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# Lateral Ankle Sprain and Subsequent Ankle Sprain Risk: A Systematic Review

**Erik A. Wikstrom, PhD, ATC*; Mary Spencer Cain, PhD*; Avinash Chandran, PhD, MS†; Kyeongtak Song, PhD, ATC*; Tasha Regan, BA*; Kimmery Migel, DPT, PT*; Zachary Y. Kerr, PhD, MPH***

*University of North Carolina at Chapel Hill; †Datalys Center for Sports Injury Research and Prevention, Indianapolis, IN

***Objective:*** To evaluate the evidence regarding the association between lateral ankle sprain (LAS) history and the subsequent LAS risk, as well as sex differences in the observed associations.

***Data Sources:*** PubMed, CINAHL, and SPORTDiscus were searched through July 2020 for articles on LAS history and incidence during the study period.

***Study Selection:*** Studies were included if they were prospective in nature and the authors reported the number of participants with and those without a history of LAS at study initiation as well as the number of participants in each group who sustained an LAS during the investigation.

***Data Extraction:*** Data were study design parameters as well as the number of participants with and those without an LAS history and the number of subsequent LASs that occurred in both groups. Risk ratios (RRs) with 95% CIs compared the risk of LAS during the study period between those with and those without an LAS history for each investigation.

***Data Synthesis:*** A total of 19 studies involving 6567 patients were included. The follow-up periods ranged from 14 weeks to 2 years. Assessment scores indicated the studies were of moderate to high quality. A significantly higher risk of LAS during the study period was observed among those with a history of LAS in 10 of 15 studies (RR range = 1.29–6.06). Similar associations were seen in 4 of 6 studies of all-male samples (RR range = 1.38–8.65) and 1 of 4 studies with an all-female sample (RR = 4.28).

***Conclusions:*** Strong evidence indicates that a previous LAS increased the risk of a subsequent LAS injury. Men with a history of LAS appeared to be at a higher risk of sustaining a subsequent LAS, but women were not. However, further data are needed to draw definitive conclusions from the limited number of sex-specific studies.

***Key Words:*** risk ratios, risk factor, epidemiology, sex

**Key Points**

- Overall, an individual with a lateral ankle sprain had a greater risk of a subsequent lateral ankle sprain than an uninjured person.
- After a lateral ankle sprain, the risk of a subsequent lateral ankle sprain was increased for men but not for women.

Lateral ankle sprain (LAS) is the most common lower extremity musculoskeletal injury[1,2] and affects individuals of all ages participating in organized sports or unstructured play.[3] The LAS is often erroneously considered a 1-time injury, but researchers[4] have estimated that up to 74% of individuals who sustain an LAS will develop persistent adverse outcomes (eg, pain, swelling, weakness, and instability), often referred to as *chronic ankle instability*. An LAS has also been linked with ankle-joint degeneration and posttraumatic osteoarthritis.[5] In addition to the long-term health-related consequences, LASs and their sequelae represent a significant financial burden on injured individuals and the health care system.[3]

Due to the extensive cost and burden of LASs, numerous authors have focused on identifying both the intrinsic (eg, balance) and extrinsic (eg, LAS history) risk factors for initial and recurrent LASs.[2,6–9] Whereas multiple factors likely contribute to the risk of recurrent LAS, an LAS history has been accepted as a major risk factor for 2 main reasons: (1) selective referencing in the existing literature (ie, only citing work supporting the case being made) and (2) an LAS causes many of the other investigated risk factors (eg, poor balance, ligamentous laxity).[10–12] This belief may be erroneous given that (1) a body of evidence[13–17] indicates that an LAS history does not increase the risk of a subsequent LAS, and (2) no systematic examination of the cumulative literature has been completed. Due to the conflicting results across the literature, a systematic examination is necessary to gain a comprehensive understanding of how an LAS history may influence the subsequent LAS risk and thus appropriately inform primary and secondary prevention strategies (ie, prevention of index injuries and subsequent rehabilitation protocols).

Epidemiologic studies[6,7,18–20] have suggested that women may be at higher risk of sustaining an initial LAS. However, fewer data exist regarding the risk of subsequent LASs among women. Only 1 study[7] of collegiate athletes showed that recurrent LASs did not differ between men and

women in sex-comparable sports. These varying results indicate the need for further examination of both sexes in comparable situations.

Therefore, the purpose of our investigation was to conduct a systematic review to evaluate evidence surrounding the association between LAS history and subsequent LAS risk, as well as sex differences in any observed associations. A secondary purpose was to evaluate whether a meta-analysis of the available literature was feasible. Based on the existing literature, we hypothesized that the risk of subsequent LAS would be higher in those with versus those without an LAS history. We also hypothesized that this association would not vary by sex, given data[7] suggesting that the risk of recurrent LAS did not differ between men and women.

## METHODS

### Search Strategy

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to perform this systematic review of the available English literature. Two researchers (M.S.C. and T.R.) conducted a systematic literature search to identify studies that addressed how an LAS history might be associated with the risk of a subsequent LAS during a follow-up study period. Three databases (PubMed, CINAHL, and SPORTDiscus) were used to search for articles from the earliest available date to July 2020. The key words used were (*ankle sprain* or lateral ankle sprain* or inversion sprain* OR history of ankle sprain**) *and* (*risk or recurrence or reinjur* or re-injur* or incidence or prevalence or injury sequence or injury order or etiolog* or aetiolog**). Additional tools, such as the reference lists of screened full-text articles and Google Scholar, were also reviewed.

### Selection Criteria

Studies included in this systematic review were required to meet the following criteria: (1) a prospective study, either experimental or observational in nature, involving human participants, with a sufficient study period (ie, follow-up duration) for the population of interest; (2) original research published as an article in a peer-reviewed journal; (3) publication in English and available in full text; (4) provided the number of participants who had or did not have a history of LAS at the start of the study; and (5) provided the number of participants in each group who sustained an LAS during the study period. Criteria related to the age of the study (ie, date published) were not imposed because the LAS incidence did not seem to change over time. A *sufficient study period* was operationally defined as at least 1 unit of time pertinent to the study population (eg, 1 season for a sporting population, 1 training block for a military population, or 1 year for a general population cohort).

### Evaluation of Study Quality

A modified Newcastle-Ottawa Quality Assessment Scale for cohort studies (NOS)[21] was used to evaluate the methodologic quality of each article's study design. Our inclusion criteria required all studies to involve individuals with a history of LAS. Because LAS history was the outcome of interest, our inclusion criteria therefore invalidated the fourth NOS item ("Demonstration that outcome of interest was not present at start of study"). As a result, this item was removed from the modified NOS. The modified NOS assessed nonrandomized study quality based on 8 items in 3 domains: (1) selection of the study groups, (2) comparability of the groups, and (3) ascertainment of the outcome of interest. The total score of the modified version ranged from 0 to 8 (2 points could be obtained from 1 item on comparability). A higher score indicated better methodologic quality. Each study was independently evaluated and scored by 2 authors (K.S. and K.M.). If any disagreement in scoring occurred, the 2 authors met to discuss their independent assessments and reach consensus.

### Data Extraction and Analysis

Two authors (M.S.C. and T.R.) independently extracted all pertinent data from the included studies. Data were study design, study duration, study location, population of interest, number of participants with and those without an LAS history, and number of subsequent LASs sustained by both groups. When available, data stratified by sex were also extracted.

We calculated study-specific estimates of LAS risk, computed as the number of participants who incurred at least 1 LAS during the study period divided by the total number of participants. We then computed study-specific risk ratios (RRs) with 95% CIs to compare the risk of a subsequent LAS during the observation period in the LAS history group with that of the no-LAS history group, which served as the referent. The following is an example of such an RR:

$$\mathrm{RR} = \frac{\left[\frac{\sum \text{Participants With a History of LAS Who Sustained an LAS During the Study Period}}{\sum \text{Participants With a History of LAS}}\right]}{\left[\frac{\sum \text{Participants Without a History of LAS Who Sustained an LAS During the Study Period}}{\sum \text{Participants Without a History of LAS}}\right]}$$

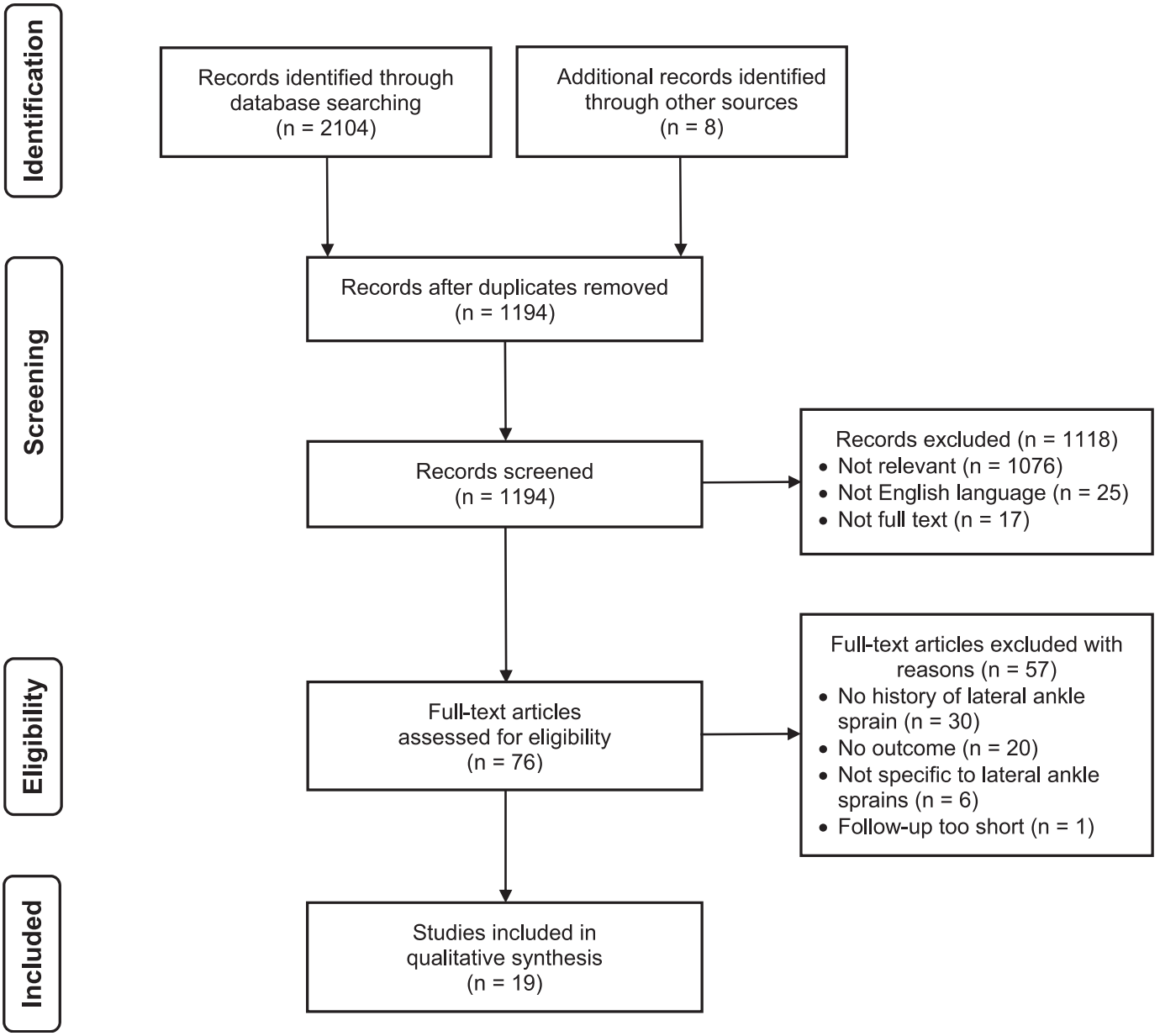


**Figure. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA): 2009 flow diagram of study-selection process.**

When possible, data for male and female participants were analyzed separately to calculate sex-stratified RRs. All RRs not including 1.00 in the 95% CI were considered statistically significant.

### Assessment of Heterogeneity

Data from all studies were then consolidated to determine the magnitude of heterogeneity across studies and whether it was appropriate to conduct a meta-analysis (ie, moderate or lower heterogeneity). Statistical heterogeneity was examined using the $I^2$ statistic. An $I^2$ value of $\geq$ 70% represented a high level of heterogeneity[22] and was used as the threshold for not performing a meta-analysis.

## RESULTS

### Articles Included

The Figure summarizes the results of the systematic search that identified a total of 2104 potential articles and 8 additional articles (eg, reference lists, Google Scholar). Overall, after we screened the potential articles by title and abstract, removed duplicates, and performed a full-text review, 19 studies were included. The studies included in the systematic review are detailed in Table 1.

### Assessment of Study Quality

All studies scored 5 points or more (of 8) on the modified NOS (mean = 6.58 $\pm$ 0.61) as seen in Table 2. From a comparability perspective, no study controlled for additional factors and, subsequently, each lost 1 quality-

**Table 1. Characteristics of Included Studies**

| Study (Year) | Study Duration | Population (Age, y) | Study Location | Total No. of Participants |
|---|---|---|---|---|
| Arnason et al[12] (2004) | 1 season (~4 mo) | Elite soccer (16–38 y) | Iceland | 517 |
| Attenborough et al[13] (2016) | 1 season (~4 mo) | Club netball (15–29 y) | Australia | 94 |
| Bahr and Bahr[27] (1997) | 1 season (TNS) | Amateur volleyball (17–28 y) | Norway | 466 |
| Barrett et al[14] (1993) | 1 season (~2 mo) | Intramural basketball (18–35 y) | United States | 569 |
| Baumhauer et al[15] (1995) | 1 season (TNS) | Collegiate lacrosse, soccer, field hockey (18–23 y) | United States | 145 |
| Cumps et al[34] (2007) | 22 wk | Elite youth and senior (division, not age) basketball (13–28 y) | Finland | 100 |
| de Noronha et al[11] (2013) | 52 wk | Active university students (18–24 y) | Brazil | 121 |
| Ekstrand and Gillquist[28] (1983) | 1 y | Elite soccer (12 teams; 17–38 y) | Sweden | 324 |
| Faude et al[29] (2006) | 1 season (TNS) | Professional soccer (17–28 y) | Germany | 143 |
| Frey et al[23] (2010) | 1 season (TNS) | Secondary school volleyball (15–18 y) | United States | 999 |
| Hartley et al[24] (2018) | 2 y | NCAA all sports (17–22 y) | United States | 551 |
| Henry et al[33] (2016) | 2 seasons (TNS) | Amateur soccer (15–23 y) | Australia | 210 |
| Hiller et al[16] (2008) | 13 mo | Secondary school dance and ballet (12–16 y) | Australia | 115 |
| Kofotolis and Kellis[30] (2007) | 2 y | Professional basketball (20–30 y) | Greece | 202 |
| Kofotolis et al[31] (2007) | 2 y | Amateur soccer (20–30 y) | Greece | 312 |
| McGuine and Keene[25] (2006) | 5 wk + Season | Secondary school soccer and basketball (15–18 y) | United States | 765 |
| Meeuwisse et al[26] (2003) | 2 y | Collegiate basketball (NA) | Canada | 448 |
| Milgrom et al[32] (1991) | Basic training: 14 wk | Military infantry recruits (NA) | Israel | 390 |
| Pourkazemi et al[8] (2018) | 1 y | Generally active (14–40 y) | Australia | 96 |

Abbreviations: NA, not available; NCAA, National Collegiate Athletic Association; TNS, time not specified.

assessment point. Four studies (21%) involved a subgroup (ie, volunteers) rather than the average member of the population of interest for the question, which resulted in the loss of 1 quality-assessment point. In the outcome domain, 4 studies (21%) did not explicitly address the percentage of participants lost at follow-up or whether that percentage was small enough to draw meaningful conclusions, and they subsequently lost 1 quality-assessment point.

## Sample Characteristics

The 19 included studies[8,11–16,23–34] contained a pooled total of 6567 participants. Of these, 4341 (66%) participants reported no LAS history, and 2226 (34%) participants reported an LAS history. Reporting of a history of LAS was not consistent across investigations.

Most studies were from Europe (42%, n = 8) and North America (32%, n = 6). Sixteen (84%) examined athletes; 2 (11%), the general or active population; and 1 (5%),

**Table 2. Modified Newcastle Ottawa Quality Assessment Scale[21] Items and Total Scores for Included Articles**

| | Item, Score (Point) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Selection[a] | | | | Comparability[b] | Outcome[c] | | | |
| Study (Year) | Q1 | Q2 | Q3 | Q4 | Q1 | Q1 | Q2 | Q3 | Total |
| Arnason et al[12] (2004) | c (0) | a (1) | a (1) | NA | a (1) | a (1) | a (1) | a (1) | 6 |
| Attenborough et al[13] (2016) | b (1) | a (1) | a (1) | NA | a (1) | a (1) | a (1) | b (1) | 7 |
| Bahr and Bahr[27] (1997) | b (1) | a (1) | b (1) | NA | a (1) | b (1) | a (1) | b (1) | 7 |
| Barrett et al[14] (1993) | b (1) | a (1) | b (1) | NA | a (1) | b (1) | a (1) | b (1) | 7 |
| Baumhauer et al[15] (1995) | b (1) | a (1) | b (1) | NA | a (1) | a (1) | a (1) | b (1) | 7 |
| Cumps et al[34] (2007) | c (0) | a (1) | b (1) | NA | a (1) | a (1) | a (1) | b (1) | 6 |
| de Noronha et al[11] (2013) | c (0) | a (1) | b (1) | NA | a (1) | a (1) | a (1) | b (1) | 6 |
| Ekstrand and Gillquist[28] (1983) | b (1) | a (1) | a (1) | NA | a (1) | b (1) | a (1) | a (1) | 7 |
| Faude et al[29] (2006) | b (1) | a (1) | a (1) | NA | a (1) | b (1) | a (1) | a (1) | 7 |
| Frey et al[23] (2010) | b (1) | a (1) | a (1) | NA | a (1) | b (1) | a (1) | d (0) | 6 |
| Hartley et al[24] (2018) | c (0) | a (1) | a (1) | NA | a (1) | a (1) | a (1) | d (0) | 5 |
| Henry et al[33] (2016) | b (1) | a (1) | a (1) | NA | a (1) | a (1) | a (1) | d (0) | 6 |
| Hiller et al[16] (2008) | b (1) | a (1) | b (1) | NA | a (1) | a (1) | a (1) | b (1) | 7 |
| Kofotolis and Kellis[30] (2007) | b (1) | a (1) | a (1) | NA | a (1) | b (1) | a (1) | b (1) | 7 |
| Kofotolis et al[31] (2007) | b (1) | a (1) | a (1) | NA | a (1) | b (1) | a (1) | a (1) | 7 |
| McGuine and Keene[25] (2006) | b (1) | a (1) | a (1) | NA | a (1) | b (1) | a (1) | b (1) | 7 |
| Meeuwisse et al[26] (2003) | b (1) | a (1) | a (1) | NA | a (1) | b (1) | a (1) | b (1) | 7 |
| Milgrom et al[32] (1991) | b (1) | a (1) | a (1) | NA | a (1) | b (1) | a (1) | d (0) | 6 |
| Pourkazemi et al[8] (2018) | a (1) | a (1) | b (1) | NA | a (1) | b (1) | a (1) | a (1) | 7 |

Abbreviations: NA, not applicable; Q, question.

[a] Q1, Representativeness of the exposed cohort; Q2, Selection of the nonexposed cohort; Q3, Ascertainment of exposure; Q4, Demonstration that outcome of interest was not present at the start of the study.

[b] Q1, Comparability of cohorts on the basis of the design or analysis.

[c] Q1, Assessment of outcome; Q2, Was follow-up long enough for outcomes to occur?; Q3, Adequacy of follow-up of cohorts.

**Table 3. Risk Ratios and 95% CIs Examining the Risk of Subsequent Lateral Ankle Sprain Among Those With Versus Those Without a History of Lateral Ankle Sprain**

| Study (Year) | Group, No. | | Group, Subsequent Lateral Ankle Sprain, No. (%) | | Risk Ratio (95% CI)[a] |
|---|---|---|---|---|---|
| | No Lateral Ankle Sprain History | Lateral Ankle Sprain History | No Lateral Ankle Sprain History | Lateral Ankle Sprain History | |
| Arnason et al[12] (2004) | 305 | 212 | 3 (1.0) | 11 (5.2) | 5.28 (1.49, 18.68)[b] |
| Attenborough et al[13] (2016) | 40 | 54 | 6 (15.0) | 5 (9.3) | 0.62 (0.20, 1.88) |
| Bahr and Bahr[27] (1997) | 234 | 232 | 10 (4.3) | 38 (16.4) | 3.83 (1.96, 7.51)[b] |
| Barrett et al[14] (1993) | 328 | 241 | 10 (3.0) | 5 (2.1) | 0.68 (0.24, 1.97) |
| Baumhauer et al[15] (1995) | 96 | 49 | 11 (11.5) | 4 (8.2) | 0.71 (0.24, 2.12) |
| Cumps et al[34] (2007) | 58 | 42 | 7 (12.1) | 7 (16.7) | 1.38 (0.52, 3.64) |
| de Noronha et al[11] (2013) | 69 | 52 | 10 (14.5) | 21 (40.4) | 2.79 (1.44, 5.40)[b] |
| Ekstrand and Gillquist[28] (1983) | 243 | 81 | 19 (7.8) | 17 (21.0) | 2.68 (1.47, 4.91)[b] |
| Faude et al[29] (2006) | 56 | 87 | 11 (19.6) | 22 (25.3) | 1.29 (0.68, 2.44) |
| Frey et al[23] (2010) | 683 | 316 | 49 (7.2) | 44 (13.9) | 1.94 (1.32, 2.85)[b] |
| Hartley et al[24] (2018) | 492 | 59 | 33 (6.7) | 24 (40.7) | 6.06 (3.86, 9.52)[b] |
| Henry et al[33] (2016) | 162 | 48 | 9 (5.6) | 5 (10.4) | 1.88 (0.66, 5.33) |
| Hiller et al[16] (2008) | 60 | 55 | 20 (33.3) | 16 (29.1) | 0.87 (0.51, 1.51) |
| Kofotolis and Kellis[30] (2007) | 64 | 138 | 8 (12.5) | 24 (17.4) | 1.39 (0.66, 2.93) |
| Kofotolis et al[31] (2007) | 180 | 132 | 55 (30.6) | 84 (63.6) | 2.08 (1.61, 2.69)[b] |
| McGuine and Keene[25] (2006) | 583 | 182 | 35 (6.0) | 27 (14.8) | 2.47 (1.54, 3.97)[b] |
| Meeuwisse et al[26] (2003) | 281 | 167 | 33 (11.7) | 27 (16.2) | 1.38 (0.86, 2.21) |
| Milgrom et al[32] (1991) | 339 | 51 | 51 (15.0) | 16 (31.4) | 2.09 (1.29, 3.36)[b] |
| Pourkazemi et al[8] (2018) | 68 | 28 | 3 (4.4) | 7 (25.0) | 5.67 (1.58, 20.36)[b] |

[a] Risk ratios compared the risk of subsequent lateral ankle sprain in the lateral ankle sprain history group versus the no lateral ankle sprain history group, which served as the referent.
[b] Indicates risk ratio was different (ie, 95% CI excluded 1.00).

military personnel. The sport-related research most commonly evaluated soccer athletes or players[12,15,24,25,28,29,31,33] (42%, n = 8) or basketball athletes or players[14,24–26,30,34] (32%, n = 6). Twelve studies[8,11–16,23,25,27–29] (63%) had a 1-season or 1-year follow-up period, whereas 5 studies[24,26,30,31,33] (26%) had follow-up periods of 2 seasons or 2 years.

## Analysis of RRs

Across individual investigations, 15 (79%) had elevated RR point estimates, suggesting that those with a history of LAS had a higher risk of sustaining a subsequent LAS (RR range = 1.29–6.06; Table 3). Of these, 10 had RRs that were statistically significant (ie, 95% CI did not include 1.00), whereas the remaining 5 demonstrated elevated RR point estimates but had a 95% CI that included 1.00. The remaining 4 (21%) without statistically significant results had point estimates < 1.00.

Notably, only 1 study presented data stratified by sex, whereas 8 presented data on a specific sex (Table 4). Across individual studies, a higher risk of LAS was suggested in those with a history of LAS in 6 studies that included data specific to male athletes (RR range = 1.38–8.65); 4 of these studies had RRs that were statistically significant (ie, 95% CI did not cross 1.00). Similarly, a higher risk of LAS in the follow-up study period was observed among those with a history of LAS (versus the referent) in 4 studies that provided data specific to female athletes (RR range = 0.62–4.28); however, only 1 of these had an RR that was statistically significant (ie, 95% CI did not cross 1.00).

**Table 4. Risk Ratios and 95% CIs Examining the Risk of Subsequent Lateral Ankle Sprain Among Those With Versus Those Without a History of Lateral Ankle Sprain by Sex**

| Sex | Study (Year) | Group, No. | | Group, Subsequent Lateral Ankle Sprain, No. (%) | | Risk Ratio (95% CI)[a] |
|---|---|---|---|---|---|---|
| | | No Lateral Ankle Sprain History | Lateral Ankle Sprain History | No Lateral Ankle Sprain History | Lateral Ankle Sprain History | |
| Male | Arnason et al[12] (2004) | 305 | 212 | 3 (1.0) | 11 (5.2) | 5.28 (1.49, 18.68)[b] |
| | Hartley et al[24] (2018) | 346 | 38 | 20 (5.8) | 19 (50.0) | 8.65 (5.09, 14.71)[b] |
| | Henry et al[33] (2016) | 162 | 48 | 9 (5.6) | 5 (10.4) | 1.88 (0.66, 5.33) |
| | Kofotolis et al[31] (2007) | 180 | 132 | 55 (30.6) | 84 (63.6) | 2.08 (1.61, 2.69)[b] |
| | Meeuwisse et al[26] (2003) | 281 | 167 | 33 (11.7) | 27 (16.2) | 1.38 (0.86, 2.21) |
| | Milgrom et al[32] (1991) | 339 | 51 | 51 (15.0) | 16 (31.4) | 2.09 (1.29, 3.36)[b] |
| Female | Attenborough et al[13] (2016) | 40 | 54 | 6 (15.0) | 5 (9.3) | 0.62 (0.20, 1.88) |
| | Faude et al[29] (2006) | 56 | 87 | 11 (19.6) | 22 (25.3) | 1.29 (0.68, 2.44) |
| | Hartley et al[24] (2018) | 146 | 21 | 13 (8.9) | 8 (38.1) | 4.28 (2.02, 9.08)[b] |
| | Kofotolis and Kellis[30] (2007) | 64 | 138 | 8 (12.5) | 24 (17.4) | 1.39 (0.66, 2.93) |

[a] Risk ratios compared the risk of subsequent lateral ankle sprain in the lateral ankle sprain history group versus the no lateral ankle sprain history group, which served as the referent.
[b] Indicates risk ratio was different (ie, 95% CI excluded 1.00).

### Heterogeneity of Studies

The observed $I^2$ value was 71% (95% CI = 50%, 89%), indicating substantial variability among the included studies. As a result, we did not pursue a meta-analysis.

## DISCUSSION

We aimed to evaluate the evidence regarding the association between LAS history and subsequent LAS risk, as well as sex differences in any observed associations. The studies were generally of high quality and involved diverse populations. Results from the systematic review supported our primary hypothesis that an LAS history is associated with a subsequent LAS risk. The results are also consistent with published findings[10,35–40] that were not included in this systematic review. However, the substantial variability among the included studies prevented us from conducting a meta-analysis. Nevertheless, these findings highlight the need to develop, implement, and evaluate prophylactic interventions that prevent index injury and provide rehabilitative strategies that prevent reinjury among individuals with an LAS history.

The exact mechanism by which an LAS history increases the subsequent LAS risk remains unclear because current theoretical models suggest that a risk of recurrent LAS and the development of chronic ankle instability are influenced by multiple factors. Yet many of these possible factors are a consequence of both an index LAS and a history of multiple LASs.[41,42] For example, a history of LAS is known to disrupt the structural integrity of the ligaments and sensorimotor function,[3] likely impairing an individual's ability to avoid injurious situations. Evidence also suggests that individuals with chronic ankle instability (ie, those with a history of multiple LASs) alter how they weight sensory information[43] and respond to fatigue,[44] which would further limit an individual's ability to mitigate risk. However, it is unclear whether these adaptations appear before chronic ankle instability develops (ie, after a history of a single LAS). Based on the known consequences of an LAS, primary prevention programs that focus on sensorimotor function (eg, balance training) are effective[45–47] in preventing first-time LAS. Similarly, comprehensive strategies that aim to restore sensorimotor function are recommended after an LAS[48,49] because of their efficacy in treating individuals with a first-time or recurrent LAS.[45–47]

Despite evidence that a history of LAS and the subsequent risk of LAS were associated in both men and women, we found more robust evidence of this association in men than in women. This is contrary to our a priori hypothesis and inconsistent with data[7] that demonstrated no sex differences in the proportion of recurrent LASs reported in National Collegiate Athletic Association athletes over a 5-year period. It is important to note that although the finding from the systematic review for women was not statistically significant, the effect estimate of 1.56 still reflected a moderate association that is worth additional research.[50] Furthermore, given the scarcity of sex-stratified data, we advocate for continued research to better determine how this association may vary by sex. This can include increasing efforts to recruit larger samples of female participants and stratifying findings by sex.

Also, the RRs in the individual studies originated from tabular methods that did not permit control of factors such as age, playing position in sport, comorbidities, and other LAS risk factors. This was primarily due to our reliance on the demographics and statistics described in the articles to calculate risk and RRs. However, from these analyses, several trends emerged. For example, the majority of studies indicating higher subsequent LAS risk in those with an LAS history involved larger samples (total sample size $\geq$ 100).[11,12,23–33,51] Cumulatively, these findings reinforce the importance of adequate power to capture effects and obtain precise effect estimates related to associations between LAS risk factors and recurrent LAS risk. Significant results were also noted across 3 populations (general or active adults, military, sporting): all 3 studies[8,11,32] in nonsporting populations demonstrated a higher risk of subsequent LAS among those with an LAS history versus those without. Despite the consistent results among nonathletes, the generalizability of these results could be enhanced with additional samples from the general population, as well as heterogeneous samples from sporting populations (ie, samples including athletes from different sports and various levels of competition). Furthermore, significant findings were noted across studies with various follow-up durations (from 14 weeks in a military population to 2 years in a sporting population). Thus, future researchers should consider time-to-event analyses to better determine how the subsequent LAS risk changes over time. Additional exploration is also needed to confirm our initial sex-specific results and to better detect whether the injury risk varies among subgroups (eg, initial injury severity, sport).

### Clinical Implications

Clinically, these results highlight the importance of (1) preventing the index LAS (ie, primary injury prevention) and (2) emphasizing the need for rehabilitative strategies (ie, secondary prevention programs) to prevent negative long-term health outcomes after an LAS. Primary[52] and secondary prevention programs are effective at reducing the LAS and recurrent LAS risks, respectively,[45–47] but strong barriers hinder consistent implementation of both. For example, a lack of coach education and perceived time constraints by coaches limit the deployment of programs designed to prevent an index LAS.[53,54] Rehabilitative programs intended to prevent recurrent LAS are hampered by an erroneous public perception that LASs are inconsequential injuries that do not need rehabilitation. Indeed, fewer than 7% of patients with LASs complete any physical therapy within 30 days of their injury.[55] Also, patients who did not seek medical care for their LASs described a greater number of recurrent LASs and worse patient-reported outcomes than those who participated in formal medical care.[56] Elucidating mechanisms to overcome these barriers should be the focus of future research.

### Limitations

This investigation, like all research, is not without limitations. First, we cannot determine whether our sample (ie, 34% with a history of LAS) represented the overall population of those with a history of LAS because this population has yet to be defined. Second, the existing literature did not document details related to prior or subsequent LASs (eg, number of previous LASs, severity of

sprains, concurrent injuries) or the presence and severity of other potential LAS risk factors; such data might have helped to explain differences among the study findings. An example of these concerns is that most but not all of the included investigations relied on participant self-reports for the LAS history. Similarly, operational definitions of LAS were not consistent across studies, and not all authors provided complete operational definitions. As noted previously, the effect estimates computed in our study were crude and therefore did not account for possible confounding factors (eg, sensorimotor function, ligamentous laxity) that could also influence the subsequent LAS risk because those data were not included in the original research reports. Our results also did not account for exposure, a common confounding variable in injury risk, and a wide variety of follow-up periods were included in this systematic review. The body of evidence was also not robust enough to permit us to assess the associations of interest within small subgroups (eg, specific sports, positions within a sport) or at different follow-up time points (eg, 1 year, 2 years), thus limiting further subgroup analyses. Finally, we could not pursue meta-analytic techniques because of a high degree of heterogeneity among studies, which was a direct result of the small body of evidence available across various subpopulations to examine the various subgroups discussed.

## CONCLUSIONS

The literature base regarding the association between an LAS history and subsequent LAS is of high quality, provides strong evidence, and supports the clinical consensus that an LAS history increases the subsequent LAS risk. Unlike female athletes, male athletes with a history of LAS appeared to be at a higher risk of sustaining a subsequent LAS. Also, substantial variability exists in the literature, which prevented us from conducting a meta-analysis.

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*Address correspondence to Erik A. Wikstrom, PhD, ATC, University of North Carolina at Chapel Hill, 311 Woollen Gym, CB#8700, Chapel Hill, NC 27599. Address email to wikstrom@unc.edu.*