The Epidemiology of Musculoskeletal Morbidity in Elite Rugby Union



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Abstract

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Over 7 million participants play rugby union throughout over 120 countries. Despite this global status, very little is known about the longer-term health outcomes of players, or how health and health-related quality of life are influenced by participation in rugby union. The aim of this thesis was to design and undertake an epidemiological study to assess overall health, the presence of morbidity, and development of osteoarthritis within former elite rugby players. In addition to establishing a study, and assessing health and morbidity, secondary aims were to compare the prevalence of morbidity in this population with age-matched representative population-based survey participants, and to examine risk factors associated with the development of osteoarthritis in this population.

A cross-sectional questionnaire study was designed to assess physician-diagnosed morbidity, playing exposure, injury history and current health status. Former rugby players for Oxford and Cambridge Universities, and members of the England Rugby Internationals Club, were invited to participate in this study. Data from the English Longitudinal Study of Ageing (ELSA) and the Health Survey for England (HSE) were used as population-based representative comparator groups.

These four studies examine the feasibility of involving rugby players in sport-related healthcare research, the prevalence of morbidity and health-related quality of life relative to the general population, the prevalence

and risk factors for osteoarthritis-related outcomes, and finally develop a prediction model of end-stage hip failure in this population.

Involving players throughout the research cycle as experts of their own experience was seen to influence the research process and questionnaire development, and ensured this process was grounded in players' beliefs and experiences. In terms of physician-diagnosed morbidity, former players were seen to demonstrate less diabetes than ELSA participants, but more osteoporosis, anxiety, osteoarthritis (OA) and joint replacement.

Risk factors for osteoarthritis-related outcomes were seen to vary between the knee, hip and shoulder, and between the definitions of osteoarthritis used (NHANES pain, physician-diagnosed OA or joint replacement). Joint-specific injury was most highly associated with osteoarthritis across all joints and definitions used.

The prediction model for hip replacement was strong (AUC 0.88), despite the relatively small development dataset, and again emphasised injury, in addition to Slipped Upper Femoral Epiphysis, age, family history, and playing in the second row, as predictive of hip replacement. This was not externally validated, however internal validation was undertaken.

This work has not only established health outcomes in this population, and developed the methodology and survey tools to replicate this work in other cohorts, but also assesses risk factors and strongly predicts poor OA outcome in this population. This work presents potential intervention opportunities for the sport to begin to address the now quantified health deficits; and also presents benefits of elite contact sports participation. These findings should support efforts to ensure healthy participation and adequate proactive management of health at the elite level, for all players.

Manuscripts arising from this work

Davies, M.A.M, Balai, E., Adams, J., Carter, J.H., Judge, A., Newton, J.L., Arden, N.K. The consultation of rugby players in co-developing a player health study: feasibility and consequences of sports participants as research partners. *Res. Involv. Engagem*. 3, 8 (2017).

Davies, M.A.M., Judge, A., Delmestri, A., Kemp, S., Stokes, K.A., Arden, N.K., Newton, J.L. Health amongst former rugby union players: A cross-sectional study of morbidity and health-related quality of life. *Sci Rep.* 1-11 (2017).

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Dedicated

To My Grandparents

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Abbreviations

AC	Acromioclavicular joint
ACL	Anterior Cruciate Ligament
ACR	American College of Rheumatology
AUROC	Area Under the Receiver Operating Curve
BMD	Bone Mineral Density
CI	Confidence Intervals
ELSA	The English Longitudinal Study of Ageing
ERIC	England Rugby Internationals Club
FAI	Femoroacetabular Impingement
GPHOA	Physician-diagnosed Hip Osteoarthritis
GPKOA	Physician-diagnosed Knee Osteoarthritis
GPOA	Physician-diagnosed Osteoarthritis
GPSOA	Physician-diagnosed Shoulder Osteoarthritis
HSE	Health Survey for England
IRR	Incident Rate Ratio
LCL	Lateral Collateral Ligament
MySQL	My Structured Query Language
MCL	Medial Collateral Ligament
MI	Multiple Imputation
MSE	Mean Squared Error
NFL	National Football League (American Football League)
NHANES	National Health and Nutrition Examination Survey
NIHR	National Institute of Health Research

OA	Osteoarthritis
OR	Odds Ratio
PCL	Posterior Cruciate Ligament
PES	Physical Education and Sport
PiiAF	The Public Involvement Impact Assessment Framework
PPI	Public and Patient Involvement
PPIE	Public and Patient Involvement and Engagement
REDCap	Research Electronic Data Capture
RFU	Rugby Football Union
RPA	Rugby Players' Association
RR	Relative Risk
SCD	Sudden Cardiac Death
SE	Standard Error
SES	Socioeconomic Status
SI	Single Imputation
SUFE	Slipped Upper Femoral Epiphysis
SMR	Standardised Morbidity Ratio
THR	Total Hip Replacement
TJR	Total Joint Replacement
TKR	Total Knee Replacement
US	United States

Overview of the Research

This thesis is concerned with examining the health of former elite rugby players, with a particular focus on the development of Osteoarthritis, and understanding risk factors that may predict detrimental health following sports participation, in this unique population. This thesis will focus on quantifying positive or negative general and musculoskeletal health outcomes following participation in rugby union, and examining individual inherent and sport-specific risk factors that are associated with negative musculoskeletal health long term.

In some ways, many concepts addressed in this thesis are by no means novel. Alongside the launch of the British Sport's Council's first campaign in 1972 to increase sports participation, aligned with the increased opportunities for sport and recreation, Bannister discussed the absence of a proven relationship between psychological and physical health, but the potential for sports to add life to years.[3] Almost half a century later, there is a notable increase in evidence supporting sport and exercise as enhancing psychological and physical health and wellbeing. However, this remains sparse particularly with regards to the effects of sport and exercise on health and ageing, and differences between sports and levels of play.

Rugby union ('rugby') is an internationally popular sport, played by over 7 million men, women and children across over 120 countries. Despite being a popular professional team sport with significant amateur and youth participation, there remains a lack of research in the long-term health effects of participation. This thesis will seek to develop a

study that begins to address these deficits in understanding, by using novel methodologies and good practice models of research as encouraged by research governing bodies.

Sports people to-date have had limited involvement in the undertaking of healthcare research aimed at reducing their injuries or improving their performance. The feasibility of involving current players as experts of their own experiences will be explored, in order to inform the research process and structure study design around their priorities and requirements. Physician-diagnosed morbidity represents a societal burden, and also a readily determined assessment of population health. Physician-diagnosed morbidity amongst former players will be compared to participants in population-based surveys using standardised morbidity ratios to determine health status in this population. The effects of health status and functional impairment will also be assessed using a measure of health-related quality of life.

Having determined the prevalence of morbidity, the prevalence of Osteoarthritis, the most common joint disorder in the world,[4] will be established within this population, in addition to risk factors associated with its development, in order to determine if there are modifiable risk factors which may provide an opportunity for intervention. A prediction model of hip replacement will be generated, with a view to producing a translatable risk score to direct clinicians, sports participants and coaches in managing osteoarthritis risk within this population.

Thesis aims and objectives

The aims of this thesis are to draw on the known health benefits and deficits of health related to physical activity and methodological advances in the epidemiology of OA and detection of early, moderate and end-stage OA to establish morbidity, musculoskeletal health and health-related quality of life amongst a newly recruited cohort of elite former rugby players, using a novel questionnaire developed to assess health in this population. The specific aims are as follows:

1. To develop and implement a novel sport-specific questionnaire examining the health status of former rugby union players ('players')

2. To examine morbidity and health-related quality of life amongst former players

3. To examine the self-reported prevalence of Osteoarthritis outcomes in former players

4. To examine risk factors for the development of self-reported Osteoarthritis outcomes in former playing populations.

5. To develop a predictive model for total hip replacement amongst former players.

Chapter 1 An Overview of the Literature

1.1 The relationship between physical activity and health

Physical activity has been defined as 'any bodily movement produced by skeletal muscles that results in energy expenditure beyond resting expenditure.'[5] By contrast, exercise has been defined as 'a subset of physical activity that is planned, structured, repetitive, and purposeful in the sense that improvement or maintenance of physical fitness is the objective.'[5]

1.1.1 Physical activity as a component of good health

Physical activity has been shown to be associated with improved health outcomes, across several states of disease and morbidity,[6–11] which will now be considered in further detail.

Cardiovascular health is positively associated with physical activity, with decreases in high blood pressure seen with an increase in physical activity,[12,13] and a 44% decrease in all-cause, and 52% decrease in cardiovascular-specific mortality seen with increased fitness.[14] Physical activity has been seen to decrease the incidence and progression of type 2 diabetes, with a 46% decrease in the relative risk of diabetes in a physically active cohort over 6 years, compared to a non-active control group.[15] A decreased risk of diabetes has been seen in trials which compare lifestyle interventions (dietary and physical activity) to control groups, demonstrating a 58% decrease in the cumulative

incidence, and 63% decrease in the relative risk of diabetes, respectively, in addition to the normalisation of glucose tolerance with increased physical activity.[16,17]

Occupational and leisure-time physical activity have been reported to be protective against the incidence and relative risk of some cancers, notably breast and colon cancers, with an approximately 30-40% decrease in the risk of colon cancer with physically active employment or biweekly recreational activity, and a 27% decreased risk of breast cancer with over 1000kcal/week energy expenditure, compared with less than 500kcal/week.[18-21] There has been further suggestion that the primary and secondary prevention of endometrial, ovarian, prostate, testicular and lung cancers may be modified with physical activity, although to date this has not been conclusive, whilst remaining reasonably well accepted for breast and colon cancers.[19]

Physical activity is associated with body composition, with more active individuals more likely to have a low body fat mass index [22]. Weight management is critical to a healthy lifestyle, with obesity having a role in the development of osteoarthritis,[23–26] metabolic syndrome,[27,28] diabetes,[29,30] cancer and the global burden of disease.[31] Participation in levels of physical activity has been seen to be the primary successful strategy for long-term weight loss,[32] which may be central to decreasing the global burden of obesity.

Cross-sectional studies have repeatedly shown habitual physical activity to be concomitant with better mental health.[33] Individuals with higher levels of physical activity have been seen to report less depression symptoms, and a decreased likelihood of depression.[34–36] Women with moderate (>7500 steps per day) ambulatory activity, and

men with 12500 steps per day or more, have been shown to have a 50% lower prevalence of depression, compared with their sedentary (<5000 steps per day) counterparts.[34] Exercise interventions in people with panic disorder have been seen to significantly decrease symptoms more than a placebo treatment, and with significantly less side effects than medication use.[37] Individuals participating in regular physical activity (daily and several times per week) have been seen to demonstrate 30% less chance of meeting the criteria for a mental disorder, or suffering from comorbid mental conditions.[38] When followed prospectively, regularly physically active participants (daily and several times per week) were seen to have a 60% lower risk of any incident mental disorder than those with no reported physical activity (less than once per month or no exercise), and a 30% lower risk than those with non-regular physical activity (1-4 times per month) at baseline.[38] The relative risk of specific morbidities amongst active compared with inactive subjects is shown below (Table 1).

Table 1. The relative reduction in morbidity with increased physical activity. Adapted from Warburton et al. (2016)

All cause mortality • 31% risk reduction • 45% risk reduction*
Cardiovascular disease • 33% risk reduction • >50% risk reduction*
Stroke • 31% risk reduction • >60% risk reduction*
Hypertension • 32% risk reduction • >50% risk reduction
Colon cancer • 30% risk reduction
Breast cancer • 20% risk reduction
Type 2 diabetes • 40% risk reduction • >50% risk reduction*
Osteoporosis • Bone adaptations to exercise are load dependant and site specific • Routine physical activity is associated with improved bone health

* Denotes reduction with aerobic fitness)

Physical activity has traditionally been embedded in the education system as physical education, and with the increasing prevalence of obesity in modern society, particularly childhood obesity,[39] embedding healthy physical activity behaviours in youths through physical education and sport (PES) activities may be a cost-effective way of increasing adulthood physical activity.[40] Higher and lower levels of physical activity may be maintained over time, particularly amongst youths,[41] which may support embedding physical activity behaviours amongst youths in order to improve youth and adult health. In addition to physical and lifestyle domains, youth PES participation has also been seen to have significant impact in affective, social and cognitive domains, and it has been

suggested that many less quantifiable but potentially equally important outcomes, such as perception of competency, socially appropriate behaviour, self-esteem and enjoyment are achieved amongst children through PES participation.[42–44]

Within specific chronic morbidities, such as cancer, osteoarthritis, chronic pain, cardiovascular disease and diabetes, physical activity has been implemented successfully for symptom management and improved disease outcome such as decreased mortality.[6,7,10,45–49] Physical activity has also been used as an intervention to improve coping and return to work for individuals in a specific health state, where the aforementioned benefits in cardiovascular health and fitness, cognition, body composition and psychological health may improve outcome. Tailored physical activity has been seen to improve return to work capacity and pain in individuals sick-listed due to chronic pain,[49] and as a coping mechanism in older individuals during smoking cessation,[50] in order to improve coping and longer-term health.

The majority of studies assessing health and physical activity have recruited participants and observed their current physical activity, or intervened in individual's routine practices, to increase their physical activity and observe the effect of this alteration on specific health outcomes. However, in addition to exercise and physical activity, individuals may also participate in organised sport as a form of physical activity, either recreationally or professionally.

Sports participation has been examined as a modifier of health to a lesser extent, and the limited number of studies of health within sports have been directed to potential health

risks associated with sports participation. However, team sports in particular may also be associated with health increments, particularly psychological and affective benefits. Resilience amongst team sports participants has been previously discussed, and shown to be associated with successful sporting performance amongst athletes.[51–55] Whilst also being associated with improved wellbeing and decreased psychological distress,[51] the longer term health implications of this, including the potential for this resilience to have a role in coping with aging and future age-related morbidity, remains unknown.

1.1.2 Physical activity as detrimental to health

Despite the significant evidence for physical activity as a predictor of better health outcome, associated with decreased mortality across a plethora of diseases and morbidities, in addition to increased physical function, musculoskeletal strength and cardiovascular fitness,, there is some evidence of physical activity being detrimental to health.

Risks of participation in physical activity are predominantly associated with cardiac events, such as the risk of myocardial infarction, or sudden cardiac death (SCD), which are transiently increased with participation in physical activity.[56] The relative risk of sudden death for competitive adolescent and young athletes (aged 12-35 years) has been seen to be 2.5 (CI 1.8-3.4), compared with non-athletes, and the relative risk of sudden death by cardiovascular disease for male athletes 2.0 (CI 1.4-2.8), and for female athletes 2.6 (CI 0.8-6.4).[57] This study also found that despite this increased risk in sudden death amongst competitive sports participants, underlying cardiovascular diseases, specifically ventricular arrhythmias, premature coronary artery disease and congenital coronary artery anomaly predisposed these individuals to cardiac arrest.[57] Within the Physician's

Health Study,[58] the risk of sudden death in male physicians aged 40-84 at baseline was significantly elevated in the one hour period following vigorous exertion, however this was seen to be lower amongst those individuals regularly participating in vigorous exertion.[59]

Another risk of participation in physical activity and exercise is that of sport and exercise injuries ('sports injuries'). Injury risk is inherent to any activity, however increased exposure to exercise and sport increases the risk of injury,[60] and injuries occurring within each sport or activity tend to have specific profiles reflecting the physiological demands of that activity. As a competitive subset of physical activity, sport may involve repetitive movement patterns, specialisation and potentially professionalism, and differ from physical activity in relationship with health and healthy participation. Individual sports also involve specific physiological demands and practices, exclusive to that one sport. Therefore, where sport specialisation may occur, an individual has repetitive sport-specific exposure, in terms of movement patterns and physiologic demands, which may produce specific health outcomes not aligned to other sports participation, or sole participation in recreational physical activity.

Sports injuries are acknowledged to be predominantly musculoskeletal in nature, such as strains, sprains and fractures.[61] The potential societal burden of sporting injuries has been subject to academic discussion, both in terms of the number of individuals who may be presenting to healthcare providers, and the financial burden on healthcare systems that sports injuries may represent. Within the United States (US), 15.7% of all injury episodes between 2004-5 were resultant of sport and exercise activities.[62] Sports injuries have been reported to cost one Australian state approximately 37.9million

Australian dollars annually in direct hospital costs, whilst in the US, 12 varsity sports across 100 high schools in North Carolina have been reported to cost an estimated 9.9million US dollars annually in medical care.[63,64] Consideration has been given as to whether these costs are sustainable,[65,66] and also should there be sequelae to these injuries, the potential future costs associated with sports injury and longer term disability.[64] Given the dominance of lower limb injuries within sports,[67–69] and known association of specific joint injuries and osteoarthritis,[70–74] sports participation, notably in conjunction with sports injury, has been considered as a risk factor for the development of osteoarthritis. [75–83]

For individuals participating in sport and exercise at the elite level (highest strata) of play, or professionally (involving financial incentive), there may be other aspects of the sporting environment, its practices and demands that may affect health, but are more in line with occupational hazards than participation in recreational or leisure time physical activity. From the beginning of a players' potential sporting career, they may be encouraged to specialise in a singular sport. Early sports specialisation becomes more prevalent with age during school, and affects specific sports disproportionately.[84–86] Some studies have reported that specialisation affects females more often than males,[85,86] although this has not been conclusive.[84] Early sports specialisation is associated with higher training loads, overuse injuries and serious overuse injuries.[85–87] For athletes who succeed to participate in the elite sporting environment, significant risk acceptance has been observed, particularly around physical and social risks, such as participation despite pain, premature return to sport, unsafe weight management strategies and a rejection of non-sports social life, even as adolescents.[88] In pursuit of success within this environment, athletes may undertake practices that are ill-advised when considering longer-term health outcomes, such as rapid weight loss techniques in order to perform in

weight-restricted sports, participating with non-specific and specific musculoskeletal pain, and training and competing when injured.[89–94] Up to 50% of combat sports athletes have been seen to use rapid weight-loss techniques, including the use of laxatives, diuretics, plastic or rubber suits and heat.[91]

The potential detriments of sporting participation may not be solely physical in nature. Mental health amongst elite athletes and sports participants has been subject to discussion within academic and media fora.[38,95–98] Whereas recreational physical activity may induce the aforementioned positive psychological outcomes of decreased anxiety and depression,[34,99–101] the elite sporting environment and its dependence on sporting successes and associated pressures, combined with potentially harmful practices such as rapid weight loss techniques, may contribute to a psychologically demanding environment.[96,102,103] Although research in this area is not conclusive, more than 46% of elite Australian athletes have reported the symptoms of at least one mental health problem,[103] despite this study having notable methodological and reporting limitations. Female athletes have been seen to suffer from more psychopathologies than males, such as generalised anxiety disorder and non-specific eating disorders, in addition to participants in aesthetic sports compared with other sports.[96]

This higher prevalence of generalised anxiety disorders amongst females may be representative of the female athlete triad, where an eating disorder is seen in combination with amenorrhea and low bone mass.[104] Eating disorders are associated with further health outcomes including osteopenia, anaemia, hypotension, bradycardia and osteoporosis.[105] However anxiety and body dysmorphia are not the sole psychopathologies that may affect athletes. Burnout, competitive failure, transition from

sport and risk-taking behaviours have all been considered amongst athlete populations, and the central roles of team physicians and support staff in managing coordinated care for athletes emphasised.[89,106]

Central risks and benefits of participation in physical activity are summarised below (Figure 1).

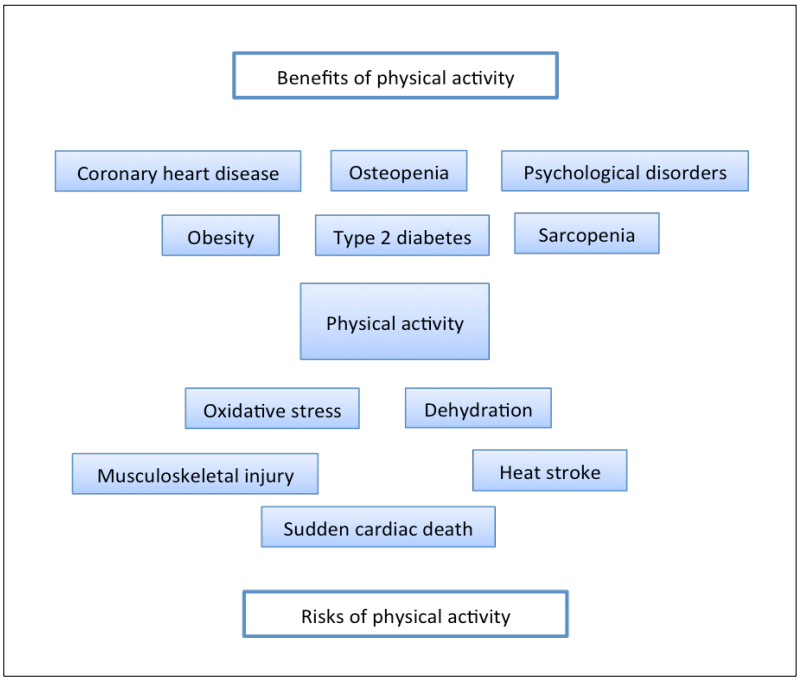


Figure 1. The benefits and risks of physical activity. Adapted from Melzer et al. (2004).

1.2 Contact Sports and Health

Due to the aforementioned central roles of team physicians in managing optimal health and performance amongst their players, and the different demands, injury profiles and effects to health with specific sports participation, individual sports have started to examine the current and longer-term implications of participation for sports players. There may also be statutory and regulatory motivations for governing body engagement

in understanding athlete health. Sports governing bodies are wide-ranging in structure, remit and their interactions with sports participants. Their functions may include revising rules, governing actions and conduct of players, managing sports funding and growth, and monitoring player welfare. Examples include the English Rugby Football Union, and Lawn Tennis Association. Full contact (sports in which participants necessary come into bodily contact with one another) and collision sports (in which the athletes purposely hit or collide with each other or inanimate objects, including the ground)[107] are often at the forefront of longer-term health considerations, due to their higher injury rates.[108] Brief consideration will be given in turn as to what is currently established within longer-term health of specific contact sports.

1.2.1 American Football

Terminology across sports is often not universal. 'Football' in the US is referred to as 'American football' in English, with the English 'football' interpreted as 'soccer' within the US. Within this thesis 'football' will be considered to be association football or soccer. American football is played widely in the US. The injury rate within American football American football is higher than other popular participation sports in American high schools such as baseball, football and basketball, with mean high school injury rates across all sports of 2.44 injuries per 1000 athlete exposures, of which 4.36 injuries per 1000 athlete injuries were attributable to American football.[109]

There has been one major long-term player health study in American football,[110,111] and to date, research within American football has considered health status mostly with regards to head injuries and their potential sequelae,[110] such as depression.[111,112] Previous research has also examined musculoskeletal health and post-traumatic osteoarthritis,[82]

alongside the potential for medication usage associated with worse longer-term health outcomes.[92] Within American football as with many other contact sports, there remains unfounded but reasonably widely-held beliefs surrounding long-term health, such as early cardiovascular mortality amongst participants, and studies have been undertaken with a view to informing these beliefs.[113] However, this approach of specific areas of focus, such as concussion and mental health status, prohibit an overall evaluation of general health and morbidity, and do not determine where participation may be beneficial and detrimental to participants. Overall, research in American football appears to be lacking in sufficient detail of player health in retirement, with notable concentration areas of research or publication, such as elite players' concussion and mental health, despite the significant grassroots and elite participation within the US and globally.

1.2.2 Australian Rules Football

Another popular contact sport is Australian Rules football. Australian Rules is responsible for a substantial number of sports injuries presenting to healthcare providers within Australia.[114,115] The significant number of injuries, and associated economic burden presented by AF participants has encouraged a proactive policy approach to the reduction and prevention of injuries.[116–118] Despite an arguably more proactive approach to player health in AF than American football, with studies exploring muscle imbalance, asymmetry and sleep quantity and quality during training camps, again there has been little research examining the longer-term health outcomes and function of former players.[119] The only former player study amongst Australian Rules league participants, with a mean age of 52 years, of which 8 years were spent in the league, showed that 77% of players had experienced at least one serious injury (hospital admission or surgery), predominantly at the knee, ankle/foot and shoulder.[119] The majority of players (62%)

were seen to have experienced more than 5 serious injuries, and 62% felt affected by their previous injury, with 60% maintaining treatment for a previous injury in their retirement.[119]

1.2.3 Rugby League

Within rugby league, there has been a significant body of research aimed at understanding and preventing injury,[120–129] and pioneering work modelling the relationship between playing load and injury within rugby league[130–132] has encouraged the adoption of more detailed epidemiological analyses of sports injuries across all sports. Despite an increased consideration for the prevalence of and risk factors for injury, again there is substantially less research that has explored longer-term health, and more holistic, person-focused outcomes. The seminal paper examining long-term health in rugby league was a preliminary investigation assessing whether there were effects of rugby league injuries in later life, amongst 28 former players.[133] This study suggested that players may suffer post-injury effects on their employment, loss of earnings and medical costs, however this study had methodological constraints such as a low sample size of elite players within one league, which may not be generalisable to other populations, and also confers causality, from a cross-sectional questionnaire study examining self-reported player injuries and self-reported occupational prospects.[133]

1.2.4 Rugby Union

Current knowledge within rugby union is more similar to rugby league than other contact sports, in that there is a relatively comprehensive, published understanding of rugby injury and its risk factors and development.[69,134–146] Rugby union may have the most detailed understanding of longer-term health outcomes compared with other

contact sports, due to the plethora of relatively recent studies examining transition from sport, joint-specific degeneration at the spine, long-term health post-concussion and health outcomes after injury.[147–151]

As the contact sport with the highest global participation, at both the elite and recreational levels, rugby union will now be considered in more detail. Where participation in rugby is seen to be associated with better health outcomes, this can be encouraged as a public health intervention to improve health. However, where rugby is associated with worse health outcomes, this needs to be considered in further detail, both for the quantification of the potential burden, and implications of this, in terms of direct or indirect societal costs.

1.3 Rugby Union

1.3.1 The Sport and its History

Rugby Union ('rugby') was established at Rugby School (England), in 1823 and has gained global popularity. The sport is played by men, women and children, and is currently one of the fastest growing female team sports globally.[152] There are many forms of rugby, with fewer players than the original fifteen-a-side version of the game; and also non-contact 'touch' and 'tag' versions of the game. Amateur players account for the majority of participants, with differing motivations of participation compared with elite professional players.

Rugby is played in schools, with rules adjusted for different age groups. For senior male participants, in addition to the professional English Premiership of the top 12 teams in England, there are professional Premiership feeder ('A') teams, and then the professional and semi-professional Championship and National Leagues 1, 2 and 3. There is also an amateur structure of regional teams and competitions for the 15-a-side version of the game, following a league organization. The playing positions within rugby union are shown below (Figure 2).

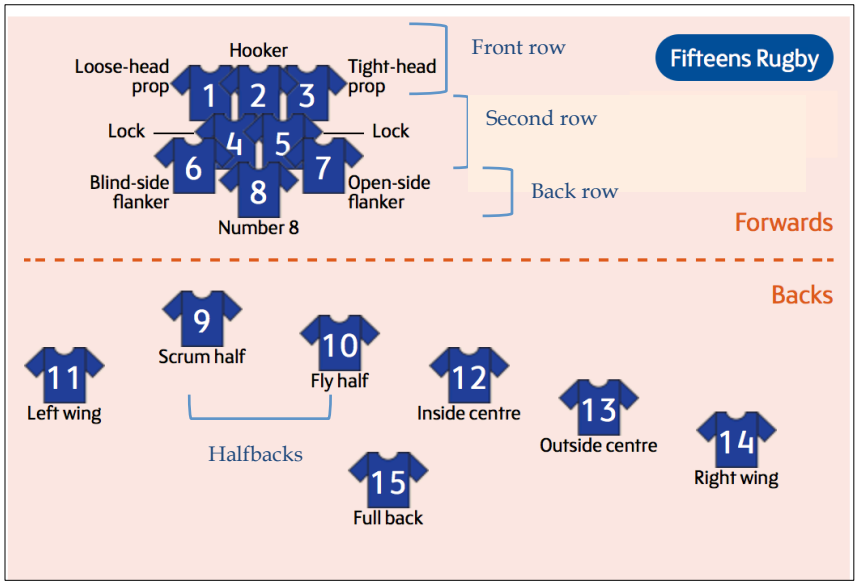


Figure 2. The names of rugby playing positions most commonly used globally. Adapted from World Rugby (2017)[153]

The structure of women's rugby is similar to men's, with a Premiership, which often features clubs parallel to those within the men's Premiership. The women's game has experienced substantial growth in the last ten years. Following England winning the Rugby World Cup in 2014, professional contracts have recently been introduced for those participating at elite level.[154] England representative squads for both sexes are

drawn from the highest performing players in the country, generally from Premiership players. There are also 'touring squads' currently predominantly for male participants, such as the Barbarians and British Lions, which arguably train and perform at the highest level of British rugby.

The culture and identity of rugby has been previously discussed in players' biographies and academic publications.[147,155–162] The sport demonstrates a strong sense of history, both in a geographical sense and familial, with players historically joining and supporting their local Club, who two or three previous generations of their family may also have played for.[163] Rugby maintaining its amateur status beyond many other sports, until 1995, contributed to a key development in the sport, the division between rugby union and rugby league in 1895. This movement not only involved rule changes and created two different styles of rugby, but also confirmed rugby union's traditionalist values, preventing the sport's commercialisation. This movement to maintain its amateur status also introduces a participation bias, whereby individuals participating and competing in the sport were not only those capable of maintaining leisure time pursuits alongside their employment, but also those with sufficient resource to risk injury by playing a collision sport, and maintain possible time lost from employment due to injury.

A summary of key developments within rugby and its division from rugby league is shown below (Table 2).

Table 2. Development of key rugby laws and changes. Updated and adapted from Brooks et al. (2008)[142]

Year	Rule change/event
1823	Rugby conceived by William Webb Ellis during a football game at Rugby School, England.
1871	Formation of the Rugby Football Union (England) and publication of the sport's laws
1877	Number of players reduced from 20 to 15
1886	World Rugby formed (formerly International Rugby Football Board and IRB)
1893	Number of points for a try becomes 3 (previously 0, 1 and 2)
1895	Separation of rugby union (amateur) and rugby league (professional)
1982	Introduction of 1m gap between teams at the lineout
1992/3	A try becomes worth 5 points The referee takes control of the scrummage ("Crouch-pause-engage") Replacement of up to 4 players for injuries The back row must remain 'bound' until the ball is out of a scrummage
1994	Tackle law changes; the tackling player must roll away and supporting players to remain on their feet
1995	Rugby becomes 'open', permitting payment and benefits
1996	Lineout supporting permitted
1997	Non-injury replacements allowed
2000	Red and yellow cards introduced for misconduct
2007	Scrum engagement sequence changed to "Crouch-touch-pause-engage"
2007	Former IRB Council approves ruling where tackles lifting a player from the ground and tipping them horizontally constitute illegal and dangerous play
2010	Amendment to World Rugby Law 10.4, further clarification of 2007 lifting tackle law
2011	Tackle laws revised penalising dangerous (high) tackles and stiff-arm tackles
2013	Further revision to scrum engagement sequence: "Crouch-bind-set"
2016	Further revision to sanctions within tackle laws, punishing reckless and accidental tackles, in addition to alterations at the breakdown and maul.
2016/7	Global trials of laws affecting uncontested scrums, penalty tries and touch and line out laws in order to increase ball-in-play time, simplify laws and avoid negative play

Law changes and enforcement within the sport, particularly those in recent decades, have been driven by motivations of player safety, the management and regulation of player behaviour, and to increase spectatorship.

1.3.2 Injury in amateur and professional rugby union

For many years prior to the professionalization of rugby union, there has been a move to better understand injury within rugby union, mostly from physicians treating rugby injuries.[138,158,163–169] This clinician-driven early injury epidemiology was initially analysis of documentation of injuries within a specific club or ground,[163,169,170] or those presenting to healthcare providers as having been attributable to rugby.[141,165,166]

Whilst not necessarily informing play, rule changes or generating guidelines, these early studies allowed recognition and identification of sports injuries with distinct pathology occurring within the sport, in addition to the identification of possible patterns of injury across the sport. These studies also provide initial comparisons between rugby injuries in different clubs, in terms of differing injury rates between different levels of play and position of play.[163,165,171]

Two early descriptive papers exploring injury within the amateur game in England in the 1970s examined all injuries resulting in time loss over 4 seasons at one ground[163] and injury incidence for rugby and football clubs in four northern counties across one season.[164] These two early studies, and a subsequent review,[171] exhibit a key methodological problem in injury surveillance. Whereas Weightman et al. (1974) uses a medical attention definition of players who stated that they were injured and sought medical treatment for this; Durkin (1977) defines injuries as time loss events which

resulted in a player being unfit for selection for the two following weeks. This may result in variation in incidence, limit the capacity for direct comparisons between populations and also lead to different aspects of injury being measured.

Durkin (1977) found injury incidence to be higher amongst backs (54.5% of all injuries) than forwards (45.5%). This finding contradicts many other papers since, which have discussed a disproportionate number of injuries among forwards compared with backs[172,173] or no difference between forwards and backs.[135,174,175] The injury definition used by Durkin (1977) encompasses two concepts that are now recognized as more distinct, injury incidence and severity. Being unfit for selection for two weeks following an injury, and requiring three weeks away from match play, may be considered a moderate or major injury.[135,174,176] The definition of injury used by Durkin (1977) therefore only captures the most severe injuries. Thus, we see the use of different case definitions for injury resulting in variations of injury incidence according to severity.

More recently, there have been methodological advances in injury epidemiology, and consensus reached surrounding the recording of incidents, in rugby and other sports.[176–178] Injury epidemiology has been described as being unique, in that an injury event is defined not only by its causative event, but also its resulting pathology.[179] An injury may not be recorded without an element of resulting pathology, such as a functional limitation resulting in time loss. For example, a blood replacement due to a laceration is now not always deemed an injurious event in rugby surveillance, as many are treated pitch side or in a temporary removal from play, and thus will not affect a player in terms of them being unavailable for selection or missing subsequent match play. Recent

surveillance programs examine the injury mechanism, location, incidence and severity, and may also derive injury risk as a product of incidence and severity.[135,180,181]

The injury risk within a full-contact collision sport such as rugby has been shown to be higher than many other sports, both at an amateur and professional level.[182,183] The injury incidence at an elite level for the top 3 participation sports in England[184] is shown below (Table 3). This table shows a relatively similar incidence of injury, despite significant difference in the definition of injury used between these studies, from medical-attention injuries, to timeloss injuries and pain (Table 3).

Table 3. Injury incidence and respective definition across popular British participation sports.

Sport	Injury Incidence	Population	Injury definition
Swimming[185]	3.04/1000 hours	34 NCAA competitive swimmers	Diagnosed by trainer or team physician: resultant of participation, required restrictions on participation or performance or medical attention.
Athletics[186]	3.57/1000 hours	292 adult and youth elite athletes	Any new musculoskeletal pain, soreness or injury resulting from training or competition which caused changes in normal training/competition to the mode, duration, intensity or frequency from current or subsequent training and/or competition.
Football[187]	8.0/1000 hours	23 European first team squads	Injury resulting from playing football and leading to a player being unable to fully participate in future training or match play (i.e. timeloss injury).

The injury incidence in rugby has been described as 81 injuries per 1000 player hours at a senior men's professional level[108] and 16.9 injuries per 1000 player hours overall at a

community level, although this varied between levels of play.[135] Despite being higher than many other participation sports played in this country, this incidence is more comparable to other full contact team sports globally (Table 4).

Table 4. Injury incidence in globally popular contact sports.

Sport	Injury Incidence	Population
Ice Hockey[188]	49.4/1000 game hours	National Hockey League players
American Football [189]	510/1000 game hours	High School football players
Australian Rules Football[190]	25.7/1000 match hours	Australian Football League players

The development of consensus statements and advances in specific injury quantification and reporting have encouraged more comparable methodologies, and with the professional era of rugby union, enabled the establishment of rigorous injury surveillance projects at the recreational and elite levels of the game over recent decades.[69,191–193] These projects have provided a platform for further study of modelling injury and injury risk, and more mechanistic understanding of risk factors for injury.[69,194–197] The prospective surveillance projects within elite rugby union have shown the most common (Table 4) and highest risk (Table 5) injuries within the English Premiership.[69]

The most common match injuries have been almost all lower limb injuries over the past four seasons (Table 5), notwithstanding concussion and more recently acromioclavicular (AC) joint injuries.[69] Hamstring muscle injuries, thigh haematoma and medial collateral ligament (MCL) injuries have been three of the five most frequently reported injuries consistently every season for the past four seasons, although there has been a general

trend towards a lower incidence of these injuries in most recent years in comparison with the 2011-12 season.[69]

There are difficulties in quantifying and reporting concussion that affect other injuries to a lesser extent. As a closed injury that is diagnosed with predominantly symptomatic reporting, if an individual is not overtly demonstrating severe concussive symptoms, either through unconsciousness, motor coordination or disorientation, the role of reporting for mild concussive symptoms will fall to the players themselves. Over recent years, concussion awareness within sport, notably rugby, has significantly increased,[69] with players now mandated to undertake concussion awareness programmes at the elite strata of the game. The increased incidence of concussive injuries over recent seasons may well be a product of this increased awareness and management, as players become more aware of these injuries, and the management by team physicians is more conservative, increasing the number of days' absence following concussion, and therefore the risk (product of severity) of those injuries.

Table 5. Incidence of most common match injuries in the English Premiership from 2011-15. Adapted from Cross et al. (2016).

Season	Injury type	Incidence (injuries per 1000 hours)
2011-12	Concussion	5.1
	Hamstring muscle	5.0
	Thigh haematoma	4.9
	Calf muscle	4.8
	Medial collateral ligament (MCL)	4.0
2012-13	Concussion	6.7
	Hamstring muscle	4.9
	Ankle syndesmosis	3.8
	MCL	3.6
	Thigh haematoma	3.3
2013-14	Concussion	10.5
	Thigh haematoma	4.2
	MCL	3.7
	Ankle lateral ligament	2.9
	Hamstring muscle	2.5
2014-15	Concussion	13.4
	Hamstring muscle	4.4
	Thigh haematoma	3.4
	MCL	3.3
	AC joint	2.9

The risk of rugby injury has been derived in recent reports as a product of injury incidence and severity (days absence).[69] As with injury incidence, the majority of highest risk injuries are seen to be lower limb injuries (Table 6), notably Anterior Cruciate Ligament (ACL) and MCL injuries. In more recent seasons concussion is increasing in risk, which may further emphasise the increased awareness and conservative management of head injury.

Table 6. Highest risk match injuries in the English Premiership from 2011-15. Adapted from Cross et al. (2016).

Season	Injury type	Risk (injuries per 1000 hours)
2011-12	ACL	186
	MCL	148
	Hamstring muscle	119
	Shoulder dislocation	108
	PCL/LCL	92
2012-13	Ankle syndesmosis	145
	MCL	141
	Hamstring muscle	130
	ACL	108
	Clavicle fracture	95
2013-14	MCL	130
	ACL	116
	Concussion	105
	Hamstring muscle	104
	Ankle syndesmosis	96
2014-15	ACL	240
	Concussion	189
	Hamstring muscle	153
	Ankle syndesmosis	142
	MCL	139

Many surveillance studies have concluded that elite players will receive at least one injury throughout the course of a season.[173,174,198] In terms of a player's risk of injury, injury incidence has been reported as similar between forwards and backs,[108] however the phase of play may be be associated with different injury profiles. The most common injuries for ball carriers are lower limb injuries such as ankle syndesmosis, quadriceps haematoma and MCL injuries, whereas tacklers have most commonly reported quadriceps haematoma, cervical stinger/burner injuries and brachial plexus stinger/burner injuries (athletically induced peripheral nerve injuries).[199] Concussion however remained the most common injury for both ball carriers and tacklers.[69]

Recurrent injuries currently account for approximately 3 injuries per 1000 hours within English professional rugby, which has decreased from an average of 8.7 injuries per 1000 hours in earlier seasons.[69] It has been suggested that this decrease may be a product of enhanced rehabilitation practices, and decreases in the severity of match injuries.[69]

Risk factors for injury have historically been explored within specific adult or youth, recreational or elite, and male or female participants.[200–208] In women's rugby, comparatively little is known about injury. Prevalence studies have not reached consensus, possibly impeded by the historically lower popularity of the sport. Injury rates of 7.1 injuries per 1000 hours within one Canadian team over a season, 37.5 injuries per 1000 hours in the 2006 World Cup, 35 injuries per 1000 hours in the 2010 World Cup, and 187 injuries per 1000 hours in the Sevens World Cup, have previously been reported.[200,201,209,210]

Within site-specific injury studies, hamstring injuries have been seen to have an incidence of 5.6 per 1000 player match hours, in the professional game. Within this study, front row forwards were seen to have the less frequent and less severe hamstring injuries, with most injuries occurring when running, and kicking injuries being the most severe type of hamstring injury.[211] Lateral ankle ligament injuries have been are the most common match injuries, alongside Achilles tendon injuries. The incidence for ankle injury was highest in the second row, and many injuries were seen to be recurrent injuries.[207] Foot injuries within rugby union have been previously described as a small but important proportion of injuries.[140] Acute injury events accounted for 73% of foot injuries, however 25% were chronic, including stress fractures, which accounted for 8% of total foot injuries.[212]

Previous research has established the injury risk associated with specific phases of play. Contact events have been seen to be the highest cause of injury within rugby,[191] with being tackled and tackling contributing to the highest injury incidence within community and elite rugby.[69,191] The scrum has historically been a focus of injury research, due to the severity of scrum injuries, notably at the spine and in the front row.[213] Whilst only accounting for 11% of injuries to forwards, the propensity for injury within scrums is higher than for any other contact event.[181,214] As a result of this, the risk factors for injury within the scrum have been isolated, such as a mismatch in experience between teams, scrum collapse and playing position, such as playing at hooker.[196,215–217] Interventions have been designed to measure force within the scrum,[218] with modifications trialled to decrease the forces players are exposed to within the scrum,[219] and then implemented and their effects evaluated.[69,220–222]

More recently, reducing the number of injuries during tackling has become a principal subject of much debate, particularly in schoolboy rugby.[223–226] Risk factors for injury in the tackle have been previously described as high speed into the tackle, high impact force, contact with the head or neck, tackles from a player's peripheral vision, differential speed tackles, and high and mid tackles from the front.[227–229] Differences in the risk for the tackler and ball carrier have been reported, with ball carriers more at risk from higher tackles to the head or neck, whereas tacklers are more at risk from low tackles.[229] Again recent tackling laws have been revised in light of this.[230]

The most prominent current focus within rugby injury management and prevention, and across other sports injury research more generally, is the consideration of acute and chronic training and playing loads (measures of stress such as heart rate, lactate, session rate of perceived exertion, or sports exposure such as minutes of match exposure or

incidences of common phases of play) as a predictor of injury. In many respects this is not a novel concern, with Quarrie et al. having established in 2001 that players exposed to higher levels of strenuous activity (>39hrs/week) missed a greater proportion of the season than those exposed to lower levels (<5hrs/week) of physical activity (RR 3.71, 95% CI 1.58-8.72).[204] However, this has now been expanded to include support for in-season training load as a risk factor for injury, with 2 standard deviation (SD) changes in training load associated with increased odds of injury for both one-week training load (OR 1.68, 95% CI 1.05-2.68) and week-to-week training load (OR 1.58, 95% CI 0.98-2.54).[195]

Another key area of focus of injury prevention research has been better understanding injury recurrence. Players injured in the season prior have been seen to have a non-significantly increased risk of injury incidence during the following season (RR 1.57, 95% CI 0.88-2.80), when compared to those not reporting injury in the 12months prior. However, individuals injured at preseason have demonstrated over twice the risk of injury (RR 2.41, 95% CI 1.34-4.32).[204] A similar finding was seen for injury severity, whereby those injured at preseason demonstrated over twice the proportion of the season missed (RR 2.25, 95% CI 0.99-5.11), when compared with non-injured individuals.[204] A meta-analysis of injury within elite rugby demonstrated a higher average severity (30 days, 95% CI 26-35) of recurrent injuries than for new injuries (20 days, 95% CI 15-24),[108] however this study also discusses that no studies have directly compared the severity of recurrent injuries to that of index injuries, and that therefore it may be more severe injuries that are becoming recurrent. Further research is currently expanding knowledge on the classification of recurrent injuries, and exploring the risk factors for the increased incidence of subsequent injury after an initial injury,[109,231–235] including the potential for risk-taking behaviours, incomplete recovery and altered

biomechanics to contribute to this increased risk.[236–238]

Despite these advances in understanding and methodology, and the apparent willingness of law makers and governing bodies within the sport to adapt the sport as a result of research findings, little attention has been giving to longer term health, other than brief indications that the injury burden may contribute to pain, osteoarthritis and affect employment in later life.[142,150] The accumulative effects of injury within rugby, number of injuries sustained throughout a player's career at the amateur or elite level and the long-term health outcomes following many of these prominent injuries either in isolation or in combination, remains unknown.

1.4 Osteoarthritis and Degeneration

Osteoarthritis is the most common joint disorder globally, with radiographic osteoarthritis (OA) being seen to affect the majority of people aged 65 years of age and older, and approximately 80% of those aged 75 and over.[239] There are several definitions of OA, from clinical OA in accordance with recognised diagnostic criteria, to symptomatic OA presenting as pain at the joint, or radiographic OA. Radiographic OA involves the presence of changes in joint structure consistent with OA, such as joint space narrowing, and the presence of osteophytes and subchondral sclerosis or cysts.[240–244]

A complexity delaying progression within the field of OA research has been the discordance between symptomatic and radiographic OA,[241,245,246] which has confused whether individuals have the disease or illness of osteoarthritis.[247] Another complexity of the discordance between radiographic disease and symptomatic disease is that

symptomatic individuals, particularly those presenting to healthcare providers, often exhibit end-stage disease.[241] Whilst pain is a valid patient-reported outcome, difficulties surrounding the use of pain as an outcome measure for research have been previously demonstrated. An example of this is with drug trials of Tanezumab and Fulranumab, where less pain was seen during treatment with these medications, however some patients demonstrated a rapidly progressing joint failure, which was considered to be a result of increased loading under analgesia.[248,249]

The burden of OA is substantial, in terms of both pain for the individual,[250,251] and societal direct and indirect resource consumption[242,252,253], which has been seen to result in a socioeconomic burden of between 1.0% and 2.5% of gross domestic product in developed countries.[254] Whilst reasonably successful treatment for end-stage OA has been developed, with knee replacement associated with rapid and substantial improvement in pain, functional status and health-related quality of life in approximately 90% of patients,[255] and approximately 90% patient satisfaction seen after hip arthroplasty [256,257], this intervention is for end-stage OA, leaving individuals with prolonged pain and potential functional deficits prior to surgery. There is also a limited lifespan to implants, with the 10 and 20 year survival rates 95.6% and 85.0% for the hip, and 96.1% and 89.7% for the knee.[258]

The current working definition of OA developed by the Osteoarthritis Research Society International (OARSI) is:

> A disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates

> maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodelling, osteophyte formation, joint inflammation and loss of normal joint function) that can culminate in illness.[259]

A lay version of this definition has also been produced.[260]

Historically the focus of OA research and treatment has been on cartilage, and delaying or preventing cartilage los however more recently there has been a broader focus of the disease,[261] as a whole joint approach involving cartilage, synovium and subchondral bone.[241] An attempted repair process in OA has also been recognised, where following a primary insult or damage,[240] which may be mechanical stress or abnormality,[261] there is a process of repair at the joint level, which then may or may not contribute to the initiation of OA.[240]

The concept of different OA phenotypes is becoming increasingly recognised with the understanding of the interplay of biomechanics, morphology, innate and environmental risk factors, and genetic components, in explaining some degree of the between-person variation in the incidence and progression of OA. [241,245]

1.4.1 The Classification of Osteoarthritis

OA may affect a single joint, or demonstrate multiple joint involvement.[74] Each affected joint has individual but potentially overlapping risk factors, with differing odds of

incident and progressive disease by joint. The hip and knee are most often studied, due to their similarities as weight bearing joints of the lower limb, higher prevalence of OA, and intervention and treatment potential. Multiple joint involvement has been termed 'generalised' or 'polyarticular OA', and there are stronger associations between the development of OA within some joints then others, with hand OA often involved in polyarticular OA, notably with the knee.[262] Generalised OA has also been considered as potentially a more evolutionary phenotype of OA.[263]

Osteoarthritis may be classified in several ways. Historically, classifications have included primary (idiopathic) and secondary OA, secondary to a specific disorder (Table 7). Primary and secondary classification is becoming less frequently used, and its rationale questioned as the identification of disease phenotypes is established,[264] and with the realisation that individuals presenting with secondary OA may also have additional inherent risk factors and a susceptibility for this.[240]

Table 7. Classification of osteoarthritis. Adapted from Arden and Nevitt (2006).[240]

Classification by joint(s) involved	
Monoarticular, oligoarticular or polyarticular (generalised)	
Chief joint site (index joint site) and localisation within the joint	
	Hip (superior pole, medial pole or concentric)
	Knee (medial, lateral or patellofemoral compartments)
	Hand (interphalangeal joints and/or thumb base)
	Spine (apophyseal joints or intervertebral disc disease)
	Others
Classification into primary and secondary forms of OA	
Primary = idiopathic	
Secondary indicates that a likely cause can be identified; causes of secondary OA:	
1.	Metabolic – examples include:
	Ochronosis
	Acromegaly
	Haemochromatosis
	Calcium crystal deposition
2.	Anatomic – examples include:
	Slipped femoral epiphysis
	Epiphyseal dysplasias
	Blount's disease
	Legge-Perthe disease
	Congential dislocation of the hip
	Leg length inequality
	Hypermobility syndromes
3.	Traumatic – examples include:
	Major joint trauma
	Fracture through a joint or osteonecrosis
	Joint surgery (e.g. meniscectomy)
	Chronic injury (occupational or arthropathies)
4.	Inflammatory – examples include:
	Any inflammatory arthropathy
	Septic arthritis
Classification by the presence of specific features:	
Inflammatory OA	
Erosive OA	
Atrophic or destructive OA	
OA with chondrocalcinosis	
Others	

OA may affect any joint, but the most common sites are: the knee, hip, hand, facet joints and feet.[242]

1.4.2 Risk factors for the development of Osteoarthritis

Age is associated with incident OA, at the knee, hip and hand.[242] Sex is also associated with the development of OA, with females being at a higher risk than males.[240,242] The development of OA is acknowledged to be a complex interplay of environmental and inherent risk factors, which are summarised below (Figure 3).

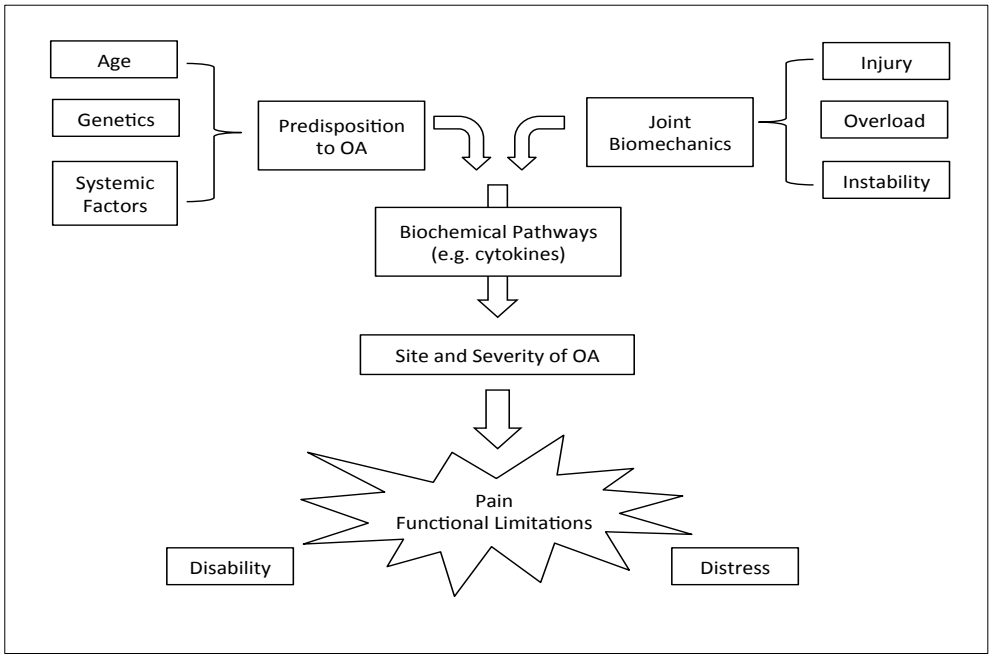


Figure 3. Osteoarthritis initiation and progression through the interaction of endogenous and environmental risk factors. Adapted from Lohmander et al. (2007). [321]

Different risk factors have differing effect sizes for the development and progression of OA, which also vary by joint. The effect size for key risk factors for OA at the most prevalent sites of the knee, hand, and hip[265] are shown below (Table 8).

Table 8. Risk factors for osteoarthritis at the knee, hand and hip.

Risk factor	Knee (OR, 95% CI)	Hand (OR, 95% CI)	Hip (OR, 95% CI)
Age	1.8 (1.4 to 2.3) / year [266]	Association with age [267,268]	Highly associated. Age 55-59, RR 2.9 (1.8 to 4.5), age 60-64, RR 5.6 (3.6 to 8.7), age 65-69, RR 9.1 (5.9 to 14.0), age>70, RR 8.7 (5.4 to 13.9)[269+]
Obesity	2.63 (2.28 to 3.05) [270]	2.59 (1.32 to 5.96) [271]	1.7 (1.3 to 2.4) [74]
Sex	1.84 (1.32-2.55) [270]	Significant difference in 10 year incidence: 5.6% (women) and 2.5% (men) [272]	Reduced incidence in males IRR 0.64 (0.48 to 0.86) [273]
Injury/Trauma	3.86 (2.61 to 5.70) [270]	0.93 (not specified) [274]	4.3 (2.2 to 8.4) [74]
Bone Mineral Density	1.0, 2.5, 2.0 and 2.3 for incident OA per quartile increase in BMD [275]	+5.8% (3.0% to 8.6%)* [276]	Increased in individuals with hip OA [277,278]
Race	Variation in pain and radiographic OA [279–281]	Higher lifetime risk amongst whites than African-Americans (p=0.031)[282], population prevalence lower in China than seen in US and UK Caucasians [283]	Little difference in lifetime risk or prevalence [284,285], however radiographic differences in compartment [284], in addition to differences in pain and disability [279]
Occupation	1.61 (1.45 to 1.78) [286] There is sufficient evidence that work associated with kneeling and squatting is causally associated with knee OA [287]	Heavy occupational load considered to be associated with hand OA [288,289]. Cleaners (OR 6.2, 95% CI 4.6 to 8.0), workers in the clothing industry (OR 5.0, 95% CI 3.9 to 6.3) and construction workers (OR 2.9, 95% CI 2.6 to 3.3) may be most at-risk [290]	Likelihood of male farmers receiving THR due to OA: 3.6 (2.1 to 6.2)[291] Increased risk of hip OA in male farmers after 1-5 years in occupation (HR, 1.63) and dose-response risk of hip OA (HR up to 4.22) [292] In male farmers with over 10 years farming (9.3, 1.9 to 44.5) [293]
Sports participation	1.17 to 3.57 [77]	Sporting and physical activity have previously been reported as not associated with hand OA [294], although there is a lack of research in this area.	0.9 to 1.6[74]

***Percentage difference in mean bone mineral density (BMD) with radiographic hand OA compared to controls**

+ Relative risk of hip replacement in female nurses

There is a notable lack of research surrounding the risk for the development of hand OA. Radiographic hand OA is significantly more prevalent than symptomatic hand OA, and despite the comparative scarcity of research at the hand compared with the knee and hip, the hand may be the joint with the most advanced understanding specific OA phenotypes.[295]

1.4.3 Defining Osteoarthritis for research

Several cohort studies have produced the most reliable population estimates of the disease to date, however differences in definitions of OA may prevent the validity of comparisons between studies and countries. As aforementioned, OA may be defined clinically, radiographically or subjectively.[242] Despite radiographic criteria (joint space width, presence of osteophytes and subchondral cysts) such as the Kellgren and Lawrence scoring system and American College of Rheumatology (ACR) criteria for the hip, knee and hand being well-established,[243,244,296,297] their historical use is largely by clinicians to distinguish OA from other joint diseases, [298] and they may be of decreased relevance for research. There has been a notable move towards sensitive, specific and responsive outcome measure for trials and studies of OA, that will begin to determine pre-radiographic and molecular stage changes.[247] Radiographic measurement and definition of OA may not be suitable for this purpose because of the established nature of structural damage when observed radiographically, and the length of time to structural change on radiograph.[241,259] The poor correlation between radiographic and symptomatic OA also reduces its patient relevance.[299]

Pain may be the most clinically meaningful measure of OA, due to the concomitant disability and substantial societal economic burden represented by OA pain.[300] Pain has been defined as:

> "An unpleasant sensory and emotional experience associated with the actual or potential tissue damage, or described in terms of such damage."[301]

Pain is acknowledged to be a complex interplay of cultural, societal, biological and psychological factors.[302] Efforts have been made to better understand OA pain, and two distinct pain profiles have been identified by an Osteoarthritis Research Society focus group initiative:[251] a dull aching pain, becoming more consistent over time, and shorter episodes of intense, unpredictable pain.[251] Despite the validity of pain as a patient-focused and societally relevant outcome, the reliable capture of such a subjective measure, and the opportunity for reporting inconsistencies according to recall period and pain fluctuations have been previously described.[300,303]

NHANES pain is an outcome frequently used in epidemiological studies. The NHANES question originated in the National Health and Nutrition Examination Survey (NHANES) in the US, which started in the 1960s, and quantified knee pain as the subject's report of having had pain in either knee for a period of at least one month.[304] A similar pain assessment to NHANES pain (the number of days of pain during the previous 30 days) has also been featured in the ACR criteria for classifying knee OA.[296] This estimate of symptomatic OA may be combined with radiographic assessment, such as the Kellgren and Lawrence scoring system,[304] however symptomatic OA defined as

standalone pain is becoming increasingly accepted as an outcome measure for OA, despite concerns around the potential for misclassification of patients.[305]

Internationally, variations of the NHANES pain question have been used across various large-scale cohort studies, with variations to the timescale of the recall period, and also in the duration of pain. Recent research has established differences in prevalence of knee pain from between 41.0% and 75.4% with variations from "knee pain lasting most days in the last month", "any knee pain in the last month", "knee pain lasting at least a month in the last year" and "any knee pain in the last year."[306] Despite previous studies having suggested that pain on most days of the last month may be too specific[307] or not have adequate diagnostic performance in comparison with clinical symptomatic knee OA,[305] this remains one of the most common measures of OA-related pain internationally in population-based cohort studies.[306]

Physician-diagnosed OA is also often used as an outcome measure within OA studies, which has been seen to demonstrate good sensitivity (0.73, 95% CI 0.86-0.95), specificity (0.96, 95% CI 0.92-0.99), and positive and negative predictive values (0.86, 95% 0.74-0.95 and 0.91, 0.86-0.95), respectively for modified ACR criteria at the knee.[308] At the hip, physician-diagnosed OA was seen to have good sensitivity (0.81, 95% CI 0.64-0.97), specificity (0.94, 95% CI 0.91-0.97) and reasonable positive predictive value (0.61, 95% CI 0.52-0.70), and stronger negative predictive value (0.98, 95% CI 0.97-0.99),[308] compared with ACR criteria for hip OA.[297]

Joint replacement may represent a reliable end-point for research, as it is reliably recorded in patient notes, reflective of end-stage OA, and will have limited susceptibility to recall bias. However, as joint replacement is reflective of end-stage disease, it is not a measure of the overall burden of the disease in its entirety, as many people with OA may not progress to surgery, and particularly for studies seeking to alter disease progression, end-stage OA may not be an appropriate outcome measure.[241] However, joint replacement is a valid measurement of self-reported OA, with all hip and knee replacements reported in an online questionnaire validated by clinical assessment.[308] Time to joint replacement, and being a candidate for joint replacement have also been considered as potential outcome measures, however studies have called for further validation work on these outcome measures, particularly with a view to their capacity to detect activity of disease-modifying osteoarthritis drugs.[309–311]

These OA-outcomes encompass different stages and severity of OA, from possible intermittent symptomatic and undiagnosed OA, physician-diagnosed OA that is sufficiently debilitating to have compelled a clinician visit, and requires sufferers to have healthcare provision and will resort in a form of early disease management, to end-stage joint disease that can no longer be managed with medication and lifestyle alteration, and warrants surgery in those without contraindications for receiving surgery.

1.5 Summary

This review has summarised literature within the main topic areas of this study: physical activity and health, sports and physical activity, contact sports and longer-term health, rugby union, and injury within rugby union, defining and classifying OA, and risk factors for the development of OA. It has been seen that there are many benefits to

cardiovascular, musculoskeletal and psychological health when participating in physical activity. However, disadvantages of physical activity and sports participation have also been examined, such as anxiety, disordered eating and unsafe weight management strategies. These disadvantages have been discussed predominantly in the context of elite sports participation, where they are most prominent, although it has also been seen that these practices also affect youth elite athletes. Osteoarthritis has been discussed as a potential outcome of both paediatric and elite sports participation.

Injury incidence within rugby union and across other popular British participation sports and global collision sports has been summarised, in addition to methodological considerations in injury surveillance studies, and the role of consensus statements in standardising and developing the reporting of injury. Injury incidence and risk factors within rugby, at the professional and amateur levels of play have been summarised. The lack of understanding of long-term health following sports participation has been highlighted, and where studies have sought to examine long-term health outcomes, particularly for full-contact sports, this has been summarised.

Clinical and research definitions of OA have been reviewed, in addition to the burden of the disease and risk factors for its development and progression. Specific definitions of NHANES pain, physician-diagnosed OA (GPOA) and joint replacement have been considered in terms of the stage of disease they represent, and individuals they may include or exclude, such as individuals with severe OA but contraindications for surgery.

Openings in the literature within the relationship between sport, physical activity and OA, and long-term health following sports participation have been emphasised as an opportunity for further research to elucidate health status and inform healthy participation for current participants, and healthy aging for players as they retire from competitive sport.

Chapter 2 Designing an epidemiological study to assess the health of former rugby players

This thesis will involve the development of a novel, sport-specific questionnaire in order to examine the playing history, previous injury, current injury and health status of former players. It is acknowledged that there may be several ways to address the questions posed for this thesis, and that different study designs and tools could be used in order to achieve this. Within this chapter, the study design and methods used throughout the thesis to establish health, injury and health-related quality of life will be discussed, and justification will be provided for the selection of these methods. An overview of the recruitment strategy and participant flow during recruitment will be provided.

2.1 Study Design

Epidemiology can be described as the study of how often diseases occur in different groups of people and why.[312] Using epidemiological methods to ascertain playing exposure and health outcomes amongst this target population will not only allow for the descriptive assessment of poor health outcomes, but also the opportunity to begin assessing risk factors and determinants for the development of positive and negative health outcomes.

Levels of evidence have previously been produced in an attempt to optimise the quality of study design and support clinical decision-making within diverse fields and disease areas.[313–315] Systematic reviews with homogeneity, and clinical trials have been

repeatedly reported as providing robust evidence with high internal validity.[315,316] A pyramid of evidence has been suggested, grading evidence based on the internal validity of these study designs (Figure 4).

Randomised-control trials are widely acknowledged to be the current gold standard in clinical research, however are of limited applicability in some disease areas, and for certain research questions. Randomised controlled trials (RCTs) may be unethical where the outcome is harmful to health, or known to be rare, and RCTs have been reported to produce non-generalisable results, as inclusion criteria may often select healthy individuals whose health status differs from both the general population overall, and individuals who may be those destined to receive the treatment or intervention.[317] Therefore, alternative and more traditional study designs may be more appropriate for specific populations and research questions. Recent studies have established the potential complementary role for population-based observational studies alongside RCTs, particularly in enhancing the generalisability of study findings.[318]

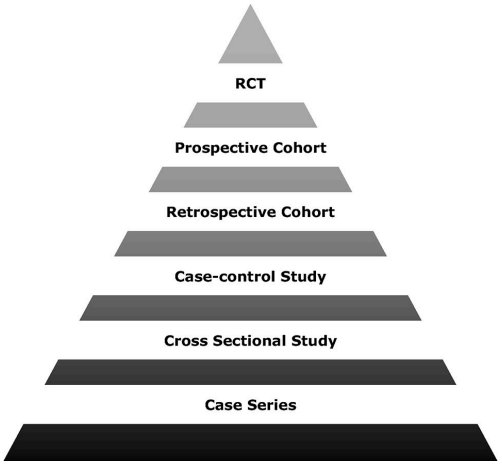


Figure 4. The pyramid of evidence. Reproduced from Ho et al [313]

For the research questions posed in this thesis, a clinical trial would be inappropriate due to randomising individuals to higher or lower rugby exposures which are not as yet established to be safe for the majority of participants, in addition to logistic considerations such as the duration between the exposure and development of longer-term health outcomes, and the low

feasibility of completing this project within a doctoral timeframe.

A prospective cohort study would be the most robust method to reliably measure playing exposure and health outcomes as they occur within a cohort of players, and to validate these reports as they occur with access to medical records. However, prospective studies require significant resource, and again the duration to the outcomes under study would be several years or even decades, and not conceivably in the scope of a doctoral project. Therefore a cross-sectional study design was implemented, in order to establish the current morbidity and musculoskeletal health within this population, in the timeframe of a doctoral degree. This study will also examine lifetime measures of potential risk factors for morbidity, and to examine their cross-sectional association with current or ever-diagnosed morbidities.

Case-control studies are of a higher level of evidence than cross-sectional studies (Figure 5). However, in order to select cases and controls for further study, case and control exposure and outcome status needs to have been determined and defined within the population, to allow case identification. Whilst being undertaken as an initial cross-sectional study, it is acknowledged that this study provides a cohort for further nested case-control studies, which are outside the scope of the thesis.

This will be a questionnaire study, in order to achieve a reasonable sample size of players that may be representative of the target population, examine multiple morbidities, and begin to statistically model their development.

2.2 Study Participants

In order to accurately examine the health of former rugby players, ideally one would assess all members of the target population, therefore all former rugby players. In the absence of the resource to contact all living former rugby players from all levels of play within England or globally, samples need to be selected, and generalisations inferred using inferential statistics where applicable.

Target populations for this study were selected as prominent rugby clubs, in regular contact with former players through well-maintained alumni records.

2.2.1 Oxbridge Blues

The Universities of Oxford and Cambridge ('Oxbridge') rugby teams ('Blues') alumni were contacted by the Club to form a pilot study. Club Managers and Administrators were engaged in the project, its steering group and decision-making, devising an appropriate recruitment strategy for each club given their existing alumni communication strategy, members and practicalities surrounding mailing lists. An overview of the criteria of alumni membership for the Oxbridge cohort is provided below (Figure 5).

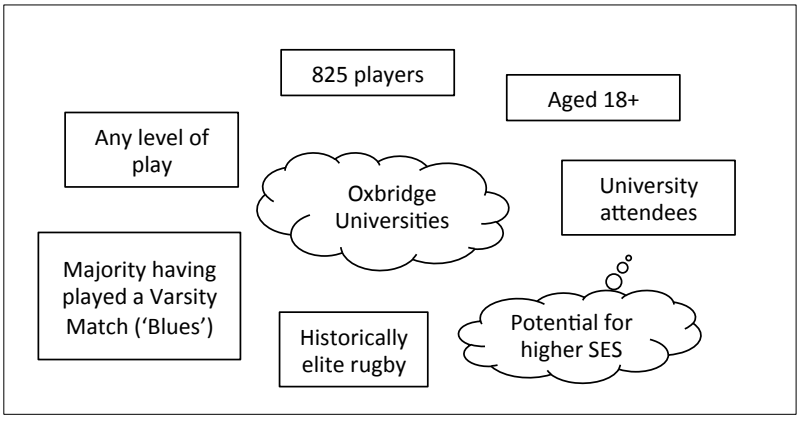


Figure 5. Criteria and features of Oxbridge rugby alumni membership

2.2.2 England Rugby Internationals Club

International rugby participation represents the highest national level of rugby performance. The England Rugby International's Club (ERIC) holds an alumni list of all former England players who have played representative games for England. The ERIC Committee were approached to support the project and participate in its steering group and management, and agreed to act as ambassadors for the study, permitting the recruitment of former England rugby players. An overview of the criteria of alumni membership for the ERIC cohort is provided below (Figure 6).

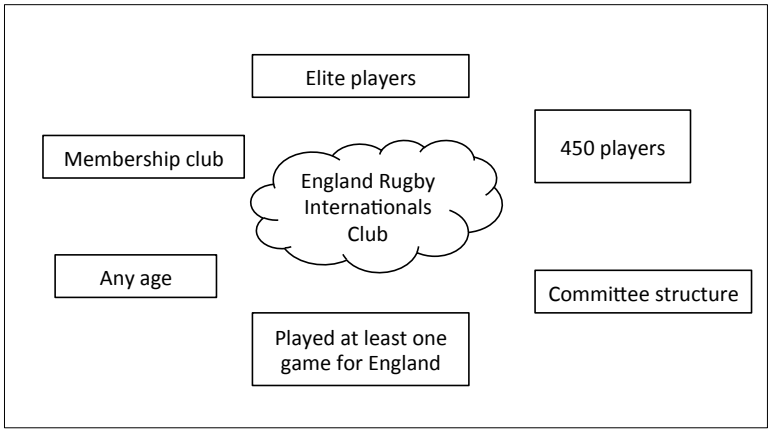


Figure 6. Criteria and features of ERIC alumni membership

Both cohorts involve players who have played representative rugby for a period of time, and therefore are not central to a specific geographical location. In order to be an Oxbridge Blue, former players will have studied at Oxford or Cambridge at a point in time and played rugby for at least one season with this Club. Blues may not be British, and may have played elite rugby within their country of birth or elsewhere. Players within ERIC will have represented England in a game of rugby at least once in their playing career, and therefore be English or of English heritage.

Both England rugby and Oxbridge may be associated with higher sociodemographic status, as University attendees and players of an elite, historically amateur sport. Therefore these cohorts may not be representative of all rugby players in terms of representing lower levels of playing level or lower socio-economic status. However, this is broadly true of rugby union historically, from its development within a British boarding school to its separation from rugby league as it maintained amateur status, thereby excluding many players of a lower socio-economic status from participation.

As representative Clubs, both study populations will be of a higher level of play than the majority of Clubs. This may be a limitation in terms of wholly understanding the relationship between participation and health, however both Clubs have well-maintained alumni mailing lists, and therefore provide an accurate denominator, potentially more so than many other lower league clubs without the same degree of alumni interaction. Playing level is also associated with injury,[191] which is known to be associated with Osteoarthritis,[319–322] pain and disability.[323,324] Therefore these Clubs provide a well-defined cohort who should be at the greatest risk of negative health outcomes, should risks be apparent. Utilising an elite cohort will also enable an initial indication as to whether there are deficits or benefits with participation in rugby union for health, and permit the more nuanced further study of the level at which these health outcomes may no longer be present, should elite participation and its increased match, training exposure and injury burden, be associated with worse health outcomes long-term.

As an elite, international club, England may be at the forefront of novel practice and its development within injury research and management. This may mean that although

players have experienced the highest exposure to injury, they will have also had the greatest access to medical professionals able to treat and rehabilitate these injuries. Optimal care and management in the acute phase may be beneficial for players in the short-term and possibly long-term. However for elite players, this may also mean increased pressure within the sporting environment and potentially an earlier return to play.[89,93,325] If the underlying mechanism of injury has not been treated or the injury sufficiently rehabilitated, this may lead to a recurrence of the injury. Recurrent injuries have been suggested to be of a greater severity than initial injuries.[108] This environmental pressure may not be as present for amateur players without financial consequences affecting their return to play, league and competition pressures or enhanced medical support, although a cultural acceptance of pain and injury in rugby at recreational levels has previously been discussed.[156,326,327] Amateur or professional players may also not necessarily always return to play, depending on the injury severity and their individual circumstances.

2.3 Recruitment

Recruitment strategies varied between cohorts and also between the Oxford and Cambridge University clubs.

2.3.1 Oxbridge Blues Recruitment (i)

Following several meetings with Club Management and Administration, a study launch email was sent, informing former and current Blues that the Clubs were working with researchers on a new player health project. Players were invited to email their interest in

participating in advance, or wait for the formal invitation two weeks later. The formal invitation was then sent with an information sheet attached, providing players with contact details for further information or study participation. Responding players were then sent a link to the online questionnaire study.

Reminder emails were sent when the response rate had decreased, with a minimum of two weeks between emails. All emails to the mailing lists were sent by Club Administrators. Drafts for email templates were sent to the Clubs by the study team for Clubs to review and revise as deemed appropriate and inline with their current communications.

Face to face recruitment was carried out at the Varsity Match 2014 in the Blues Village, a meeting point for alumni from both Universities. Flyers were circulated, and players were able to return these to study staff in secure designated locations. Players who had completed these were then emailed the study information sheet.

2.3.2 Oxbridge Blues Recruitment (ii)

In addition to the approach outlined above, and as a result of the lower than expected recruitment rate to the online pilot study, a postal follow up for Oxford Blues was coordinated to understand if a postal approach may be a more effective method of recruitment for this population. An abbreviated postal questionnaire was developed and sent to former players, with an information sheet, consent form and return envelope. The Club enclosed a letter mirroring the introductory email and coordinated the player

addresses for these within their existing data protection practices. This process contributed the greatest number of players, but with a similar response rate.

2.3.3 England Rugby Internationals Club Recruitment

Following the recruitment of the Blues Study, a modified recruitment strategy was undertaken with former England International players. An initial email was sent to players from the Club Secretary stating ERIC's support and collaboration in this project. The email described the study and stated that the study team would be present at a forthcoming general meeting and International game match day to answer any questions and provide further information.

The week after this launch event, players were emailed further details of the study and an address to contact should they wish to participate, with the attached information sheet. Players were offered the option of participating online, receiving a postal questionnaire or a telephone interview. Two reminder emails were sent before the study was closed.

A postal approach was taken for individuals on the database without an email address. Where emails were undeliverable, the Club Secretary checked if players had postal addresses and if so, they were added to the postal approach.

Reminders were sent for the postal approach as a message from the Secretary, in a scheduled Six Nations players' ticket application.

Between the second and third reminder emails, researchers attended two World Cup warm-up games to again discuss the study with players, collect email addresses if players wished to provide these, and answer any questions to further increase our visibility and the study response rate. The recruitment strategy for the ERIC online (Figure 7) and postal participants (Figure 8) are shown below.

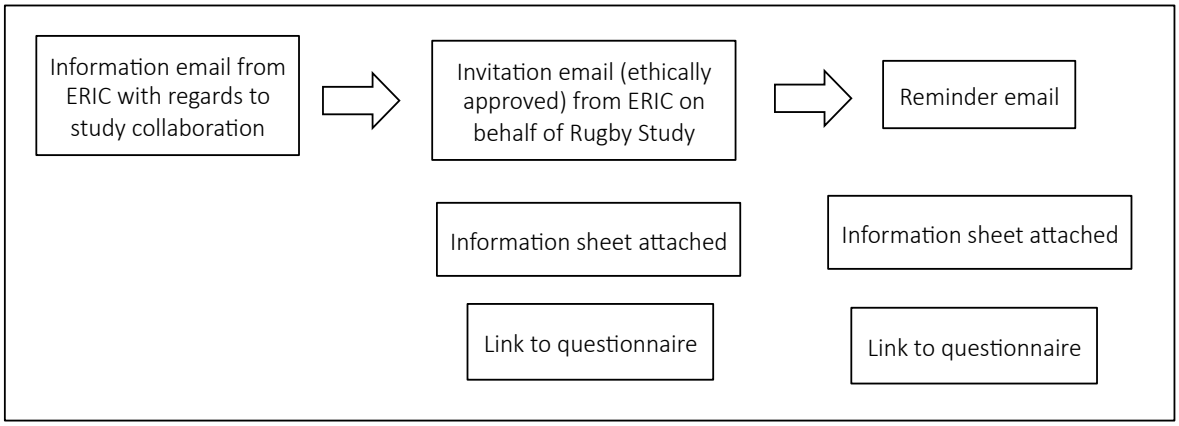


Figure 7. Recruitment of former English international rugby players using an internet-based methodology.

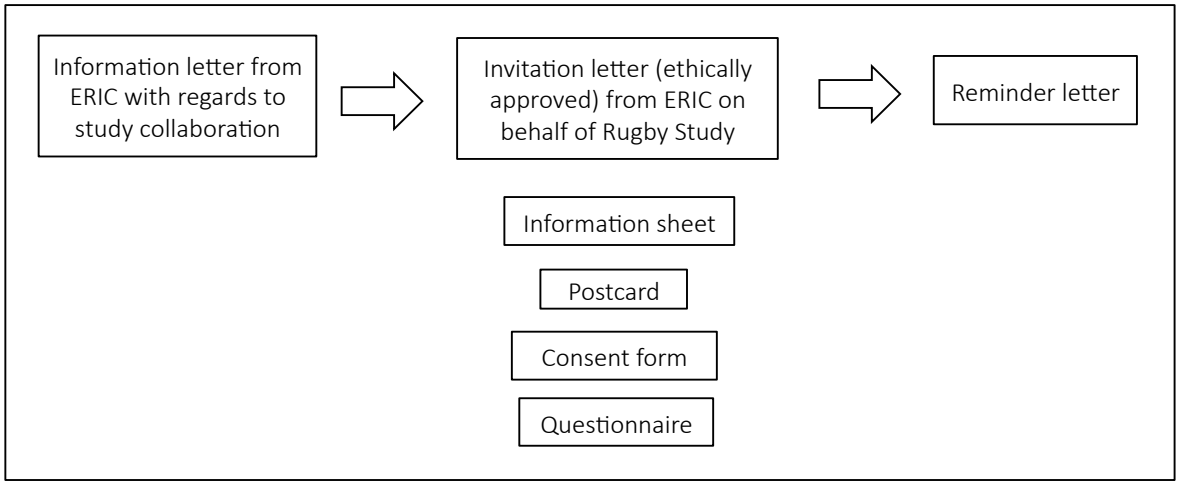


Figure 8. Recruitment of former English international rugby players using postal methodology.

2.4 Population comparisons

Population comparator groups allow for an approximation of health status in the general or a reference population, for comparison with recruited study samples. As primary data collection was undertaken with ERIC members and former Blues players, there were limitations surrounding the recruitment of a control population, both in terms of logistics and the selection of a control group, and how to measure physical activity and joint loading for comparison with rugby players.

The use of population-based surveys as a control population for recruited former rugby playing cohorts provides a large, nationally representative comparator group, with a similar health status estimate to the general population, across multiple morbidities.

2.4.1 The Health Survey for England

The Health Survey for England (HSE) is an annual cross-sectional survey of adults and children living in England. The 2014 dataset was selected as a recent representative survey of an English sample population,[328] which used the EQ-5D as a measure of health-related quality of life. [329]

2.4.2 The England Longitudinal Study of Ageing

The English Longitudinal Study of Aging (ELSA) is a longitudinal study, which has selected a representative subset of participants from HSE to monitor for multiple morbidities and health outcomes over time.[330] Selected respondents to the HSE in 1998, 1999 or 2001, aged 50 or over, residing in private households in England were invited to

participate in ELSA as 'Core members' of the study. Core members of this ELSA cohort at baseline ('Wave 1') were used as a nationally representative comparison population. Female participants were removed for this analysis.

The data were made available through the UK Data Archive. ELSA was developed by a team of researchers based at the NatCen Social Research, University College London and the Institute for Fiscal Studies. The data were collected by NatCen Social Research. The funding is provided by the National Institute of Aging in the United States, and a consortium of UK government departments coordinated by the Office for National Statistics. The developers and funders of ELSA and the Archive do not bear any responsibility for the analyses or interpretations presented here.[330]

2.5 Data Management

A data management plan was developed by researchers (MD) and agreed with the data manager (AD) and study team (NKA and JN). Data for the initial Blues study was stored differently from that obtained in the postal follow up and ERIC study. Initially a MySQL database was created with a custom-built specific interface. Data capture was standardized through the same interface being presented for participants, into which they enter data themselves. Data entry validation was also built into this interface. Repeat samples were collected prior to the interface's launch, and participants who had completed double data entry were asked to provide feedback on the interface and their experiences of completing the questionnaire.

The Oxford Blues postal study and ERIC study both used an abbreviated questionnaire, which was designed and formatted to be completed by post. A Research Electronic Data Capture (REDCap) database[331] was created, and the survey tool was used for online participants for the ERIC study and moving forwards.

2.6 Quality assurance and control

All data collection and storage processes were agreed between the study team, including data management staff, and data were checked for accuracy and outliers. Data entry was undertaken over eight weeks by one individual (MD), with double data entry undertaken at a later date, and these documents merged and assessed for differences by a third individual.

A study email account hosted by the University was requested, and regularly monitored throughout the duration of the study (MD). Open communication was encouraged with researchers, and particularly in the initial online study of Oxbridge Blues, participants were provided with a free text box, where they could evaluate the process and anonymously disclose any further information they wished to, which was directly sent to researchers.

Data dictionaries were produced for each questionnaire, and analysis was undertaken from the variable names and labels stored within data dictionaries produced by the respective management software. All data analysis was undertaken anonymously, with identifiable information stored on encrypted hard drives separately from participant

data. The research team all undertook Good Clinical Practice training courses at the commencement of the project (August 2013-January 2014).

The UK Data Archive, ELSA and HSE have their own quality assurance procedures documented elsewhere.[332] ELSA and HSE data underwent the same procedures documented above for data storage, checking and analysis.

2.7 Ethical Compliance

Following the development of a recruitment strategy with the clubs and the assembly of all player-facing documents, an application for ethical approval was submitted and approved following ethical review by the University of Oxford Medical Sciences Division Central University Research Ethics Committee, reference MSD-IDREC-C1-2014-020: The health outcomes of professional and amateur rugby (Appendix 2). Subsequent amendments were made to personalise study documents with specific club branding, collect data from current players in addition to former players in order to exclude these from analyses, recruit face-to-face, and collect questionnaires by proxy where an individual's family has responded on their behalf, and the individual may have a primary outcome of interest for the study.

2.8 Copyright and Intellectual Property Rights

The Rugby Questionnaire (The Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis Rugby Epidemiology Questionnaire©) has been granted copyright through Isis Innovation at the University of Oxford, to Madeleine Davies and Stefan

Kluzek. Anyone wishing to use or adapt the questionnaire should seek written permission from the authors.

Data is being collected and funded through the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis (Grant reference 20194). Any ensuing project proposals are subject to the authors' involvement in receiving a satisfactory analysis plan and agreeing with the use of the questionnaire and/or data for the proposed project.

2.9 Study Steering Group

From the outset of the project, a study steering group was created, with the shared decision-making capacity and management of logistic considerations and overarching supervision of the study. This steering group was devised to coordinate key project stakeholders, from the sport's governing body, players' unions, clubs and players. The invitation for participation in the steering group is shown in Appendix 3. This group met quarterly throughout the first three years of the project.

2.10 Role in Study Design and Processes

The study team was comprised of a doctoral researcher (MD), and the supervision team, (JN and NKA), which was expanded during the course of the project (AJ and KS). MD was responsible for participant recruitment, club engagement and study logistics, with joint decision-making in conjunction with the supervision team. MD was responsible for managing the email account and stakeholders, coordination and output of steering group meetings, ethical approval and compliance, obtaining and managing data from population-based comparator groups. The development of the database and survey tools

was led by a Data Manager and supported by the study team, with joint responsibility for testing these prior to their implementation.

All statistical analysis was undertaken by MD, with supervision and management by AJ. MD had sole access to all study data, and bears responsibility for all data and analysis presented within the thesis.

2.11 Study Outcome Measures

The main outcome measures within this cross-sectional study are examining health status, morbidity and health-related quality of life. The main outcome measures in each chapter will now be examined in more detail.

2.11.1 Health status and morbidity

Health status and the presence of morbidity will be assessed by examining physician-diagnosed morbidity during a player's lifetime, parallel to the approach undertaken within the population-based comparator populations. Physician-diagnosed morbidity was assessed within collected cohorts using the question: "Have you ever been told you have any of the following by a Doctor?"

2.11.2 Health-related quality of life

Health-related quality of life was assessed using the EQ-5D.[329] The EQ-5D was selected as a valid and reliable measurement of health-related quality of life, which has been seen to maintain validity and reliability across different geographical and disease populations.[333–337] The EQ-5D assesses the level of reported problems (none, slight, moderate, severe or inability) an individual suffers within each of 5 dimensions:

mobility, self-care, usual activities, pain or discomfort and anxiety or depression. The 5-level EQ-5D-5L was used within rugby due to its increased capacity to discriminate participants with slight, moderate or severe problems within a dimension. The EQ-5D-5L has also been shown to provide stronger evidence of validity compared with the EQ-5D-3L.[338] Permission for the use of the EQ-5D-5L was achieved by registering the project with Euro-QoL who then emailed a license for the use of the EQ-5D-5L to the researcher (MD).

2.11.3 Osteoarthritis

As previously discussed, OA may affect any joint,[242] and is understood to have several thus far mostly uncharacterised disease phenotypes,[241,247,308] despite initial attempts to define radiographic and symptomatic disease phenotypes, predominantly at the hand.[284,339,340] This study will measure several OA-outcomes, which may all be representative of different stages of disease progression, particularly in this contact sports population. The response of players to pain and injury has been previously discussed as potentially having some cultural influence,[156,326] and whilst the validity of these measures and an overall player health study will be co-developed with players in order to understand where data collection may be less reliable (Chapter 4), the assessment of multiple OA-outcomes has several advantages. It will substantially expand current knowledge within the field, determine the cross-sectional stage of OA where players may be at a specific age, particularly if this is rapidly progressing post-traumatic OA, and also be more likely to provide an estimate of their OA status irrespective of healthcare provision, pain tolerance and propensity for surgery, which may all affect individual OA measures.

In collecting NHANES pain, significant variation in prevalence, sensitivity and specificity have been seen with relatively minor differences in phraseology.[303,306] The NHANES pain question used within this study was: "Have you had any pain in your knees on most days of the last month?" This question is most similar to the "gold standard" NHANES question against which other variations have been measured.[306] It is also similar to the ACR criteria for knee OA: "Have you had knee pain on most days of the last month,"[296] which has demonstrated higher specificity (72.7%), but less sensitivity (45.4%) of three variations of the NHANES question, against the outcome of a greater than grade 1 overall osteophyte classification on radiograph.[303] This definition may therefore be expected to exclude a high percentage of non-cases compared to radiographic OA, whilst also potentially not capturing as high a percentage of cases as other methods of OA assessment. However, this variation has also been seen to indicate the highest rate of disability, compared with other NHANES phraseology, and may therefore be a robust measure of the burden of joint-specific disability in this population.

Physician-diagnosed OA has been seen to have good sensitivity and specificity compared to ACR clinical criteria at the knee and hip,[308] (see 1.4.3) and whilst requiring participants to have healthcare provision and have sought a diagnosis for their joint pain, this is therefore a reasonable population-level assessment for the burden of OA. Physician-diagnosed OA will be recorded as "Have you ever been told you have wear and tear, degeneration or osteoarthritis by a doctor?" Joint-specific physician-diagnosed OA (GPOA) will be determined by deriving a binary response per joint from side-specific responses to: "If yes, where? Please circle which joints and sides, or specify other."

Case definitions in epidemiological studies have been previously described as needing to be clear, concise, valid, reliable and easily measured in clinic and the general population.[341] Joint replacement is an acknowledged 'hard endpoint' in OA,[311] due to its relatively reliable reporting from clinicians and the general population, decreased susceptibility to recall bias, simple measurement, and reliability of representing end-stage joint failure. Joint replacement will be collected as "Have you ever had joint replacement surgery?" Joint-specific joint replacement will be derived from side-specific binary responses at the hip, knee and shoulder for "If yes, please indicate the number below for each joint and side."

Whilst each definition of OA used here will encompass different stages of OA progression within the population as a whole, and radiographs or clinical consultations will not be undertaken to validate that players reporting OA-outcomes currently have or have had clinical OA, and therefore definitively reported the outcome of interest, these measures will indicate the burden of the pain and disability present amongst former players, their Primary Health Care utilisation attributable to OA, and end-stage disease where symptom management and intervention has not been successful, and joint failure and thus replacement has occurred.

2.12 Overview of Statistical Methodology

2.12.1 Data preparation

Participants with any complete fields within the database will have their data extracted from the databases. Participants who have registered but with all fields incomplete, will not be considered as participants. All data will be extracted, and checked for accuracy and outliers with cross-tabulations (MD). Labels will be generated for variables where these are not attached at the point of extraction, as for the initial questionnaire study amongst Blues, and the logic checked for any dependant variables, in addition to missingness within dependant and all other variables (MD). Variables required in analysis plans and not collected directly will be derived from collected variables (MD).

2.12.2 Descriptive statistics

Statistical analyses will be undertaken using Stata (Version 13.1). In addition to cross-tabulations for data checking, frequencies, means and ranges will be assessed to ensure data accuracy. Descriptive statistics (mean (standard deviation) for continuous variables, and number (percentage) for categorical variables) will be produced for all variables collected. Descriptive statistics calculated in this thesis will include means, ranges, and standard deviations.

2.12.3 Inferential and predictive statistics

Whereas descriptive statistics may summarise information surrounding the person, place or time, inferential statistics further expand this analysis to begin to generalise from a study sample towards a population. Within this thesis, standardised morbidity

ratios will be used to assess the differences between observed morbidity within the rugby playing population, and expected morbidity based on the comparator populations and distribution of morbidity therein.

Further analysis will then begin to explore risk factors for OA prevalence, examining the association between individual sporting and non-sporting risk factors for OA-outcomes, at the person and joint level.

The final stage of analysis for this thesis will be predictive analysis, developing a predictive model for end-stage osteoarthritis of the hip amongst this former playing cohort. A priori analysis plans were agreed within the study team for each analysis forming a chapter of this thesis. Any analyses conducted following initial a priori analyses will be specified as post-hoc analyses.

2.13 Participant flow

2.13.1 Oxbridge Blues

109 Oxbridge Blues registered for an account in order to complete the questionnaire. 19 of these did not proceed past the initial screen to answer any questions, and therefore 90 participant records were carried through to analysis from the original online questionnaire.

The abbreviated postal follow up to this study resulted in an additional 79 former Blues players.

2.13.2 England Rugby Internationals Club

150 ERIC members participated in this study by a combination of telephone, online and postal participation.

The participant flow from recruitment to data analysis is shown below (Figure 9). The resultant 259 male, former elite, age-specified players form the sample analysed throughout the thesis.

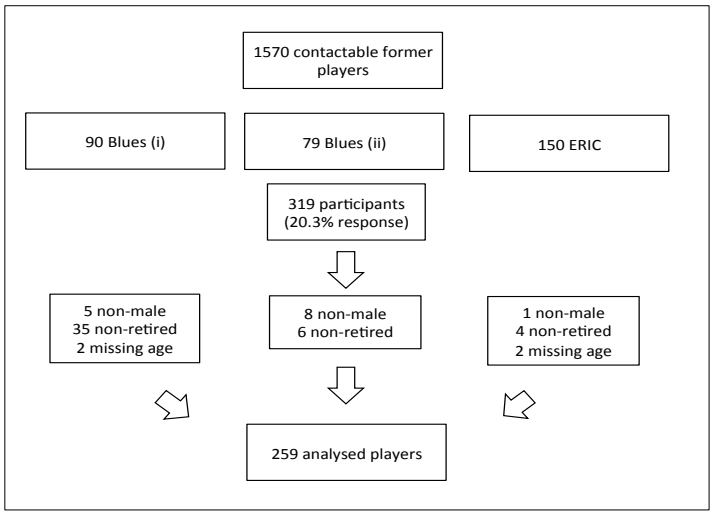


Figure 9. Primary data collection of rugby players from alumni membership lists to recruitment, including the exclusion of players missing or not specifying their sex as male, their age and former playing status.

2.13.3 The Health Survey for England

Variables from the 2014 HSE associated with identifying participants, their demography and health-related quality of life were extracted from the UK Data Archive. Non-male participants (n=5456), and those outside the age range (24-95) of rugby participants (n=1363) were excluded from analyses. Age within HSE is capped at 90, and therefore any HSE participants aged 90 or above will be shown as 90. Participants missing data due to non-completion of the self-complete HSE booklet (n=280) were also excluded (Figure 10).

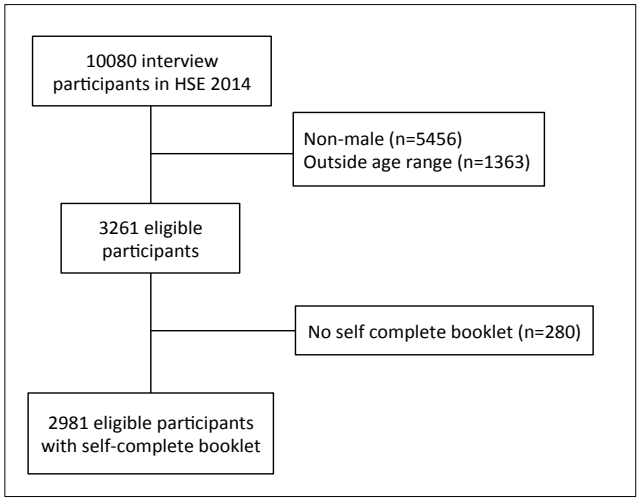


Figure 10. Selection of the Health Survey for England (HSE) study sample from HSE 2014 participants

2.13.4 The English Longitudinal Study of Ageing

The English Longitudinal Study of Ageing (ELSA) selected a representative sample of participants from HSE to monitor for multiple morbidities and health outcomes over time, from 2002 onwards.[330] The representative sample selected for ELSA participation were study participants from HSE in 1998, 1999 or 2001, aged 50 or over, residing in private households in England.

The first point of ELSA data collection (Wave 1) was used as a cross-sectional representative population comparison of morbidity for rugby respondents. Young partners, female participants and partners other than core members (those individuals over 50 years who had been selected from HSE) were removed from analysis so only the original 'core member' sample remained (Figure 11).

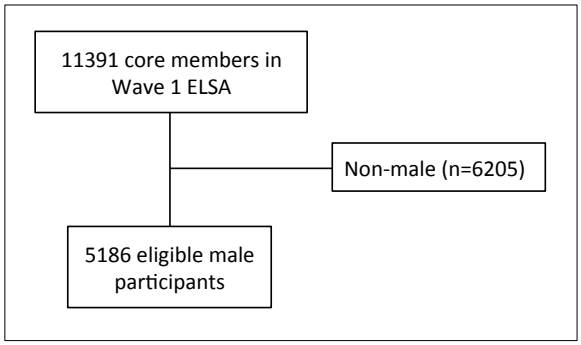


Figure 11. Selection of the English Longitudinal Study of Ageing sample from ELSA Wave 1 participants

Chapter 3 Data

An overview of the descriptive statistics for the demographics and primary outcomes of each chapter for former players, ELSA participants and HSE participants is provided below for reference (Tables 9-12).

Table 9. Characteristics of rugby, ELSA and HSE cohorts. Results are expressed as mean (±SD) or n(%)

Characteristic	Rugby (N=259)		ELSA (N=5186)		HSE (N=2981)	
Age (yr)						
Mean (SD)	259	60.1 ± 16.1	5186	64.9 ± 10.0	2981	53.4 ± 16.3
Median (range)	259	62.0 (70.8)	5186	64.0 (49.0)	2981	52.0 (66.0)
Categorised: 20-29 30-39 40-49 50-59 60-69 70-79 80-89 90-99		5 (2%) 31 (12%) 37 (14%) 50 (19%) 44 (17%) 64 (25%) 27 (10%) 1 (1%)		0 0 0 1916 (37%) 1611 (31%) 1174 (23%) 447 (9%) 38 (1%)		224 (8%) 460 (15%) 603 (20%) 553 (19%) 579 (19%) 373 (12%) 171 (6%) 18 (1%)
White ethnicity – no. (%)	206	199 (97%)	5148	4973 (97%)	2978	2713 (91%)
Height (m)	252	1.82 ± 0.07	4856	1.73 ± 0.07	2963	1.76 ± 0.07
Weight (kg)	254	94.0± 15.2	4739	82.2 ± 13.1	2912	84.2 ± 14.8
BMI (kg/m^2)*	249	28.1 ± 3.7	4720	27.5 ± 3.8	2896	27.0 ± 4.3
BMI Categories:	249				2896	
Underweight		0				25 (1%)
Normal range		41 (17%)				989 (34%)
Overweight (pre-obese)		148 (59%)				1272 (44%)
Obese Class I		50 (20%)				467 (16%)
Obese Class II		8 (3%)				114 (4%)
Obese Class III		2 (1%)				29 (1%)
Ever smoker	257	25 (10%)	5104	3824 (74%)	2981	1832 (62%)
Marital status:	207		5185		3258	
Single/never married		6 (3%)		324 (6%)		471 (15%)
Married		171 (83%)		3916 (76%)		1991 (61%)
Separated		1 (1%)		64 (1%)		64 (2%)
Divorced		14 (7%)		399 (8%)		214 (7%)
Widowed		12 (6%)		482 (9%)		136 (4%)
Other		3 (2%)		0		382 (12%)
Employed or retired[1]	251	246 (98.0%)				

Table 10. Lifetime rugby playing exposure. The results are expressed as mean (±SD) or *number (%)

Variable	All former (n=259)	Mean (SD)	Median (IQR)
Amateur status	256	*214 (84%)	-
Age at first schoolboy game (years)	256	10.2 (2.5)	11 (3)
Number of matches	205	377 (189)	350 (250)
Total years of rugby	243	22.2 (5.3)	22 (6)
Number of years at the highest level	254	4.7 (3.4)	4 (5)

Table 11. OA-outcomes for former rugby players. Results are expressed as number (%)

OA-outcome	n	Former players (n=259)
Any GPOA	253	152 (60.1%)
Any joint replacement	253	60 (23.7%)
NHANES hip pain	253	50 (19.8%)
NHANES knee pain	254	99 (39.0%)
NHANES shoulder pain	254*	70 (27.6%)
GPOA at the hip	252	43 (17.1%)
GPOA at the knee	252	96 (38.1%)
GPOA at the shoulder	252	39 (15.5%)
Hip replacement	254	39 (15.4%)
Knee replacement	254	23 (9.1%)
Shoulder replacement	254	8 (3.2%)

Table 12. EQ-5D results of reported problems amongst former players and HSE participants

EQ-5D-5L reported problems in rugby players		EQ-5D-3L reported problems in HSE	
Mobility (n=249)		**Mobility (n=2867)**	
I have no problems in walking about	131 (52.6%)	I have no problems in walking about	2335 (81.4%)
I have slight problems in walking about	78 (31.3%)	I have some problems in walking about	525 (18.3%)
I have moderate problems in walking about	30 (12.1%)		
I have severe problems in walking about	10 (4.0%)		
I am unable to walk about	0	I am confined to bed	7 (0.3%)
Self-care (n=247)		**Self-care (n=2856)**	
I have no problems washing or dressing myself	224 (90.7%)	I have no problems with self-care	2684 (94.0%)
I have slight problems washing or dressing myself	19 (7.7%)	I have some problems washing or dressing myself	161 (5.6%)
I have moderate problems washing or dressing myself	3 (1.2%)		
I have severe problems washing or dressing myself	0		
I am unable to wash or dress myself	1 (0.4%)	I am unable to wash or dress myself	11 (0.4%)
Usual activities (n=249)		**Usual activities (n=2855)**	
I have no problems doing my usual activities	159 (63.9%)	I have no problems with performing my usual activities	2416 (84.6%)
I have slight problems doing my usual activities	61 (24.5%)	I have some problems with performing my usual activities	384 (13.5%)
I have moderate problems doing my usual activities	24 (9.6%)		
I have severe problems doing my usual activities	4 (1.6%)		
I am unable to do my usual activities	1 (0.4%)	I am unable to perform my usual activities	55 (1.9%)
Pain/discomfort (n=249)		**Pain/discomfort (n=2859)**	
I have no pain or discomfort	54 (21.7%)	I have no pain or discomfort	1925 (67.3%)
I have slight pain or discomfort	130 (52.2%)	I have moderate pain or discomfort	833 (29.1%)
I have moderate pain or discomfort	56 (22.5%)		
I have severe pain or discomfort	9 (3.6%)		
I have extreme pain or discomfort	0	I have extreme pain or discomfort	101 (3.5%)

Anxiety/depression (n=249)		**Anxiety/depression (n=2857)**	
I am not anxious or depressed	212(85.14%)	I am not anxious or depressed	2384 (83.4%)
I am slightly anxious or depressed	26 (10.44%)	I am moderately anxious or depressed	419 (14.7%)
I am moderately anxious or depressed	9 (3.61%)		
I am severely anxious or depressed	2 (0.8%)		
I am extremely anxious or depressed	0	I am extremely anxious or depressed	54 (1.9%)
Health today (n=229)		**Health today (n=2666)**	
	79.2 (14.5)		77.8(18.0)

Chapter 4 Player involvement in the development of an epidemiological study assessing health status amongst former rugby players*

Global sports governing bodies, national rugby unions, and elite leagues have specific structures to address areas of concern for player welfare, and to assess and mitigate risks to player health within sport. Research or audit findings that improve player welfare may be trialled for efficacy against current performance, and subsequently initiatives may be adopted, potentially consulting with or receiving feedback from players' unions. However, this process of legislative change for health protection within rugby is one example of how within the elite sporting environment, applied research is historically conducted without player consultation, collaboration or involvement. Players are currently typically consulted after initial research and further intervention studies, regarding initiatives, which are ideologically developed in order to protect their welfare, or mitigate risks to their short or long-term health.

Despite the increasingly persuasive argument for the widespread adoption of public involvement in research to increase its quality, relevance and impact,[342] public involvement in research remains more frequently implemented within certain disease areas and populations, with involvement being most regularly reported within mental health, followed by black and minority ethnic (BME) or indigenous health.[343] It has been previously considered that involvement may be most integrated into research areas where longer-term service use or service dependency is undertaken, or where there may

* This chapter has been reproduced as a manuscript accepted for publication (Davies et al., 2017)

be a cultural mistrust or hostility towards services and service providers.[344] Involvement has yet to be routinely integrated within sports research, sports science and medicine, or by key stakeholders who may be able to encourage this as routine good practice, as in other areas of healthcare science and medicine. In addition to increasing research quality, relevance and impact, involvement also gives voice to those who will ultimately be affected by research outcomes.

This chapter will describe the involvement of rugby players across the research cycle of this player health study, evaluating the process and describing how player involvement may benefit research and researchers.

4.1 Public Involvement

Public involvement in research is defined as research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them.[1] Public involvement embodies democratic values, involving lay representation and promoting a patient-focused and patient-driven agenda for service provision.[345] Historically, these values have not translated into healthcare research and routine academic practice, albeit with a significant increase in involvement activities and their reporting between 1999 and 2006, in the UK and internationally.[343]

Public involvement, often termed 'patient and public involvement' (PPI) or 'patient and public involvement and engagement' (PPIE) may take many forms, and can occur at any stage of the research cycle, from commissioning to report writing.[346] Despite being endorsed for every stage of the research cycle, study designs and disease areas,[1,347]

involvement has been reported as predominantly focusing on question identification and prioritisation.[343] Examples of public involvement throughout the research cycle are shown below (Figure 12).

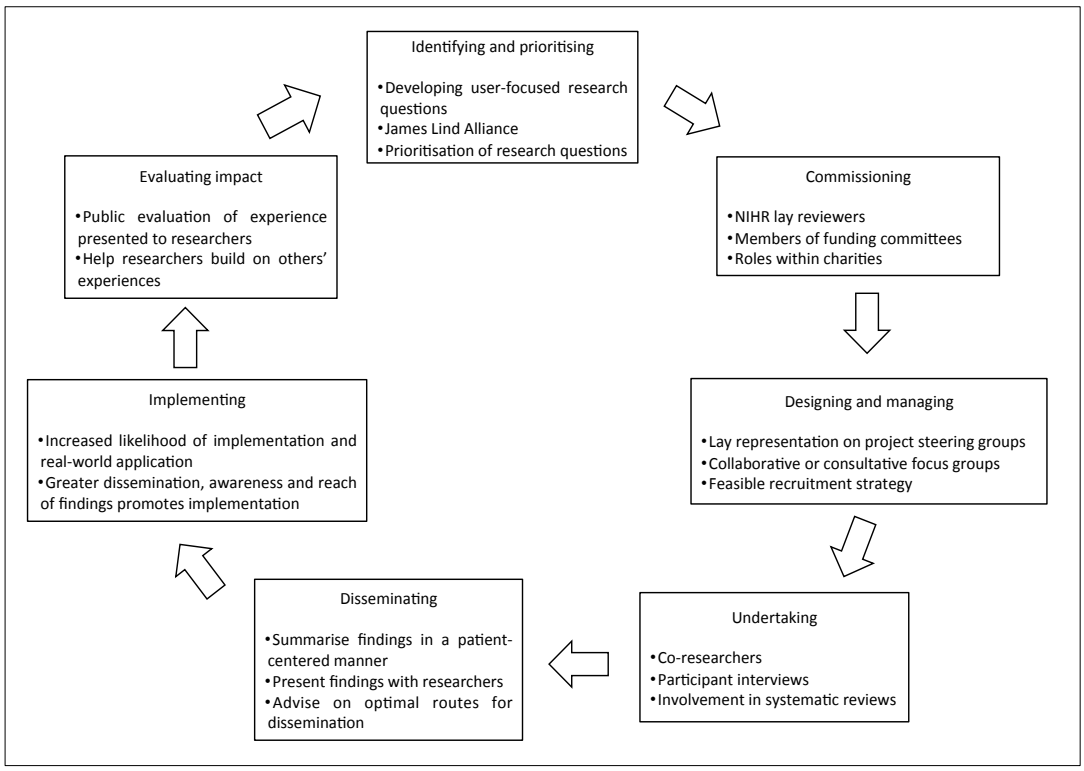


Figure 12. The involvement of patients and members of the public across the research cycle. Adapted from Hayes (2012)[1] and National Institute for Health Research (2014)[2].

4.1.1 Why involve members of the public in research?

The justification for involving members of the public in research has previously been described as being epistemological, moralistic and consequentialist. Epistemological motivation refers to what can be learnt from the experiential knowledge of patients, moralistic refers to the accountability to, and right of, the public to be involved in research projects and decision-making which may ultimately alter or transform their healthcare.[348] Consequentialist arguments describe an improved product after

involvement, in terms of research quality, relevance and impact,[349–353] when involving the public, and that involvement may have benefits for both researchers and members of the public who are involved in research.[354]

The National Institute for Healthcare Research (NIHR) has used an epistemological model of evidencing engagement throughout the research cycle as mandatory for all funding within the NIHR.[2] The Department of Health has been vocal in its support for patient involvement in research, stating that relevant service users and carers or their representative groups should be involved wherever possible in the design, conduct, analysis and reporting of research,[347] and also discussing that research with the active involvement of service users is a key feature of a quality research culture.[347]

4.1.2 How should the public be involved in research?

INVOLVE, an NIHR-funded advisory group for the integration of public involvement in research, emphasises ways of involving members of the public throughout the research cycle (as shown in Figure 14), and also stresses the differences between collaboration, consultation, involvement and engagement.[1] Public involvement in research is aspiring towards active collaboration with members of the public as co-researchers and co-applicants, ensuring the entire research process is accessible to and ideally guided by members of the public, service users and potential service users. The importance of working with members of the public who will provide knowledge and perspective at odds with those represented within the research team has been discussed as central to successful involvement.[1,344]

4.1.3 Rugby players as a population disempowered in healthcare decision-making

The growth of professional rugby union over the last two decades has further promoted values within the sport of a non-acceptance of pain and injury within the sport, where players with pain or injury may not be truthful or prompt in their reporting, or play despite pain as they chose to not consciously acknowledge pain or an injury.[156] It has also added a financial incentive to this collision sport, where injury is not only associated with an intrinsic experience of pain, loss of function and absence from competition, but also further potential financial loss of earnings and future potential earnings, if there are performance or competition-related incentives for players, and limited future playing opportunities if on-going injuries or health considerations are acknowledged.

Elite sports people within many sports become tradable commodities, where their capacity to perform effectively, thus their health and function is an asset of the Club. Sports people may not traditionally be viewed as disempowered or marginalised, however they could be considered as such regarding their ability to make individual and unconstrained choices concerning their health and healthcare, such as surgery and return to play decisions, in an elite sporting environment. Within this environment, players may be less able to seek individualised care and have the ultimate healthcare decision-making capacity of members of the public. In elite environments, squad availability, league position and upcoming games may influence healthcare decisions, which may also involve a team of support staff with varied interests, such as coaches, managers, and institutional healthcare providers such as physicians and medical officers. The complexity of return to play decisions has been previously described, due to

the difficulty in managing return to play within an elite sporting environment, including whether a full recovery from injury is necessary for both training and competition, if this may be of more or less importance at different times within the season, and low level compliance of players with return to play advice, and adherence to guidelines.[94,325,327]

Whilst amateur and recreational sports participants may not experience the same highly pressured elite-sporting environment, this may also influence the healthcare they receive. Whilst decision-making at the elite level may be subject to the aforementioned extrinsic influences, these environments also provide specialist first-class injury management, and novel techniques to promote recovery post-injury. Recreational athletes, who may be otherwise healthy individuals, could present to primary care providers with a sporting injury, and be treated by physicians without expertise in sporting injury or an understanding of the sporting environment and its culture. In addition, recreational sports participants may not be as actively involved in their provision as more chronic service users, partly due to their shorter admission or consultation periods, and therefore have little opportunity to influence their care and management.

In examining the health status of former rugby participants, there needs to be an awareness of player sentiment around health and healthcare. There have been numerous high-profile reports in the mainstream media regarding specific incidences of player health mismanagement, or former players feeling post-retirement that they can now discuss a culture that either encouraged or refused to actively dissuade players from taking risks with their health. As a sport with recent professionalization, the group being

assessed for former health status will not only encompass amateur and professional players in terms of level of play, but also in terms of decade of play, where those from earlier years will have only had the opportunity to play at an amateur level. This may mean that older amateur players have a more egalitarian view of their healthcare during their era, as they may have had an increased influence on both healthcare provision and decision-making than younger, professionalised players.

Player involvement in study design will empower former players to be engaged in open discussions about their health status as sports participants for the first time to date, and allow researchers a better understanding of player perceptions of their own healthcare control during their playing career.

4.1.4 Rugby players as experts of their own experiences and environment

Experiential knowledge has previously been discussed as a potentially important output of involvement in research.[344] Involvement may enhance the quality and appropriateness of research for certain populations, in addition to developing topics grounded in the reality of users experiences.[346]

Sports participants acquire extensive experiential knowledge, which may be unique to their sporting environment. Sport-specific vocabulary may symbolise an exclusive dialect, and contribute to a sport-specific subculture or society.[147] The experiential knowledge of players about their own environment, and the current ethos and attitude to health and research amongst players is unique. Involving players in research is the only way to ensure player experiences are truly encompassed and represented within a research study.

4.1.5 Potential player hostility towards health status research

Public involvement in research has been particularly encouraged when groups may be hostile to services or service providers.[344,355] There has been a historical disconnect within rugby union between the sport's administrators, such as the Rugby Football Union (RFU) and World Rugby, and players and Clubs. A fundamental example of this occurred during the sport's professionalisation, when many clubs defected to play other codes of rugby football and receive financial incentives for participation, and national team performance suffered.[356]

Sporting unions have several roles, including increasing participation for young people, the promotion of values of sportsmanship and competition through the sport, and to grow sports for spectators and participants, on a global scale. Sports governing bodies may have roles to both protect player health, and potentially have contractual obligations towards a duty of care for contracted players, with a statutory responsibility to proactively manage risks of participation amongst those engaged in the sport. These roles may not always be straightforward, whereby the union's roles in increasing spectatorship and participation may be at odds with their responsibility to ensure safe participation, if health status and risk within these groups have not been established. Should participation in rugby union involve health risks that are above and beyond those of individuals without participation in rugby union, there may be a role of national and international governing bodies in better understanding these risks, and proactively managing and mitigating them for players at all levels of play.

There has been increasing concern surrounding the long term health of sports participants after their playing career, particularly post-injury within contact sports, and associated with sports concussion.[71,223,226,357] Many other sports such as football, Australian rules football and National Football League (NFL) have examined longer-term player health and reported these before rugby union,[111,119,358] and there is the potential for former players, particularly those with morbidity that they may attribute to rugby, to feel somewhat disregarded by the sport, in terms of their welfare provision post-retirement.[147]

Recent widespread scrutiny of player health in rugby union,[223,226,359] may affect the attitude of former and current players to research. The implementation of player involvement in the study, and understanding player opinion in more detail will assist in anticipating player perception of the study, and mitigating potential player concerns. Player concerns may include the portrayal of rugby union, where collectively held player values may result in an unwillingness to cast the sport in a negative light.[147]

Public involvement has been used to ensure study methodology is culturally and linguistically appropriate for potential participants,[355] and also to identify cultural matters which may need to be considered and adapted in the study design phase.[355,360] With an awareness of the broader context of health in rugby union, and that there may be conflicting sentiments amongst former players, it is important that this player health study remains player-centred and culturally sensitive in every possible dimension, and that player experience is informing the study wherever possible. Many individuals reflect on a successful playing career and with affection on the friendships, achievements

and character-forming experiences provided by the sport, whilst others may have experienced a more traumatic transition into retirement from sport.[147]

4.1.6 Accurate data collection in a population accepting of pain

The focus of this thesis is the accurate collection, analysis and interpretation of data examining player health, pain, disability and function following participation in elite rugby union. Osteoarthritis, as a globally prevalent disabling disease, associated with pain and disability,[242,361] and increased following sporting injury,[71,74,362] is a particular disease of interest. However, it is acknowledged that this population, who may provide an accelerated model of post-traumatic joint degeneration, may also be a group liable to conscious or unconscious cultural misrepresentation of pain and injury.[156,326]

By participating in a contact collision sport, rugby players may have an altered pain tolerance or increased pain threshold which may prevent or lessen their self-report of pain and likelihood of physician consultation for joint pain, when compared to the general population, and also be associated with their rugby exposure ('survival') at this level of competition.

Player involvement in designing a questionnaire to assess pain, injury and disability may assist with more accurately capturing data, in addition to researchers being able to directly discuss with players whether upon receiving a questionnaire assessing pain, injury and health, players may over- or under-estimate these factors, and if so what influence this may have. This notion of involvement in research improving the content and face validity of measuring tools has previously been acknowledged.[346,363]

4.2 Chapter aims

The aim of this chapter is to document and describe the involvement of players within the design, development and decision-making of a player health study. The chapter will focus on how rugby players were involved in the study, the feasibility and outcomes of this, and reflect on the experience. The aims of player involvement within the study were multifaceted. Primarily from the conception of the study, it was necessitated that the study would be player-focused and allow players an equal opportunity to direct the research process. Sports governing bodies were actively engaged in the study, motivated by the aforementioned requirement to better understand player health. Aware of historic contrasts between governing body, Club and player opinions, researchers were keen to engage all stakeholders in the project and ensure their equal contribution to study design, management, interpretation and dissemination.

Researchers were keen to understand players' thoughts on the study, practicalities and recruitment, any preconceptions and their consideration on the likelihood of over- or under-reporting any outcomes of interest.

4.3 Format

Players were involved across the research cycle in several ways.

4.3.1 Collaborative management

Collaborative study management was achieved with lay representation on the study steering group. This included stakeholders from the sport's governing body, player-

representing bodies, participating Clubs and former players. This group was responsible for the management and appraisal of methodology including the recruitment strategy, results, interpretation, dissemination, press releases and coordinating lay summaries of the research undertaken.

4.3.2 Scoping discussions

Individual scoping discussions were undertaken with current and former, recreational and elite players during the design phase and before the dissemination of results. These informal sessions were aimed at understanding player sentiments on the feasibility of a player health study, key areas of interest and methodologies that may be most successful in order to contact and encourage participation amongst their peers. These discussions helped to adapt study design and recruitment strategies.

4.3.3 Player consultancy

Players were consulted in small group fora, which informed the study design, questionnaire content and recruitment methodology.

4.3.4 Collaboration in testing data collection procedures

Players were involved in testing data collection platforms, both for the ease of use, test-retest validity and reliability, and to feedback to researchers on their experience. Six former players were involved in test-retest validity assessments of the original questionnaire platform, providing feedback on any difficulties, which were then relayed to programmers to be remedied.

This chapter will focus predominantly on player consultancy within fora, the format, suggestions and outcomes of this. Terminology within involvement is diverse, with the terms 'patients', 'participants', 'consumers', 'collaborators', 'co-researchers' and 'consultants' previously used, depending on the research area and level of involvement. Within this context, those involved will be referred to as 'players', as their involvement was resultant of experiential knowledge due to their sports participation.

4.4 The fora

Player fora were semi-structured open forum discussions for players, established within a high-ranking Collegiate University setting. Current players, contactable through the University's male and female rugby teams' mailing lists, were approached by the respective administrators to attend one of two sessions. A description of the aims of the session and the overall player health study were included in the initial email. Sessions times and locations were scheduled according to player availability, and when confirmed, the session timings were again publicised using social media and routine communications within the University rugby mailing lists.

Players who expressed an interest following the initial call and confirmed their availability for a session were sent further details of the session's structure. They were informed of the player health study's ethical approval and that the session would be an informal open forum discussion of their thoughts and views on the structure and content of paper and online-format questionnaires, in order to inform the project's development.

Sessions were audio-recorded and transcribed by the player-lead, and reviewed by a member of the study team present at the sessions. The fora followed good research governance principles.

The fora were not intended to be the research activity of qualitative focus groups seeking to generate new knowledge, but were designed to be player-led group discussions, where players could inform researchers in designing and implementing an appropriate study design, which would accurately encompass player experiences and player-prioritised research aims.

The fora were led by a player-lead, with the support of a researcher in attendance. The player lead was a medical student on a research placement, with limited prior exposure to the research project. Fora were carried out in one of two College locations central to focus group contributors. Eleven players participated in the fora, with five in one session and six in the other. Ten players were male and one was female.

The multidisciplinary research team produced a topic guide for the sessions with the player-lead in collaboration with an experienced qualitative researcher. Players involved in the fora did not receive any research training prior to the fora, but the player-lead had several meetings with the research team, was given an overview of the project, and attended two meetings discussing topic guides and conducting fora, led by the qualitative researcher experienced in chairing focus groups.

Players were informed that information disclosed to the group would be anonymised after transcription, and treated confidentially and that the aims of the session were questionnaire and study feedback, and therefore there were no right or wrong responses. Prompts and probes were used in conversation where appropriate. Suggestions were extracted from transcripts by the player-lead and a researcher present at the sessions (MD). All player suggestions were discussed by the research team (JN, NKA and MD) and where possible implemented by a researcher who had been present at the fora (MD). Suggestions mentioned in both fora, or repeatedly by different players within a group were prioritised for inclusion.

4.4.1 Resultant alterations

Both fora communicated easily, freely discussing their playing experiences in order to inform the design of the study. During the review of the draft questionnaire, players asked questions which were often answered or discussed between the groups, before clarification was sought from the player-lead.

Players openly justified their comments and opinions with their playing history. Group consensus was not sought or encouraged, and the groups seemed comfortable demonstrating contrasting views. However players mostly agreed on concepts and considered issues in a cyclical manner, developing each other's ideas and demonstrating similar experiences. Specific alterations resulting from the fora are presented below (Table 13).

Table 13. Resultant alterations from consultative player fora

Player suggestions	Change resulting from player involvement
Use event markers	Event markers created for some questions, such as 'How often were you concussed?' becoming 'How often were you removed from play due to concussion?' to minimize recall bias.
Use ratios for incidence	Categories of 'every (n) games' to assess the incidence of more frequent injuries.
Long-term outcomes associated with other sports or injuries being separate from rugby	Categories of training, playing and non-rugby created for each injury reported.
Save and come back later	Players are now able to save information and re-enter the platform at a later point in time, to assist with sections such as Family History where this information may not be immediately available.
Reorder in order of importance	Current pains and primary outcome sections were placed earlier in the questionnaire.
Alter occupation categories	An additional category was added so players can put 'professional sports player' which previously would have had to be 'skilled manual worker'.
Include mental health status	Questions on anxiety and depression were added as players felt that this was relevant and that it would not act as a deterrent for participation

4.4.2 The group's views

Players were keen to ensure questions were phrased optimally and achieved this by relating their experience and understanding of the question back to the group. Comments such as 'I would put' demonstrated a consideration of the question's results, and an immersion in the project that often resulted in alterations to the final phraseology. Players suggested qualifications of questions, and when they would be unable to answer questions.

Both groups discussed the difficulty of accurately examining pain amongst former players. Players discussed their individual current pains, and the differences between acute and more long-term pain, and differences in pain between their joints.

Based on players' experiences and interests, or areas players considered pertinent to this population and important for the game to better understand, additional questions were suggested. Players were also asked directly what they would add to the questionnaire. Their suggestions included the availability of medical staff, and support following an injury. The way an injury affected a player's ability to work was considered both a valid marker of severity and also important to players in terms of its impact on their daily life. In addition to considering their own experience, players also discussed the experiences of others in games they had played in, or elite level games they had watched. This confirms the epistemological motivation for player involvement, and enables questionnaire alteration to mirror experiences, which may otherwise not have been captured.

Players asked the player-lead and researcher many questions during the sessions, mostly with regards to the rationale behind question choices, if these were standardised measures, and the aim of specific questions, so that players could consider if this concept was satisfactorily captured with that question. This demonstrated researcher and player-lead accountability to the players.

Players were made aware during the session that the questionnaire would be sent to former players at various amateur and professional levels of play. Players discussed the differences between former and current players in terms of their outlook and experiences of amateur and professional exposure, and often referred to their 'dads generation' as the older target audience. Recall bias, changes within the sport and its organisation over time, and a contrasting mentality between generations were discussed.

Some specific examples of players' reflections on the concepts and practicalities of the study are provided below (Table 14).

Table 14. Examples of player reflections and comments during the fora.

Topic	Player comments
Definition and interpretation of current pain	"So with the current pains thing, I, quite a lot of the time, a lot of my joints and stuff hurts" "I feel the pain in my knees is different to the pain I feel in my back" "What do people call pain? Like everyone kind of… a bit of a tweak after a game is different to – "
Additional question suggestions	"Did you get much support immediately after" (injury) "Did it affect your ability to work?" "Do you have strapping?" "Even if you are at a Club, like, how available the physios were?" "Something about the perceptions of warm up?"
Researcher accountability	"The family history only seems to be congenital…family physical things. Have you considered including neurology on that?" "Is there any mention of other sports, which lead to injuries? For example, things like boxing or martial arts?" "Where it says 'Have you ever been advised to not play or train for 3 weeks following a head injury?' is that 3 weeks a standard don't play thing?
Contrasting current and former player mentality and experience	"If you went to my dad's generation, he would probably tell you concussion's not a thing, because he's like that" "I'm sure former players would probably underestimate how many times that happened, because current players would remember" "The game has also changed quite a bit" "That just wouldn't have occurred'

4.5 Discussion

Key findings from the involvement activities described in this chapter are that the involvement of sports participants as consultants within fora is feasible for studies wishing to involve sporting cohorts with minimal inconvenience to those involved, and limited resource, and that sporting participants are a cohort capable of readily assuming a critical reviewer role, with little training, due to their existing experiential knowledge.

Significant experiential knowledge was demonstrated within fora, and it has been shown that this knowledge can contribute to alterations in study design, questions and functionality, which may facilitate player experience in participating in the player health study, and enable the more accurate collection of data for this group.

4.5.1 Sports participants as research partners

This is the first occasion to our knowledge, in which sports participants have been involved in research to specifically inform the research agenda with their experience. Within these sessions, players assumed the role of researchers, discussing how certain questions could be phrased for accurate response, and examining the bias that may be introduced with certain terminology. Female and male clubs were approached to be involved in the fora, however the uptake of female players was notably less than for males. This may be a reflection of participation in rugby union more generally and throughout the University, with more male players participating at College and University levels.

Players asked researchers if they had considered certain elements, issues or topics, contributing to addressing content validity. This also held researchers accountable to the fora, not only ensuring the effectiveness of questions and their outcomes, but also demonstrating involvement as a form of empowerment [348], for a group who may potentially be affected by the outcomes of this study to have been involved in its design, prioritisation and objectives.

Within this consultant role, topics of questionnaire fatigue and recall bias were raised, considered and addressed by players. This resulted in researchers observing similar processes to those experienced during initial questionnaire design, and appeared to validate some of the reflection processes previously navigated by researchers. The concept of players exploring and vocalising similar considerations to researchers may be due to similar experiences between players and the research team, or similarities in the values, assumptions and priorities of players and the researchers. The impact of involvement has previously been considered to be greatest where the skills and experiences of those involved differ from the research team.[344] As researchers and players were both undergraduate and postgraduate students at the same University this similar reflection process may be a result of shared values and experience.

Methods of actively empowering patients and members of the public to become involved in research have previously been suggested,[364,365] and research training for the public has been discussed as enabling members of the public to critique the research cycle more effectively and improve public confidence in articulating their sentiments.[354] During these fora, possibly due to the specific sporting population, players' prior

acquaintance with each other at a University or College level, or status as students of a high-ranking University, players readily assumed the critiquing researcher role desired within public consultations. Players appeared comfortable to appraise the questionnaire and research team, without a specific focus of the session being their empowerment or a notion of perceived power exchange. Players did not receive specific research training, which has been recommended in involvement, and described as assisting with more effective critique of research by those involved,[354,366] however, as student athletes with multiple demands on their time, researchers were concerned that an additional training session would have reduced attendance and proved too demanding for those involved.

The tutorial system in which many of the student-athletes will participate during their studies may influence their ease in debate and critique, as this group may be acclimatised to contributing to discussion, and developing each other's ideas. Training in involvement also introduces concerns of professionalization, with the potential of losing a 'lay perspective', either directly through training activities, or as a result of research knowledge and experiences gained through multiple projects.[367,368] Researchers were concerned that players undergoing training in research methodology may lose an ideological lay perspective, which was of substantial value to researchers, more so than obtaining critique on a perceived even footing, when this may be less applicable for this population.

The involvement of a rugby-playing medical student as group lead who was previously known to the majority of players, and had experienced limited exposure to the study with no official study role, but an awareness of the project and session aims, may have

facilitated the groups' interaction and success. The notion that user involvement is facilitated by a perceived lack of significant operationalized power structure between the users and researchers, and that the perception of equality is vital has been previously discussed,[369] and may have facilitated dialogue during these sessions.

Impact has been discussed as being associated with what users are asked to contribute.[344] In this exercise, players were given a very open brief of informing, correcting and providing feedback on the study, design, questionnaire and functionality, as opposed to other involvement activities such as amending consent forms and information sheets for lay understanding. Fora outcomes may have been more impactful and changes more substantial as a result of the initial, open brief given to players.

4.5.2 Session structure

A topic guide was used to broadly structure conversation and receive feedback on specific perceived weaknesses in the questionnaire, and study design. The topic guide followed the questionnaire structure, from first impressions through to any additional suggestions. Whilst this may have structured conversation more than necessary in a patient involvement forum, this structure also ensured players had many opportunities to comment on specific questions, ensured the entire questionnaire was discussed, and allowed relatively high-level and specific feedback, with inter-group consensus within relatively short fora sessions.

The session format of two fora, led by a student with a topic guide sufficiently detailed to stimulate conversation, address areas of researcher concern and provide session

structure, without relying on researcher input, allowed the session to be player-led. The research team was mindful of allowing the groups to feel capable of expressing opinions and concerns without having to, or feeling that they must find fault and make alterations to the study.

A member of the study team (MD) was present as an observer for the sessions. This provided the opportunity to observe the initial reaction of players to the questionnaire. Interpretation of these responses provided insight for the quantitative study team into potential motivators and deterrents for participation upon receiving the questionnaire. This opportunity has influenced methods of recruitment by including incentives, encouraging clubs to be ambassadors for the research, involving the teams' medical staff, considering timing in the season when questionnaires are sent, and considering designated times when players can participate together.

4.5.3 Strengths and weaknesses

The involvement of players within this questionnaire and study design was an informative process for the researchers, resulting in several changes to the questionnaire, and increased confidence of researchers that the questionnaire was approved by players and would collect player-centred information in the most precise way.

The questionnaire structure, specific questions and online functionality were altered and improved following recommendations (Table 12). Questions that may be more difficult for players to answer were highlighted to researchers, even if the fora or study team felt limited in scope to alter this whilst maintaining the study's overall aims.

As a consultative activity, the sessions were led by one particular player, who had delegated responsibilities for the sessions from the study team, as opposed to being truly led by a group of player-partners in collaborative decision-making that would be directly implemented. Researchers felt that player-collaboration and direction was present in other aspects of the study, and that the purpose of this session was more targeted feedback, which led to a consultative approach using a topic guide for structure.

The action taken in response to suggestions during involvement sessions has been highlighted as affecting the impact of PPI alterations,[344] whereby researchers maintaining significant power within collaborative projects, may not fully involve patients, or treat involvement as a tokenistic exercise, not fully integrating their suggestions into studies, thereby reducing the potential impact of the sessions. As researchers were conscious of balancing time constraints and practicality with as much player-control as possible, the majority of suggestions were implemented unless there was a strong argument for their non-inclusion. These were also agreed by three members of the study team, all of which were ambassadors of user involvement, not viewing involvement as detrimental to the research process.[367]

Further player involvement in the application of alterations and suggestions may have helped to ensure suggestions were embedded without bias from the study team, and that players maintained their authority throughout the process. However, researchers were concerned with burdening players, and the team felt that as ambassadors of

involvement, player suggestions would be integrated where feasible. The main reasons for non-inclusion were where player suggestions may be less relevant for former players or where a suggestion would involve multiple smaller questions to be accurately captured, therefore taking too much space within the questionnaire for a secondary study objective. Secondary fora, demonstrating where changes had been incorporated, and agreeing this with fora members, may have assisted to balance the level of involvement, to prevent this from being such a consultative approach, and move towards a more collaborative approach.

The need for more critical evaluation of involvement activities has been previously discussed and efforts have been made to improve the reporting of such activities and evaluate them[1,370] to prevent involvement being treated as a tokenistic exercise.[351] The number of changes in the questionnaire as a result of the fora, and process of players considering research questions, limitations and outcomes using their previous experience to inform this demonstrates the worth of these sessions within this project. Players did not, however, formally evaluate the process as has been suggested previously in the literature.[370,371] Within other studies, evaluation has been a questionnaire completed by forum members, to appraise the session and improve future activities.[371] This type of assessment may have been useful for this study, not necessarily to improve the output or impact of the involvement sessions, but to evaluate researchers, by ensuring players felt involved and heard during the sessions, and to suggest ways of improving player involvement for future studies.

A limitation to this exercise is that this was a consultative activity, and not fully collaborative. Although a player-lead facilitated the sessions, the group did not approve ensuing alteration or observe their suggestions being implemented in the study and questionnaire. This was predominantly because additional time demands on players would have been involved in this, and as student athletes, researchers were conscious to not excessively burden players.

The groups for this exercise were locally available to researchers and currently playing at an amateur level of play. Fora with retired players may have been useful in order to receive any additional feedback from a group with different experiences, who had also played in the amateur era of the sport and may have a different approach to the questionnaire based on these experiences. Fora attendees being current amateur players may however benefit the study by ensuring the relevance of the research project to this population who will be most influenced by the translated results, and who also form the majority of the playing population.

Diversity amongst involvement groups has been discussed as a difficulty within involvement research, where harder to reach groups, such as minority ethnic populations, older people, those with disabilities and those feeling they have little to contribute may be less inclined to participate.[346,372] Whilst diversity in experiential knowledge has been described as key to generating impactful outcomes,[344] the additional time needed to achieve a diverse group has been previously discussed.[373] The fora members for this exercise were not diverse, as they were young and mostly male, Caucasian University attendees at a high-ranking university. However, these attendees were similar to the current playing population within and outside of the University environment in this respect, as the target population for this study is an older, but still

majority male population of a relatively high socio-economic status, including cohorts recruited as former University attendees. Therefore, the fora members may be well aligned in experience and beliefs with the target population, as has been previously recommended.[1]

Patient involvement in research has previously been reported to increase the credibility of research,[355,374,375] and final reports with stakeholders.[376] However within this project, stakeholders appeared to not be as invested in player involvement, and player involvement appeared to be viewed as more of a time consuming additional process, than a necessary indication of good practise to generate a player-informed project. This may be due to the lack of player involvement in previous projects, and the absence of involvement's adoption into sporting research at present.

Discussion of the impact of public involvement has increased over recent years.[334,337,369,370] Difficulties in measuring impact, in terms of measuring the benefits involvement brings to a study and its processes, when this is mostly observational or anecdotal, qualitative data, and weaknesses in reporting standards have been discussed.[344,379] The GRIPP checklist[370] has been developed to improve the reporting of public involvement, alongside initiatives such as the Patient Involvement Impact Assessment Framework (PiiAF), and critical appraisal guidelines.[351] Clinical trials have been discussed as a way of more accurately quantifying the impact of involvement, whereby involvement is treated as an intervention, and its impact in one exposed (involved) group could be assessed over another non-exposed (not involved) group.[344] However this approach applies the quantitative and results-focused principles of evidence-based medicine to

public involvement, which may not be appropriate, or beneficial when considering individuals' experiences across a multitude of varying projects and research areas,[344] and also validates a more critical approach to involvement, far-removed from its ideal as a routine component of good research practise.[351] Measurement of impact within this chapter evolved predominantly around the recommendations from players, and the ensuing changes to the questionnaire and study design.

Players did not appear to seek to drastically influence the aims and objectives of the study. This may be that they did not feel empowered to do so, that they did not feel this was appropriate, or that they were satisfied with the researchers' existing aims. Players also did not re-prioritise research questions or aims, but did suggest changes that were incorporated where this was feasible. The main reasons for non-inclusion were that these might not influence long-term health outcomes in any reliable way (e.g. strapping of joints), or the difficulty of question integration into the existing functionality of the platform, balanced against the potential utility of these answers (e.g. 'Did you get much support immediately after?' would need to be integrated into the functionality of each injury for each joint, and require free text data collection, which would also cause additional complications when coding this in the analysis phase).

4.5.4 Main findings

The research team reflected upon player involvement in the study as very successful, however due to the multiple motivations for its inclusion in the study, including moralistic and ethical motivation within this charity-funded project, one could argue that with moralistic rationale for the involvement of sportspeople, the activity could not

be unsuccessful, if the sessions occurred and players attended. However, experiential and consequentialist elements were also demonstrated, with players divulging their experiences, and the process and questionnaire being altered as a result.

This study did not seek to create generalizable information with regards to players' experiences, nor examine similarities and differences between the experiences of players and how these could define the study. This chapter aimed to involve, and justify the involvement, of sporting participants in research, demonstrate that this is feasible within a DPhil project, and present the contributions and adaptations that this involvement process brought.

The main findings of this chapter are that sports participants can feasibly be involved in research with a similar justification to that of patients and members of the public. Sports participants were comfortable to participate in this activity, and experiential knowledge was exchanged, leading to alterations in the study such as goal setting, outcomes and the collection of sport-specific variables, informed by player experiences.

These findings justify and encourage the increased involvement of sports participants within research, and demonstrate that in addition to ethical and political imperatives of involving those in studies who will be affected by the results, consequentialist rationale for involvement is also satisfied.

Chapter 5 Health and morbidity amongst former elite rugby players*

Despite the global participation of over 7million individuals in rugby union across 120 countries,[380] the potential for increased morbidity, pain, disability and decreased quality of life amongst former players following their retirement from amateur or professional competition remains unexplored.

The World Health Organisation defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."[381] Despite some deliberation as to whether this maintains its relevance given increases in chronic disease and long-term morbidity,[382,383] this remains the most widely used definition of health. Population health has been given a broader definition by Dunn and Hayes (1999), including social and societal influences which may affect health: "the health of the population as measured by health status indicators and as influenced by social, economic, and physical environments, personal health practices, individual capacity and coping skills, human biology, early childhood development, and health services."[384]

Population health may examine the health status of particular groups with a view to examining health policies, outcomes, determinants, and interventions that could ameliorate health in a specific population of interest.[385] Sporting populations are unique cohorts with varying rates of injury, joint-specific loading and training patterns, and the potential for sporting subcultures and cultural norms to vary health behaviours.[156,326] Examining health outcomes amongst sports people and considering specific sporting

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populations for their longer term health not only assists in understanding health outcomes and determinants, but also indicates where there may be need for further intervention, in order to ensure informed and healthy sports participation for the highest number of participants.

The motivation for exploring athlete health is multifaceted, and health service providers, sports governing bodies and clinicians will all approach athlete health from a different position. Many aspects of player health may also be affected by level of participation, such as the duty of care of participants. A minority of players perform at a professional elite level, and at this level, sports governing bodies and clubs must proactively examine the exposure of their employees to health risks and understand how their employment may affect their health status both in the acute and longer-term. There are also moralistic concerns surrounding employment within elite sport. Before embarking on a career as a professional rugby player, and during their career are players sufficiently informed about the potential risks to their health? During a professional playing career does a player remain in control of their own health, and capable of influencing clinical decision making irrespective of their status in a team? Are clinical decisions made during and following their playing career informed by an awareness of longer term health outcomes, or are players being treated as commodities where their long-term health is being actively forsaken in favour of rapid return to play and commercial gain? With the absence of longer term health and morbidity data, clinicians may arguably have impaired decision-making, by not being supported in their awareness of longer term effects following their decision-making, or the likely health trajectory for individual athletes with specific sporting exposures.

However, at the recreational level of participation, the duty of care to participants moves from an employer's statutory responsibility to more of a public health concern. Sporting participation is encouraged in schools due to the known physical, social and psychological benefits of participation,[6,98] and there is a governmental initiative to increase participation in team sports across the country, including in rugby union.[386] Players, parents, teachers and policy makers need to have access to sufficiently clear data about the risks and benefits of participation, and a duty of care to ensure that within schools, children's safety is ensured and adverse risks can be monitored, limited and mitigated in order to ensure participant safety, and child safeguarding. The absence of such data in rugby union to date has been topical with on-going clinical academic debate.[226,386–388]

Where there are consequences to sports participation, these may also represent a future societal health cost. A high prevalence of injury, pain and potential long-term disability within sporting populations will place an additional burden on healthcare systems. In addition to the acute injury period, where up to 54.1% of schoolboy rugby injuries have been seen to result in emergency consultation with healthcare providers [387], the presence of increased morbidity or deteriorating health after playing will increase resource consumption amongst these groups. In addition to an individual's health affecting their individual daily activities and productivity, individuals with a worsened health state may subsequently rely on their support network. Besides these indirect burdens of disability, there are also direct financial implications of medications, consultations, investigatory procedures and therapies. In chronic conditions the use of health care resource may be of a longer duration, and possibly necessary to sustain the individual for their lifespan.

For players themselves, potential deficits in physical, mental and social health and wellbeing may affect their everyday lives and their functional capacity. The psychological impact of this may be more severe in contact sports participants, who have previously demonstrated higher physicality and movement competency. Movement competency is a central component of physical literacy,[389] which is generally developed in childhood and has been defined as 'the motivation, confidence, physical competence, understanding and knowledge to maintain physical activity at an individually appropriate level throughout life.'[390]

The emotional adjustment necessary for career transition from elite sport ("retirement") at a young age has been previously examined, including coping strategies used by semi-professional athletes during their career transition and contributors to their transition success, such as a lesser emotional investment in sport or lesser athletic identity during their career.[147,391] An early retirement from sporting activity not only involves emotional adjustment for players,[155,391,392] but also affects a players' identity, by both losing a sporting identity,[147] and also a career transition, at a point in which they have already achieved mastery in a specific environment. Establishing longer-term health and morbidity in this population will help prepare future generations of players for their likely health status following sports participation. In addition to identifying morbidities which may provide targets for intervention, players' expectations around longer-term health and function may be proactively managed, which may thus improve their health outcomes.[393]

In an aging population with increasing multimorbidity and resource consumption,[394] specific populations at risk of worse health in the longer term may provide intervention

opportunities to reduce health care expenditure. An increased understanding of modifiable risk factors and intervention targets for the reduction of rugby's contribution to societal health burdens will therefore benefit both players and health care providers. No studies to date have examined long-term overall rugby player health status, as compared with a general population comparator group, or examined risk factors that may contribute to adverse outcomes. For the aforementioned rationale of a duty of care, informed participation and safeguarding of players, protection of public health and potential resultant societal burden, this chapter will begin to consider rugby as a means of altering health status for participants. Given the elevated injury risk in rugby union compared with other elite sports,[108,142] rugby players may be at a higher risk for negative health outcomes in later life, and therefore an appropriate population with the potential for prevalent morbidity, where the interactions between health, physical activity, sports participation and sports injury can begin to be defined.

Firstly, the self-reported medical history of a group of elite rugby players will be examined, and secondly their health-related quality of life will be assessed. Population-based survey data from the English Longitudinal Study of Aging (ELSA) and the Health Survey for England (HSE) will be used to compare health outcomes between former University and International rugby players, and participants of these nationally representative population-based surveys.

5.1 Methodology

5.1.1 Study design

This chapter's design will be a cross-sectional comparison of self-reported physician-diagnosed morbidity and health-related quality of life, amongst former elite rugby players and members of the general population, who have participated in HSE and ELSA.

5.1.2 Participants

Former Oxbridge Blues and England Rugby Internationals Club (ERIC) participants specifying their sex as male, age and status as retired players (n=259) will be assessed alongside representative population controls from HSE and ELSA, as described in Chapter 2 (2.12).

ELSA 'core' members (those approached for ELSA aged 50+, and not their partners or other household occupants) were aged 50 and above, therefore age- and gender-matched comparison populations were not produced for those less than 50 years old. Standardised morbidity ratios will therefore exclude individuals less than 50 years of age. Joint replacement was only collected for individuals aged 60 or over in ELSA, so standardised morbidity ratios for joint replacement will compare individuals aged 60 years or above. Initial prevalence tables will examine all rugby players and all ELSA members, in addition to prevalence amongst rugby players aged 50 and above, and ELSA participants (Figure 13).

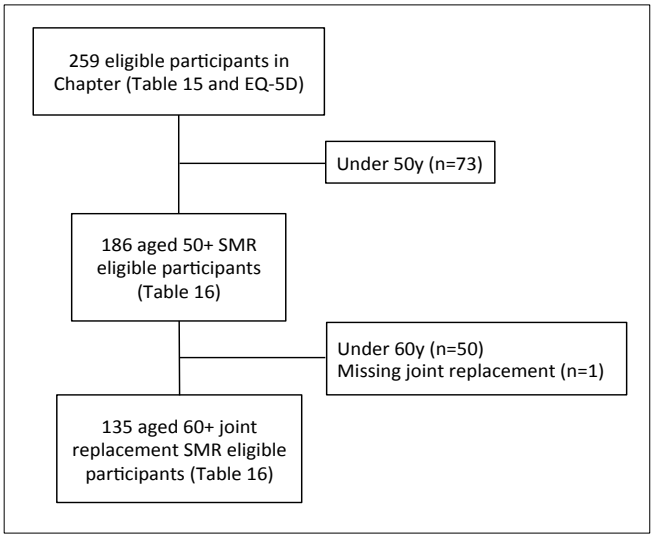


Figure 13. Rugby player analyses in this chapter, from prevalence data to inclusion in standardised morbidity ratio analyses

5.1.3 Statistical methods

Age standardised morbidity ratios[395] were calculated to demonstrate where health amongst former rugby players exceeded or was inferior to that of the age-standardised reference population.

Standardised morbidity ratios were calculated using the following formula.[396]

$$\text{SMR} = \frac{\text{the number of observed morbidity cases}}{\text{the number of morbidity cases if the age-sex specific prevalence was the same as those of the } \textit{standard} \text{ population}} = \frac{\Sigma\, di}{\Sigma Ei}$$

All cohorts were categorised into age bands (20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90-99). The number of participants in each age group was calculated for each cohort,

in addition to the number of participants with each morbidity, in each age group. ELSA was used as the reference population.

Disease prevalence per age category in ELSA =

$$\frac{\text{(n diseased in age category of ELSA)}}{\text{(n population in age category in ELSA)}}$$

This ELSA disease rate was then used to produce an expected rate of disease for each disease in each age category of the playing populations.

Disease prevalence expected in rugby cohort =

(Disease prevalence per age category in ELSA) x (population per age category in rugby cohort)

Standardised morbidity ratios were produced by dividing the number of diseased participants in each group by the number expected in that group from the ELSA reference value.

Descriptive statistics will be presented for EQ-5D responses within each domain: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. As HSE uses the EQ-5D-3L, whereas rugby uses the 5-level EQ-5D-5L, responses will be

dichotomised to a 'no problems' (EQ-5D '1' scoring) or 'problems' (EQ-5D '2+' scoring) variable.[329]

5.1.4 Variable selection

Variables from ELSA associated with identifying participants, their demography and health status (morbidity) were extracted from the UK Data Archive. Demographic variables that were missing from ELSA but previously collected in HSE ('Wave 0') were retrieved from the UK Data Archive at Wave 1, and carried forwards into the cross-sectional analysis where participants had previously been missing ('not applicable'). Wave 1 and Wave 0 datasets were merged using the unique patient identifier maintained throughout all Waves of ELSA.

The original phrasing associated with each morbidity variable is included in Appendix 4.

5.1.4.1 Morbidity

The prevalence of self-reported physician-diagnosed morbidity was assessed through a medical history in both sporting cohorts and ELSA. Variables were a priori selected as being contributors to poor health, and derived as binary variables (Table 15).

Table 15. Morbidities selected for comparison across cohorts

Health dimension	Variable
Respiratory	Asthma
Cardiovascular	Diabetes
	High blood pressure
	Heart problems
	Stroke
Mental	Anxiety
	Depression
	Dementia
Musculoskeletal	Osteoporosis
	Osteoarthritis
	Joint replacement (any)
	Hip replacement
	Knee replacement

Health-related quality of life

The 5-level EQ-5D-5L was used for primary data collection within rugby due to its increased capacity to discriminate participants with slight, moderate or severe problems within a dimension. The EQ-5D-5L has also been shown to provide stronger evidence of validity compared with the EQ-5D-3L.[338]

A general population comparison using the EQ-5D-5L was not available at the time of analysis. The English normative population provided by EuroQol is currently based on the EQ-5D-3L. Data will be presented for the EQ-5D-5L in sporting cohorts, EQ-5D-3L in HSE participants, and then a two-level variable of 'any problems' or 'no problems' will be derived for each domain, to permit comparison between these two populations.

5.1.5 Data harmonisation

Harmonisation was required where different question phraseology had been used, or different categories had been provided for parallel questions.

Where different question wording had been used, an additional variable was generated which would encompass the meaning of both questions. An example of this, for smoking where an 'ever smoke' variable was created, is shown below (Table 16).

Table 16. An example of variable harmonisation between cohorts

Cohort	Original variable	Question wording	Options
Rugby		Do you smoke?	Yes, No, Ex-smoker or don't know
ELSA Wave 1	hesmk	Have you ever smoked cigarettes?	
ELSA Wave 0	smkevr	Whether ever smoked cigarette/cigar/pipe	

Questions within ELSA reporting cardiovascular-related conditions or chronic illnesses were asked as one overarching question with a card showing possible diagnoses, and up to 10 variables generated where more than one of these diagnoses had occurred. A variable per illness was derived by producing a binary variable where an individual had reported a specific condition in response to any of the ten possible variables (Appendix 4).

The phrasing of a specific morbidity was not always parallel between groups, such as "diabetes" in rugby and "diabetes or high blood sugar" in ELSA and "high blood pressure" in rugby and "high blood pressure or hypertension" in ELSA (Appendix 4).

Where self-reported heart problems (binary variable) had been assessed within rugby, specific self-reported cardiac events in ELSA were combined to produce a comparable variable. Specific cardiac events in ELSA included angina, heart attack, heart murmur and an abnormal heart rhythm (Appendix 4).

Morbidities were condensed to a binary variable (yes/no) describing the presence or absence of each condition, and were given the same name across both rugby cohorts and ELSA.

Where categories differed in original variables, new variables were created with categories that would encompass the outcome of both variables in the original question. Examples of variables with different categories between the cohorts included marital status and ethnicity.

In ELSA, ethnicity is collapsed to white or non-white in order to avoid disclosure, whereas the primary data collection in rugby cohorts offered categories of white, mixed, black, Asian, other, don't know or a refusal to answer option. For marital status, ELSA includes more flexibility than the data categories within rugby, which were based on those used by the Office of National Statistics in the UK. In these cases, an overarching variable was derived to encompass both sets of categories (Table 17).

Table 17. The derivation of novel categories to encompass responses to multiple categorical variables.

ELSA categories	Rugby categories	Derived variable
Single, that is never married	Never married	Never married
Married, first and only marriage	Married	Married
Remarried, second or later marriage		
Legally separated	Separated	Separated
Divorced	Divorced	Divorced
Widowed	Widowed	Widowed
	Other	Other
	Don't know	Don't know

5.1.6 Missing data

5.1.6.1 Participants

Study participants missing responses for outcomes of interest will be:

i. Examined to see if the participant has completed the majority of other fields in the questionnaire
ii. Examined to see if it is the same participants who are repeatedly missing fields of interest
iii. Tabulated to see if there is a logic in the way participants have answered questions which may provide meaning to their missingness

As the questionnaire involved retrospective data collection, which may introduce recall bias, participants were given the option of answering 'don't know'. Participants answering 'don't know' were made missing for that outcome of interest.

The English Longitudinal Study of Ageing

ELSA used several codes to differentiate between missingness (-1: not applicable, -9: refusal, -8: don't know). Variables such as height, weight and BMI, measured during participation in HSE were carried through to the baseline data for ELSA. There were several options for these demographic data, the raw values (including 'unreliable measurements'), a variable detailing whether each measurement (height, weight, BMI) was valid, and then categories of BMI including or excluding unreliable measurements. Limited criteria for assessing the validity were presented, and as ELSA data will be compared to self-reported rugby data with known validity limitations, the raw height, weight and BMI data were used for analysis, with unreasonable outlier values made missing.

Within the validity variable for each ELSA measurement, those considered not valid were categorised into: not usable, refused, attempted but not obtained and not attempted. Reasons for not attempting measurements included participants being unstable on their feet or uneven ground for weighing scales.

The demographic data presented for ELSA (Table 18) shows a varying number of missing between variables. The rationale behind this missing data as provided by ELSA is detailed in Appendix 6.

5.2 Results

5.2.1 Participants

319 former Oxbridge and England rugby players (aged 60.1y± 16.1), with a mean playing exposure of 22.2 years (±5.3), completed this questionnaire study (20.3% response rate). Morbidity and health-related quality of life analyses were restricted to former players who confirmed male sex, former playing status and age (n=259). The majority of these former players responded to the questionnaire as England Rugby Internationals Club ('ERIC') members (n=142). Data is presented for all rugby players irrespective of age, and then when matched on age with ELSA participants for SMR analyses, players who were younger than 50 years (60 years for joint replacement) were no longer eligible, and were excluded.

5.2.2 Demographics

Former players were aged (mean(SD)) 60.1(16.1) years, whereas ELSA participants were 64.9(10.0) years, and HSE participants 53.4(16.3) years. The majority of participants were of a white ethnicity. The mean BMI of all cohorts was >25 kgm^2 (28.1kgm^2, 24.5 kgm^2 and 27.0kgm^2 for players, ELSA and HSE, respectively) therefore classified as pre-obese according to the World Health Organisation.[397] Smoking, marital and employment status are summarised below (Table 18). Former players were predominantly amateur players (83.6%) whose average total years of play was over two decades (22.2y).

Table 18. Descriptive characteristics of the rugby, ELSA and HSE cohorts. The results are expressed as mean (±SD) or number (%)

Characteristic	Rugby (N=259)		ELSA (N=5186)		HSE (N=2981)	
Age (yr)						
Mean (SD)	259	60.1 ± 16.1	5186	64.9 ± 10.0	2981	53.4 ± 16.3
Median (range)	259	62.0 (70.8)	5186	64.0 (49.0)	2981	52.0 (66.0)
Categorised: 20-29 30-39 40-49 50-59 60-69 70-79 80-89 90-99		5 (2%) 31 (12%) 37 (14%) 50 (19%) 44 (17%) 64 (25%) 27 (10%) 1 (1%)		0 0 0 1916 (37%) 1611 (31%) 1174 (23%) 447 (9%) 38 (1%)		224 (8%) 460 (15%) 603 (20%) 553 (19%) 579 (19%) 373 (12%) 171 (6%) 18 (1%)
White ethnicity – no. (%)	206	199 (97%)	5148	4973 (97%)	2978	2713 (91%)
Height (m)	252	1.82 ± 0.07	4856	1.73 ± 0.07	2963	1.76 ± 0.07
Weight (kg)	254	94.0± 15.2	4739	82.2 ± 13.1	2912	84.2 ± 14.8
BMI (kg/m^2)*	249	28.1 ± 3.7	4720	27.5 ± 3.8	2896	27.0 ± 4.3
BMI Categories:	249				2896	
Underweight		0				25 (1%)
Normal range		41 (17%)				989 (34%)
Overweight (pre-obese)		148 (59%)				1272 (44%)
Obese Class I		50 (20%)				467 (16%)
Obese Class II		8 (3%)				114 (4%)
Obese Class III		2 (1%)				29 (1%)
Ever smoker	257	25 (10%)	5162	3824 (74%)	2981	1832 (62%)
Marital status:	207		5185		3258	
Single/never married		6 (3%)		324 (6%)		471 (15%)
Married		171 (83%)		3916 (76%)		1991 (61%)
Separated		1 (1%)		64 (1%)		64 (2%)
Divorced		14 (7%)		399 (8%)		214 (7%)
Widowed		12 (6%)		482 (9%)		136 (4%)
Other		3 (2%)		0		382 (12%)
Amateur status	256	214 (84%)				
Total years of play						
Mean (SD)	245	22.2 ± 5.3				
Median (range)	245	22.0 (33)				
Employed or retired[1]	251	246 (98.0%)				

ELSA – The English Longitudinal Study of Ageing

HSE – The Health Survey for England
BMI – Body Mass Index

5.2.3 The prevalence of morbidity

Morbidity differed between the cohort of rugby players, and ELSA participants aged 50 and above (Table 19). The most prevalent morbidities amongst rugby players were osteoarthritis (60%), high blood pressure (28%) and joint replacement (24%), whereas the most prevalent morbidities amongst ELSA participants were high blood pressure (37%), heart problems (24%) and osteoarthritis (15%).

Table 19. The prevalence of morbidity amongst rugby players and ELSA participants.

	Rugby players (n=259) Aged 24-95		Rugby players (n=186) Aged 50-95		ELSA (n=5186) Aged 50-99	
Morbidity	Number of respondents	Number (%)	Number of respondents	Number (%)	Number of respondents	Number (%)
Asthma	245	24 (10%)	176	11 (6%)	5184	524 (10%)
Diabetes	238	5 (2%)	171	5 (3%)	5184	464 (9%)
High blood pressure	245	68 (28%)	178	66 (36%)	5184	1905 (37%)
Heart problems	241	43 (18%)	174	40 (22%)	5184	1236 (24%)
Stroke	198	6 (3%)	148	6 (3%)	5184	264 (5%)
Anxiety	242	18 (7%)	174	11 (6%)	5184	175 (3%)
Depression	241	15 (6%)	174	9 (5%)	5184	218 (4%)
Dementia	197	2 (1%)	147	2 (1%)	5184	36 (1%)
Osteoporosis	240*	9 (4%)	174	8 (4%)	5184	76 (1%)
Osteoarthritis	253	152 (60%)	184	112 (60%)	5017	729 (15%)
Joint replacement	253	60 (24%)	184	59 (32%)	3181•	202 (6%)
Hip replacement	254	39 (15%)	185	39 (21%)	3181•	126 (4%)
Knee replacement	254	23 (9%)	185	22 (12%)	3181•	80 (3%)

* denotes participant(s) responding 'don't know' made to missing.
• 60+ for joint replacement variables.

5.2.4 Health-related quality of life

Former players reported higher values of health today on the visual analogue scale (79.2) than participants in the HSE (77.8). No players reported incapacity within mobility, extreme pain/discomfort, or extreme anxiety and depression, whereas 0.3% of HSE participants reported confinement due to mobility, 3.5% reported extreme pain/discomfort and 1.9% reported extreme anxiety or depression. The highest number of any reported problems (2+) was seen within the domains of pain/discomfort (78.3% and 32.6% respectively), and mobility (47.4% and 18.5%).

When EQ-5D domains were dichotomised to problems (2+) or no problems (1) per domain, within the domains of mobility, pain/discomfort and usual activities, reported problems were twice as prevalent for former players in comparison with the HSE reference population (Figure 14).

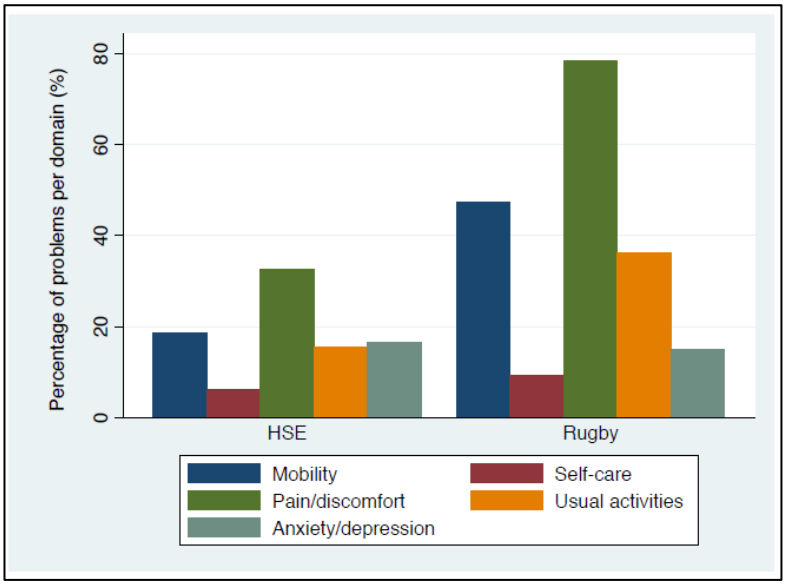


Figure 14. Percentage of EQ-5D problems per domain amongst Health Survey for England and rugby participants

5.2.5 Standardised morbidity ratios

Standardised morbidity ratios (SMR) are presented as the age-matched ratio of the rate of morbidity amongst former players aged 50 and over (60 and over for joint replacement) against the rate of disease in ELSA, where SMRs greater than 1 represent increased morbidity in comparison with a reference population.

Musculoskeletal morbidities of osteoarthritis (4.00, 95% CI 3.32-4.81), osteoporosis (2.69, 95% CI 1.35-5.38) hip replacement (6.42, 95% CI 4.69-8.79) and knee replacement (5.64, 95% CI 3.72-8.57) were significantly increased amongst former players compared with the reference population (Table 19). Anxiety was also more likely amongst former players than ELSA participants (2.00, CI 1.11-3.61). Depression (1.34, 95% CI 0.70-2.58) and dementia (1.40, 95% CI 0.35-5.61) were elevated amongst former players in comparison with the ELSA participants; however this did not reach statistical significance.

Diabetes was significantly reduced amongst former players compared with ELSA participants (0.28, 95% CI 0.11-0.66). Asthma, high blood pressure, heart problems and stroke demonstrated a reduced SMR (<1), which did not reach statistical significance (Table 20).

Table 20. Age standardised morbidity ratios for rugby players aged 50+ (n=186) against an ELSA reference population (n=5186)

Morbidity	Prevalence	Expected prevalence*	SMR	95% CI
Asthma	11 (6%)	18 (10%)	0.60	0.33 to 1.08
Diabetes	5 (3%)	18 (10%)	**0.28**	**0.11** to **0.66**
High blood pressure	66 (36%)	71 (38%)	0.92	0.73 to 1.18
Heart problems	48 (22%)	50 (27%)	0.80	0.59 to 1.09
Stroke	6 (3%)	11 (6%)	0.52	0.23 to 1.16
Anxiety	11 (6%)	6 (3%)	**2.00**	**1.11** to **3.61**
Depression	9 (5%)	7 (4%)	1.34	0.70 to 2.58
Dementia	2 (1%)	1 (1%)	1.40	0.35 to 5.61
Osteoporosis	8 (4%)	3 (2%)	**2.69**	**1.35** to **5.38**
Osteoarthritis	112 (60%)	28 (15%)	**4.00**	**3.32** to **4.81**
Joint replacement	59 (32%)	10 (5%)	**6.02**	**4.66** to **7.77**
Hip replacement	39 (21%)	6 (3%)	**6.42**	**4.69** to **8.79**
Knee replacement	22 (12%)	4 (2%)	**5.64**	**3.72** to **8.57**

*Denotes n to the nearest whole number

5.3 Discussion

5.3.1 Main findings

Key findings from this study, based on over 250 former elite rugby players, are that there are differences in morbidity and health-related quality of life between former rugby players and participants in representative population-based surveys. Amongst participants aged 50 and above, age-matched standardised morbidity ratios show diabetes to be significantly lower amongst former players (0.28, 95% CI 0.11-0.66), whereas osteoporosis (2.69, 95% CI 1.35-5.38), osteoarthritis (4.00, 95% CI 3.32-4.81), joint replacement (6.02, 95% CI 4.66-7.77), and site-specific joint replacement at the hip (6.42, 95% CI 4.69-8.79) and knee (5.64, 95% CI 3.72-8.57) are significantly more likely amongst former players than ELSA participants. Other cardiovascular outcomes of high blood

pressure, stroke and heart problems were reduced amongst players when compared with the reference population in SMR analyses, but this did not reach statistical significance.

Problems with health-related quality of life (EQ-5D 2+) were most highly reported amongst rugby players in each domain. This was most notable for pain/discomfort (78.3%), mobility (47.4%), and usual activities (38.1%), where reported problems were twice as prevalent amongst rugby players. This comprehensive approach to analyses and health status is seminal within rugby union, and by undertaking SMR analyses against a nationally representative population, may advance sports epidemiology towards using patient-orientated routinely collected outcome data of a high quality.

5.3.2 Strengths and limitations

Key strengths of this study include the national representativeness of ERIC participants, and the cohorts not mandating geographical inclusion or exclusion criteria, the comprehensive approach to player health including multiple morbidities and health-related quality of life, and the comparability of questions and definitions across cohorts within the chapter.

A main limitation for this chapter is not having a population-based control group that encompasses younger ages. ELSA is one of few population-based surveys to assess all health outcomes measured in this chapter, however it also only features participants aged 50 and over and therefore differences in morbidity amongst younger participants will not be captured in this study. Many of the morbidities examined in this chapter are

highly associated with age, and a younger population-based cohort with more similar age ranges would have increased the sample size for analyses, and provided more detail on health status in younger and older players.

The cross-sectional study design prevents the examination of morbidity over time or discussion of causality between rugby exposure and the development of morbidity. Whilst permitting a more complete analysis of health status with this cross-sectional approach, it also prevents discussion of the causality of outcomes; and we therefore are not able to infer that rugby is causing or influencing these outcomes.

Morbidity and health-related quality of life amongst former elite players may not be generalisable to the entire playing population. The majority of players do not play at the elite level, and these results may not represent morbidity amongst other populations such as females and recreational players. Females have different inherent risks of morbidity, and therefore were excluded from analyses to ensure generalisability to former, male, elite players, of that generation. However, these results indicate morbidities which are increased beyond the reference population, and therefore in need of management and prevention. Elite players represent a tightly phenotyped cohort with an explicit denominator who may demonstrate the most significant health burden and therefore increased the feasibility of generating positive findings within this study, should there be differences in health status. Future research should seek to understand the extent to which these morbidities are seen amongst recreational players, and in the modern era of the sport.

For less common morbidities (<5% prevalence) in this relatively small sample, drawing robust inferences is challenging. Morbidities such as osteoporosis and dementia with small numbers of cases and wider confidence intervals may require further study in order to validate and support these findings.

This study was designed to assess morbidity, health related quality of life, and overall health status. Therefore, a cross-sectional study design was the most feasible study design to use moderate resource and assess multiple morbidities within this population. In order to encourage response rate, the length of the questionnaire was central. Concurrent diseases may affect health related quality of life, and congenital morbidity has not been collected. Worse health, as indicated by the EQ-5D, may be resultant of other morbidity that we are not able to account for. However, the presence of congenital disorders and other concurrent diseases may reasonably be reduced amongst elite sporting participants, and the potential for external unqualified previous morbidity or trauma to influence outcomes remains consistent for both sporting and representative populations. Multi-morbidity has not been explored within this chapter, which may further elucidate health status for these populations. However, this was not the focus of this chapter, but will be a focus of future work within this cohort.

All study outcomes are reported by players themselves, which may be a less robust measure of morbidity than direct measurement, or a further validation study from patient records. However, this approach permitted the assessment of multiple morbidities within project timescales, and self-reported outcomes were consistent between all cohorts. Self-reported morbidity outcomes were also of physician-diagnosed morbidity, and therefore participants reporting these outcomes should have previously

undertaken physician consultation and investigation, thereby increasing the sensitivity of reported outcomes. Within osteoarthritis, online self-reported physician diagnosed knee and hip osteoarthritis have correctly identified most cases and non-cases of clinical OA, compared with the gold standard. [308] This study suggested that these case definitions had utility for the identification of community and population-base lower limb OA.[308]

Whilst there were not specific inclusion or exclusion criteria besides data cleaning in order to improve generalisability, as a self-report questionnaire which was undertaken predominantly online, those without the capacity to consent or complete the questionnaire, be that physical function, access to computers or lower literacy levels, may have not chosen to participate by proxy.

Whilst study participation was reasonable, the overall response rate amongst former players was approximately 20%. Players who were more inclined to participate may be those with pre-existing medical diagnoses, particularly if players feel that these are associated with rugby. Conversely, people with dementia or depression will be ess likely to participate. Therefore, there should be some caution surrounding the interpretation of these results as fully generalizable to former elite rugby players, and a consideration that these may be biased towards players with worse health.

There was not an available representative population comparison for the EQ-5D-5L at the time of analysis. A 'problems' or 'no problems' variable per domain was derived in order to compare between EQ-5D questionnaire results, despite the further information

provided by the EQ-5D-5L. This approach has been previously been used by EuroQoL.[329] However, the EQ-5D-5L would have allowed a more standardised comparison, and provided a more detailed assessment of health-related quality of life differences between these populations.

Similarities in morbidity phraseology were considered to be a strength of the study, however variables with differences included diabetes, where individuals in ELSA were asked a broader definition of diabetes, including 'high blood sugar', which may include individuals who are pre-diabetic. This may have inflated the prevalence of these diagnoses, and would affect the SMR results in favour of healthier rugby players, due to the more specific case definition in this population. Therefore the specific phraseology used to assess each morbidity (Appendices 4 and 5) should be considered alongside the interpretation of these results.

5.3.3 Interpretation

The results from this chapter can be interpreted as demonstrating that health differs between former, elite rugby players, and participants of population-based health surveys, and that former rugby players may exhibit decreased morbidity within some domains compared to an age and gender-standardised reference population, however they may also exhibit increased morbidity in other domains.

In addition to the aforementioned potential limitations of self-reported outcomes, differences in age between cohorts, the association of morbidities with age, and response

bias, there are further considerations that should be considered in the interpretation of this chapter.

Players who have been recruited to this study were selected as elite players of Oxbridge Universities or the English International team. Both university attendees and international sports participants may be of a higher socioeconomic status than participants in both the HSE and ELSA, and socioeconomic status is positively associated with health.[398] This may mean that elite players, as a population largely from higher socioeconomic backgrounds, are predisposed to better health, and less morbidity, than the representative populations. This may affect the results of the study as reduced morbidity amongst players due to socioeconomic status would bias the standardised morbidity ratio in favour of elite rugby players having a better health status compared to the reference population. As parallel measures of socio-economic status were not available in both cohorts, we were unable to account for this. As a population with a higher socioeconomic status, and involving participants of a higher level of education, recruited due to their prior attendance of a high-ranking academic institution, there is the potential for former players to have had increased consultation than the reference population. This may be resultant of increased healthcare provision after an elite playing career, or an increased awareness from players of their physical functioning and health status, having participated in elite sport, and therefore having an increased awareness of and eagerness for an explanation for any symptoms that may be abnormal for them.

Osteoarthritis-related outcomes, such as physician-diagnosed OA, joint replacement and hip and knee replacement were most significantly elevated amongst players in comparison with the reference population. The definition of OA used within the rugby

questionnaire was "Have you ever been told you have wear and tear, degeneration or Osteoarthritis by a doctor?" Including 'wear and tear' within this definition is acknowledged to lessen the sensitivity of diagnoses, and thereby increase the prevalence of self-reported physician diagnosed OA. However, participants may have less recall of the specific morbidity or what 'type' of arthritis they have been previously diagnosed with, but aware that this diagnosis included an explanation of 'wear and tear' or degeneration of the joints, as this phraseology has traditionally been associated with OA.[23,399] This more inclusive definition of OA may have increased the prevalence of physician-diagnosed OA amongst former players, and therefore increased the standardised morbidity ratio for this morbidity.

Harder endpoint outcomes of joint replacement, hip and knee replacement were also significantly higher amongst former players, and therefore we can be reasonably confident that OA outcomes are increased amongst former players beyond those of the general population. Understanding differences in socioeconomic status and the potential for differences in the uptake of joint replacement between the populations would further increase our confidence in this finding. However, increases in OA outcomes have previously been observed in other sporting populations particularly team sports and weightlifting athletes,[400,401] which supports this finding amongst former rugby players. This finding could potentially be explained by sporting injury amongst former sports participants,[72,321,362,402–404] or repetitive microtrauma[117,405] during participation in collision sports, increased surgical intervention in the pursuit of a faster return to play,[70] or increased joint loading in terms of both body mass and repetitive sport-specific loading patterns throughout a career. The extent of this difference may support proactively managing OA risk in former elite playing populations. Initial OA management includes guidance on OA care, education on the condition and non-pharmacological management

with exercise and weight loss.[406] Weight management and exercise are components of a healthy lifestyle, and the emphasis of this to players transitioning from the game, and physicians in general practice, may increase awareness and begin to manage this increased 4- to 6-fold increased risk of OA outcomes.

Results were not presented for the entire cohort, but for players included in this analysis, who confirmed their age, gender and retired status. Of these criteria, most players were excluded due to missing playing status, or their status as currently playing rugby. Ensuring participants were male and former players was considered to be data cleaning, aimed at ensuring the sample for analysis is wholly representative of the target population, and generalizable to that group. It is acknowledged that these values may be missing as players believed these answers, such as sex, to be evident. However, the importance of reliable data, which represents the morbidity and health-related quality of life status of the target population, was deemed to be more important than potentially excluding a subset of participants who may not be representative, through still playing, and therefore potentially reporting fewer morbidities and more current pain and discomfort due to maintained rugby exposure and potentially acute sporting injury.

Excluding non-core members from ELSA reduced the number of eligible participants for analyses; however the initial core member sample was nationally representative and this was a priority for the matched reference populations. Many of the morbidities under examination in this study are associated with age, and HSE includes data from infants. As the focus of this study was health amongst adult males, participants younger than the rugby age groups were excluded, as including younger participants may artificially

inflate standardised morbidity ratios towards worse health outcomes amongst rugby players.

Participants in HSE without self-complete booklet data (n=280) were also excluded. Participants who had not completed the self-complete booklet may be HSE participants with lower literacy levels, or illnesses preventing their participation in a questionnaire study. However, this booklet contained EQ-5D data, and therefore participants without this data would be missing key outcomes of interest.

5.3.4 Comparison to other studies

Diabetes is associated with numerous chronic health conditions, and predisposes individuals to cardiovascular disease, blindness, kidney disease and depression.[29] We found the rates of diabetes were significantly reduced amongst former players, in comparison with ELSA participants. Risk factors for diabetes include age, ethnicity, family history, smoking, obesity and physical activity.[30] As rugby and ELSA participants were matched on age and of similar ethnicity, these risk factors should not explain the significant difference between the groups. Family history was not available for rugby players, and therefore we were unable to account for this. Significantly less rugby players had smoked than ELSA participants (10% and 74% respectively), which could feasibly contribute to these statistical differences.

Obesity was similar between the groups (BMI 28.1 and 27.5 respectively), with both groups being classified as pre-obese.[397] However, BMI has been discussed as an invalid measure of adiposity in many athletic populations,[407] as a high BMI amongst individuals

with a high lean muscle mass may represent a high fat-free mass to fat mass ratio, and using the World Health Organisation categorisation, 65% of players within semi-finalist teams at the 2003 Rugby World Cup were classified as overweight, and 25% obese.[408] As no other measures of adiposity were obtained, the hypothesis of a higher BMI masking a lower level of adiposity amongst rugby players, and therefore lower risk for diabetes cannot be tested, but may partly explain the difference in standardised morbidity ratios.

The most probable explanation for the significant difference in diabetes prevalence between former players and ELSA participants may be increased lifetime physical activity amongst former rugby players. Sporting and non-sporting physical activity has previously been associated with decreased prevalence of type 2 diabetes,[8] and moderate intensity physical activity has been associated with a 30% reduction in diabetes (RR 0.69), which was sustained as a 17% reduction after adjustment for BMI.[409]

Other cardiovascular outcomes, such as high blood pressure, heart problems and stroke were reduced amongst former players, but the results did not reach statistical significance. This may suggest protective effects of elite rugby participation on cardiovascular health, which we may have been underpowered to detect, or were masked by the older ages of both players and the population comparison group. Cardiovascular outcomes are relatively frequent and highly associated with age,[410,411] and therefore as opposed to being prevented by participation in rugby union, these may be delayed, whereby members of the general population develop worse cardiovascular health at an earlier age than rugby players. Weight management and players' higher level of physical activity may be protective, however these outcomes are highly associated with age. Therefore, SMR analyses of players aged 50+ may disguise this

association between participation in elite rugby union and better cardiovascular health, however this analysis would need to be replicated in a younger cohort and with more players within each age group, in order to establish this.

We found that self-reported osteoporosis was significantly increased amongst former players in comparison with ELSA participants. This result was unexpected, and will therefore require further investigation. Previously, higher total body bone mineral density, and regional bone mineral density has been found amongst rugby players, and physical activity has been shown to be preventative of osteoporosis [412–414]. Therefore osteoporosis in later life amongst this elite, highly weight bearing, sporting population may be counterintuitive. Osteoporosis was the outcome for which most uncertainty was indicated ('don't know'), and there is the potential that some players may have confused prior diagnoses of osteoporosis and osteoarthritis. However, 'don't know' responses were treated as missing, and therefore those answered as uncertain will not have influenced this analysis directly, however may indicate uncertainty around the term or its diagnosis.

Players were significantly taller than ELSA participants, and lean body stature has previously been considered as an indication for hip fracture.[415] Whilst these former players may not be lean individuals, due to their current BMI falling predominantly in the WHO overweight category, and the high BMI values seen amongst elite rugby players,[408] height may partially explain the differences in osteoporosis between these populations, or represent a mechanistic rationale for the difference in osteoporosis results which we are unable to further define within this study.

Anxiety was twice as prevalent amongst former players as it was amongst the ELSA population, although this remained a relatively rare outcome (6% and 3% respectively). Using the EQ-5D, 85% of players reported no current problems with anxiety or depression. Potential explanations for the higher likelihood of anxiety amongst former players may be character traits amongst elite sporting populations contributing to poorer mental health outcomes, or distressing effects of career transition.[147,416] Physician-diagnosed anxiety, as with other morbidity outcomes, were examined as 'ever' morbidity, without a specific timeframe. This may also therefore include any diagnoses from players' transition time. The elite playing population under study is inclusive of International players and former Oxbridge students. The mental health status of University students has been subject to previous discussion, and moderate severity anxiety has been seen to have an increased prevalence (47.1%) amongst students, compared with stress and depression.[417] It is therefore hypothesised that the increased SMR for former players may be a product of the elite International and University population recruited.

5.3.5 Generalisability

Oxbridge University and England rugby cohorts are by nature elite, and whilst the target population is representative of elite players at the time, it may not be representative of lower level rugby players, or modern era players. Lower level rugby players may demonstrate better health than elite players, due to less injury within lower levels of the community game.[191] However player match hours may be higher for recreational/social participants, than for amateur and semi-professional participants,[194] meaning these players may be more exposed to sport, but less exposed to injury.

As former players participating in a cross-sectional study, the players within this study must be within a certain age range, and therefore decade of play. The sport of rugby union has changed significantly over these decades with rule changes, notably the professionalization of rugby union which is known to be associated with a higher number of injuries.[172,418] Modern rugby union will be very different to that played by participants in this study, in terms of injury incidence and severity, phases and styles of play, which may be explained by game-related factors such as increased ball in play time.[183] Therefore, the health status measured within this cohort may not reflect that of elite players today. Elite players of today will be unlikely to achieve the playing durations seen within this cohort, due to the increases in speed and physicality within the game, partly encouraged by professionalization. This may mean health outcomes for current elite players would be improved beyond those seen here, with less morbidity due to the improved injury management, training load management and shorter career duration. However, the increased number of collisions, body mass and speed of players, and number of games per season [142] may also affect overall health, increasing the potential long-term musculoskeletal burden for these players. Without further data to elucidate differences in playing load and demands between players of this and the modern era, the findings presented here may not be generalizable outside of the elite, male playing population of that era.

5.4 Main findings and conclusion

The main findings of this chapter are that there are differences in morbidity and health related quality of life between former elite rugby players, and a representative group of the adult general population. Musculoskeletal morbidities, such as physician-diagnosed osteoarthritis, joint replacement and osteoporosis were increased amongst rugby players, whereas diabetes was reduced. Former players also experienced more problems

with pain/discomfort, mobility and their usual activities than the reference population.

This chapter suggests opportunities for intervention targets, which may allow early detection, and risk factor modification, in this group at a significantly increased risk of negative health outcomes, such as osteoarthritis and joint replacement. It also suggests that individuals at risk of diabetes may be encouraged towards physical activity such as rugby union, and that elite sports participation may be protective of this element of cardiovascular health. Further research to identify what motivates these increases and decreases is necessary in order to increase the relevance of public health messaging, and target interventions to where they may be most successfully implemented.

Chapter 6 Rugby playing load as a risk factor for osteoarthritis: A cross-sectional multivariable analysis

Osteoarthritis (OA) is a leading cause of pain and disability that is known to affect quality of life[419,420] and has been associated with mortality.[421,422] Despite discussion of different OA phenotypes and the on-going refinement of OA definition in order to provide potential therapeutic targets,[259,423] OA remains relatively poorly understood, with a substantial societal burden. The end-stage treatment of OA, joint replacement is estimated to cost over £850 million annually,[253] which is projected to increase.[258] Post-traumatic OA, defined as OA following joint trauma, may be a more progressive form of OA,[424] and therefore individuals with a history of joint injury may provide an accelerated model of OA development, and potentially end-stage disease.

Previous chapters have suggested an increased prevalence of joint replacement, at the person and joint-levels, amongst former rugby players. Amongst the general population risk factors for OA have been well described (1.4.2.), however amongst contact sports participants such as rugby players, the risk factors may well be different. Furthermore, the lack of clarity surrounding sport-specific risk factors and their association with OA in the absence of injury has been previously described.[319,425,426] In this popular participation sport, acknowledged to have an elevated exposure to severe injury,[108,427] there is a need to identify sporting and injury-related risk factors which may be contributing to this elevated risk.

The aims of this chapter are to establish the associations between rugby playing exposure and OA-outcome at the knee, hip and shoulder. This chapter will explore which risk factors are associated with OA, and how this differs according to the site and definition of OA used.

6.1 Methodology

This chapter will use a cross-sectional study design, of rugby-specific playing load exposures and self-reported OA-outcomes collected during the player health study. The recruitment, setting and data collection strategies for this study have been previously described (Chapter 2).

6.1.1 Participants

Data from male, former, age-specified rugby players recruited to the player health study will be analysed within this chapter (n=259).

6.1.2 Variable selection

Rugby-specific risk factors with biological plausibility of being associated with OA, through playing exposure to rugby, or suspected mechanisms of OA, were obtained through self-reported playing history in the player health questionnaire. These were a priori selected following a literature review, and the data obtained from the questionnaire.

Rugby-specific risk factors encompassing elements of playing exposure were a priori selected as possible risk factors for OA. These were as follows:

1. The total number of years of play (continuous variable) – derived from:

   An individual's age at their last competitive season (years) and their age at first 'schoolboy' or casual game (years)

2. The number of years an individual spent at their highest level of play (continuous variable):

   For how many years did you play at this level?

3. The number of matches a player participated in during their career (continuous variable):

   Approximately how many matches (playing for at least half the match) did you take part in during your career? (Continuous variable)

4. An individual's age at their first schoolboy game (continuous variable):

   Age at first 'schoolboy' or casual game"

The number of years an individual had played at their highest level of play was derived and inclusive of International play, but also included other levels of play, such as players who had not played International rugby, but had played within the Premiership, or their individual reported highest level of play.

All numerical variables were continuous variables for the analyses, in order to maintain power by not losing degrees of freedom with the use of categorical variables.

Outcomes reflecting the prevalence of self-reported OA at the joint level will be derived from the following questions, for the knee hip and shoulder:

1. NHANES pain (binary variable):
   "Have you had any pain in your (hip or groin/knees/shoulders) on most days of the last month?"

2. Physician-diagnosed OA (binary variable):
   "Have you ever been told you have wear and tear, degeneration or Osteoarthritis by a doctor? If yes, where? "

   Hip – left/right (binary variable)

   Knee – left/right (binary variable)

   Shoulder – left/right (binary variable)

3. Joint replacement (binary variable):
   "Have you ever had joint replacement surgery?" (Binary variable)

   If yes, please indicate the number below for each joint and side:

   Hip – left/right (categorical variable)

   Knee – left/right (categorical variable)

   Shoulder – left/right (categorical variable)

Confounding variables are other variables that may affect the true association between an exposure and the outcome of interest. All models will be adjusted for age and current weight as these may be associated with rugby exposure, and are highly associated with OA-outcomes. Retired players who are older may have played more years of rugby, and will have an increased likelihood of an OA diagnosis. Retired players who are heavier

will have an increased risk of OA, and their weight may have affected, or be affected by, playing exposure.

Models were adjusted for weight as opposed to BMI as BMI is known to be an inaccurate measurement of obesity in athletes, particularly rugby players,[428,429] and it is hypothesised that BMI as a measure of somatotype, may also reflect other player selection factors rather than weight-bearing load at specific joints.

The derivation of confounding variables is shown below.

Age at questionnaire completion (continuous variable) – derived from:

Date of birth (DD/MM/YY)

Weight (kg, continuous variable) – derived from:

Weight: (kg) / (stones/pounds)

Joint injury is known to be highly associated with NHANES pain, OA and joint replacement, particularly at the hip and knee.[72–74,270,321] The relationship between injury and OA has been described more commonly at the knee than the hip and the shoulder. Whilst being highly associated with the OA-outcomes assessed in this chapter (OA pain, physician-diagnosed OA and joint replacement), injury may also be associated with playing load. Match injury has been shown to occur on average at least once per season for professional players, or approximately 70 injuries per professional team per season.[181] Therefore, those individuals playing for more seasons or games, with an increased

playing load throughout their career, may also be at an increased risk of OA, but resultant from accumulated injuries, and not rugby itself. Therefore, within the relationship between playing load and OA prevalence, it was considered that injury should be treated as though it is on the causal pathway, due to its known association with OA, and also its incidence within rugby union. I will not be adjusting for injury in all models, but presenting this side by side as a joint-specific risk factor for OA.

6.1.3 Statistical methods

Data analysis was undertaken using Stata 13.1. Descriptive statistics (mean (standard deviation) for continuous variables (median (IQR) if non-normally distributed), and number (percentage) for categorical variables) are presented for all exposure and outcome variables for the cohort of former players (n=259).

Univariable logistic regression was used to examine the relationship between sport-specific predictors and binary joint-specific OA-outcomes of NHANES pain, joint replacement or GPOA at the knee, hip and shoulder. These analyses were then adjusted for age, and age and weight respectively. Any site-specific injury, and rugby site-specific injuries are also presented as risk factors for all binary OA-outcomes.

Regression diagnostics were undertaken to check the assumptions of the logistic regression model in all produced final models. The assumptions that were tested were linearity of effect on the outcome, looking for outliers. Fractional polynomials were used to test the evidence of linearity. Where there was evidence of non-linearity on the outcome, the risk factor variable was categorised. This occurred for the total years of

play risk factor, which was categorised into year groups (<20 and 20+) and total number of matches during an individual's career (career matches), which was categorised into match exposure groups (<300 and 300+), with a data-driven approach, depending on the cut point for that outcome.

Values of less than 50 matches within a career were excluded as anomalous due to their high leverage (influence on the models). This is shown in Appendix 7, in addition to an example of a fractional polynomial plot for a model where linearity was not met, and after categorization (Appendix 8).

Regression results for the number of matches an individual played in their career is shown per 50 matches. The association of playing load with OA-outcomes at the knee will be shown in detail. The results for the hip and shoulder will be summarised, and appear fully in the appendices.

6.2 Results

6.2.1 Participants

Former players were a mean age of 60 years, with an average weight of 94 kg (Table 21). Demographics for this cohort are shown in more detail in Chapter 4 (4.3.2).

Table 21. Demographics and player load risk factors of former rugby players

Variable	All former (n=259)	Mean (SD)	Median (IQR)
Age (years)	259	60.1 (16.1)	62 (27)
Weight (kg)	254	94.0 (15.2)	91 (17.6)
Age at first schoolboy game (years)	256	10.2 (2.5)	11 (3)
Number of matches	205	377 (189)	350 (250)
Total years of rugby	243	22.2 (5.3)	22 (6)
Number of years at the highest level	254	4.7 (3.4)	4 (5)

6.2.2 Risk factor variables

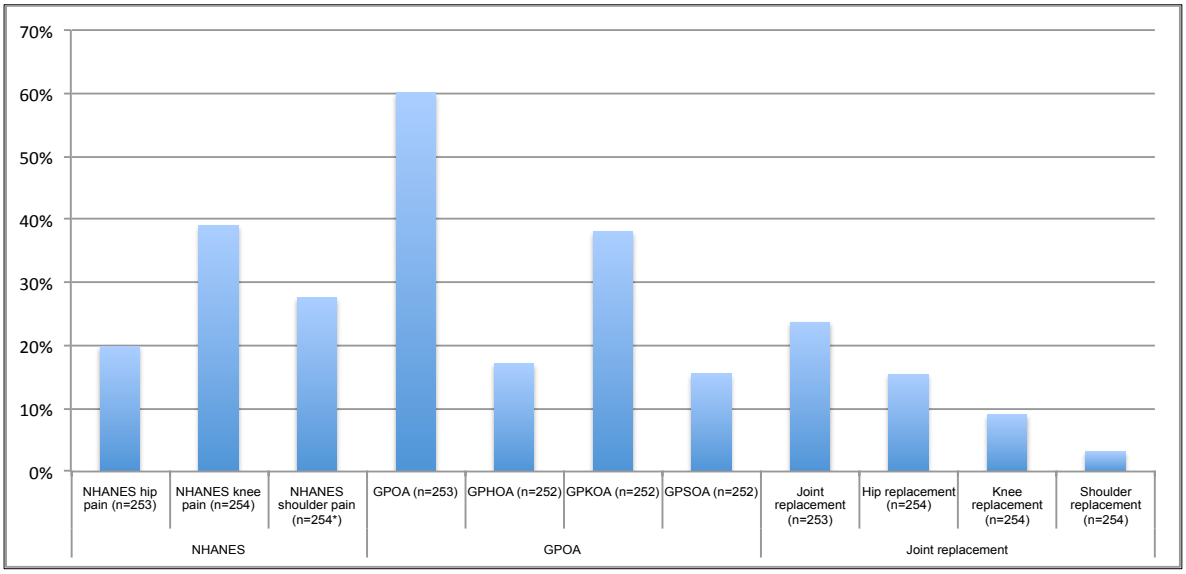
Players were on average 10 years old at their first schoolboy game, and played for over 20 years. Players played at their highest level of participation for over 4 years, and played approximately 377 games throughout their career, although a substantial standard deviation and interquartile range were seen for this risk factor, suggesting a wide within-group variance amongst this cohort (Chapter 3).

6.2.3 Outcome variables

A high proportion of former players reported physician-diagnosed OA (60.1%), and more than 1 in 5 former players had experienced joint replacement surgery (23.7%).

The most prevalent outcome at the joint level was NHANES pain at the knee (39.0%). The most prevalent outcomes at the hip and shoulder were also NHANES pain (Figure 15).

Figure 15. OA outcomes of joint replacement, NHANES pain and physician-diagnosed OA, at the knee, hip and shoulder of former rugby players.



6.2.4 The association of playing exposure with OA outcomes at the knee

6.2.4.1 NHANES knee pain

No rugby-related exposures were associated with a higher risk of NHANES knee pain (NHKP). Each year of participation in rugby union was associated with a non-significant 1% decrease in the odds of NHKP, which remained robust when adjusted for age, and age and weight respectively (Table 22). The number of years a player spent at their highest level of play was associated with a non-significant 5% decrease per year in the odds of NHKP (p=0.165). Career matches and age at first game appeared to have little effect on NHKP (Table 22).

Table 22. Logistic regression analyses of playing load risk factors for NHANES pain at the knee

	NHANES Knee Pain			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	242	0.99 (0.94-1.04)	0.759	242	0.99 (0.95-1.04)	0.780	237	0.99 (0.94-1.04)	0.650
Years at highest level	249	0.95 (0.88-1.02)	0.165	249	0.95 (0.88-1.03)	0.182	244	0.95 (0.88-1.03)	0.218
Number of matches (per 50 matches)	201	1.01 (0.93-1.09)	0.808	201	0.99 (0.92-1.08)	0.873	197	1.00 (0.92-1.09)	0.954
Age at first schoolboy game (years)	252	1.01 (0.92-1.12)	0.772	252	0.99 (0.89-1.10)	0.840	247	0.98 (0.88-1.10)	0.766

6.2.4.2 Physician-diagnosed knee OA

The effect of playing exposure appeared more pronounced for GPKOA than for NHKP. The total number of years of rugby an individual had played was associated with a 5% higher risk of GPKOA per year (p=0.047), which when adjusted for age remained associated with a 5% higher risk of GPKOA per year (p=0.047). After adjustment for age and weight, this attenuated to a 4% higher risk per year, and became non-significant (p=0.107). When categorised due to non-linearity, more than 20 years of rugby was associated with two and a half times (OR 2.51) the risk of GPKOA (p=0.001).

The number of years an individual played at their highest level of play was seen to have no effect on GPKOA (Table 22), whereas the number of matches a player played during their career was associated with a 3% higher but non-significant risk of GPKOA per 50 matches (p=0.275) in univariable logistic regression. After adjustment for age, this was a 2% higher risk of GPKOA per year (p=0.591), which became non-significantly protective

after adjustment for age and weight (Table 23). A player's age at their first game was seen to have little effect on their risk of GPKOA (Table 23).

Table 23. Logistic regression analyses of playing load risk factors for physician-diagnosed OA at the knee

	GPOA Knee			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	238	**1.05 (1.00-1.11)**	**0.047**	238	**1.05 (1.00-1.11)**	**0.047**	233	1.04 (0.99-1.10)	0.107
Years at highest level	247	1.00 (0.93-1.08)	0.919	247	1.01 (0.93-1.08)	0.896	242	1.00 (0.92-1.08)	0.970
Number of matches (per 50 matches)	196	1.03 (0.95-1.12)	0.275	196	1.02 (0.94-1.11)	0.591	192	0.99 (0.91-1.08)	0.870
Age at first schoolboy game (years)	249	0.99 (0.89-1.09)	0.813	249	0.97 (0.87-1.08)	0.590	244	0.97 (0.87-1.08)	0.573
Total years of rugby (categorised)	252	**2.51 (1.43-4.38)**	**0.001**	252	**2.56 (1.46-4.50)**	**0.001**	247	**2.34 (1.32-4.14)**	**0.004**

Knee replacement

Higher risks of knee replacement (TKR) were seen with higher rugby exposures, but the majority of these exposures did not reach statistical significance. Each year of participation in rugby union was associated with a 6% increase in the odds of TKR, but this association did not reach significance (p=0.131). Adjusting for age demonstrated a stronger association, with each year being associated with an 8% increased likelihood of knee replacement, which was a borderline significant association (p=0.081). However adjusting for weight in addition to age decreased this association (Table 24).

Each year at a player's highest level of play was associated with a 3-4% higher risk of TKR, which did not reach significance (p=0.696). The number of matches a player played in their career was associated with an 18% increase in their odds of TKR (OR 1.18) per 50 matches (p=0.010). Adjusting for age lowered the effect of this association (OR 1.13), however it remained of borderline significance (p=0.050). After adjustment for age and weight, an 11% increase risk was sustained, but this was no longer significant (p=0.128). When categorised, higher numbers of career matches (>300) were associated with almost a four-fold increase (OR 3.80) in the risk of knee replacement, but this risk estimate did not reach statistical significance (p=0.081). After adjusting for age, age and weight respectively, the effect of the number of matches on knee replacement was slightly attenuated (OR 3.65 and OR 2.81), and remained non-significant (p=0.097 and p=0.193).

Table 24. Logistic regression analyses of playing load risk factors for joint replacement at the knee

	TJR Knee			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	240	1.06 (0.98-1.15)	0.131	240	1.08 (0.99-1.17)	0.081	235	1.06 (0.98-1.16)	0.141
Years at highest level	249	1.03 (0.90-1.16)	0.696	249	1.04 (0.92-1.17)	0.509	244	1.03 (0.91-1.17)	0.597
Number of matches (per 50 matches)	198	**1.18 (1.04-1.33)**	**0.010**	198	**1.13 (1.00-1.28)**	**0.050**	194	1.11 (0.97-1.26)	0.128
Age at first schoolboy game (years)	251	1.04 (0.87-1.24)	0.638	251	0.88 (0.72-1.09)	0.242	246	0.87 (0.70-1.07)	0.172
Number of matches (categorised)	198	3.80 (0.85-17.09)	0.081	198	3.65 (0.79-16.81)	0.097	194	2.81 (0.59-13.27)	0.193

A summary of the association between playing exposure and OA-outcomes at the knee in final adjusted multivariable models is shown below (Figure 16).

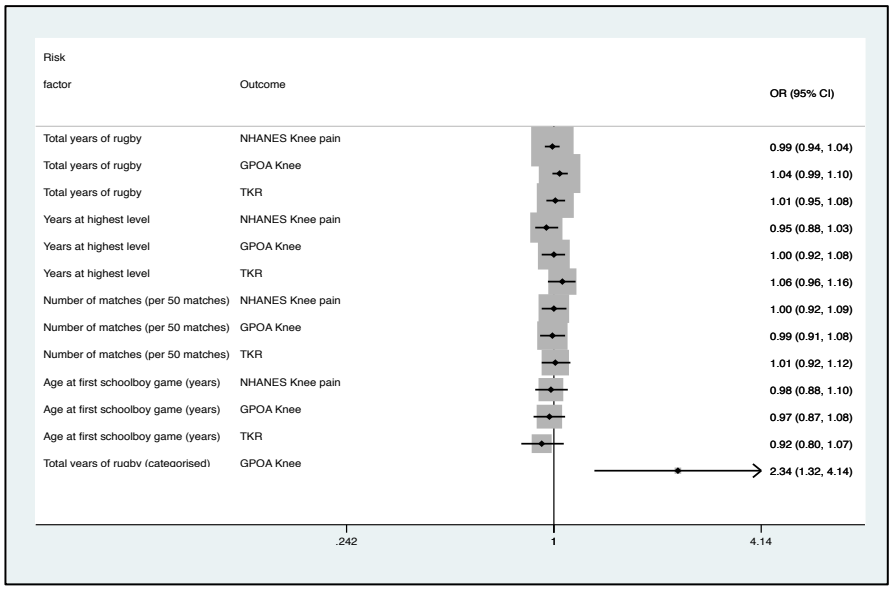


Figure 16. Final models adjusted for age and weight for the association between rugby exposure and OA-outcome at the knee.

6.2.5 The association of playing exposure with OA outcomes at the hip

6.2.5.1 NHANES hip pain

No significant associations were seen between rugby playing load and NHANES hip pain (NHHP). All playing exposures were slightly and non-significantly protective in final models (OR 0.91-OR 0.99). The highest association for NHHP was for the age of a player at their first game, where each year older a player was, demonstrated a 9% lower odds of NHHP, which did not reach statistical significance (Appendix 9).

6.2.5.2 Physician-diagnosed hip OA

There were no significant associations between rugby exposure and GPOA at the hip. The number of career matches was associated with a 5% increase in GPHOA (p=0.348), which became slightly and non-significantly protective after adjustment for age and weight (OR 0.99). The age of a player at their first game of rugby was associated with 7%

lower odds of GPHOA per year in univariable analysis, but this did not reach significance (p=0.355). When adjusting for age and age and weight, a player's age at their first game was associated with a 7% reduction per year of age in the risk of GPHOA per year, which did not reach statistical significance (Figure 17).

6.2.5.3 Hip replacement

There were no significant associations between rugby exposure and joint replacement at the hip. The number of years at a player's highest level of play was associated with a 3% higher likelihood of hip replacement per year in the fully adjusted model, but this association did not reach significance (p=0.583).

The number of career matches was associated with a non-significant 5% higher likelihood of THR in unadjusted univariable logistic regression (p=0.346), but after adjustment for age and weight, this became 1% less per year (p=0.839). The age of a player at their first game was associated with an 8% increase in the likelihood of THR per year of age (p=0.292), which became non-significantly protective (OR 0.91) from the unadjusted model when adjusting for age (p=0.257).

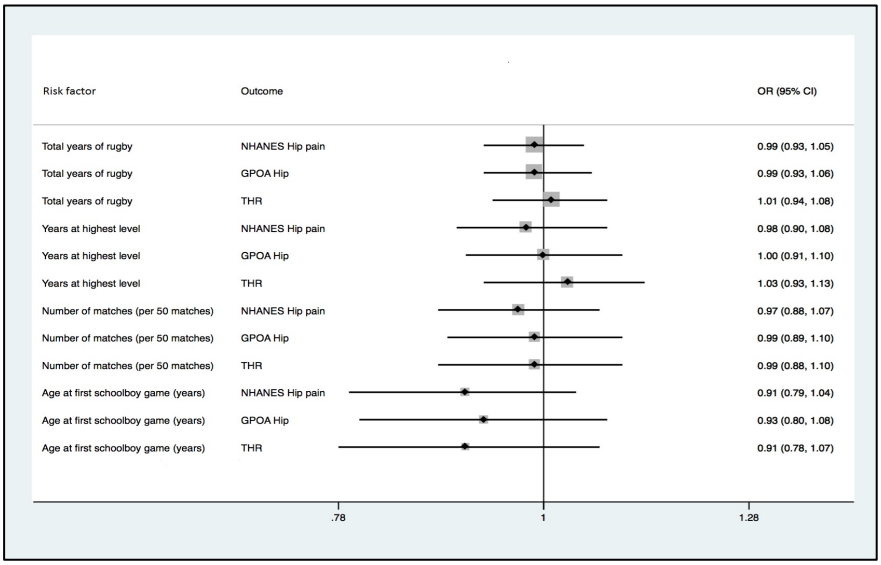


Figure 17. Final models adjusted for age and weight for the association between rugby exposure and OA-outcome at the hip.

6.2.6 The association of playing exposure with OA outcomes at the shoulder

6.2.6.1 NHANES shoulder pain

No rugby exposures were significantly associated with NHANES shoulder pain (NHSP). The number of years an individual played at their highest level of play was associated with 4% lower likelihood of NHANES shoulder pain per year, which did not reach significance (p=0.303). The number of career matches was associated with a non-significant 4% increase in the risk of NHSP per 50 matches (p=0.396). A player's age at their first schoolboy game was associated with a 5% increase in NHSP per year (older), which did not reach statistical significance (p=0.453). Adjusting for age and age and weight respectively had less effect on the models than for knee and hip models (Appendix 9).

6.2.6.2 Physician-diagnosed shoulder OA

The total years of rugby an individual played was associated with 5% higher odds of physician-diagnosed shoulder (GPSOA) per year in univariable analysis, which was of borderline statistical significance (p=0.056). Adjusting for age had little effect on this model (p=0.057), however adjusting for age and weight slightly attenuated this association (OR 1.06), which became non-significant (p=0.109). The number of years an individual played at their highest level of play was associated with 11% lower odds of GPSOA after adjustment for age and weight, which was of borderline significance (p=0.068). The total number of career matches was associated with a 10% increase in the likelihood of GPSOA per 50-match increase (OR 1.10), which was of borderline statistical significance (p=0.07). However when adjusted for age and weight, this was attenuated (OR 1.08, p=0.186). The age at which a player played their first schoolboy game was associated with 4% higher odds of GPSOA per year (p=0.637).

6.2.6.3 Shoulder replacement

A player's total years of rugby was associated with a 3% lower likelihood of shoulder replacement per year across all models, which did not reach statistical significance (final model, p=0.625). The number of years a player had played at their highest level of rugby was associated with a 3% higher likelihood of shoulder replacement, but this did not reach significance (p=0.772). The number of career matches an individual played increased their risk of shoulder replacement by 18% per 50 matches in univariable analysis, however this did not reach statistical significance (p=0.178). When adjusted for age and weight, this association lessened (OR 1.14), and remained non-significant (p=0.293). An individual's age at their first schoolboy game was associated with a non-

significant 16% higher risk of shoulder replacement per year of age (p=0.282), which lowered to a 7% higher risk when adjusted for age and weight (p=0.664).

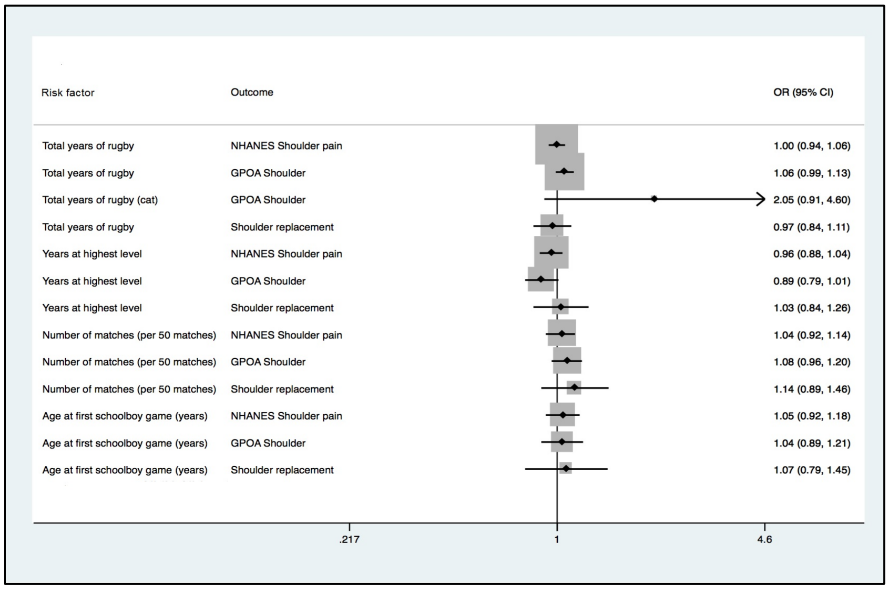


Figure 18. Final models adjusted for age and weight for the association between rugby exposure and OA-outcomes at the shoulder.

6.2.7 The association of joint injury and rugby injury with OA-outcomes

6.2.7.1 Injury and knee OA

Knee injury was associated with almost 5 times the risk of NHKP (p=0.000). When adjusted for age, the odds of NHKP were higher (OR 5.44), and when adjusted for age and weight, knee injury and NHKP were more highly associated (OR 5.47), whilst remaining highly significant (p=0.000). Rugby-specific knee injury was also associated with almost 5 times the risk of NHKP (OR 4.76), which again was stronger when adjusting for age and weight (OR 5.74).

Knee injury was also associated with almost 5 times the risk of GPKOA (p=0.000), which again became stronger when adjusted for age and weight (Appendix 11). Rugby-specific knee injury was associated with over 3 times the risk of GPKOA (OR 3.64), which was higher when adjusted for age (OR 4.01) however was slightly lowered (OR 3.97), when adjusting for age and weight, whilst remaining highly significant (p=0.000).

Knee injury was also associated with a 33% greater risk of TKR, which did not reach statistical significance (p=0.534). Adjusting for age was seen to increase the effect size (OR 2.07), but this remained non-significant (p=0.139). Adjusting for age and weight again influence this association (OR 2.35), which remained non-significant (p=0.093). Rugby injury at the knee was associated with a non-significant 57% higher likelihood of TKR (p=0.339). After adjusting for age, players with a rugby knee injury had over twice the risk of TKR (OR 2.52), but this was of borderline statistical significance (p=0.067). When adjusting for age and weight, this association became statistically significant (p=0.047), with injured players being almost at three times the risk of having knee replacement (OR 2.80).

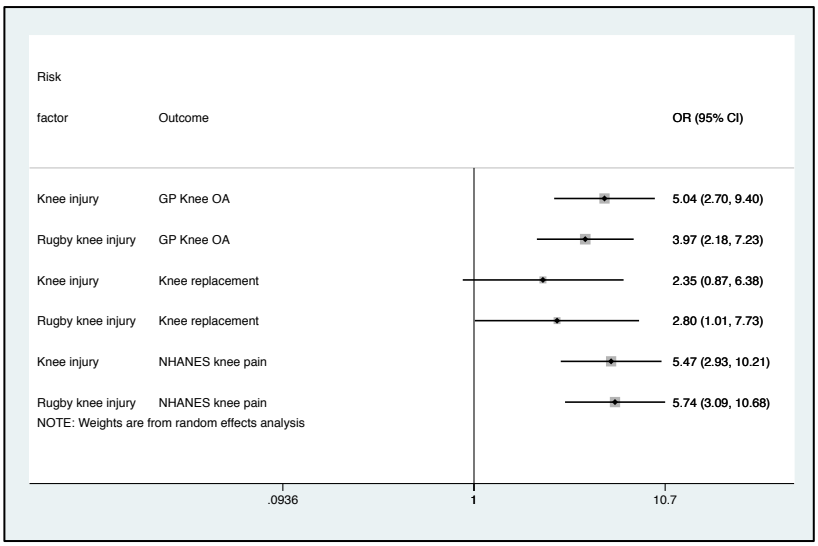


Figure 19. Final models adjusted for age and weight for the association of any knee injury and rugby-specific knee injury with OA-outcomes at the knee.

6.2.7.2 Injury and hip OA

Hip injury and rugby-specific (playing or training) hip injury, were significantly associated with hip OA across all OA-outcomes and all unadjusted and adjusted models ($p<0.011$)

In univariable logistic regression, hip injury was significantly associated with GPHOA (OR 4.39), and rugby-specific hip injury was also significantly associated with GPHOA (OR 3.64). Adjusting for age, and age and weight respectively, increased the effect of injury on OA-outcome, and the final models presented over 7 times the likelihood of GPHOA with injury (OR 7.30), and over 5 times the likelihood of GPHOA with rugby injury (OR 5.81).

Hip injury (OR 6.28) and rugby-specific hip injury (OR 4.73) were also significantly associated with hip replacement across all models ($p=0.000$). Adjusting for age increased the effect of injury on hip replacement (OR 21.5 and OR 13.8 respectively), however adjusting for age and weight in the final model lowered the likelihood of hip replacement compared to the previous model adjusted for age, for any hip injury (OR 20.76) and rugby-specific hip injury (OR 13.22) respectively.

Hip injury and rugby-specific hip injury were significantly associated with NHHP (OR 2.49 and 3.16 respectively). Adjusting for age was seen to increase the effect of injury on NHHP, however adjusting for age and weight slightly lowered this, producing a final

model of more than double the likelihood of NHHP with hip injury (p=0.006) and over three times the likelihood of NHHP with rugby injury (p=0.002).

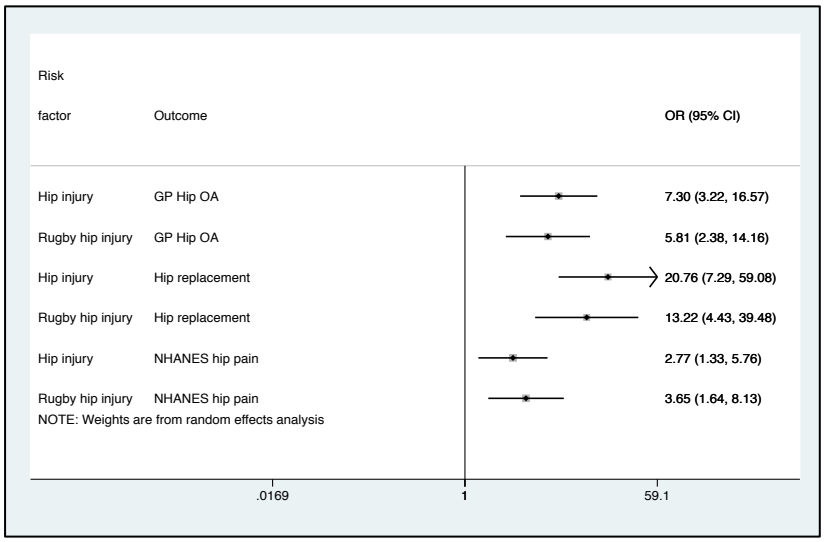


Figure 20. Final models adjusted for age and weight for the association of hip injury and rugby-specific hip injury with OA-outcomes at the hip.

6.2.7.3 Injury and shoulder OA

Shoulder injury and rugby-specific shoulder injury, were significantly associated with all shoulder OA-outcomes, across all models.

Shoulder injury and rugby-specific shoulder injury were highly associated with NHSP in all models. Shoulder injury was seen to increase the likelihood of NHSP over 7 times (OR 7.14). Adjusting for age further increased this association (OR 7.21), as did adjustment for age and weight (OR 8.08). Rugby-specific shoulder injury was associated with over 5 times the odds of NHSP (OR 5.20). Adjusting for age, and age and weight

respectively increased this association, with over 5 times the risk of NHSP for those with a rugby-specific shoulder injury (OR 5.88) in the fully adjusted model (p=0.000).

Shoulder injury, and rugby-specific shoulder injury, were associated with over 6 times and just under 6 times the likelihood of GPSOA respectively (OR 6.22 and 5.93). Adjusting for age, and then age and weight, increased the strength of the association to over 7 times the likelihood of GPSOA following shoulder injury (OR 7.07) and rugby-specific shoulder injury (OR 7.77).

The association between rugby-specific shoulder injury and shoulder replacement was strongest of all regression models in this chapter, albeit with wide confidence intervals. Shoulder injury and rugby-specific shoulder injury were highly associated with shoulder replacement (OR 10.87 and 12.39 respectively), and after adjusting for age this association increased, with injured players over 13 times as likely to experience shoulder replacement (p=0.018), and those with rugby-specific shoulder injury over 15 times as likely to report shoulder replacement (p=0.012). After adjusting for age and weight, the likelihood of shoulder replacement was almost 12 times higher after injury (OR 12.91), whereas for rugby-specific shoulder injury, the likelihood of GPSOA was over 22 times the likelihood (OR 22.41).

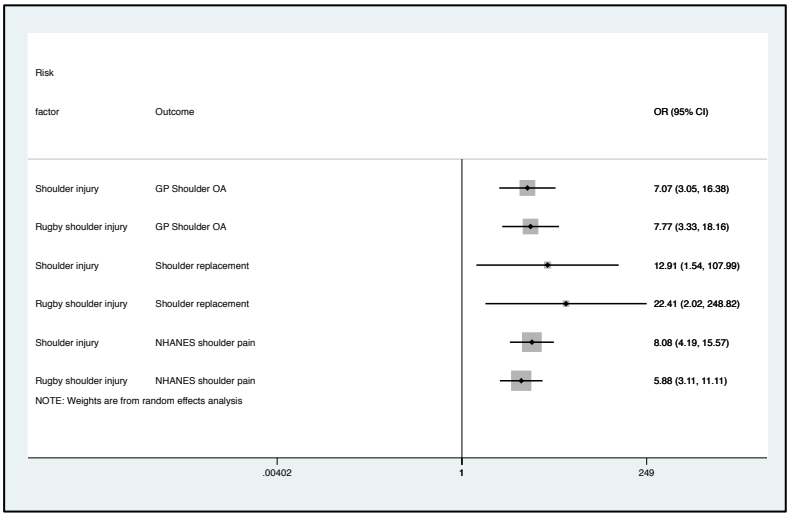


Figure 21. Final models adjusted for age and weight for the association of any shoulder injury and rugby-specific shoulder injury with OA-outcomes at the shoulder.

6.3 Discussion

6.3.1 Main findings

Key findings from this chapter are that playing load influences OA-outcome, and that this varies between joints and OA-outcomes. Results were most consistent for the knee, where smaller confidence intervals were seen, and the total years of play was associated with a 5% increase in GPKOA per year, and over two and a half times the risk of GPKOA when playing for over 20 years, in unadjusted logistic regression, which remained over twice the risk (OR 2.34) in the fully adjusted model, categorised due to nonlinearity. Playing exposure was also associated with KOA when assessing the total number of matches. There was an 18% increase in the risk of TKR per 50 matches (p=0.010), which became 11% and was attenuated after adjustment for age. There were also borderline associations for playing exposure with shoulder replacement, but these did not reach statistical significance.

Injury was highly associated with the development of OA across all joints and OA-outcomes, aside from the association between knee injury and knee replacement, which was not associated in univariable analysis (p=0.534), although this approached significance when adjusted for age and weight (p=0.093). The associations were strongest between shoulder injuries and replacement and hip injuries and replacement.

The relationship of injury with OA-outcomes differed between joints. At the hip and shoulder, the associations were strongest between injury and replacement, followed by GPOA and NHANES pain, whereas at the knee, the association was strongest for NHANES pain, followed by GPOA and joint replacement.

6.3.2 Strengths and limitations

Strengths of this chapter include that it has established a way to measure lifetime playing exposure, albeit with relatively crude measurements, examined the association between rugby and osteoarthritis for the first time, across multiple sites, and with multiple measures of OA representing different stages of disease. This chapter also presents the first evidence within rugby union of injury being associated with worse longer term outcomes, and therefore intervention targets within this population.

A key limitation for this chapter is the cross-sectional study design. Whilst being the only feasible method of data collection to answer these questions in the timescale of a doctoral program, causality in these cross-sectional associations cannot be inferred, and therefore we are unable to conclude that there is a causal association between any risk factors and OA-outcomes.

There is the possibility of a reporting bias, where individuals who have experienced OA-outcomes may reflect negatively on their playing experiences, thereby inflating the values consciously or unconsciously and over-reporting rugby exposures. The player involvement process (Chapter 4) undertaken in this study was designed to mitigate this concern. However, the possibility remains that there could be a responder bias, with individuals with significant joint problems being at an increased likelihood of responding to the questionnaire.

All of the playing load measures used in this chapter are relatively crude lifetime measurements, which have been self-reported. All outcome measures are also self-reported. These measurements may not be precise, and if repeated with the same players, or validated against playing records, there may be some variation. The crude lifetime nature of these measurements should be considered in their interpretation, and the purpose of this chapter is not to specifically define cut points of 'healthy' playing exposure or excess risk, but to establish whether a player's established elevated OA-outcomes are associated with their rugby playing exposures, and if so, at which joints and in which direction.

In a cohort recruited as elite participants of a contact sport, there may be other population-driven biases that affect OA-outcome and reporting. Players who have maintained a career spanning more years, more years at an elite level, a higher match exposure and started at a younger age may be those who are more pain tolerant and therefore less susceptible to OA pain. There was a substantial within-group difference in

risk factors such as number of games within an individual's career. This wide variance could be an effect of recall bias, or support a 'healthy players affect', should individuals who are more injury-adverse, for example due to biomechanical or innate physiological characteristics, be those 'surviving' to reach higher levels of elite sporting exposure. The number of years at the highest level of play was associated with an 11% reduction per year in the risk of shoulder replacement, which was of borderline significance (p=0.068). This may represent a survival effect at the highest level of play in this cross-sectional study, where those remaining at a higher level of play are those capable of sustaining a longer duration career, a 'healthy player' effect.

Almost 200 regression analyses have been undertaken within this chapter, which encourages the consideration of multiple testing and increases the possibility of a false positive, i.e. a significant association detected where this is not the case. However, as all the outcomes are correlated and similar associations with the outcome are to be expected, this was considered to be less of an issue than for studies where outcomes are not correlated, and therefore no adjustment or corrections to analyses have been undertaken.

The sample size is relatively small, particularly for rarer outcomes, such as those at the shoulder. Results with fewer observations should be cautiously interpreted, due to the increased potential leverage of outliers. The interpretation of logistic regression results may not necessarily be understandable in terms of risk per year, in comparison with categorical variables. However, the relatively small sample size meant continuous risk factors were favourable, and results should be more accurate as a result of this. There are also stratifications that could be carried out to test for interactions, for example, amateur

or professional career status, which may affect the influence of the risk factor on the outcome between these two groups. However, again due to sample size and concerns around the accuracy of these potential findings, these stratifications were not undertaken.

6.3.3 Interpretation

The results from this chapter can be interpreted as providing little evidence for an association between playing exposure and OA-outcomes at the shoulder and hip, however demonstrating an influence of playing load, particularly the total years of play, at the knee. The relationship between playing exposure and OA outcome has been seen to vary by joint, and the knee in particular may be more susceptible to an influence from playing exposure than the hip or shoulder.

Severe joint injury, and severe rugby-specific joint injury were highly associated with the development of symptomatic, clinical and end-stage OA across the knee, hip and shoulder. These data suggest that interventions aimed at reducing the significantly higher prevalence of OA seen amongst former rugby players, should be directed towards the prevention of severe injuries, particularly those occurring during rugby itself.

The majority of measures were continuous, and interpretation needs to be carefully considered where there may be small effect sizes, such as an odds ratio of 1.03, but this may be per year. For this reason, the number of career matches was categorised,

however other variables were kept continuous in order to use less degrees of freedom in analyses.

For NHANES pain at the knee and hip, playing exposures were non-significantly protective, with the majority of odds ratios <1.00. This may be resultant of increased weight management and the role of physical activity on lower limb pain longer term, or due to pain tolerance and resilience in those who reach higher playing exposures. The total years of rugby did not appear to influence NHSP, and the number of years at the highest level of play was also slightly and non-significantly protective of NHSP. However, a player's total number of career matches was associated with a non-significant 4% higher risk of NHSP per 50 matches, and there was a non-significant 5% higher risk of NHSP with each year older a youth was at their first game. This suggests that there may be an effect that we were underpowered to detect, and that whereas increased rugby exposure may be beneficial for lower limb pain in the longer term, there may be a different mechanism at the shoulder, where contact sports exposure is not protective.

OA pain is known to vary between individuals and temporally within the same individuals.[430] Pain is acknowledged to be a multifactorial experience, with interplay of sensory and emotional contributors, which may be inherent or learnt. Self-efficacy and pain catastrophising are psychosocial factors that have been acknowledged to influence OA pain.[431,432] Elite rugby players as contact sports participants may be a population who demonstrate higher self-efficacy and are by nature adverse to pain catastrophising, in addition to learnt pain resilience and an increased pain threshold. These factors may contribute to the broadly protective effect of playing exposure on NHANES pain at the

lower limb. OA pain has also been seen to be associated with obesity, with individuals with higher BMIs demonstrating an incremental increase in OA pain, at the hip and knee.[24,433] As a cohort of former elite sports participants, players may have lower adiposity, which is contributing to decreased pain despite potential structural damage. Without direct measurement of adiposity and joint imaging, we are unable to further elucidate this.

For GPOA, the total years of play was seen to have an influence at the knee (OR 2.34), but not at the hip (OR 0.99). At the shoulder there was a 6% higher risk in GPSOA per year of play, but this did not reach significance (p=0.109). This may represent different mechanisms behind joint pain, or different risk factor's interactions between joints, for example microtrauma or meniscal injury at the knee driving an association, whereas at the hip obesity management achieved through rugby may be lowering metabolic risk in a joint less prone to direct rugby-related trauma. The age of an individual at their first schoolboy game was non-significantly protective of GPKOA and GPHOA, with younger players at an increased risk, but not for GPSOA. This again may suggest differing OA mechanisms by joint, but also may be resultant of adaptation to rugby union at this age. There has been significant academic and media discussion surrounding the tackle in rugby union,[225,386,434–436] including suggestions that the tackle should be banned in youth versions of rugby union, and that this may be misguided as tackle technique may be crucial for learning to tackle safely, and decreasing injury at the tackle.[225] Whilst the results presented in this chapter do not show a statistically significant association of rugby exposure and OA-outcome, the older a player is at their first game, the higher their association with OA-outcome at the shoulder, varying from 4% per year for GPSOA, to 7% higher risk per year for shoulder replacement. In univariable analysis this was higher at a 16% higher risk per year, which did not reach significance (p=0.282).

For joint replacement, the majority of playing exposures were associated with non-significantly higher risks of poor outcomes. At the knee all playing exposures were non-significantly increased amongst those with TKR, aside from the age at which a player started playing (OR 0.87). This 13% decrease in the risk of TKR per year was an interesting finding, however did not reach significance (p=0.172). Similar findings were seen for THR with non-significant higher odds of THR for the total years of rugby and years at the highest level (OR 1.01 and 1.03), but not for the total number of matches (OR 0.99) and age at first game (p=0.257), despite a 9% decrease in risk per year. At the shoulder however, in addition to the aforementioned non-significant 7% higher risk of replacement, there was also a non-significant higher risk of replacement with the number of matches (OR 1.14), and years at the highest level of play (OR 1.03), although the total years of play remained non-significantly protective (OR 0.97). This may suggest that the age of an individual at their first game was more protective at the knee and hip than for the shoulder, again suggesting different mechanisms for longer term pain and OA between the weight bearing and non-weight bearing joints.

Hip replacement was of particular interest in terms of the association of playing exposure and development of OA, as previous studies have found a weak positive relationship between regular prolonged physical activity and hip OA,[74] in addition to Femoroacetabular impingement deformity being increased in athletic populations, particularly those exposed to higher playing loads during adolescence,[437–439] and recent findings of hip abnormalities on MRI amongst young elite rugby players.[440] In this chapter, each year older a player was at their first game of rugby was associated with a 7-9% lower risk of OA-outcome at the hip, which may suggest an association with age, such as youth joint loading, but these results did not reach significance.

Although the age of a player at their first game has been measured, the level of loading at specific ages has not been measured due to difficulties of assessing this in a lifetime measurement, and the recall bias it may be susceptible to. However, given the potential for sports specialisation, notably early sport specialisation to be detrimental to health and musculoskeletal development,[441–443] there may be affects of earlier or later loading in adolescence, which we have not been able to determine in this study. A prospective study using imaging and more precise measures of playing exposure over a short timeframe may be more appropriate to further describe the effects of rugby playing load, particularly within youth and adolescent sport, and those specialising in rugby at this age, on musculoskeletal health and joint-specific mechanisms for potential OA. Using imaging may be effective in determining earlier osteoarthritis-related changes, which may permit intervention for players and isolate potential mechanisms for the effect of playing load on musculoskeletal health.

Injury is known to be associated with OA-outcomes at the knee and hip, [73,74,444,445], and has been discussed as a risk factor for persistent shoulder pain.[446] These findings were replicated in our study, with joint-specific injury, and rugby playing or training joint-specific injuries were highly associated with OA-outcomes. The increased risk of OA observed amongst former elite rugby players (Chapter 5) may be most effectively managed by reducing all injury, and rugby-specific injuries within this population, at the knee hip and shoulder, and potentially other joints. Injury prevention within sports is its own research field, and efforts have been made to understand how to effectively reduce injury risk, such as with the implementation of movement control programmes and aiming to improve neuromuscular control.[447–450]

6.3.4 Generalisability

Given the significant changes in rugby union over recent decades, further study or sensitivity analyses within more recently retired professional players will need to be undertaken to understand the generalisability of these results to the modern professional era. As previously discussed, playing load over a player's career, in terms of the ball-in-play time, the number of games per season, the number of collisions per game, and body mass within those collisions have increased with professionalism. These changes to the sport may influence the playing exposures, the risk of injury and the OA-prevalence in the longer term.

The trends of association in univariable analyses of playing exposure and KOA may be affected by this increased musculoskeletal loading, which may have drastically increased for modern players. Playing load within youth sports may also have increased between players who are now a mean age of 60 and played their first game at a mean age of 10, and those players contracted to elite academies during their adolescence.

Specific sports medicine provision has also increased with the sport's professionalisation and over recent decades including the availability of qualified pitch-side care, which may improve injury management, particularly with more enforced removal from play. This may lead to more structured return-to-play practices for players in the modern era, but also the potential for faster return to play from more severe injuries with increased clinical guidance, which may again further increase playing load, particularly on destabilised or not sufficiently rehabilitated and strengthened joints.

This study would need to be expanded or validated in another playing population, and potentially the predictors validated or more robust player load measures used in order to ensure these results are directly translatable and generalizable to other groups of players, particularly to the modern era of professional rugby players.

6.4 Main findings and conclusion

The main findings from this chapter are that rugby playing load appears to influence OA-outcome, and that this varies with OA-measurement and between joints, however in the majority of models this did not reach statistical significance. Injury and rugby injury were highly predictive of OA-outcomes at all joints, and therefore may provide the most evident targets for intervention in order to reduce the increased risk of OA seen amongst former rugby players.

Chapter 7 Hip replacement amongst former rugby players: creating and validating a prediction model

7.1 Introduction

The prevalence of OA amongst former rugby players has been shown to be a significant burden, with elevated osteoarthritis-related outcomes at the knee and hip in comparison with the general population (Chapter 5), with the highest increase in joint-specific morbidity seen at the hip (SMR 6.42, CI 4.69-8.79). Despite having quantified this additional burden, and examined risk factors that may be associated with this (Chapter 6), these analyses have limited applicability in terms of translating this risk, establishing the interactions between multiple potential predictors, and are not readily communicable to players and as population health messages.

The implementation of prediction models to estimate risk, inform patients about the likely future course of their illness, and aid healthcare decision making has been described as a foundation of modern medicine and clinical practice.[451] Prediction model tools such as Fracture Risk Assessment Tool (FRAX) have been translated and validated in diverse geographical areas and populations, and become routinely used both in clinical practice by physicians and freely available to members of the public wishing to understand their risk.

Developing a prediction model of future risk of hip replacement in this cohort of elite former rugby players will permit the identification of individuals with the highest

likelihood of hip replacement, allowing clinicians and sports governing bodies to monitor and proactively manage the risk amongst their players. The development of a prediction model will also allow players to monitor their own risk, and understand their likelihood of hip replacement in later life given their sporting and medical history. Therefore, developing a prediction model of the most prominent musculoskeletal burden and prevalent morbidity amongst this cohort permits players more control of their health in the elite sporting environment, increases their awareness of risk management and modification, and empowers the sport, its players and administrators to proactively manage this risk.

7.2 Chapter aims

The aims of this chapter are to develop and validate a prediction model in order to establish the likelihood of hip replacement amongst elite rugby players for a given set of potential risk factors.

Having developed this model, secondary aims of the chapter are to internally validate this model, develop a risk score, and undertake sensitivity analyses on the univariable screening approach to predictor selection, using lasso regression.

7.3 Methodology

7.3.1 Sources of data

This chapter will develop the model using data collected in a cross-sectional study of former elite rugby players, between 2014 and 2016.

7.3.2 Participants

The study setting is within elite rugby union, using data from 259 respondents to a player health questionnaire from three elite English clubs (Chapter 2). Players with missing data for the outcome of hip replacement were also excluded (n=5), and therefore 254 participants' data is included in this chapter.

7.3.3 Outcome

The outcome for this predictive model is a dichotomous variable representing self-reported hip replacement, at the person level. This outcome is derived from the questions "Have you ever had joint replacement surgery?" and "If yes, please indicate the number below for each joint and side:" which led to responses for "Hip: left" and "Hip: right", which were combined to produce 'any' hip replacement.

7.3.4 Candidate predictors

Identification of candidate predictors for prediction modelling from the literature and clinical expertise has been previously suggested.[452] Known risk factors for hip replacement from the literature that were available in the study were selected (Table 25), in addition to novel, hypothesised rugby-related risk factors for hip replacement.

7.3.4.1 Known predictors of outcome

Risk factors associated with hip OA and replacement include age, sex, BMI, SUFE, hip dysplasia, injury and a family history of osteoarthritis,[74,453] and therefore these predictors were included in the model.

7.3.4.2 Novel potential rugby-related predictors of outcome

Novel sport-specific predictor variables reflected a players' overall rugby exposure, such as position of play, age at first game, level of play, professional status, number of hours per week training, and number of games in their career. Playing BMI was selected as a measure of adiposity during a players' playing career. The variable type for each candidate predictor is specified in Appendix 12.

Table 25.Candidate predictors for prediction model of hip replacement.

Candidate Predictors	Variable type
Age at first game (years)	Continuous
Total years of play (years)	Continuous
Level of play International Premiership Premiership 'A' league Premiership Academy University team RFU Championship/National league Non-Premiership or Championship Club Other – please specify Don't know	Categorical
Playing BMI	Continuous
Position of play Prop Hooker Second row Flanker Number 8 Scrum half Fly half Centre Winger Full back	Categorical
Professional status	Categorical
Number of games in career	Continuous
Hours per week training youth (hours)	Continuous
Hours per week training player (hours)	Continuous
Slipped Upper Femoral Epiphysis	Binary
Hip dysplasia	Binary
Severe hip injury	Binary
Age (years)	Continuous
BMI	Continuous
Family history hip OA	Binary

7.3.4.3 Data reduction

Model overfitting is a central problem in prediction modelling, which can cause optimism of the model's performance in new subjects.[452,454] Particularly in datasets with relatively small sample sizes, and uncommon binary outcomes. Overfitting is caused by idiosyncrasies within the development dataset, which may result in worse predictive performance when applied to an external dataset. Overfitting is particularly a problem in a dataset with a limited sample size, where random variation in the dataset is more likely to be captured in the fitted model.[454]

An event per variable ratio (EPV) of 10 has been suggested in order to reduce overfitting.[455,456] This means that data reduction is often necessary, to reduce clinically relevant or hypothesised candidate predictors to a more suitable number, relative to the sample size and number of individuals with the outcome of interest.

In order to reduce the degrees of freedom used in these regression analyses, categorical predictors were reduced to a minimum number of categories. Although relevant for the accurate collection of players' true characteristics, a higher number of categories may be less relevant to hip replacement risk in comparison with other risk factors in this exploratory prognostic model. Categorical candidate predictors such as position of play and level of play were reduced by combining positions that may represent similar positional demands (Table 26).

Table 26.Data reduction by combining categories of level of play.

Level of play	Label	New category	New label
1	International	1	International
2	Premiership	2	High level
3	Premiership 'A' league	2	
4	RFU Championship/National League	3	Tier two
5	University first team		
6	University second team		
7	Non-Premiership or championship club	4	Recreational
8	Premiership club academy	2	High level
9 Other	e.g. Middlesex County, Llanelli 1st team Pre-premiership first class Welsh 1st division	 2 2 2 2	Individually assigned and agreed by study team consensus (NKA, JN and MD)

Candidate predictors were further revised based on clinical and sporting judgment of the most potentially relevant candidate predictors to this question, such as playing BMI above current BMI (Table 27).

It was hypothesised that a player's BMI during their playing career may contribute to joint-specific loading over time, and therefore that an increased BMI during elite participation in rugby union may be more relevant to the development of poor musculoskeletal outcome in a weight bearing joint. It has previously been suggested that prediction models should use clinically available predictors in order to facilitate their generalisability and future utility.[457] Current playing BMI will increase the utility of this model, permitting players the opportunity to prospectively monitor their hip replacement risk. In contrast, post-retirement BMI would mean the model is based on players' future post retirement, and therefore less clinically relevant.

Table 27.Candidate predictors with revised categories.

Predictor	Variable type
Age	Continuous
Playing BMI	
Amateur or professional	Binary
Hours per week training as a youth	
Hours per week training as a player	
Primary position of play	Categorical
Position of play: 1 Position of play: 2 Position of play: 3 Position of play: 4 Position of play: 5	Front row Second row Back row Half-back Centre/wing/fullback
Number of games during career	Continuous
Total years of play	
Level of play	Categorical
Level of play: 1 Level of play: 2 Level of play: 3 Level of play: 4	International High level Tier two Recreational
Slipped Upper Femoral Epiphysis (SUFE)	Binary
Hip dysplasia	Binary
Hip injury	Binary
Family history of osteoarthritis	Binary

7.3.5 Statistical methods

All statistical analysis was undertaken using Stata 13.1 and R 3.3.2 (R Foundation for Statistical Computing). Descriptive statistics (mean (SD) and median (IQR) for continuous variables and number (%) for categorical) were derived for all candidate predictors and the outcome variable.

The relatively small sample size and relative rarity of the outcome dictated the approach to model development. An initial simple approach was taken, using univariable logistic

regression and forward selection. Forward selection is a relatively simplistic approach to model development, and there are limitations to forward selection, univariable screening and backwards elimination, which may result in unstable predictor selection and less discriminating models, and models with less calibration than shrinkage methods.[454,458,459] Following a univariable approach to predictor selection, lasso regression, a more complicated penalised method of risk factor selection [460] was undertaken with all candidate predictors.

7.3.5.1 Selection of candidate predictors

Forward selection using univariable logistic regression was used to decrease the number of candidate predictors, and non-significant predictors were excluded. Predictor variables were assessed for outliers and kept continuous where possible.

7.3.5.2 Regression modelling assumptions and diagnostics

Regression model assumptions, such as linearity of the effect of continuous predictors on the outcome were assessed using fractional polynomials.

A full multivariable logistic regression model was produced with all candidate variables. This was then also produced with only significant variables from univariable analyses, and further non-significant variables in the multivariable model were excluded.

The linktest was undertaken to examine the specification of error within the model, and the model was checked for multicollinearity within the model and for influential observations.

Multicollinearity was assessed with the command 'collin', for tolerances of <0.1, or a VIF>10.

Influential observations were examined using Pearson residuals, deviance residuals and Pregibon leverage. These were plotted against the predicted probabilities and case numbers for review.

7.3.5.3 Missing data

Participants with missing predictor variables were included in analyses, and this data was imputed using single imputation. Multiple imputation (MI) with chained equation was undertaken, with the first imputed dataset stored as the single imputation ready for lasso regression. Age and the outcome variable were the only variables not imputed, as these were inclusion criteria.

Continuous predictors were assessed for normality prior to imputation. Variables not normally distributed were assessed for which transformation to use (Appendix 13) and transformed for MI. Descriptive statistics were repeated on the imputed datasets to ensure the imputation was successful. The multivariable prediction model was then repeated for the imputed dataset.

7.3.5.4 Model performance

Model performance was assessed by calibration and discrimination. Calibration is the ability of a model to determine how closely the predicted probabilities of hip replacement agree with the observed probabilities of hip replacement.[461,462] Discrimination is the ability of a model to discriminate between people who experience hip replacement and those who do not. The c-index is a measure of concordance, which is often used to measure model discrimination.[458,463]

Model calibration was measured using the Hosmer-Lemershow test, and model discrimination was calculated as the Area Under the Receiver Operating Characteristic (AUROC) curve in these logistic regression analyses, determined using the 'lroc' command.

7.3.5.5 Model validation

Model validation should be undertaken before a risk model is implemented in clinical practice, and typically internal validation using bootstrapping, or external validation using patient data not used in the development model, is undertaken.[454] Bootstrapping is often used to estimate quantities associated with sampling distribution of estimators,[464] and produces an imitation dataset by randomly sampling patients from the original dataset.[454] Two hundred bootstrap resamples with replacement were undertaken in R to perform a bias-corrected estimate of predictive ability.

7.3.5.6 Risk score

A risk score was generated from coefficients of predictor variables, fitted to the outcome, and the sensitivity and specificity of this model derived.

7.3.5.7 Lasso regression

Due to the accepted limitations of univariable selection, lasso regression, as a form of penalized regression with a flexible shrinkage approach was undertaken, due to its suitability when the events per variable are low.[454]

7.4 Results

7.4.1 Participants

Of the 254 participants eligible for this study, 39 (15.35%) had the outcome of interest.

Descriptive statistics of the participant demographics, predictors and respondents per variable, are shown below (Table 28).

Table 28. Descriptive statistics for participant demographics and predictor variables.

Explanatory variable	Respondents	Mean (SD) or n (%)	Median (IQR)
Age	254	60.5 (16.0)	63.3 (47.0-73.2)
BMI	246	29.3 (9.1)	28.4 (26.5-30.5)
Outcome (Hip replacement)	254	39 (15.4%)	-
Playing BMI	248	27.9 (2.6)	27.7 (26.1-29.2)
Amateur playing status	251	211 (84.1%)	
Hours per week training as a youth	189	7.6 (4.5)	6.0 (5.0-10.0)
Hours per week training as a player	215	10.5 (6.3)	9.0 (6.0-15.0)
Primary position of play: Front row Second row Back row Half-back Centre/wing/fullback	244	39 (16.0%)	-
		25 (10.3%)	-
		49 (20.1%)	-
		25 (10.3%)	-
		106 (43.4%)	-
Number of games during career	201	378.4 (189.0)	350 (250-500)
Total years of play	240	22.3 (5.3)	22.0 (19.0-26.0)
Level of play: 1. International, representative (e.g. Barbarians, Lions) 2. Professional, Premiership, Premiership 'A', Club and County 3. University, National League 4. Non-premiership or championship club	249	35 (14.1%)	-
		136 (54.6%)	-
		60 (24.1%)	-
		18 (7.2%)	-
Slipped Upper Femoral Epiphysis (SUFE)	249	4 (1.6%)	-
Hip dysplasia	249	8 (3.2%)	-
Hip injury	248	50 (20.2%)	-
Family history of any osteoarthritis	228	27 (11.8%)	-

7.4.2 Model development

7.4.2.1 Univariable logistic regression

In univariable logistic regression analyses, age, hip dysplasia, hip injury and the playing position of the back row were associated with hip replacement (Table 29).

Table 29. The association between risk factors and hip replacement in univariable logistic regression.

Explanatory variable	n	p-value	OR (CI)
Age	254	**0.000**	**1.07 (1.04-1.10)**
Age at first schoolboy game	251	0.292	1.08 (0.94-1.23)
Number of games during career	201	0.274	1.00 (1.00-1.00)
Total years of play	240	0.897	1.00 (0.93-1.06)
Playing BMI	246	0.409	0.94 (0.82-1.08)
Hours per week training as a player	215	0.595	1.02 (0.96-1.07)
Hours per week training as a youth	189	0.204	1.05 (0.97-1.14)
Professional status	211	-	1*
Slipped Upper Femoral Epiphysis (SUFE)	249	0.073	6.21 (0.85-45.54)
Hip dysplasia	249	**0.012**	**6.30 (1.50-26.44)**
Family history of any osteoarthritis	228	0.111	2.16 (0.84-5.58)
Hip injury	248	**0.000**	**6.28 (3.00-13.13)**
Playing position°	244		
Second row		0.567	1.64 (0.30-8.83)
Back row		**0.048**	**3.89 (1.01-14.95)**
Half-back		0.964	1.04 (0.16-6.73)
Centre/wing/full back		0.170	2.45 (0.68-8.85)
Level of play°	249		
Professional, Premiership etc		0.196	0.56 (0.23-1.35)
University, National League		**0.050**	**0.32 (0.10-1.00)**
Non-Premiership or Championship		0.107	0.17 (0.02-1.47)

*Omitted: Amateur status predicts failure perfectly, therefore variable excluded.

° First category used as reference category: Front row for position of play, and International/representative for level of play.

Playing position categories were also further combined according to the predictive significance of the categories (Front row, second row or halfback/back row/centre, wing or fullback). The playing position of the back row was associated with hip replacement, but other positions of play were not (Table 29). Therefore position of play was further categorised following univariable analyses (Table 30).

Table 30. Categorisation of position of play according to univariable effect of posititon of play on hip replacement.

Explanatory variable	n	p-value	OR (CI)
Position of play (additional categorization)	244		
2. Back row		0.017	3.28 (1.24-8.71)
3. Centre/wing/fullback		0.107	2.07 (0.85-5.02)

7.4.2.2 Regression diagnostics

The assumption of linearity was not met for age, and therefore this variable was categorised at 60years (Figure 22).

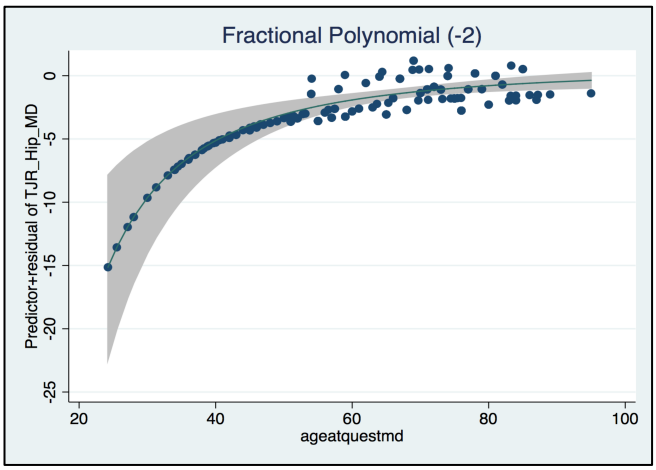


Figure 22. Fractional polynomial plot of age and hip replacement.

7.4.2.3 Full multivariable logistic regression model

In the full model of all candidate predictors irrespective of their univariable association with hip replacement, previous hip injury, age and playing in the back row were associated ($p<0.01$) with hip replacement (Table 31).

Table 31. The association of candidate predictors with hip replacement in the full multivariable model irrespective of univariable association (n=103).

Explanatory variable	P-value	Odds Ratio (95% CI)
Age at first schoolboy game	0.598	0.90 (0.59-1.35)
Number of games during career	0.482	1.00 (0.99-1.00)
Total years of play	0.086	1.20 (0.97-1.47)
Playing BMI	0.707	1.09 (0.70-1.67)
Hours per week training as a player	0.218	1.11 (0.94-1.32)
Hours per week training as a youth	0.743	0.98 (0.85-1.13)
Professional status	1 (omitted)	n/a
Slipped Upper Femoral Epiphysis (SUFE)	0.334	6.32 (0.15-265.62)
Hip dysplasia	0.914	0.78 (0.01-77.34)
Family history of any osteoarthritis	0.106	5.55 (0.70-44.38)
Hip injury	**0.001**	**28.79 (4.14-199.99)**
Level of play		
Professional, Premiership, Premiership 'A', Club and County	0.571	2.13 (0.16-29.08)
University, National League	0.969	0.94 (0.05-17.84)
Non-premiership or championship club	0.354	10.03 (0.08-1316.23)
Age (categorised)	**0.003**	**46.65 (3.81-570.62)**
Position of play		
Second row	**0.004**	**31.25 (2.96-329.57)**
Centre, wing or full-back	0.115	6.83 (0.63-74.49)

When only significant candidate predictors from univariable analyses were used in a multivariable model, all variables remained highly associated with hip replacement ($p \leq 0.05$), other than hip dysplasia (Table 32).

Table 32. Full multivariable model for hip replacement, using only significant candidate predictors from univariable analyses (n=208).

Explanatory variable	P-value	Odds Ratio (95% CI)
Slipped Upper Femoral Epiphysis (SUFE)	**0.011**	**46.91 (2.46-894.28)**
Hip dysplasia	0.763	0.64 (0.03-11.85)
Family history of any osteoarthritis	**0.026**	**4.46 (1.20-16.65)**
Hip injury	**0.000**	**11.85 (3.72-37.80)**
Age (categorised)	**0.000**	**28.84 (6.24-133.38)**
Position of play		
Second row	**0.029**	**4.79 (1.17-19.54)**
Centre, winger or full back	**0.013**	**5.16 (1.40-18.98)**

Hip dysplasia was then excluded from this model, to produce a final model of predictors highly associated with hip replacement (Table 33).

Table 33. Final model of significant predictors of hip replacement (n=211).

Explanatory variable	P-value	Odds Ratio (95% CI)
Slipped Upper Femoral Epiphysis (SUFE)	**0.009**	**41.38 (2.54-674.49)**
Family history of any osteoarthritis	**0.029**	**4.25 (1.16-15.63)**
Hip injury	**0.000**	**11.90 (3.76-37.67)**
Age (categorised)	**0.000**	**28.63 (6.19-132.40)**
Position of play		
Second row	**0.024**	**5.05 (1.24-20.56)**
Centre, winger or full back	**0.012**	**5.20 (1.44-18.83)**

7.4.3 Missing data

MI with chained equation was undertaken, with missing observations imputed (Table 34).

Table 34. Candidate predictors with multiple imputation of missing values.

Explanatory variable	Complete	Incomplete	Imputed	Total
Slipped Upper Femoral Epiphysis (SUFE)	**249**	**5**	**5**	**254**
Hip dysplasia	**249**	**5**	**5**	**254**
Family history of any osteoarthritis	**228**	**26**	**26**	**254**
Amateur or professional status	**251**	**3**	**3**	**254**
Hip injury	**248**	**6**	**6**	**254**
Hours per week training as a youth	**189**	**65**	**65**	**254**
Hours per week training as a professional	**215**	**39**	**39**	**254**
Age at first schoolboy game	**251**	**3**	**3**	**254**
Total years of participation	**240**	**14**	**14**	**254**
Playing BMI	**246**	**8**	**8**	**254**
BMI	**246**	**8**	**8**	**254**
Level of play	**249**	**5**	**5**	**254**
Number of matches in a players' career	**201**	**53**	**53**	**254**
Position of play	**244**	**10**	**10**	**254**

When the multivariable model of previously significant predictors was repeated in the imputed dataset, SUFE, family history, injury and age were more strongly associated with the outcome; however the association between position of play and hip replacement was slightly decreased, whilst remaining highly significant (Table 35).

Table 35. Multivariable model of significant predictors repeated in the imputed dataset (n=254).

Explanatory variable	P-value	Odds Ratio (95% CI)
Slipped Upper Femoral Epiphysis (SUFE)	**0.004**	**67.31 (3.74-1210.08)**
Family history of any osteoarthritis	**0.013**	**4.37 (1.36-14.00)**
Hip injury	**0.000**	**19.50 (6.36-59.75)**
Age (categorised)	**0.000**	**50.09 (10.54-238.00)**
Position of play		
Second row	**0.017**	**4.94 (1.32-18.45)**
Centre, winger or full back	**0.015**	**4.46 (1.34-14.87)**

7.4.4 Model performance

7.4.4.1 Calibration

In order to determine how closely the predicted probabilities of hip replacement agreed with the observed probabilities of hip replacement, the predicted outcome was generated, and the group divided into 10 quantiles of estimated probabilities. Only 9 distinct quantiles were formed due to ties, and the results from this are shown in Appendix 15, and Figure 23 (p=0.0767).

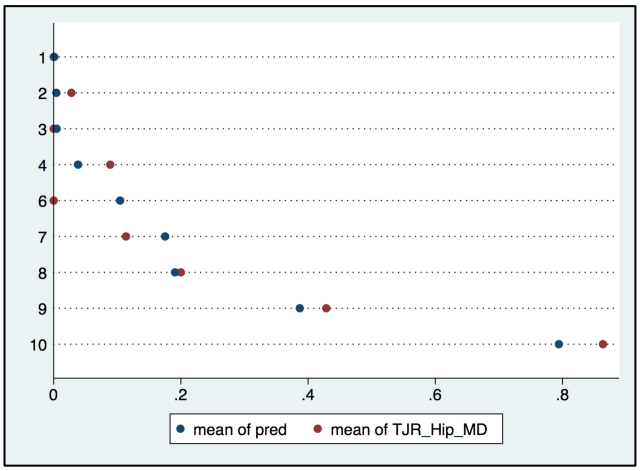


Figure 23. Quantiles of estimated probabilities and predicted outcome of the prediction model.

7.4.4.2 Discrimination

Prediction accuracy (discrimination) of this model was assessed by the area under the Receiver Operating Curve (AUROC), which represented the c-index. The AUROC for this final model was 0.8838 (Figure 24).

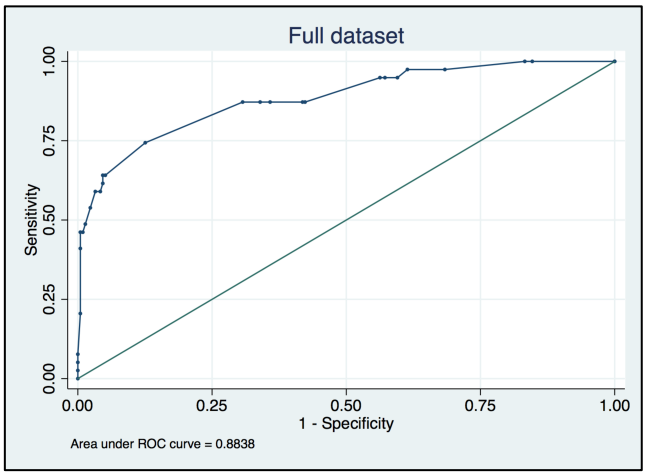


Figure 24. Prediction accuracy of the model, assessed by the area under the receiver operating curve (AUROC).

This AUROC was used to determine a cut point for the model's sensitivity and specificity. With a cut point of 0.1906, model sensitivity was 74.36%, and specificity was 87.44%, with 85.43% correctly classified.

7.4.5 Regression diagnostics

The link test is a specification link test for single equation models. The test regresses explanatory predictors on the prediction, and prediction squared. Although it is a test for the specification of the dependant variables, it is often used as a test that the risk factor variables are correctly specified.[465] In the link test, the prediction-squared value was significant (p=0.027). This suggests that there may be a problem with the model specification.

Multicollinearity was not observed using the 'collin' command (tolerance 0.9782-0.9916 and VIF 1.01-1.02), as shown in Appendix 15 (Table 56).

Individual observations may have significant influence on a model. Pearsons residuals, deviance residuals and Pregibon leverage were assessed for potential observations with a significant influence on the model.

Coefficient sensitivity was tested using the 'ldfbeta' command to observe the difference between the regression coefficient for all data, and the regression coefficient without the observation (Appendix 12).

7.4.6 Development of a risk score

The risk score was derived from the coefficients for each predictor within the final model, with the total risk score as the sum of all predictors' individual scores (Table 36).

Table 36. Risk score development from the regression coefficients of each predictor.

Predictor	Category (Label)	Label	Regression coefficient	Reference value	Final risk score
Age	1 2	(<60) (>60)	3.914	0 1	0 39
Hip injury	0 1	None Injury	2.970	0 1	0 30
Playing position	1 2 3	Front row, second row or half-back Back row Centre, wing or full-back	 1.598 1.494	0 1 2	0 16 32
SUFE	0 1	None SUFE	4.209	0 1	0 42
Family history	0 1	None Family history	1.473	0 1	0 15

The AUROC was derived for this model (Figure 25, AUROC = 0.8819), and the threshold of whether or not a player is at high risk of hip replacement determined using bootstrapping with 1000 repetitions. A cut point of 55 points (95% CI 48.36-61.64) was suggested as the observed threshold, and 'roctab' was used to calculate the AUROC at this cut point. With a cut point of 55, the risk score was seen to have sensitivity of 74.36%, specificity of 87.44%, and 85.43% correctly classified (Appendix 15).

When a logistic model of the risk score was fitted on the outcome, the same sensitivity and specificity was observed with a cut point of 0.1882.

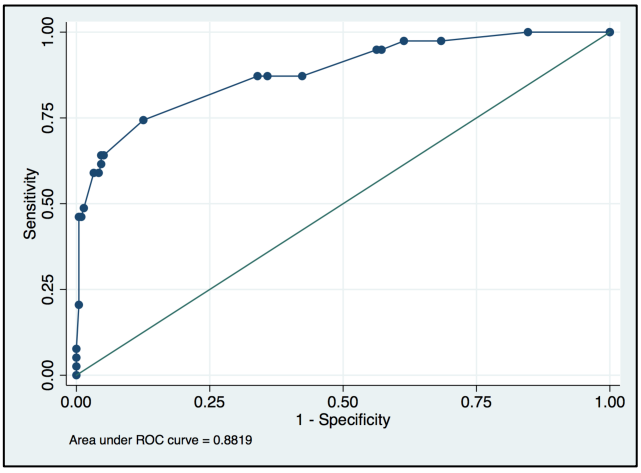


Figure 25. ROC curve of the risk score for hip replacement

With a cut point of 55, 29 players were seen to have THR (51.8%), compared with 10 (0.05%) players with a score <55 (Figure 26).

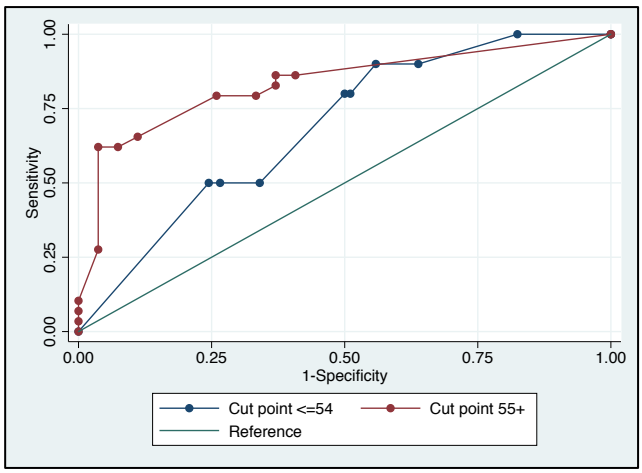


Figure 26. The AUROC for the cut point for hip replacement

7.4.7 Model validation: bootstrapping

In order to internally validate the model, the model was repeated in R with 200 bootstrap repetitions, with replacement. The bias-corrected association between the observed risk and predicted risk is shown below (Figure 27).

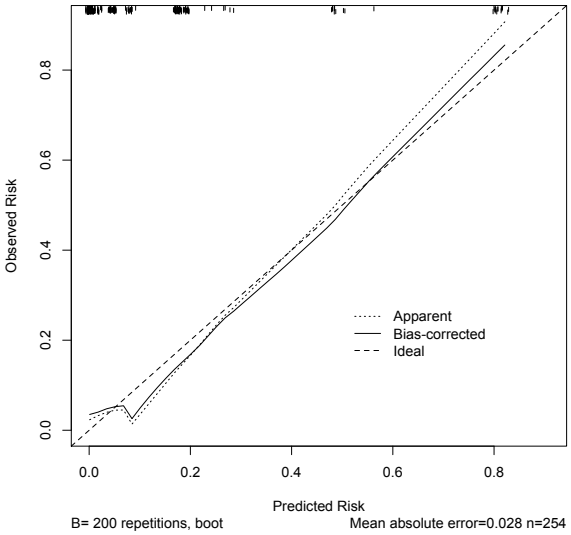


Figure 27. Bias-corrected association between observed risk and predicted risk of hip replacement, using 200 bootstrap repetitions with replacement.

The c-statistic was derived for this model, and provided an optimism-corrected measure of concordance (0.856).

7.4.8 Model validation: coefficient shrinkage in a potentially over fitted prediction model

7.4.8.1 Methodology

Univariable forward selection was used in this chapter due to the small study sample size and relatively few people with the outcome of interest. However there are limitations associated with forward selection, and alternate methods of risk factor selection are becoming increasingly favoured by researchers.[454] Lasso regression has been discussed as a powerful method of risk factor selection, using shrinkage of the coefficients within the model, to determine the number of predictors that may lead to the best fit within the model.

With an awareness that the previously developed model may be over fitted, and that the sample size and the small number of individuals with the outcome of interest has led to a potentially less robust method of predictor selection, lasso regression was undertaken in this cohort. The lasso analysis was undertaken in order to determine, from all candidate risk factors for the prediction model, how many predictors would produce the best fit of the model, with the least error in model fitting, and the ranking of candidate predictors that should be included in this final regression model.

Single imputation was undertaken with the original candidate predictors for analysis within this chapter. The categorisation of position of play and age were maintained for this analysis, and current BMI was included in addition to playing BMI, as this sensitivity analysis was data driven using all available candidate predictor variables. A logistic regression model was fitted using the Lasso and Elastic-Net Regularized Linear

Models ('glmnet') function in R. The model underwent 10-fold cross-validation, with the mean-squared error (MSE) used to assess the non-zero coefficients, and therefore the significant predictors. This process was undertaken with the minimum average mean-squared error, and also using 1 standard error.

7.4.8.2 Results

The shrinkage of coefficients of predictor variables is shown below (Figure 28).

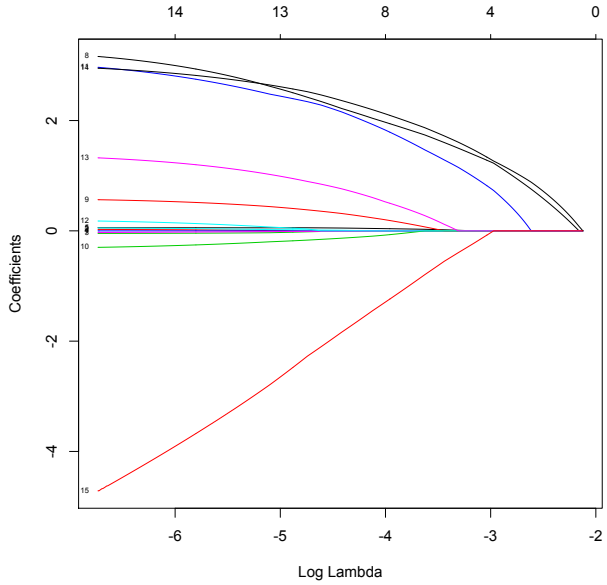


Figure 28. Shrinkage of coefficients towards lambda using lasso regression.

Using minimum average mean-squared error to assess non-zero coefficients, 10 variables were selected for inclusion in the model. However, using 1 standard error to assess non-zero coefficients resulted in three variables selected for inclusion in the model (Table 37).

Table 37. Lasso regression for the shrinkage of coefficients using MSE and 1SE.

Minimum average MSE		1 Standard error of the MSE	
Ranking	Variable	Ranking	Variable
1	Hip injury	1	Hip injury
2	Age	2	Age
3	SUFE	3	SUFE
4	Professional status		
5	Family history		
6	Playing position		
7	Level of play		
8	Hours per week training as a youth		
9	Total years of rugby		
10	Current BMI		

The effect of the number of variables in the model on the model's mean-squared error is shown below (Figure 29).

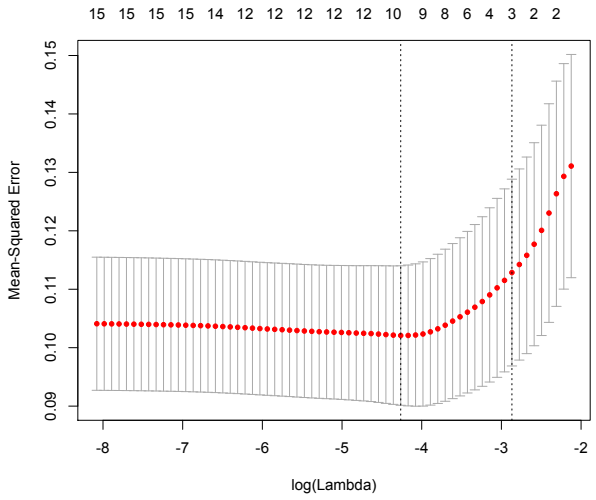


Figure 29. The effect of the number of variables on mean-squared error.

The logistic regression model was re-fitted in Stata, only including those variables selected by lasso regression.

For the MSE model with 10 variables, injury, age, SUFE, family history and the playing positions of centre, wing or full-back were highly predictive of hip replacement (Table 38).

Table 38. The prediction of hip replacement with risk factors selected by lasso regression using MSE (n=214).

Explanatory variable	P-value	Odds Ratio (95% CI)
Injury	**0.000**	**25.13 (6.98-90.48)**
Age	**0.000**	**23.04 (6.61-115.22)**
SUFE	**0.013**	**33.59 (2.13-529.90)**
Amateur or professional status	**(Omitted)**	**1**
Family history	**0.010**	**7.67 (1.64-35.89)**
Position		
Second row	**0.004**	**0.61 (2.04-45.21)**
Centre, winger or full back	**0.017**	**5.38 (1.36-21.37)**
Level of play		
Professional, Premiership	**0.189**	**0.41 (0.11-1.55)**
University, National League	**0.152**	**0.30 (0.56-1.56)**
Non-Premiership or Championship	**0.289**	**0.25 (0.02-3.21)**
Hours per week training as a youth	**0.334**	**1.05 (0.95-1.17)**
Total years playing rugby	**0.260**	**1.05 (0.96-1.15)**
BMI	**0.416**	**0.95 (0.84-1.07)**

The predictive performance of the minimum MSE model was measured by the AUROC (Figure 30).

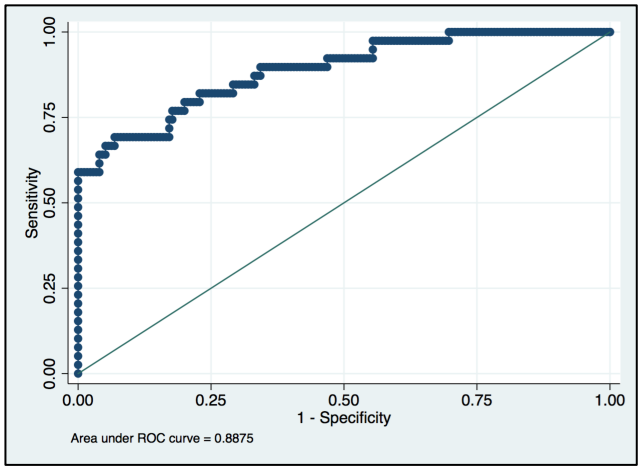


Figure 30. The performance of the prediction model after lasso regression using MSE for the shrinkage of coefficients.

For the 1 SE model with 3 variables, injury, age and SUFE were highly predictive of hip replacement (Table 39).

Table 39. The prediction of hip replacement with risk factors selected by lasso regression using 1SE

Explanatory variable	P-value	Odds Ratio (95% CI)
Injury	**0.000**	**15.72 (5.57-44.38)**
Age	**0.000**	**32.04 (7.92-129.59)**
SUFE	**0.009**	**38.29 (2.50-587.44)**

The predictive performance of the 1SE model was measured by the AUROC (Figure 31).

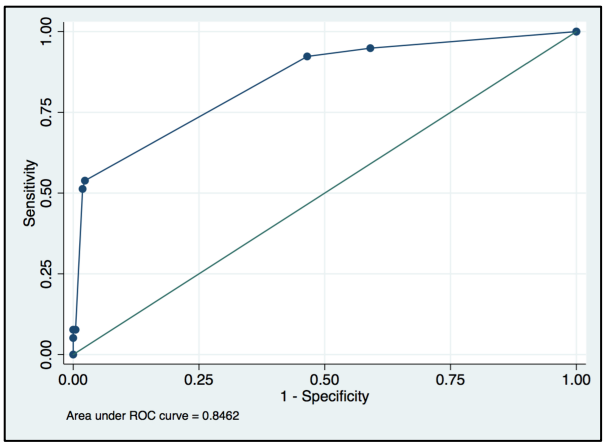


Figure 31. The performance of the prediction model after lasso regression using 1SE for the shrinkage of coefficients.

7.5 Discussion

7.5.1 Key results

Key results from this chapter are that it is feasible to develop a prediction model within this dataset, and that it has strong predictive accuracy (AUROC 0.88) which is sustained after internal validation (AUROC 0.856), despite the relative rarity of the outcome (15%). The model indicates that age, injury and SUFE are highly predictive of hip replacement amongst rugby players. Sensitivity analyses using lasso regression selected similar candidate predictors, and maintained a strong level of predictive accuracy, whether selected using the average MSE or 1SE.

7.5.2 Strengths and limitations

Strengths of this study include the robustness of the outcome, as hip replacement is a major surgery representing end-stage osteoarthritis, which is not likely to be influenced by response bias or uncertainty around reporting. Joint replacement has previously been

described as an attractive outcome criterion due to the large numbers of operations undertaken, and financial burden of surgery.[466] Although joint replacement surgery may be post-traumatic, and not elective for OA, this is estimated to be less than 5% of all hip replacements, which was in accordance with ELSA data in Chapter 5, and therefore we can be reasonably sure that these replacements represent end-stage osteoarthritis.

The binary outcome of any hip replacement at the person-level does not distinguish between unilateral or bilateral, primary or secondary hip replacement. However this chapter was aimed at exploring the risk factors which would contribute to an individual's risk of joint replacement, and therefore those with multiple joint involvement, or worse outcomes after surgery requiring further surgery, or who have survived to the stage of a secondary replacement, are of less interest than the modelling of any hip replacement.

Another strength of this analysis is that all predictors are readily available and measurable, as has been previously recommended in developing a prediction model.[457] However, this strength may also be a limitation in developing a complete understanding of the development of this outcome. Many other developmental risk factors which are known to predict hip replacement and hip osteoarthritis, particularly imaging and biomarkers such as lateral centre edge (LCE) angle, Extrusion Index, alpha angle and Gosvig's Triangular Index,[467] were not measured within this study and as risk factors for hip replacement, may have increased the model's performance if included. These risk factors for hip replacement may also be of an increased importance in this former elite sporting population. However, the current model was developed with collected risk factors from an epidemiological survey, and aiming to be more applicable to routine

athlete care, and not inclusive of all known imaging and biological risk factors for hip replacement.

Future research to establish how imaging and other known morphological measurements associated with OA interact with the risk factors measured within this study will help to better define the mechanisms contributing to this outcome, within this population. Although the detail and mechanism of this outcome may not be fully explored with the risk factors presented within this chapter, imaging risk factors in particular such as alpha angle and LCE angle may not be readily available to players and their clinicians, and therefore their inclusion within this model may decrease the clinical and patient application and utility of this model. The model also already demonstrates strong predictive accuracy, and therefore any improvement of the model with additional risk factors may be marginal.

A potential limitation to this study is that whilst being readily available, many of the candidate predictors were also relatively crude measures. The initial study design was a cross-sectional study of retired players, and therefore the majority of risk factors were lifetime measurements, such as total years of play and the number of games played during a players' career. These may not be the most specific or accurately reported predictors, and as continuous measures, may have more recall bias than if reported as categorical exposures. Continuous measures have been used where possible due to our relatively small sample size and number of individuals with the outcome of interest, however as a continuous predictors, if a player wished to understand their risk of 5-year versus 10-year risk of replacement following playing exposure, this is not as interpretable from the work undertaken in this chapter.

The data for this analysis was obtained in a cross-sectional study of retired players, and as with other chapters may be susceptible to response bias to the initial survey, has used self-reported data, and participants are all former players reporting lifetime exposure to rugby and current health status, alongside 'ever' morbidities, specific surgeries and health outcomes. The majority of players participating in this study were elite amateur players who are now in their 60s, and as the professionalization of rugby union was relatively recent, the model may be limited in its application to other recreational or new-era professional players.

Logistic regression was the choice of model for this analysis, which comparatively involves less model assumptions than for linear regression, such as the distribution of the outcome, and more relatively interpretable results than more complex multivariable prognostic modelling, or other methods which could have been used for this prediction modelling.[458,468]

The model also demonstrated that the independent variables used might not be correctly specified in the link test. It has been previously discussed that where there is a problem with risk factor specification in the link test in a logistic regression model, one may be forced to accept this or reconsider the specification of independent variables as the only specification of the dependant variable that can be altered would be to change likelihood functions.[465]

7.5.3 Interpretation

This model is the first attempt to identify individuals at risk of hip replacement within rugby union, and after appropriate external validation, may be useful to advise recently retired rugby players and team physicians to understand the likelihood of hip replacement for rugby-playing individuals given their playing history, injury history and demographics.

Within the final model using univariable logistic regression and forward selection, and in both sensitivity analyses with lasso regression using average MSE and 1SE, SUFE was the strongest predictor of hip replacement. SUFE is a disorder of adolescent hips, which is seen to involve the displacement of the capital femoral epiphysis from the metaphysis.[469] SUFE affects both sexes, although primarily males with a 3:2 ratio, involves the left leg more than right, and is associated with obesity.[470] Over 63% of children with SUFEs have been seen to be on or over the 90th percentile for weight.[470] Risk factors for SUFE may also include greater acetabular depth and endocrine irregularities such as hypothyroidism, panhypopituitarism, growth hormone abnormality and hypogonadism.[469] Injury has also been considered as a risk factor for SUFE, with trauma being discussed as a potential cause of SUFE,[471] and specific case studies documenting where a traumatic lower limb impact has caused individuals to present to an emergency department with SUFE.[472]

In addition to SUFEs being predictive of hip replacement in this sample, there was also a higher prevalence of SUFE (1.6%) in this study than would be expected in the general population, with the incidence of SUFEs being 3.41 per 100,000 people under age 25, and

10.8 per 100,000 in groups most at risk.[473] As previously discussed (Chapters 5 and 6), temporality is not determined in a cross-sectional study. Rugby players may be more exposed to SUFE as a result of their youth sporting (and potentially rugby) participation and increased hip trauma, or individuals with SUFE potential may be more predisposed to playing rugby, either due to their increased adiposity encouraging participation in a contact sport, or potential endocrine irregularities also encouraging delayed participation in rugby union.

Age was highly predictive of hip replacement across all models. Age is highly associated with the development of hip OA, with the prevalence of radiographic hip OA increasing with age,[474,475] and also being associated with an increased likelihood of hip replacement.[269] The association between age and hip replacement observed within this population suggests that those who have experienced hip replacement are older than those who haven't, and that players should expect their risk of hip replacement when aged over 60 to be significantly higher than when they were less than 60.

The other significant predictor of hip replacement across all models was severe (4 week time loss definition) hip injury. Severe hip injury (1 week offloading definition) has previously been reported to increase the odds of hip osteoarthritis (being listed for hip replacement due to OA), with an overall 4.3 times higher risk of hip OA. This increased risk of hip replacement with injury was higher for men (OR 24.8, 95% CI 3.1-199.3) than for women (OR 2.8, 95% CI 1.4-5.9).[74] Injury was defined by Cooper et al. (1998) as the inability to weight bear for >1 week, at least 1 year before the onset of hip pain, and reported hip injuries included falls, road traffic accidents and sporting injury. [74] Injury is a known risk factor for OA in other joints such as the knee,[70,71] and the strong association

of hip injury with hip replacement in this chapter further supports a similar, but lesser documented affect of injury at the hip.

Whilst SUFE and age may not be the most modifiable risk factors within this population, injury presents a potentially modifiable predictor of prevalent end-stage hip OA amongst current and future generations of former rugby participants, which may reduce their risk of hip replacement in later life.

Within the model generated using univariable selection of predictors, playing in the second row and as a centre, winger or full back, were significantly associated with hip replacement above and beyond other playing positions. Originally this categorical variable had 10 categories, which were combined to 5 categories based on knowledge of the sport and its positional demands, in addition to injuries associated with specific positions in injury surveillance studies. This was then further combined based on the association of playing positions with hip replacement in univariable analysis. These categories were combined to reduce the EPV of the model, and to balance the level of detail initially collected in the study, with the potential mechanisms for negative joint outcomes and relevance in comparison with other predictors. For example, of the 15 playing positions in rugby union, both 1 and 3 will be props, and 1, 2 and 3 will constitute the front row. Although the demands and injury location may differ based on where in the front row they play, and thus other roles in the game they may have (such as the hooker throwing in), compared to the second row, back row or backs, these players will generally have a more similar somatotype within the front row, and the positional demands of front row scrummaging on joints at the shoulder, spine, hip and knee. Therefore these groups were combined. However given the significance of playing

in the second row, this categorisation may have impacted the results, and in order to accurately determine the risk of each individual playing position for hip replacement, a larger sample size would be required.

Within a dataset of this size, there will be few players within each category for the positions of play. Therefore, the apparent association of playing in the second row could be due to a high proportion of the individuals with hip replacement being amongst the 25 players (10.3%) who have played the majority of their career in the second row, by chance. However, there is also the possibility that there is a biological mechanism increasing second row players to hip replacement, either through injury, or another mechanism, such as joint specific repetitive loading. Joint-specific loading of players in the second row may be their central positioning in the scrum, with additional players' weight from their own team and the opposition's team in the scrum through their lower limb joints, or a position-specific increased game exposure, such as a higher number of ball carries. Second row players may be more exposed to ball carries taken directly into contact, increasing their running distance whilst subject to the external forces of tacklers' weight, or increased collision forces during tackles, particularly if these lead to mauls with a player being held up in the tackle, or at a line out, with additional players adding their weight to the collision at speed.

Family history was also predictive of hip replacement in the univariable prediction model. Whilst this finding is to be expected, due to the known strong genetic influence in OA,[476] and the heritability of end-stage hip OA being estimated at 27%,[477] it presents support that this known predictor is of maintained significance in this sporting population, despite the increased prominence of other predictors. Family history also

presents an innate risk factor, which will be consistent from birth for players, although familial diagnosis of OA may occur at any time. Family history may therefore present an easily monitored risk factor, which in terms of translating these results to a clinically meaningful tool to reduce hip replacement amongst players, is easy to measure at any time point, easily understood if a player maintains familial contact, and can encourage the adjustment of other modifiable risk factors, given an individual's family history of OA.

7.5.4 Generalisability

The findings of this chapter may be generalisable to other former elite rugby playing populations, and also therefore to current elite players in order to prospectively manage their risk given their clinical and playing history. However, further external validation of this model will need to be undertaken to observe the model's performance in an external dataset. Having been developed in a relatively small dataset, the effect of random noise in this development dataset could be substantial, and despite bootstrap validation and the sensitivity analyses undertaken using lasso regression, external validation would increase the likelihood that this model will perform as well in novel patient groups as in the development dataset, and that it may be clinically applicable to guide player and clinician decision-making.

When considering the generalisability of these findings, further consideration needs to be given to the unique population from which the development dataset is drawn. As previously discussed, this group of elite players are not representative of lower levels of play, which form the majority of the playing population, and the predictors of hip replacement may be different for lower level players. All players within the

development dataset were also former players, who had played primarily within the sport's amateur era. Whilst current players may be able to use this model to support their decision-making after it's external validation, as the sport has changed significantly with professionalism, this model and the risk of hip replacement may have altered between generations, and therefore have limited applicability to modern era and future generations of rugby players.

As this cohort was a wholly elite, albeit amateur rugby playing cohort, the development of a prediction model of hip replacement amongst recreational players would help the understanding of the interaction between playing history and innate risk factors at different levels of the game. Recreational rugby players may in many ways represent an entirely different demographic, with lower physical activity, potentially lower socio-economic status and less routine medical care than elite players. All of these factors may influence health outcomes, and would support the generation of a novel model amongst recreational players before translating these results beyond the elite strata of play.

7.6 Main findings and conclusions

The main findings of this chapter are that it is feasible to develop a prediction model of hip replacement with good predictive accuracy, in a relatively small dataset, and that within this model, SUFE, age, family history, hip injury, and playing in the second row, are seen to predict hip replacement.

Whilst requiring cautious interpretation due to the size of the dataset and lack of external validation, this model strongly predicts hip replacement, and demonstrates that

rugby exposures such as position of play may have a role in the development of end-stage hip OA, alongside developmental conditions such as SUFE and acquired potentially modifiable risk factors such as injury. Whilst requiring additional validation before being widely implemented, in its current form this model encourages prevention and optimal management of SUFE in adolescence, and emphasises the importance of injury prevention for future health, disability and the societal burden of OA. The potential influence of playing position demonstrates that big datasets within this field may provide an opportunity to support safe participation, by informing game stakeholders of previously unknown affects to health that may be influenced by previous sporting participation.

Chapter 8 Conclusions and Future Research

8.1 Summary of the findings

Each chapter of this doctoral thesis has presented novel findings further describing the relationship between participation in rugby union and long-term health. It is feasible to implement patient and public involvement within sports-related research and player health studies, and this process encourages alterations to the research design and process. The presence of morbidity within former rugby union participants has been established, with significant increases seen in anxiety, osteoporosis, osteoarthritis, joint replacement, and hip and knee replacement compared with the general population. Twice the prevalence of problems have been reported for health-related quality of life, within the domains of mobility, pain/discomfort and usual activities, in comparison with the general population.

In the assessment of playing exposure as a risk factor for OA, only the total years of play during a player's career was associated with physician-diagnosed knee OA in univariable analysis, and when adjusted for age. However, rugby-specific joint injury was associated with all OA-outcomes in fully adjusted models, and the only models that showed a non-significant association were knee injury, and rugby-specific knee injury as risk factors for knee replacement. This demonstrated that broadly there was not strong evidence for an association between playing exposure and OA outcome, however this varied in direction and effect size between joints, and the outcome measure used. The final results chapter within this thesis found SUFE, age, family history, hip injury and playing in the second row to strongly predict hip replacement.

Given the aim of this thesis to design, develop and undertake an epidemiological study of overall health, morbidity and the development of OA in former elite rugby players, this thesis has been successful in achieving its aims. An epidemiological study has been designed and implemented, recruiting over 40% of former English International rugby players. The prevalence of physician-diagnosed morbidity has been quantified, and measured relative to a population-based survey comparator group, and OA-prevalence and risk factors have been identified within this population.

Prior to the undertaking of this thesis, there was very little detail surrounding player health within rugby union, despite suggestions that osteoarthritis may be increased post-injury, and pose a risk to health in this population.[150,183] During the course of the doctorate, evidence suggesting worse longer-term health within this population has increased,[149,151] but these studies have been very focused on potential neurodegeneration and subclinical deficits, post-concussion. This doctoral project has contributed to knowledge within the field by providing a holistic overview of health, morbidity and function, using clinically relevant but patient-focused measurements and methodology.

The deficits in health which have been determined, particularly with regards to OA and joint replacement, at over four- and six-times the risk in this population compared with the general population, have been emphasised. As evident areas of concern, these data suggest that there may be opportunities for intervention to protect long-term player health. Within logistic regression models, and the predictive model of hip replacement, the prominent modifiable risk factor isolated due to its association with poor-OA outcomes has been joint-injury. The logical implementation of this finding would be increased efforts to reduce injury within rugby, and an increased importance of reducing

injury, not just for participation and performance, but also considering the increases in longer-term joint replacement, disability and pain in this population. However, injury prevention is very much an established field in itself, with on-going research evaluating not just injury incidence, but also injury prevention strategies and the successful implementation of prevention strategies, in any sport, and also within individual sports, including rugby union.[116,478–484]

Recent research within rugby union has demonstrated the potential impact of the implementation of prevention programmes, with three weekly sessions of a pre-activity movement control exercise programme being seen to reduce overall match injury incidence by 70%, and concussion incidence by almost 60%.[449] This thesis highlights the importance of these initiatives and their routine, encouraged and mandated inclusion within the sport at all levels of play, both for injury prevention, the protection of longer term player health, and for reduced longer-term healthcare resource consumption amongst this population. Given the extent of SMR findings, I believe there is reason for concern and considered efforts to improve health within this population, with the caveat that longitudinal surveillance with more robust measures are needed to definitively determine to what extent players and stakeholders should be concerned.

Further joint-specific analyses, such as those undertaken within Chapter 7 may elucidate intervention opportunities within this population. SUFE was highly predictive of hip replacement. The optimal clinical management and diagnosis of SUFE such as time to surgery and risk of avascular necrosis after slips have previously discussed as inadequate and in need of further randomised controlled trials to inform clinical decision making.[485,486] Given the predictive capacity of SUFE for longer-term end-stage

joint failure within this population, increased study as to the correct management and outcome of this within athletic populations, and awareness of athletes with a history of SUFE, may be pivotal opportunities for managing health amongst athletes and decreasing the likelihood of progression to end-stage joint failure. Profiling other joints in this way may also indicate further opportunities for increased prevention and management of specific conditions that may predict poor outcome. Again more robust, longitudinal measures could further clarify these prevention and management opportunities.

A central finding of this thesis is that rugby playing load throughout a player's career is not significantly associated with OA-outcomes, and therefore this population do not present as a group at significantly higher risk of OA after exposure to higher playing loads, in terms of numbers of matches or years of play. This finding is pivotal for the sport, in terms of directing efforts for OA prevention. These findings advocate that comparatively, effort should be invested into injury prevention rather than changes in playing exposure, to reduce OA in this cohort.

Despite the research within this doctorate being comprehensive and supporting gaps in the existing literature, there remains substantially more work to be undertaken within this field. Although it has been concluded that playing exposure is not associated with OA-outcome, crude self-reported lifetime measurements have been used, and there is the potential that these risk factors measured in other ways may have resulted in an association with OA-outcome. Relatively novel technologies such as GPS and accelerometers may provide opportunities for innovative, more sensitive measures of playing exposure, and other measures of playing exposure which cannot be reliably

determined in a questionnaire study, such as the number of tackles and collisions a player is exposed to, their playing biomechanics and joint shape and morphology may have a role in the development of OA, but were outside the scope of this thesis.

8.2 Strengths and limitations

Central strengths of this thesis include:

i. The number of players relative to other longer-term health studies, and the opportunity this has provided to undertake more detailed inferential analyses and begin to explore risk factors and predict poor outcome
ii. The recruitment strategy, in achieving a known denominator, and therefore the capacity to quantify generalisability beyond the study sample
iii. The elite playing cohort
iv. The holistic view of health and morbidity presented
v. The capacity for further case-control studies to be undertaken with this population given their cross-sectional demographics and health status
vi. Reproducible methodology which can be implemented in other sports to quantify health, examine risk factors for poor health in other sports, and differences in the effects of sports participation given an individual's inherent physiology (e.g. SUFE, family history), with a view to safer participation in physical activity.

As previously discussed, numerous study designs could have been implemented in order to address the questions posed within this thesis. The cross-sectional study design utilised was a feasible, timely manner in which to acquire substantial data on various

outcomes of interest, this being the first study to examine the prevalence and risk factors for adverse health outcomes within this population. However this cross-sectional study design does not provide additional information in timing of disease onset, and also introduces elements of recall bias, which may affect results. Each chapter that has started to ascertain more detail on the association and interaction between playing exposures and health has been limited in discussing causality as a result of this cross-sectional study design, albeit whilst substantially advancing knowledge in this previously neglected field of research.

An emphasis of this study has been on understanding OA prevalence within this population, however radiographs remain a key component of establishing the diagnosis of OA, that have not been undertaken within this project. Initially these were included in the project proposal, however due to the poor correlation between radiographic and symptomatic OA, and an uncertainty as to how non-symptomatic radiographic OA may be interpreted in this population, these were not undertaken. Future research will seek to examine OA by radiograph and MRI within this population.

The cross-sectional approach of this study limits discussion of causality, but may also restrict the measurement of OA in some respects. Players within this study will be on a continuum of OA, from possessing healthy joints to end-stage joint failure. Where an individual is on this spectrum at the time of data collection is the only measurement of OA that we have – and not what has happened before or after this. It is known that risk factors for the incidence and progression of OA vary, and that post-traumatic OA is more rapidly progressing. However, we have little detail on the temporality of these

events, we are unable to discuss progression, or examine time to joint replacement. However there is the capacity for these players to be followed up in the future.

The elite playing population may be considered as a limitation, as it provides a relatively focused view of the relationship between health and rugby, which may not be the same at lower levels of the game. And therefore potentially the more significant societal burden may be the recreational playing population who form the greater number of players, compared with players at the elite level of play. However, this initial study undertook this focused view both as a doctoral research project, and as a first effort to quantify health within this population, whereby an elite population was selected both due to the quality of playing records in achieving a reliable denominator and as any positive and negative associations with health may be most evident for players with the highest playing exposure, enabling the estimation of a dose-response, should this exist.

A central limitation to this thesis lies in the generalisability of these findings. Rule changes that the game has been subject to, notably with the introduction of professionalism, may mean the game that the majority of participants played in, and therefore our results, are more representative of health status following elite, amateur rugby participation, or participation in previous eras such as the 1970s and 1980s, before the scoring was as it currently is within the game, and replacements for injuries were permitted (1.3.1). This may make results less relevant to current players, or players retiring post-professionalism. The effect of this can be deliberated, in terms of whether higher exposures, such as ball-in-play time will amplify health deficits amongst this population, particularly at the joint-level, or whether greater healthcare provision and specialist clinical environments including cryotherapy, strength and conditioning,

recovery and nutrition may be beneficial in managing acute inflammation and injury, and therefore have a role in improving players' long-term health, have yet to be determined. Further research within recently retired and retiring professional players may begin to elucidate some of these considerations.

8.3 Translation and implications for clinical practice

There are translatable main findings within each results chapter. Public involvement has been eagerly endorsed as an indication of good research practice, which is feasible to implement in studies with sports participants, and results in alterations to studies and their processes. Given the novel establishment of health status amongst former rugby players, there are evident intervention targets, notably musculoskeletal health deficits determined in Chapter 5, which need to be proactively managed and prevented for future generations of players. Whilst an unanticipated finding that requires further validation, the increased risk of osteoporosis amongst players may lend itself to intervention, such as increased nutritional advice for older and retiring players, and the utilisation of a FRAX-type score to ensure that players are not further predisposed to increased morbidity or negative sequelae resultant of their morbidity.

The increased risk of osteoarthritis is a main finding which may also lend itself to translation for player benefit. Initial OA management includes weight and pain management and lifestyle modification, such as increased physical activity and exercise. These modifications may be enforced for retiring players, with increased 'healthy aging' guidance, and the potential to empower players as they retire from sport to control their own health and begin a prevention cycle of weight management and maintenance of cardiovascular fitness.

As the number of reported problems for mobility, pain/discomfort and usual activities were twice as prevalent as in the general population, there may be functional deficits within this cohort, which again present as intervention opportunities to improve players' quality of life by ensuring they are able to function and have capacity to complete activities of daily living. A multidisciplinary team encompassing physicians, players' unions, player representatives and governing bodies would be best place to develop standards to support retired and retiring players, given the novel findings presented within this thesis.

Diabetes has been seen to be significantly lower, and other cardiovascular measures lower, but not reaching statistical significance. These findings demonstrate that there may be health states for which participation in rugby, as a competitive contact sport, may be beneficial. Lifetime physical activity data were not available to indicate the mechanism by which this may be achieved, and other factors such as socioeconomic status and smoking were not taken into account within this analysis, however this presents initial indication that elite rugby may potentially be considered as protective against physician-diagnosed diabetes.

Joint injury and rugby-specific joint injury are most highly associated with OA-outcome, and represent modifiable risk factors during player's careers, and therefore a key opportunity for clinicians, researchers and the sport's stakeholders to begin to prevent OA and protect longer-term health with increased efforts on injury prevention amongst participants. As previously discussed, injury prevention within rugby is a growing field of study that has been successful in determining injury risks, and this study ought to support the importance of these efforts.

SUFE was predictive of hip replacement, alongside injury, playing position and non-modifiable predictors such as family history and age. There has been discussion of optimal management of SUFE, but little discussion of SUFE in athletic populations. Individuals at risk of high training and playing loads with elite participation in sport may represent an unusual population in terms of differences in the clinical management of their condition, given their likely future exposure. These athletes may be best managed by sports physicians aware of future sport-specific demands, and consideration should be given to the importance of sports physicians providing this care having full access to players' medical histories and adequate resource for their care during a playing career, in addition to a clear transition of care and ideally follow-up when these players retire from competitive sport. There may be an argument for discouraging participation in rugby union or contact sports after SUFE. However, given the cross-sectional nature of this study, there is lack of detail in the temporality of this. Players may have experienced SUFE prior to rugby exposure, during rugby exposure, or there may be other factors such as hormonal profiles that make individuals who are more likely to play rugby also more likely to experience SUFE. Further research is needed on the temporality of this finding to determine what may be causing the SUFE exposure within this population, and how this can be best clinically managed at the time and longer term.

The results from this study are being disseminated back to the participating clubs and players, in manuscripts, conference proceedings, and in the wider media. The purpose behind conference proceedings, which are predominantly for clinical sports medicine audiences is to encourage proactive management and consideration of OA and OA risk across players' and athlete's careers.

8.4 Future research

The holistic overview of health provided in this study is relatively novel across all sporting populations, and undertaking a similar approach to Chapter 5 in establishing the risks of morbidity across multiple sports will not only assist with clear public health messaging and inform healthy participation in physical activity, but also significantly enhance our understanding of longer-term athlete health.

Future research within this population should initially seek to validate these findings with more accurate measures, such as clinical assessment where this is available, in addition to validating the association of playing exposure and OA-outcomes in larger samples, and externally validating the prediction model generated in Chapter 7. To determine causality a prospective study would need to be established, and if this study could be developed from existing cohorts, such as the Premiership Injury Surveillance on-going within the English Premiership at present, this would present an ideal opportunity to prospectively measure these playing exposures, and also incident morbidity as this occurs amongst players.

This thesis has solely examined the health of male rugby participants. The women's game is one of the fastest growing team sports globally, and female sex has been established as a risk factor for OA. Female participants may therefore represent a population potentially at a higher risk of poor outcomes after participation in rugby union. The replication and expansion of this study into female rugby participants will be able to begin establishing female athlete health, and quantifying health within this population.

Recreational rugby union has not been included in this thesis, and as this population form the majority of the playing population, future research should seek to quantify health status within former participants at lower levels of the game, and data collection is underway to replicate this study within recreational playing populations.

8.5 Individual learning points and advancement of knowledge

This thesis has documented my navigation of developing an epidemiological study to assess sports participant health. From developing a proposal and protocol, to obtaining ethical approval, database design, questionnaire development, the development of a recruitment strategy, modification of a recruitment strategy, data extraction, cleaning and analysis; I have developed an understanding of the entire research process, and the logistics and potential difficulties and key considerations which are critical in this process.

Main learning points from this process have been the importance of establishing a concise protocol early within the study, as a guide for any difficulties which may occur, and attempting to 'future proof' the study, in terms of asking questions which will still be relevant in years to come, collecting data in a format that it will be analysed in, and ensuring that it is also stored in an easily extractable management facility, ideally readily coded and labelled for analysis. Where key outcomes such as OA have multiple definitions that probably encompass multiple concepts or phenotypes, determining these key outcome measurements with multiple measures may enable an increased understanding of the disease, and also permit the identification of risk factors for different hypotheses, such as metabolic or inflammation-driven pain, alongside end-

stage post-traumatic OA resultant of injury. Again it is hoped that this methodology will ensure the study findings remain relevant despite future research, which will further elucidate our understanding of OA beyond these measurements.

8.6 Conclusion

This player health study has substantially expanded our knowledge about long-term health and rugby union. Modifiable risk factors have been quantified and established, and targets for OA and broader health management within this population have been indicated. Clarifying these areas of further research and implementing proactive OA and health management based on these findings will permit informed healthcare decision-making for athletes, and increase healthy sports participation for all players.

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Appendix 1: Data Management Plan

Data Management Plan: Rugby Study

Admin Details

Project Name: Data Management Plan: Rugby Study

Principal Investigator / Researcher: Madi Davies

Description: The Rugby Study is the first research study to extensively examine long-term health outcomes after playing amateur and professional rugby; in terms of the long-term musculoskeletal and overall health outcomes. The project seeks to calculate the prevalence of Osteoarthritis and other long-term musculoskeletal health consequences within former elite players.

Institution: University of Oxford

Data Collection

What data will you collect or create?

The project will use a cross-sectional questionnaire study design. The questionnaire is divided into Core questions and Rugby Extension questions. Core data is that which will be collected for all other sports within the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis, and provides a comprehensive epidemiological overview of players' health. The Rugby Extension questions are sport-specific, and will be used to examine the influence of sport-specific risk factors on the development of Osteoarthritis (OA).

The comprehensive questionnaire includes the following sections: Demographics, Playing History, Current Pain, Past Injury, Current Injuries, Medical History, Family History, History of Puberty, Medications, General Health, Occupation, Physical Activity, in addition to validated OA-specific questionnaires.

Do your chosen formats and software enable sharing and long-term access to the data?

The data collected is a combination of predominantly text and numeric fields. This will be collected online for approximately 500 ex-rugby players of various levels of play. Data will be stored on Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science (NDORMS) servers, based at the University of Oxford, with restricted access and daily back up to an offsite location. The formats and software utilised are compatible with Good Clinical Practice recommendations, similar studies International, and using procedures agreed with a Data Manager.

How will the data be collected or created?

Data is being collected online through a University of Oxford interface, created by an external contractor but managed by a Data Manager at NDORMS. Data will also be collected by postal questionnaire, and entered by one member of the study team (MD). Data being saved into the platform will be transferred to a MySQL database, consisting of 87 tables. Tables are structured according to the data they are collecting.

Data capture is standardised, with participants being presented with the same interface into which they are entering data themselves, with the same guidance from the system, in terms of 'more information' boxes on certain questions. There is data entry validation built into the platform, where pages with missing fields are flagged up to the user, number fields such as 'age', 'month' and 'year' only permitting the entry of probable answers. If postal questionnaires are entered, the researcher will also be subject to parallel data entry validation procedures, in addition to double data entry.

Documentation and Metadata

What documentation and metadata will accompany the data?

A copy of the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis Rugby Epidemiology Questionnaire©, or a detailed knowledge of the questions within this questionnaire is necessary to read and interpret the dataset as a whole. In the future, if individual questions were of interest to a third party, the question and subsequent data could be extracted.

Madeleine Davies and Stefan Kluzek, who have created the original questionnaire, with contributions from several team members within Epidemiology, copyright the questionnaire. Requests for access to the questionnaire itself must be made in writing directly to Madeleine Davies.

The Data Manager is responsible for the development and management of data dictionaries, which will accompany any data exchange and be utilised during data analysis.

Ethics and Legal Compliance

How will you manage any ethical issues?

The study has received ethical approval from the Central University Research Ethics Committee at the University of Oxford. Through the information sheet and consent form, players have been made aware that:

- Information will be stored on secure servers, separate to identifiable data.
- Data will be analysed anonymously
- Only the Study Team will have access to raw data
- Anonymous data may be shared with national and international collaborators

- Only designated members of the Centre have access to study data, this will be anonymous data, stored on secure University servers and deleted at the end of the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis.

How will you manage copyright and Intellectual Property Rights (IPR) issues?

The Rugby Questionnaire (The Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis Rugby Epidemiology Questionnaire©) has been registered as intellectual property through Isis Innovation at the University of Oxford, to Madeleine Davies and Stefan Kluzek.

The data is being collected through the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis, and resulting data will be available for use throughout the Centre. This is subject to the authors' involvement in receiveing a satisfactory analysis plan and agreeing with the use of the questionnaire and/or data for the proposed project.

Data sharing will be at the discretion of the study team, and the study management Steering Group.

Storage and Backup

How will the data be stored and backed up during the research?

During the research, data will be stored on University of Oxford servers, which are backed up daily to a secure off-site location.

How will you manage access and security?

Identifiable data is being stored elsewhere to participant data. Access is limited to named members of the study team, who have undergone Good Clinical Practice training. Paper questionnaires will be entered by one member of the study team (MD) who has received Good Clinical Practise training.

Selection and Preservation

Which data are of long-term value and should be retained, shared, and/or preserved?

All data will be stored throughout the duration of the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis (‘the Centre’), in order to permit additional analyses outside the scope of this doctoral thesis to be undertaken by the study team.

Anonymous data will be shared in accordance with previously outlined application procedure, to the study steering group. Identifiable data such as first name, surname and email address will be preserved securely in order to identify players for Phase 2 study and invite them to participate in specific follow-up studies, subject to further ethical applications.

The Centre aims and those of our research group are to work as openly and collaboratively as possible. As rugby is one of many sports which will be involved in multiple intersport comparisons over the next 5-10 years to help explore the relationship between sport, exercise, injury and Osteoarthritis, it is reasonable to believe that this data will be kept for upto 10 years to facilitate epidemiological studies further exploring this relationship within sports within the Centre, but also other sports externally who would like to participate in this collaborative effort to establish and understand healthy aging within sporting populations.

What is the long-term preservation plan for the dataset?

This data is considered to need to be retained to permit future collaborative analyses, and in-depth study for Phase 2 projects isolated during Phase 1 analyses. The primary dataset will remain stored at the University of Oxford, or within the Centre, for this purpose. This involves no direct costs or archiving charges.

Data Sharing

How will you share the data?

Data will be shared with appropriate research groups, with significant epidemiological and musculoskeletal research expertise. Data sharing will be conditional on a satisfactory methodology, analysis plan, and engagement with the study, in addition to being subject to data sharing or collaboration agreements, agreed through the University of Oxford.

Are any restrictions on data sharing required?

Exclusive use of the data will be required until the final rugby study data analysis is complete and publication strategy established, which is envisaged to be two years from the end of data collection. The study team will work actively to communicate with potential collaborators and finalise sharing agreements in a timely manner where possible.

Secure data exchange and software compatibility will be examined on a case-by-case basis.

Responsibilities and Resources

Who will be responsible for data management?

The Centre Manager will maintain overall responsibility for data management and good management procedures. Madi Davies is leading the study and will take responsibility for

overseeing and reviewing this Data Management Plan, in conjunction with the Database Manager, Web Developer and University IT Management.

All data management responsibility will remain within the Centre and the University of Oxford site, irrespective of additional collaborators.

What resources will you require to deliver your plan?

There is no charge for the data repositories this study will use.

Technical expertise is adequately provided within the team at present, however discussions over project maintenance have not been conclusive to date.

Appendix 2: Ethical Permissions

MEDICAL SCIENCES INTER DIVISIONAL RESEARCH ETHICS COMMITTEE
Research Services, University of Oxford

University Offices, Wellington Square, Oxford, OX1 2JD
Tel: +44(0)1865 616577 Fax: +44(0)1865 280467
ethics@medsci.ox.ac.uk http://www.medsci.ox.ac.uk



CONFIDENTIAL

Ref: MSD-IDREC-C1-2014-020

6th March 2014

Miss Madeleine Davies
Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal
Botnar Research Centre, Nuffield Orthopaedic Centre
Headington
Oxford

Dear Madeleine

CUREC checklist

I am writing to acknowledge receipt of your CUREC-1 form for your project: **The health outcomes of professional and amateur rugby**

On the basis of the information you have provided this has now been approved by the Medical Sciences IDREC **subject to:**

a) **receipt of the hard copy of your application signed by your head of department (Please note that should this not appear or the head of department is unwilling to sign then this approval would not be valid);**

b) **your following the BPS guidelines for online research;**

c) **it is your responsibility to comply with the requirements for administering any tests or questionnaires and if in doubt to contact the publisher of those tests or questionnaires.**

The reference number for this project is **MSD-IDREC-C1-2014-020** and is valid for a period of **36** months from the CUREC 1 approval date, **20th February 2014**. Please may I remind you that your project may be reviewed at some stage during an annual audit of projects.

Amendments

Should you at some stage alter some of the techniques or procedures then you should first undertake a checklist (CUREC-1) to see whether these changes alter the ethics of the research. If these remain the same then the committee will require notification of the changes to lodge with the project. If they do not remain the same then you may need to complete a CUREC-2 form and undergo further scrutiny by the committee.

Please do not hesitate to contact me if you have any queries about this.

Yours sincerely

Gill Halstead
Research Ethics Co-ordinator, Medical Sciences

Appendix 3: Steering Group Invitation





INVITATION TO BE A MEMBER OF THE STEERING GROUP FOR THE FOLLOWING STUDY:

PROJECT TITLE - HEALTH OUTCOMES IN PROFESSIONAL AND AMATEUR RUGBY

This research project is investigating the long-term health consequences of playing rugby.

The University of Oxford, as part of the Arthritis Research UK Centre of Excellence for Sport Exercise and Osteoarthritis, has initiated this project in collaboration with the RFU and Rugby Players Association. If successful, it will inform the global rugby playing community of issues surrounding the health consequences of rugby, and further this field extensively.

You have been invited as the research group:

'A Phase 1 cross-sectional study investigating the risk factors and prevalence of Osteoarthritis (OA) within rugby union and the prevalence of significant injury, including concussion: An Oxford University Blues Pilot Study.'

This invitation is for selected individuals involved in OURFC and project stakeholders to become involved with the planning and progress of this study.

THE RESEARCH STUDY

Rugby is an international sport, with over 5 million players throughout 117 countries. Between England, Ireland, Scotland and Wales, there are an estimated 2.4 million registered and unregistered participants.

Injury occurrence within rugby is well documented and monitored through injury surveillance initiatives. However, there is very little research examining the long-term effects of playing rugby on joints and also wider health consequences, in terms of the physical impact of exposure to the sport at amateur and professional levels.

The project is being designed and lead by the Epidemiology Unit at the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science (NDORMS), University of Oxford. The University of Oxford are leading this study as part of the Arthritis Research UK Centre of Excellence for Sport, Exercise and Osteoarthritis, which comprises seven universities working collaboratively to better understand the relationship between sport, exercise and OA.

Phase 1 study –

Stage 1: A pilot study of a cross-sectional questionnaire, among ex-players of the Oxford University Blues rugby team.

Stage 2: A Cross-sectional study of retired amateur and professional rugby union players.

Methodology: The questionnaire is accessed and completed through an online platform, and asks players about their previous injuries, how these were treated and their severity, current injuries and current pain, other health problems and risk factors.

Concussion is a topical issue within contact sports in general. We will scope the self-reported incidence of concussive episodes amongst retired professional and amateur players. The data produced from this study will impact rugby unions globally, and demonstrate to players and the rugby community the investment in and importance of long-term player welfare.

THE ROLE

We are seeking individuals with broad and varied experience to help direct this project. The role will be to discuss and inform the direction of the study, such as the recruitment of potential participants, progression of the study, and communication and dissemination of results. You would use your past experiences to direct the project's progress.

The Principle Investigator is responsible for ensuring you have sufficient knowledge of the project to fulfill your role, and that you have all the information and support you require.

The role involves attending and providing input at Steering Group meetings. You will be available for occasional email contact outside of these meetings. The study is expected to last March 2014 until March 2017.

FREQUENCY OF MEETINGS

The Steering Group will meet 3 times annually, depending on the project's progress. It is envisaged that this will be 3 meetings in the first year and potentially decrease, as deemed appropriate by the Group. The meetings will be scheduled to last two hours. Outside of these meetings, you may be asked to work with members of the study team on specific tasks, if you are able to do so.

PERSONAL SPECIFICATION

- To be familiar with rugby union
- To have knowledge of, or an interest in, injury associated with rugby union
- To be able to attend meetings
- To have an interest in research and the research process
- To have time to commit to the project
- To be comfortable working in a team

REIMBURSEMENT

Travelling expenses for Steering Group meetings will be covered.

WHOM TO CONTACT

If you would like any further information on this opportunity or to register your interest, please contact Madi Davies, the Principle Investigator for further information (therugbystudy@ndorms.ox.ac.uk or telephone 01865 223436).

Appendix 4: Phrasing and Derivation of Morbidity Variables

ELSA		Rugby			Harmonised variable
Has a doctor ever told you that you have (or have had) any of the conditions on this card?		Have you ever been told you have any of the following by a Doctor?			
Variable name	Possible response	Variable name	Phrasing	Possible response	Binary variables
hedia01-10	Value = 96.0 Label = None of these Value = 1.0 Label = High blood pressure or hypertension Value = 2.0 Label = Angina Value = 3.0 Label = A heart attack (including myocardial infarction or coronary… Value = 4.0 Label = Congestive heart failure Value = 5.0 Label = A heart murmur Value = 6.0 Label = An abnormal heart rhythm Value = 7.0 Label = Diabetes or high blood sugar Value = 8.0 Label = A stroke (cerebral vascular disease) Value = -9.0 Label = Refusal Value = -8.0 Label = Don't Know Value = -1.0 Label = Not applicable Value = 95.0 Label = Any other heart trouble (SPECIFY)	diabetes high_blood_ pressure heart_proble ms stroke	Diabetes High blood pressure Heart problems (e.g. heart attack or angina) Stroke	1 Yes 2 No 3 Don't know 1 Yes 2 No 3 Don't know 1 Yes 2 No 3 Don't know 1 Yes 2 No 3 Don't know	Diabetes Highbloodpressure Heart problems Stroke
hedib01-10	Value = 96.0 Label = None of these Value = 1.0 Label = Chronic lung disease such as chronic bronchitis or emphysema Value = 2.0 Label = Asthma Value = 3.0*** Label = Arthritis (including osteoarthritis , or rheumatism) Value = 4.0 Label = Osteoporosis, sometimes called thin or brittle bones Value = 5.0 Label = Cancer or a malignant tumour (excluding minor skin cancers) Value = 6.0 Label = Parkinson s disease Value = 7.0 Label = Any emotional, nervous or psychiatric problems Value = 8.0 Label = Alzheimers disease Value = 9.0*** Label = Dementia, organic brain syndrome, senility or any other seri.. Value = -9.0 Label = Refusal Value = -8.0 Label = Don't Know Value = -1.0 Label = Not applicable	asthma dementia	Asthma Dementia	1 Yes 2 No 3 Don't know 1 Yes 2 No 3 Don't know	Asthma Dementia
heji	Have you ever had any joint replacements? Value = 1.0 Label = Yes Value = 2.0*** Label = No	jreplacement	Have you ever had joint replacement surgery?	1 Yes 2 No 3 Don't know	jreplacement

*** Denotes dependancy of another variable(s) on value

Appendix 5: Morbidity Variables with Dependencies

hepsy1-9	What type of emotional, nervous or psychiatric problems do/did you have? Value = 1.0 Label = Hallucinations Value = 2.0 Label = Anxiety Value = 3.0 Label = Depression Value = 4.0 Label = Emotional problems Value = 5.0 Label = Schizophrenia Value = 6.0 Label = Psychosis Value = 7.0 Label = Mood swings Value = 8.0 Label = Manic depression Value = -9.0 Label = Refusal Value = -8.0 Label = Don't Know Value = -1.0 Label = Not applicable Value = 95.0 Label = Something else	anxiety depression	Anxiety Depression	1 Yes 2 No 3 Don't know 1 Yes 2 No 3 Don't know	Anxiety Depression
heart1-3	Which types of arthritis do you have? Value = 1.0 Label = ... osteoarthritis? Value = 2.0 Label = ... rheumatoid Arthritis? Value = 3.0 Label = ... some other kind of arthritis? Value = -9.0 Label = Refusal Value = -8.0 Label = Don't Know Value = -1.0 Label = Not applicable	osteoarthritis	Have you ever been told you have wear and tear, degeneration or Osteoarthritis by a doctor?	1 Yes 2 No 3 Don't know	Osteoarthritis
hejia1-6	Which joints did you have replaced? Value = 1.0 Label = Hip Value = 2.0 Label = Both hips Value = 3.0 Label = Knee Value = 4.0 Label = Both knees Value = 5.0 Label = Hips(s) and knee(s) Value = 6.0 Label = Other joint Value = -9.0 Label = Refusal Value = -8.0 Label = Don't Know Value = -1.0 Label = Not applicable	jreplacement_ joint	If yes, where?	jreplacement_joint_1 (Left hip) 2 jreplacement_joint_2 (Right hip) 3 replacement_joint_3 (Left knee) 4 jreplacement_joint_4 (Right knee) jreplacement_joint_5 (Left ankle) jreplacement_joint_6 (Right ankle) 7 jreplacement_joint_7 (Left shoulder) 8 jreplacement_joint_8 (Right shoulder) 9jreplacement_joint_9 (Left wrist) 10 jreplacement_joint_10 (Right wrist) 11 jreplacement_joint_11 (Left hand) 12 jreplacement_joint_12 (Right hand) 13 jreplacement_joint_13 (Other – please specify)	TJR_hip TJR_knee

Appendix 6: Missingness in the English Longitudinal Study of Ageing

Table 40. Missingness of variables extracted from the English Longitudinal Study of Ageing.

Variable	Response
Gender	
Male	5,186 (45.5%)
Female	6,204 (54.5%)
(-8 Don't know)	1 (0.0%)
Ethnicity	
White	10,995 (96.5%)
Non-white	320 (2.8%)
(-8 Don't know)	1 (0.0%)
(-9 refusal)	9 (0.1%)
(-1 not applicable)	66 (0.6%)
Ever smoking	
Yes	3,824 (73.7%)
No	1,338 (25.8%)
(-8 Don't know)	5 (0.1%)
(-9 refusal)	1 (0.0%)
(-1 not applicable)	18 (0.4%)
Marital status	
Single (never married)	324 (6.3%)
Married (1st and only)	3,258 (62.8%)
Remarried (2nd or later)	658 (12.7%)
Legally separated	64 (1.2%)
Divorced	399 (7.7%)
Widowed	482 (9.3%)
(-9 refusal)	1 (0.0%)
Height	
Value specified	4,856 (93.6%)
(-1 not applicable)	201 (3.9%)
.	129 (2.5%)
Height (-1 not applicable)	
Refused	40 (24.9%)

Attempted but not obtained	65 (20.5%)
Not attempted	173 (54.6%)
Weight	
Value specified	4,740 (91.4%)
(-1 not applicable)	317 (6.1%)
.	129 (2.5%)
Weight (-1 not applicable)	
Refused	79 (24.9%)
Attempted but not obtained	65 (20.5%)
Not attempted	173 (54.6%)
BMI	
Value specified	4,721 (91.0%)
(-1 not applicable)	336 (6.5%)
.	129 (2.5%)
BMI (-1 not applicable)	
Refused	82 (24.4%)
Attempted but not obtained	67 (19.9%)
Not attempted	187 (55.7%)
Hedib01 (Asthma, OP, OA, emotional/nervous disorders, dementia)	
None	2,935 (56.6%)
Value specified	2,249 (43.4%)
(-8 Don't know)	1 (0.0%)
(-9 refusal)	1 (0.0%)
Hedia01 (HBP, heart problems, diabetes, stroke)	
None	2,480 (47.8%)
Value specified	2,704 (52.1%)
(-8 Don't know)	2 (0.0%)
Heart1 (OA)	
Value specified	1,173 (22.6%)
(-8 Don’t know)	169 (3.3%)
(-1 not applicable)	3,844 (74.1%)

Appendix 7: Outliers within Logistic Regression Modeling

Outliers are acknowledged to have a high leverage on models. The example below (Figure 32) shows the effect of a low number of matches during a player's career on joint replacement, both before and after the three lower values (<50) were excluded (Figure 33).

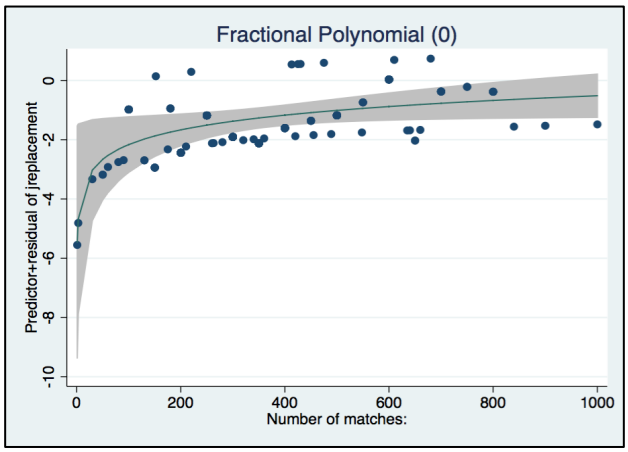


Figure 32. Fractional polynomial plot of the number of matches in a player's career and their predicted risk joint replacement

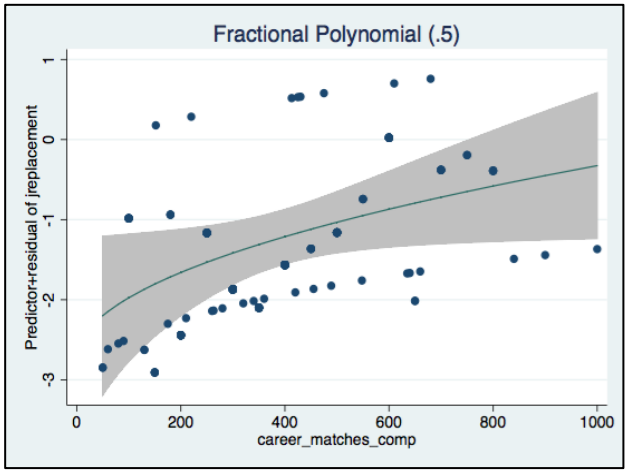


Figure 33. Fractional polynomial plot of the number of matches in a player's career and their predicted risk joint replacement, after the exclusion of low values with high leverage.

Appendix 8: Assumption of Linearity within Logistic Regression Modeling

The figures shown below (Figures 34 and 35) are examples of where the logistic regression assumption of linearity of the risk factor's effect on the outcome was not met. These were therefore produced as categorical variables for the risk factor with that specific outcome.

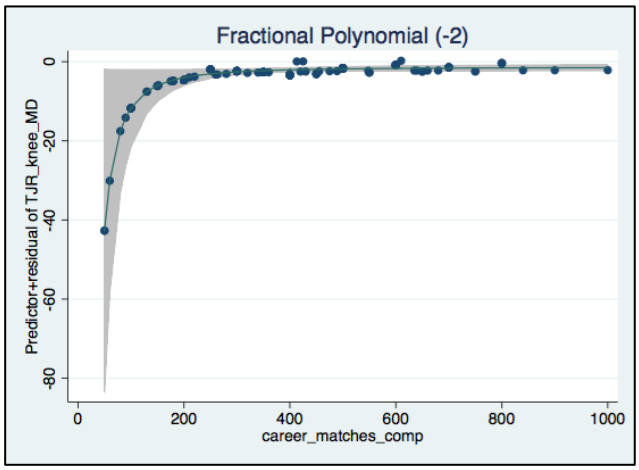


Figure 34. The assumption of linearity was not met for the effect of the continuous 'career matches' variable on the risk of TKR.

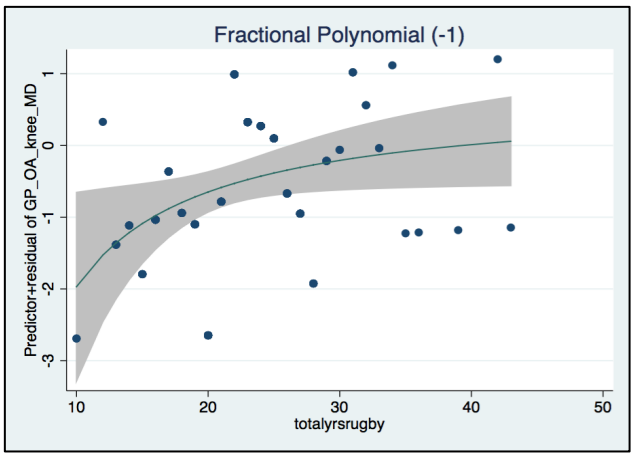


Figure 35. The assumption of linearity was also not met for the effect of the 'total years of rugby' on GPKOA.

Appendix 9: The Effect of Playing Exposure on OA-outcome at the Hip

Table 41. Logistic regression analyses of playing load risk factors for NHANES pain at the hip.

	NHANES Hip			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	241	0.99 (0.93-1.05)	0.673	241	0.99 (0.93-1.05)	0.685	237	0.99 (0.93-1.05)	0.721
Years at highest level	248	0.99 (0.90-1.08)	0.789	248	0.99 (0.90-1.08)	0.802	244	0.98 (0.90-1.08)	0.738
Number of matches (per 50 matches)	198	0.99 (0.90-1.09)	0.778	198	0.97 (0.88-1.07)	0.585	195	0.97 (0.88-1.07)	0.549
Age at first schoolboy game (years)	250	0.93 (0.82-1.06)	0.282	250	0.91 (0.79-1.05)	0.189	246	0.91 (0.79-1.04)	0.172

Table 42. Logistic regression analyses of playing load risk factors for physician-diagnosed OA at the hip.

	GPOA Hip			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	238	0.99 (0.93-1.06)	0.873	238	1.00 (0.94-1.07)	0.968	233	0.99 (0.93-1.06)	0.789
Years at highest level	247	1.00 (0.90-1.10)	0.929	247	1.00 (0.91-1.11)	0.920	242	1.00 (0.91-1.10)	0.990
Number of matches (per 50 matches)	196	1.05 (0.95-1.16)	0.348	196	1.02 (0.92-1.12)	0.712	192	0.99 (0.89-1.10)	0.808
Age at first schoolboy game (years)	249	1.02 (0.89-1.16)	0.812	249	0.93 (0.80-1.08)	0.345	244	0.93 (0.80-1.08)	0.355

Table 43. Logistic regression analyses of playing load risk factors for hip replacement.

	TJR Hip			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	240	1.00 (0.93-1.06)	0.897	240	1.01 (0.95-1.08)	0.723	235	1.01 (0.94-1.08)	0.823
Years at highest level	249	1.02 (0.92-1.12)	0.719	249	1.04 (0.94-1.14)	0.461	244	1.03 (0.93-1.13)	0.583
Number of matches (per 50 matches)	198	1.05 (0.95-1.16)	0.346	198	1.00 (0.91-1.11)	0.931	194	0.99 (0.88-1.10)	0.839
Age at first schoolboy game (years)	251	1.08 (0.94-1.23)	0.292	251	0.91 (0.78-1.07)	0.275	246	0.91 (0.78-1.07)	0.257

Appendix 10: The Effect of Playing Exposure on OA-outcome at the Shoulder

Table 44. Logistic regression analyses of playing load risk factors for NHANES pain at the shoulder.

	NHANES Shoulder			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	240	0.99 (0.94-1.05)	0.789	240	0.99 (0.94-1.05)	0.773	235	1.00 (0.94-1.06)	0.926
Years at highest level	249	0.96 (0.88-1.04)	0.341	249	0.96 (0.88-1.04)	0.333	244	0.96 (0.88-1.04)	0.303
Number of matches (per 50 matches)	199	1.02 (0.94-1.11)	0.637	199	1.02 (0.94-1.12)	0.583	195	1.04 (0.92-1.14)	0.396
Age at first schoolboy game (years)	251	1.03 (0.92-1.15)	0.589	251	1.05 (0.93-1.19)	0.388	246	1.05 (0.92-1.18)	0.453

Table 45. Logistic regression analyses of playing load risk factors for physician-diagnosed OA at the shoulder.

	GPOA Shoulder			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	238	1.07 (1.00-1.14)	0.056	238	1.07 (1.00-1.14)	0.057	233	1.06 (0.99-1.13)	0.109
Years at highest level	247	0.90 (0.80-1.02)	0.097	247	0.91 (0.80-1.02)	0.101	242	0.89 (0.79-1.01)	0.068
Number of matches (per 50 matches)	196	1.10 (0.99-1.21)	0.070	196	1.10 (0.99-1.22)	0.072	192	1.08 (0.96-1.20)	0.186
Age at first schoolboy game (years)	249	1.03 (0.90-1.18)	0.651	249	1.04 (0.89-1.20)	0.645	244	1.04 (0.89-1.21)	0.637
Total years of rugby (categorised)	252	2.26 (1.02-4.99)	0.044	252	2.29 (1.03-5.09)	0.041	247	2.05 (0.91-4.60)	0.082

Table 46. Logistic regression analyses of playing load risk factors for shoulder replacement.

	TJR Shoulder			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Total years of rugby	240	0.97 (0.84-1.11)	0.630	240	0.98 (0.86-1.12)	0.733	235	0.97 (0.84-1.11)	0.625
Years at highest level	249	1.03 (0.84-1.27)	0.769	249	1.04 (0.85-1.27)	0.715	244	1.03 (0.84-1.26)	0.772
Number of matches (per 50 matches)	198	1.18 (0.93-1.49)	0.178	198	1.14 (0.90-1.45)	0.282	194	1.14 (0.89-1.46)	0.293
Age at first schoolboy game (years)	251	1.16 (0.88-1.53)	0.282	251	1.08 (0.80-1.47)	0.614	246	1.07 (0.79-1.45)	0.664

Appendix 11: The Effect of Injury on OA-outcomes at the Hip and Shoulder

Table 47. Logistic regression analysis of hip injury as a risk factor for physician-diagnosed hip OA.

	GPOA Hip			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Hip injury	246	4.39 (2.15-8.96)	0.000	246	6.64 (2.99-14.74)	0.000	241	7.30 (3.22-16.57)	0.000
Rugby (playing or training) hip injury	238	3.64 (1.65-8.02)	0.000	238	5.27 (2.21-12.55)	0.000	233	5.81 (2.38-14.16)	0.000

Table 48. Logistic regression analysis of hip injury as a risk factor for hip replacement.

	Hip replacement			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Hip injury	248	6.28 (3.00-13.13)	0.000	248	21.50 (7.56-61.15)	0.000	243	20.76 (7.29-59.08)	0.000
Rugby (playing or training) hip injury	240	4.73 (2.10-10.68)	0.000	240	13.81 (4.64-41.08)	0.000	235	13.22 (4.43-39.48)	0.000

Table 49. Logistic regression analysis of hip injury as a risk factor for NHANES hip pain.

	NHANES hip pain			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Hip injury	245	2.49 (1.23-5.05)	0.011	245	2.83 (1.36-5.90)	0.005	241	2.77 (1.33-5.76)	0.006
Rugby (playing or training) hip injury	237	3.16 (1.47-6.78)	0.003	237	3.70 (1.66-8.21)	0.001	233	3.65 (1.64-8.13)	0.002

Table 50. Logistic regression analysis of shoulder injury as a risk factor for physician-diagnosed shoulder OA

	GPOA Shoulder			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Shoulder injury	246	6.22 (2.79-13.85)	0.000	246	6.54 (2.91-14.72)	0.000	241	7.07 (3.05-16.38)	0.000
Rugby (playing or training) shoulder injury	238	5.93 (2.73-12.84)	0.000	238	6.43 (2.92-14.17)	0.000	233	7.77 (3.33-18.16)	0.000

Table 51. Logistic regression analysis of shoulder injury as a risk factor for shoulder replacement.

	Shoulder replacement			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Shoulder injury	248	10.87 (1.32-89.79)	0.027	248	13.11 (1.56-109.84)	0.018	243	12.91 (1.54-107.99)	0.018
Rugby (playing or training) shoulder injury	240	12.39 (1.47-104.79)	0.021	240	15.79 (1.83-136.63)	0.012	235	22.41 (2.02-248.82)	0.011

Table 52. Logistic regression analysis of shoulder injury as a risk factor for NHANES shoulder pain.

	Shoulder replacement			Adjusted for age			Adjusted for age and weight		
Risk factor	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Shoulder injury	245	7.14 (3.81-13.40)	0.000	245	7.21 (3.81-13.61)	0.000	240	8.08 (4.19-15.57)	0.000
Rugby (playing or training) shoulder injury	237	5.20 (2.83-9.56)	0.000	237	5.21 (2.81-9.65)	0.000	232	5.88 (3.11-11.11)	0.000

Appendix 12: The Variable Type of Candidate Predictors

Table 53. The variable type of candidate predictors.

Candidate Predictors	Variable type
Age at first game (years)	Continuous
Total years of play (years)	Continuous
Level of play	Categorical
Level of play: 1 Level of play: 2 Level of play: 3 Level of play: 4 Level of play: 5 Level of play: 6 Level of play: 7 Other	
Playing BMI	
Position of play	Categorical
Position of play: 1 Position of play: 2 Position of play: 3 Position of play: 4 Position of play: 5 Position of play: 6 Position of play: 7 Position of play: 8 Position of play: 9 Position of play: 10 Position of play: 11 Position of play: 12 Position of play: 13 Position of play: 14 Position of play: 15	
Professional status (categorical)	Categorical
Number of games in career (continuous)	Continuous
Hours per week training youth (hours)	
Hours per week training player (hours)	
Slipped upper femoral epiphysis (binary)	Binary
Hip dysplasia (binary)	Binary
Severe hip injury (binary)	Binary
Age (years)	Continuous
BMI	
Family history hip OA (binary)	Binary

Appendix 13: The Development of a Prediction Model

Continuous variables must be normally distributed for imputation. Examples of provided for normally distributed (Figure 36) and skewed (Figure 37) predictor variables. These variables were then transformed, using a function selected with the 'gladder' command (Figure 38).

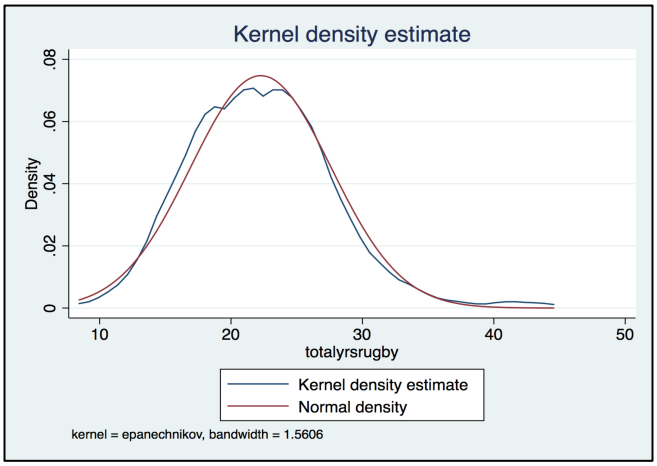


Figure 36. Assessing normality of continuous predictor variables before imputation: A normal distribution

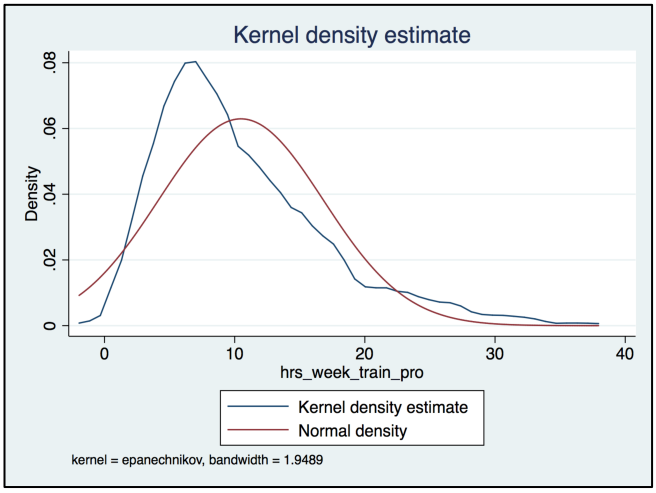


Figure 37. Assessing normality of continuous predictor variables before imputation: A skewed distribution

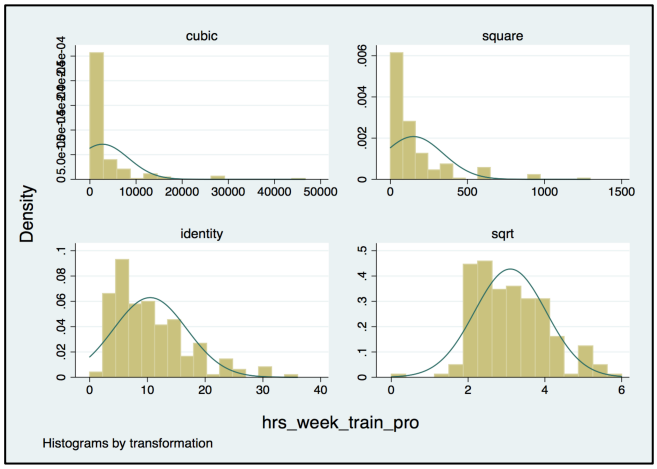


Figure 38. Transforming continous predictor variables without normal distribution: using 'gladder' command to assess which transformation should be performed

Appendix 14: Single Imputation of Candidate Predictors

Multivariate imputation			Imputations	= 1
Chained equations			added	= 1
Imputed: m=1			updated	= 0
Initialization: monotone			Iterations	= 10
sufe_ndk:	augmented logistic regression		burn-in	= 10
hip_dysp:	augmented logistic regression			
fam_hist_hip~d:	logistic regression			
injury_hip_md:	logistic regression			
schoolboy_ga~l:	linear regression			
totalyrsrugby:	linear regression			
playing_BMI:	linear regression			
sqrt_hrs_wee~o:	linear regression			
sqrt_hrs_wee~h:	linear regression			
level_play_cat:	ordered logistic regression			
play2:	multinomial logistic regression			
career_match~l:	predictive mean matching			
Observations per m				
Variable	Complete	Incomplete	Imputed	Total
sufe_ndk	249	5	5	254
hip_dysp	249	5	5	254
fam_hist_hip~d	228	26	26	254
injury_hip_md	248	6	6	254
schoolboy_ga~l	251	3	3	254
totalyrsrugby	240	14	14	254
playing_BMI	246	8	8	254
sqrt_hrs_wee~o	215	39	39	254
sqrt_hrs_wee~h	189	65	65	254
level_play_cat	249	5	5	254
play2	244	10	10	254
career_match~l	201	53	53	254

Appendix 15: Model Performance

Table 54. Model calibration: ten quantiles of predicted probabilities and observed probabilities of hip replacement

Group	Probability	Observed 1	Expected 1	Observed 0	Expected 0	Total
1	0.0010	0	0.0	33	33.0	33
2	0.0042	1	0.2	35	35.8	36
3	0.0047	0	0.1	15	14.9	15
5	0.0455	4	1.7	41	43.3	45
6	0.1723	0	2.6	25	22.4	25
7	0.1752	5	7.7	39	36.3	44
8	0.1907	4	3.8	16	16.2	20
9	0.4817	6	5.4	8	8.6	14
10	0.9964	19	17.5	3	4.5	22

Table 55. Selection of a cutpoint for the risk score based on the area under the receiver operating curve.

Cutpoint	Sensitivity	Specificity	Correctly Classified	LR+	LR-
(>= 0)	100.00%	0.00%	15.35%	1.0000	
(>= 15)	100.00%	15.35%	28.35%	1.1813	0.0000
(>= 16)	97.44%	31.63%	41.73%	1.4251	0.0811
(>= 30)	97.44%	38.60%	47.64%	1.5870	0.0664
(>= 31)	94.87%	42.79%	50.79%	1.6583	0.1198
(>= 39)	94.87%	43.72%	51.57%	1.6857	0.1173
(>= 45)	87.18%	57.67%	62.20%	2.0597	0.2223
(>= 46)	87.18%	64.19%	67.72%	2.4342	0.1997
(>= 54)	87.18%	66.05%	69.29%	2.5676	0.1941
(>= 55)	74.36%	87.44%	85.43%	5.9212	0.2932
(>= 57)	64.10%	94.88%	90.16%	12.5291	0.3783
(>= 58)	64.10%	95.35%	90.55%	13.7820	0.3765
(>= 60)	61.54%	95.35%	90.16%	13.2308	0.4034
(>= 61)	58.97%	95.81%	90.16%	14.0883	0.4282
(>= 69)	58.97%	96.74%	90.94%	18.1136	0.4241
(>= 70)	48.72%	98.60%	90.94%	34.9146	0.5201
(>= 72)	46.15%	99.07%	90.94%	49.6156	0.5435
(>= 84)	46.15%	99.53%	91.34%	99.2303	0.5410
(>= 85)	20.51%	99.53%	87.40%	44.1024	0.7986
(>= 99)	7.69%	100.00%	85.83%		0.9231
(>= 112)	5.13%	100.00%	85.43%		0.9487
(>= 126)	2.56%	100.00%	85.04%		0.9744
(> 126)	0.00%	100.00%	84.65%		1.0000
	Obs	ROC Area	Std.Err.	95% CI	
	254	0.8819	0.0323	0.8186	0.9452

Table 56. Output of the 'collin' assessment of multicollinearity within the model.

Variable	VIF	SQRT VIF	Tolerance	R-Squared
Age	1.01	1.00	0.9916	0.0084
Injury	1.02	1.01	0.9785	0.0215
Position of play	1.01	1.01	0.9893	0.0107
SUFE	1.02	1.01	0.9801	0.0199
Family history	1.02	1.01	0.9782	0.0218
Mean VIF	1.02			

Bibliography

1. Hayes, H., Buckland, S. & Tarpey, M. *Briefing notes for researchers: Public Involvement in NHS, public health and social care research*. (2012).

2. NHS National Institute for Health Research. Patient and public involvement in health and social care research: A handbook for researchers. (2014).

3. Bannister, R. Sport, physical recreation, and the national health. *Br. Med. J.* **4,** 711–5 (1972).

4. Arden, N. & Nevitt, M. C. in *Oxford Textbook of Osteoarthritis and Crystal Arthropathy* (eds. Doherty, M., Bijlsma, J., Arden, N., Hunter, D. J. & Dalbeth, N.) (Oxford University Press, 2016).

5. Caspersen, C. J., Powell, K. E. & Christenson, G. M. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* **100,** 126–31 (1985).

6. Warburton, D. E. R., Nicol, C. W. & Bredin, S. S. D. Health benefits of physical activity: the evidence. *CMAJ* **174,** 801–809 (2006).

7. Hayes, C. & Kriska, A. Role of Physical Activity in Diabetes Management and Prevention. *J. Am. Diet. Assoc.* **108,** (2008).

8. Helmrich, S. P., Ragland, D. R., Leung, R. W. & Paffenbarger, R. S. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. *N. Engl. J. Med.* **325,** 147–52 (1991).

9. Colberg, S. R. Physical activity: The forgotten tool for type 2 diabetes management. *Frontiers in Endocrinology* **3,** (2012).

10. Richardson, C. R., Kriska, A. M., Lantz, P. M. & Hayward, R. A. Physical activity and mortality across cardiovascular disease risk groups. *Med. Sci. Sports Exerc.* **36,** 1923–1929 (2004).

11. Blondell, S. J., Hammersley-Mather, R. & Veerman, J. Does physical activity prevent cognitive decline and dementia?: A systematic review and meta-analysis

of longitudinal studies. *BMC Public Health* **14,** 1–12 (2014).

12. Pescatello, L. S. *et al.* Short-term effect of dynamic exercise on arterial blood pressure. *Circulation* **83,** 1557–1561 (1991).

13. McKune, A. J. *et al.* Autonomic cardiac regulation, blood pressure and cardiorespiratory fitness responses to different training doses over a 12 week group program in the elderly. *Arch. Gerontol. Geriatr.* **70,** 130–135 (2017).

14. Blair, S. N. *et al.* Changes in physical fitness and all-cause mortality. Prospective Study of Healthy and Unhealthy Men. *Jama* **273,** 1093–1098 (1995).

15. Pan, X. R. *et al.* Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* **20,** 537–44 (1997).

16. Eriksson, K. F. & Lindgärde, F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmö feasibility study. *Diabetologia* **34,** 891–8 (1991).

17. Tuomilehto, J. *et al.* Prevention of Type 2 Diabetes Mellitus By Changes in Lifestyle Among Subjects With Impaired Glucose Tolerance. *N. Engl. J. Med.* **344,** 1343–1350 (2001).

18. Sesso, H. D., Paffenbarger, R. S. & Lee, I. M. Physical activity and breast cancer risk in the College Alumni Health Study (United States). *Cancer Causes Control* **9,** 433–439 (1998).

19. Thune, I. & Furberg, A. S. Physical activity and cancer risk: dose-response and cancer, all sites and site-specific. *Med. Sci. Sports Exerc.* **33,** S530-NaN-S610 (2001).

20. Zhang, Y. *et al.* Occupational and leisure-time physical activity and risk of colon cancer by subsite. *J Occup Env. Med* **48,** 236–243 (2006).

21. Brownson, R. C., Zahm, S. H., Chang, J. C. & Blair, A. Occupational risk of colon cancer. *Am. J. Epidemiol.* **130,** 675–687 (1989).

22. Kyle, U. G., Morabia, A., Schutz, Y. & Pichard, C. Sedentarism affects body fat mass index and fat-free mass index in adults aged 18 to 98 years. *Nutrition* **20,** 255–260 (2004).

23. Musumeci, G. *et al.* Osteoarthritis in the XXIst century: risk factors and behaviours that influence disease onset and progression. *Int. J. Mol. Sci.* **16,** 6093–112 (2015).

24. Marks, R. Obesity profiles with knee osteoarthritis: correlation with pain, disability, disease progression. *Obesity (Silver Spring).* **15,** 1867–1874 (2007).

25. Mooney, R. A., Sampson, E. R., Lerea, J., Rosier, R. N. & Zuscik, M. J. High-fat diet accelerates progression of osteoarthritis after meniscal/ligamentous injury. *Arthritis Res. Ther.* **13,** R198 (2011).

26. Kluzek, S., Newton, J. L. & Arden, N. K. Is osteoarthritis a metabolic disorder? *Br. Med. Bull.* **115,** 111–121 (2015).

27. Després, J.-P. & Lemieux, I. Abdominal obesity and metabolic syndrome. *Nature* **444,** 881–7 (2006).

28. Grundy, S. M. Obesity, metabolic syndrome, and cardiovascular disease. *J. Clin. Endocrinol. Metab.* **89,** 2595–600 (2004).

29. Public Health England. Adult obesity and type 2 diabetes About Public Health England. 1–39 (2014). doi:2014211

30. Deshpande, A. D., Harris-Hayes, M. & Schootman, M. Epidemiology of diabetes and diabetes-related complications. *Phys. Ther.* **88,** 1254–1264 (2008).

31. Haslam, D. W. & James, W. P. T. Obesity. in *Lancet* **366,** 1197–1209 (2005).

32. Wing, R. R. & Phelan, S. Long-term weight loss maintenance. **82,** 222–225 (2005).

33. Ströhle, A. Physical activity, exercise, depression and anxiety disorders. *J. Neural Transm.* **116,** 777–784 (2009).

34. McKercher, C. M. *et al.* Physical Activity and Depression in Young Adults. *Am. J. Prev. Med.* **36,** 161–164 (2009).

35. Teychenne, M., Ball, K. & Salmon, J. Physical activity and likelihood of depression in adults: A review. *Prev. Med. (Baltim).* **46,** 397–411 (2008).

36. Harris, A. H. S., Cronkite, R. & Moos, R. Physical activity, exercise coping, and depression in a 10-year cohort study of depressed patients. *J. Affect. Disord.* **93,** 79–85 (2006).

37. Broocks, A. *et al.* Comparison of aerobic exercise, clomipramine, and placebo in the treatment of panic disorder. *Am. J. Psychiatry* **155,** 603–609 (1998).

38. Ströhle, A. *et al.* Physical activity and prevalence and incidence of mental disorders in adolescents and young adults. *Psychol. Med.* **37,** 1657–1666 (2007).

39. Murray, a W. & Wilson, N. I. L. Changing incidence of slipped capital femoral epiphysis: a relationship with obesity? *J. Bone Joint Surg. Br.* **90,** 92–4 (2008).

40. Shephard, R. J. & Trudeau, F. The Legacy of Physical Education: Influences on Adult Lifestyle. *Pediatr. Exerc. Sci.* **12,** 34–50 (2000).

41. Kelder, S. H., Perry, C. L., Klepp, K. I. & Lytle, L. L. Longitudinal tracking of adolescent smoking, physical activity, and food choice behaviors. *Am. J. Public Health* **84,** 1121–1126 (1994).

42. Fox, K. R. The effects of exercise on self perceptions and self-esteem. *Int. J. Sport Psychol.* **31,** 228–240 (2000).

43. Bailey, R. Physical Education and Sport in Schools: A Review of Benefits and Outcomes. *J. Sch. Health* **76,** 397–401 (2006).

44. Fox, K. R. The Self-Esteem Complex and Youth Fitness. *Quest* **40,** 230–246 (1988).

45. Wannamethee, G., Shaper, A. G. & Macfarlane, P. W. Heart-Rate, Physical-Activity, and Mortality From Cancer and Other Noncardiovascular Diseases. *Am. J. Epidemiol.* **137,** 735–748 (1993).

46. Kampert, J. B., Blair, S. N., Barlow, C. E. & Kohl, H. W. Physical activity, physical fitness, and all-cause and cancer mortality: A prospective study of men and women. *Ann. Epidemiol.* **6,** 452–457 (1996).

47. Williamson, W. *et al.* Behavioural physical activity interventions in participants with lower-limb osteoarthritis: a systematic review with meta-analysis. *BMJ Open* **5,** e007642 (2015).

48. Susko, A. M. & Kelley Fitzgerald, G. The pain-relieving qualities of exercise in knee osteoarthritis. *Open Access Rheumatology: Research and Reviews* **5,** 81–91 (2013).

49. Andersen, L. N. *et al.* Efficacy of Tailored Physical Activity or Chronic Pain Self-Management Programme on return to work for sick-listed citizens: A 3-month

randomised controlled trial. *Scand. J. Public Health* **43,** 694–703 (2015).

50. Treviño, L. A. *et al.* Physical activity as a coping strategy for smoking cessation in mid-life and older adults. *Addict. Behav.* **39,** 885–888 (2014).

51. Nezhad, M. A. S. & Besharat, M. A. Relations of resilience and hardiness with sport achievement and mental health in a sample of athletes. *Procedia - Soc. Behav. Sci.* **5,** 757–763 (2010).

52. Morgan, P. B. C., Fletcher, D. & Sarkar, M. Defining and characterizing team resilience in elite sport. *Psychol. Sport Exerc.* **14,** 549–559 (2013).

53. Sarkar, M. & Fletcher, D. How Should We Measure Psychological Resilience in Sport Performers? *Meas. Phys. Educ. Exerc. Sci.* **17,** 264–280 (2013).

54. Sarkar, M. & Fletcher, D. Psychological resilience in sport performers: a review of stressors and protective factors. *J. Sports Sci.* **0,** 37–41 (2014).

55. Fletcher, D. & Sarkar, M. A grounded theory of psychological resilience in Olympic champions. *Psychol. Sport Exerc.* **13,** 669–678 (2012).

56. Warburton, D. E. R., Taunton, J., Bredin, S. S. D. & Isserow, S. H. The risk-benefit paradox of exercise. *BC Med. J.* 210–218 (2016).

57. Corrado, D., Basso, C., Rizzoli, G., Schiavon, M. & Thiene, G. Does Sports Activity Enhance the Risk of Sudden Death in Adolescents and Young Adults? *J. Am. Coll. Cardiol.* **42,** 1959–1963 (2003).

58. Steering Committee of the Physicians' Health Study Research Group. Final report on the aspirin component of the ongoing Physicians' Health Study. Steering Committee of the Physicians' Health Study Research Group. *N. Engl. J. Med.* **321,** 129–35 (1989).

59. Albert, C. M. *et al.* Triggering of sudden death from cardiac causes by vigorous exertion. *N. Engl. J. Med.* **343,** 1355–1361 (2000).

60. Pollock, M. L. *et al.* Effects of frequency and duration of training on attrition and incidence of injury. 31–36 (1977).

61. Franklin, B. A. & Billecke, S. Putting the Benefits and Risks of Aerobic Exercise in Perspective. *Curr. Sports Med. Rep.* **11,** 201–208 (2012).

62. Bergen, G., Chen, L. H., Warner, M. & Fingerhut, L. A. *Injury in the United States: 2007 Chartbook*. (2008).

63. Knowles, S. B. *et al.* Cost of injuries from a prospective cohort study of North Carolina high school athletes. *Inj. Prev.* **13,** 416–422 (2007).

64. Finch, C. F., Kemp, J. L. & Clapperton, A. J. The incidence and burden of hospital-treated sports-related injury in people aged 15+ years in Victoria, Australia, 2004-2010: A future epidemic of osteoarthritis? *Osteoarthr. Cartil.* **23,** 1138–1143 (2015).

65. Marshall, S. W. & Guskiewicz, K. M. Sports and recreational injury: the hidden cost of a healthy lifestyle. *Inj. Prev.* **9,** (2003).

66. Shephard, R. J. Can we afford to exercise, given current injury rates? *Inj. Prev.* **9,** 99–100 (2003).

67. Hootman, J. M., Dick, R. & Agel, J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J. Athl. Train.* **42,** 311–9 (2007).

68. Hootman, J. M. *et al.* Epidemiology of musculoskeletal injuries among sedentary and physically active adults. *Med. Sci. Sports Exerc.* **34,** 838–844 (2002).

69. Cross, M. *et al. England Professional Rugby Injury Surveillance Project 2014-15 Season Report*. (2016).

70. Dare, D. & Rodeo, S. Mechanisms of Post-traumatic Osteoarthritis After ACL Injury. *Curr. Rheumatol. Rep.* **16,** 448 (2014).

71. Lohmander, L. S., Englund, P. M., Dahl, L. L. & Roos, E. M. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am. J. Sports Med.* **35,** 1756–69 (2007).

72. Roos, E. M. Joint injury causes knee osteoarthritis in young adults. *Curr. Opin. Rheumatol.* **17,** 195–200 (2005).

73. Gelber, A. C. *et al.* Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. *Ann. Intern. Med.* **133,** 321–8 (2000).

74. Cooper, C. *et al.* Individual risk factors for hip osteoarthritis: obesity, hip injury, and physical activity. *Am. J. Epidemiol.* **147,** 516–22 (1998).

75. Cymet, T. C. & Sinkov, V. Does long-distance running cause osteoarthritis? *J. Am. Osteopath. Assoc.* **106,** 342–345 (2006).

76. Lane, N. E. *et al.* Running, osteoarthritis, and bone density: initial 2-year longitudinal study. *Am. J. Med.* **88,** 452–9 (1990).

77. Spector, T. D. *et al.* Risk of osteoarthritis associated with long-term weight-bearing sports: A radiologic survey of the hips and knees in female ex-athletes and population controls. *Arthritis Rheum.* **39,** 988–995 (1996).

78. Vingård, E., Alfredsson, L., Goldie, I. & Hogstedt, C. Sports and osteoarthrosis of the hip. An epidemiologic study. *Am. J. Sports Med.* **21,** 195–200 (1993).

79. Neusel, E., Arza, D., Rompe, G. & Steinbrück, K. Long-term roentgenologic studies in peak performance javelin throwers. *Sportverletz. Sportschaden* **1,** 76–80 (1987).

80. Niek van Dijk, C.; Lim, L.S.L, Poortman, A.; Strubbe, E.H., Marti, R, K. Degenerative Joint Disease in Female Ballet Dancers. *Am. J. Med.* (1995).

81. Fitzgerald, B. & McLatchie, G. R. Degenerative joint disease in weight-lifters. Fact or fiction? *Br. J. Sports Med.* **14,** 97–101 (1980).

82. Golightly, Y. M., Marshall, S. W., Callahan, L. F. & Guskiewicz, K. Early-onset arthritis in retired National Football League players. *J. Phys. Act. Health* **6,** 638–643 (2009).

83. Krajnc, Z. *et al.* Increased risk of knee injuries and osteoarthritis in the non-dominant leg of former professional football players. *Wien. Klin. Wochenschr.* **122 Suppl,** 40–3 (2010).

84. Post, E. G. *et al.* High School Sport Specialization Patterns of Current Division I Athletes. *Sports Health* **9,** 148–153 (2016).

85. Post, E. G. *et al.* The Association of Sport Specialization and Training Volume With Injury History in Youth Athletes. *Am. J. Sports Med.* 36354651769084 (2017). doi:10.1177/0363546517690848

86. Pasulka, J., Jayanthi, N., McCann, A., Dugas, L. R. & LaBella, C. Specialization patterns across various youth sports and relationship to injury risk. *Phys.*

Sportsmed. **0,** 00913847.2017.1313077 (2017).

87. Jayanthi, N., Pinkham, C., Dugas, L., Patrick, B. & LaBella, C. Sports Specialization in Young Athletes: Evidence-Based Recommendations. *Sport. Heal. A Multidiscip. Approach* **5,** 251–257 (2013).

88. Schnell, A., Mayer, J., Diehl, K., Zipfel, S. & Thiel, A. Giving everything for athletic success! - Sports-specific risk acceptance of elite adolescent athletes. *Psychol. Sport Exerc.* **15,** 165–172 (2014).

89. Dijkstra, H. P., Pollock, N., Chakraverty, R. & Alonso, J. M. Managing the health of the elite athlete: a new integrated performance health management and coaching model. *Br. J. Sports Med.* **48,** 523–31 (2014).

90. Mendes, S. H. *et al.* Effect of rapid weight loss on performance in combat sport male athletes: does adaptation to chronic weight cycling play a role? *Br. J. Sports Med.* **47,** 1155–60 (2013).

91. Franchini, E., Brito, C. J. & Artioli, G. G. Weight loss in combat sports: physiological, psychological and performance effects. *J. Int. Soc. Sports Nutr.* **9,** 52 (2012).

92. Cottler, L. B. *et al.* Injury, pain, and prescription opioid use among former National Football League (NFL) players. *Drug Alcohol Depend.* **116,** 188–194 (2011).

93. Fenton, L. T. & Pitter, R. Keeping the Body in Play. *Res. Q. Exerc. Sport* **81,** 212–223 (2010).

94. Murphy, P. & Waddington, I. Are Elite Athletes Exploited? *Sport Soc.* **10,** 239–255 (2007).

95. Hassmén, P., Koivula, N. & Uutela, A. Physical Exercise and Psychological Well-Being: A Population Study in Finland. *Prev. Med. (Baltim).* **30,** 17–25 (2000).

96. Schaal, K. *et al.* Psychological balance in high level athletes: gender-based differences and sport-specific patterns. *PLoS One* **6,** e19007 (2011).

97. Hughes, L. & Leavey, G. Setting the bar: Athletes and vulnerability to mental illness. *Br. J. Psychiatry* **200,** 95–96 (2012).

98. Steptoe, A. & Butler, N. Sports participation and emotional wellbeing in

adolescents. *Lancet (London, England)* **347,** 1789–92 (1996).

99. Taylor, C. B., Sallis, J. F. & Needle, R. The relation of physical activity and exercise to mental health. *Public Health Rep.* **100,** 195–202 (1985).

100. Strawbridge, W. J., Deleger, S., Roberts, R. E. & Kaplan, G. A. Physical activity reduces the risk of subsequent depression for older adults. *Am. J. Epidemiol.* **156,** 328–334 (2002).

101. Guszkowska, M. [Effects of exercise on anxiety, depression and mood]. *Psychiatr. Pol.* **38,** 611–20

102. Rice, S. M. *et al.* The Mental Health of Elite Athletes: A Narrative Systematic Review. *Sport. Med.* **46,** 1333–1353 (2016).

103. Gulliver, A., Griffiths, K. M., Mackinnon, A., Batterham, P. J. & Stanimirovic, R. The mental health of Australian elite athletes. *J. Sci. Med. Sport* **18,** 255–261 (2015).

104. Fenichel, R. M. & Warren, M. P. Anorexia, bulimia, and the athletic triad: Evaluation and management. *Curr. Osteoporos. Rep.* **5,** 160–164 (2007).

105. Miller, K. K. Medical Findings in Outpatients With Anorexia Nervosa. *Arch. Intern. Med.* **165,** 561 (2005).

106. Mendelsohn, F. A. & Warren, M. P. Anorexia, Bulimia, and the Female Athlete Triad: Evaluation and Management. *Endocrinology and Metabolism Clinics of North America* **39,** 155–167 (2010).

107. Farlex. Segen's Medical Dictionary. *Farlex, Inc* (2012). Available at: http://medical-dictionary.thefreedictionary.com/triple+therapy.

108. Williams, S., Trewartha, G., Kemp, S. & Stokes, K. A meta-analysis of injuries in senior men's professional Rugby Union. *Sports Medicine* **43,** 1043–1055 (2013).

109. Williams, J. Z. *et al.* Epidemiological Patterns of Initial and Subsequent Injuries in Collegiate Football Athletes. 1171–1178 (2011). doi:10.1177/0363546516685317

110. Guskiewicz, K. M. *et al.* Association between recurrent concussion and late-life cognitive impairment in retired professional football players. *Neurosurgery* **57,** 719-26-26 (2005).

111. Guskiewicz, K. M. *et al.* Recurrent concussion and risk of depression in retired professional football players. *Med. Sci. Sports Exerc.* **39,** 903–9 (2007).

112. Didehbani, N., Munro Cullum, C., Mansinghani, S., Conover, H. & Hart, J. Depressive symptoms and concussions in aging retired NFL players. *Arch. Clin. Neuropsychol.* **28,** 418–24 (2013).

113. Selden, M. a, Helzberg, J. H. & Waeckerle, J. F. Early cardiovascular mortality in professional football players: fact or fiction? *Am. J. Med.* **122,** 811–814 (2009).

114. Gabbe, B. & Finch, C. A profile of Australian football injuries presenting to sports medicine clinics. *J. Sci. Med. Sport* **4,** 386–395 (2001).

115. Finch, C., Valuri, G. & Ozanne-Smith, J. Sport and active recreation injuries in Australia: evidence from emergency department presentations. *Br. J. Sports Med.* **32,** 220–5 (1998).

116. Finch, C. A new framework for research leading to sports injury prevention. *J. Sci. Med. Sport* **9,** 3- (2006).

117. Saxon, L., Finch, C. & Bass, S. Sports participation, sports injuries and osteoarthritis implications for prevention. *Sports Medicine* **28,** 123–135 (1999).

118. Bekker, S., Paliadelis, P. & Finch, C. F. The translation of sports injury prevention and safety promotion knowledge: insights from key intermediary organisations. *Heal. Res. Policy Syst.* **15,** 25 (2017).

119. King, T., Rosenberg, M., Braham, R., Ferguson, R. & Dawson, B. Life after the game--injury profile of past elite Australian football players. *J. Sci. Med. Sport* **16,** 302–6 (2013).

120. Gabbett, T. J. & Jenkins, D. G. Relationship between training load and injury in professional rugby league players. *J. Sci. Med. Sport* **14,** 204–209 (2011).

121. Stephenson, S., Gissane, C. & Jennings, D. Injury in rugby league: a four year prospective survey. *Br. J. Sports Med.* **30,** 331–334 (1996).

122. Gibbs, N. Common Rugby League Injuries: Recommendations for Treatment and Preventative Measures. *Sport. Med.* **18,** 438–450 (1994).

123. Lovell, M. E. & Rostron, P. Referral of professional Rugby League players to the

orthopaedic service: A review of 447 injuries in 147 players. *Sport. Exerc. Inj.* **2,** 103–107 (1996).

124. Gissane, C., Jennings, D., Kerr, K. & White, J. A. A pooled data analysis of injury incidence in rugby league football. *Sports Med.* **32,** 211–6 (2002).

125. Hoskins, W., Pollard, H., Hough, K. & Tully, C. Injury in rugby league. *Journal of Science and Medicine in Sport* **9,** 46–56 (2006).

126. Gabbett, T. J. Incidence, site, and nature of injuries in amateur rugby league over three consecutive seasons. *Br. J. Sports Med.* **34,** 98–103 (2000).

127. Gabbett, T. J. Incidence of injury in junior and senior rugby league players. *Sports Medicine* **34,** 849–859 (2004).

128. Gabbett, T. J. Incidence of injury in semi-professional rugby league players. *Br. J. Sports Med.* **37,** 36–43 (2003).

129. Gissane, C. Injury in rugby league: A four year prospective survey. *Br. J. Sports Med.* **30,** 331–334 (1996).

130. Gabbett, T. J., Jenkins, D. G. & Abernethy, B. Physical collisions and injury in professional rugby league match-play. *J. Sci. Med. Sport* **14,** 210–215 (2011).

131. Gabbett, T. J., Ullah, S., Jenkins, D. & Abernethy, B. Skill qualities as risk factors for contact injury in professional rugby league players. *J. Sports Sci.* **30,** 1421–1427 (2012).

132. Gabbett, T. J. & Domrow, N. Relationships between training load, injury, and fitness in sub-elite collision sport athletes. *J. Sports Sci.* **25,** 1507–19 (2007).

133. Meir, R. A., McDonald, K. N. & Russell, R. Injury consequences from participation in professional rugby league: a preliminary investigation. *Br. J. Sports Med.* **31,** 132–134 (1997).

134. Fuller, C. W., Brooks, J. H. M. & Kemp, S. P. T. Spinal injuries in professional rugby union: a prospective cohort study. *Clin. J. Sport Med.* **17,** 10–6 (2007).

135. Roberts, S. P., Trewartha, G., England, M., Shaddick, G. & Stokes, K. A. Epidemiology of time-loss injuries in English community-level rugby union. *BMJ Open* **3,** e003998 (2013).

136. Quarrie, K. L., Cantu, R. C. & Chalmers, D. J. Rugby union injuries to the cervical spine and spinal cord. *Sports Med.* **32,** 633–653 (2002).

137. Jakoet, I. & Noakes, T. D. A high rate of injury during the 1995 Rugby World Cup. *S. Afr. Med. J.* **88,** 45–7 (1998).

138. Davies, J. E. & Gibson, T. Injuries in Rugby Union football. *Br. Med. J.* **2,** 1759–1761 (1978).

139. Swain, M. S., Pollard, H. P. & Bonello, R. Incidence, severity, aetiology and type of neck injury in men's amateur rugby union: a prospective cohort study. *Chiropr. Osteopat.* **18,** 18 (2010).

140. Pearce, C. J., Brooks, J. H. M., Kemp, S. P. T. & Calder, J. D. F. The epidemiology of foot injuries in professional rugby union players. *Foot Ankle Surg.* **17,** 113–118 (2011).

141. McCoy, G. F., Piggot, J., Macafee, A. L. & Adair, I. V. Injuries of the Cervical Spine in Schoolboy Rugby Football. *J Bone Jt. Surg Br* **66,** 500–3 (1984).

142. Brooks, J. H. M. & Kemp, S. P. T. Recent Trends in Rugby Union Injuries. *Clin Sport. Med* **27,** 51–73 (2008).

143. Kuster, D., Gibson, A., Abboud, R. & Drew, T. Mechanisms of cervical spine injury in rugby union: a systematic review of the literature. *Br. J. Sports Med.* **46,** 550–4 (2012).

144. Trewartha, G., Preatoni, E., England, M. E. & Stokes, K. A. Injury and biomechanical perspectives on the rugby scrum: a review of the literature. *Br. J. Sports Med.* **49,** 425–33 (2015).

145. Chalmers, D. J., Samaranayaka, A., Gulliver, P. & McNoe, B. Risk factors for injury in rugby union football in New Zealand: a cohort study. *Br. J. Sports Med.* **46,** 95–102 (2012).

146. Viljoen, W. & Saunders, C. Training volume and injury incidence in a professional rugby union team. *South African J. Sport. Med.* **21,** 97–101 (2009).

147. McKenna, J. & Thomas, H. Enduring injustice: a case study of retirement from professional rugby union. *Sport. Educ. Soc.* **12,** 19–35 (2007).

148. O'Brien, C. P. 'Rugby neck': cervical degeneration in two front row rugby union players. *Clin. J. Sport Med.* **6,** 56–59 (1996).

149. McMillan, T. M. *et al.* Long-term health outcomes after exposure to repeated concussion in elite level: rugby union players. *J. Neurol. Neurosurg. Psychiatry* **0,** 1–7 (2016).

150. Lee, A. J., Garraway, W. M., Hepburn, W. & Laidlaw, R. Influence of rugby injuries on players' subsequent health and lifestyle: beginning a long term follow up. *Br. J. Sports Med.* **35,** 38–42 (2001).

151. Decq, P. *et al.* Long-term consequences of recurrent sports concussion. *Acta Neurochir. (Wien).* **158,** 289–300 (2016).

152. World Rugby. More women are playing rugby than ever before. (2015). Available at: http://www.worldrugby.org/news/60275?lang=en.

153. World Rugby. A Beginners's Guide to Rugby Union : The positions. Available at: https://passport.worldrugby.org/?page=beginners&p=10. (Accessed: 10th May 2017)

154. England Rugby. England Women to award professional contracts for 2016/17. Available at: http://www.englandrugby.com/news/england-women-award-professional-contracts-for-2016/. (Accessed: 10th May 2017)

155. Kanemasu, Y. & Molnar, G. Life after Rugby: Issues of Being an 'Ex' in Fiji Rugby. *Int. J. Hist. Sport* **31,** 1389–1405 (2014).

156. Howe, P. D. An Ethnography of Pain and Injury in Professional Rugby Union: The Case of Pontypridd RFC. *Int. Rev. Sociol. Sport* **36,** 289–303 (2001).

157. Light, R. & Kirk, D. High School Rugby, the Body and the Reproduction of Hegemonic Masculinity. *Sport. Educ. Soc.* **5,** 163–176 (2000).

158. Myers, P. T. Injuries presenting from rugby union football. *Med. J. Aust.* **2,** 17–20 (1980).

159. Leonard, J. *Jason Leonard: Full Time the Autobiography of a Rugby Legend*. (Willow, 2009).

160. Moore, B. *What goes on tour stays on tour*. (Simon & Schuster, 2014).

161. Healey, A. *Me and my mouth: the Austin Healey story*. (Monday, 2006).

162. Dawson, M. & Spink, A. *Nine lives: the autobiography*. (Willow, 2004).

163. Durkin, T. E. A survey of injuries in a 1st class Rugby Union Football Club from 1972-1976. *Br. J. Sports Med.* **11,** 7–11 (1977).

164. Weightman, D. & Browne, R. C. Injuries in Rugby and Association Football. *Br. J. Sports Med.* **8,** 183–187 (1974).

165. Roy, S. P. The nature and frequency of rugby injuries: a pilot study of 300 injuries at Stellenbosch. *S. Afr. Med. J.* **48,** 2321–7 (1974).

166. Williams, J. P. & McKibbin, B. Cervical spine injuries in Rugby Union football. *BMJ* **2,** 1747–1747 (1978).

167. Sparks, J. P. Rugby Football Injuries, 1980-1983. 71–75 (1983).

168. Sparks, J. P. Half a million hours of rugby football. The injuries. **15,** 30–32 (1981).

169. Davidson, R. M. Schoolboy Rugby injuries, 1969-1986. *Med. J. Aust.* **147,** 119–20 (1987).

170. Walkden, L. Immediate post-injury considerations in rugby football [proceedings]. *Br. J. Sports Med.* **12,** 39–40 (1978).

171. Murphy, W. & Shuttleworth, J. Risk factors in Rugby Union football [proceedings]. *Br. J. Sports Med.* **12,** 48–50 (1978).

172. Bathgate, A., Best, J. P., Craig, G. & Jamieson, M. A prospective study of injuries to elite Australian rugby union players. *Br. J. Sports Med.* **36,** 265–269 (2002).

173. Targett, S. G. R. Injuries in professional rugby union. 280–285. (1998).

174. Brooks, J. H. M., Fuller, C. W., Kemp, S. P. T. & Reddin, D. B. Epidemiology of injuries in English professional rugby union: part 1 match injuries. *Br. J. Sports Med.* **39,** 757–766 (2005).

175. Hughes, D. C. & Fricker, P. A. A Prospective Survey of Injuries to First-Grade Rugby Union Players. *Clinical Journal of Sport Medicine* **4,** 249–256 (1994).

176. Fuller, C. W. *et al.* Consensus statement on injury definitions and data collection

procedures for studies of injuries in rugby union. *Br. J. Sports Med.* **41,** 328–31 (2007).

177. Fuller, C. W. *et al.* Consensus statement on injury definitions and data collection procedures in studies of football (soccer) injuries. *Scandinavian Journal of Medicine and Science in Sports* **16,** 83–92 (2006).

178. McCrory, P. *et al.* Consensus statement on concussion in sport - the Third International Conference on Concussion in Sport held in Zurich, November 2008. *Phys. Sportsmed.* **37,** 141–59 (2009).

179. Langley, J. What is an injury? *Inj. Prev.* **10,** 69–71 (2004).

180. Moore, I. S., Ranson, C. & Mathema, P. Injury Risk in International Rugby Union: Three-Year Injury Surveillance of the Welsh National Team. *Orthop. J. Sport. Med.* **3,** 2325967115596194 (2015).

181. Brooks, J. H. M., Fuller, C. W., Kemp, S. P. T. & Reddin, D. B. Epidemiology of injuries in English professional rugby union: part 1 match injuries. *Br. J. Sports Med.* **39,** 757–66 (2005).

182. Nicholl, J. P., Coleman, P. & Williams, B. T. The epidemiology of sports and exercise related injury in the United Kingdom. *Br. J. Sports Med.* **29,** 232–238 (1995).

183. Brooks, J. H. M. & Kemp, S. P. T. Recent trends in rugby union injuries. *Clin. Sports Med.* **27,** 51–73 (2008).

184. Sport England. *Once a week participation in funded sports amongst people aged 16 years and over (April 2015 - March 2016)*. (2016).

185. Chase, K. I., Caine, D. J., Goodwin, B. J., Whitehead, J. R. & Romanick, M. a. A prospective study of injury affecting competitive collegiate swimmers. *Res. Sports Med.* **21,** 111–23 (2013).

186. Jacobsson, J. *et al.* Injury patterns in Swedish elite athletics: annual incidence, injury types and risk factors. *Br. J. Sports Med.* **47,** 941–52 (2013).

187. Ekstrand, J., Hägglund, M. & Waldén, M. Injury incidence and injury patterns in professional football: the UEFA injury study. *Br. J. Sports Med.* **45,** 553–558 (2011).

188. McKay, C. D., Tufts, R. J., Shaffer, B. & Meeuwisse, W. H. The epidemiology of

professional ice hockey injuries: a prospective report of six NHL seasons. *Br. J. Sports Med.* **48,** 57–62 (2014).

189. Moretz, A., Rashkin, A. & Grana, W. A. Oklahoma high school football injury study: a preliminary report. *J. Okla. State Med. Assoc.* **71,** 85–8 (1978).

190. Orchard, J. Epidemiology of injuries in the Australian Football League, seasons 1997-2000. *Br. J. Sports Med.* **36,** 39–44 (2002).

191. Roberts, S. P., Trewartha, G., England, M., Shaddick, G. & Stokes, K. a. Epidemiology of time-loss injuries in English community-level rugby union. *BMJ Open* **3,** 1–8 (2013).

192. Palmer-Green, D. S. *et al.* Match injuries in English youth academy and schools rugby union: an epidemiological study. *Am. J. Sports Med.* **41,** 749–755 (2013).

193. Palmer-Green, D. S. *et al.* Training activities and injuries in English youth academy and schools rugby union. *Am. J. Sports Med.* **43,** 475–81 (2015).

194. Roberts, S. P., Trewartha, G., England, M. & Stokes, K. A. Collapsed scrums and collision tackles: what is the injury risk? *Br. J. Sports Med.* **49,** 536–40 (2015).

195. Cross, M. J., Williams, S., Trewartha, G., Kemp, S. P. & Stokes, K. A. The Influence of In-Season Training Loads on Injury Risk in Professional Rugby Union. *Int. J. Sports Physiol. Perform.* **11,** 350–5 (2016).

196. Trewartha, G., Preatoni, E., England, M. E. & Stokes, K. A. Injury and biomechanical perspectives on the rugby scrum: A review of the literature. *Br. J. Sports Med.* (2014). doi:10.1136/bjsports-2013-092972

197. Williams, S., West, S., Cross, M. J. & Stokes, K. A. Better way to determine the acute: chronic workload ratio? *Br. J. Sports Med.* **51,** bjsports-2016 (2016).

198. Bird, Y. N. *et al.* The New Zealand Rugby Injury and Performance Project: V. Epidemiology of a season of rugby injury. *Br. J. Sports Med.* **32,** 319–325 (1998).

199. Weinstein, S. M. Assessment and rehabilitation of the athlete with a 'stinger'. A model for the management of noncatastrophic athletic cervical spine injury. *Clin. Sports Med.* **17,** 127–35 (1998).

200. Schick, D. M., Molloy, M. G. & Wiley, J. P. Injuries during the 2006 Women's

Rugby World Cup. *Br. J. Sports Med.* **42,** 447–51 (2008).

201. Carson, J. D., Roberts, M. A. & White, A. L. The epidemiology of women's rugby injuries. *Clin. J. Sport Med.* **9,** 75–8 (1999).

202. Schneiders, A. G., Takemura, M. & Wassinger, C. A. A prospective epidemiological study of injuries to New Zealand premier club rugby union players. *Phys. Ther. Sport* **10,** 85–90 (2009).

203. Brooks, J. H. M., Fuller, C. W., Kemp, S. P. T. & Reddin, D. B. An assessment of training volume in professional rugby union and its impact on the incidence, severity, and nature of match and training injuries. *J. Sports Sci.* **26,** 863–73 (2008).

204. Quarrie, K. L. *et al.* The New Zealand rugby injury and performance project. VI. A prospective cohort study of risk factors for injury in rugby union football. *Br. J. Sports Med.* **35,** 157–166 (2001).

205. Fuller, C. W. *et al.* Injury risks associated with tackling in rugby union. *Br. J. Sports Med.* **44,** 159–67 (2010).

206. McIntosh, A. S., McCrory, P., Finch, C. F. & Wolfe, R. Head, face and neck injury in youth rugby: incidence and risk factors. *Br J Sport. Med* **44,** 188–193 (2010).

207. Sankey, R. A., Brooks, J. H. M., Kemp, S. P. T. & Haddad, F. S. The epidemiology of ankle injuries in professional rugby union players. *Am. J. Sports Med.* **36,** 2415–24 (2008).

208. Fuller, C. W., Taylor, A. & Molloy, M. G. Epidemiological study of injuries in international Rugby Sevens. *Clin. J. Sport Med.* **20,** 179–184 (2010).

209. Taylor, A. E., Fuller, C. W. & Molloy, M. G. Injury surveillance during the 2010 IRB Women's Rugby World Cup. *British Journal of Sports Medicine* **45,** 1243–1245 (2011).

210. Gabb, N., Trewartha, G., Kemp, S. & Stokes, K. A. Epidemiology of injuries in a women's international rugby sevens world cip squad. *Br. J. Sports Med.* **48,** 596–598 (2014).

211. Brooks, J. H. M., Fuller, C. W., Kemp, S. P. T. & Reddin, D. B. Incidence, Risk, and Prevention of Hamstring Muscle Injuries in Professional Rugby Union. *Am. J.*

Sports Med. **34,** 1297–1306 (2006).

212. Pearce, C. J., Brooks, J. H. M., Kemp, S. P. T. & Calder, J. D. F. The epidemiology of foot injuries in professional rugby union players. *Foot Ankle Surg.* **17,** 113–118 (2011).

213. Silver, J. R. Injuries of the spine sustained during rugby. *Br. J. Sports Med.* **26,** 253–258 (1992).

214. Fuller, C. W., Brooks, J. H. M., Cancea, R. J., Hall, J. & Kemp, S. P. T. Contact events in rugby union and their propensity to cause injury. *Br. J. Sports Med.* **41,** 862–7; discussion 867 (2007).

215. Brown, J. C. *et al.* The incidence of rugby-related catastrophic injuries (including cardiac events) in South Africa from 2008 to 2011: a cohort study. *BMJ Open* **3,** 1–10 (2013).

216. Wetzler, M. J., Akpata, T., Laughlin, W. & Levy, A. S. Occurrence of Cervical Spine Injuries During the Rugby Scrum. *Am. J. Sport.* **26,** 177–180 (1998).

217. Taylor, A. E., Kemp, S., Trewartha, G. & Stokes, K. a. Scrum injury risk in English professional rugby union. *Br. J. Sports Med.* **48,** 1066–8 (2014).

218. Preatoni, E., Stokes, K. A., England, M. E. & Trewartha, G. The influence of playing level on the biomechanical demands experienced by rugby union forwards during machine scrummaging. *Scand. J. Med. Sci. Sport.* **23,** 520–528 (2013).

219. Cazzola, D., Preatoni, E., Stokes, K., England, M. & Trewartha, G. Does a Modified Rugby Scrum Engagement Process Improve the Stability of the Scrum and Minimise the Likelihood of Scrum Collapse? *Br. J. Sports Med.* **48,** 577–578 (2014).

220. Cazzola, D., Preatoni, E., Stokes, K. A., England, M. E. & Trewartha, G. A modified prebind engagement process reduces biomechanical loading on front row players during scrummaging: a cross-sectional study of 11 elite teams. *Br. J. Sports Med.* **49,** 541–6 (2015).

221. Hendricks, S., Lambert, M. I., Brown, J. C., Readhead, C. & Viljoen, W. An evidence-driven approach to scrum law modifications in amateur rugby played in South Africa. *Br J Sport. Med* **48,** 1115–9 (2014).

222. Reboursiere, E. *et al.* Impact of the national prevention policy and scrum law changes on the incidence of rugby-related catastrophic cervical spine injuries in French Rugby Union. *Br. J. Sports Med.* 1–5 (2016). doi:10.1136/bjsports-2016-096122

223. Kmietowicz, Z. World Rugby must review rules on tackling, says public health expert. *BMJ* **351,** h5049 (2015).

224. Jewett, R. *et al.* School sport participation during adolescence and mental health in early adulthood. *J. Adolesc. Health* **55,** 640–4 (2014).

225. Tucker, R., Raftery, M. & Verhagen, E. Injury risk and a tackle ban in youth Rugby Union: reviewing the evidence and searching for targeted, effective interventions. A critical review. *Br. J. Sports Med.* **50,** 921–925 (2016).

226. Carter, M. The unknown risks of youth rugby. *BMJ* **350,** (2015).

227. Fuller, C. W. *et al.* Injury risks associated with tackling in rugby union. *Br. J. Sports Med.* **44,** 159–67 (2010).

228. Garraway, W. M. *et al.* Factors influencing tackle injuries in rugby union football. *Br. J. Sports Med.* **33,** 37–41 (1999).

229. Quarrie, K. L. & Hopkins, W. G. Tackle Injuries in Professional Rugby Union. *Am. J. Sports Med.* **36,** 1705–1716 (2008).

230. Tucker, R. Has rugby applied high tackle laws, or have referees stopped enforcing them? The Science of Sport. Available at: http://sportsscientists.com/2017/04/rugby-applied-high-tackle-laws-referees-stopped-enforcing/. (Accessed: 8th May 2017)

231. Finch, C. F. & Cook, J. Categorising sports injuries in epidemiological studies: the subsequent injury categorisation (SIC) model to address multiple, recurrent and exacerbation of injuries. *Br. J. Sports Med.* **1,** 1276–1280 (2013).

232. Finch, C. F., Cook, J., Kunstler, B. E., Akram, M. & Orchard, J. Subsequent Injuries Are More Common Than Injury Recurrences. *Am. J. Sports Med.* 36354651769194 (2017). doi:10.1177/0363546517691943

233. Shrier, I. *et al.* A multistate framework for the analysis of subsequent injury in

sport (M-FASIS). *Scand. J. Med. Sci. Sports* **26,** 128–39 (2016).

234. Shrier, I. & Steele, R. J. Classification systems for reinjuries: a continuing challenge. *Br. J. Sports Med.* **48,** 1–3 (2013).

235. Von Rosen, P. & Heijne, A. How should we categorise self-reported data on subsequent injuries? *Eur. J. Sport Sci.* **17,** 621–628 (2017).

236. Dvorak, J. *et al.* Risk factor analysis for injuries in football players. Possibilities for a prevention program. *Am. J. Sports Med.* **28,** 69–74 (2000).

237. Hamilton, G. M., Meeuwisse, W. H., Emery, C. A., Steele, R. J. & Shrier, I. Past injury as a risk factor: An illustrative example where appearances are deceiving. *Am. J. Epidemiol.* **173,** 941–948 (2011).

238. Knowles, S. B., Marshall, S. W. & Guskiewicz, K. M. Issues in estimating risks and rates in sports injury research. *J. Athl. Train.* **41,** 207–215 (2006).

239. Felson, D. T. Epidemiology of hip and knee osteoarthritis. **10,** (1988).

240. Arden, N. & Nevitt, M. C. Osteoarthritis: Epidemiology. *Best Practice and Research: Clinical Rheumatology* **20,** 3–25 (2006).

241. Glyn-Jones, S. *et al.* Osteoarthritis. in *The Lancet* **386,** 376–387 (2015).

242. Litwic, A., Edwards, M. H., Dennison, E. M. & Cooper, C. Epidemiology and burden of osteoarthritis. *Br. Med. Bull.* **105,** 185–99 (2013).

243. Altman, R. *et al.* The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. *Arthritis Rheum.* **33,** 1601–1610 (1990).

244. Kellgren, J. & Lawrence, J. Radiological assessment of osteoarthritis. *Ann. Rheum. Dis.* **16,** 494 (1957).

245. Dieppe, P. A. & Lohmander, L. S. Pathogenesis and management of pain in osteoarthritis. *Lancet* **365,** 965–973 (2005).

246. Dahaghin, S. *et al.* Prevalence and determinants of one month hand pain and hand related disability in the elderly (Rotterdam study). *Ann. Rheum. Dis.* **64,** 99–104 (2005).

247. Kraus, V. B. *et al.* Call for standardized definitions of osteoarthritis and risk stratification for clinical trials and clinical use. *Osteoarthr. Cartil.* **23,** 1233–41 (2015).

248. Chevalier, X., Eymard, F. & Richette, P. Biologic agents in osteoarthritis: hopes and disappointments. *Nat. Rev. Rheumatol.* **9,** 400–410 (2013).

249. Seidel, M. F., Wise, B. L. & Lane, N. E. Nerve growth factor: An update on the science and therapy. *Osteoarthr. Cartil.* **21,** 1223–1228 (2013).

250. Bedson, J. Chronic knee pain and osteoarthritis : an labels , diagnosis epidemiological study of investigation in and general practice. (2006).

251. Hawker, G. a *et al.* Understanding the pain experience in hip and knee osteoarthritis--an OARSI/OMERACT initiative. *Osteoarthritis Cartilage* **16,** 415–22 (2008).

252. Gupta, S., Hawker, G. A., Laporte, A., Croxford, R. & Coyte, P. C. The economic burden of disabling hip and knee osteoarthritis (OA) from the perspective of individuals living with this condition. *Rheumatology* **44,** 1531–1537 (2005).

253. Chen, a., Gupte, C., Akhtar, K., Smith, P. & Cobb, J. The Global Economic Cost of Osteoarthritis: How the UK Compares. *Arthritis* **2012,** 1–6 (2012).

254. Hiligsmann, M. *et al.* Health economics in the field of osteoarthritis: An Expert's consensus paper from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). *Semin. Arthritis Rheum.* **43,** 303–313 (2013).

255. NIH Consensus Statement on Total Knee Replacement. *NIH Consens. State. Sci. Statements* **20,** 1–34 (2003).

256. Mancuso, C. A., Salvati, E. A., Johanson, N. A., Peterson, M. G. & Charlson, M. E. Patients' expectations and satisfaction with total hip arthroplasty. *J. Arthroplasty* **12,** 387–396 (1997).

257. Jones, C. A., Voaklander, D. C., Johnston, D. W. & Suarez-Almazor, M. E. Health related quality of life outcomes after total hip and knee arthroplasties in a community based population. *J. Rheumatol.* **27,** 1745–52 (2000).

258. Bayliss, L. E. *et al.* The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. *Lancet* (2017). doi:10.1016/S0140-6736(17)30059-4

259. Kraus, V. B., Blanco, F. J., Englund, M., Karsdal, M. A. & Lohmander, L. S. Call for standardized definitions of osteoarthritis and risk stratification for clinical trials and clinical use. *Osteoarthr. Cartil.* **23,** 1233–1241 (2015).

260. Blackburn, S., Rhodes, C., Higginbottom, A. & Dziedzic, K. The oarsi standardised definition of osteoarthritis: A lay version. *Osteoarthr. Cartil.* **24,** S192 (2016).

261. Brandt, K. D., Dieppe, P. & Radin, E. L. Etiopathogenesis of osteoarthritis. *Rheum. Dis. Clin. North Am.* **34,** 531–59 (2008).

262. Vignon, E. Hand osteoarthritis and generalized osteoarthritis: a need for clarification. *Osteoarthritis Cartilage* **8 Suppl A,** S22–S24 (2000).

263. Hutton, C. W. Generalised osteoarthritis: an evolutionary problem? *Lancet* **1,** 1463–1465 (1987).

264. Herrero-Beaumont, G., Roman-Blas, J. A., Castañeda, S. & Jimenez, S. A. Primary Osteoarthritis No Longer Primary: Three Subsets with Distinct Etiological, Clinical, and Therapeutic Characteristics. *Semin. Arthritis Rheum.* **39,** 71–80 (2009).

265. Oliveria, S. A., Felson, D. T., Reed, J. I., Cirillo, P. A. & Walker, A. M. Incidence of symptomatic hand, hip, and knee osteoarthritis among patients in a health maintenance organization. *Arthritis Rheum.* **38,** 1134–1141 (1995).

266. Toivanen, A. T. *et al.* Obesity, physically demanding work and traumatic knee injury are major risk factors for knee osteoarthritis-a population-based study with a follow-up of 22 years. *Rheumatology* **49,** 308–314 (2010).

267. Haugen, I. K. *et al.* Prevalence, incidence and progression of hand osteoarthritis in the general population: the Framingham Osteoarthritis Study. *Ann Rheum Dis* **70,** 1581–1586 (2011).

268. Busby, J., Tobin, J., Ettinger, W., Roadarmel, K. & Plato, C. C. A longitudinal study of osteoarthritis of the hand: the effect of age. *Ann Hum Biol* **18,** 417–424 (1991).

269. Karlson, E. W. *et al.* Total hip replacement due to osteoarthritis: The importance of

age, obesity, and other modifiable risk factors. *Am. J. Med.* **114,** 93–98 (2003).

270. Blagojevic, M., Jinks, C., Jeffery, A. & Jordan, K. P. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthr. Cartil.* **18,** 24–33 (2010).

271. Grotle, M., Hagen, K. B., Natvig, B., Dahl, F. A. & Kvien, T. K. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. *BMC Musculoskelet. Disord.* **9,** 132 (2008).

272. Grotle, M., Hagen, K. B., Natvig, B., Dahl, F. A. & Kvien, T. K. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. *BMC Musculoskelet Disord* **9,** 132 (2008).

273. Srikanth, V. K. *et al.* A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthr. Cartil.* **13,** 769–781 (2005).

274. Wilder, F. V., Barrett, J. P. & Farina, E. J. Joint-specific prevalence of osteoarthritis of the hand. *Osteoarthr. Cartil.* **14,** 953–957 (2006).

275. Zhang, Y. *et al.* Bone mineral density and risk of incident and progressive radiographic knee osteoarthritis in women: the Framingham Study. *J. Rheumatol.* **27,** 1032–7 (2000).

276. Hart, D. J., Mootoosamy, I., Doyle, David, V. & Spector, T. D. The relationship between osteoarthritis (Oa) and osteoporosis in the general population: The chingford study. *Ann. Rheum. Dis.* **53,** 158–162 (1994).

277. Nevitt, M. C. *et al.* Radiographic osteoarthritis of the hip and bone mineral density. The Study of Osteoporotic Fractures Research Group. *Arthritis Rheum.* **38,** 907–16 (1995).

278. Burger, H. *et al.* Association of radiographically evident osteoarthritis with higher bone mineral density and increased bone loss with age. The Rotterdam Study. *Arthritis Rheum.* **39,** 81–6 (1996).

279. Allen, K. D. *et al.* Racial differences in self-reported pain and function among individuals with radiographic hip and knee osteoarthritis: the Johnston County Osteoarthritis Project. *Osteoarthr. Cartil.* **17,** 1132–1136 (2009).

280. Zhang, Y. *et al.* Comparison of the Prevalence of Knee Osteoarthritis between the Elderly Chinese Population in Beijing and Whites in the United States: The Beijing Osteoarthritis Study. *Arthritis Rheum.* **44,** 2065–2071 (2001).

281. Golightly, Y. M. & Dominick, K. L. Racial variations in self reported osteoarthritis symptom severity among veterans. *Aging Clin. Exp. Res.* **4,** 264–9 (2005).

282. Qin, J. *et al.* Lifetime Risk of Symptomatic Hand Osteoarthritis: The Johnston County Osteoarthritis Project. *Arthritis Care Res. (Hoboken).* **0,** (2017).

283. Zeng, Q. Y. *et al.* Rheumatic diseases in China. *Arthritis Res. Ther.* **10,** R17 (2008).

284. Nelson, A. E. *et al.* Characterization of individual radiographic features of hip osteoarthritis in African American and white women and men: The Johnston County Osteoarthritis Project. *Arthritis Care Res.* **62,** 190–197 (2010).

285. Murphy, L. B. *et al.* One in four people may develop symptomatic hip osteoarthritis in his or her lifetime. *Osteoarthr. Cartil.* **18,** 1372–1379 (2010).

286. McWilliams, D. F., Leeb, B. F., Muthuri, S. G., Doherty, M. & Zhang, W. Occupational risk factors for osteoarthritis of the knee: a meta-analysis. *Osteoarthritis Cartilage* **19,** 829–39 (2011).

287. McMillan, G. & Nichols, L. Osteoarthritis and meniscus disorders of the knee as occupational diseases of miners. *Occup. Environ. Med.* **62,** 567–75 (2005).

288. Kalichman, L. & Hernández-Molina, G. Hand osteoarthritis: An epidemiological perspective. *Seminars in Arthritis and Rheumatism* **39,** 465–476 (2010).

289. Toba, N. *et al.* Prevalence and involvement patterns of radiographic hand osteoarthritis in Japanese women: The Hizen-Oshima study. *J. Bone Miner. Metab.* **24,** 344–348 (2006).

290. Rossignol, M. *et al.* Primary osteoarthritis of hip, knee, and hand in relation to occupational exposure. *Occup. Environ. Med.* **62,** 772–777 (2005).

291. Franklin, J., Ingvarsson, T., Englund, M. & Lohmander, S. Association between occupation and knee and hip replacement due to osteoarthritis: a case-control study. *Arthritis Res. Ther.* **12,** R102 (2010).

292. Andersen, S., Thygesen, L. C., Davidsen, M. & Helweg-Larsen, K. Cumulative

years in occupation and the risk of hip or knee osteoarthritis in men and women: a register-based follow-up study. *Occup. Environ. Med.* **69,** 325–330 (2012).

293. Croft, P., Coggon, D., Cruddas, M. & Cooper, C. Osteoarthritis of the hip: an occupational disease in farmers. *BMJ* **304,** 1269–72 (1992).

294. Jones, G., Cooley, H. M. & Stankovich, J. M. A cross sectional study of the association between sex, smoking, and other lifestyle factors and osteoarthritis of the hand. *J. Rheumatol.* **29,** 1719–1724 (2002).

295. Kloppenburg, M. & Kwok, W.-Y. Hand osteoarthritis—a heterogeneous disorder. *Nature Reviews Rheumatology* **8,** 22–31 (2011).

296. Altman, R. *et al.* Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum.* **29,** 1039–1049 (1986).

297. Altman, R. *et al.* The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis Rheum.* **34,** 505–514 (1991).

298. Moskowitz, R. W., Altman, R. D., Hochberg, M. C., Buckwalter, J. A. & Goldberg, V. M. *Osteoarthritis: diagnosis and medical/surgical management - 4th ed.* (Lippincott Williams & Wilkins, 2007).

299. Bedson, J. & Croft, P. R. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. *BMC Musculoskelet. Disord.* **9,** 116 (2008).

300. Neogi, T. The Epidemiology and Impact of Pain in Osteoarthritis. *Osteoarthr. Res. Soc.* **21,** 1145–1153 (2013).

301. IASP Taxonomy - IASP. Available at: http://www.iasp-pain.org/Taxonomy. (Accessed: 14th May 2017)

302. IOM. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.* (The National Academies Press, 2011).

303. O'Reilly, S. C., Muir, K. R. & Doherty, M. Screening for pain in knee osteoarthritis:

which question? *Ann. Rheum. Dis.* **55,** 931–3 (1996).

304. Anderson, J. J. & Felson, D. T. Factors Associated With Osteoarthritis of the Knee in the first National Health and Nutrition Examination Survey (HANES I). *Am. J. Epidemiol.* **128,** 179–189 (1988).

305. LaValley, M., McAlindon, T. E., Evans, S., Chaisson, C. E. & Felson, D. T. Problems in the development and validation of questionnaire-based screening instruments for ascertaining cases with symptomatic knee osteoarthritis. *Arthritis Rheum.* **44,** 1105–1113 (2001).

306. Leyland, K. M. *et al.* Measuring the variation between self-reported osteoarthritis pain assessments. *Osteoarthr. Cartil.* **24,** S8 (2016).

307. Hart, D. J., Leedham-Green, M. & Spector, T. D. The prevalence of knee osteoarthritis (Oa) in the general population using different clinical criteria: The chingford study. *Arthritis Rheumatol.* **30,** 72 (1991).

308. Ratzlaff, C., Koehoorn, M., Cibere, J. & Kopec, J. Clinical validation of an Internet-based questionnaire for ascertaining hip and knee osteoarthritis. *Osteoarthr. Cartil.* **20,** 1568–1573 (2012).

309. Gossec, L. *et al.* OARSI/OMERACT initiative to define states of severity and indication for joint replacement in hip and knee osteoarthritis. An OMERACT 10 special interest group. in *Journal of Rheumatology* **38,** 1765–1769 (2011).

310. Dougados, M. *et al.* OARSI/OMERACT criteria of being considered a candidate for total joint replacement in knee/hip osteoarthritis as an endpoint in clinical trials evaluating potential disease modifying osteoarthritic drugs. *J. Rheumatol.* **36,** 2097–2099 (2009).

311. Dougados, M. *et al.* Requirement for total hip arthroplasty: an outcome measure of hip osteoarthritis? *J. Rheumatol.* **26,** 855–61 (1999).

312. Coggon, D. (David), Rose, G. A. (Geoffrey A. & Barker, D. J. P. (David J. P. *Epidemiology for the uninitiated*. (BMJ Books, 2003).

313. Ho, P. M., Peterson, P. N. & Masoudi, F. A. Evaluating the evidence. Is there a rigid hierarchy? *Circulation* **118,** 1675–1984 (2008).

314. Brighton, B., Bhandari, M., Tornetta, P. & Felson, D. T. Hierarchy of Evidence: From Case Reports to Randomized Controlled Trials. *Clin. Orthop. Relat. Res.* **413,** 19–24 (2003).

315. Tomlin, G. *et al.* Research Pyramid: A New Evidence-Based Practice Model for Occupational Therapy. *Am. J. Occup. Ther.* **65,** 189–196 (2011).

316. Phillips, B. *et al. Appendix 2. Reccomendations based on the Centre for Evidence Based Medicine (Oxford) Gradation System*. (1998).

317. Sanson-Fisher, R. W., Bonevski, B., Green, L. W. & D'Este, C. Limitations of the Randomized Controlled Trial in Evaluating Population-Based Health Interventions. *Am. J. Prev. Med.* **33,** 155–161 (2007).

318. Booth, C. M. & Tannock, I. F. Randomised controlled trials and population-based observational research: partners in the evolution of medical evidence. *Br. J. Cancer* **110,** 551–555 (2014).

319. Bennell, K., Hunter, D. J. & Vicenzino, B. Long-term effects of sport: preventing and managing OA in the athlete. *Nat. Rev. Rheumatol.* **8,** 747–52 (2012).

320. Torii, S. Relation between the experience of major joint injury in collegiate athletic activity and arthralgia in later life. *Japanese J. Clin. Sport. Med. 2005* **13,**

321. Lohmander, L. S., Englund, P. M., Dahl, L. L. & Roos, E. M. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am. J. Sports Med.* **35,** 1756–69 (2007).

322. Conaghan, P. G. Update on osteoarthritis part 1: current concepts and the relation to exercise. *Br. J. Sports Med.* **36,** 330–3 (2002).

323. Kettunen, J. a, Kujala, U. M., Kaprio, J., Koskenvuo, M. & Sarna, S. Lower-limb function among former elite male athletes. *Am. J. Sports Med.* **29,** 2–8 (2001).

324. Lohmander, L. S., Ostenberg, a, Englund, M. & Roos, H. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum.* **50,** 3145–52 (2004).

325. Beardmore, A. L., Handcock, P. J. & Rehrer, N. J. Return-to-play after injury: practices in New Zealand rugby union. *Phys. Ther. Sport* **6,** 24–30 (2005).

326. Liston, K., Reacher, D., Smith, A. & Waddington, I. Managing Pain and Injury in Non-Elite Rugby Union and Rugby League: a case study of players at a British University. *Sport in Society* (2006).

327. Hollis, S. J., Stevenson, M. R., McIntosh, A. S., Shores, E. A. & Finch, C. F. Compliance with return-to-play regulations following concussion in Australian schoolboy and community rugby union players. *Br J Sport. Med* **46,** 735–740 (2012).

328. NatCen Social Research, U. C. L. D. of E. and P. H. *Health Survey for England, 2014 [data collection]. UK data service*. (2016). doi:http://dx.doi.org/10.5255/UKDA-SN-7919-1

329. Van Reenen, M. & Janssen, B. *EQ-5D-5L User Guide: Basic information on how to use the EQ-5D-5L instrument*. (EuroQol Research Foundation, Rotterdam., 2015).

330. Marmot, M. *et al.* English Longitudinal Study of Ageing: Waves 0-7, 1998-2015. [data collection]. 24th Edition. (2017).

331. Harris, P. A. *et al.* Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. *J. Biomed. Inform.* **42,** 377–381 (2009).

332. UK Data Archive - Our Quality Control. Available at: http://www.data-archive.ac.uk/curate/archive-quality. (Accessed: 16th May 2017)

333. Janssen, M. F., Lubetkin, E. I., Sekhobo, J. P. & Pickard, A. S. The use of the EQ-5D preference-based health status measure in adults with Type 2 diabetes mellitus. *Diabetic Medicine* **28,** 395–413 (2011).

334. Pickard, A. S. *et al.* Use of a preference-based measure of health (EQ-5D) in COPD and asthma. *Respir. Med.* **102,** 519–536 (2008).

335. Johnson, J. A. & Pickard, A. S. Comparison of the EQ-5D and SF-12 health surveys in a general population survey in Alberta, Canada. *Med. Care* **38,** 115–21 (2000).

336. Johnson, J. A. & Coons, S. J. Comparison of the EQ-5D and SF-12 in an adult US sample. *Qual. Life Res.* **7,** 155–166 (1998).

337. Fransen, M. & Edmonds, J. Reliability and validity of the EuroQol in patients with osteoarthritis of the knee. *Rheumatology (Oxford).* **38,** 807–13 (1999).

338. Conner-Spady, B. L. *et al.* Reliability and validity of the EQ-5D-5L compared to the EQ-5D-3L in patients with osteoarthritis referred for hip and knee replacement. *Qual. Life Res.* **24,** 1775–84 (2015).

339. Nelson, A. E. *et al.* Brief Report: Differences in multijoint symptomatic osteoarthritis phenotypes by race and sex: The Johnston County Osteoarthritis Project. *Arthritis Rheum.* **65,** 373–377 (2013).

340. Kraus, V. B. *et al.* The Genetics of Generalized Osteoarthritis (GOGO) study: study design and evaluation of osteoarthritis phenotypes. *Osteoarthr. Cartil.* **15,** 120–127 (2007).

341. Spector, T. D. & Hochberg, M. C. Methodological problems in the epidemiological study of osteoarthritis. *Ann. Rheum. Dis.* **53,** 143–6 (1994).

342. Thompson, J. *et al.* Health researchers' attitudes towards public involvement in health research. *Heal. Expect.* **12,** 209–220 (2009).

343. Boote, J., Wong, R. & Booth, A. 'Talking the talk or walking the walk?' A bibliometric review of the literature on public involvement in health research published between 1995 and 2009. *Heal. Expect.* **18,** 44–57 (2012).

344. Staley, K. 'Is it worth doing?' Measuring the impact of patient and public involvement in research. *Res. Involv. Engagem.* **1,** 1–10 (2015).

345. Baggott, R. A Funny thing happened on the way to the forum? Reforming patient and public involvement in the NHS in England. *Public Administration* **83,** 533–551 (2005).

346. Brett, J. *et al.* Mapping the impact of patient and public involvement on health and social care research: A systematic review. *Heal. Expect.* 1–14 (2012). doi:10.1111/j.1369-7625.2012.00795.x

347. Department of Health. Research governance framework for health and social care (Second edition, 2005). *Health Soc. Care Community* **10,** 1–54 (2005).

348. Boote, J., Baird, W. & Beecroft, C. Public involvement at the design stage of primary health research: A narrative review of case examples. *Health Policy (New. York).* **95,** 10–23 (2010).

349. Koniotou, M., Halter, M., Evans, B. A., Porter, A. & Gaze, S. Developing a model to involve service users in a multi-centred trial of a complex intervention in pre-hospital emergency care. *Emerg. Med. J.* **32,** e9.1-e9 (2015).

350. Adams, J. & Lempp, H. Patients' and carers' direct involvement in musculoskeletal research and service delivery: what are the benefits and challenges? *Rheumatology* **53,** i7 (2014).

351. Wright, D., Foster, C., Amir, Z., Elliott, J. & Wilson, R. Critical appraisal guidelines for assessing the quality and impact of user involvement in research. *Health Expect.* **13,** 359–68 (2010).

352. Chalmers, I. What do I want from health research and researchers when I am a patient? *BMJ* **310,** 1315–1318 (1995).

353. Entwistle, V. A., Renfrew, M. J., Yearley, S., Forrester, J. & Lamont, T. Lay perspectives: advantages for health research. *BMJ* **316,** 463–466 (1998).

354. Mockford, C. *et al.* A SHARED study-the benefits and costs of setting up a health research study involving lay co-researchers and how we overcame the challenges. *Res. Involv. Engagem.* **2,** 8 (2016).

355. Burrus, B. B., Liburd, L. G. & Burroughs, A. Maximizing participation by black americans in population-based diabetes research: The project direct pilot experience. *J. Community Health* **23,** 15–27 (1998).

356. Woolgar, J. *England : the official R.F.U. history*. (Virgin Books, 1999).

357. Maffulli, N., Longo, U. G., Gougoulias, N., Loppini, M. & Denaro, V. Long-term health outcomes of youth sports injuries. *Br. J. Sports Med.* **44,** 21–5 (2010).

358. Roos, H. Are there long-term sequelae from soccer? *Clin. Sports Med.* **17,** 819–831 (1998).

359. Godlee, F. NHS is not (yet) in crisis, but what about school rugby? *BMJ* **350,** h78 (2015).

360. Corneli, A. L. *et al.* Involving communities in the design of clinical trial protocols: The BAN Study in Lilongwe, Malawi. *Contemp. Clin. Trials* **28,** 59–67 (2007).

361. Das, S. K. & Farooqi, A. Osteoarthritis. *Best Pract. Res. Clin. Rheumatol.* **22,** 657–675

(2008).

362. Caine, D. J. & Golightly, Y. M. Osteoarthritis as an outcome of paediatric sport: an epidemiological perspective. *Br. J. Sports Med.* **45,** 298–303 (2011).

363. Graham, T., Rose, D., Murray, J., Ashworth, M. & Tylee, A. User-generated quality standards for youth mental health in primary care: a participatory research design using mixed methods. *BMJ Qual. Saf.* **23,** 857–66 (2014).

364. Piper, S. How To Empower Patients And Involve The Public. *Nurs. Stand.* **29,** 37–41 (2014).

365. Leppo, A. & Perälä, R. User involvement in Finland: the hybrid of control and emancipation. *J. Health Organ. Manag.* **23,** 359–71 (2009).

366. INVOLVE. *Briefing notes for researchers: involving the public in the NHS, public health and social care research.* (INVOLVE, 2012).

367. Cassidy, J. Why patient representation might harm science? *Breast Cancer Res.* **9,** S4 (2007).

368. Dudley, L. *et al.* A little more conversation please? Qualitative study of researchers' and patients' interview accounts of training for patient and public involvement in clinical trials. *Trials* **16,** 190 (2015).

369. Staniszewska, S., Jones, N., Newburn, M. & Marshall, S. User involvement in the development of a research bid: barriers, enablers and impacts. *Health Expect.* **10,** 173–83 (2007).

370. Staniszewska, S., Brett, J., Mockford, C. & Barber, R. The GRIPP checklist: strengthening the quality of patient and public involvement reporting in research. *Int. J. Technol. Assess. Health Care* **27,** 391–9 (2011).

371. Gooberman-Hill, R. *et al.* Designing a placebo device: involving service users in clinical trial design. *Heal. Expect.* **16,** E100–E110 (2013).

372. Abma, T. A. Patient participation in health research: Research with and for people with spinal cord injuries. *Qual. Health Res.* **15,** 1310–1328 (2005).

373. Gooberman-Hill, R., Horwood, J. & Calnan, M. Citizens' juries in planning research priorities: process, engagement and outcome. *Heal. Expect.* **11,** 272–281

(2008).

374. Thompson, J. *et al.* Health researchers' attitudes towards public involvement in health research. *Heal. Expect.* **12,** 209–220 (2009).

375. Domecq, J. P. *et al.* Patient engagement in research: a systematic review. *BMC Health Serv. Res.* **14,** 89 (2014).

376. Dobbs, L. & Moore, C. Engaging Communities in Area-based Regeneration: The Role of Participatory Evaluation. *Policy Stud.* **23,** 157–171 (2002).

377. Mockford, C., Staniszewska, S., Griffiths, F. & Herron-Marx, S. The impact of patient and public involvement on UK NHS health care: A systematic review. *International Journal for Quality in Health Care* **24,** 28–38 (2012).

378. Staniszewska, S. *et al.* Developing the evidence base of patient and public involvement in health and social care research: The case for measuring impact. *Int. J. Consum. Stud.* **35,** 628–632 (2011).

379. Petit-Zeman, S. & Locock, L. Health care: Bring on the evidence. *Nature* **501,** 160–161 (2013).

380. World Rugby. Player Numbers. (2016). Available at: http://www.worldrugby.org/development/player-numbers. (Accessed: 13th August 2016)

381. World Health Organization. *Consititution of the World Health Organisation*. (2006).

382. Huber, M. Health: how should be define it? *BMJ* **343,** 235–237 (2011).

383. Shilton, T., Sparks, M., McQueen, D., Lamarre, M.-C. & Jackson, S. Proposal for new definition of health. *BMJ* **343,** d5359–d5359 (2011).

384. Dunn, J. R. & Hayes, M. V. Toward a lexicon of population health. *Can. J. Public Heal.* **90,** 7–10 (1999).

385. Kindig, D. & Stoddart, G. What is population health? *Am. J. Public Health* **93,** 380–3 (2003).

386. Freitag, A., Kirkwood, G. & Pollock, A. M. Rugby injury surveillance and prevention programmes: are they effective? *BMJ* **350,** h1587 (2015).

387. Nicol, A., Pollock, A., Kirkwood, G., Parekh, N. & Robson, J. Rugby union injuries in Scottish schools. *J. Public Health (Bangkok).* **33,** 256–261 (2011).

388. Godlee, F. NHS is not (yet) in crisis, but what about school rugby? *BMJ* **350,** h78–h78 (2015).

389. Rudd, J. *et al.* A holistic measurement model of movement competency in children. *J. Sports Sci.* **34,** 477–485 (2016).

390. Whitehead, M. Physical Literacy: Philosophical Considerations in Relation to Developing a Sense of Self, Universality and Propositional Knowledge. *Sport. Ethics Philos.* **1,** 281–298 (2007).

391. Grove, J. R., Lavallee, D. & Gordon, S. Coping with retirement from sport: The influence of athletic identity. *J. Appl. Sport Psychol.* **9,** 191–203 (1997).

392. Cosh, S., Crabb, S. & Lecouteur, A. Elite athletes and retirement: Identity, choice, and agency. *Aust. J. Psychol.* **65,** 89–97 (2013).

393. Goldsmith, L. *et al.* The importance of informational, clinical and personal support in patient experience with total knee replacement: a qualitative investigation. *BMC Musculoskelet. Disord.* **18,** 1–13 (2017).

394. Brilleman, S. L. *et al.* Implications of comorbidity for primary care costs in the UK: A retrospective observational study. *Br. J. Gen. Pract.* **63,** (2013).

395. Rothman, K. J. *Modern epidemiology.* (Little, Brown, 1986).

396. Kirkwood, B. B. & Sterne, J. *Essential medical statistics*. *Malden, MA: Blackwell Science* (2003). doi:10.1002/sim.1961

397. Body mass index - BMI. (2017). Available at: http://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi. (Accessed: 9th January 2017)

398. Cutler, D. M., Lleras-Muney, A. & Vogl, T. in *The Oxford Handbook of Health Economics* (2012). doi:10.1093/oxfordhb/9780199238828.013.0007

399. Daghestani, H. N. & Kraus, V. B. Inflammatory biomarkers in osteoarthritis. *Osteoarthritis Cartilage* **23,** 1890–6 (2015).

400. Kujala, U. M. *et al.* Knee osteoarthritis in former runners, soccer players, weight lifters, and shooters. *Arthritis Rheum.* **38,** 539–46 (1995).

401. Kujala, U. M., Kaprio, J. & Sarna, S. Osteoarthritis of weight bearing joints of lower limbs in former elite male athletes. *Br. Med. J.* **308,** 231–234 (1994).

402. Gelber, A. C. *et al.* Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. *Ann. Intern. Med.* **133,** 321–328+I16 (2000).

403. Molloy, M. G. & Molloy, C. B. Contact sport and osteoarthritis. *Br. J. Sports Med.* **45,** 275–7 (2011).

404. Valderrabano, V., Hintermann, B., Horisberger, M. & Fung, T. S. Ligamentous posttraumatic ankle osteoarthritis. *Am. J. Sports Med.* **34,** 612–620 (2006).

405. Andersson, S. *et al.* Degenerative joint disease in female ballet dancers. *Am. J. Sports Med.* **23,** 295–300 (1986).

406. *Osteoarthritis: Care and management in adults. Clinical guideline CG177. Methods, evidence and recommendations.* (2014).

407. Nevill, A. M., Stewart, A. D., Olds, T. & Holder, R. Relationship between adiposity and body size reveals limitations of BMI. *Am. J. Phys. Anthropol.* **129,** 151–156 (2006).

408. King, N. A., Hills, A. P. & Blundell, J. E. High Body Mass Index is not a barrier to physical activity: Analysis of international rugby players' anthropometric data. *Eur. J. Sport Sci.* **5,** 73–75 (2005).

409. Jeon, C. Y., Lokken, R. P., Hu, F. B. & Van Dam, R. M. Physical activity of moderate intensity and risk of type 2 diabetes: A systematic review. *Diabetes Care* **30,** 744–752 (2007).

410. Allen, C. L. & Bayraktutan, U. Risk factors for ischaemic stroke. *Int. J. Stroke* **3,** 105–16 (2008).

411. Wolf, P. A. & Colaboradores. Probability of Stroke: A Risk Profile From the Framingham Study. *Stroke* **22,** 312–318 (1991).

412. Morel, J., Combe, B., Francisco, J. & Bernard, J. Bone mineral density of 704 amateur sportsmen involved in different physical activities. *Osteoporos. Int.* **12,**

152–157 (2001).

413. Elloumi, M., Courteix, D., Sellami, S., Tabka, Z. & Lac, G. Bone mineral content and density of Tunisian male rugby players: Differences between forwards and backs. *Int. J. Sports Med.* **27,** 351–358 (2006).

414. Egan, E., Reilly, T., Giacomoni, M., Redmond, L. & Turner, C. Bone mineral density among female sports participants. *Bone* **38,** 227–233 (2006).

415. Meyer, H. E., Falch, J. A., O'Neill, T., Tverdal, A. & Varlow, J. Height and body mass index in oslo, norway, compared to other regions of europe: do they explain differences in the incidence of hip fracture? *Bone* **17,** 347–350 (1995).

416. Cosh, S., LeCouteur, A., Crabb, S. & Kettler, L. Career transitions and identity: a discursive psychological approach to exploring athlete identity in retirement and the transition back into elite sport. *Qual. Res. Sport. Exerc. Heal.* **5,** 1–22 (2012).

417. Bayram, N. & Bilgel, N. The prevalence and socio-demographic correlations of depression, anxiety and stress among a group of university students. *Soc. Psychiatry Psychiatr. Epidemiol.* **43,** 667–672 (2008).

418. Garraway, W. M. Impact of professionalism on injuries in rugby union. *Br. J. Sports Med.* **34,** 348–351 (2000).

419. Moskowitz, R. W. The burden of osteoarthritis: clinical and quality-of-life issues. *Am. J. Manag. Care* **15,** S223-229 (2009).

420. Groessl, E. J., Kaplan, R. M. & Cronan, T. a. Quality of well-being in older people with osteoarthritis. *Arthritis Rheum.* **49,** 23–8 (2003).

421. Hochberg, M. C. Mortality in osteoarthritis. *Clin. Exp. Rheumatol.* **26,** (2008).

422. Nuesch, E. *et al.* All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. *BMJ* **342,** d1165 (2011).

423. Abramson, S. B., Berenbaum, F., Hochberg, M. C. & Moskowitz, R. W. Introduction to OARSI FDA initiative OAC special edition. *Osteoarthr. Cartil.* **19,** 475–477 (2011).

424. Lieberthal, J., Sambamurthy, N. & Scanzello, C. R. Inflammation in joint injury and post-traumatic osteoarthritis. *Osteoarthr. Cartil.* **23,** 1825–34 (2015).

425. Lohkamp, M., Kromer, T. O. & Schmitt, H. Osteoarthritis and joint replacements of the lower limb and spine in ex-professional soccer players: A systematic review. *Scand. J. Med. Sci. Sports* 1–12 (2017). doi:10.1111/sms.12846

426. Hunter, D. J. & Eckstein, F. Exercise and osteoarthritis. *J. Anat.* **214,** 197–207 (2009).

427. Fuller, C. W. Catastrophic Injuries in Rugby Union: An Assessment of the Risk. **2007,** (2007).

428. Hind, K., Gannon, L., Brightmore, A. & Beck, B. Insights into relationships between body mass, composition and bone: findings in elite rugby players. *J. Clin. Densitom.* **18,** 172–8

429. Duthie, G. High Body Mass Index is not a barrier to physical activity: Analysis of international rugby players' anthropometric data. *Eur. J. Sport Sci.* **5,** 77 (2005).

430. Hunter, D. J. *et al.* The symptoms of OA and the genesis of pain. *Rheum Dis Clin North Am.* **34,** 1–19 (2009).

431. Keefe, F. J., Lefebvre, J. C., Maixner, W., Salley, a N. & Caldwell, D. S. Self-efficacy for arthritis pain: relationship to perception of thermal laboratory pain stimuli. *Arthritis Care Res.* **10,** 177–184 (1997).

432. Keefe, F. J. *et al.* The relationship of gender to pain, pain behavior, and disability in osteoarthritis patients: the role of catastrophizing. *Pain* **87,** 325–334 (2000).

433. Andersen, R. E., Crespo, C. J., Bartlett, S. J., Bathon, J. M. & Fontaine, K. R. Relationship between body weight gain and significant knee, hip, and back pain in older Americans. *Obes. Res.* **11,** 1159–62 (2003).

434. Quarrie, K. L. & Hopkins, W. G. Tackle Injuries in Professional Rugby Union. *Am. J. Sports Med.* **36,** 1705–1716 (2008).

435. Patricios, J. Tackles , tears and troubles … a South African Sports Medicine Association perspective. *Br. J. Sports Med.* **50,** 893–893 (2016).

436. Murray, A. D., Murray, I. R. & Robson, J. Rugby Union: faster, higher, stronger: keeping an evolving sport safe. *Br. J. Sports Med.* **48,** 73–4 (2014).

437. de Silva, V., Swain, M., Broderick, C. & McKay, D. Does high level youth sports participation increase the risk of femoroacetabular impingement? A review of the

current literature. *Pediatr. Rheumatol.* **14,** 16 (2016).

438. Philippon, M., Schenker, M., Briggs, K. & Kuppersmith, D. Femoroacetabular impingement in 45 professional athletes: Associated pathologies and return to sport following arthroscopic decompression. *Knee Surgery, Sport. Traumatol. Arthrosc.* **15,** 908–914 (2007).

439. Byrd, J. W. T. Femoroacetabular Impingement in Athletes, Part 1: Cause and Assessment. *Sport. Heal. A Multidiscip. Approach* **2,** 321–333 (2010).

440. Farrell, G. *et al.* 95% prevalence of abnormality on hip MRI in elite academy level rugby union: A clinical and imaging study of hip disorders. *J. Sci. Med. Sport* **19,** 893–897 (2016).

441. Caine, D. J. & Golightly, Y. M. Osteoarthritis as an outcome of paediatric sport: an epidemiological perspective. *Br. J. Sports Med.* **45,** 298–303 (2011).

442. Brenner, J. S. Sports Specialization and Intensive Training in Young Athletes. *Pediatrics* **138,** 154–157 (2016).

443. Mostafavifar, A. M., Best, T. M. & Myer, G. D. Early sport specialisation, does it lead to long-term problems? *Br. J. Sports Med.* **47,** 1060–1061 (2013).

444. Cooper, C. *et al.* Risk factors for the incidence and progression of radiographic knee osteoarthritis [In Process Citation]. *Arthritis Rheum* **43,** 995–1000 (2000).

445. Richmond, S. a *et al.* Are joint injury, sport activity, physical activity, obesity, or occupational activities predictors for osteoarthritis? A systematic review. *J. Orthop. Sports Phys. Ther.* **43,** 515-B19 (2013).

446. Meislin, R. J., Sperling, J. W. & Stitik, T. P. Persistent shoulder pain: epidemiology, pathophysiology, and diagnosis. *Am. J. Orthop.* **34,** 5–9 (2005).

447. Hewett, T. E. Biomechanical Measures of Neuromuscular Control and Valgus Loading of the Knee Predict Anterior Cruciate Ligament Injury Risk in Female Athletes: A Prospective Study. *Am. J. Sports Med.* **33,** 492–501 (2005).

448. Padua, D. A. *et al.* Fatigue, vertical leg stiffness, and stiffness control strategies in males and females. *J. Athl. Train.* **41,** 294–304 (2006).

449. Hislop, M. D. *et al.* Reducing musculoskeletal injury and concussion risk in

schoolboy rugby players with a pre-activity movement control exercise programme: a cluster randomised controlled trial. *Br. J. Sports Med.* **15,** bjsports-2016-097434 (2017).

450. Zazulak, B. T., Hewett, T. E., Reeves, N. P., Goldberg, B. & Cholewicki, J. Deficits in Neuromuscular Control of the Trunk Predict Knee Injury Risk: A Prospective Biomechanical-Epidemiologic Study. *Am. J. Sports Med.* **35,** 1123–1130 (2007).

451. Moons, K. G. M., Royston, P., Vergouwe, Y., Grobbee, D. E. & Altman, D. G. Prognosis and prognostic research: what, why, and how? *BMJ* **338,** b375 (2009).

452. Steyerberg, E. W. *Clinical Prediction Models. Ewout W. Steyerberg. Clinical Prediction Models.* (2009). doi:10.1007/978-0-387-77244-8

453. Flugsrud, G. B., Nordsletten, L., Espehaug, B., Havelin, L. I. & Meyer, H. E. Risk factors for total hip replacement due to primary osteoarthritis: A cohort study in 50,034 persons. *Arthritis Rheum.* **46,** 675–682 (2002).

454. Pavlou, M. *et al.* How to develop a more accurate risk prediction model when there are few events. *BMJ* **351,** h3868 (2015).

455. Concato, J., Peduzzi, P., Holford, T. R. & Feinstein, A. R. Importance of events per independent variable in proportional hazards analysis I. Background, goals, and general strategy. *J. Clin. Epidemiol.* **48,** 1495–1501 (1995).

456. Peduzzi, P., Concato, J., Kemper, E., Holford, T. R. & Feinstein, a R. A simulation study of the number of events per variable in logistic regression analysis. *J. Clin. Epidemiol.* **49,** 1373–1379 (1996).

457. Steyerberg, E. W. *Clinical Prediction Models*. (Springer-Verlag, 2009). doi:10.1007/978-0-387-77244-8

458. Steyerberg, E. W., Eijkemans, M. J. C., Harrell, F. E. & Habbema, J. D. F. Prognostic Modeling with Logistic Regression Analysis: In Search of a Sensible Strategy in Small Data Sets. *Med. Decis. Mak.* **21,** 45–56 (2001).

459. Harrell, F. E. *Regression modeling strategies. With applications to linear models, logistic regression, and survival analysis. Springer Series in Statistics* (2001). doi:10.1007/978-1-4757-3462-1

460. Tibshirani, R. Regression Selection and Shrinkage via the Lasso. *Journal of the Royal Statistical Society B* **58,** 267–288 (1996).

461. Van Houwelingen, J. C. & Le Cessie, S. Predictive value of statistical models. *Stat. Med.* **9,** 1303–1325 (1990).

462. Miller, M. E., Hui, S. I. U. L. & Tierney, W. M. Validation Techniques for Logistic Regression Models. **10,** 1213–1226 (1991).

463. Harrell, F. E., Califf, R. M., Pryor, D. B., Lee, K. L. & Rosati, R. A. Evaluating the yield of medical tests. *JAMA* **247,** 2543–6 (1982).

464. Boos, D. D. Introduction to the Bootstrap World. *Stat. Sci.* **18,** 168–174 (2003).

465. Stata.com. Linktest - specification link test for single-equaton models. *Stata* 1–4 (1999).

466. Altman, R. D. *et al.* Total joint replacement of hip or knee as an outcome measure for structure modifying trials in osteoarthritis. *Osteoarthr. Cartil.* **13,** 13–19 (2005).

467. Thomas, G. E. R. *et al.* Subclinical deformities of the hip are significant predictors of radiographic osteoarthritis and joint replacement in women. A 20 year longitudinal cohort study. *Osteoarthr. Cartil.* **22,** 1504–1510 (2014).

468. Harrell, F. E. H., Lee, K. L. & Mark, D. B. Tutorial in biostatistics multivariable prognostic models. *Stat. Med.* **15,** 361–387 (1996).

469. Parsons, S. J., Barton, C., Banerjee, R. & Kiely, N. T. Slipped upper femoral epiphysis. *Curr. Orthop.* **21,** 215–228 (2007).

470. Loder, R. T. The Demographics of Slipped Capital Femoral Epiphysis. *Clinical orthopaedics and related research* 8–27 (1996).

471. Ambrose, G. B. & McLaughlin, H. L. Slipped Upper Femoral Epiphysis and trauma. (1960).

472. Thavarajah, D., Maroju, R. S. & Narayanaswamy, L. Slipped upper femoral epiphysis - A case of a 'dodgem hip'. *Ann. R. Coll. Surg. Engl.* **91,** 2–3 (2009).

473. Montgomery, R. J. (iv) Slipped upper femoral epiphysis. *Orthop. Trauma* **23,** 169–174 (2009).

474. Lawrence, J. S., Bremner, J. M. & Bier, F. Osteo-arthrosis. Prevalence in the population and relationship between symptoms and x-ray changes. *Ann. Rheum. Dis.* **25,** 1–24 (1966).

475. Kellgren, J. H. Osteoarthrosis in patients and populations. *Br. Med. J.* **2,** 1–6 (1961).

476. Lanyon, P., Muir, K., Doherty, S. & Doherty, M. Assessment of a genetic contribution to osteoarthritis of the hip: sibling study. *BMJ* **321,** 1179–83 (2000).

477. Chitnavis, J. *et al.* Genetic Influences in End-Stage Osteoarthritis: Sibling Risks of Hip and Knee Replacement for Idiopathic Osteoarthritis. *J Bone Jt. Surg Br* **79–B,** 660–664 (1997).

478. Cross, M. J., Williams, S., Trewartha, G., Kemp, S. P. & Stokes, K. A. The Influence of In-Season Training Loads on Injury Risk in Professional Rugby Union. *Int. J. Sports Physiol. Perform.* (2015). doi:10.1123/ijspp.2015-0187

479. Brooks, J. H. M. & Kemp, S. P. T. Injury-prevention priorities according to playing position in professional rugby union players. *Br. J. Sports Med.* **45,** 765–775 (2011).

480. Gianotti, S. M., Quarrie, K. L. & Hume, P. A. Evaluation of RugbySmart: A rugby union community injury prevention programme. *J. Sci. Med. Sport* **12,** 371–375 (2009).

481. Walsh, A. J. *et al.* The prevention of spinal injuries in rugby football. *Paraplegia* **32,** 442–453 (1994).

482. Hendricks, S. & Lambert, M. Tackling in rugby: Coaching strategies for effective technique and injury prevention. *Int. J. Sport. Sci. Coach.* **5,** 117–136 (2010).

483. Brown, J., Lubbe, S., Lambert, M., van Mechelen, W. & Verhagen, E. Effectiveness of the Boksmart intervention: the association between knowledge, education and perceptions and injury prevention behaviour in rugby union players. *Br. J. Sports Med.* **48,** 575 (2014).

484. Quarrie, K. L., Gianotti, S. M., Hopkins, W. G. & Hume, P. A. Effect of nationwide injury prevention programme on serious spinal injuries in New Zealand rugby union: ecological study. *BMJ* **334,** 1150–1150 (2007).

485. Lowndes, S., Khanna, A., Emery, D., Sim, J. & Maffulli, N. Management of

unstable slipped upper femoral epiphysis: A meta-analysis. *Br. Med. Bull.* **90,** 133–146 (2009).

486. Tosounidis, T. *et al.* Prognostic significance of stability in slipped upper femoral epiphysis: a systematic review and meta-analysis. *J. Pediatr.* **157,** 674–681 (2010).