Sport and Osteoarthritis: Is there a link?

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Causation: OA prevention & treatment?
1. Does sport cause OA: how will we know?
2. What exercise minimizes the risk of adult OA?
3. What exercise is best for those with OA?
Why is the question important?

Exercise 'can be as good as pills'

By Michelle Roberts
Health editor, BBC News online

Sporty fortysomethings put pressure on NHS
Physical activity guidelines

- Are many doctors & healthcare workers aware of their existence?....
- How does this effect their practice?
- Great guidelines: dissemination needs work

Examples of physical activity that meet the guidelines:

- Moderate-intensity physical activity: causes adults to get warmer and breathe harder and their hearts to beat faster, but they should still be able to carry on a conversation.
  - Walking
  - Cycling

- Vigorous-intensity physical activity: causes adults to get extremely hot and breathe extremely fast.
  - Swimming
  - Sports such as running or football

Physical activities that strengthen muscles include lifting body weight or anything against a resistance. They should involve using all the major muscle groups.
- Examples include:
  - Exercising with weights
  - Carrying or moving heavy loads such as groceries

Minimising sedentary behaviour may include:
- Reducing time spent watching TV, using the computer or playing video games
- Taking regular breaks from sitting
- Snacking more wisely such as swapping a long sandwich for a healthier fruit ball

What are the benefits of being active daily?
- Reduces risk of a range of diseases, e.g., coronary heart disease, stroke, type 2 diabetes
- Helps maintain a healthy weight
- Helps maintain balance
- Reduces symptoms of depression and anxiety

For further information: Start Active. Stay Active: A report on physical activity for health from the Chief Medical Officer (2011)
Physical activity guidelines: older people

- **Strength training**
- **Balance & co-ordination**

1. Older adults who participate in any amount of physical activity gain some health benefits, including maintenance of good physical and cognitive function. Some physical activity is better than none, and more physical activity provides greater health benefits.

2. Older adults should aim to be active daily. Over a week, activity should add up to at least 150 minutes (2½ hours) of moderate-intensity activity in bouts of 10 minutes or more - one way to approach this is to do 30 minutes on at least 5 days a week.

3. For those who are already regularly active at moderate intensity, comparable benefits can be achieved through 75 minutes of vigorous-intensity activity spread across the week in a combination of moderate and vigorous activity.

4. Older adults should also undertake physical activity to improve muscle strength on at least two days a week.

5. Older adults at risk of falls should incorporate physical activity to improve balance and co-ordination on at least two days a week.

6. All older adults should minimise the amount of time spent being sedentary (sitting) for extended periods.

Individual physical and mental capabilities should be considered when interpreting the guidelines.

**Examples of physical activity that meet the guidelines**

**Moderate intensity physical activities** will cause older adults to get warmer and breathe harder and their hearts to beat faster, but they should still be able to carry on a conversation. Examples include:
- Walking
- Stretching
- Dancing

**Vigorous intensity physical activities** will cause older adults to get warmer and breathe much harder and their hearts to beat rapidly, making it more difficult to carry on a conversation. Examples include:
- Climbing stairs
- Running

**Physical activities that strengthen muscles** involve using body weight or working against a resistance. This should involve at least two of the major muscle groups. Examples include:
- Weightlifting
- Push-ups
- Squats

**Activities to improve balance and co-ordination may include**
- Tai Chi
- Yoga

**Minimising sedentary behaviour may include**
- Reducing time spent watching TV
- Being regular walk breaks around the garden or street
- Breaking up sedentary times such as swapping a long bus or car journey for walking part of the way

**What are the benefits of being active daily?**
- Helps maintain cognitive function
- Reduces cardiovascular risk
- Helps maintain ability to carry out daily living activities
- Improves mood and can improve self-esteem
- Reduces the risk of falls

For further information, **Start Active, Stay Active: A report on physical activity for health from the four home countries**.
Association of "Weekend Warrior" and Other Leisure Time Physical Activity Patterns With Risks for All-Cause, Cardiovascular Disease, and Cancer Mortality

Gary O'Connor, PhD; Min Lee, ScD; Mark Harner, PhD; Ellinam Samples, PhD

IMPORTANCE More research is required to clarify the association between physical activity and health in "weekend warriors" who perform all their exercise in 1 or 2 sessions per week.

OBJECTIVE To investigate associations between the weekend warrior and other physical activity patterns and the risks for all-cause, cardiovascular disease (CVD), and cancer mortality.

DESIGN, SETTING, AND PARTICIPANTS This pooled analysis of household-based surveillance studies included 11 cohort-based respondents to the Health Survey for England and Scottish Health Survey with prospective linkage to mortality records. Respondents 40 years or older were included in the analysis. Data were collected from 1994 to 2012 and analyzed in 2016.

EXPOSURES Self-reported leisure time physical activity, with activity patterns defined as inactive (reporting no moderate- or vigorous-intensity activities), insufficiently active (reporting >150 min/wk in moderate-intensity and <75 min/wk in vigorous-intensity activities), weekend warrior (reporting >150 min/wk in moderate-intensity or >75 min/wk in vigorous-intensity activities from 1 or 2 sessions), and regularly active (reporting >150 min/wk in moderate-intensity or >75 min/wk in vigorous-intensity activities from 3 sessions). The insufficiently active participants were also characterized by physical activity frequency.

MAIN OUTCOMES AND MEASURES All-cause, CVD, and cancer mortality ascertained from death certificates.

RESULTS Among the 63,561 adult respondents (48.9% male; 51.1% female; mean [SD] age, 58.4 [11.9] years), 8,802 deaths from all causes, 2,780 deaths from CVD, and 2,536 deaths from cancer occurred during 656,199 person-years of follow-up. Compared with the inactive participants, the hazard ratio (HR) for all-cause mortality was 0.66 (95% CI, 0.62-0.70) in insufficiently active participants who reported 1 or 2 sessions per week, 0.70 (95% CI, 0.60-0.83) in weekend warrior participants, and 0.65 (95% CI, 0.58-0.73) in regularly active participants. Compared with the inactive participants, the HR for CVD mortality was 0.60 (95% CI, 0.52-0.69) in insufficiently active participants who reported 1 or 2 sessions per week, 0.60 (95% CI, 0.45-0.82) in weekend warrior participants, and 0.59 (95% CI, 0.48-0.73) in regularly active participants. Compared with the inactive participants, the HR for cancer mortality was 0.83 (95% CI, 0.73-0.94) in insufficiently active participants who reported 1 or 2 sessions per week, 0.82 (95% CI, 0.63-1.06) in weekend warrior participants, and 0.79 (95% CI, 0.66-0.94) in regularly active participants.

CONCLUSIONS AND RELEVANCE Weekend warriors and other leisure time physical activity patterns characterized by 1 or 2 sessions per week may be sufficient to reduce all-cause, CVD, and cancer mortality risks regardless of adherence to prevailing physical activity guidelines.

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Johnson County OA project

• Association between meeting Physical Activity guidelines & knee outcomes in 1522 adults >45yrs
• Follow-up time 6.5yrs (4.0-10.2)
• Minnesota Leisure Time Physical Activity questionnaire
• Incident knee OA: KL grade 2 or above
• Meeting HHS Physical Activity guidelines (150mins/wk) was not associated with incident knee OA
• Those with >300mins/wk had non-significant increased risk when compared to those who were inactive: <10mins/wk
1. Does sport cause OA: how will we ever know?
2. What exercise minimizes the risk of OA in adults?

- Easy answers?: Systematic reviews, meta-analyses
- Definitions
- Arthritis Research UK Centre Sport, Exercise & OA
- Cohorts:
  - Cross-sectional:
    - Football
    - Olympians
  - Prospective:
    - Ankles
    - Runners
- Conclusions

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Does sports participation (including level of performance and previous injury) increase risk of osteoarthritis? A systematic review and meta-analysis

Gui Tran, Toby O Smith, Adam Grice, Sarah R Kingsbury, Paul McCrory, Philip G Conaghan

ABSTRACT

Background To assess the relationship between sport and osteoarthritis (OA), and specifically to determine whether previous participation, in terms of level (elite or non-elite), type of sport, intensity or previous injury, was associated with OA.

Methods This systematic review was developed using PRISMA guidelines. Databases were searched (to May 2015). Narrative review and meta-analysis (with risk ratio (RR) and 95% CI) approaches were undertaken where appropriate. Study quality was assessed using GRADE.

Results 46 studies were included. Narratively, 31 studies reported an increased risk of OA, with 19 demonstrating an increased risk in elite athletes. There was an increased risk after sports exposure (independent of type: RR 1.37; 95% CI 1.14 to 1.64; 21 studies). It remained unclear whether there was a difference in risk of OA between elite and non-elite athletes (RR 1.37; 95% CI 0.84 to 2.22; 17 studies). The risk was higher in soccer (RR 1.42; 95% CI 1.14 to 1.77; 15 studies) but lower in runners (RR 0.86; 95% CI 0.53 to 1.41; 12 studies). 9 studies showed an association with the intensity of sport undertaken and OA. 5 studies demonstrated a higher prevalence of OA following micro-avulsion and anterior cruciate ligament tears. Overall, the evidence was of GRADE ‘very low’ quality.

Conclusions There was very low-quality evidence to support an increased relationship between sports participation and OA in elite participants. It is unclear whether there is a difference in risk between elite and non-elite participants with further prospective studies needed to evaluate this. Pooled findings suggested that significant injuries were associated with OA in soccer players.

It is important as it potentially provides a population where interventions may prevent subsequent OA.

There have been several narrative reviews investigating sporting activities and their relationship with OA, with conflicting conclusions. For example, O’Doherty et al determined that elite level running increased the risk of OA, although there was no associated risk in recreational runners. Similarly, Conaghan and Lequesne et al argued that elite sports participation may increase the risk of OA, and that the risk for runners in particular may be dependent on the rate of miles run. In contrast, Cymet and Sinkov concluded that there was no increased risk of knee or hip OA in runners.

A systematic review in 2003 demonstrated moderate evidence that sporting activity was associated with hip OA, although OA in other joints was not explored. In a review of OA and physical activity, Vignon et al found sport to be a risk factor for knee and hip OA, with increased risk associated with both intensity (including duration) of sports participation. These systematic reviews, however, did not investigate individual sports, and nor did the authors investigate other joints except the knee or hips, or the role of previous sporting injuries. Furthermore, there has been no systematic review exploring the relationship between OA and elite sport compared with non-elite sport.

This systematic review aims to examine the relationship between OA and the top 32 most popular English sports by participation, which represents the majority of the 1.7 million adults who participated in sports. It specifically aims to examine if there is a relationship between previous participation in sports, the level of sports participated in (ie, elite, non-elite), intensity of participation (ie, high, low), and the risk of OA.
What are the findings?

- There is low-quality or very low-quality evidence to support an increased association of sports participation and the occurrence of osteoarthritis (OA) in elite participants.
- There is very low-quality evidence to suggest that soccer, especially in the elite setting, may increase the risk of OA, whereas running may not.
- For non-elite participants, the relationship is unclear and further prospective cohort studies need to be undertaken.
- Overall, there were conflicting results, based on low-quality evidence, in determining an association between previous sporting injuries and OA, although pooled findings suggest that ACL injuries and meniscectomies may contribute to OA in soccer players.

How might it impact on clinical practice in the future?

- Improve awareness that there may be an increased risk of OA in elite athletes, particularly soccer players, and those who get injured.
- This may influence prehabilitation and rehabilitation of these athletes.
- Be aware that high-intensity sporting activity may potentially be associated with OA, although further research needs to be undertaken to understand this.
- Understand that this needs to be balanced with the substantial benefits of participating in sports (physical and mental well-being) where >30 min of activity/day is advised.
Are Joint Injury, Sport Activity, Physical Activity, Obesity, or Occupational Activities Predictors for Osteoarthritis? A Systematic Review

Osteoarthritis (OA) is a significant health problem worldwide, affecting approximately 10% of men and 18% of women over 60 years of age. OA typically affects weight-bearing joints, is historically diagnosed later in life, and is a major cause of morbidity, disability, and pain. The onset of OA increases with age, and up to half of people over 50 years of age report symptomatic OA. Some physical risk factors may also be associated with an increased rate of early onset of OA and require further investigation. For example, longitudinal studies provide evidence of a significantly increased risk of knee OA 12 to 20 years post-knee injury (e.g., meniscus or anterior cruciate ligament injury). In addition, there is evidence that knee and ankle injuries, physical activity, obesity, and occupational activity are associated with an increased risk of OA.
Definitions

• OA Phenotypes
• Stages of OA: XR, MRI
• OA in different joints
• Pain: Symptomatic OA
• Exercise/Physical Activity
“A group of overlapping disorders with different aetiologies but similar biologic, morphologic and clinical outcomes. The disease processes affect articular cartilage, subchondral bone, synovium, capsule and ligaments. Ultimately, cartilage degenerates with fibrillation, fissures, ulceration and full thickness loss of joint surface.”

NIAMS, NIA, AF, OREF (1995)
Synovium
Inhibition of synovial inflammation
- Arachidonic acid pathway inhibitors (e.g. Licofelone)
- p38 pathway inhibitors (e.g. MK2)
- Inducible nitric oxide synthase (iNOS) inhibitors

Cartilage
Inhibition of catabolic proteases
- Specific MMP inhibitors (e.g. MMP13)
- Aggrecanase inhibitors (ADAMTS4, ADAMTS5)
Anabolic promotion
- Growth Factors (e.g. FGF2, FGF18)
- BMP7
Novel combinations of known targets
- e.g. Protease inhibitor + anabolic

Subchondral Bone
Inhibition of osteoclast activity
- Protease inhibitors (e.g. CatK)
- Apoptosis inducers (e.g. Strontium Ranelate)
Bone vasculature targets
- Angiogenic modulators
- Candidate drug repurposing (from CV Therapeutic area)

Skeletal Muscle
[combination with adjuvant exercise program]
Inhibition of myofibrillar degradation
- Selective androgen receptor modulators (SARMs)
- B2-adrenergic agonists
Modulation of muscle fibre type
- Recombinant thyroid hormone
- B2-adrenergic agonists

Adipose Tissue
[combination with adjuvant weight-loss program]
Modulation of adipokine signalling
- Leptin pathway inhibitors (e.g. Leptin mAb)
- Resistin pathway inhibitors
- APN pathway activators (e.g. recombinant/mimetic APN)
Different phenotypes of OA

- Inflammatory OA
- Cartilage driven OA
- Bone driven OA
- Trauma/injury OA
What is OA?...what to study?

Pain  Structure  Surgical

centre for sport, exercise & osteoarthritis
Conceptual model for the pathogenesis of osteoarthritis: **confounders**

**Systemic factors**
- Age
- Gender
- Obesity (weight)
- Genetics
- Bone density
- Nutrition
- Sex hormones

**Mechanical factors**
- Occupation - joint loading
- Elite athletics
- Joint deformity /alignment
- Obesity (weight)
- Injury, surgery
- Muscle weakness

\[ \text{Susceptibility of joints to damage and repair failure} \]
\[ \text{Site and severity of OA} \]

Nevitt MC, Arden NK 2006

centre for sport, exercise & osteoarthritis
Which joint do we study?
Knee Osteoarthritis: Radiographic changes

- Only 30-50% of patients with radiographic Knee OA have knee pain
Pain processing
Conceptual model for the pathogenesis of osteoarthritis

**Systemic factors**
- Age
- Gender
- Obesity (weight)
- Genetics
- Bone density
- Nutrition
- Sex hormones

**Mechanical factors**
- Occupation - joint loading
- Elite athletics
- Joint deformity /alignment
- Obesity (weight)
- Injury, surgery
- Muscle weakness

Susceptibility of joints to damage and repair failure

Site and severity of OA

Symptomatic OA

Pain factors

[Image: Conceptual model for the pathogenesis of osteoarthritis]
Exercise, Sport and OA: What joint ‘insult’
OA - a multifactorial disease: which risk factor?
Type of study

- Case-control
- Cohort
- Meta-analysis
Methodology

- **Case-control:**
- Cohort
- Meta-analysis

Select population and collect baseline data

Osteoarthritis (Cases)

No osteoarthritis (Control)

Compare case and control groups during follow up
Methodology

- Case-control
- Cohort
- Meta-analysis

Hypothesized sequence of post injury OA development

Injury → Pre-clinical OA → Clinical OA → Joint replacement

Cohort study
Risk factor: ‘Exposure’

Outcome

Exercise

Timing: Present

Osteoarthritis

Future

No osteoarthritis

www.sportsarthritisresearch.org
Meta-analysis
Meta-analysis
Overview of the Arthritis Research UK Centre for Sport, Exercise and OA

Prof Mark E Batt
Centre Director: Nottingham

Prof Nigel Arden
Deputy-Director: Oxford
Every sufferer knows that arthritis is a very unpleasant condition. It seems to be generally random in its choice of victims, but there is much evidence to suggest that it frequently attacks old injuries sustained during participation in exercise or in sports. There are two possible responses; treatment of the condition after it has been diagnosed, and prevention.

I am very pleased to know that The Institute of Sports and Exercise Medicine has joined with Arthritis Research UK to look into ways of preventing osteoarthritis developing after exercise or sport. I know that any advance in techniques for the prevention of this painful condition will be warmly welcomed by the large number of sufferers.
Sports injury and OA Research Centre

Vision:

To create an international multidisciplinary collaborative research Centre to reduce the risk and impact of Osteoarthritis due to acute and overuse injuries in sport
• Nottingham University Hospitals NHS Trust
• Nottingham University
• Oxford University
• Southampton University
• Loughborough University
• Bath University
• Leeds University
• University College London
ARUK Sports Injury and OA Centre: A Centre for a new sport led research agenda
International Collaboration

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Sports Advisory Group
Sport, exercise, injury & OA

Everyday exercisers

Sports active

Elites
Centre cohorts: 2013-2017

- Football
- Olympians
- Runners: HALO
- Significant ankle ligament injury: SALI
- Cricket
- Rugby
- Military
Knee Osteoarthritis in Retired Professional Footballers vs. General Population
A Case Control Study

Gwen S. Fernandes, PhD
Research Fellow
The University of Nottingham, UK
• 300 million players
• 47% professional footballers retire due to injury
• 32% prevalence lower limb OA
• Knee OA in football:
  - 16% elite footballers
  - 4.2% non-elite footballers
  - 1.6% controls
Background

• Football (soccer) - popular sport

• Intensity over a prolonged period

• Injuries – Risk of knee osteoarthritis (OA)

• Limited Evidence

• The Industrial Injuries Advisory Council (IIAC): is football an occupational risk factor for OA?
  • “evidence did not prove compelling in the absence of injury.” {IIAC Paper 15, 2005}
  • Doubling or more of risk

1. Drawer and Fuller 2001
2. Turner et al., 2000
3. Elleuch et al., 2008
4. Krajnc et al., 2010
5. Roos et al., 1994
6. Ariliani et al., 2014
Objectives:

1. To determine and compare the prevalence of Knee OA outcomes specifically in ex-footballers vs. the general population
   - Knee Pain (KP)
   - Radiographic Knee OA (RKOA)
   - Total Knee Replacement (TKR)

2. To determine the main attributable risks for any increased prevalence found.
Methods

Questionnaires

• Knee Pain
in and around the knee for most days of the last one month

• Total Knee Replacement
Self-reported unilateral or bilateral TKR

• Risk Factors
Age, body mass index (BMI), knee alignment, 2D4D ratio, nodal OA, family history and knee injury.

Radiographs

• Nottingham Line Drawing Atlas (NLDA)
• Kellgren Lawrence (KL) Scale
  • Definite joint space narrowing + definite osteophyte
• Chondrocalcinosis (CC)
Methods: Recruitment

Inclusion Criteria:
- Male
- Aged 40 years and over
- Held a contract with a professional football club

Ex-Footballers

Questionnaire Survey
(n=4775)

Questionnaire Responses
(n=1207)

Bilateral Radiographic Assessments
(n=470)

General Population

Questionnaire Survey
(n=40,505)

Questionnaire Responses
(n=9017)

Male, n=4085

Bilateral Radiographic Assessments
(n=491)
## Results

<table>
<thead>
<tr>
<th></th>
<th>Footballers n=1207</th>
<th>Controls n=4085</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>59.0 (11.7)</td>
<td>62.9 (10.4)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>27.3 (3.2)</td>
<td>27.5 (4.7)</td>
<td>0.139</td>
</tr>
<tr>
<td>Pattern 3, 2D4D Digit Ratio, n (%)</td>
<td>733 (60.7)</td>
<td>2237 (54.8)</td>
<td>0.003*</td>
</tr>
<tr>
<td>Nodal OA, n (%)</td>
<td>86 (7.1)</td>
<td>218 (5.6)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Knee Injury, n (%)</td>
<td>778 (64.5)</td>
<td>953 (23.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>High Risk Occupation, n (%)</td>
<td>742 (61.5)</td>
<td>2185 (53.5)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Malalignment, n (%)</td>
<td>193 (16.0)</td>
<td>278 (6.8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Body Pain, n (%)</td>
<td>901 (74.7)</td>
<td>2574 (69.8)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Painkillers, n (%)</td>
<td>423 (35.04)</td>
<td>1289 (31.55)</td>
<td>0.02</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td>355 (29.4)</td>
<td>1868 (45.7)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>
Prevalence of Knee Pain

%  

- 40-44  
- 45-49  
- 50-54  
- 55-59  
- 60-64  
- 65-69  
- 70-74  
- 75-79  
- 80+

- ex-footballers  
- controls

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Prevalence of RKOA

![Prevalence of RKOA graph]

- **Ex-footballers**
- **Controls**

www.sportsarthritisresearch.org
Prevalence of TKR

% of Ex-footballers and Controls over Age Groups

- Ex-footballers
- Controls

Age Groups:
- 40-44
- 45-49
- 50-54
- 55-59
- 60-64
- 65-69
- 70-74
- 75-79
- 80+

Sources:
- www.sportsarthritisresearch.org
Summary

• Prevalence of KP and RKOA is greater in ex-footballers and occurs earlier

• KP, TKR, RKOA and CC are all 1.5-2.5 times higher (after adjustment)

• Injury, BMI and High Risk Occupations are the main attributable risk factors

• This supports consideration of Knee OA as an occupational hazard.
Caveats

- Recall Bias
- Selection Bias
- Generalisability

Future Work

- Nested Case Control within ex-footballers [OARSI Abstract 2179 Amsterdam]
- Data need replication in other populations/countries
- Ankle OA: with cognition, mental health
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• SPIRE Healthcare
• Football Association (FA)
Great Britain’s Olympians Study: Protecting Olympic athletes from osteoarthritis

Dale Cooper1,2, Brigitte E. Scammell1,2,3, Debbie Palmer-Green2, Mark E. Batt1,2,3

1Division of Rheumatology, Orthopaedics and Dermatology, School of Medicine, University of Nottingham, 2Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis, University of Nottingham, 3Nottingham University Hospitals NHS Trust
Objectives

(1) Describe the injury patterns, the prevalence of pain, and osteoarthritis (OA) in Great Britain’s (GB) Olympians;

(2) Determine in GB Olympians aged 40 years and older the risk of pain and OA at three joints - the hip, knee and the lumbar spine; and

(3) Identify the individual risk factors associated with joint pain and OA in GB Olympians aged 40 years and older.
Methods

• Cross-sectional with an internal nested-case control study.

• A web-based and / or paper questionnaire was distributed by email and / or post to 2742 GB Olympians living in 30 different countries:

  • The presence of OA was defined by a self-reported physician-diagnosis.
  • Pain was self-reported using a body manikin, and defined as pain in or around the selected joint on most days for at least one month. The most severe limb was selected as the index joint for data analysis, if bilateral.
  • Six separate models of binary logistic regression were constructed to examine the covariates that were associated with pain/OA at the hip, knee, and the lumbar spine.
Summary

(1) Injury appeared to be constantly the strongest risk factor for pain at the knee, hip and the lumbar spine, as well as OA at the hip and knee;

(2) In GB Olympians aged 40 years and older, the knee was most likely affected by OA, and the lumbar spine by pain; and

(3) Participation in weight-bearing loading sports was associated with hip and knee pain, but not hip and knee OA.
Significant ankle ligament injury study: SALI
Dr Laura Wyatt PhD
Background: Ankle injuries

• Ankle sprains account for up to 5% emergency department visits each year

• Often thought of as benign injuries

• As many as half of people who suffer a significant ankle injury do not fully recover.
Background: Ankle OA

- Most research to date has focused on knee and hip osteoarthritis (OA)
- Injury is a risk factor for ankle OA
- Around 70% of ankle OA is a result of injury
- Little is known about ankle OA and the types of people who suffer a significant ankle injury.
SALI: Multi-centre prospective longitudinal cohort study

LEEDS: Leeds General Infirmary and St James University hospital ED

EDINBURGH: Royal Infirmary of Edinburgh ED

NOTTINGHAM: Queen’s Medical Centre ED & Urgent Care centre

NIHR adopted: Aim to recruit 3000-4000 participants and 200 controls from Emergency Departments

centre for sport, exercise & osteoarthritis
Aims

1. To determine the prevalence of persistent ankle pain and dysfunction following significant ankle ligament injury (SALI) presenting to ED

2. To identify risk factors for poor PROMs following SALI

3. To determine the incidence of ankle OA following SALI

4. To identify risk factors for developing ankle OA following SALI

1. To understand latency of ankle OA onset following SALI.
Eligibility criteria

- Ottawa Ankle Rules **positive**
- **Negative** for ankle fracture on x-ray.
Exclusion criteria

• Patients under the age of 18 or over 70 yrs old.

• Any patients with x-ray reported fractures (excepting flake fractures)

• Fracture injuries of the hind foot, midfoot or forefoot

• Patients with any other significant concurrent injuries e.g., contralateral ankle injury and upper limb injuries

• Patients who are not independently living

• Patients who are not able to read English.
Questionnaires

SALI questionnaires will be completed at each of the 7 time points.

Questionnaires will include 4 sections:

- **Baseline questions** (including age, gender, BMI, occupation, education, diet, puberty history, family joint health, history of OA, knee alignment, 2D:4D ratio, foot position and hypermobility).
- **Index injury and injury history**
- **Functional assessment** (ankle function prior to injury, stiffness, function).
- **Quality of life** (Physical activity, sport and leisure, general health, medication use and history of disease, ED-5D-5L questionnaire).
Nested case-control study

• Control patients will also be recruited (n = 200)

• Age and gender matched recruited from the Accident and Emergency department

• Any patient who has not had a significant ankle injury (ankle pain/function affected for more than 7 days and/or the ankle injury caused them to present to a hospital emergency department).
Retention

• Maintain telephone and email contact with participants

• Annual SALI newsletter sent to participants

• Participants entered into a prize draw for completion of questionnaire at each time points - two tickets to a major sporting event

• Access to GP Read notes (if retention falls in future) – consent form covers consent to relevant sections of medical notes being looked at by authorised individuals.
Recruitment

• Commenced Oct 2016

• **222** participants recruited so far
Running and Walking studies
National Runners and Walkers Health Study

- 74,752 runners & 14,625 walkers
- Studies 1991 & 1997
- Runners half as likely as walkers to develop hip OA leading to a THR
- Runners who ran most had the lowest risk of OA – in part due to lower BMI

www.sportsarthritisresearch.org
Does running protect against knee osteoarthritis? Or promote it? Assessing the current evidence

Richard D Leech, Kim L Edwards, Mark E Batt

Running is extremely popular and knee osteoarthritis is one of the most common musculoskeletal conditions requiring healthcare intervention, thus the question of whether recreational (non-elite) running is associated with knee osteoarthritis has considerable personal and public health significance. The potential exists for a paradox relating to recreational running and joint health: promoting running may have unknown consequences for knee joint health, conversely, discouraging physical activity will negatively impact overall health, increasing the burden on healthcare systems. Additionally, risks (and/or benefits) associated with recreational running may not remain static but vary throughout life. Much remains unknown and the running research base to inform clinical decision-making is thin.

We aim to highlight the limitations of the current body of research and stimulate a wider debate regarding how this evidence is interpreted and conveyed. We also provide guidance on how future research should be structured and implemented, rather than considering recreational running in isolation.

For the purpose of this editorial, we cite 10 key papers that explicitly report the effect of recreational running and the risk of knee osteoarthritis.1–5 Many of these studies found no significant relationship between recreational running and knee osteoarthritis.4,5 A recently published abstract goes further, suggesting running may protect the knee joint from osteoarthritis.4 Conversely, a new systematic review identified long-distance running as a significant risk factor,9 but importantly, only at elite levels. One small study (n=20) found the number of years training was significantly greater in those runners with degenerative joint changes compared to those without, but there was no difference in weekly mileage between the two groups. Additionally, potential confounders remained as age was not adjusted for and the degenerative joint group had a greater history of injury.10

Overall, the ‘weight’ of available evidence, albeit limited, suggests that recreational running may protect the knee joint from osteoarthritis, but more research is needed to understand the underlying mechanisms and to inform clinical practice.

unknown; and specifically how much running (if any) is too much? Identification of a dose or load-response and defined individualised hazards ratios of running would be groundbreaking. A prospective, longitudinal, observational study is required to identify known and novel risk factors for knee osteoarthritis among recreational runners. The study must include a wide-range of running ability while encompassing training parameters such as volume, intensity and terrain. Collaborations with sporting organisations would stimulate interest, provide resources and aid translation of findings. Ideally, the population should include sufficient numbers of younger (<30 years of age) athletes for long-term analysis.

There is a clear self-selection bias in the current research that largely examines older participants who remain able to run in later life.5 Generalising the conclusions from such research is difficult. Future research will require larger populations and a sufficiently long follow-up to enable identification of disease onset and development. Follow-up periods applied by other authors to analyse disease progression (9–11 years) may prove insufficient. Once participants are identified with joint pain/osteoarthritis, they must be retained within the study to enable ongoing review, as the risk factors for symptom development, incidence and progression may not be the same.
Running and Knee Osteoarthritis

A Systematic Review and Meta-analysis

Kate A. Timmins, PhD, Richard D. Leech, MSc, Mark E. Batt, MB Chir, DM, FFSEM, and Kimberley L. Edwards, PhD
Investigation performed at the University of Nottingham, Nottingham, UK

Background: Osteoarthritis (OA) is a chronic condition characterized by pain, impaired function, and reduced quality of life. A number of risk factors for knee OA have been identified, such as obesity, occupation, and injury. The association between knee OA and physical activity or particular sports such as running is less clear. Previous reviews, and the evidence that informs them, present contradictory or inconclusive findings.

Purpose: This systematic review aimed to determine the association between running and the development of knee OA.

Study Design: Systematic review and meta-analysis.

Methods: Four electronic databases were searched, along with citations in eligible articles and reviews and the contents of recent journal issues. Two reviewers independently assessed the titles and abstracts using prespecified eligibility criteria. Full-text articles were also independently assessed for eligibility. Eligible studies were those in which running or running-related sports (e.g., triathlon or orienteering) were assessed as a risk factor for the onset or progression of knee OA in adults. Relevant outcomes included: (i) diagnosis of knee OA, (ii) radiographic markers of knee OA, (iii) knee joint surgery for OA, (iv) knee pain, and (v) knee-associated disability. Risk of bias was judged by use of the Newcastle-Ottawa scale. A random-effects meta-analysis was performed with case-control studies investigating arthroplasty.

Results: After de-duplication, the search returned 1322 records. Of these, 103 full-text articles were assessed, 25 were eligible, describing 15 studies: 11 cohort (6 prospective) and 4 case-control studies. Findings of studies with a diagnostic OA outcome were mixed. Some radiographic differences were observed in runners, but only at baseline within some subgroups. Meta-analysis suggested a protective effect of running against surgery due to OA: pooled odds ratio 0.48 (95% CI, 0.30-0.71). The R² was 9% (95% CI, 0%-73%). Evidence relating to symptomatic outcomes was sparse and inconclusive.

Conclusion: With this evidence, it is not possible to determine the role of running in Knee OA. Moderate- to low-quality evidence suggests no association with OA diagnosis, a positive association with knee OA, and a negative association with knee OA surgery. Conflicting results may reflect methodological heterogeneity. More evidence from well-designed, prospective studies is needed to clarify the contradictions.

Keywords: osteoarthritis, running, physical activity, knee joint, systematic review.
The HALO Study: Runners Cohort

Background:

The role, positive or detrimental, that running plays in knee joint health remains unclear.

Aim:

Develop a prospective, longitudinal, observational study that includes recreational runners from a variety of backgrounds and review them over >15 years, periodically assessing their running behaviour and change in health status over time.
Runners Study: Objectives

• Examine the association between running behaviour and potential risk factors for knee OA for recreational runners compared to non-runners.

• Examine the association between knee-related functional outcomes and potential risk factors for knee OA for recreational runners compared to non-runners.

• Examine the association between joint symptoms (e.g. pain) and levels of physical activity.
Runners Study: Construct

Recruitment:

• Significant support provided by parkrun UK and parkrun Australia

• Approximately: n=3,100 (UK) and n=400 (Australia)

Study Design:

• Baseline questionnaire, initial 1 year follow-up (subsequently every 2-5 years for >15 years)
Physical Activity Profile

Occupation

Recreation / Sport

Running Behaviour

Joint Health Status

Symptoms

Injury History

OA Diagnosis

KOOS

Clinical Tests

Leg length

ROM

Limb / joint circumference

Crepitus

OARSI Performance-based Tests

30-second chair stand

Timed up and go

4x10m walk

6 minute walk

Stair climb

Functional Tests

Single leg balance

Triple hop for distance

Star excursion

KOOS

centre for sport, exercise & osteoarthritis
Conclusions:

• The literature is currently sparse & confusing
• Evidence overall suggests that exercise is good for joints and MSK health
• Need large scale collaborative research to fully describe the effects of exercise on OA in terms of:
  • Timing
  • Type
  • Threshold
Dose-response: Exercise & OA

Risk of Osteoarthritis!

Exercise!
Next steps: 2017-2022

- Football ankle study
- Recreational studies
- Netball study
- Muscle in OA
- Equipoise benefits of sport studies
Thank you & Questions
What exercise minimises the risk of OA in adults?
What exercise minimises the risk of osteoarthritis in adults?

- Discordance between knee joint symptoms & XR
- 33% >60yrs have radiographic knee OA
  - 15-81% have Sx (Systematic review Bedson J 2009)
- UK: 84,000 TKR in 2011
- The evidence:
  - Longitudinal cohorts
  - Cross-sectional data
  - Systematic reviews
# Risk factors Knee OA

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older age</td>
<td>Higher incidence</td>
</tr>
<tr>
<td>Female</td>
<td>Higher incidence</td>
</tr>
<tr>
<td><em>Obesity</em></td>
<td>Higher incidence</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Higher incidence</td>
</tr>
<tr>
<td><em>Sports</em></td>
<td>High impact, torsion, overuse</td>
</tr>
<tr>
<td><em>Trauma</em></td>
<td>Post injury OA</td>
</tr>
<tr>
<td><em>Muscle dysfunction/weak</em></td>
<td>Inactivity, poor training</td>
</tr>
<tr>
<td><em>Proprioception</em></td>
<td>↑ with age, ACLR, comorbidity</td>
</tr>
<tr>
<td>Genetics</td>
<td>Variable expression</td>
</tr>
</tbody>
</table>
Risk factors Knee OA: Obesity

- 62% UK adult population overweight or obese
- £5.1B illness-related obesity cost
- Obesity increases risk of Knee OA x3
- A 5kg wt loss => 50% Knee OA risk reduction
Johnson County OA project

- Association between meeting Physical Activity guidelines & knee outcomes in 1522 adults >45yrs
- Follow-up time 6.5yrs (4.0-10.2)
- Minnesota Leisure Time Physical Activity questionnaire
- Incident knee OA: K-L grade 2 or above
- Meeting HHS Physical Activity guidelines (150mins/wk) was not associated with incident knee OA
- Those with >300mins/wk had non-significant increased risk when compared to those who were inactive: <10mins/wk
Sport and OA

Risk of OA related to elite vs. recreational and likelihood of joint injury (strongest risk factor):

• Recreational/occupational: literature split – no consensus
• Knee OA: occupational disease: miners, farmers...football?
• Running – probably no increased risk except for high milers
• Elite sport: Injury
  • Repetitive, high intensity, loading: jumping/twisting/cutting
  • Football: Prevalence elite 14% hip & 15.5% knee vs. 4% in non elite
  • Positional: ice hockey goalies
What exercise minimises the risk of osteoarthritis in adults?

• Benefits of Exercise:
  • Chronic disease
    • Prevention
    • treatment
  • Weight/Obesity
  • Mental health
  • Certain cancers
  • Society
  • Healthcare cost

• No evidence that exercise in the absence of injury causes OA
What exercise minimises the risk of osteoarthritis in adults?

- Running does not cause OA: does not ‘wear out’ joints
- Interplay between genes and environment
- Strongest risk factors: obesity, family history, female, injury
- Prescription:
  - Meet UK Physical Activity Guidelines: aerobic & strength
  - Cross-train
  - Consider non-impact loading if appropriate
  - Avoid significant acute injury (directional change, collision)
  - Try not to be over-weight (‘Catch 22’)
  - Understand your family history
What is Sport and Exercise Medicine?
The specialty of Sport and Exercise Medicine (SEM) is concerned with the accurate diagnosis, management and prevention of medical conditions and injury in those who participate in physical activity.

*SEM is made up of three elements:*
1. Exercise as a way to improve health
2. Exercise as treatment for illness
3. Treatment of injuries from sport

Within NHS services, SEM consultants deliver two broad provisions, Exercise Medicine and Musculoskeletal services, across primary, secondary and intermediate care.
What exercise is best in managing adults with established OA?
Overview

• Background
• Why prescribe exercise in OA
• Evidence for specific exercise
• Barriers to exercise
• Summary
Background

• Lifetime risk undergoing knee or hip arthroplasty significantly less than risk symptomatic OA (Culliford DJ et al Osteo Cart 2012, Murphy L et al Arthr Rheum 2008, Murphy LB et al Osteo Cart 2010)

• OA associated with an increased mortality SMR 1.55 (1.4-1.7 95% ci) (Nuesch et al BMJ 2011)

• Co-morbidity from OA is great

• OA patients should avoid inactivity (EULAR, OARSI, ACR, NICE)
Exercise and the Primary prevention of disease

- Ischaemic Heart Disease: 40% risk reduction
- Stroke: 27% risk reduction
- Colonic cancer: 25% risk reduction
- Breast cancer: 24% risk reduction
- Type 2 diabetes: 30% risk reduction
- Hypertension: 50% risk reduction
- Dementia: 30% risk reduction (Alzheimer’s)
Background facts

• OA patients have increased pain and a lower level of activity (Moskowitz M J Managed Care RW 2009)

• OA patients have reduced QoL (Bijlsma JW et al Lancet 2011, Rosemann T et al Journ Orthop Surg Res 2007)

• People with OA have reduced muscle strength (Moskowitz RW 2009)
Background facts

• Muscle strength correlates with pain and functional disability  (Jan MH Physical Therapy 2008)

• Higher levels of pain are associated with lower activity and greater functional decline  (Dieppe PA & Lohmander LA 2005, Jordan J et al 1997, van Dijk GM et al 2008)


• High anxiety and fear avoidance beliefs are associated with lower levels of activity  (Scopaz KA 2009)
Cycle of pain and inactivity in OA

- Pain
- Fear avoidance
- Reduced muscle strength
- Functional decline
- Reduced activity
Why prescribe exercise in OA?

• Exercise reduces pain (Fransen M and McConnell S Cochrane review 2009)

• Exercise improves function (Vincent KR PM R 2012 Resistance exercise for knee OA)

• Exercise improves self efficacy and self management (Vincent KR 2012)

• Weight loss, other chronic co-morbidities
NICE guidance 2013

• Core guidelines:

  1) Access to the appropriate information about OA and self-management

  2) Encourage patients to be active and participate in exercise, and

  3) Weight loss if patients are overweight or obese.

Non-pharmacological treatment

• Walking aids and braces
• Local heat and cold therapy
• Shock-absorbing shoes and insoles

Pharmacological treatment

• Paracetamol
• Oral or topical non-steroidal anti-inflammatory drugs (NSAIDs)
• Opioids
• Transcutaneous electrical nerve stimulation (TENS)
• Capsaicin
OARSI Guidelines for the Non-surgical Management of Knee OA

Core Treatments
Appropriate for all individuals
- Land-based exercise
- Weight management
- Strength training
- Water-based exercise
- Self-mgmt and education

Recommended treatments*
Appropriate for the following OA types:

Knee-only OA without co-morbidities
- Biomechanical interventions
- Intra-articular Corticosteroids
- Topical NSAIDs
- Walking Cane
- Oral COX-2 Inhibitors (selective NSAIDs)
- Capsaicin
- Oral Non-selective NSAIDs
- Duloxetine
- Acetaminophen (Paracetamol)

Knee-only OA with co-morbidities
- Biomechanical interventions
- Walking Cane
- Intra-articular Corticosteroids
- Oral Non-selective NSAIDs
- Duloxetine
- Biomechanical Interventions
- Acetaminophen (Paracetamol)

Multi-joint OA without co-morbidities
- Oral COX-2 Inhibitors (selective NSAIDs)
- Intra-articular Corticosteroids
- Oral Non-selective NSAIDs
- Duloxetine
- Biomechanical Interventions
- Acetaminophen (Paracetamol)

Multi-joint OA with co-morbidities
- Pain therapy
- Biomechanical interventions
- Intra-articular Corticosteroids
- Oral COX-2 Inhibitors (selective NSAIDs)
- Duloxetine

*OARSI also recommends referral for consideration of surgical or orthopedic surgery if more conservative treatment modalities are found ineffective.
Hip OA

• Evidence for improvement in pain, not in disability

• All exercise (water and land)
  • Meta-analysis on exercise vs no exercise (Hernandez-Molina G et al 2008)
    • Pain relief -0.38 (-0.68 - 0.08)

• Land vs non-exercise
  • Pain -0.49 (-0.77 - 0.29)
  • Not significant for self reported physical function
Knee OA

• Effect size of aerobic exercise
  • pain  0.52 (95% CI, 0.34 to 0.70)
  • disability  0.46 (95% CI, 0.25 to 0.67)

• Effect size of quads strengthening
  • pain 0.32 (0.23 to 0.42)
  • disability 0.32 (0.23 to 0.41)
  (Roddy et al Ann Rheum Dis 2005)

• Effect size of all exercise on pain and function
  (Fransen M et al Cochrane Database Syst Rev 2009)
  • Pain SMD 0.4 (0.3-0.5)
  • Function SMD 0.37 (0.25-0.49)

• Equivalent to analgesics and NSAIDs
Knee OA

- Exercise decreases pain and improves function in 50-75%

- No difference between strength and aerobic exercise (Bicshoff and Roos Curr Opin Rheum 2003)

- No difference between low and high intensity exercise (Brosseau L Cochrane Database Syst Rev 2003)
Aquatic exercise

- **Aquatic = land exercise** (Batterham et al. BMC Musculoskeletal Disorders 2011)

- Benefits in QoL, mental health and pain

- Small to moderate effect on function for hip and knee OA
  - SMD 0.26 (95% ci 0.11 to 0.42)

- Large effect on pain for hip and knee combined
  - SMD 0.86 (0.25 to 1.47)  
    (Bartels EM et al Cochrane Database Syst Rev 2008)

- Aquatic minor superiority over land for short term pain  (Uthman OA et al BMJ 2013)
Summary of exercise interventions

• Significant evidence for exercise intervention in OA for pain and function: ACR, EULAR, NICE guidance

• Moderate to large effect sizes

• Combination strength, flexibility and aerobic work

• Aquatic and land equally effective

• Include higher intensity

• DoH recommendations to reduce co-morbidity
Barriers and Motivation
Promoting adherence

• Supervised exercise more effective (part or whole) (Jordan JL et al Cochrane Database Syst Rev 2010)

• Supplementary written information (Jordan JL 2010)

• Self Mx program increase adherence (Veenhof C Arthr Rheum 2006)

• Reminders, feedback, support, rewards (van Dulmen 2007)

• Goal setting (Bravata DM et al JAMA 2007)

• Graded progressive activity (Jordan JL 2010)

• Consultant consultations increase adherence to aerobic exercise (Ravaud et al BMJ 2009)
Future research

• Longer term intervention and outcomes
• How to increase adherence?
• Which patients benefit the most?
• Cost effectiveness analyses
• Joints other than the knee
• What is the most effective regimen:
  • Intensity?
  • Duration?
  • Type?
  • Frequency?
Recommendations

- Exercise is central to the self management of OA
- The evidence is indisputable
- Target exercise for improved health not just pain and function in OA
- Combine aerobic, strength, flexibility and balance
- Medical role in removing barriers to participation, including pain control
“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”
References

• *Osteoarthritis: the care and management of osteoarthritis in adults.* NICE guideline; Draft for consultation, August 2013: 1-38.


