Title	The Incidence and Prevalence of Ankle Sprain Injury: A Systematic Review and Meta-Analysis of Prospective Epidemiological Studies
Authors(s)	Doherty, Cailbhe, Delahunt, Eamonn, Caulfield, Brian, Hertel, Jay, Ryan, John, Bleakley, Chris J.
Publication date	2014-01
Publication information	Doherty, Cailbhe, Eamonn Delahunt, Brian Caulfield, Jay Hertel, John Ryan, and Chris J. Bleakley. "The Incidence and Prevalence of Ankle Sprain Injury: A Systematic Review and Meta-Analysis of Prospective Epidemiological Studies." Springer, January 2014. https://doi.org/10.1007/s40279-013-0102-5.
Publisher	Springer
Item record/more information	http://hdl.handle.net/10197/8348
Publisher's statement	The final publication is available at Springer via http://dx.doi.org/10.1007/s40279-013-0102-5.
Publisher's version (DOI)	10.1007/s40279-013-0102-5

Title: The incidence and prevalence of ankle sprain injury: a systematic review and meta-analysis of prospective epidemiological studies.

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Word Count: 5570.

Acknowledgements

This study was supported by the Health Research Board (HRA_POR/2011/46) as follows: PI – Eamonn Delahunt; Co-investigators – Chris Bleakley and Jay Hertel; PhD student – Cailbhe Doherty).

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Key Words:

Ankle Sprain, Inclusion Criteria, Incidence Rate, Prevalence Period

ABSTRACT

Context: ankle sprain is one of the most common musculoskeletal injuries, yet a contemporary review and meta-analysis of prospective epidemiological studies investigating ankle sprain does not exist.

Objective: to provide an up-to-date account of the incidence rate and prevalence period of ankle sprain injury unlimited by timeframe or context activity.

Data Sources: systematic review and meta-analyses of English articles using relevant computerised databases. Search terms included Medical Search Headings for the ankle joint, injury and epidemiology.

Study selection: the following inclusion criteria were used: the study must report epidemiology findings of injuries sustained in an observed sample; the study must report ankle sprain injury with either incidence rate or prevalence period among the surveyed sample, or provide sufficient data from which these figures could be calculated; the study design must be prospective.

Data extraction: independent extraction of articles was performed by two authors using pre-determined data fields.

Data synthesis: 181 prospective epidemiology studies from 149 separate papers were included. The average rating of all the included studies was 6.67/11. 116 studies were considered high quality and 65 were considered low quality. The main findings of the meta-analysis demonstrated a higher incidence of ankle sprain in females compared to males (13.6 versus 6.94 per 1000 exposures), in children compared to adolescents (2.85 versus 1.94 per 1000 exposures) and adolescents compared to adults (1.94 versus 0.72 per 1000 exposures). The sport category with the highest incidence of ankle sprain was indoor/court sports, with a cumulative incidence rate of 7 per 1000 exposures or 1.37 per 1000 athlete exposures and 4.9 per 1000 hours. Low quality studies tended to underestimate the incidence of ankle sprain when compared to high quality studies (0.54 versus .12 per 1000 exposures). Ankle sprain prevalence period estimates were similar across sub-groups. Lateral ankle sprain was the most commonly observed type of ankle sprain.

Conclusions: females were at a higher risk of sustaining an ankle sprain compared to males, children compared to adolescents and adults, with indoor and court sports the highest risk activity. Studies at a greater risk of bias were more likely to underestimate the risk of ankle sprain. Participants were at a significantly higher risk of sustaining a lateral ankle sprain compared with syndesmotic and medial ankle sprains.

1. Introduction:

Ankle sprain accounts for between 3% and 5% of all Emergency Department visits in the UK, equating to approximately 5,600 incidences per day (1). Despite the high prevalence and severity of lifestyle-limiting symptoms that follow the acute episode (2) (3), ankle sprains are oftentimes regarded as benign injuries that will resolve quickly with limited treatment (4, 5).

Ankle sprain in sport may result in varying degrees of debilitation, including decreased performance, absence from competition and adverse psychological effects (6). Following an acute ankle sprain, pain, swelling and ecchymosis are common, which may contribute to reduced mobility and function, as well as occupational absence. The incidence of residual symptoms following acute ankle sprain is variable, but has been reported with rates of between 40% and 50% (7-10). The vast extent of these residual symptoms have prompted the creation of several homogenous subsets (mechanical insufficiencies which include arthrokinematic restrictions, laxity, synovial changes and degeneration, and functional insufficiencies, which include impaired proprioception, postural control, neuromuscular control and strength deficits) of a heterogenous condition referred to as chronic ankle instability (CAI) (11). CAI has been defined as an encompassing term used to classify a subject with both mechanical and functional instability of the ankle joint. To be classified 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 (12).

Ankle sprain has high societal economic costs associated with the diagnosis, treatment, and loss of work productivity contingent with the severity of injury. It has been reported that one quarter of all people who sustain an ankle sprain are unable to attend school or work for more than seven days following the initial injury (13). The economic burden of ankle sprain cannot be disputed, as the mean total cost of one ankle sprain in the Netherlands has been reported to be approximately €360 (14) equating to an estimated annual cost of €84,240,000 in the Netherlands alone.

Musculoskeletal injury is also a persistent and primary health concern for military populations as it is a leading cause of hospitalisation and accounts for a significant amount of lost duty time (15). The yearly cost of military musculoskeletal injuries has been estimated to equate to nearly €1 billion (US dollars), with ankle sprain the 7th most prevalent injury subgroup (16). Military musculoskeletal injuries results in both short term and long term disability, and places a substantial burden on the medical system (17). Ankle sprains are one of the most common musculoskeletal injuries and present a significant issue for military healthcare practitioners (18-22)

The consequences of the developed insufficiencies following an acute ankle sprain extend beyond the context of active populations (23). It has recently been acknowledged that CAI is a leading cause of post-traumatic ankle joint osteoarthritis (24-26). Furthermore, it has previously been demonstrated that chronic peripheral joint injury such as CAI negatively alters central mechanisms of motor control, leading to an increased risk of falls (27, 28). Therefore, investigating the incidence of ankle sprain and including data relating to various populations is of clinical relevance.

The first step of the United States' public health model of injury prevention and control (17) involves identifying the scope and magnitude of musculoskeletal injuries through injury surveillance. It is only by adopting this paradigm that methodological and intervention specificity can be achieved to meet the demands of distinct groups with the aim of injury prevention and control. (17). A systematic review by Fong et al. indicated that the ankle joint is the second most commonly injured joint in those who participate in sport related activities (29). Since the completion of this review, a number of epidemiological surveillance papers investigating ankle sprain injury in a variety of samples have been published.

Therefore, identifying the scope and magnitude of ankle sprain injury stands to be updated and advanced via the use of appropriate statistical techniques in meta-analysis of eligible studies. The aim of this systematic review and meta-analysis is to examine ankle sprain prevalence period and incidence rate unrestricted by sample activity context. This analysis will be limited to prospective studies only. Our main objectives are to determine if ankle sprain incidence rate and prevalence period is affected by age, gender and the nature of sporting activity. We will also consider whether incidence and prevalence figures are influenced by study quality. Such an analysis will meet the first criterion required to tackle issues of injury prevention and control. Surveillance of ankle sprain in a number of population types stands to elucidate the contrasting patterns of ankle sprain injury in a variety of settings.

2. Methodology

The study protocol was developed using the framework outlined in the guidelines provided by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyes) statement. (30)

2.1 Literature Search Strategy

In July 2012, we undertook a computerized literature search of the following databases from inception: Web of Science, CINAHL, Cochrane Central Register of Controlled Trials, PEDro, Embase, Pubmed and SportDiscus. The database search was further supplemented with a single related-citation search on PubMed (National Centre for Biotechnology Information, U.S. National Library of Medicine. Home page. http://www.ncbi.nlm.nih.gov/pubmed. Accessed July 2012)-this retrieved a set of articles closely related to ankle sprain injuries. The search strategy was designed with the purpose of extracting epidemiological studies of ankle sprain injury in multiple population groups. Recurrent sprain and chronic ankle instability are pathologies frequently described in the aforementioned investigations. This was accounted for in the formulation of the following search strategy:

Population-specific and patient-specific search terms were combined using Boolean operators as follows: (1) ankle OR “ankle joint”, (2) injury OR injuries OR strain OR strains OR sprain OR sprains OR rupture OR ruptures OR repeated OR multiple OR recurrent OR instability OR "recurrent instability" OR "chronic instability" OR “functional instability” OR “mechanical instability”, (3) "ankle instability" OR "chronic ankle sprain” (4) epidemiology OR epidemiologic OR epidemiological OR survey OR statistics OR pattern OR patterns OR incidence OR incidences OR prevalence OR prevalences (5) (1 AND [2 OR 3] AND 4).

The search strategy was limited to full text studies published in the English language. Published abstracts were followed up for full-text publication, but were not included as independent papers.

One investigator (CD) reviewed all the titles produced by the database searches, and retrieved suitable abstracts. Implied suitability via abstract review dictated the retrieval of full texts. These were included in the review if they fulfilled the required selection criteria.

2.2 Selection Criteria

No blinding of study author, place of publication, or results occurred. The following inclusion criteria were used:

(1) The study must report epidemiology findings of injuries sustained in an observed sample.
(2) The study must report ankle sprain injury with either incidence rate or prevalence period among the surveyed sample, or provide sufficient data from which these figures could be calculated.
(3) The study design must be prospective.

No restrictions were placed on the participant age, gender or activity level. Review articles and individual case studies were excluded. Abstracts from conferences were not reviewed for inclusion because of their limited availability in the electronic databases.

2.3 Assessment of Study Quality

Two authors (C.D & C.B) evaluated study quality, which gives an indication of risk of bias. Study quality was assessed using an adapted version of the STROBE guidelines for rating observational studies (31)-all included studies were rated on 11 specific criteria which were derived from items 5, 6, 7, 8, 9, 12, 14 and 15 of the original checklist (figure 1).
The observational studies were considered as having a low risk of bias if they were determined as high quality (score of ≥7/11) or a high risk of bias if they were low quality (≤6/11). Final study ratings for each reviewer were collated and examined for discrepancies. Any inter-rater disagreement was resolved by consensus decision. Once consensus was reached for all study ratings, overall quality scores were collated by summing those criteria, providing a score out of 11.

2.4 Data Management and Statistical Analysis

Three authors (C.D, C.B & E.D) extracted key data onto an Excel spread-sheet template. Studies were classified by injury focus (whether injuries of all types or ankle injuries in isolation were reported), sample demographics (region, age-group, period of completion, sample size, gender, context activity), method of diagnosis (independent trained healthcare worker, author or subject report) and duration (number of seasons). Data relating to prevalence period and incidence rate were recorded for the subgroups of gender (male; female), age (child; adolescent; adult), quality (high; low) and activity (field sports; ice & water sports; court sports; outdoor sports)

Prevalence period represents the ratio of the number of events (ankle sprains) existing in a population over a specified time to the study population in that time. Incidence rate is the ratio of the number of events commencing during a specified time to the average population during the same period of time.

$$Prevalence\ period = \frac{Sum\ of\ ankle\ sprains\ existing\ over\ a\ specified\ time}{Population\ at\ that\ time}$$

$$Incidence\ per\ 1000\ units\ of\ exposure = \frac{Sum\ of\ ankle\ sprains\ commencing\ over\ a\ specfified\ time}{Sum\ of\ exposure\ units\ for\ all\ included\ samples}\ x1000$$

Articles reporting incidence were divided according to the unit of exposure used (e.g. per thousand athlete exposures or per thousand hours). In situations where data was presented in other forms (e.g. per 10000 units of exposure), efforts were made to synthesize data by converting them to a common unit of exposure when possible. Cumulative incidence rate figures combined the units of athlete exposure and hours of exposure to provide a resultant value. In the presence of any unclear or missing data, authors were contacted by email for clarification.

2.4.1 Meta-Analysis

For each study, standard error and variance were calculated for prevalence period and incidence rate estimates. Individual study estimates were then pooled based on the following subgroups: gender, sport category, study quality and age.

The gender subgroup was classified as male or female based on a surveyed sample of 60-100% male or female subjects respectively. Age was classified by three broad categories: children (aged: 0 to ≤12 years); adolescent (aged: ≥13 to ≤17 years); adult (aged: ≥18 years). Study quality was classified into two categories: high quality (≥7/11) or low quality (≤6/11). Sport was categorised by field, indoor/court, ice/water and outdoor sports (table 1).

Studies were weighted by sample size and separate analyses were undertaken for prevalence period and incidence rate data. Data were then assessed for heterogeneity using Microsoft Excel 2010 (32), based on the Q test in conjunction with the I^2 statistic. The significance for Chi^2 was set at $P < 0.1$. The I^2 statistic was used to quantify inconsistency using the following formula $I^2 = [(Qdf\ )/Q] \times 100\%$, where Q is the Chi^2 statistic and df its degrees of freedom. I^2 values greater than 50% were considered to represent substantial heterogeneity (33). In cases were substantial heterogeneity were present, a random effects model was used for meta-analysis. Accordingly, prevalence and incidence were used to enable several forest plots. A 95% CI was used in the analysis. The horizontal bars in the plots represent the range of confidence interval (CI), and also give an indication of the study weight (smaller width=larger weight).

3. Results.

3.1 Search Strategy

The search strategy returned a total of 10524 articles for review. Articles were included based on a group consensus. Refer to figure 2 for information pertaining to the total number of studies screened, assessed for eligibility and included in the analysis (with reasons for exclusions at each stage). A total of 181 prospective epidemiology studies from 149 separate papers were included in the systematic review and meta-analyses (20, 34-179).

3.2 Methodological Quality

The average rating of all the included studies was 6.67/11 (6.94 for all the male studies, 7.41 for all the female studies and 5.81 for all the studies with mixed gender samples; 6.57 for all studies with only child samples, 7.56 for adolescent-only samples and 6.64 for adult-only samples). 116 studies were considered high quality (≥7/11), having a low risk of bias, and 65 were considered low quality (≤6/11), having a high risk of bias. Consensus was reached for all items on initial discussion. No studies were excluded from analysis based on the rating of methodological quality.

3.3 Characteristics of the Included Studies

Some studies consisted of entirely male (75) and female (44) samples, while a number of studies included mixed samples (36). 26 studies included mixed samples but did not report the distribution of males and females.

122 off the 181 studies had adult-only samples, 25 had adolescent-only samples and 11 children-only. A number of studies had mixed samples-adults, adolescents and children combined (10), adults and adolescents only (3) or children and adolescents only (4). 6 studies were unclear of their sample age demographics.

94 of the included studies reported injury as a function of exposure. 87 studies reported ankle sprain as a % of all injuries. Of the 94 studies that did report exposure, 42 reported ankle sprain per 1000 athlete exposures, 44 per 1000 hours, 5 per 1000 days, and 1 each per 1000 jumps, player games and person years. All except 16 of these 94 studies also reported ankle sprain period prevalence. Similarly, the nature of injury diagnosis differed substantially between studies. 153 studies used the diagnosis of an independent medical professional, 4 used that of the authors themselves, 4 used coaches, 11 used the subjects' own report and 7 used a mix of all.

173 studies reported on sporting populations and the remaining 8 included military populations. Twenty one (12%) papers included a surveyed sample of 0-100 participants, seventy five (41%) had 100-200 participants, nineteen (10%) had 500-1000 participants, seventeen (9%) had 1000-2000

participants, fourteen (8%) had 2000-5000 participants, twenty-five (14%) had 5000-10000 participants and 10 (6%) had over 10000 participants. A group of authors responsible for 13 of the included studies was contacted to provide clarification of their surveyed sample sizes.

The total number of sports analysed was 37. Sports were sub-classified into 4 categories (Table 1). Five papers reported re-sprains within the surveyed sample. Three of these five were surveying ankle sprain injuries in isolation (56, 63, 180) and two reported ankle sprains among all injuries (97, 181). For the purposes of prevalence period and incidence rate estimates, the total number of sprains/re-sprains were used in the prevalence period and incidence rate calculations.

3.4 Findings-Meta Analyses

Figures 3-9 and table 2 present pooled estimates (95% CI's) for each sub-group. There was a high degree of heterogeneity across studies within each of the subgroups ($p<0.01$), (Table 2) and random effects models were used in all cases.

Indoor and court sports were the highest risk activity, based on cumulative incidence and prevalence figures, whereas outdoor sports presented the lowest risk activity subgroup. Females were more likely to sustain an ankle sprain than males, and children more likely than adolescents and adults.

3.4.1 Sport

Pooled cumulative incidence was 7 ankle sprains per 1000 exposures (CI: 6.8 to 7.1) for court sports, 3.7 per 1000 exposures (CI: 3.3 to 4.17) for ice/water sports, 1.0 per 1000 exposures (CI: 0.9 to 1.05) for field sports and 0.88 per 1000 exposures (CI: 0.73 to 1.02) for outdoor sports -see figure 6. There was a high degree of heterogeneity in all subgroups (Table 2). We found similar findings when incidence data was reported based exposures per 1000 hours and per 1000A/E (Table 2).

Pooled Prevalence of ankle sprain for indoor/court sports was 12.17% (CI: 12.01 to 12.33), 4.36% for water/ice sports (CI: 3.92 to 4.79), 11.3% for field based sports (CI: 11.15 to 11.44) and 11.65% for outdoor pursuits sports (CI: 11.33 to 11.97).

3.4.2 Study Quality

High quality (≥7/11) studies had a pooled cumulative incidence rate of 11.55 per 1000 exposures (CI: +/-0.18) and a pooled prevalence period of 11.88% [CI: 10.56 to 13.19]. Pooled incidence rate figures were reduced in low quality (≤6/11) studies with 0.54 ankle sprains per 1000 exposures (CI: 0.49 to 0.59 and a pooled prevalence of 11.18% [CI: 6.59 to 15.78]). See figure 5.

3.4.3 Gender

Meta-analysis for gender revealed a cumulative incidence rate of 13.6 per 1000 exposures (CI: 13.25 to 13.94) for females and 6.94 per 1000 exposures (CI: 6.8 to 7.09) for males. Incidence figures for gender were also calculated separately per 1000 hours and per 1000 athlete exposures (Table 2). Pooled prevalence of ankle sprains was 10.55% (CI: 10.84 to 11.15) in females and 10.99% (CI: 10.84 to 11.15) for males. See figure 4.

3.4.4 Age

Meta-analysis for age sub-groups revealed a pooled cumulative incidence of 0.72 per 1000 exposures (CI: 0.67 to 0.77) in adults, 1.94 (CI: 1.73 to 2.14) for adolescents and 2.85 (CI: 2.51 to 3.19) for children. 12.62% of all injuries were ankle sprains in children (CI: 11.81 to 13.43), 10.55% in adolescents (CI: 9.92 to 11.17) and 11.41% (CI: 11.28 to 11.54) in adults. See figure 3.

3.4.5 Sprain Diagnosis

11 of the 181 included studies reported specific diagnoses pertaining to the type of ankle sprain incurred by the surveyed sample (Lateral, medial or syndesmotic). 4 of these studies were investigating lateral/inversion sprains in isolation; 1 reported incidence as a percentage of all injuries (and not by specific sprain diagnosis) and therefore could not be considered for this aspect of analysis (Table 3).

Weighted percentage was calculated using the following formula:

$$Weighted\ percentage\left(ankle\,sprain\,type\right)=\frac{\sum_{i=1}^{n}total\,ankle\,sprains\times percentage\left(ankle\,sprain\,type\right)}{\sum_{i=1}^{n}total\,ankle\,sprains}$$

Data collected from the 6 included studies identified a weighted prevalence period of 15.31 for lateral ankle sprains. Lateral ankle sprain was also the most commonly incurred type of ankle sprain based on incidence rate units of athlete exposure, years and hours when compared to medial and syndesmotic ankle sprains (Table 7).

3.4.6 Military Populations

7 studies with entirely military samples were included in the analysis. Each paper surveying military population subgroups employed unique methods of reporting exposure. The risk of ankle sprain was determined per 1000 (parachute) jumps (3.8 lateral ankle sprains per 1000 jumps; 1.08 syndesmotic sprains per 1000 jumps), per 1000 person-years (58.4 per 1000 person years) and as a percentage- 2.8% in one study, and 17.7% in another.

4. Discussion.

The search strategy identified data pertaining to the incidence rate and prevalence period of ankle sprain in a variety of settings from 181 prospective studies in 149 separate research papers. Injury patterns were reported for 37 different sports, and military populations (174 studies were sports related and 7 were military related). Separate meta-analyses were completed for incidence rate and prevalence period data for the subgroups of age, gender, sport and study quality, thus providing evidence for the highest risk activities and populations. Results of these analyses identify the scope and magnitude of ankle sprain injury, thus allowing for methodological and intervention specificity to meet the demands of distinct groups.

Findings from this review revealed a wide variation in ankle sprain incidence estimates, and meta-analyses indicate that females and children were the highest risk population subgroups for sustaining an ankle sprain, with indoor and court sports the highest risk activity. Furthermore, studies with high bias underestimated the risk of ankle sprain. The meta-analysis revealed minimal variation in ankle sprain prevalence related to the sample subgroups. The prevalence of ankle sprain was equal between males and females, between studies of high and low bias, and between age sub-groups. Ice and water sports had the lowest overall prevalence within the sport subcategory.

We devised a rating system for the purpose of determining the methodological quality of the included studies. Assessing the quality of observational epidemiology research has been the focus for a number of research groups (182-186). Hagglund et al. (187), outline key attributes that an epidemiological study should possess, recommending that the design should be prospective, with a clear definition of injury (prospective studies provide a more realistic representation of injury patterns as a result of superior experimental control and data collection techniques), whereby exposure data is collected over the course of at least one entire season (187). Our rating system was a modified version of the STROBE guidelines for rating observational studies (31), and was based on 11 separate variables. We considered this checklist of 11 items essential for good reporting of these observational studies, thus facilitating a feasible means to assess the quality and potential bias of 181 studies.

Meta-analysis of the cumulative incidence rate and prevalence period data by study quality revealed clear differences between high and low quality papers. One hundred sixteen studies were considered high quality and 65 were considered low quality based on this system. Only 2 studies scored full marks on the criteria outlined, with 9 studies scoring 10/11. The pooled estimate of ankle sprain incidence rate in low quality studies (0.54 per 1000 cumulative units of exposure) was 21 times less than that of high quality studies (11.55 per 1000 cumulative units of exposure). Very few of the included studies adhered to the criteria described by Hagglund et al. (187). A potential reason for the tendency of lower quality studies (as measured by our rating system) to underestimate the incidence rate of ankle sprain injury could relate to the absence of a medical professional to appropriately diagnose potential injuries. Indeed, 28 of the included studies did not use an independent medical professional for the diagnosis of injuries in the surveyed sample, with coaches, authors or subjects themselves reporting injury, raising concerns over internal validity secondary to investigator error through reporting bias. Additionally, the lack of a qualified medical professional will corrupt the definition and classification of injury (figure 2; criteria 1 & 3). Considering the high rate of morbidity following an acute ankle sprain (2) (3), the consequences of this methodological inadequacy could theoretically put the injured population at risk of prolonged lifestyle-limiting symptoms secondary to the absence of astute intervention in the acute phase of injury.

Findings of the meta-analysis of cumulative incidence rate and prevalence period by gender elucidated a higher risk of ankle sprain in females compared to males. Of the 94 studies that did report exposure figures for gender, 42 reported ankle sprain per 1000 athlete exposures and 44 reported ankle sprain per 1000 hours, giving a cumulative incidence rate of 13.6 sprains per 1000 exposures for females versus 6.94 per 1000 exposures for males. Gender was the only sub-group whereby sufficient data existed to analyse incidence rate per cumulative exposures, and per hour and athlete exposure separately (table 2). Thirty six of the included studies had mixed gender samples, reporting the exact sample size with specific details of the number of male and female participants. Fifteen of these 36 studies reported injury as a function of exposure (hours or athlete exposures) 6 reported no differences in injury rates between males and females (64) (188) (80) (189) (190) (142), 2 reported a higher risk of injury for men (57) (115) and 2 a higher risk for women (191, 192). Two papers (5 studies) did not report separate injury data for males and females (193) (107) [4 separate studies]. Differences in study design, such as definition of the injury or different data collection methods, may explain these contradictory results.

Women have been reported to sustain more knee joint injuries than men, especially ACL injuries (194). However, to the authors' knowledge, this is the first meta-analysis to determine a higher incidence rate of ankle sprain in females compared to males. Efforts to prevent ankle sprain injury in females should therefore focus on the factors that increase the susceptibility of women to injury and furthermore to develop interventions to facilitate the prevention of these injuries. The anatomical (195-197), hormonal (197-199) and neuromuscular (199, 200) (201) differences that exist between the sexes (202) do not necessarily explain the observed increased risk of ankle sprain in females; this analysis serves to expose possible differences in injury risks between the genders, but can only hypothesize as to their cause. Future research could focus on whether gender differences are activity-specific, and thus related to training behaviours, or whether the difference in risk are related to anatomical or physiological gender differences.

The existence of a higher risk of ankle sprain in children compared to adolescents (2.85 versus 1.94 per 1000 exposures) and adolescents compared to adults (1.94 versus 0.72 per 1000 exposures) as demonstrated by the meta analysis (figure 3) is a significant finding, as injury at a young age can negatively affect a child's ability to participate in activity and may trigger long-term sequelae such as early onset of osteoarthritis (203) (204). None of the included studies surveyed a sample of children, adolescents and adults giving specific data relating to exposure and number of ankle sprains for each distinct age group. Childhood and adolescence are considered to be periods of development in which the individual is at an amplified risk of injury (205). Appropriate neuromuscular control is ubiquitous to the successful completion of dynamic sporting manoeuvres. Whereas preferred patterns of coordination are established in adults ((206, 207), young children do not show the same consistency in patterns of coordination (208). Similarly, increased 'motor awkwardness' during adolescence may result from an immaturely developed sensorimotor system, thus increasing the challenge of even simple motor control tasks (204). The increased risk of ankle sprain in children and adolescents compared to adults could therefore be the result of a developing dynamic motor control system exploring the state space of movement patterns prior to settling in a number of preferred movement 'attractor' states (209, 210).

Meta-analysis by sport category revealed that indoor and court sports (7 per 1000 cumulative exposures) had the highest risk of ankle sprain followed by ice and water sports (3.7 per 1000 cumulative exposures), field sports (0.9 per 1000 exposures) and finally outdoor sports (0.87 per 1000 exposures). Pooled prevalence estimates revealed that ice/water sports had the lowest prevalence of ankle sprains of the 4 sub-groups of sport. The high incidence rate combined with low prevalence period can be explained by a higher overall incidence of injury in these sports but a greater tendency toward shoulder, knee and predominantly head injuries (34, 35).

Several studies not included in our analysis have previously reported that ankle sprain is one of the most common, if not the most common, injury in indoor and court sports such as basketball (211) (212-217), volleyball (218-221), tennis (222-224) and wrestling (225-227), thus explaining the trend for a higher risk of ankle sprain in indoor/court sports. There is also an abundance of literature investigating injury epidemiology in field based sports (98 of the studies included in our analysis were field-based focused). The high risk of ankle sprain has promoted an appropriate research response, as a large number of methodologically rigorous randomised control trials now exist investigating the effect of different interventions in injury rehabilitation (54, 228-231) and prevention (232-234).

In contrast to the clear disparity illustrated by the meta-analyses of incidence rate estimates between the subcategories of quality, gender, age and sport, meta-analyses of the same sub-ategories elucidated very similar prevalence period estimates.

Prevalence is a measure independent of exposure. Ninety-seven of 181 studies reported injury as a function of exposure. By incorporating exposure in the calculation of injury rates across a surveyed sample, incidence rate determines the number of events of interest occurring per projected amount of activity undertaken-thus providing an estimation of risk. In contrast, prevalence is a ratio of the number of the surveyed sample incurring an ankle sprain to the total sample, and is independent to the amount of activity undertaken. A possible reason for the contrasting findings between incidence rate and prevalence period is that in a given group or activity the proportion of people who sustain ankle sprains is similar, but the introduction of exposure separates these groups via the determination of risk per unit of activity completed; females and children are at a higher risk of sustaining an ankle sprain per exposure in the same activities compared to males or adolescents and adults, respectively. The disparity of incidence rate estimates by study quality and the lack thereof regarding prevalence period estimates cannot however be explained by the introduction of a unit of exposure. Rather, we propose that a study of higher quality will be predisposed to a more accurate determination of injury as a function of exposure, both in the correct and appropriate diagnosis of injury and the evaluation of levels of exposure for each surveyed subject.

Findings from the systematic review indicate that of the 3 most common clinical classifications of ankle sprain, lateral ankle sprain presents the greatest risk, followed by syndesmotic (high) ankle sprain and finally deltoid (medial) ligament sprain (based on incidence rate figures for exposure units of athlete exposure, year and hour)-see table 7. Only 6 of the 181 included studies reported sprain diagnosis without focusing on ankle sprain injury in isolation, giving sufficient data to determine incidence rate and/or prevalence period (45, 164, 235-237). Both a muscle driven computer simulation (238) and a cadaveric model (239)) have shown that plantarflexion and inversion increase strain on the lateral ligaments of the ankle. The higher risk of sustaining a lateral ligament sprain can be attributed to relative lower load to failure rate of the lateral ligamentous complex when compared to the medial and syndesmotic ligament groups (240) and reduced arthrokinematic restriction credited to decreased contact of the talus within the ankle mortise in the plantar-flexed and inverted position (241).

The systematic review identified that injury surveillance in military populations utilised varying measures of exposure, limiting the pooling of data. Seven studies were included in the review investigating military samples (43, 45, 242-246). Ankle sprain was reported per 1000 (parachute) jumps (3.8 lateral ankle sprains per 1000 jumps; 1.08 syndesmotic sprains per 1000 jumps) (45), per 1000 person-years (58.4 per 1000 person years) (166) and as a percentage, 2.8% in one study (43), and 17.7% in another (20).

These data outline the extent to which ankle sprain injury is a persistent and primary health concern for military populations-an abundance of available military epidemiology research also exists that didn't meet our inclusion criteria. Six papers surveying military populations were excluded from our analysis as they were retrospective in design (19, 247-251). In accordance with this, several intervention studies have been conducted with the primary aim of reducing in the incidence of ankle sprains in military populations (45, 252).

This is the first systematic review to incorporate meta-analyses of data from epidemiological studies relating to ankle sprain injury. A similar review was published in 2007 and included studies from 1977 to 2005 (29). Apart from the incorporation of meta-analyses of injury data, several key factors separate this study from the study by Fong et al (2007). The review by Fong et al. did not include military populations, did not use a rating system for the included studies and did not report specific data relating to sprain diagnosis. Another key difference is that for studies that reported the injury incidence for several body sites, the combined percentages were divided evenly for each included body site, thus introducing a critical source of bias. Furthermore, the search undertaken for the present study was completed in July 2012, and as such adds over 6 years of prospective evidence to the results presented in the review by Fong et al (2007).

Despite the strengths of this systematic review and meta-analyses, it is important to consider several limitations when interpreting the results. Studies were not included if they were published in non-English languages, which may influence the outcomes of our analyses, despite the probability that authors of high quality surveys would aim for publication in high-impact journals published in the English language in the pursuit of superior dissemination of output data.

It was also our intention to adhere to the framework outlined in the guidelines provided by the PRISMA statement (30). With specific reference to criteria 15 relating to the assessment of publication bias, we encountered difficulty in assessing and establishing the possibility of selective reporting of outcomes by individual studies. It was unfeasible to check if all the included 149 papers had published a protocol prior to their collection of data and compare the predicted outcomes to those published to determine any discrepancy. Furthermore, as required by our outlined inclusion criteria, all included studies reported the primary outcome – incidence rate or prevalence period, so there is no risk of selective reporting at an individual study level. Funnel plotting to determine cumulative risk of publication bias was considered to be more applicable to reviews involving interventional type studies, rather than descriptive epidemiology.

A number of methodological issues were identified among the included studies that should be addressed in future observational studies. Only 1 study scored full marks on the checklist developed for this analysis. We would recommend that epidemiological studies standardize their reporting according to the STROBE guidelines for reporting observational studies (31), thus allowing for proper interpretation of the available data to produce better estimates of incidence rate and prevalence period of ankle sprain injury (253).

5. Conclusions.

We found further evidence that individuals can incur an ankle sprain during various physical activity and sport activities. Female gender, lower age and athletes competing in indoor and court sports are the subgroups most at risk of ankle sprain. Lower quality studies are more likely to underestimate the risk of ankle sprain. Participants were at a significantly higher risk of sustaining a lateral ankle sprain compared with syndesmotic and medial ankle sprains. This analysis provides valuable information for researchers internationally in studies of epidemiology and intervention.

Table 1: The sub-categories of sport

Field Sports	Indoor + Court Sports	Ice/Water Sports	Outdoor Sports
American Football	Aeroball	Skiing	Orienteering
Australian Football	Basketball	Ice Hockey	Parachuting
Baseball	Cheerleading	Ice skating	Rock climbing
Cricket	Dance	Kitesurfing	Small wheel devices
Field Hockey	Floorball	Windsurfing	Trampoline
Gaelic Football	Gymnastics		Track and field
Lacrosse	Handball		Ultimate Frisbee.
Rugby	Netball		
Softball	Volleyball		
	Pole vault		
	Teamgym		
	Tennis		
	Wrestling		

<u>Table 2:</u> Pooled random effects estimates for ankle sprain incidence rate and prevalence period for the subgroups of study quality, gender, age and sport (95% CI).

	Cumulative Incidence per 1000 Exposures 8297.1. p<0.01 = 98.01%. n=98	**Incidence per 1000 Athlete Exposures**	**Incidence per 1000 Hours**	**Prevalence** 186945.32; p<0.01; = to 99.96%) n=160
High χ^2 17160.68. p<0.01 I^2 = 99.49%	0.12 (CI: 0.11 to 0.12). n=85			11.88% (CI: 10.56 to 13.19). n=116
Low χ^2 5171.39; p<0.01 I^2 = 99.07%	0.54 (CI: 0.49 to 0.59). n=12			11.19% (CI: 6.59 to 15.78). n=65
Male χ^2 14766.76; p<0.01 I^2 = 98.57%	6.94 (CI: 6.8 to 7.09). n=50	1.05 (CI: 0.78 to 1.31). n=24	6.16 (5.61 to 6.71). n=26	10.99% (CI: 10.84 to 11.15). n=86
Female χ^2 3337.87; p<0.01 I^2 = 98.71%	13.6 (CI: 13.25 to 13.94). n=32	1.17 (CI: 0.83 to 1.51). n=20	2.71 (CI: 1.71 to 3.71). n=12	10.55% (CI: 10.84 to 11.15). n=49
Child Q: 220.4; p<0.01 I^2 = 96.37%	2.85 (CI: 2.51 to 3.19). n=11			12.62% (CI: 11.81 to 13.43). n=15
Adolescent Q: 945.26; p<0.01 I^2 = 98.1%	1.94 (CI: 1.73 to 2.14). n=24			10.55% (CI: 9.92 to 11.17). n=32
Adult Q: 28813.04; p<0.01 I^2 = 99.69%	0.72 (CI: 0.67 to 0.77). n=97			11.41% (CI: 11.28 to 11.54). n=122
Field Sports Q: 19756.74; p<0.01 I^2 = 99.63%	1 (CI: 0.95 to 1.05). n=63	1.18 (CI: 0.86 to 1.50). n=26	3.85 (CI: 3.45 to 4.24). n=37	11.3% (CI: 11.15 to 11.44). n=101
Indoor/Court Sports Q: 6017.52; p<0.01 I^2 = 99.4%	7 (CI: 6.82 to 7.18). n=23	1.37 (CI: 1.05 to 1.7). n=16	4.9 (CI: 3.3 to 6.5). n=7	12.17% (CI: 12.01 to 12.33). n=44
Ice/Water Sports Q: 119.19; p<0.01 I^2 = 92.44%	3.74 (CI: 3.3 to 4.17). n=9	0.47 (CI: 0.22 to 0.71). n=6	0.5 (CI: 0.25 to 0.7). n=3	4.36% (CI:3.92 to 4.79). n=14
Outdoor Sports Q: 315.61; p<0.01 I^2 = 97.46%	0.88 (CI: 0.73 to 1.02). n=5			11.65% (CI: 11.33 to 11.97). n=13

Table 3: The incidences of lateral, medial and syndesmotic ankle sprain according to available data.

Diagnosis	Weighted prevalence period %	Incidence Per 1000:	Athlete exposures	Jumps	Days	Years	Hours
LATERAL	15.31		0.93	3.8	0.85	52.98	0.49
MEDIAL			0.06			2.19	0.2
SYNDESMOTIC			0.38	1.08		3.21	0.11

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<u>Table 1:</u> The sub-categories of sport

Field Sports	Indoor + Court Sports	Ice/Water Sports	Outdoor Sports
American Football	Aeroball	Skiing	Orienteering
Australian Football	Basketball	Ice Hockey	Parachuting
Baseball	Cheerleading	Ice skating	Rock climbing
Cricket	Dance	Kitesurfing	Small wheel devices
Field Hockey	Floorball	Windsurfing	Trampoline
Gaelic Football	Gymnastics		Track and field
Lacrosse	Handball		Ultimate Frisbee.
Rugby	Netball		
Softball	Volleyball		
	Pole vault		
	Teamgym		
	Tennis		
	Wrestling		

Table 2
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Table 2: Pooled random effects estimates for ankle sprain incidence rate and prevalence period for the subgroups of study quality, gender, age and sport (95% CI).

	Cumulative Incidence per 1000 Exposures 8297.1. *p*<0.01 = 98.01%. n=98	**Incidence per 1000 Athlete Exposures**	**Incidence per 1000 Hours**	**Prevalence** 186945.32; *p*<0.01; = to 99.96%) n=160
High χ^2 17160.68. *p*<0.01 I^2 = 99.49%	0.12 (CI: 0.11 to 0.12). n=85			11.88% (CI: 10.56 to 13.19). n=116
Low χ^2 5171.39; *p*<0.01 I^2 = 99.07%	0.54 (CI: 0.49 to 0.59). n=12			11.19% (CI: 6.59 to 15.78). n=65
Male χ^2 14766.76; *p*<0.01 I^2 = 98.57%	6.94 (CI: 6.8 to 7.09). n=50	1.05 (CI: 0.78 to 1.31). n=24	6.16 (5.61 to 6.71). n=26	10.99% (CI: 10.84 to 11.15). n=86
Female χ^2 3337.87; *p*<0.01 I^2 = 98.71%	13.6 (CI: 13.25 to 13.94). n=32	1.17 (CI: 0.83 to 1.51). n=20	2.71 (CI: 1.71 to 3.71). n=12	10.55% (CI: 10.84 to 11.15). n=49
Child Q: 220.4; *p*<0.01 I^2 = 96.37%	2.85 (CI: 2.51 to 3.19). n=11			12.62% (CI: 11.81 to 13.43). n=15
Adolescent Q: 945.26; *p*<0.01 I^2 = 98.1%	1.94 (CI: 1.73 to 2.14). n=24			10.55% (CI: 9.92 to 11.17). n=32
Adult Q: 28813.04; *p*<0.01 I^2 = 99.69%	0.72 (CI: 0.67 to 0.77). n=97			11.41% (CI: 11.28 to 11.54). n=122
Field Sports Q: 19756.74; *p*<0.01 I^2 = 99.63%	1 (CI: 0.95 to 1.05). n=63	1.18 (CI: 0.86 to 1.50). n=26	3.85 (CI: 3.45 to 4.24). n=37	11.3% (CI: 11.15 to 11.44). n=101
Indoor/Court Sports Q: 6017.52; *p*<0.01 I^2 = 99.4%	7 (CI: 6.82 to 7.18). n=23	1.37 (CI: 1.05 to 1.7). n=16	4.9 (CI: 3.3 to 6.5). n=7	12.17% (CI: 12.01 to 12.33). n=44
Ice/Water Sports Q: 119.19; *p*<0.01 I^2 = 92.44%	3.74 (CI: 3.3 to 4.17). n=9	0.47 (CI: 0.22 to 0.71). n=6	0.5 (CI: 0.25 to 0.7). n=3	4.36% (CI:3.92 to 4.79). n=14
Outdoor Sports Q: 315.61; *p*<0.01 I^2 = 97.46%	0.88 (CI: 0.73 to 1.02). n=5			11.65% (CI: 11.33 to 11.97). n=13

<u>Table 3:</u> The incidences of lateral, medial and syndesmotic ankle sprain according to available data.

Diagnosis	Weighted prevalence period %	Incidence Per 1000:	Athlete exposures	Jumps	Days	Years	Hours
LATERAL	15.31		0.93	3.8	0.85	52.98	0.49
MEDIAL			0.06			2.19	0.2
SYNDESMOTIC			0.38	1.08		3.21	0.11

Figure 1
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Materials and Methods.	
1. Describe the setting or participating locations.	/1
2. Describe relevant dates (period of recruitment, exposure, follow-up, data collection).	/1
3. Statement concerning institutional review board approval and consent provided.	/1
4. Give the inclusion and exclusion criteria.	/1
5. Describe ankle injury history.	/1
6. Describe methods of follow-up.	/1
Data Sources/Measurement.	
1. Provide a definition of injury.	/1
2. Verification of injury by *independent* medical professional.	/1
3. Classification of injury (grade, medial / lateral).	/1
4. Indicate the number of participants with missing data and explain how this was addressed.	/1
5. Exposure data measured and presented.	/1
Final Score:	**/11**

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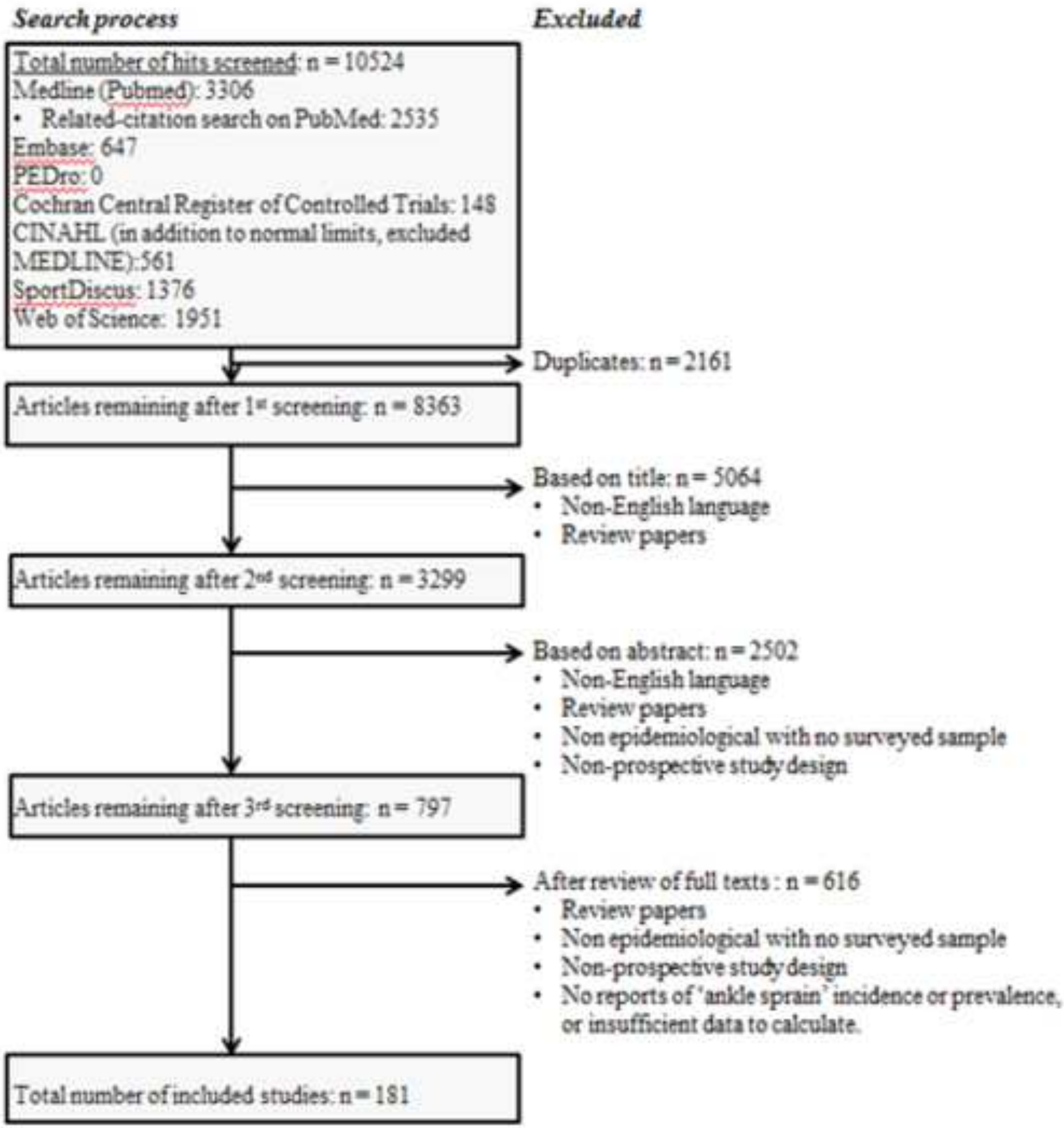

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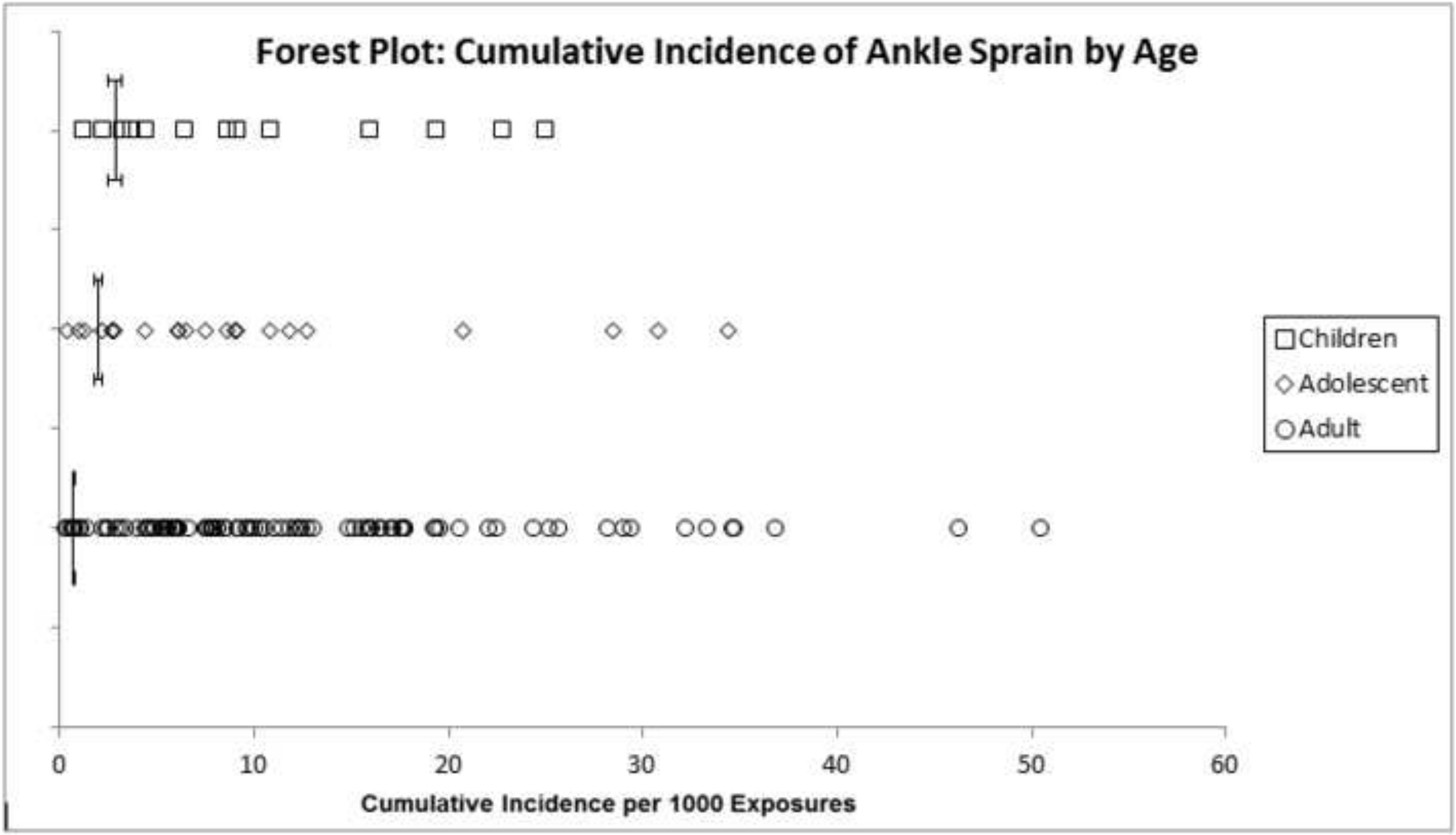

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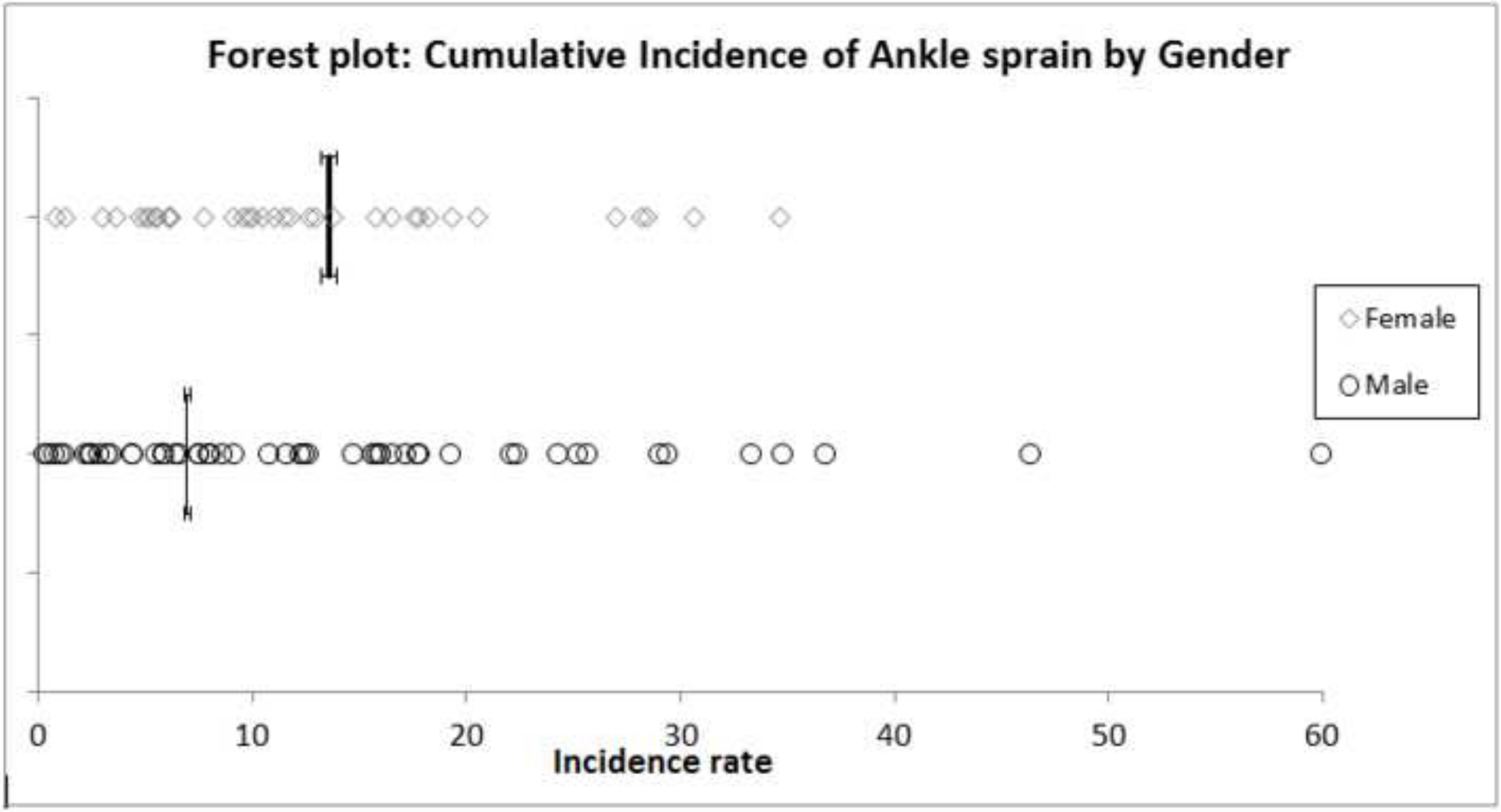

Figure 5

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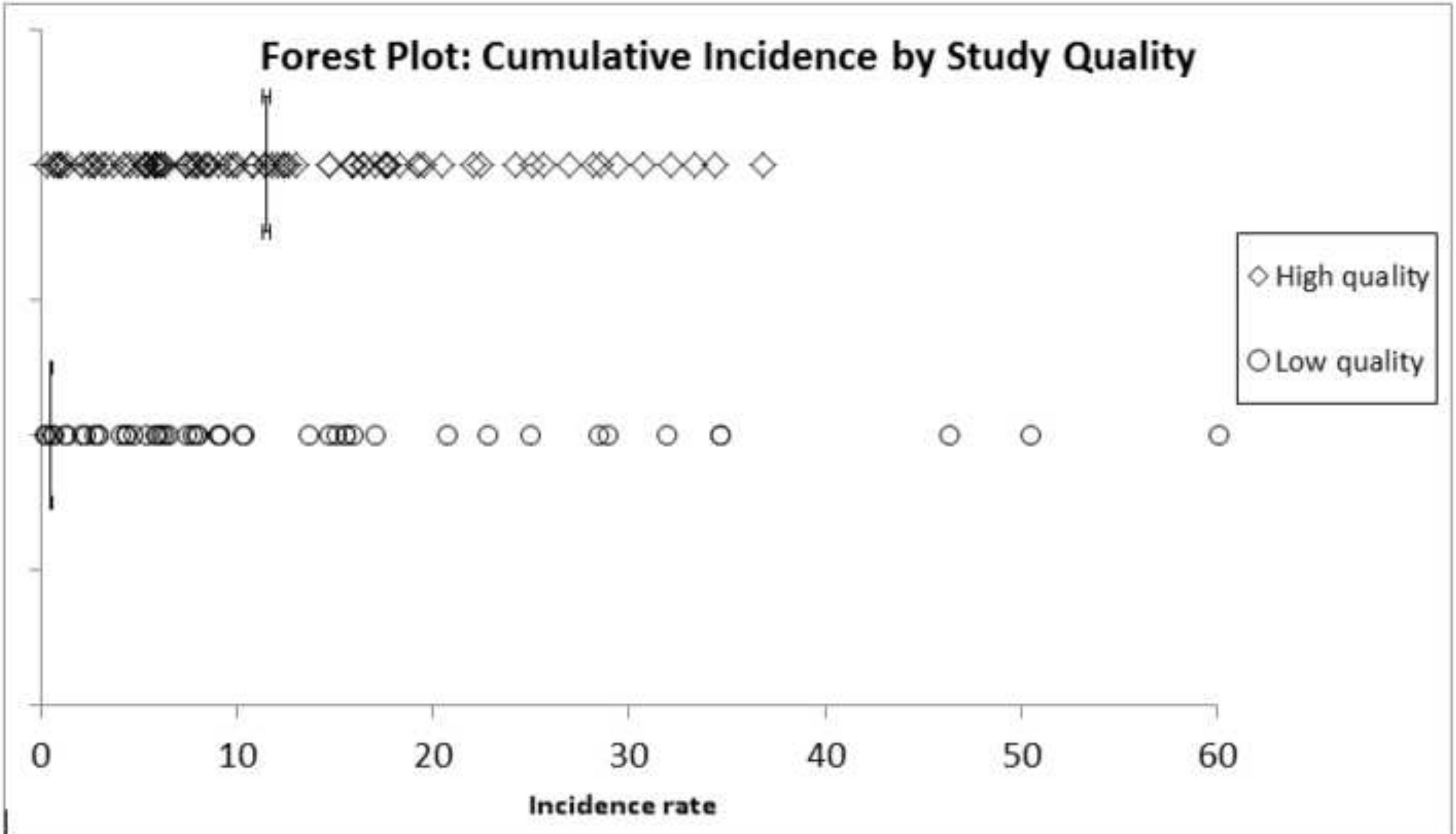

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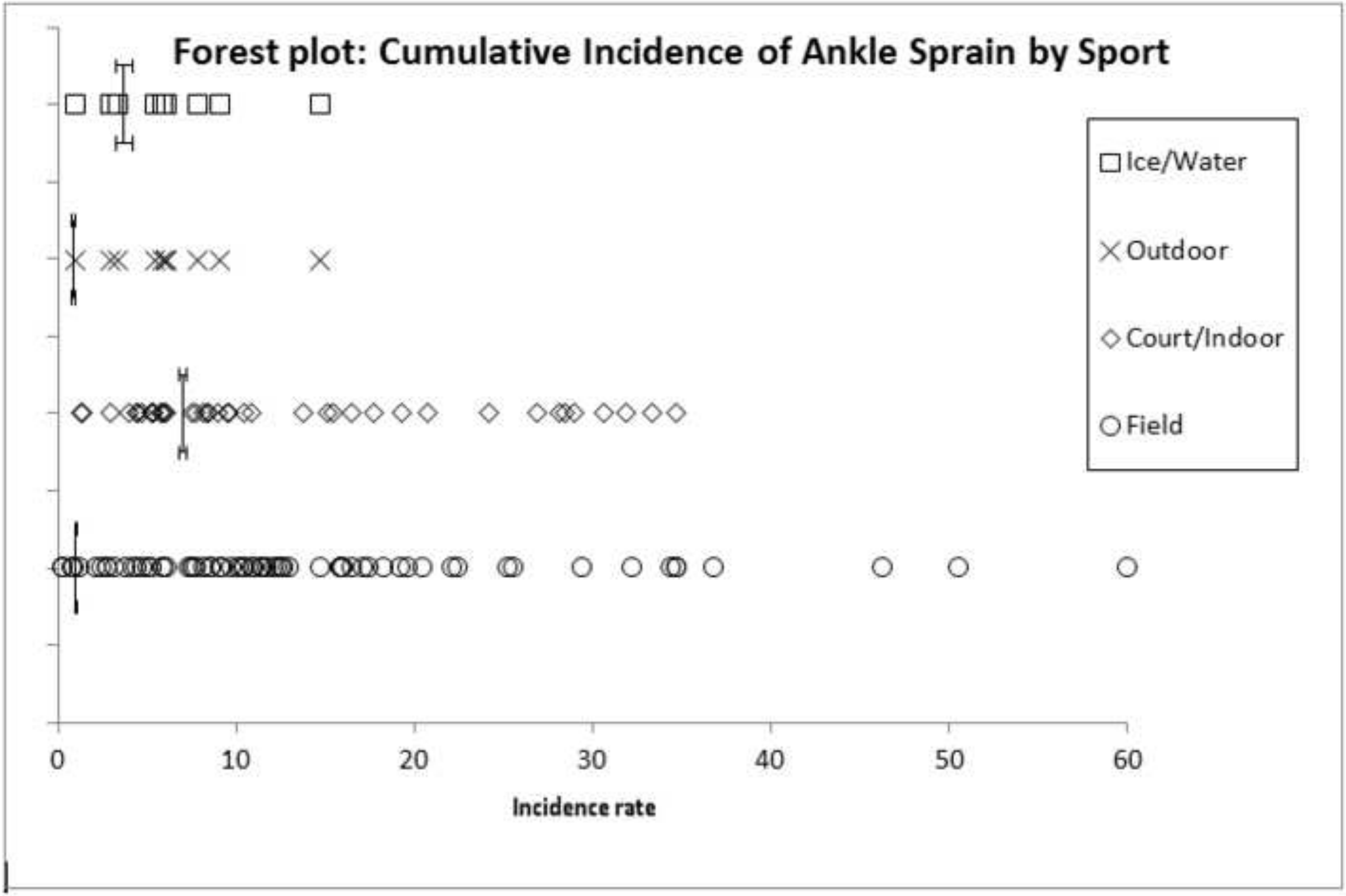

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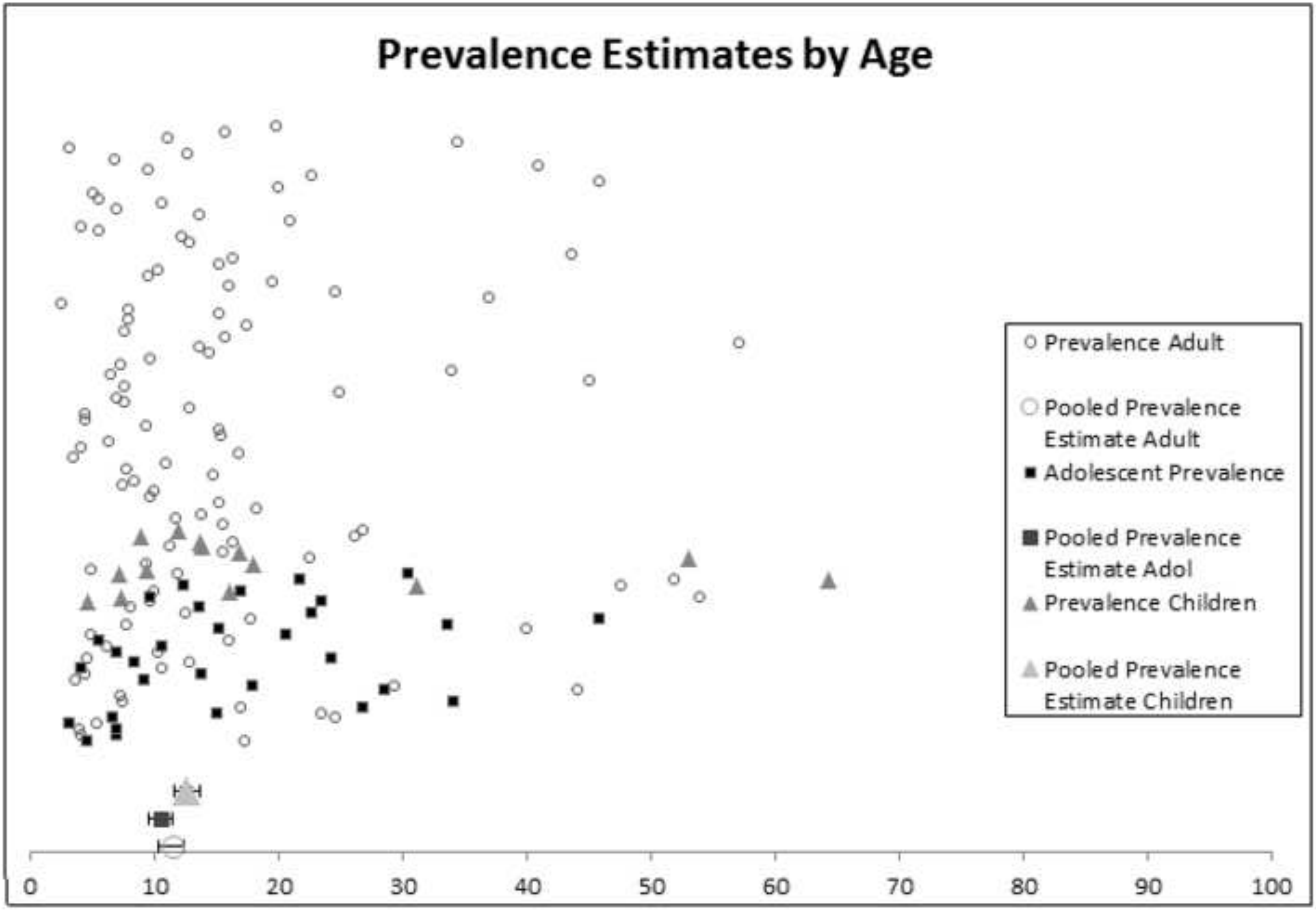

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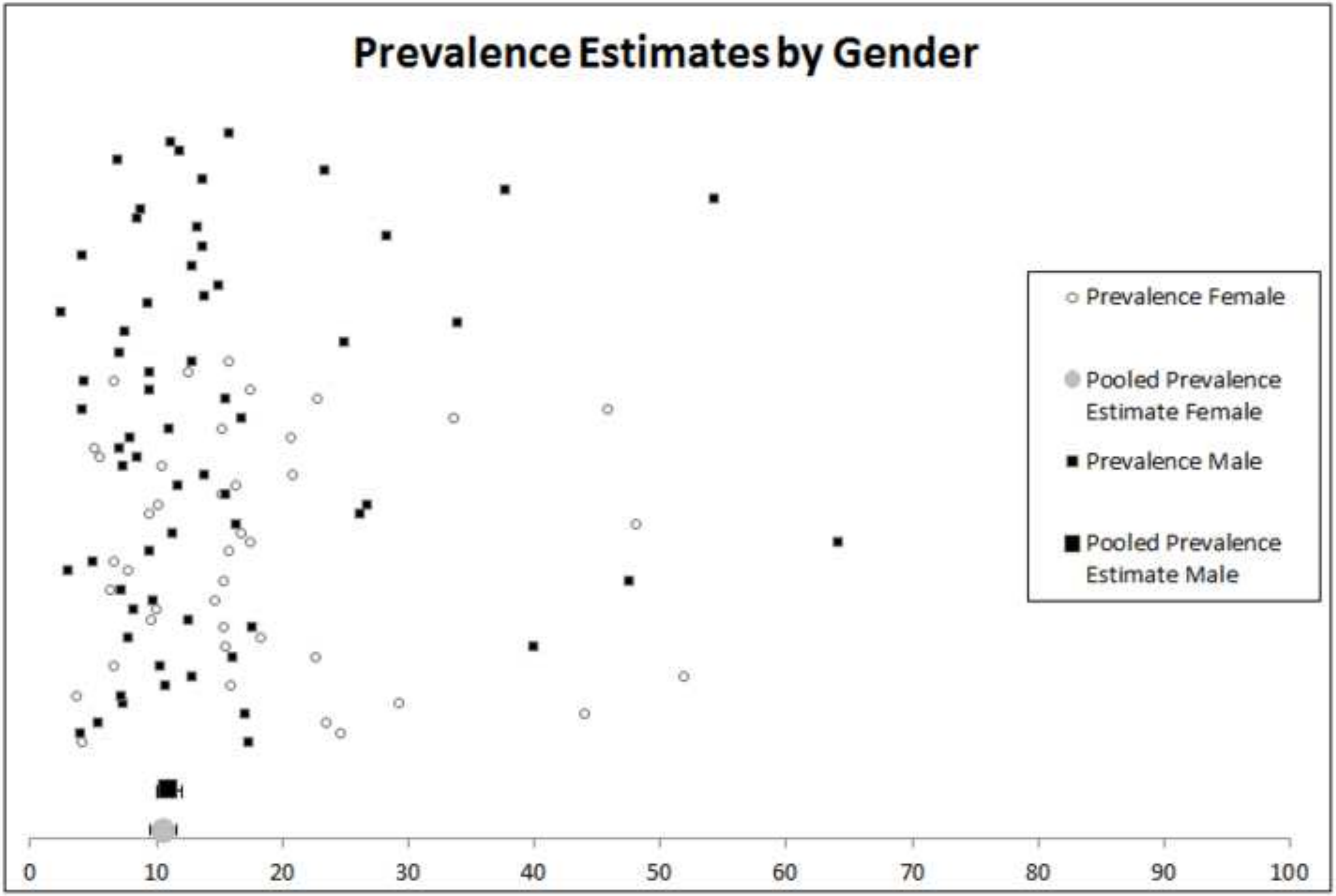

Figure 9

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