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

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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 health care burden. The recurrence rates of LAS are high, leading to a large percentage of LAS patients developing chronic ankle instability (CAI). This chronicity is associated with decreases in physical activity levels and quality of life and associates with increasing rates of ankle post-traumatic osteoarthritis, all of which generate financial costs that are larger than many have realized. The literature review that follows expands this paradigm and introduces emerging areas that are that should be prioritized for continued research, supporting a companion position statement paper that proposes recommendations for utilizing this summary of information, as well as needs for specific future research.

Musculoskeletal injuries have the potential to outweigh the health benefits of participation in physical activity and organized 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 health care burden. The injury mechanism is characterized 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 LAS are high, leading to a large percentage of LAS patients 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. 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 the ankle joint OA surgical cases. Additionally, the onset of ankle joint PTOA is occurring earlier in the 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 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 health care 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 that should be prioritized for continued research. In a companion position statement paper, the Executive Committee of the International Ankle Consortium proposes recommendations for utilizing this summary of information, as well as needs for specific future research based on this evidence review that follows. 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 health care 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 organized into two sections that will: (A) establish the burden of LAS and (B) raise awareness of the mid- and long-term consequences of LAS.

Comment [PG1]: Add in citation from BJSM that will follow once its available

Section A: Establishing Lateral Ankle Sprain Prevalence and Burden

Defining Lateral Ankle Sprain

LAS is the most common lower limb musculoskeletal injury in physically active persons.[3] Acute LAS has been defined by Delahunt *et al*[4] and endorsed by the International Ankle Consortium[5-7] 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.[8] In an attempt to develop a comprehensive understanding of the mechanisms of LAS in football, Andersen *et al*[9] 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.[8]

Fong *et al*[10] reported the first-ever kinematic analysis of a LAS, which occurred accidentally during testing in their research laboratory. A male athlete performing a series of cutting test trials incurred a LAS during the 4th 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 characterized by a rapid inversion and internal rotation which was initiated 0.06 seconds 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.[11-13] 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.

More recently, Mok *et al*[14] and Fong *et al*[15] used a model-based image-matching motion analysis technique to describe the kinematic characteristics of un-calibrated video recordings of ankle joint sprains incurred during live sporting events. Mok *et al*[14] 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*[15] 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.[16] Furthermore, peak inversion was noted to occur rapidly after

initial contact (typically 0.09 – 0.13 seconds).

Epidemiology of Lateral Ankle Sprain

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 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*[17] 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*[8] included a meta-analysis of prospective studies and provided pooled incidence figures, sub-grouped by sport, age and gender. In conjunction with earlier reports,[17] indoor/court sports had the highest incidence rates estimated as 7 ankle sprains per 1,000 exposures.[8] There were also differences according to athletes' gender, with higher incidences estimated in females (13.6 per 1,000 exposures) compared to males (6.94 per 1,000 exposures). Incidence rates also varied across age cohorts, with the highest figure of 2.85 ankle sprains per 1,000 exposures reported in young athletes (under 12 years of age), followed by adolescents (aged 12-18 years) (1.94 per 1,000 exposures), then adults (0.72 per 1,000 exposures).[8] 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*[8] can be limited by study heterogeneity. Prospective injury data extracted from large regional datasets 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 United States. Using this database, Hootman *et al*[18] 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 1,000 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 1,000 AE) and male basketball players (1.3 ankle sprains per 1,000 AE), and in female (1.3 ankle sprains per 1,000 AE) and male soccer players (1.24 ankle sprains per 1,000 AE).[18] High participation in sports such as soccer (estimated 265 million soccer players worldwide[19]) or basketball (estimated 450 million basketball players worldwide[20]) 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 United States, with the incidence of ankle sprains reported to be between 34.95[21] to 45.14[22] sprains per 1000 person-years. Based on a conservative estimate of 100 exposures per year, these equate

to approximately 0.35 to 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.[18]

Another important patient cohort to consider is the general population presenting to an ED in the early stages post- ankle injury. In the United Kingdom (UK), 3-5% of all ED presentations are for LAS, [23 24] equating to 5600 daily incidents[23] or 1-1.5 million visits annually.[24] 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.[25] 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.[26] 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 United States accessed ED data sets from the National Electronic Injury Surveillance System (NEISS).[3 27] Lambers *et al*[27], 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, 181–230). Similarly, Waterman *et al*[3] reported rates of 2.15 per 1000 person-years during a four-year review. A 25-year review of the Dutch Injury Surveillance System undertaken by Kemler *et al*[28] is the largest ED data set analyzed 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 United States.[3 27] In the same report Kemler *et al*[28] also analyzed 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- and long-term consequences, are a good indicator of the severity of an injury. However, economic evaluations aid policy makers 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 analysis of intervention effectiveness to determine if an intervention comes with a tolerable financial investment relative to a favorable 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.[29-36] However, we will restrict ourselves here to a rough description of the costs associated with ankle sprains. For an expanded background on the methodology employed in economic evaluations in sports medicine, we refer to text books on this topic.[37 38] 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. Also, 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, as well as the costs for the employer. We employ this societal perspective in this section, with sub-divisions solely in direct and indirect costs. As such, data derived from insurance registries are not discussed here.

In the United States, Knowles *et al*[39] 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 (i.e. Quality Adjusted Life Years lost). Costs for specific injuries were not calculated, but the mean societal costs for a joint sprain ($9,196; 95%CI $6,856 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 United States high school athletes reside within this range.

These cost are higher than what is reported in studies that only include the short-term costs of ankle sprains, i.e. costs incurred from the moment of injury occurrence to recovery.[31 36 40] Cooke *et al*[40] 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.[41] It may be clear that patients who require hospitalization after emergency care have higher costs than patients who do

not require further hospital care, respectively €6,217 and €842 in the Dutch situation.[41] 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*[36] and Hupperets *et al*[31] Both studies reported on the costs of all ankle sprains sustained by a sporting population. Hupperets *et al*[31] 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*[36] 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,[42] 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*[3] of 628,000 ankle sprains annually in the United States and apply the estimations from Knowles *et al*[39] of $10,000 (the low end of the 95% CI for treating ankle injury), there would be over $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 less than 50% of LAS patients may seek formal care,[43] 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, etc. Presentation of direct costs of ankle sprains provides insight into the concrete burden to the healthcare system. Cooke *et al*[40] describe the total direct costs of standard care for ankle sprains presenting at British EDs to be £135. Verhagen et al.[36] valued these costs at €43, and Hupperets et al.[31] at €61. Naturally the direct costs of ankle sprains treated at EDs are lower, while specialized 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.[31 36 40 41]

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 economical 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% to 90% of the total costs of ankle sprains.[31 32 36 39 40] Within the general population of the UK, Cooke *et al*[40] 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 to £135 of direct healthcare costs. Specifically in sports, Verhagen *et al*[36] 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 standardized 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*[31] 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.[51]

Long-term costs

Most of the cost analyses reviewed above focus on the short-term treatment and management for LAS. However, as is discussed later in this review, there is a very high rate of re-injury and subsequent development of CAI. Additionally, the long-term consequences of ankle injury are being recognized 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% to 85% of the surgical cases for end-stage ankle joint PTOA.[44-47] Patients with CAI are at an increased risk of PTOA,[44 45 47-52] 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 utilized for CAI patients with successful restoration of self-reported outcomes and functional measurements. [53-65] 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 CAI patients. Additionally, we have no data to demonstrate that conservative management is effective at improving indices of long-term success, such as quality of life years. Therefore, while likely to improve the quality of life of CAI patients, it is difficult to conclude what the cost effectiveness of conservative management (i.e. physiotherapy) is relative to 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, CAI patients may seek non-conservative management options in the form of surgical reconstruction. The modified Brostrom procedure is the most commonly employed surgical procedure, with consistent reporting of associated long-term successful outcomes.[66-70] 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.[66] However, there is little to no data that has assessed the comprehensive costing and quality of life 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 CAI patients that have failed with conservative management. However, more research is needed to consider the indirect costs and assessments of quality of life 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 PTOA patients stem from the CAI patient population.[44 47 49 50] 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*[71] performed a cost effectiveness analysis of operative and non-operative treatments with an emphasis on incremental cost-effectiveness ratio (ICER), which considers direct and indirect costs along with quality of life 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 United States. 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 quality of life.[71] This means that the best option for patients with end stage OA is a very costly surgery. This surgery optimizes the quality of life and minimizes the indirect costs compared to 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.[8] 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.[8] 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.[43] Contemporary figures suggest that the true incidence rate in the general population is around 5.5 times higher than figures derived from EDs.[28] To provide the most accurate estimate of population-based incidence rates, epidemiology studies should focus on 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 associate with the management and treatment for LAS, as well as 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 policy makers 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 in the short- and long-term. In regards to LAS, the direct costs are, as with other injuries, lower than the indirect costs. Although cost estimates differ between countries, depending upon the different insurance and medical systems, the sheer magnitude of LAS make 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 costings, but more comprehensive assessments of LAS management and treatment are still needed. It is likely that with more complete analyses across societies, we will realize that our current figures are underestimated.

Section B: Mid- and Long-Term Consequences of Lateral Ankle Sprains

Development and Onset of CAI

As an isolated, acute injury, it is common to consider LAS 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 re-injury rate. Additionally, what causes CAI to develop in some patients but not in others has not been established definitively. Subsequently, we will summarize hypotheses that are currently being considered

Post-acute deficits following LAS

Most patients with LAS have resolution of primary inflammatory symptoms in a relatively short period of time with conservative treatment,[72-74] and a high likelihood of rapid return to activity.[75] Subsequently, there is an assumption that LAS is an inconsequential injury once the sub-acute 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 follow-up of LAS patients are lingering disabling symptoms including pain and decreased function.[76]

The early work by Gerber *et al*[77] 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 LAS patients 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 LAS patients presented with full function; and 25% of patients still reported pain.[77] Konradsen *et al*[78], at the7-year follow- up of 648 LAS patients, 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.[78]

Retrospective assessment of the population with a history of previous LAS demonstrates lingering symptoms and functional deficits. It is worth noting that 32% to 74% of individuals with a previous history of LAS suffer chronic symptoms.[78-80] Hiller *et al*[81], 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*[82], 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 greater than 10 years.

There may be a host of functional and sensorimotor deficits that persist in the months following LAS.[83 84] Patients with LAS exhibit deficits in balance and movement coordination in the weeks and months following acute injury.[85-88] Doherty *et al*[89-96] 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 a 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 re-injury.

Recurrent injury

LASs have the highest recurrence rates of all lower limb musculoskeletal injuries,[18 97-99] with a two-fold increased risk of re-injury in the year following injury occurrence.[36 100] 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.[36 101]

It is suggested that neuromuscular functioning is altered after an initial LAS due to damage of the ankle ligament receptors.[102] Resulting functional deficits include limited postural control, decreased maximal strength of the evertor muscles and prolonged muscle reaction time.[83 103] Even after successful return to play**,** ongoing deficits in neuromuscular control may contribute to a higher risk of a recurrent injury.[104] For example, individuals with a history of ankle sprain have greater fatigue-induced alterations of dynamic postural control.[105 106] It may be that further damaging of the already impaired ankle function after LAS recurrences is a significant contributor to CAI.

From Lateral Ankle Sprain to Chronic Ankle Instability

Many patients have ongoing pain, giving way and a feelings of instability in their ankle,[63] leading to persistent disability, which are characteristic features of CAI.[4] Hertel[107] 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)[108] 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)[109 110]. Delahunt *et al*[4] expanded the inclusion criteria that define insufficiencies in CAI as an encompassing term used to classify a person with both mechanical and functional instability of the ankle joint. They specified that in order to be categorized as having CAI, residual symptoms (''giving way'' and feelings of ankle joint instability) should be present for a minimum of one year post-initial sprain.

The Hertel model[107] was revised by Hiller *et al*[111] 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,[112 113] with the intent to differentiate functional limitations that may coexist with other impairments in CAI patients. More recently, the Executive Committee of the International Ankle Consortium published a position statement regarding 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.[5-7]

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,[17 82 98] and typically within a short period of time.[78 91-93 96] In a recent systematic review of the prevalence of CAI in sporting

populations, Attenborough *et al*[114] indicated that CAI is a highly prevalent condition (>25%) in sports such as handball, basketball, soccer, and volleyball. This has been confirmed in more recent investigations of collegiate and high school athletes in which the prevalence of CAI was approximately 25% in those athletes with a previous history of injury.[115 116] Within the performing arts population, such as ballet, over 50% of the dancers with a history of ankle sprain report CAI.[117] This CAI prevalence trend extends out to the general population in which over 20% of the general population with ankle injury reported having chronic issues.[82] 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,[118] it may be that our current societal awareness of CAI prevalence and its consequences on physical activity are poorly appreciated.[119 120] There is evidence to suggest that regardless of a first time or recurrent LAS, athletes are more likely to be returned to activity within 1 week of the injury.[75] 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 an application of ice and a brief period of rest. In fact, it has been reported that over half of sport players who sprained an ankle did not seek any type of care.[43 121] A secondary analysis from the work by Hiller *et al*[82] 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.[24 61 122] 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.[23 63 88 123] This means that many patients with a LAS are susceptible to inadequate restoration of disease oriented outcomes of ROM, arthrokinematics, strength, balance and neuromuscular control.[124] While this has not been supported directly in the literature, it is likely that a lack of attention to those factors are contribute to ongoing ankle instability, re-injury, and a decline in patient-oriented outcomes, all of which are characteristic of CAI.

An advantage of entry into a formalized health care 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.[75] This aggressive approach may neglect 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*[125] 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, randomized control trials are needed to determine optimal dosage of initial management and rehabilitation for a return to activity timeline that minimizes lingering instability and re-injury for LAS patients. 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 CAI patients that persist throughout the lower extremity.[55 81 83-86 104-106 118 126-152] These documented deficits have expanded on the original theory by Freeman *et al*[109] that ankle ligamentous injury created a "de-afferentation" whereby balance deficits would persist after LAS. Additionally, a collection of work has suggested there are adaptations within the central nervous system that may explain some of these observed sensorimotor changes in CAI patients.[149 153-162]

However, those observed patterns have been generated from retrospective study designs, limiting the conclusions that a LAS definitely creates these deficits in the CAI population. Doherty *et al*[89-96 163-168] have conducted a large longitudinal prospective study to examine the onset of sensorimotor deficits following a LAS. In that series of papers, LAS patients were assessed at the time of their acute injury, as well as 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 persist compared to 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 the acute LAS is incurred. Couple this with a potential lack of adequate care for LAS as we suggest above, and one can begin to understand how re-injury 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] (2015) 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 Osteoarthritis Development

Based on 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 both acute LAS and CAI. Ankle joint OA, regardless of etiology, represents a significant physical burden to the individual as evidenced by an average 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 (e.g. 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.[47] Additionally, between 70-80% of all ankle joint OA cases are post-traumatic in nature,[44 172-174] 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 (i.e. primary, secondary, PTOA) and up to 80% of ankle joint PTOA cases.[44 47 172-174] It is important to note that roughly 50% of ankle joint PTOA patients with a history of ligamentous injury reported only a single LAS while the remaining patients reported recurrent sprains and/or instability.[44 172 174] The end stage ankle joint PTOA patients in these investigations were, on average 51.5[174] and 58[44] years of age, with Valderabanno et al.[44] noting an age range of 22-90 years of age. Based on their data, Valderrabano et al.[47] 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 a 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 CAI patients (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 LAS patients sooner after the initial inciting injury than previously anticipated. For the chronically unstable ankle, the evidence is focused on patients reporting for lateral ligament stabilization 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 upon arthroscopic review.[48 49 178-187]

On the low end of the range reported in the literature, Sammarco and DiRaimondo[182 188] noted only 21% of CAI patients had degenerative changes of any kind in the ankle joint at the time of a lateral ligament stabilization procedure. Hintermann et al.[178] found cartilage lesions in 55% of CAI patients via arthroscopic evaluation performed on average less than 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.[49] illustrated that 95% of chronically unstable ankles examined arthroscopically had chondral lesions, with an average age of only 20 years. Komenda[181] and Ferkel & Chams[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 & Chams[179] also found intra-articular problems in 95% of CAI patients, with a mean age 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 LAS patients 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 unilateral LAS patients (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*[50] noted that both young, physically active CAI participants and LAS "copers" (i.e. those whom 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 fiber 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 timeframe relative to initial LAS. While these findings within "asymptomatic" (i.e. 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 diagnosis of end stage ankle joint OA, which from the work by Valderrabono *et al*[47] may not develop for 25-30 years after sustaining the 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 etiology of these degenerative changes/intra-articular problems has not yet been established. Taga *et al*[49] 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 osteocondral lesion. Epidemiological research regarding ankle joint PTOA etiology would appear to support this hypothesis, as roughly half of PTOA patients reporting ligamentous injury only report a single injury event.[44 174] The degenerative changes noted in LAS copers also suggest that a single LAS is sufficient to cause degenerative changes.[50] Lee *et al*[52] examined a series of patients reporting for arthroscopic marrow stimulation surgery. This sample was then examined for a history of a 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 approximately 28 months.

If the initial LAS is an underlying cause of osteochondral lesions, recurrent LASs and episodes of giving way likely exacerbate the contact stress adaptations,[51] further advancing degenerative changes. While speculative, this would place a premium on restoring appropriate biomechanics and motor control following a LAS in order to mitigate cartilage degeneration. Supporting this hypothesis, Golditz *et al*[189] found that mediolateral time to stabilization, a

measure of dynamic postural stability recorded while landing from a jump, was correlated to the increased relaxation times (i.e. 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 Co-Morbidity Risk

Throughout this paper, the prevalence, financial impact, and high rate of ankle sprain re-injury and lingering instability illustrate the impact of this musculoskeletal injury. However, the contributions of musculoskeletal disease on health care and societal concerns extend beyond those factors. Specifically, patients with CAI present with decreases in quality of life[79 190-194] and physical activity,[78 119 120 195 196] as well as accelerated onset of ankle joint OA,[44 45 48 49 51 197 198] oftentimes as early as the 3rd decade of life.[50] These factors all contribute to a paradigm of compromised health and wellness, which are established correlates with co-morbidity 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 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 instill 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.[75] At face value, this is true and achievable through therapeutic and pharmaceutical interventions, and most patients with a LAS can return to ADLs, occupational activity and recreational/sporting activities in a relatively short period of time.[75] However, what is not appreciated in the general population, and perhaps in the medical community, is that LAS patients, especially those that transition into CAI patients, 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*[199] 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.[195] Finally, this research group reported these "CAI" mice to have lower levels of activity levels using the running wheels throughout their lifespan compared to the uninjured mice, suggesting a negative influence of the ankle injury on lifelong physical activity.[120] 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 lifelong decline in physical activity, which is an important factor to consider in understanding the larger impact on health status.

The negative influence of ankle injury history on physical activity has also been documented in human populations. During a seven-year follow-up to injury by Konradsen *et al*,[78] 72% of over 600 enrolled LAS patients self-reported remaining functionally impaired, including inability to perform sports and physical activity, due to their 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 aging or chronic inflammation. In a survey of the general population, Hiller *et al*[82] 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*[196] 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 aging. 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-age adults. Hubbard-Turner and Turner[119] have shown that young adults with CAI engage in lower self-selected levels of physical activity compared to age-matched individuals with no history of ankle injury. Using pedometers, college-aged students in their early twenties with CAI demonstrated significantly fewer weekly steps taken and minutes engaged in moderate to vigorous activity compared to a non-injured cohort. Collectively, this work indicates that a history of LAS associates with a decline in physical

activity well after symptoms of the acute injury subside, but this decline is not necessarily a product of aging.

A consequence of physical activity decline is the likelihood of an increase in BMI. In a large study of over 800,000 individuals, Herskovich *et al*[200] found that males and females who were obese or overweight were more likely to have CAI (range of OR: 1.19-3.29) compared to those with a 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.[44 45 48-50] 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 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 quality of life (QOL). Evidence is mounting that a LAS may initiate a degradation in QOL levels in patients long after they have recovered from the acute symptoms of the injury. Anandacoomarasamy and Barnsley[79], using the SF-36 general health subscale, found in a small cohort of 19 lateral ankle sprain patients a decrease in QOL over a two-year period compared to age matched controls. The majority (74%) of these injured subjects

still had lingering pain, swelling, and/or lingering instability at the two-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[190] found similar declines in QOL compared to individuals without ankle sprain history. The authors of that study do not describe the amount of time since suffering the acute lateral ankle sprains 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*[191 193 194] also have considered the effect of ankle injury history on QOL, as well as 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 to non-injured and LAS coper populations.[194] 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.[191] 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.[193] 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*[191 193 194] illustrates that the degradation in QOL occurs as LAS patients downgrade into CAI populations. Alarmingly, this is being

observed in young adult patients under the age of 30. Simon and Docherty[201] report similar a phenomenon, but in a broader age range of the population. Former Division I collegiate athletes (n=232) who were between the ages of 40-60 years self-reported their current QOL using the American Academy of Orthopaedic Surgeons Lower Limb Questionnaire and the Short Form - 36v2. Even with this older age range, individuals with CAI reported decreased function and QOL compared with individuals without CAI. The largest differences were seen on the American Academy of Orthopaedic Surgeons Lower Limb Questionnaire, as well as the Physical Component Summary Score and physical function scales of the SF-36v2.[201]

Section B Summary

It is important to contextualize the trend of CAI and the associated consequences as it translates to at least 1 out of every 5 people in the public who incur a LAS will go on to report chronic problems.[82] These trends are higher in athletic populations (at least 1 of 3)[114 116] and among dancers (1 out of 2)[117]. When examining the trends within the general public, individuals with chronic ankle problems report increased modification of functional activity and reduced overall health compared to 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 CAI patients 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 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. The limited data we have show similar CAI related issues impact older adult populations as well, suggesting this injury and its consequence are more complex than initially understood, with persistence throughout the lifespan. Additionally, this is an issue not only impacting the competitive athlete, but is being reported throughout the general population. More epidemiological work, especially longitudinal studies, are needed to quantify the threats to general health as a means of defining the comprehensive health care burden from LAS. Because of the links of LAS and CAI to physical activity, BMI, QOL, and OA, it will be important to ascertain potential associations of ankle injury to other disease co-morbidities. This will emphasize the need for improved comprehensive treatment of acute LAS and CAI beyond the goal of returning to exercise and sport.

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