for all but two of the remaining studies

J. Tharapos '03

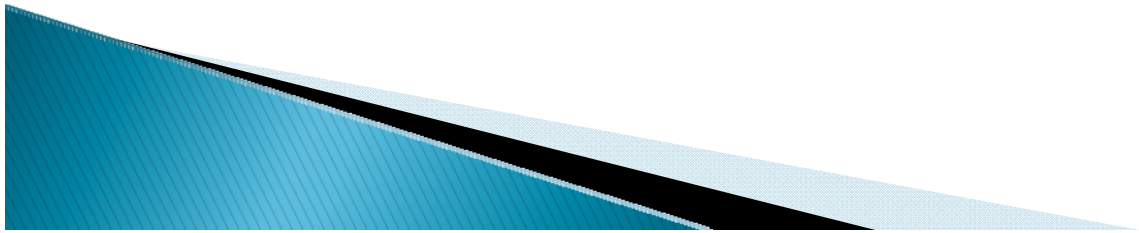
Waist and pathology



Malliaras et al 06

How does fat affect tendons?

- Cytokines
  - Visceral fat excretes pro-inflammatory cytokines
    - IL-6, IL-1
  - Also factors known to be associated with bone-tendon junction pathology
    - TNF-a
- Lipid deposition
  - In arteries
    - Vascular compromise
  - In tendons
    - Tendolipomatosis
      - Seen in familial hypercholesterolaemia
    - Cholesterol levels linked to Achilles tendinopathy
    - 70% of those examined had elevated cholesterol levels (Gaida et al 09)



Lipids

- = Tot Chol, = LDL
- ↑ Triglyceride
- ↓ %HDL-C
- ↑ TG/HDL-C
- ↑ APO-B

Variable	Achilles	Control	p
Chol (mmol/L)	5.47 (1.02)	5.16 (1.00)	0.094
TG (mmol/L)	**1.22 (0.77)**	**0.96 (0.47)**	**0.039**
HDL (mmol/L)	1.44 (0.39)	1.58 (0.48)	0.097
%HDL	**27.6 (8.5)**	**31.9 (10.3)**	**0.016**
LDL (mmol/L)	3.37 (0.86)	3.14 (0.93)	0.166
LDL/HDL	2.53 (0.98)	2.18 (0.93)	0.052
TG/HDL	**0.941 (0.746)**	**0.691 (0.459)**	**0.036**
ApoB (mg/L)	**1005 (230)**	**896 (231)**	**0.017**

Clinical application

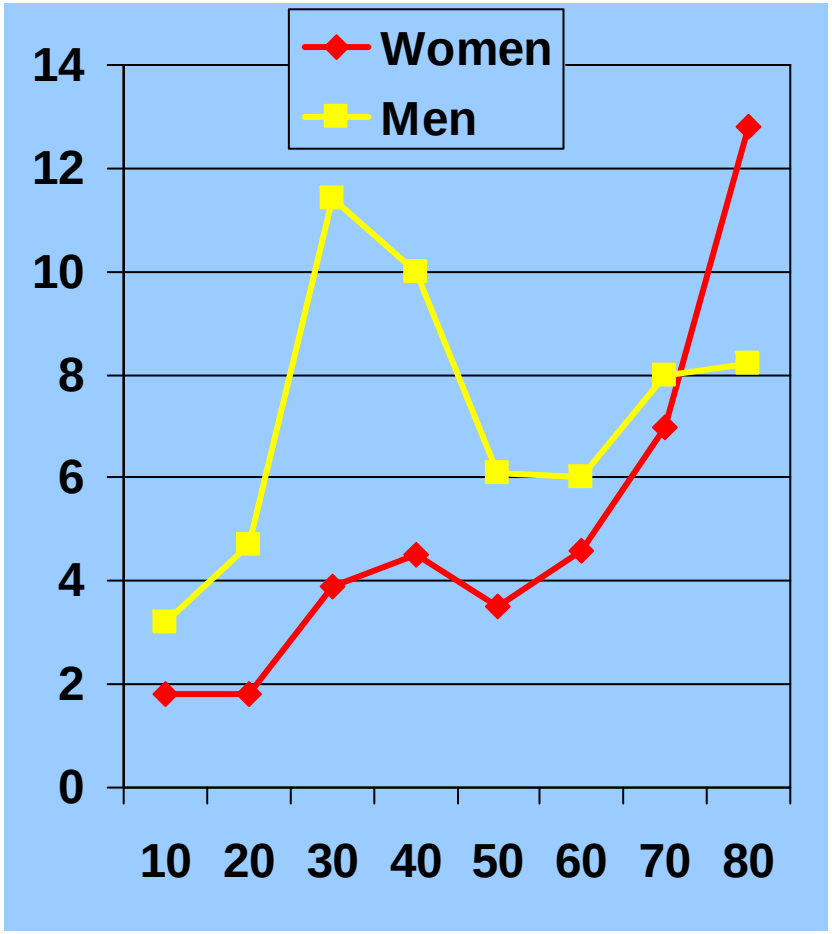
- If you exercise (increased load)
  - With a genetic predisposition to tendon disease and/or central fat storage
  - AND you are fat
- You may have a series of factors that leave you vulnerable to tendon disease

Factors that affect the Achilles

- So how might fat explain other populations with tendinopathy?
  - Sedentary people might have higher fat mass
    - Surgery in athletic and not athletic populations
      - NA were shorter, heavier (higher BMI), higher subcutaneous fat
        - 25/48 good result cf 32/45, VISA 88 cf 74
        - Suffered more wound infection and sensitivity, more hypertrophic scarring, more repeat surgery
        - Maffulli et al 07
  - Middle aged men have higher visceral fat levels
  - Post menopausal women change fat deposition from subcutaneous to visceral

Factors that affect the Achilles

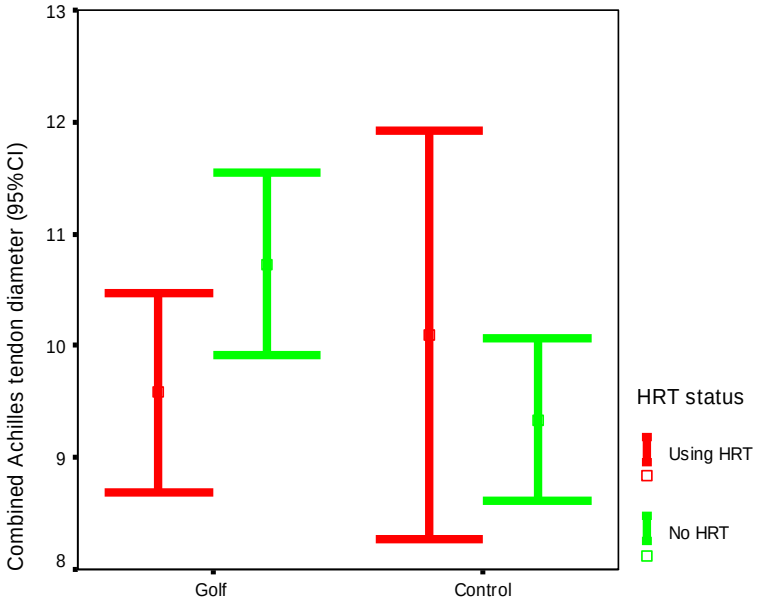
- Sex
  - Women get less Achilles mid-tendinopathy than men
    - Is oestrogen a factor?
- Female hormones may be protective of tendons
  - Non-load related tendinopathy in post-menopausal women
  - Increased incidence in rupture post menopause



Role of female hormones in Achilles tendinopathy

- 95 post-menopausal women
  - Achilles tendon US
  - VISA-A score
  - Golfers and controls
  - Current and never HRT
- Results
  - Positive effect from HRT
  - Negative effect from golf
    - More pathology
    - Larger tendons

Cook et al 2007

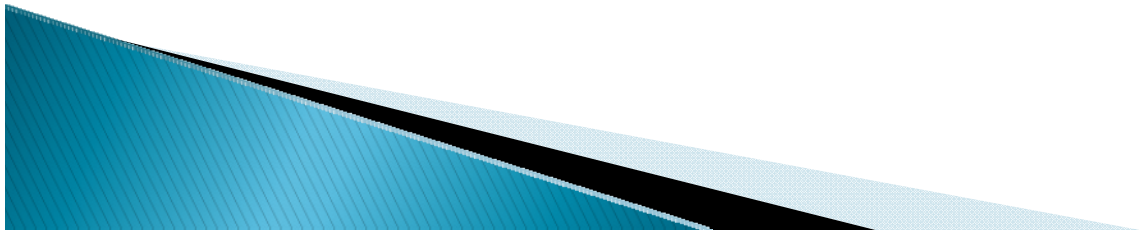


Summary

- Tendinopathy has a range of factors that contribute to it
- Occurs in tendons with a variety of loads
  - The pathology is likely the same
  - The aetiology is likely different
- Understanding and addressing the factors associated with the condition may improve outcomes

Why do eccentric programs work?

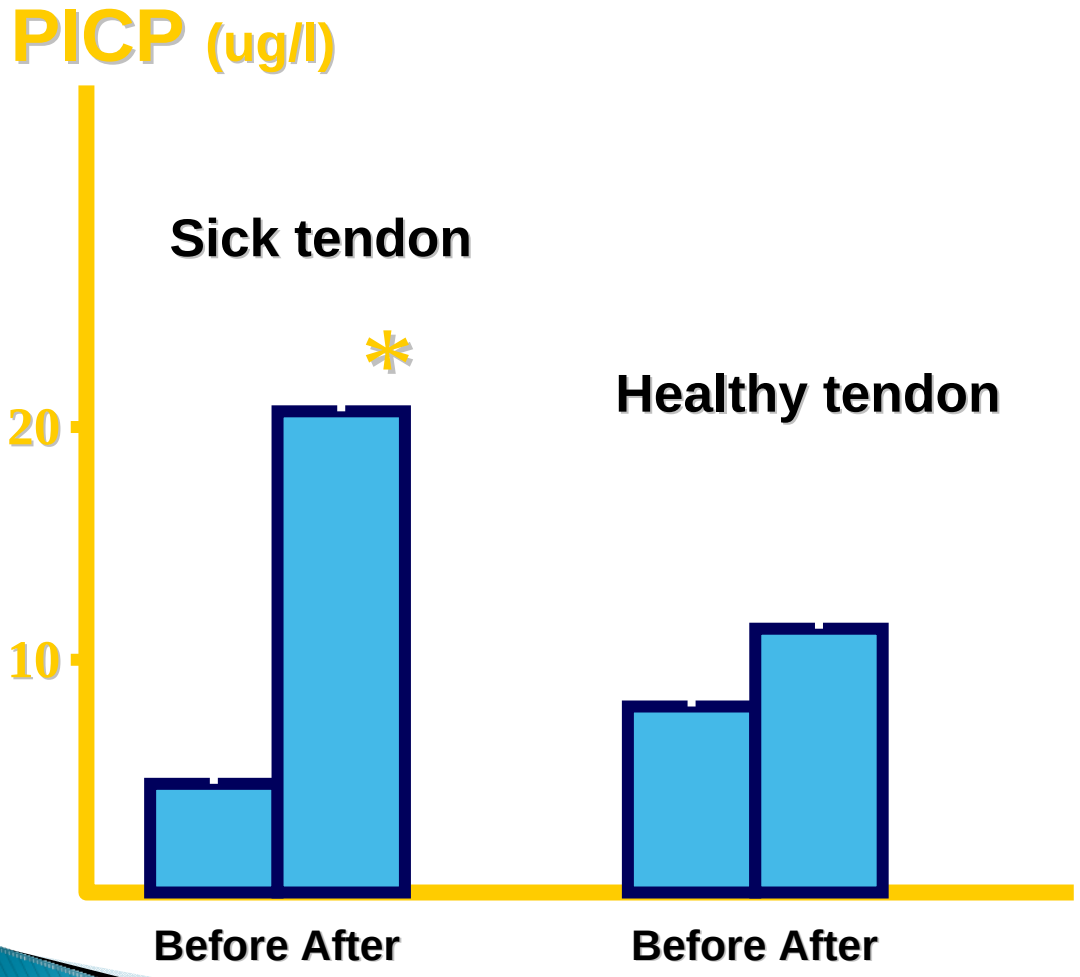
- Decreased eccentric strength?
  - Haglund-Akerlind 93
- Neuroirritant
  - Soft tissue firm tissue interface
- Muscle effects
  - Increased length of MTU
- Effects on matrix structure
- Fluctuating length-force relationship
  - Rees 2008
- Decrease in cross sectional area after eccentric exercise
  - Bryant et al 08



Effects of a single bout of exercise

- A single bout of eccentric exercise
  - decreases cross-sectional area in normal tenons
  - In abnormal tendon increased tendon
    - Signal by 31%
    - Volume by 17%
      - Shalabi 04

Effect of an eccentric exercise program



Activity related Achilles tendon pain (>3 months)

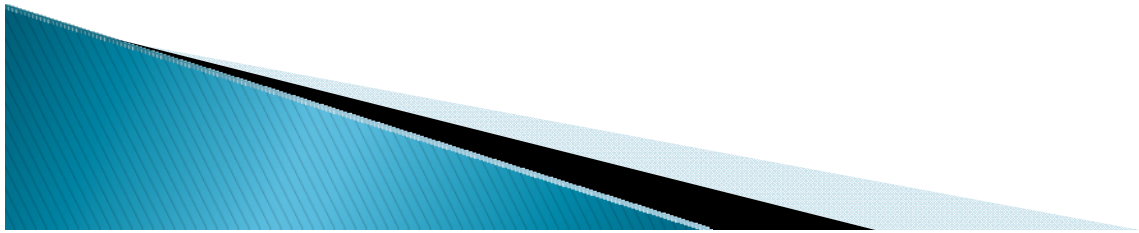
Elite football players 12 weeks training

Microdialysis
Achilles region
Sick + healthy side
(n=10)

Langberg, Ellingsgaard & Kjær 07

Benefits and limitations of eccentric recipes

- Benefits
  - Easy to apply
  - Known outcomes
  - Both programs are progressive tendon loading
- Limitations
  - Population specific
    - Most evidence in middle aged recreational athletes
      - Alfredson program yields very good results in older, pre-surgical cohorts *Alfredson 1998, 2000, 2001*
      - Evidence in elite?
        - Do these athletes need a speed program?
      - Evidence in non athletic cohort
        - Poorer outcome Maffulli 06



Not just eccentric exercise

- Achilles
  - All did general and specific strength
    - Not just eccentrics
  - Randomised 2 groups
    - One allowed to stay active
      - <5/10 pain
    - One rehab only
- No difference in outcome
  - Silbernagel (in press)

Eccentric exercise compared to stretching

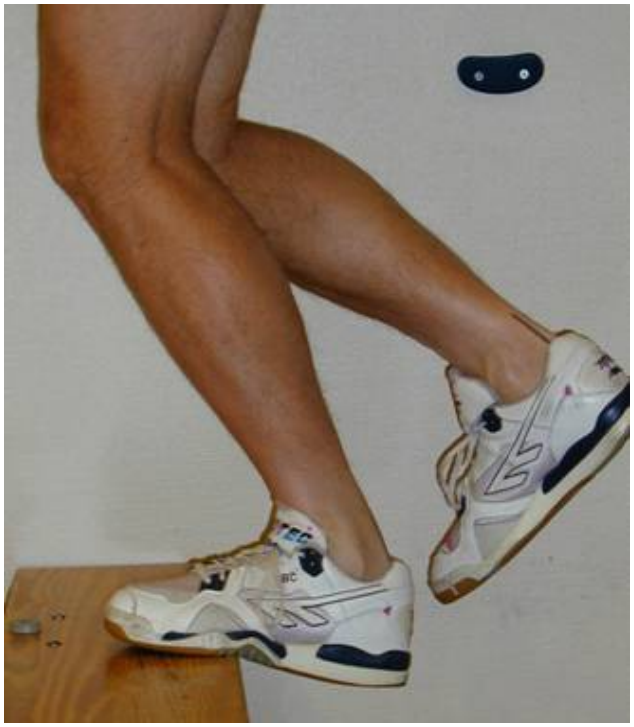
- Eccentric vs stretching Lateral elbow tendinopathy RCT
  - n=38
  - Matched age, symptoms
  - 3 sets of 5 reps with dumbbell
  - Started at 1 kg (M) and 0.5 kg (F)
    - Increased weight 10% weekly
    - Exercises intended to be pain free

- Svernlov & Adolfsson 01

- 71% vs 39% completely recovered @ 12 mths
  - $p = 0.09$
- Greater increase in grip strength in exercise group
  - $p < 0.05$

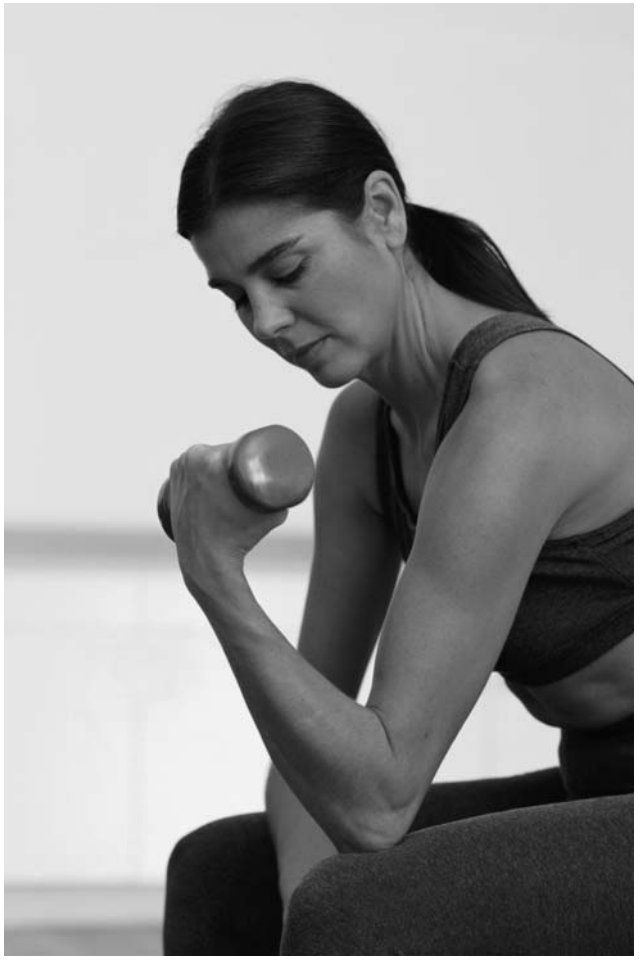
Eccentric exercise compared to stretching

- Achilles RCT, n=45
  - Eccentric vs 30 s stretch both bent and straight knee
- No difference (?) in outcome
  - 3 and 12 months
- Issues
  - Follow up
  - Outcome measures
    - US, palpation and unvalidated questionnaires
      - Norregaard et al 07

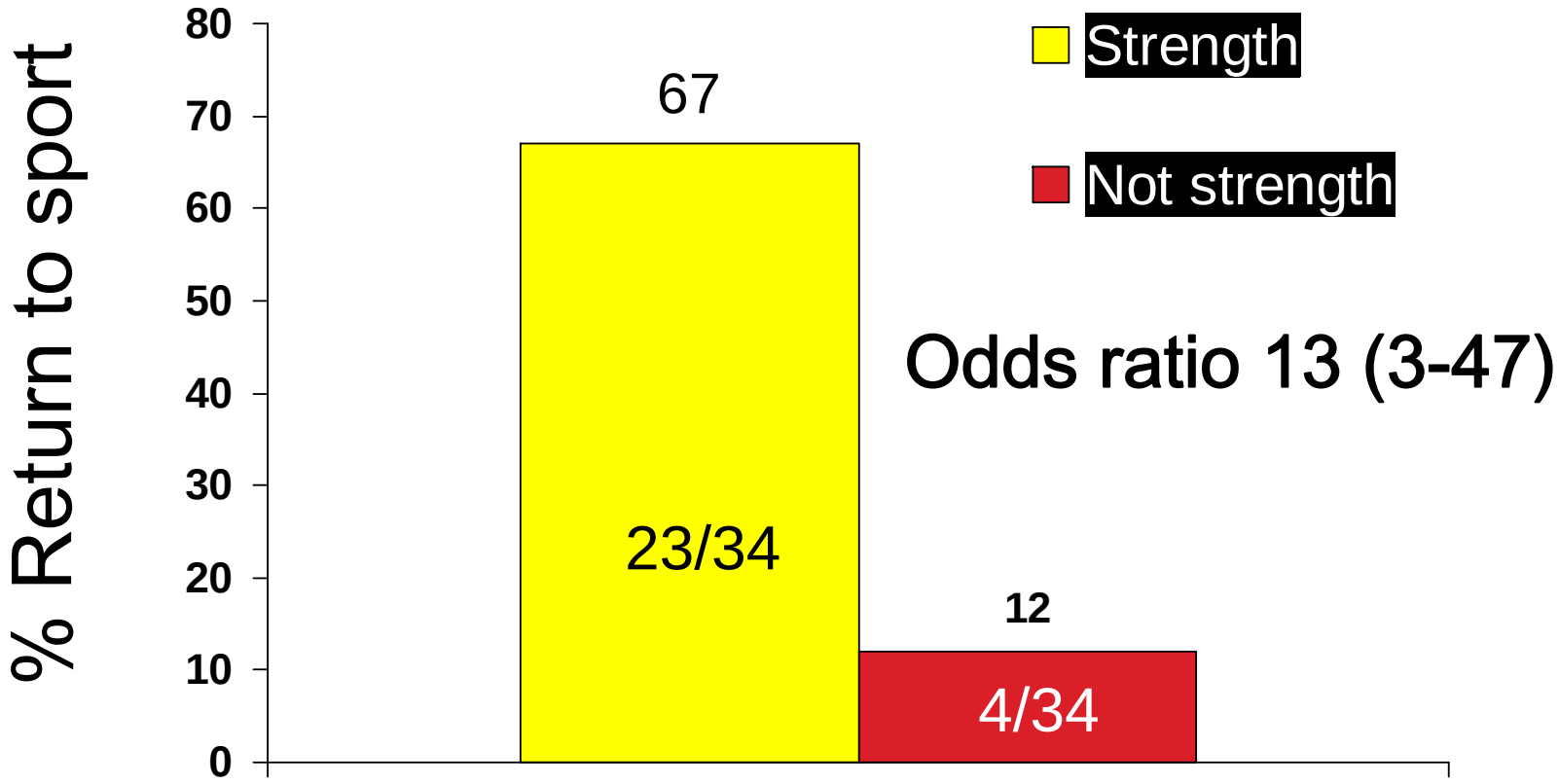


Not just eccentric exercise

- High load resistance training
  - Patellar tendon
    - 3 groups
      - Decline squat, heavy load resistance, control
  - Heavy slow resistance better than decline at 12 weeks
    - Kongsgaard et al (in press)
  - Similar results with Bronstromm machine
    - Frohm et al



Any exercise helps tendons



Holmich, Lancet, 1999

As long as it has an eccentric part

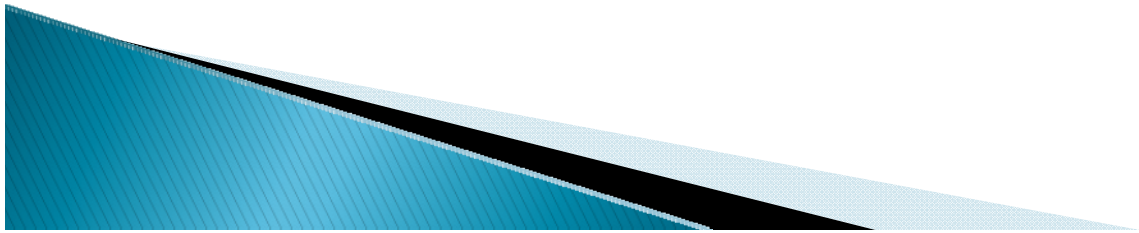
- Randomized controlled trial
- Heel drops
  - n=22
- Heel raises
  - n=22
- Same routine

- 82% success rate in eccentric group
  - VAS from 69 to 12
- 36% success rate in concentric group
  - p<.002

Mafi, Lorentzon, Alfredson, KSSTA, 2001

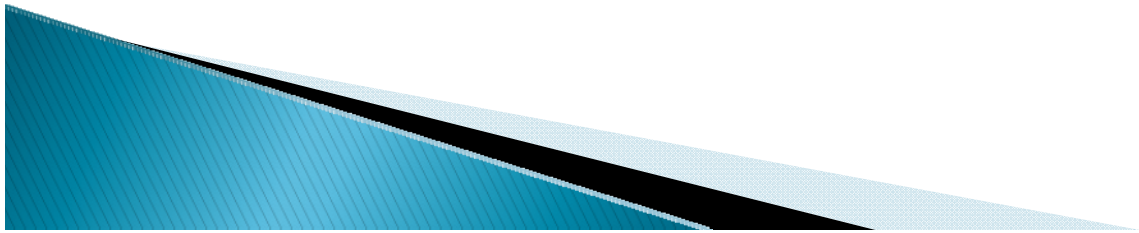
Eccentric exercise in season

- Unsuccessful in patellar tendon
  - Visnes, Fredberg
- Soccer players
  - Randomised to intervention or control
    - Intervention stretching and eccentric exercise
      - 25 times each leg, 3 sets, 3 times a week
  - No difference in outcome
    - 9% of normals developed US changes both groups
    - RR of developing symptoms 2.8 (1.6,4.9) in both groups if US abnormal at baseline
- Eccentrics have never been shown to have a preventative role
  - In-season loads are high



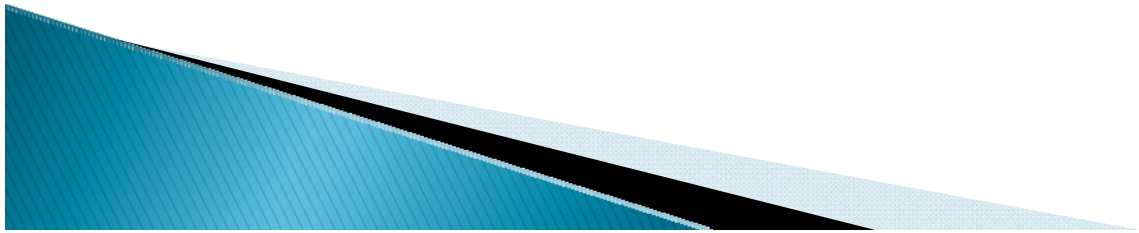
Summary of eccentric programs

- Good starting point
  - Especially in the population they have been shown effective
- Will it adapt the muscle-tendon unit to required load capacity?
  - Yes – go right ahead, remember it is NOT a muscle strengthening program
  - No – add more or do different program
- Have strategies and time frames to vary program if necessary
  - Added interventions
  - Altered interventions



Tendon rehabilitation

- The cornerstones of tendon rehabilitation is a good assessment
  - Defining the stage of tendinopathy
    - Patient history
    - Diagnostic ultrasound
  - Quantify tendon symptoms & function
    - Loading tests
- And then providing the right stimulus to the tendon
  - Modify the tendon load
    - Training
    - Biomechanical
  - Progressive loading/exercise program as required
    - Affected by presentation, timing



Define the stage – Patient history

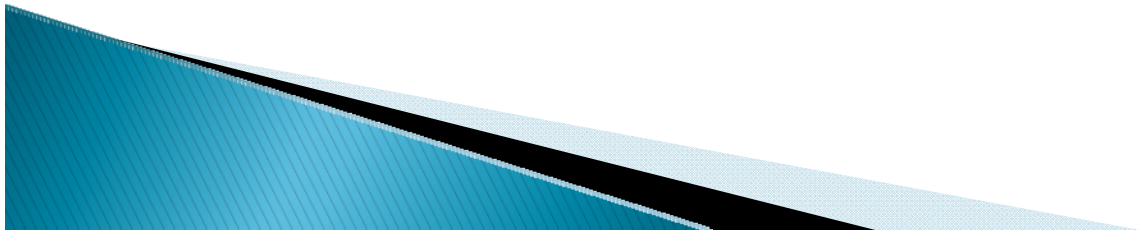
- Age
- History of onset
  - First episode?
  - Exercise history
    - Periods of down-time
- Person factors
  - General health
    - Diabetes, inflammatory diseases, gout
  - Lipid profile
    - Waist girth
    - Cholesterol
  - Other tendinopathies
  - Biomechanics

Physical assessment

- Confirm pain localisation
  - Include related structures
- Assess load – pain response
  - Progressive load
  - Pain score /10
- Irritability
  - 24 hour response to training load
  - Morning stiffness in Achilles
- Assess kinetic chain
  - Atrophy
  - ROM – Ankle, foot and other m-t units
  - Strength, power, fatigability
  - Dynamic, sports-related function

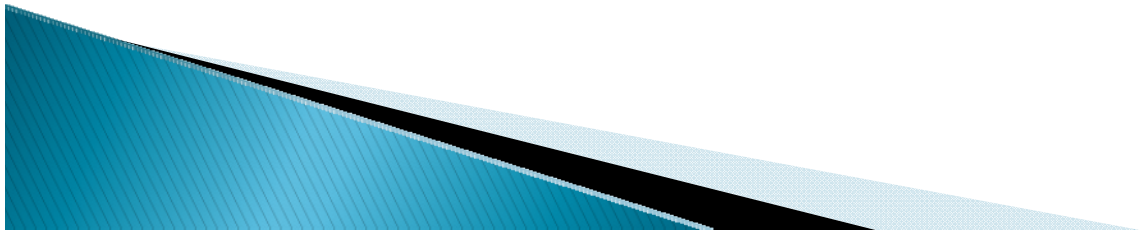
What are we trying to achieve with rehab?

- Avoid exacerbation of the tendon cells/matrix
  - Unload the affected tendon
- Remodelling of matrix through graduated and specific loading
    - Is the sub-acute tendinopathy weak? – probably not
- Maintain/improve function of muscle, kinetic chain and athlete
  - Load progression geared towards a return to sport



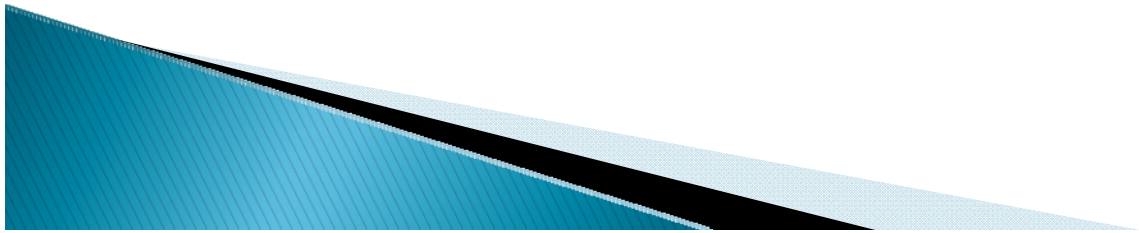
Tendon unloading and reloading

- Prolonged periods of unloading are not beneficial to the matrix
  - Greater than 2-3 weeks
- Mechano-transduction theory would support slower/lower impulse loading in acute phase
  - Less likely to up-regulate the tenocytes or matrix
- Elastic function loading sessions only every 3rd or 4th day *Langberg 1999, Cook 2003, Silbernagel 2004*
- Structure high, low, medium tendon load day
  - Strength day, power day, energy storage day



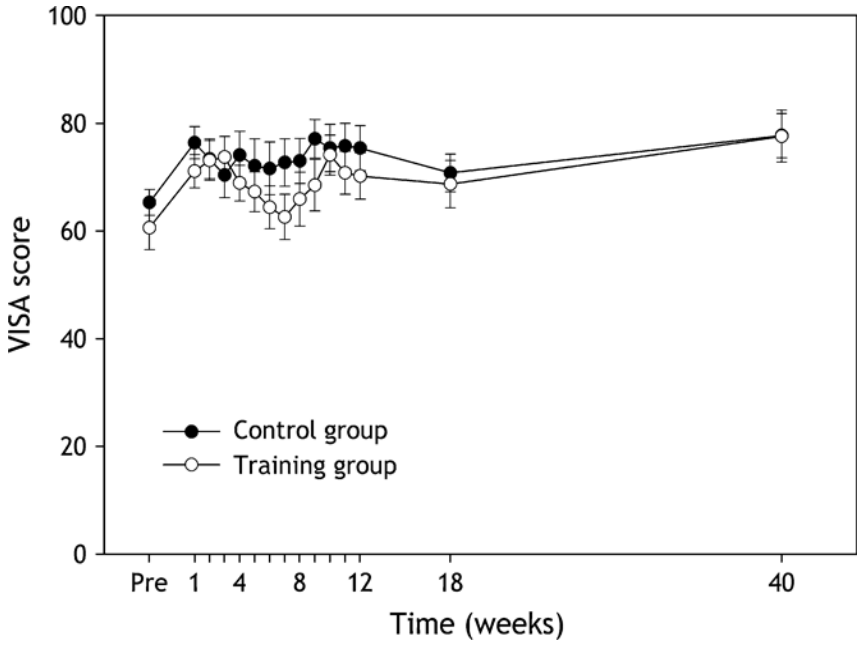
What else?

- Prehab in those with known tendinopathy and/or symptoms
  - Maintain strength always
- Monitoring
  - Use provocative tests
- Early intervention
  - Stitch in time approach
- Training planning
  - Ideal vs real
  - Negotiate with coach….



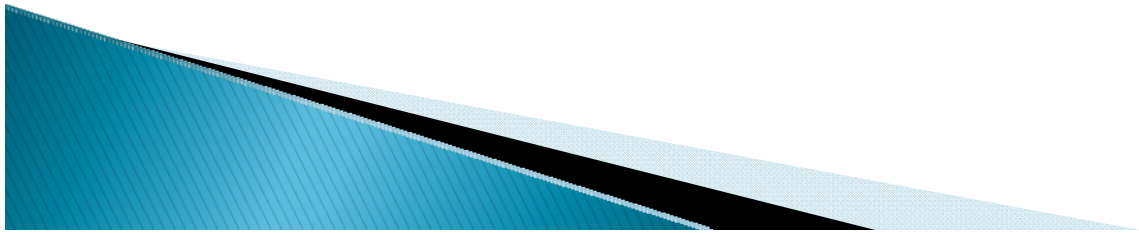
What doesn't help?

- High load drills/exercises with little recovery
  - Plyometrics
- Painful eccentric programs
  - in acute onset pain, in-season
- Rehab using solely eccentric exercise
- Ultrasound & frictions
  - Tenocyte activation
- Glucosamine compounds
  - Inhibition of breakdown of aggrecan



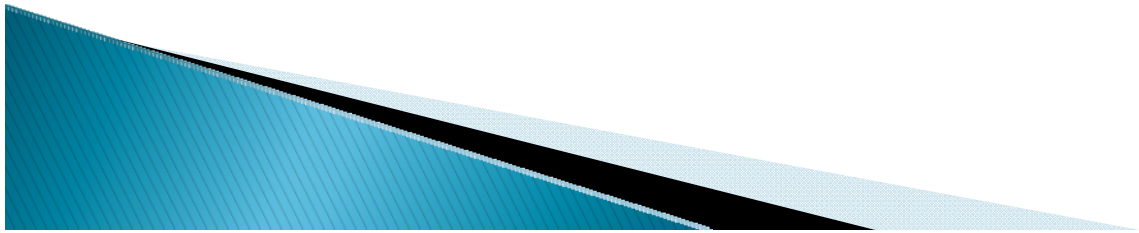
Current thoughts

- Staging the condition is a key to optimal medical and rehabilitation management
- Latent (24 hr) pain response is probably the most useful guide to load progression
- Early tendinopathies are essentially load management
- High load, painful eccentric programs are not indicated in all tendinopathies



Treating tendinopathy

- Identify if you think compression is a factor
  - If so, limit the compression on the tendon
- Identify factors that might influence outcome
  - Fat is easy
  - Genes, sex a bit harder
- Identify if they are in a population that responds to an eccentric program
  - Middle ages recreational athletes
    - If so, start with that
    - Otherwise consider other factors that might impact on outcome



Summary

- Exercise is the most potent stimulus to maintain and remodel the matrix
- Maintenance and prevention
  - Kinetic chain analysis
  - Off season pre-habilitation
  - In season maintenance of strength
  - Regular monitoring & early intervention
  - Care with programming of change of load

There is no magic bullet!