BJSM Online First, published on June 3, 2016 as 10.1136/bjsports-2016-096189

Evidence review for the 2016 International Ankle Consortium consensus statement on the prevalence, impact and long-term consequences of lateral ankle sprains

Phillip A Gribble,[1] Chris M Bleakley,[2] Brian M Caulfield,[3] Carrie L Docherty,[4] François Fourchet,[5] Daniel Tik-Pui Fong,[6] Jay Hertel,[7] Claire E Hiller,[8] Thomas W Kaminski,[9] Patrick O McKeon,[10] Kathryn M Refshauge,[8] Evert A Verhagen,[11] Bill T Vicenzino,[12] Erik A Wikstrom,[13] Eamonn Delahunt[14]

For numbered affiliations see end of article.

Correspondence to
Dr Phillip A Gribble, Charles Wethington, Jr. Building, Room 206C, 900 South Limestone, College of Health Sciences, University of Kentucky, Lexington, KY 40536-0200, USA; phillip.gribble@uky.edu

Accepted 12 May 2016

Linked

▸ http://dx.doi.org/10.1136/bjsports-2016-096188

To cite: Gribble PA, Bleakley CM, Caulfield BM, *et al*. *Br J Sports Med* Published Online First: [*please include* Day Month Year] doi:10.1136/bjsports-2016-096189

ABSTRACT
Lateral ankle sprains (LASs) are the most prevalent musculoskeletal injury in physically active populations. They also have a high prevalence in the general population and pose a substantial healthcare burden. The recurrence rates of LASs are high, leading to a large percentage of patients with LAS developing chronic ankle instability. This chronicity is associated with decreased physical activity levels and quality of life and associates with increasing rates of post-traumatic ankle osteoarthritis, all of which generate financial costs that are larger than many have realised. The literature review that follows expands this paradigm and introduces emerging areas that should be prioritised for continued research, supporting a companion position statement paper that proposes recommendations for using this summary of information, and needs for specific future research.

Musculoskeletal injuries have the potential to outweigh the health benefits of participation in physical activity and organised sport, and the perceived risk of injury could also act as a deterrent to future participants.[1 2] Lateral ankle sprains (LASs) are the most prevalent musculoskeletal injury in physically active populations. They also have a high prevalence in the general population and pose a substantial healthcare burden. The injury mechanism is characterised by a high velocity inversion and internal rotation of the ankle/foot complex. The treatment for acute LAS is quite variable, with many patients returning to activity in a short period of time; however, half of the population may never seek initial care.

The recurrence rates of LASs are high, leading to a large percentage of patients with LAS developing chronic ankle instability (CAI). The lingering ankle instability contributes to ongoing disability and sensorimotor control deficits, which associate with decreased physical activity and quality of life (QOL). Not surprisingly, we are seeing that patients with a history of LAS and CAI dominate ankle joint post-traumatic osteoarthritis (PTOA) cases, which comprise the majority of ankle joint OA surgical cases. Additionally, the onset of ankle joint PTOA is occurring earlier in one's lifespan than most would assume.

While the direct costs for treatment of an isolated acute LAS are relatively low, compounding these costs are the indirect costs accruing from follow-up care and time loss. Considering that LAS injury is the most prevalent musculoskeletal injury in physically active populations, the societal costs are larger than most would comprehend. As these costs for management of acute LAS are combined with the costs of managing the loss of physical activity and treatments for likely onset and care for ankle joint PTOA, it is easy to formulate the healthcare burden that emerges from a seemingly 'simple' LAS injury.

The literature review that follows expands the paradigm we describe above, and introduces emerging areas that are to be prioritised for continued research. In a companion position statement paper, the Executive Committee of the International Ankle Consortium proposes recommendations for using this summary of information, as well as needs for specific future research based on this evidence review that follows.[3] Therefore, the Executive Committee of the International Ankle Consortium presents this review of the evidence that demonstrates that LAS, and the development of CAI, serve as a conduit to a significant global healthcare burden. We illustrate this paradigm as a mechanism to promote efforts to improve prevention and early management of LAS. We believe this will reduce the prevalence of CAI and associated sequelae that have led to the broader public health burdens of decreased physical activity and early onset ankle joint PTOA. Ultimately, this can contribute to healthier lifestyles and promotion of physical activity. Our review of evidence is organised into two sections that will: (A) establish the burden of LAS and (B) raise awareness of the mid-term and long-term consequences of LAS.

SECTION A: ESTABLISHING LAS PREVALENCE AND BURDEN

Defining LAS

LAS is the most common lower limb musculoskeletal injury in physically active persons.[4] Acute LAS has been defined by Delahunt *et al*[5] and endorsed by the International Ankle Consortium[6–8] as "an acute traumatic injury to the lateral ligament complex of the ankle joint as a result of excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot."

Mechanism of injury

Ankle sprains are particularly prevalent in field and court sports.[9] In an attempt to develop a comprehensive understanding of the mechanisms of LAS in football, Andersen *et al*[10] reviewed videotape recordings of 26 ankle sprains in Norwegian and Icelandic elite football from the 1999–2000 season. They reported that the two most frequent injury mechanisms were: (1) player-to-player contact with impact by an opponent on the medial aspect of the leg just before or at foot strike, resulting in a laterally directed force causing the player to land with the ankle in a vulnerable, inverted position or (2) forced plantar flexion where the injured player hit the opponent's foot when attempting to shoot or clear the ball. Both of these mechanisms can be described as contact mechanisms of injury. However, qualitative analysis and reporting of injury mechanisms based on visual inspection of recorded injuries is not without limitations. Furthermore, non-contact mechanisms of ankle sprain are reported to be more common than contact mechanisms of injury.[9]

Fong *et al*[11] reported the first-ever kinematic analysis of an LAS, which occurred accidentally during testing in their research laboratory. A male athlete performing a series of cutting test trials incurred an LAS during the fourth test trial. During the injury sustaining trial, the ankle was 7° more internally rotated and 6° more inverted at initial contact when compared with the preceding three 'normal' test trials in which no adverse result occurred. The injury trial was characterised by a rapid inversion and internal rotation which was initiated after 0.06 s following initial contact. Interestingly, in contrast to previously purported mechanisms of injury, dorsiflexion was observed throughout the injury trial. A number of other authors have reported the kinematic patterns observed during accidental LASs incurred during controlled laboratory testing.[12–14] All observations confirmed the presence of a rapid increase in inversion and internal rotation with or without the presence of plantar flexion. Thus, it can be considered that LASs occur as a consequence of a sudden rapid inversion and internal rotation loading of the foot and ankle complex irrespective of sagittal plane position.

Recently, Mok *et al*[15] and Fong *et al*[16] used a model-based image-matching motion analysis technique to describe the kinematic characteristics of uncalibrated video recordings of ankle joint sprains incurred during live sporting events. Mok *et al*[15] reported on two LASs incurred during the 2008 Beijing Summer Olympic Games. The injuries occurred during the women's high jump qualification round and a field hockey match. For the high jump injury, the ankle joint was 30° inverted, 28° internally rotated and 5° plantar flexed at initial contact. Following initial contact there was a sudden rapid increase in inversion (maximum=142°) and internal rotation (maximum=37°). The field hockey injury was a contact mechanism, whereby the defending player accidentally stood on the attacking player's foot provoking an inversion moment and subsequent LAS. Additionally, Fong *et al*[16] described the kinematic characteristics of LASs recorded during five televised tennis matches. In all instances, the ankle joint was inverted at the time of initial contact, which is a vulnerable position and posited as an inciting mechanism of LAS.[17] Furthermore, peak inversion was noted to occur rapidly after initial contact (typically 0.09–0.13 s).

Epidemiology of LAS

In this section, we will illustrate that LAS is the most common injury incurred among physically active populations. Commonly, these injuries are considered only to be an issue for athletes; but as the evidence shows, LASs are an injury that impacts many aspects of physical activity. Additionally, the distribution of LASs within the general population is quite large as demonstrated from the emergency department (ED) data. It is important to demonstrate the prevalence of LAS throughout society to establish the foundation for the public healthcare burden we present in this paper.

There is an abundance of epidemiological data delineating patterns of ankle injury in sporting activities. In 2007, Fong *et al*[18] reviewed 227 epidemiological studies, across 70 sports, involving a total of 201 600 individuals. In 24 of the 70 included sports (34%), the ankle joint was the most commonly injured body part. A recently published systematic review by Doherty *et al*[9] included a meta-analysis of prospective studies and provided pooled incidence figures, subgrouped by sport, age and gender. In conjunction with earlier reports,[18] indoor/court sports had the highest incidence rates estimated as 7 ankle sprains per 1000 exposures.[9] There were also differences according to athletes' gender, with higher incidences estimated in women (13.6 per 1000 exposures) compared with men (6.94 per 1000 exposures). Incidence rates also varied across age cohorts, with the highest figure of 2.85 ankle sprains per 1000 exposures reported in young athletes (under 12 years of age), followed by adolescents (aged 12–18 years; 1.94 per 1000 exposures), then adults (0.72 per 1000 exposures).[9] In both reviews, there was consistent evidence that the majority of ankle injuries were diagnosed as sprains; of which 80–90% were LASs.

Although it is interesting to compare data across multiple sports and nationalities, pooled incidence figures, such as those presented by Doherty *et al*[9] can be limited by study heterogeneity. Prospective injury data extracted from large regional data sets may be more reliable by ensuring consistency in study methods, injury definitions and medical verification over time. The National Collegiate Athletic Association (NCAA) Injury Surveillance System (ISS) has captured injury data across 16 collegiate sports over the past 27 years in the USA. Using this database, Hootman *et al*[19] report that ankle ligament sprains are the most common injury in NCAA sports, accounting for 15% of all reported injuries, with an overall incidence of 0.83 sprains per 1000 athletic exposures (AE). Their data also show that incidence rates differ across sports, with the highest figures reported in basketball and soccer. Interestingly their reported rates were consistent across gender cohorts, with similar figures in female (1.15 ankle sprains per 1000 AE) and male basketball players (1.3 ankle sprains per 1000 AE), and in female (1.3 ankle sprains per 1000 AE) and male soccer players (1.24 ankle sprains per 1000 AE).[19] High participation in sports such as soccer (estimated 265 million soccer players worldwide[20]) or basketball (estimated 450 million basketball players worldwide[21]) provides further context to the global burden associated with ankle sprains in sport.

It is important to consider that other physically active populations, such as military personnel, are also at high risk of ankle sprain. Two of the largest studies in this area have used retrospective audits of injury data recorded (prospectively) over a 7–9-year period in the USA, with the incidence of ankle sprains reported to be between 34.95[22] and 45.14[23] sprains per 1000 person-years. On the basis of a conservative estimate of 100 exposures per year, these equate to ~0.35–0.45 ankle sprains per 1000 exposures, figures that are comparable to many sporting populations such as softball, baseball, and both ice and field hockey.[19]

Another important patient cohort to consider is the general population presenting to an ED in the early stages of postankle injury. In the UK, 3–5% of all ED presentations are for LAS,[24 25] equating to 5600 daily incidents[24] or 1–1.5 million visits annually.[25] One of the first audits of ED attendances was undertaken in a single region of Denmark in 1994 and estimated an incidence of 7.0 ankle sprains per 1000 person-years.[26] A decade later, slightly lower incidence rates of 5.2 per 1000 people per year were estimated based on data captured from EDs across four large health districts in the UK.[27] Interestingly, this study also noted marked age–sex differences, with the highest incidence figures reported in girls aged 10–14 years (12.8 per 1000 person-years).

Two studies in the USA accessed ED data sets from the National Electronic Injury Surveillance System (NEISS).[4 28] Lambers *et al*,[28] using data from 119 815 patient presentations in a single year, reported that ankle sprains were the most common reason for presenting to an ED, estimating an incidence of 2.06 ankle sprains per 1000 person-years (95% CI 181 to 230). Similarly, Waterman *et al*[4] reported rates of 2.15 per 1000 person-years during a 4-year review. A 25-year review of the Dutch Injury Surveillance System undertaken by Kemler *et al*[29] is the largest ED data set analysed to date. Interestingly, they reported a steady decline in ankle sprains between 1986 and 2010, from 3.0 per 1000 person-years, down to 2.1 per 1000 person-years, but these figures are generally consistent with those reported in the USA.[4 28] In the same report, Kemler *et al*[29] also analysed data from a 10-year National Survey in the Netherlands. Although separate figures were not available for ankle sprains, an interesting finding was that ankle injury rates more than doubled over a 10-year period, from 8.2 per 1000 person-years in 2000, up to 17.5 in 2010. This likely indicates that LASs are still occurring at a high rate, but fewer individuals may be seeking treatment from an ED.

Financial burden

Sports injuries in general and ankle sprains in particular have a significant financial impact on society. Most injuries require clinical care, and may also lead to production loss due to work absenteeism and disablement. From a clinical perspective, the sports time lost, and the short-term and long-term consequences are a good indicator of the severity of an injury. However, economic evaluations aid policymakers in their decisions to place focus on specific sports, injuries and interventions. An economic interpretation of injury severity in terms of direct (healthcare) costs and indirect (productivity loss) costs provides a single understandable figure that unifies many of the clinical injury outcomes. A description and valuation of costs is also vital for an analysis of intervention effectiveness to determine if an intervention comes with a tolerable financial investment relative to a favourable clinical outcome. Weighting these factors in a cost-effectiveness analysis provides a tool to quantify the required investment to prevent, effectively diagnose or treat LAS.[30–37] However, we will restrict ourselves here to a rough description of the costs associated with ankle sprains. For an expanded background on the methodology used in economic evaluations in sports medicine, we refer to text books on this topic.[38 39] It should be noted that there are large differences in valuation of costs and market prices between countries, and as such cost data from different countries should be compared with caution. Moreover, cost data are subject to change over time due to factors such as inflation, changes in the healthcare system or effectiveness of provided care. Consequently, we have chosen only to report on costs published after the year 2000 to provide the most contemporary overview to date of the financial burden of LAS.

Societal costs

The most comprehensive cost perspective is the 'societal' perspective, which represents the costs of an injury for society regardless of who pays. Costs from a societal perspective include the out-of-pocket expenses for the injured individual, the costs for provided clinical care, and the costs for the employer. We use this societal perspective in this section, with subdivisions solely in direct and indirect costs. As such, data derived from insurance registries are not discussed here.

In the USA, Knowles *et al*[40] prospectively calculated the costs associated with musculoskeletal injuries in high school athletes. This study is unique as in addition to the short-term direct and indirect costs, they also attached a monetary value to lost health in the long term (ie, quality-adjusted life years lost). Costs for specific injuries were not calculated, but the mean societal costs for joint sprain ($9196; 95%CI $6856 to $11 536) and ankle injuries ($11 925; 95% CI $10 188 to $13 662) were reported. Given that ankle sprains are among the most commonly reported injuries, it is likely that the mean societal costs for LASs in the USA high school athletes reside within this range.

These costs are higher than what is reported in studies that only include the short-term costs of ankle sprains, that is, costs incurred from the moment of injury occurrence to recovery.[32 37 41] Cooke *et al*[41] reported the societal cost of ankle sprains in a population of British ED patients to be £940. This amount is comparable to what is found in the Netherlands, where the costs of ankle sprains presenting at an ED are calculated to be €823.[42] It may be clear that patients who require hospitalisation after emergency care have higher costs than patients who do not require further hospital care, respectively €6217 and €842 in the Dutch situation.[42] Those patients who present at an ED have in general more severe injuries, which can be illustrated by the societal costs of ankle sprains as reported by Verhagen *et al*[37] and Hupperets *et al*.[32] Both studies reported on the costs of all ankle sprains sustained by a sporting population. Hupperets *et al*[32] reported specifically on the costs associated with recurrent ankle sprains that were sustained in the year after athletes were deemed fit to return to play. The costs of these recurrences were estimated at €447 per injury, by which it can be concluded that both primary and secondary ankle sprains are associated with a significant financial burden and that prevention is duly warranted.

Verhagen *et al*[37] estimated the societal costs of all ankle sprains sustained in an amateur volleyball population to be €360. Given that the annual total number of ankle sprains in the Netherlands is projected at about 580 000,[43] this would give a rough annual cost of €208 million per annum for ankle sprains due to sports alone. Similarly, if one was to take the estimation by Waterman *et al*[4] of 628 000 ankle sprains annually in the USA and apply the estimations from Knowles *et al*[40] of $10 000 (the low end of the 95% CI for treating ankle injury), there would be more than $6.2 billion in annual costs, an alarmingly high amount for an injury that is deemed minor and relatively easy to prevent.

These estimations must only be accepted as approximations, and not as validated documentation of costs. Another factor to remember is that <50% of patients with LAS may seek formal care,[44] leading to likely underestimation of true costs. Clearly, more comprehensive estimations of societal costs are needed. We hope that our rough estimations presented here will stimulate others to follow through with validated analyses.

Direct costs

Part of the societal cost comprises the direct costs of injury due to consumed healthcare. These costs include, among others, the consultation costs of caregivers, the operational costs of diagnostics, prescribed and over-the-counter medications and so on. Presentation of direct costs of ankle sprains provides insight into the concrete burden to the healthcare system. Cooke *et al*[41] describe the total direct costs of standard care for ankle sprains presenting at British EDs to be £135. Verhagen *et al*[37] valued these costs at €43, and Hupperets *et al*[32] at €61. Naturally the direct costs of ankle sprains treated at EDs are lower, while specialised care provided in a clinic is generally more elaborate and expensive. It is impossible to provide a breakdown of the healthcare consumption per injury, but what is generally described is that most direct costs go into consultation with caregivers of which most are physiotherapists.[32 37 41 42]

Indirect costs

In addition to the direct healthcare costs associated with acute LASs, these injuries are also linked to indirect costs associated with time lost from activities. In sport and military settings, this impact is intuitive as it means time lost in training and likely a decrease in either game or combat readiness. However, in a private and business setting, the injury creates time lost from leisure time and work. Both carry a financial impact related to a loss of paid (work) and unpaid (leisure time) productivity, and both should be considered when describing the burden of LAS from a societal economic perspective. Naturally, when only interested in the cost perspective from an employer's point of view, time lost from unpaid work is not a meaningful measure; albeit the side note should be made that quality leisure time has been linked to increased vitality and productivity, by which a loss of leisure time is entangled to a financial burden for the employer nonetheless.

Indirect injury costs due to lost productivity make up 70–90% of the total costs of ankle sprains.[32 33 37 40 41] Within the general population of the UK, Cooke *et al*[41] observed an average of 6.9 days of paid work lost due to ankle sprains treated by means of standard care, adding at least an additional £805 pounds in lost productivity costs for each ankle sprain to the overall costs, compared with £135 of direct healthcare costs. Specifically in sports, Verhagen *et al*[37] demonstrated that ankle sprains sustained by Dutch recreational volleyball players led to an average of 2.3 days of working time lost and 29.8 hours of unpaid leisure time lost per injury. These times were economically valued, based on standardised rates, at a mean of €318 of indirect costs per injury. This was in contrast to €43 of direct healthcare costs per injury. Similarly, Hupperets *et al*[32] showed that recurrent ankle sprains sustained in a general Dutch sporting population lead to an average of €385 indirect costs in contrast to €61 of direct healthcare costs. Unfortunately, a breakdown between paid and unpaid work was not given.[45]

Long-term costs

Most of the cost analyses reviewed above focus on the short-term treatment and management for LAS. However, as discussed later in this review, there is a very high rate of reinjury and subsequent development of CAI. Additionally, the long-term consequences of ankle injury are being recognised with the rise of documented ankle joint degenerative disease, specifically, the onset of ankle joint PTOA. Patients with a history of LAS make up 70–85% of the surgical cases for end-stage ankle joint PTOA.[46–49] Patients with CAI are at an increased risk of PTOA,[45–47 49 50–53] suggesting that CAI represents an important contribution to the early stages of ankle joint degeneration and may even be a key mediator driving the disease process. This will be discussed in greater detail in section B of this consensus statement.

Conservative management using a variety of physiotherapy techniques can be used for patients with CAI with successful restoration of self-reported outcomes and functional measurements.[54–66] While the cost analyses for management and early rehabilitation for LAS have been discussed previously in this section, to our knowledge, there has been little cost analyses of conservative treatment for patients with CAI. Additionally, we have no data to demonstrate that conservative management is effective at improving indices of long-term success, such as QOL years. Therefore, while likely to improve the QOL of patients with CAI, it is difficult to conclude what the cost-effectiveness of conservative management (ie, physiotherapy) is relative to the standard of care, which is often nothing.

As CAI progresses, and symptoms, such as lingering pain, instability and reduction in function persist with or without physiotherapy, patients with CAI may seek non-conservative management options in the form of surgical reconstruction. The modified Brostrom procedure is the most commonly used surgical procedure, with consistent reporting of associated long-term successful outcomes.[67–71] A recent prospective comparative study concluded similar functional success between the suture anchor or the suture bridge techniques of the Brostrom procedure, but better cost-effectiveness for the surgical event with the suture anchor technique.[67] However, there is little to no data that has assessed the comprehensive costing and QOL analysis of these surgical techniques relative to conservative management for CAI. The direct surgical costs are greater than non-surgical management of ankle instability, introducing financial burden for potentially effective treatment for patients with CAI that have failed with conservative management. However, more research is needed to consider the indirect costs and assessments of QOL using long-term follow-ups to determine the extent to which these surgical techniques contribute to increasing or decreasing the financial burden of ankle instability.

Unfortunately, an alarmingly high percentage of patients with PTOA stem from the CAI patient population.[45 46 49 51] At present, ankle replacement via arthroplasty or arthrodesis represent the few options available for patients with ankle degenerative disease once symptoms become intolerable and activity levels are compromised. As with surgical reconstruction, there are few studies that have compared conservative management for ankle OA with surgical fusion or replacement for the ankle. Nwachukwu *et al*[72] performed a cost-effectiveness analysis of operative and non-operative treatments with an emphasis on incremental cost-effectiveness ratio, which considers direct and indirect costs along with QOL years. Their analysis was based on the cost of ankle fusion ($16 754) and ankle replacement ($21 423) from the 2012 Nationwide Inpatient Sample from the USA. Ankle replacement procedures are more expensive than non-operative management, but this technique was optimal in 83% of the analyses when considering direct and indirect costs, along with factors that impact QOL.[72] This means that the best option for patients with end-stage OA is a very costly surgery. This surgery optimises the QOL and minimises indirect costs compared with conservative management in these patients. While ankle replacement is a successful treatment option, it presents a major financial burden that emerges from patients with a history of LAS.

Section A summary

Contact and non-contact mechanisms of LAS exist. An inverted position of the ankle joint at initial contact is a particularly vulnerable position and has been identified as a key characteristic feature of the LAS injury mechanism. There is clear evidence that LASs commonly occur during sporting activity. Incidence figures in excess of 2.0 LASs per 1000 AE are consistently reported in popular field and court sports.[9] Incidence rates in sport also tend to vary according to age and gender, with some of the highest figures reported in young/adolescent female athletes.[9] As LASs also occur during activities of daily living, it is important to determine population-based incidence rates. Estimates from EDs range from 2 to 7 ankle sprains per 1000 person-years, but these figures may be an underestimation due to the growing number of patients attending primary care practice or self-managing their ankle sprain.[44] Contemporary figures suggest that the true incidence rate in the general population is around 5.5 times higher than figures derived from EDs.[29] To provide the most accurate estimate of population-based incidence rates, epidemiological studies should focus on the National Survey data that encompasses both medical and non-medically treated ankle sprains. While LAS is the most common injury sustained in the physically active population, the documented prevalence of LAS demonstrates this is not an injury associated exclusively with sporting and competitive athlete groups. Therefore, we must consider the financial costs that are associated with the management and treatment for LAS, and the long-term consequences that persist.

Economic consequences of injury add a new layer of severity outcome measures to describe the burden of injury, aiding policymakers in their decisions to place focus on specific sports, injuries or interventions. Costs are described in direct (medical costs) and indirect (work time lost) costs, and can be described for the short term and for the long term. With regard to LAS, direct costs are, as with other injuries, lower than indirect costs. Although cost estimates differ between countries, depending on the different insurance and medical systems, the sheer magnitude of LAS makes the societal costs substantial. Usually such estimations do not include the long-term consequences of LAS, providing a significant underestimation of the actual financial burden LAS poses to society. We have identified the current information that depicts the direct and indirect costs, but more comprehensive assessments of LAS management and treatment are still needed. It is likely that with more complete analyses across societies, we will realise that our current figures are underestimated.

SECTION B: MID-TERM AND LONG-TERM CONSEQUENCES OF LASS

Development and onset of CAI

As an isolated, acute injury, it is common to consider LAS an an innocuous injury from which a patient can recover fairly quickly. However, a significant number of people experience ongoing problems including residual symptoms of instability, decreased function and activity restrictions in the months and years following LAS. It is common for these patients to develop CAI, and experience a substantial reinjury rate. Additionally, what causes CAI to develop in some patients but not in others has not been established definitively. Subsequently, we will summarise the hypotheses that are currently being considered.

Postacute deficits following LAS

Most patients with LAS have resolution of primary inflammatory symptoms in a relatively short period of time with conservative treatment,[73–75] and a high likelihood of rapid return to activity.[76] Subsequently, there is an assumption that LAS is an inconsequential injury once the subacute phase has passed. However, the consideration for successful treatment of LAS does not usually extend beyond the assessment of return to activity. What is observed commonly in the follow-up of patients with LAS are lingering disabling symptoms including pain and decreased function.[77]

The early work by Gerber *et al*[78] illustrates this pattern. Among a group of military cadets presenting with a total of 67 LAS of varying severity, 78% of the grade 1 and 48% of the grade 2 or 3 patients with LAS had returned to full military demands by 6 weeks, but with 28% of all the patients still reporting pain. However, at a 6-month follow-up (n=61), only 72% of all patients with LAS presented with full function and 25% of patients still reported pain.[78] Konradsen *et al*,[79] at the7-year follow-up of 648 patients with LAS, found >30% still had pain, swelling or recurrent injury (three or more severe sprains/year). Among those reporting ankle disability at the 7-year follow-up, >70% felt functionally impaired.[79]

Retrospective assessment of the population with a history of previous LAS demonstrates lingering symptoms and functional deficits. It is worth noting that 32–74% of individuals with a previous history of LAS suffer chronic symptoms.[79–81] Hiller *et al*,[82] in a systematic review of 55 papers that included patients with recurrent ankle sprain history (at least 2) found characteristics such as altered foot positioning during gait, decreased dynamic postural stability and talar radiographic changes in patients with recurrent LAS. In a cross-sectional analysis by Hiller *et al*,[83] 29% of the general population reported a history of LAS, and 28% reported chronic ankle issues (pain, weakness, swelling or instability), of which 52% reported duration >10 years.

There may be a host of functional and sensorimotor deficits that persist in the months following LAS.[84 85] Patients with LAS exhibit deficits in balance and movement coordination in the weeks and months following acute injury.[86–89] Doherty *et al*,[90–97] following patients for up to 12 months following a first-time acute LAS, observed a host of aberrant movement patterns that differed from individuals without an LAS. They concluded from their collective work that the LAS injury creates sensorimotor deficits that have not resolved in spite of the patients returning to activity, which may have implications for reinjury.

Recurrent injury

LASs have the highest recurrence rates of all lower limb musculoskeletal injuries,[19 98–100] with a twofold increased risk of reinjury in the year following injury occurrence.[37 101] However, it should be noted that a number of studies describing LAS recurrence rates are biased, failing to control for details such as player function and/or position, which can influence injury risk in some sports. Volleyball is a good example, where attacking players have a higher LAS risk than other players.[37 102]

It is suggested that neuromuscular functioning is altered after an initial LAS due to damage of the ankle ligament receptors.[103] Resulting functional deficits include limited postural control, decreased maximal strength of the evertor muscles and prolonged muscle reaction time.[84 104] Even after successful return to play, ongoing deficits in neuromuscular control may contribute to a higher risk of a recurrent injury.[105] For example, individuals with a history of ankle sprain have greater fatigue-induced alterations of dynamic postural control.[106 107] It may be that further damage of the already impaired ankle function after LAS recurrences is a significant contributor to CAI.

From LAS to CAI

Many patients have ongoing pain, giving way and feelings of instability in their ankle,[64] leading to persistent disability, which are characteristic features of CAI.[5] Hertel[108] proposed a model of CAI that denoted the occurrence of repetitive bouts of lateral ankle instability, resulting in numerous ankle sprains. His model integrated previous concepts of (1) mechanical instability (pathologic laxity after ankle-ligament injury)[109] and/or (2) functional instability (occurrence of recurrent ankle instability and the sensation of joint instability due to the contributions of proprioceptive and neuromuscular deficits).[110 111] Delahunt *et al*[5] expanded the inclusion criteria that define insufficiencies in CAI as an encompassing term used to classify a person with mechanical and functional instability of the ankle joint. They specified that in order to be categorised as having CAI, residual symptoms ('giving way' and feelings of ankle joint instability) should be present for a minimum of 1-year postinitial sprain.

The Hertel model[108] was revised by Hiller *et al*[112] in an effort to explain the inconsistencies in CAI research that were associated with the misconception that CAI is a homogeneous condition. These authors proposed that CAI should be considered as a heterogeneous condition including several homogeneous subgroups. Subsequently, the new model included seven subgroups integrating the concept of perceived instability instead of functional instability. This emerged from the development of questionnaires quantifying functional instability through the assessment of perceived instability,[113 114] with the intent to differentiate functional limitations that may coexist with other impairments in patients with CAI. Recently, the Executive Committee of the International Ankle Consortium published a position statement regarding the selection criteria for patients with CAI in controlled research focused on defining the acute LAS history and the functional limitations since injury through self-reported giving-way episodes and validated patient-reported outcome tools.[6–8]

Prevalence of CAI

There is a concerning trend in the literature for the prevalence of CAI. CAI develops in up to 70% of patients with a history of LAS,[18 83 99] and typically within a short period of time.[79 92–94 97] In a recent systematic review of the prevalence of CAI in sporting populations, Attenborough *et al*[115] indicated that CAI is a highly prevalent condition (>25%) in sports such as handball, basketball, soccer and volleyball. This has been confirmed in recent investigations of collegiate and high school athletes in which the prevalence of CAI was ~25% in those athletes with a previous history of injury.[116 117] Within the performing arts population, such as ballet, more than 50% of the dancers with a history of ankle sprain report CAI.[118] This CAI prevalence trend extends out to the general population in which more than 20% of the general population with ankle injury reported having chronic issues.[83] Within that study, chronicity following ankle sprain was most commonly associated with sporting activity.

While the development of CAI has been linked to the severity of LAS,[119] it may be that our current societal awareness of CAI prevalence and its consequences on physical activity are poorly appreciated.[120 121] There is evidence to suggest that regardless of a first time or recurrent LAS, athletes are more likely to return to activity within 1 week of the injury.[76] When combining this evidence with the current prevalence trends in the literature, it is apparent that CAI is a persistent, if not a recalcitrant, condition that is underappreciated and underestimated with regard to its public health burden.

Theories for CAI development

While the prevalence and characteristics of CAI are well established, the causes for CAI development have not been established definitively. One hypothesis surrounds the culture of LAS being an innocuous injury. Thus, many individuals do not seek initial care from any type of practitioner, preferring a 'it will be fine' approach, perhaps with application of ice and a brief period of rest. In fact, it has been reported that more than half of sport players who sprained an ankle did not seek any type of care.[44 122] A secondary analysis from the work by Hiller *et al*[83] found a similar distribution where half of the people in a sample of the general population with an ankle sprain (n=136/219) did not seek formal medical care. It may be that lack of medical assessment and appropriate care is more likely to lead to the development of CAI, but due to the difficulty of recruiting this population, there is no definitive evidence to support this hypothesis.

A second theory that may contribute to CAI development relates to the standard of care administered for LAS, which may be too passive or too aggressive. The management of LAS in many EDs is limited to advice on controlling acute inflammatory symptoms and restoration of joint range of motion.[25 62 123] Discharge criteria are often vague and clinicians will routinely avoid prognostication relating to recovery; and typically, there is inadequate follow-up care to ensure restoration of function.[24 64 89 124] This means that many patients with an LAS are susceptible to inadequate restoration of disease-oriented outcomes of range of motion (ROM), arthrokinematics, strength, balance and neuromuscular control.[125] While this has not been supported directly in the literature, it is likely that a lack of attention to those factors contribute to ongoing ankle instability, reinjury and a decline in patient-oriented outcomes, all of which are characteristics of CAI.

An advantage of entry into a formalised healthcare system is follow-up rehabilitation to address the factors listed above in an effort to restore function and reduce sources of disability. However, among clinical care for athletic populations, often there is an emphasis on rapid return to activity once pain is reduced and weight bearing is achieved.[76] This aggressive approach may neglect the critical outcomes and allow disability to persist. Athletic patients may return to activities before physiological healing stages have completed, leaving patients with potentially inadequate structural integrity and initiation of inefficient neuromuscular control patterns. Therefore, there are potential negative consequences from little to no follow-up rehabilitation, as well as the other end of the spectrum which is overly aggressive care and return to activity that may be too accelerated. A paradigm by Delahunt *et al*[126] proposes a 'road map' to help determine LAS patient needs and deficits that can shape clinical care decisions. Using these and other potential approaches, prospective, randomised control trials are needed to determine the optimal dosage of initial management and rehabilitation for a return to activity timeline that minimises lingering instability and reinjury for patients with LAS. These should also include long-term follow-up assessments to determine successful patient outcomes.

A third theory for CAI development involves aberrant sensorimotor and neuromuscular patterns that are observed in this population. Numerous retrospective studies have documented alterations in balance, gait and movement patterns in patients with CAI that persist throughout the lower extremity.[56 82 84–87]

[105–107 119 127–152] These documented deficits have expanded on the original theory by Freeman[110] that ankle ligamentous injury created a 'deafferentation' whereby balance deficits would persist after LAS. Additionally, a collection of work has suggested that there are adaptations within the central nervous system that may explain some of these observed sensorimotor changes in patients with CAI.[149 153–162]

However, those observed patterns have been generated from retrospective study designs, limiting the conclusions that an LAS definitely creates these deficits in the CAI population. Doherty *et al*[90–97 163–168] have conducted a large longitudinal prospective study to examine the onset of sensorimotor deficits following an LAS. In that series of papers, patients with LAS were assessed at the time of their acute injury, and at 6-month and 12-month follow-ups. This collective work has demonstrated that postural control and multiple aberrant movement patterns during a variety of functional tasks are present and are persistent compared with non-injured cohorts. Additionally, these neuromuscular alterations appear in conjunction with patient-reported disability and instability, suggesting that the foundation for CAI may begin to develop shortly after incurring acute LAS. Couple this with a potential lack of adequate care for LAS as suggested above, one can understand how reinjury and CAI can easily develop.

A final potential theory for consideration is how genetic factors may play a role in developing CAI. While genetic factors have been implicated in lower limb soft tissue injuries,[169 170] to date there is only one study of genetic factors in LAS. Shang *et al*[171] reported that Chinese soldiers with the ACTN3 RR genotype had fewer acute ankle sprains than a control group of soldiers with the same ethnic background and similar lifestyles. There was no relationship between genotype frequency and severity of sprain. This preliminary work gives initial support to the hypothesis that genetics may be involved in the development of CAI; however, continued work, including prospective studies, are needed to confirm these relationships and what interventions might be needed.

Post-traumatic OA development

On the basis of the above evidence, a clear link has been made between LAS and the development of CAI. While less well known, ankle joint PTOA has also been linked to acute LAS and CAI. Ankle joint OA, regardless of its aetiology, represents a significant physical burden to the individual as evidenced by an average 36-Item Short Form Health Survey (SF-36) physical component score of 32±8.[172] This profound physical limitation was noted in patients who averaged 53 years of age and represents subjective physical limitations comparable to those reported by patients with end-stage kidney disease, congestive heart failure, and cervical pain and radiculopathy.[172] Research has also outlined that patients with end-stage ankle joint OA, as measured radiographically, tend to be younger than patients with other lower extremity joint degeneration (eg, knee or hip OA) and appear to present with faster functional loss with progression to the final stages of ankle joint OA in 10–20 years.[49] Additionally, between 70 and 80% of all ankle joint OA cases are post-traumatic in nature,[46 172–174] likely explaining the younger onset and faster functional loss.

Ligamentous injury and instability play a substantial role in the development of ankle joint PTOA. More specifically, LASs account for 13–21.7% of all ankle joint OA cases (ie, primary, secondary, PTOA) and up to 80% of ankle joint PTOA cases.[46 49 172–174] It is important to note that roughly 50% of patients with ankle joint PTOA with a history of ligamentous injury reported only a single LAS while the remaining patients reported recurrent sprains and/or instability.[46 172 174] The patients with end-stage ankle joint PTOA in these investigations were, on average 51.5[174] and 58[46] years of age, with Valderrabano *et al*[46] noting an age range of 22–90 years. On the basis of their data, Valderrabano *et al*[49] suggest a latency period of 26 years for the development of ankle joint PTOA following a single severe LAS and 28 years following recurrent LASs. It is important to remember that the patients in these investigations were being treated for end-stage OA, which likely inflates the projected latency period. Similarly, in a 20-year follow-up study, Lofvenberg *et al*[175] reported 13% of 49 ankles with CAI had radiographic evidence of OA, but also reported 8.7% PTOA in a group that had recently sustained an LAS. The duration of time since the 'recent' LAS or if the injury was a first-time sprain was not reported. These studies document consistent rates of ankle joint PTOA development following LAS, but Canale and Belding[176] observed a much higher percentage of patients with CAI (48%) who had radiographic evidence of degenerative OA at an 11-year follow-up.

While the studies above discuss the findings of radiographic evidence of ankle joint degeneration in patients with diagnosed ankle joint PTOA, a large body of evidence demonstrates early degenerative changes, osteochondral lesions, and/or intra-articular pathologies in a high percentage of patients with LAS sooner after the initial inciting injury than previously anticipated. For the chronically unstable ankle, the evidence is focused on patients reporting for lateral ligament stabilisation and arthroscopic procedures. One of the first empirical reports observed that 26 of 30 patients (87%) who had a history of recurrent LAS for at least 10 years had evidence of arthritic changes via arthroscopic evaluation.[177] It is important to note that the chief complaint was chronic pain following a history of LAS and not CAI. Other reports demonstrate that 21–95% of patients with CAI have degenerative changes on arthroscopic review.[50 51 178–187]

On the low end of the range reported in the literature, Sammarco and DiRaimondo[182] noted only 21% of patients with CAI had degenerative changes of any kind in the ankle joint at the time of a lateral ligament stabilisation procedure. Hintermann *et al*[178] found cartilage lesions in 55% of patients with CAI via arthroscopic evaluation performed on average <2 years after the initial LAS. Similarly, Takao *et al*[184] noted that 50% of his 72 patients (average age 29 years) had degenerative changes but only 29% had osteochondral lesions. The mean time from injury to arthroscopic evaluation was only 7 months. On the other end of spectrum, Taga *et al*[51] illustrated that 95% of chronically unstable ankles examined arthroscopically had chondral lesions, with an average age of only 20 years. Komenda and Ferkel[181] and Ferkel andChams[179] noted that 91% of patients with an unstable ankle had degenerative changes at the ankle joint, but only 25% of the patients (mean age 31 years) had chondral lesions. Ferkel and Chams[179] also found intra-articular problems in 95% of patients with CAI, with a mean age of 28 years. The mean time from initial injury was just over 2 years.

As stated earlier, the above data are all from patients needing a surgical procedure to treat their CAI-associated symptoms. Thus, it is possible that the percentages of reported ankle joint OA, which have mostly included 'symptomatic' patients seeking medical attention, could be higher than in individuals who sustain recurrent episodes of giving way and recurrent LAS, but who do not feel the need to seek out medical care. However, it is difficult to determine if these individuals that at present are not seeking medical attention would also have degenerative changes given the lack of cartilage imaging performed for LAS and CAI. To date, few studies have considered the interaction of symptoms with documented degenerative changes. Van Ochten *et al*[186] reported that 40–55% of patients with LAS in general practice with an average of 37 years had Kellgren and Lawrence scores of >1 within the talocrural and talonavicular compartments, regardless of presenting with persistent instability and functional limitations. In a companion paper, the contralateral limb of a subset of those same patients with unilateral LAS (n=195) were scanned, with significant evidence of radiographic changes only present in the injured ankle.[187] This group suggests that the LAS initiated the degenerative changes, but self-reported dysfunction does not necessarily help identify early development of PTOA.[186 187]

Further, Golditz *et al*[45] noted that both young, physically active CAI participants and LAS 'copers' (ie, those who had sprained their ankle but not developed symptoms of CAI) had higher T2 relaxation times relative to uninjured controls. Increased relaxation times indicate a loss of water content and collagen fibre integrity. Most importantly, these CAI and LAS coper participants were 24.5 and 25.3 years of age, respectively, and had their initial LAS within 5 years of their MRI. These findings strongly support ankle degeneration in a small time frame relative to initial LAS. While these findings within 'asymptomatic' (ie, those not seeking medical care) participants are consistent with arthroscopic evaluations, additional research using MRI to quantify early degenerative changes are needed. The illustration of rapid ankle joint degeneration could be a precursor to the diagnosis of end-stage ankle joint OA, which from the work by Valderrabano *et al*[49] may not develop for 25–30 years after sustaining acute LAS. These emerging relationships requires follow-up research to determine how early degeneration and end-stage ankle OA relate, and if there are any viable interventions for this timeline.

The underlying aetiology of these degenerative changes/intra-articular problems has not yet been established. Taga *et al*[51] have reported that 89% of acutely sprained ankles had osteochondral lesions in patients whose mean age was 19 years. The authors suggest that acute LAS may be sufficient to cause an osteochondral lesion. Epidemiological research regarding ankle joint PTOA aetiology would appear to support this hypothesis, as roughly half of patients with PTOA reporting ligamentous injury only report a single injury event.[46 174] The degenerative changes noted in LAS copers also suggest that a single LAS is sufficient to cause degenerative changes.[45] Lee *et al*[53] examined a series of patients reporting for arthroscopic marrow stimulation surgery. This sample was then examined for a history of single LAS (copers) or CAI. As all participants were required to have osteochondral lesions, this investigation provides additional evidence that a single LAS is sufficient to cause osteochondral lesions, with an average duration of symptoms among the groups of ∼28 months.

If the initial LAS is an underlying cause of osteochondral lesions, recurrent LASs and episodes of giving way likely exacerbate contact stress adaptations,[52] further advancing degenerative changes. While speculative, this would place a premium on restoring appropriate biomechanics and motor control following an LAS in order to mitigate cartilage degeneration. Supporting this hypothesis, Golditz *et al*[188] found that mediolateral time to stabilisation, a measure of dynamic postural stability recorded while landing from a jump, was correlated to the increased relaxation times (ie, worse cartilage health) in both 'asymptomatic' CAI participants and LAS copers. This suggests that ankle OA, even if asymptomatic, may be associated with functional deficits; and if allowed to persist could amplify and perhaps accelerate expected limitations in activity levels as ankle joint health begins to deteriorate. This is clearly speculative as no study to date has determined the effectiveness of any conservative or surgical interventions for LAS or CAI at mitigating cartilage degeneration.

Impact on physical activity, quality of life and comorbidity risk

Throughout this paper, the prevalence, financial impact and high rate of ankle sprain reinjury and lingering instability illustrate the impact of this musculoskeletal injury. However, the contributions of musculoskeletal disease on healthcare and societal concerns extend beyond those factors. Specifically, patients with CAI present with decreases in QOL[80 189–193] and physical activity,[79 120 121 194 195] as well as accelerated onset of ankle joint OA,[46 47 49–53] oftentimes as early as the third decade of life.[45] These factors all contribute to a paradigm of compromised health and wellness, which are established correlates with comorbidity risk. Therefore, we must consider that the links to health-related consequences and the broader impact of ankle instability are becoming more tangible.

Physical activity-related consequences

The importance of physical activity as a conduit to good physical and emotional health is well accepted. Injury is one factor that creates short-term and long-term interruption to physical activity. The abundance of LASs, as we have discussed earlier, illustrates the immediate and short-term disruptions in ADLs and recreational/sport physical activity. The pain and swelling that accompany acute ankle joint injury are difficult to ignore, and instil noticeable weight-bearing challenges and alterations to gait and movement coordination, temporarily downgrading physical activity. The general population perceives the threat to physical activity is removed once initial pain is reduced and swelling subsides, and a complete recovery is attainable in a matter of days.[76] At face value, this is true and achievable through therapeutic and pharmaceutical interventions, and most patients with an LAS can return to ADLs, occupational activity and recreational/sporting activities in a relatively short period of time.[76] However, what is not appreciated in the general population, and perhaps in the medical community, is that patients with LAS, especially those that transition into patients with CAI, are susceptible to lingering disruptions in physical activity throughout the lifespan.

Using animal models, the negative influence of acute and CAI on physical activity has been illustrated. Hubbard-Turner *et al*[196] induced acute ankle instability in mice by transecting lateral ankle ligaments, and then monitored self-selected physical activity during the first 4 weeks after injury, representing the acute phase of injury recovery. Injured mice groups spent less time on a running wheel with slower walking speeds than uninjured mice. In a companion study, the research group monitored the mice as they recovered from the induced injury. They observed that the injured mice developed CAI-like symptoms as evidenced by more foot slips (giving way) during balance and gait activities.[194] Finally, this research group reported these 'CAI' mice to have lower levels of activity levels using the running wheels throughout their lifespan compared with the uninjured mice, suggesting a negative influence of the ankle injury on lifelong physical activity.[121] This mouse model indicates that with LAS, physical activity declines immediately, and it is likely that the injured individuals will develop CAI, mimicking what has been discussed in human populations previously in this review. The work by this group also suggests that ankle injury triggers a life-long decline in physical activity, which is an important factor to consider in understanding the larger impact on health status.

The negative influence of history of ankle injury on physical activity has also been documented in human populations. During a 7-year follow-up to injury by Konradsen *et al*,[79] 72% of more than 600 enrolled patients with LAS self-reported remaining functionally impaired, including their inability to perform sports and physical activity, due to ankle injury. The median age was 29 years, and only a small percentage of patients still reported pain (16%) and swelling (22%), suggesting that the lingering disruptions in functional ability years after injury were not due to ageing or chronic inflammation. In a survey of the general population, Hiller *et al*[83] observed that 55% of those with ankle sprain report limitations in physical activity that result in an inability to participate in tasks that could be performed before injury. Ankle sprains may also impact occupational activity and demands. Verhagen *et al*[195] from a 6.5-year follow-up of 577 patients with LAS, report that 15% had lingering 'handicaps' to their occupational activities, while 6% were unable to maintain their occupational activities at all. These discussed studies encompass large cross-sectional population samples, challenging the notion that these disruptions to physical activity from ankle sprain are simply a product of ageing. While none of these studies used age as a covariate to examine that question, it appears that the majority of the participants in these studies were young and middle-aged adults. Hubbard-Turner and Turner[120] have shown that young adults with CAI engage in lower self-selected levels of physical activity compared with age-matched individuals with no history of ankle injury. Using pedometers, college-aged students in their early 20s with CAI demonstrated significantly fewer weekly steps taken and minutes engaged in moderate-to-vigorous activity compared with a non-injured cohort. Collectively, this work indicates that a history of LAS associates with a decline in physical activity well after symptoms of acute injury subside, but this decline is not necessarily a product of ageing.

A consequence of physical activity decline is the likelihood of an increase in body mass index (BMI). In a large study of more than 800 000 individuals, Hershkovich *et al*[197] found that men and women who were obese or overweight were more likely to have CAI (range of OR 1.19–3.29) compared with those with healthy weight. However, this study did not quantify the level of physical activity among the study participants. While the negative long-term impact of LAS on physical activity and the potential effect on BMI is being established, a specific explanation for these negative impacts has not been clearly articulated. As discussed in the previous sections, LASs are likely to develop into CAI with the increasing number of documented cases of early onset of ankle joint PTOA.[45–47 50 51] Associations with lingering ankle pain and instability that persist in CAI populations should be considered when attempting to form links to the diminished levels of physical activity. Additionally, we must consider how psychosocial changes that may accompany ankle injury may influence patient-selected levels of physical activity. Exploring these and other factors will be important for the development of effective strategies to overcome limitations to physical activity.

Quality of life-related consequences

Related to the limitations in physical activity, an additional consequence of injury is a likely decline in the patient's QOL. Evidence is mounting that an LAS may initiate a degradation in QOL levels in patients long after they have recovered from acute symptoms of the injury. Anandacoomarasamy and Barnsley,[80] using the SF-36 general health subscale, found in a small cohort of 19 patients with LAS a decrease in QOL over a 2-year period compared with age-matched controls. The majority (74%) of these injured participants still had lingering pain, swelling and/or lingering instability at the 2-year follow-up. Using the same assessment in a larger cohort of 68 individuals with a history of at least one ankle sprain and ongoing instability, Arnold *et al*[189] found similar declines in QOL compared with individuals without a history of ankle sprain. The authors of that study do not describe the amount of time since suffering acute LASs for their injured participants, but do designate that the participants were free from any acute symptoms. This suggests that while there should have been a substantial time for recovery from the injury, there was a significant decline in QOL.

Houston *et al*[190 192 193] also have considered the effect of ankle injury history on QOL, and what factors might help explain this decline. In a systematic review, this group concluded that patients with CAI demonstrated disability and deficits in function on ankle-specific patient-reported outcome measures, as well as generic health-related QOL outcome measures compared with non-injured and LAS coper populations.[193] In their own case–control study, this group reported that individuals with CAI displayed decreased function using the Disablement in the Physically Active Scale, while simultaneously displaying increased levels of fear of injury using the Fear-Avoidance Beliefs Questionnaire and the Tampa Scale of Kinesiophobia.[190] Additionally, this group has demonstrated that the ankle-specific disability measures can be explained with physical and functional clinical measures, such as balance, strength or ROM.[192] This suggests that clinical and functional impairments that are addressed in rehabilitation may be able to reduce ankle-specific disability, but there is a need for more comprehensive assessment of these patients during rehabilitation for LAS to address what factors may be creating long-term threats to QOL.

The work described by Houston *et al*[190 192 193] illustrates that the degradation in QOL occurs as patients with LAS downgrade into CAI populations. Alarmingly, this is being observed in young adult patients under the age of 30 years. Simon and Docherty[198] report a similar phenomenon, but in a broader age range of the population. Former Division I collegiate athletes (n=232) who were between the ages of 40 and 60 years self-reported their current QOL using the American Academy of Orthopaedic Surgeons Lower Limb Questionnaire and the Short Form-36 V.2. Even with this older age range, individuals with CAI reported decreased function and QOL compared with individuals without CAI. The largest differences were seen in the American Academy of Orthopaedic Surgeons Lower Limb Questionnaire, and in the Physical Component Summary Score and physical function scales of the SF-36 V.2.[198]

Section B summary

It is important to contextualise the trend of CAI and the associated consequences as it translates to at least one out of every five people in the public who incur an LAS will go on to report chronic problems.[83] These trends are higher in athletic populations (at least 1 of 3)[115 117] and among dancers (1 out of 2).[118] When examining the trends within the general public, individuals with chronic ankle problems report increased modification of functional activity and reduced overall health compared with their non-injured counterparts in the community. It is apparent that CAI is a highly prevalent condition, especially in those who are physically active. The lingering deficits in disease and patient-oriented outcome measures observed in patients with

CAI are likely persisting beyond the LAS. More investigation is needed to determine the source of these issues that lead to chronicity, from which more effective prevention and treatment strategies can be developed. If these are not addressed, these patients are likely to develop long-term issues that may threaten physical activity and general health.

The evidence is growing that an important consequence of LAS, and the subsequent high rate of CAI, is ankle joint PTOA, affecting a disproportionately young population group, and subsequently increasing the number of disability-affected life years. Patients with a history of LAS make up the majority of the surgical cases for end-stage ankle joint PTOA. Emerging information is supporting that CAI represents an important period in the early stages of ankle joint degeneration and may even be a key mediator driving the disease process. Continued work in this area is needed to elucidate fully the paradigms between LAS, CAI and ankle joint PTOA.

The documentation of reductions in physical activity, increases in BMI and declines in QOL from ankle sprain history in animal and human models is growing. It appears that this paradigm of negative consequences from LAS is independent of age-related declines in QOL, and manifests itself early after the initial injury when patients are still adolescents and/or young adults. It has been shown from the limited data that similar CAI-related issues impact older adult populations as well, suggesting that this injury and its consequence are more complex than have initially understood, with persistence throughout one's lifespan. Additionally, it should be noted that this issue not only impacts competitive athletes, but is being reported throughout the general population. More epidemiological work, especially longitudinal studies, is needed to quantify the threats to general health as a means of defining the comprehensive healthcare burden from LAS. Owing to the links of LAS and CAI to physical activity, BMI, QOL and OA, it will be important to ascertain the potential associations of ankle injury to other disease comorbidities. This will emphasise the need for improved comprehensive treatment of acute LAS and CAI beyond the goal of returning to exercise and sport.

Author affiliations
[1]University of Kentucky, College of Health Sciences, Lexington, Kentucky, USA
[2]Department of Life and Health Sciences, Ulster University, Jordanstown, Carrickfergus, UK
[3]University College Dublin, Insight Centre for Data Analytics, Dublin, Ireland
[4]Indiana University, School of Public Health, Bloomington, Indiana, USA
[5]Physiotherapy Department, Hôpital La Tour, Geneva, Switzerland
[6]National Centre for Sport and Exercise Medicine—East Midlands, School of Sport, Exercise and Health Sciences, Loughborough University, Loughborough, Leicestershire, UK
[7]Departments of Kinesiology and Orthopaedic Surgery, University of Virginia, Charlottesville, Virginia, USA
[8]University of Sydney, College of Health, Sydney, New South Wales, Australia
[9]Department of Kinesiology and Applied Physiology, University of Delaware, Newark, Delaware, USA
[10]Department of Exercise and Sport Sciences, Ithaca College, Ithaca, New York, USA
[11]Department of Public and Occupational Health, VU University Medical Center, Amsterdam, The Netherlands
[12]University of Queensland, School of Health and Rehabilitation Sciences: Physiotherapy, Brisbane, Queensland, Australia
[13]Department of Exercise & Sport Science, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
[14]University College Dublin, School of Public Health, Physiotherapy and Sports Science, Dublin, Ireland

Twitter Follow Phillip Gribble at @gribblepa, Evert Verhagen at @Evertverhagen and Erik Wikstrom at @ea_wikstrom

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Finch C, Owen N, Price R. Current injury or disability as a barrier to being more physically active. *Med Sci Sports Exerc* 2001;33:778–82.
2 Telford A, Finch CF, Barnett L, *et al*. Do parents' and children's concerns about sports safety and injury risk relate to how much physical activity children do? *Br J Sports Med* 2012;46:1084–8.
3 Gribble PA, Bleakley C, Caulfield B, *et al*. 2016 consensus statement of the International Ankle Consortium: prevalence, impact and long-term consequences of lateral ankle sprains. *Br J Sports Med* 2016;[in press]
4 Waterman B, Owens B, Davey S, *et al*. The epidemiology of ankle sprains in the United States. *J Bone Joint Surg Am* 2010;92:2279–84.
5 Delahunt E, Coughlan GF, Caulfield B, *et al*. Inclusion criteria when investigating insufficiencies in chronic ankle instability. *Med Sci Sports Exerc* 2010;42:2106–21.
6 Gribble PA, Delahunt E, Bleakley C, *et al*. Selection criteria for patients with chronic ankle instability in controlled research: a position statement of the International Ankle Consortium. *Br J Sports Med* 2014;48:1014–18.
7 Gribble PA, Delahunt E, Bleakley C, *et al*. Selection criteria for patients with chronic ankle instability in controlled research: a position statement of the International Ankle Consortium. *J Orthop Sports Phys Ther* 2013;43:585–91.
8 Gribble PA, Delahunt E, Bleakley CM, *et al*. Selection criteria for patients with chronic ankle instability in controlled research: a position statement of the International Ankle Consortium. *J Athl Train* 2014;49:121–7.
9 Doherty C, Delahunt E, Caulfield B, *et al*. The incidence and prevalence of ankle sprain injury: a systematic review and meta-analysis of prospective epidemiological studies. *Sports Med* 2014;44:123–40.
10 Andersen TE, Floerenes TW, Arnason A, *et al*. Video analysis of the mechanisms for ankle injuries in football. *Am J Sports Med* 2004;32(1 Suppl):69s–79s.
11 Fong DT, Hong Y, Shima Y, *et al*. Biomechanics of supination ankle sprain: a case report of an accidental injury event in the laboratory. *Am J Sports Med* 2009;37:822–7.
12 Gehring D, Wissler S, Mornieux G, *et al*. How to sprain your ankle—a biomechanical case report of an inversion trauma. *J Biomech* 2013;46:175–8.
13 Kristianslund E, Bahr R, Krosshaug T. Kinematics and kinetics of an accidental lateral ankle sprain. *J Biomech* 2011;44:2576–8.
14 Terada M, Gribble PA. Jump landing biomechanics during a laboratory recorded recurrent ankle sprain. *Foot Ankle Int* 2015;36:842–8.
15 Mok KM, Fong DT, Krosshaug T, *et al*. Kinematics analysis of ankle inversion ligamentous sprain injuries in sports: 2 cases during the 2008 Beijing Olympics. *Am J Sports Med* 2011;39:1548–52.
16 Fong DT, Ha SC, Mok KM, *et al*. Kinematics analysis of ankle inversion ligamentous sprain injuries in sports: five cases from televised tennis competitions. *Am J Sports Med* 2012;40:2627–32.
17 Tropp H. Commentary: functional ankle instability revisited. *J Athl Train* 2002;37:512–15.
18 Fong DTP, Hong YL, Chan LK, *et al*. A systematic review on ankle injury and ankle sprain in sports. *Sports Med* 2007;37:73–94.
19 Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J Athl Train* 2007;42:311–19.
20 FIFA. Secondary FIFA. http://www.fifa.com/worldfootball/bigcount/
21 FIBA: worldwide basketball player numbers. Secondary FIBA: worldwide basketball player numbers. http://www.fiba.com/pages/eng/fc/FIBA/quicFact/p/openNodeIDs/962/selNodeID/962/quicFacts.html
22 Cameron KL, Owens BD, DeBerardino TM. Incidence of ankle sprains among active-duty members of the United States Armed Services from 1998 through 2006. *J Athl Train* 2010;45:29–38.
23 Bulathsinhala L, Hill OT, Scofield DE, *et al*. Epidemiology of ankle sprains and the risk of separation from service in U.S Army Soldiers. *J Orthop Sports Phys Ther* 2015;45:477–84.
24 Cooke M, Lamb S, Marsh J, *et al*. A survey of current consultant practice of treatment of severe ankle sprains in emergency departments in the United Kingdom. *Emerg Med J* 2003;20:505–7.
25 Lamb SE, Marsh JL, Hutton JL, *et al*. Mechanical supports for acute, severe ankle sprain: a pragmatic, multicentre, randomised controlled trial. *Lancet* 2009;373:575–81.
26 Holmer P, Sondergaard L, Konradsen L, *et al*. Epidemiology of sprains in the lateral ankle and foot. *Foot Ankle Int* 1994;15:72–4.
27 Bridgman SA, Clement D, Downing A, *et al*. Population based epidemiology of ankle sprains attending accident and emergency units in the West Midlands of England, and a survey of UK practice for severe ankle sprains. *Emerg Med J* 2003;20:508–10.
28 Lambers K, Ootes D, Ring D. Incidence of patients with lower extremity injuries presenting to US emergency departments by anatomic region, disease category, and age. *Clin Orthop Relat Res* 2012;470:284–90.
29 Kemler E, van de Port I, Valkenberg H, *et al*. Ankle injuries in the Netherlands: trends over 10-25 years. *Scand J Med Sci Sports* 2015;25:331–7.

30 Anis AH, Stiell IG, Stewart DG, *et al*. Cost-effectiveness analysis of the Ottawa Ankle Rules. *Ann Emerg Med* 1995;26:422–8.
31 Derksen RJ, Coupe VM, van Tulder MW, *et al*. Cost-effectiveness of the SEN-concept: Specialized Emergency Nurses (SEN) treating ankle/foot injuries. *BMC Musculoskelet Disord* 2007;8:99.
32 Hupperets MD, Verhagen EA, Heymans MW, *et al*. Potential savings of a program to prevent ankle sprain recurrence: economic evaluation of a randomized controlled trial. *Am J Sports Med* 2010;38:2194–200.
33 Janssen KW, Hendriks MR, van Mechelen W, *et al*. The cost-effectiveness of measures to prevent recurrent ankle sprains: results of a 3-arm randomized controlled trial. *Am J Sports Med* 2014;42:1534–41.
34 Lin CW, Uegaki K, Coupe VM, *et al*. Economic evaluations of diagnostic tests, treatment and prevention for lateral ankle sprains: a systematic review. *Br J Sports Med* 2013;47:1144–9.
35 Olmsted LC, Vela LI, Denegar CR, *et al*. Prophylactic ankle taping and bracing: a numbers-needed-to-treat and cost-benefit analysis. *J Athl Train* 2004;39:95–100.
36 Ramasubbu B, McNamara R, Okafor I, *et al*. Evaluation of safety and cost-effectiveness of the low risk ankle rule in one of Europe's Busiest Pediatric Emergency Departments. *Pediatr Emerg Care* 2015;31:685–7.
37 Verhagen EA, van Tulder M, van der Beek AJ, *et al*. An economic evaluation of a proprioceptive balance board training programme for the prevention of ankle sprains in volleyball. *Br J Sports Med* 2005;39:111–15.
38 Drummond M, Sculpher G, Thorrance M, *et al*. *Methods for the economic evaluation of health care programmes*. 3rd edn. New York: Oxford University Press, 2013.
39 Bosmans J, Heymans M, Hupperets M, *et al*. Cost-effectiveness studies. In: Verhagen E, Van Mechelen W, eds. *Sports injury research*. Oxford: Oxford University Press, 2010:195–210.
40 Knowles SB, Marshall SW, Miller T, *et al*. Cost of injuries from a prospective cohort study of North Carolina high school athletes. *Inj Prev* 2007;13:416–21.
41 Cooke MW, Marsh JL, Clark M, *et al*. Treatment of severe ankle sprain: a pragmatic randomised controlled trial comparing the clinical effectiveness and cost-effectiveness of three types of mechanical ankle support with tubular bandage. The CAST trial. *Health Technol Assess* 2009;13:iii, ix-x, 1-121.
42 De Boer AS, Schepers T, Panneman MJ, *et al*. Health care consumption and costs due to foot and ankle injuries in the Netherlands, 1986-2010. *BMC Musculoskelet Disord* 2014;15:128.
43 Consument en Veiligheid. Cijfers over sportblessures. Secondary Consument en Veiligheid. Cijfers over sportblessures. https://www.veiligheid.nl/sportblessures/kennis/cijfers-over-sportblessures
44 McKay GD, Goldie PA, Payne WR, *et al*. Ankle injuries in basketball: injury rate and risk factors. *Br J Sports Med* 2001;35:103–8.
45 Golditz T, Steib S, Pfeifer K, *et al*. Functional ankle instability as a risk factor for osteoarthritis: using T2-mapping to analyze early cartilage degeneration in the ankle joint of young athletes. *Osteoarthr Cartil* 2014;22:1377–85.
46 Valderrabano V, Horisberger M, Russell I, *et al*. Etiology of ankle osteoarthritis. *Clin Orthop Relat Res* 2009;467:1800–6.
47 Valderrabano V, Pagenstert G, Horisberger M, *et al*. Sports and recreation activity of ankle arthritis patients before and after total ankle replacement. *Am J Sports Med* 2006;34:993–9.
48 Nieuwe Weme RA, van Solinge G, N Doornberg J, *et al*. Total ankle replacement for posttraumatic arthritis. Similar outcome in postfracture and instability arthritis: a comparison of 90 ankles. *Acta Orthop* 2015;86:401–6.
49 Valderrabano V, Hintermann B, Horisberger M, *et al*. Ligamentous posttraumatic ankle osteoarthritis. *Am J Sports Med* 2006;34:612–20.
50 Hirose K, Murakami G, Minowa T, *et al*. Lateral ligament injury of the ankle and associated articular cartilage degeneration in the talocrural joint: anatomic study using elderly cadavers. *J Orthop Sci* 2004;9:37–43.
51 Taga I, Shino K, Inoue M, *et al*. Articular cartilage lesions in ankles with lateral ligament injury. An arthroscopic study. *Am J Sports Med* 1993;21:120–6; doi: discussion 26-7.
52 Bischof JE, Spritzer CE, Caputo AM, *et al*. In vivo cartilage contact strains in patients with lateral ankle instability. *J Biomech* 2010;43:2561–6.
53 Lee M, Kwon JW, Choi WJ, *et al*. Comparison of outcomes for osteochondral lesions of the talus with and without chronic lateral ankle instability. *Foot Ankle Int* 2015;36:1050–7.
54 Cain MS, Garceau SW, Linens SW. Effects of a four week biomechanical ankle platform system protocol on balance in high school athletes with chronic ankle instability. *J Sport Rehabil* 2015.
55 De Ridder R, Willems TM, Vanrenterghem J, *et al*. Effect of a home-based balance training protocol on dynamic postural control in subjects with chronic ankle instability. *Int J Sports Med* 2015;36:596–602.
56 Donovan L, Hertel J. A new paradigm for rehabilitation of patients with chronic ankle instability. *Phys Sportsmed* 2012;40:41–51.
57 Hale SA, Fergus A, Axmacher R, *et al*. Bilateral improvements in lower extremity function after unilateral balance training in individuals with chronic ankle instability. *J Athl Train* 2014;49:181–91.
58 Hale SA, Hertel J, Olmsted-Kramer LC. The effect of a 4-week comprehensive rehabilitation program on postural control and lower extremity function in individuals with chronic ankle instability. *J Orthop Sports Phys Ther* 2007;37:303–11.
59 Hall EA, Docherty CL, Simon J, *et al*. Strength-training protocols to improve deficits in participants with chronic ankle instability: a randomized controlled trial. *J Athl Train* 2015;50:36–44.
60 Holmes A, Delahunt E. Treatment of common deficits associated with chronic ankle instability. *Sports Med* 2009;39:207–24.
61 Linens SW, Ross SE, Arnold BL. Wobble board rehabilitation for improving balance in ankles with chronic instability. *Clin J Sport Med* 2015;26(1):76–82.
62 McCriskin BJ, Cameron KL, Orr JD, *et al*. Management and prevention of acute and chronic lateral ankle instability in athletic patient populations. *World J Orthop* 2015;6:161–71.
63 O'Driscoll J, Delahunt E. Neuromuscular training to enhance sensorimotor and functional deficits in subjects with chronic ankle instability: a systematic review and best evidence synthesis. *Sports Med Arthrosc Rehabil Ther Technol* 2011;3:19.
64 van Ochten JM, van Middelkoop M, Meuffels D, *et al*. Chronic complaints after ankle sprains: a systematic review on effectiveness of treatments. *J Orthop Sports Phys Ther* 2014;44:862–71.
65 Webster KA, Gribble PA. Functional rehabilitation interventions for chronic ankle instability: a systematic review. *J Sport Rehabil* 2010;19:98–114.
66 Wortmann MA, Docherty CL. Effect of balance training on postural stability in subjects with chronic ankle instability. *J Sport Rehabil* 2013;22:143–9.
67 Cho BK, Kim YM, Park KJ, *et al*. A prospective outcome and cost-effectiveness comparison between two ligament reattachment techniques using suture anchors for chronic ankle instability. *Foot Ankle Int* 2015;36:172–9.
68 Hsu AR, Ardoin GT, Davis WH, *et al*. Intermediate and long-term outcomes of the modified Brostrom-Evans procedure for lateral ankle ligament reconstruction. *Foot Ankle Spec* 2016;9:131–9.
69 Girard P, Anderson RB, Davis WH, *et al*. Clinical evaluation of the modified Brostrom-Evans procedure to restore ankle stability. *Foot Ankle Int* 1999;20:246–52.
70 Petrera M, Dwyer T, Theodoropoulos JS, *et al*. Short- to medium-term outcomes after a modified Brostrom repair for lateral ankle instability with immediate postoperative weightbearing. *Am J Sports Med* 2014;42:1542–8.
71 Nery C, Raduan F, Del Buono A, *et al*. Arthroscopic-assisted Brostrom-Gould for chronic ankle instability: a long-term follow-up. *Am J Sports Med* 2011;39:2381–8.
72 Nwachukwu BU, McLawhorn AS, Simon MS, *et al*. Management of end-stage ankle arthritis: cost-utility analysis using direct and indirect costs. *J Bone Joint Surg Am* 2015;97:1159–72.
73 Bleakley CM, McDonough SM, MacAuley DC. Some conservative strategies are effective when added to controlled mobilisation with external support after acute ankle sprain: a systematic review. *Aust J Physiother* 2008;54:7–20.
74 Bleakley CM, McDonough SM, MacAuley DC, *et al*. Cryotherapy for acute ankle sprains: a randomised controlled study of two different icing protocols. *Br J Sports Med* 2006;40:700–5. doi:discussion 05.
75 Petersen W, Rembitzki IV, Koppenburg AG, *et al*. Treatment of acute ankle ligament injuries: a systematic review. *Arch Orthop Trauma Surg* 2013;133:1129–41.
76 Medina McKeon JM, Bush HM, Reed A, *et al*. Return-to-play probabilities following new versus recurrent ankle sprains in high school athletes. *J Sci Med Sport* 2014;17:23–8.
77 van Rijn RM, van Os AG, Bernsen RM, *et al*. What is the clinical course of acute ankle sprains? A systematic literature review. *Am J Med* 2008;121:324–31.e6.
78 Gerber JP, Williams GN, Scoville CR, *et al*. Persistent disability associated with ankle sprains: a prospective examination of an athletic population. *Foot Ankle Int* 1998;19:653–60.
79 Konradsen L, Bech L, Ehrenbjerg M, *et al*. Seven years follow-up after ankle inversion trauma. *Scand J Med Sci Sports* 2002;12:129–35.
80 Anandacoomarasamy A, Barnsley L. Long term outcomes of inversion ankle injuries. *Br J Sports Med* 2005;39:e14.
81 Braun BL. Effects of ankle sprain in a general clinic population 6 to 18 months after medical evaluation. *Arch Fam Med* 1999;8:143–8.
82 Hiller CE, Nightingale EJ, Lin CW, *et al*. Characteristics of people with recurrent ankle sprains: a systematic review with meta-analysis. *Br J Sports Med* 2011;45:660–72.
83 Hiller CE, Nightingale EJ, Raymond J, *et al*. Prevalence and impact of chronic musculoskeletal ankle disorders in the community. *Arch Phys Med Rehabil* 2012;93:1801–7.
84 Hertel J. Sensorimotor deficits with ankle sprains and chronic ankle instability. *Clin Sports Med* 2008;27:353–70.
85 McKeon PO, Hertel J. Systematic review of postural control and lateral ankle instability, part I: can deficits be detected with instrumented testing. *J Athl Train* 2008;43:293–304.
86 Bastien M, Moffet H, Bouyer LJ, *et al*. Alteration in global motor strategy following lateral ankle sprain. *BMC Musculoskelet Disord* 2014;15:436.

87 Wikstrom EA, Naik S, Lodha N, *et al*. Bilateral balance impairments after lateral ankle trauma: a systematic review and meta-analysis. *Gait Posture* 2010;31:407–14.
88 Goldie PA, Evans OM, Bach TM. Postural control following inversion injuries of the ankle. *Arch Phys Med Rehabil* 1994;75:969–75.
89 Punt IM, Ziltener JL, Laidet M, *et al*. Gait and physical impairments in patients with acute ankle sprains who did not receive physical therapy. *PM R* 2015;7:34–41.
90 Doherty C, Bleakley C, Hertel J, *et al*. Single-leg drop landing movement strategies 6 months following first-time acute lateral ankle sprain injury. *Scand J Med Sci Sports* 2015;25:806–17.
91 Doherty C, Bleakley C, Hertel J, *et al*. Dynamic balance deficits 6 months following first-time acute lateral ankle sprain: a laboratory analysis. *J Orthop Sports Phys Ther* 2015;45:626–33.
92 Doherty C, Bleakley C, Hertel J, *et al*. Dynamic balance deficits in individuals with chronic ankle instability compared to ankle sprain copers 1 year after a first-time lateral ankle sprain injury. *Knee Surg Sports Traumatol Arthrosc* 2016;24:1086–95.
93 Doherty C, Bleakley C, Hertel J, *et al*. Single-leg drop landing movement strategies in participants with chronic ankle instability compared with lateral ankle sprain 'copers'. *Knee Surg Sports Traumatol Arthrosc* 2016;24:1049–59.
94 Doherty C, Bleakley C, Hertel J, *et al*. Locomotive biomechanics in persons with chronic ankle instability and lateral ankle sprain copers. *J Sci Med Sport* 2015.
95 Doherty C, Bleakley C, Hertel J, *et al*. Inter-joint coordination strategies during unilateral stance following first-time, acute lateral ankle sprain: a brief report. *Clin Biomech (Bristol, Avon)* 2015;30:636–9.
96 Doherty C, Bleakley C, Hertel J, *et al*. Coordination and symmetry patterns during the drop vertical jump, 6-months after first-time lateral ankle sprain. *J Orthop Res* 2015;33:1537–44.
97 Doherty C, Bleakley C, Hertel J, *et al*. Lower limb interjoint postural coordination one year after first-time lateral ankle sprain. *Med Sci Sports Exerc* 2015;47:2398–405.
98 Nelson AJ, Collins CL, Yard EE, *et al*. Ankle injuries among United States high school sports athletes, 2005–2006. *J Athl Train* 2007;42:381–7.
99 Swenson DM, Yard EE, Fields SK, *et al*. Patterns of recurrent injuries among US high school athletes, 2005-2008. *Am J Sports Med* 2009;37:1586–93.
100 Yeung MS, Chan KM, So CH. An epidemiological survey on ankle sprain. *Br J Sports Med* 1994;28:112–16.
101 Beynnon BD, Murphy DF, Alosa DM. Predictive factors for lateral ankle sprains: a literature review. *J Athl Train* 2002;37:376–80.
102 Bahr R, Bahr IA. Incidence of acute volleyball injuries: a prospective cohort study of injury mechanisms and risk factors. *Scand J Med Sci Sports* 1997;7:166–71.
103 Zech A, Hubscher M, Vogt L, *et al*. Neuromuscular training for rehabilitation of sports injuries: a systematic review. *Med Sci Sports Exerc* 2009;41:1831–41.
104 Holme E, Magnusson SP, Becher K, *et al*. The effect of supervised rehabilitation on strength, postural sway, position sense and re-injury risk after acute ankle ligament sprain. *Scand J Med Sci Sports* 1999;9:104–9.
105 Steib S, Zech A, Hentschke C, *et al*. Fatigue-induced alterations of static and dynamic postural control in athletes with a history of ankle sprain. *J Athl Train* 2013;48:203–8.
106 Gribble PA, Hertel J, Denegar CR. Chronic ankle instability and fatigue create proximal joint alterations during performance of the Star Excursion Balance Test. *Int J Sports Med* 2007;28:236–42.
107 Gribble PA, Hertel J, Denegar CR, *et al*. The effects of fatigue and chronic ankle instability on dynamic postural control. *J Athl Train* 2004;39:321–9.
108 Hertel J. Functional anatomy, pathomechanics, and pathophysiology of lateral ankle instability. *J Athl Train* 2002;37:364–75.
109 Tropp H, Odenrick P, Gillquist J. Stabilometry recordings in functional and mechanical instability of the ankle joint. *Int J Sports Med* 1985;6:180–2.
110 Freeman M. Instability of the foot after injuries to the lateral ligament of the ankle. *J Bone Joint Surg Br* 1965;47B:669–77.
111 Hertel J. Functional instability following lateral ankle sprain. *Sports Med* 2000;29:361–71.
112 Hiller CE, Kilbreath SL, Refshauge KM. Chronic ankle instability: evolution of the model. *J Athl Train* 2011;46:133–41.
113 Docherty CL, Gansneder BM, Arnold BL, *et al*. Development and reliability of the ankle instability instrument. *J Athl Train* 2006;41:154–8.
114 Hiller CE, Refshauge KM, Bundy AC, *et al*. The Cumberland ankle instability tool: a report of validity and reliability testing. *Arch Phys Med Rehabil* 2006;87:1235–41.
115 Attenborough AS, Hiller CE, Smith RM, *et al*. Chronic ankle instability in sporting populations. *Sports Med* 2014;44:1545–56.
116 Attenborough AS, Sinclair PJ, Sharp T, *et al*. A snapshot of chronic ankle instability in a cohort of netball players. *J Sci Med Sport* 2015;19:379–83.
117 Tanen L, Docherty CL, Van Der Pol B, *et al*. Prevalence of chronic ankle instability in high school and division I athletes. *Foot Ankle Spec* 2014;7:37–44.
118 Simon J, Hall E, Docherty C. Prevalence of chronic ankle instability and associated symptoms in university dance majors: an exploratory study. *J Dance Med Sci* 2014;18:178–84.
119 Pourkazemi F, Hiller CE, Raymond J, *et al*. Predictors of chronic ankle instability after an index lateral ankle sprain: a systematic review. *J Sci Med Sport* 2014;17:568–73.
120 Hubbard-Turner T, Turner MJ. Physical activity levels in college students with chronic ankle instability. *J Athl Train* 2015;50:742–7.
121 Hubbard-Turner T, Wikstrom EA, Guderian S, *et al*. An acute lateral ankle sprain significantly decreases physical activity across the lifespan. *J Sports Sci Med* 2015;14:556–61.
122 Kaur J, Sinha A. Prevalence of ankle sprain and service utilization among players of Punjab. *Int J Ther Rehabil Res* 2015;4:16–24.
123 Prado MP, Mendes AA, Amodio DT, *et al*. A comparative, prospective, and randomized study of two conservative treatment protocols for first-episode lateral ankle ligament injuries. *Foot Ankle Int* 2014;35:201–6.
124 Aiken AB, Pelland L, Brison R, *et al*. Short-term natural recovery of ankle sprains following discharge from emergency departments. *J Orthop Sports Phys Ther* 2008;38:566–71.
125 Kerin F, Delahunt E. Physiotherapists' understanding of functional and mechanical insufficiencies contributing to chronic ankle instability. *Athl Train Sports Health Care* 2011;3:125–30.
126 Delahunt E, Caulfield B, Doherty C. Question 16: what criteria should be used to diagnose a patient with chronic ankle instability? In: McKeon P, Wikstrom E, eds. *Quick questions in ankle sprains: expert advice in sports medicine*. Thorofare, New Jersey, USA: Slack Incorporated, 2015:83–86.
127 Arnold BL, De La Motte S, Linens S, *et al*. Ankle instability is associated with balance impairments: a meta-analysis. *Med Sci Sports Exerc* 2009;41:1048–62.
128 Brown C, Bowser B, Simpson KJ. Movement variability during single leg jump landings in individuals with and without chronic ankle instability. *Clin Biomech (Bristol, Avon)* 2012;27:52–63.
129 Brown CN, Padua DA, Marshall SW, *et al*. Variability of motion in individuals with mechanical or functional ankle instability during a stop jump maneuver. *Clin Biomech (Bristol, Avon)* 2009;24:762–8.
130 Brown CN, Padua DA, Marshall SW, *et al*. Hip kinematics during a stop-jump task in patients with chronic ankle instability. *J Athl Train* 2011;46:461–7.
131 Hubbard TJ, Kramer LC, Denegar CR, *et al*. Contributing factors to chronic ankle instability. *Foot Ankle Int* 2007;28:343–54.
132 Munn J, Sullivan SJ, Schneiders AG. Evidence of sensorimotor deficits in functional ankle instability: a systematic review with meta-analysis. *J Sci Med Sport* 2010;13:2–12.
133 Sefton JM, Hicks-Little CA, Hubbard TJ, *et al*. Sensorimotor function as a predictor of chronic ankle instability. *Clin Biomech (Bristol, Avon)* 2009;24:451–8.
134 Wikstrom EA, Tillman MD, Chmielewski TL, *et al*. Discriminating between copers and people with chronic ankle instability. *J Athl Train* 2012;47:136–42.
135 Wikstrom EA, Tillman MD, Chmielewski TL, *et al*. Self-assessed disability and functional performance in individuals with and without ankle instability: a case control study. *J Orthop Sports Phys Ther* 2009;39:458–67.
136 Witchalls J, Blanch P, Waddington G, *et al*. Intrinsic functional deficits associated with increased risk of ankle injuries: a systematic review with meta-analysis. *Br J Sports Med* 2012;46:515–23.
137 Chinn L, Dicharry J, Hertel J. Ankle kinematics of individuals with chronic ankle instability while walking and jogging on a treadmill in shoes. *Phys Ther Sport* 2013;14:232–9.
138 Drewes LK, McKeon PO, Paolini G, *et al*. Altered ankle kinematics and shank-rear-foot coupling in those with chronic ankle instability. *J Sport Rehabil* 2009;18:375–88.
139 Feger MA, Donovan L, Hart JM, *et al*. Lower extremity muscle activation in patients with or without chronic ankle instability during walking. *J Athl Train* 2015;50:350–7.
140 Terada M, Bowker S, Thomas AC, *et al*. Alterations in stride-to-stride variability during walking in individuals with chronic ankle instability. *Hum Mov Sci* 2015;40:154–62.
141 Terada M, Pietrosimone B, Gribble PA. Individuals with chronic ankle instability exhibit altered landing knee kinematics: potential link with the mechanism of loading for the anterior cruciate ligament. *Clin Biomech (Bristol, Avon)* 2014;29:1125–30.
142 Terada M, Pietrosimone BG, Gribble PA. Alterations in neuromuscular control at the knee in individuals with chronic ankle instability. *J Athl Train* 2014;49:599–607.
143 Terada M, Harkey MS, Wells AM, *et al*. The influence of ankle dorsiflexion and self-reported patient outcomes on dynamic postural control in participants with chronic ankle instability. *Gait Posture* 2014;40:193–7.
144 Terada M, Pfile KR, Pietrosimone BG, *et al*. Effects of chronic ankle instability on energy dissipation in the lower extremity. *Med Sci Sports Exerc* 2013;45:2120–8.
145 Gribble P, Robinson R. Differences in spatiotemporal landing variables during a dynamic stability task in subjects with CAI. *Scand J Med Sci Sports* 2010;20:e63–71.

146 Gribble PA, Robinson RH. An examination of ankle, knee, and hip torque production in individuals with chronic ankle instability. *J Strength Cond Res* 2009;23:395–400.
147 Gribble PA, Robinson RH. Alterations in knee kinematics and dynamic stability associated with chronic ankle instability. *J Athl Train* 2009;44:350–5.
148 Ross SE, Guskiewicz KM. Examination of static and dynamic postural stability in individuals with functionally stable and unstable ankles. *Clin J Sport Med* 2004;14:332–8.
149 Wikstrom EA, Bishop MD, Inamdar AD, *et al*. Gait termination control strategies are altered in chronic ankle instability subjects. *Med Sci Sports Exerc* 2010;42:197–205.
150 Wikstrom EA, Fournier KA, McKeon PO. Postural control differs between those with and without chronic ankle instability. *Gait Posture* 2010;32:82–6.
151 Wikstrom EA, Tillman MD, Borsa PA. Detection of dynamic stability deficits in subjects with functional ankle instability. *Med Sci Sports Exerc* 2005;37:169–75.
152 Wikstrom EA, Tillman MD, Chmielewski TL, *et al*. Dynamic postural control but not mechanical stability differs among those with and without chronic ankle instability. *Scand J Med Sci Sports* 2010;20:e137–44.
153 Harkey M, McLeod M, Terada M, *et al*. Quadratic association between corticomotor and spinal-reflexive excitability and self-reported disability in participants with chronic ankle instability. *J Sport Rehabil* 2015.
154 Harkey M, McLeod M, Van Scoit A, *et al*. The immediate effects of an anterior-to-posterior talar mobilization on neural excitability, dorsiflexion range of motion, and dynamic balance in patients with chronic ankle instability. *J Sport Rehabil* 2014;23:351–9.
155 McLeod MM, Gribble PA, Pietrosimone BG. Chronic ankle instability and neural excitability of the lower extremity. *J Athl Train* 2015;50:847–53.
156 Needle AR, Palmer JA, Kesar TM, *et al*. Brain regulation of muscle tone in healthy and functionally unstable ankles. *J Sport Rehabil* 2013;22:202–11.
157 Needle AR, Swanik CB, Schubert M, *et al*. Decoupling of laxity and cortical activation in functionally unstable ankles during joint loading. *Eur J Appl Physiol* 2014;114:2129–38.
158 Pietrosimone BG, Gribble PA. Chronic ankle instability and corticomotor excitability of the fibularis longus muscle. *J Athl Train* 2012;47:621–6.
159 Wikstrom EA, Hubbard-Turner T, McKeon PO. Understanding and treating lateral ankle sprains and their consequences: a constraints-based approach. *Sports Med* 2013;43:385–93.
160 Hass CJ, Bishop MD, Doidge D, *et al*. Chronic ankle instability alters central organization of movement. *Am J Sports Med* 2010;38:829–34.
161 Klykken LW, Pietrosimone BG, Kim KM, *et al*. Motor-neuron pool excitability of the lower leg muscles after acute lateral ankle sprain. *J Athl Train* 2011;46:263–9.
162 Van Deun S, Staes FF, Stappaerts KH, *et al*. Relationship of chronic ankle instability to muscle activation patterns during the transition from double-leg to single-leg stance. *Am J Sports Med* 2007;35:274–81.
163 Doherty C, Bleakley C, Hertel J, *et al*. Postural control strategies during single limb stance following acute lateral ankle sprain. *Clin Biomech (Bristol, Avon)* 2014;29:643–9.
164 Doherty C, Bleakley C, Hertel J, *et al*. Lower extremity function during gait in participants with first time acute lateral ankle sprain compared to controls. *J Electromyogr Kinesiol* 2015;25:182–92.
165 Doherty C, Bleakley C, Hertel J, *et al*. Inter-joint coordination strategies during unilateral stance 6-months following first-time lateral ankle sprain. *Clin Biomech (Bristol, Avon)* 2015;30:129–35.
166 Doherty C, Bleakley CM, Hertel J, *et al*. Laboratory measures of postural control during the star excursion balance test after acute first-time lateral ankle sprain. *J Athl Train* 2015;50:651–64.
167 Doherty C, Bleakley C, Hertel J, *et al*. Balance failure in single limb stance due to ankle sprain injury: an analysis of center of pressure using the fractal dimension method. *Gait Posture* 2014;40:172–6.
168 Doherty C, Bleakley C, Hertel J, *et al*. Lower extremity coordination and symmetry patterns during a drop vertical jump task following acute ankle sprain. *Hum Mov Sci* 2014;38:34–46.
169 Collins M, Raleigh SM. Genetic risk factors for musculoskeletal soft tissue injuries. *Med Sport Sci* 2009;54:136–49.
170 September AV, Schwellnus MP, Collins M. Tendon and ligament injuries: the genetic component. *Br J Sports Med* 2007;41:241–6; doi:discussion 46.
171 Shang X, Li Z, Cao X, *et al*. The association between the ACTN3 R577X polymorphism and noncontact acute ankle sprains. *J Sports Sci* 2015;33:1775–9.
172 Saltzman CL, Zimmerman B, O'Rourke M, *et al*. Impact of comorbidities on the measurement of health in patients with ankle osteoarthritis. *J Bone Joint Surg Am* 2006;88A:2366–72.
173 Brown TD, Johnston RC, Saltzman CL, *et al*. Posttraumatic osteoarthritis: a first estimate of incidence, prevalence, and burden of disease. *J Orthop Trauma* 2006;20:739–44.
174 Saltzman CL, Salamon ML, Blanchard GM, *et al*. Epidemiology of ankle arthritis: report of a consecutive series of 639 patients from a tertiary orthopaedic center. *Iowa Orthop J* 2005;25:44–6.
175 Lofvenberg R, Karrholm J, Lund B. The outcome of nonoperated patients with chronic lateral instability of the ankle: a 20-year follow-up study. *Foot Ankle Int* 1994;15:165–9.
176 Canale ST, Belding RH. Osteochondral lesions of the talus. *J Bone Joint Surg Am* 1980;62:97–102.
177 Harrington KD. Degenerative arthritis of the ankle secondary to long-standing lateral ligament instability. *J Bone Joint Surg Am* 1979;61:354–61.
178 Hintermann B, Boss A, Schafer D. Arthroscopic findings in patients with chronic ankle instability. *Am J Sports Med* 2002;30:402–9.
179 Ferkel RD, Chams RN. Chronic lateral instability: arthroscopic findings and long-term results. *Foot Ankle Int* 2007;28:24–31.
180 Kibler WB. Arthroscopic findings in ankle ligament reconstruction. *Clin Sports Med* 1996;15:799–804.
181 Komenda GA, Ferkel RD. Arthroscopic findings associated with the unstable ankle. *Foot Ankle Int* 1999;20:708–13.
182 Sammarco GJ, DiRaimondo CV. Surgical treatment of lateral ankle instability syndrome. *Am J Sports Med* 1988;16:501–11.
183 Sugimoto K, Takakura Y, Okahashi K, *et al*. Chondral injuries of the ankle with recurrent lateral instability: an arthroscopic study. *J Bone Joint Surg Am* 2009;91:99–106.
184 Takao M, Uchio Y, Naito K, *et al*. Arthroscopic assessment for intra-articular disorders in residual ankle disability after sprain. *Am J Sports Med* 2005;33:686–92.
185 van Dijk CN, Bossuyt PM, Marti RK. Medial ankle pain after lateral ligament rupture. *J Bone Joint Surg Br* 1996;78:562–7.
186 van Ochten JM, Mos MC, van Putte-Katier N, *et al*. Structural abnormalities and persistent complaints after an ankle sprain are not associated: an observational case control study in primary care. *Br J Gen Pract* 2014;64:e545–53.
187 van Putte-Katier N, van Ochten JM, van Middelkoop M, *et al*. Magnetic resonance imaging abnormalities after lateral ankle trauma in injured and contralateral ankles. *Eur J Radiol* 2015;84:2586–92.
188 Golditz T, Welsch GH, Pachowsky M, *et al*. A multimodal approach to ankle instability: Interrelations between subjective and objective assessments of ankle status in athletes. *J Orthop Res* 2016;34:525–32.
189 Arnold BL, Wright CJ, Ross SE. Functional ankle instability and health-related quality of life. *J Athl Train* 2011;46:634–41.
190 Houston MN, Van Lunen BL, Hoch MC. Health-related quality of life in individuals with chronic ankle instability. *J Athl Train* 2014;49:758–63.
191 Simon JE, Docherty CL. Current health-related quality of life is lower in former Division I collegiate athletes than in non-collegiate athletes. *Am J Sports Med* 2014;42:423–9.
192 Houston MN, Hoch JM, Gabriner ML, *et al*. Clinical and laboratory measures associated with health-related quality of life in individuals with chronic ankle instability. *Phys Ther Sport* 2015;16:169–75.
193 Houston MN, Hoch JM, Hoch MC. Patient-reported outcome measures in individuals with chronic ankle instability: a systematic review. *J Athl Train* 2015;50:1019–33.
194 Wikstrom EA, Hubbard-Turner T, Woods S, *et al*. Developing a mouse model of chronic ankle instability. *Med Sci Sports Exerc* 2015;47:866–72.
195 Verhagen RA, de Keizer G, van Dijk CN. Long-term follow-up of inversion trauma of the ankle. *Arch Orthop Trauma Surg* 1995;114:92–6.
196 Hubbard-Turner T, Wikstrom EA, Guderian S, *et al*. Acute ankle sprain in a mouse model. *Med Sci Sports Exerc* 2013;45:1623–8.
197 Hershkovich O, Tenenbaum S, Gordon B, *et al*. A large-scale study on epidemiology and risk factors for chronic ankle instability in young adults. *J Foot Ankle Surg* 2015;54:183–7.
198 Simon J, Docherty C. Current health-related quality of life in older adults with chronic ankle instability. *Br J Sports Med* 2015;49(Supplement 1):A10.

BJSM

Evidence review for the 2016 International Ankle Consortium consensus statement on the prevalence, impact and long-term consequences of lateral ankle sprains

Phillip A Gribble, Chris M Bleakley, Brian M Caulfield, Carrie L Docherty, François Fourchet, Daniel Tik-Pui Fong, Jay Hertel, Claire E Hiller, Thomas W Kaminski, Patrick O McKeon, Kathryn M Refshauge, Evert A Verhagen, Bill T Vicenzino, Erik A Wikstrom and Eamonn Delahunt

Br J Sports Med published online June 3, 2016