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Invited Review

# Meta-analysis of risk factors for racehorse catastrophic musculoskeletal injury in flat racing

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ABSTRACT

Studies of racehorse injury or fatality in various countries have identified common, and in some cases conflicting, risk factors. We conducted a systematic search of the relevant literature published from 1990 to 2017. Peer-reviewed articles were included if they reported the incidence of fatal or catastrophic musculoskeletal injury (CMI) in Thoroughbred flat races ($n = 21$) or risk factors for CMI ($n = 65$). Pooled effect sizes were estimated using the random-effects DerSimonian–Laird model. The pooled incidence of CMI was 1.17 (95% confidence interval 0.90, 1.44) per 1000 race starts. Almost 300 factors have been investigated in epidemiological studies for potential associations with CMI. Factors found to have consistent evidence of increasing risk of CMI are: (1) Horse-level factors such as older horse age and age at first start, male sex, and higher race class or lower claiming price; (2) Race-level factors such as firmer track conditions on turf and wetter conditions on dirt, longer race distance, and a greater number of starters; and (3) Management-related factors including more time since previous start, greater number of starts, longer career length, issues identified at pre-race examination, previous injury, and recent administration of medication or injections. Studies investigating recent cumulative distance of high-speed exercise were conflicting and suggestive of at least two mechanisms of injury related to the accumulation of bone damage: (1) In well adapted bone following a period of intense training; and (2) In poorly adapted bone at relatively low levels of training intensity. Future studies should evaluate success of interventions and mechanisms for injury.



## Introduction

There have been several reviews of the epidemiology of racehorse musculoskeletal injury (MSI) that summarised the incidence of injury or fatality in various countries, and identified common and conflicting risk factors (Riggs, 2002; Stover, 2003; Parkin, 2007, 2008; Clegg, 2011; Verheyen, 2013; Maeda et al., 2016). Issues raised by these reviews included different case definitions of injury or fatality, lack of quantification of risk, inconsistency in reporting of risk factors, and failure to account for the multifactorial nature of injuries in epidemiological modelling. A history of epidemiological studies of racehorse injuries also detailed the progression from the late 1960's commencing with largely descriptive studies, through univariable studies of associations, to today's more advanced multi-level multivariable models (Parkin, 2008).

Evidence-based research leading to strategies that improve racehorse welfare and rider safety is required. Meta-analysis is a means of summarising the evidence-base using systematic statistical methods (Egger et al., 2001). We aimed to conduct a meta-analysis that provides a consolidated resource for assessing findings from new studies with those historically, to identify gaps in reporting of epidemiological studies that make it difficult to compare results, and to provide the basis for a consensus statement on future reporting of racehorse injury epidemiological studies. We expected considerable heterogeneity across studies due to differences in racehorse populations internationally, due to differences in study design (e.g. case-control versus cohort studies), and differences in assessment of outcomes (e.g. differences in effect size) (Stroup et al., 2000).

## Materials and methods

### *Search strategy and selection criteria*

We conducted a systematic search of relevant literature identified in previous reviews of racehorse injury (Riggs, 2002; Stover, 2003; Parkin, 2007, 2008; Clegg, 2011; Verheyen, 2013; Maeda et al., 2016), and a Scopus and Google Scholar search

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of literature published between 1 January 1990 and 1 November 2017. The title and abstract of original or review articles (in English) were searched for three term categories. These terms were combined using the Boolean operator 'AND'. They included keywords indicating the term (1) 'Horse'; including horse OR equine OR Thoroughbred OR racehorse* OR racing; (2) 'Injury'; including injur* OR fatal OR non-fatal OR nonfatal OR catastrophic OR fracture*; and (3) 'Epidemiology'; including epidemiolog* OR risk OR predict* OR model* OR univariable OR multivariable OR regression. Two investigators (PLH; AMW) independently assessed the relevancy of identified articles. Article information was entered into a custom database. Each article was initially classified into three categories (exclude; unsure; include). Articles assessed as eligible for full-text screening were stored in a citation manager (Endnote X8 Thomson Reuters; 2017; see Supplementary Table S1 in the online version at DOI: 10.1016/j.tvjl.2018.11.014). Inclusion criteria were: (1) Original peer-reviewed research article; (2) Cohort; case-control; case-crossover or cross-sectional observational study; (3) Addressing risk factors and/or incidence of fatal catastrophic musculoskeletal injury (CMI) in Thoroughbred flat racing, trialling and/or training, and (4) Denominator data calculating risk and/or incidence pertaining to the number of race starts (e.g. incidence reported as per 1,000 starts).

Exclusion criteria were studies reporting solely: (1) Risk in training days; (2) Non-bone related CMIs only (e.g. tendon and ligament studies); (3) Non-fatal or non-CMI only (e.g. lameness); (4) Other racing disciplines (e.g. jumps racing, Quarter Horse racing).

This study has been conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2015) and Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE) (Stroup et al., 2000) protocols. Fig. 1 presents a flowchart of studies identified, reviewed, and excluded from the meta-analysis.

*Data analysis*

For each included study, data were extracted on study location (country and/or state), study year(s), outcome assessed and its definition, study type (e.g. case-control, cohort), type of regression model (univariable, multivariable and/or multi-level model), whether fatalities for horses in training were also included (race, train, both), and definitions of fatality or CMI. The key information from each included study are summarised in the Supplementary Table S2 in the online version at DOI: 10.1016/j.tvjl.2018.11.014.

To determine CMI incidence from cross-sectional studies, the number of racehorse CMIs (numerator) and the number of starts (denominator) were extracted. We considered outcomes of CMI reported from within 24 h to up to 3 days post race-day injury, or that then failed to race or trial for 6 months from the date of a race-day injury. In most jurisdictions, outcomes were determined after race-day following post-mortem, or per mandatory reporting of death to the respective racing authority. Sudden deaths or non-CMI related fatalities were excluded from incidence calculations. Pooled incidence estimates were obtained from a random-effects model weighted by sub-group (country), and displayed in a forest plot with 95% confidence intervals (95% CI) using the METAPROP package in Stata (Nyaga et al., 2014). Confidence intervals were based on the Clopper–Pearson exact binomial procedure (Newcombe, 1998). The I-squared measure was used as the test for heterogeneity across studies (Higgins et al., 2003).

For each study risk factor, we extracted the beta coefficient ($\beta$), odds ratio (OR), relative risk (RR), hazard ratio (HR), or incidence rate ratio (IRR) and their 95% CIs. Effect sizes (ES) from both univariable and multivariable regression were extracted where available. Where studies have a low prevalence of the outcome, the HR and RR can be approximated to the OR (Lee, 1994; Schmidt and Kohlmann, 2008), however, because most studies reported ORs, those that used HRs or RRs have been reported separately. We used calculations recommended by Altman and Bland (2011) to derive *P*-values (where only CIs were reported) and CIs (where only *P*-values were reported). Meta-analysis was restricted to study factors reported in two or more publications that used different study populations, and that were statistically significant in at least one publication. Where distance units differed between studies, ORs were unit converted back into the regression coefficient ($\ln(OR_{furlong}) = \beta_{furlong}$) indicating a per unit increase or decrease from furlongs to per 1000 m (1 km) as follows:

$$\beta_{metre} = \beta_{furlong}/201.168 \text{ metres}$$

$$OR_{1000\ metres} = \exp\left(\beta_{metre}\ 1000\right)$$

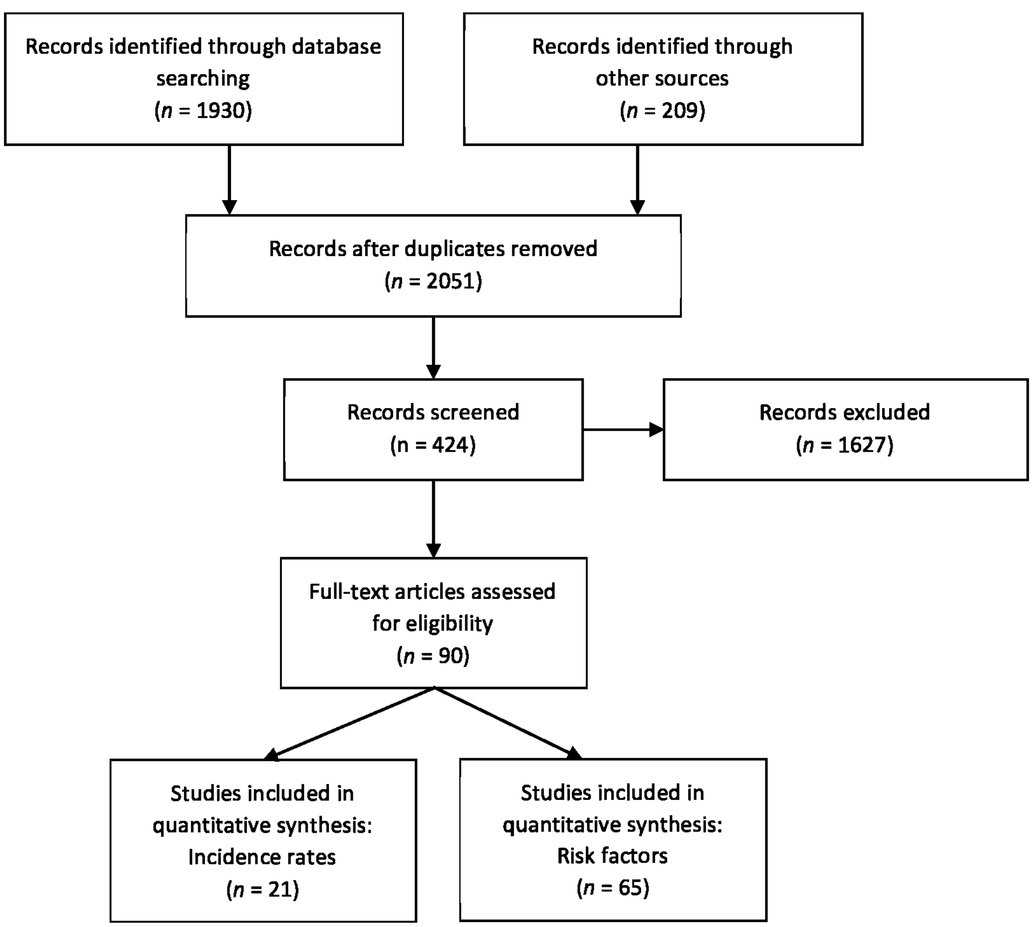


**Fig. 1.** PRISMA flow chart of studies identified, reviewed, and excluded from the meta-analysis.

Pooled ES and 95% CI were estimated using random-effects under the DerSimonian–Laird model in the METAN package in Stata (Harris et al., 2010). The random-effects model was appropriate due to known variability within studies related to country, study design, study period, and definitions. There were insufficient studies to stratify by: (1) Univariable and multivariable analysis, (2) Fatal, non-fatal, and all MSIs, and; (3) Study type (cohort, cross-sectional, case-control).

Statistical analyses and forest plots were produced using Stata/SE, v.14.2 (StataCorp, College Station). Fig. 3 was produced in R v.3.4.0 (R Core Team, R Foundation for Statistical Computing) using the HH package (Heiberger, 2017).

## Results

### *Incidence of catastrophic musculoskeletal injuries*

The pooled CMI incidence was 1.17 (95% CI 0.90, 1.44) per 1000 race starts (Fig. 2). Pooled incidence of CMI for Australia and New Zealand were significantly lower than that observed in the United States ($P < 0.001$) and Canada (0.011), but not significantly different from Hong Kong ($P = 0.608$) and the United Kingdom (UK; $P = 0.091$). However, Australian rates have not been updated this decade, and we were unable to determine whether rates changed over time due to overlapping or unavailability of yearly raw data for all studies. Not included in Fig. 2 are incidence rates from Japan (Oikawa et al., 1994; Mizuno, 1996; Oikawa and Kusunose, 2005) and Switzerland (Schweizer et al., 2016) because fatal and non-fatal fractures were combined in these studies.

### *Risk factors for catastrophic musculoskeletal injuries*

A reported 296 study factors have been investigated for associations with CMI (see Supplementary Table S3 in the online version at DOI: 10.1016/j.tvjl.2018.11.014). Fig. 3 presents a summary of key factors significant in at least two studies.

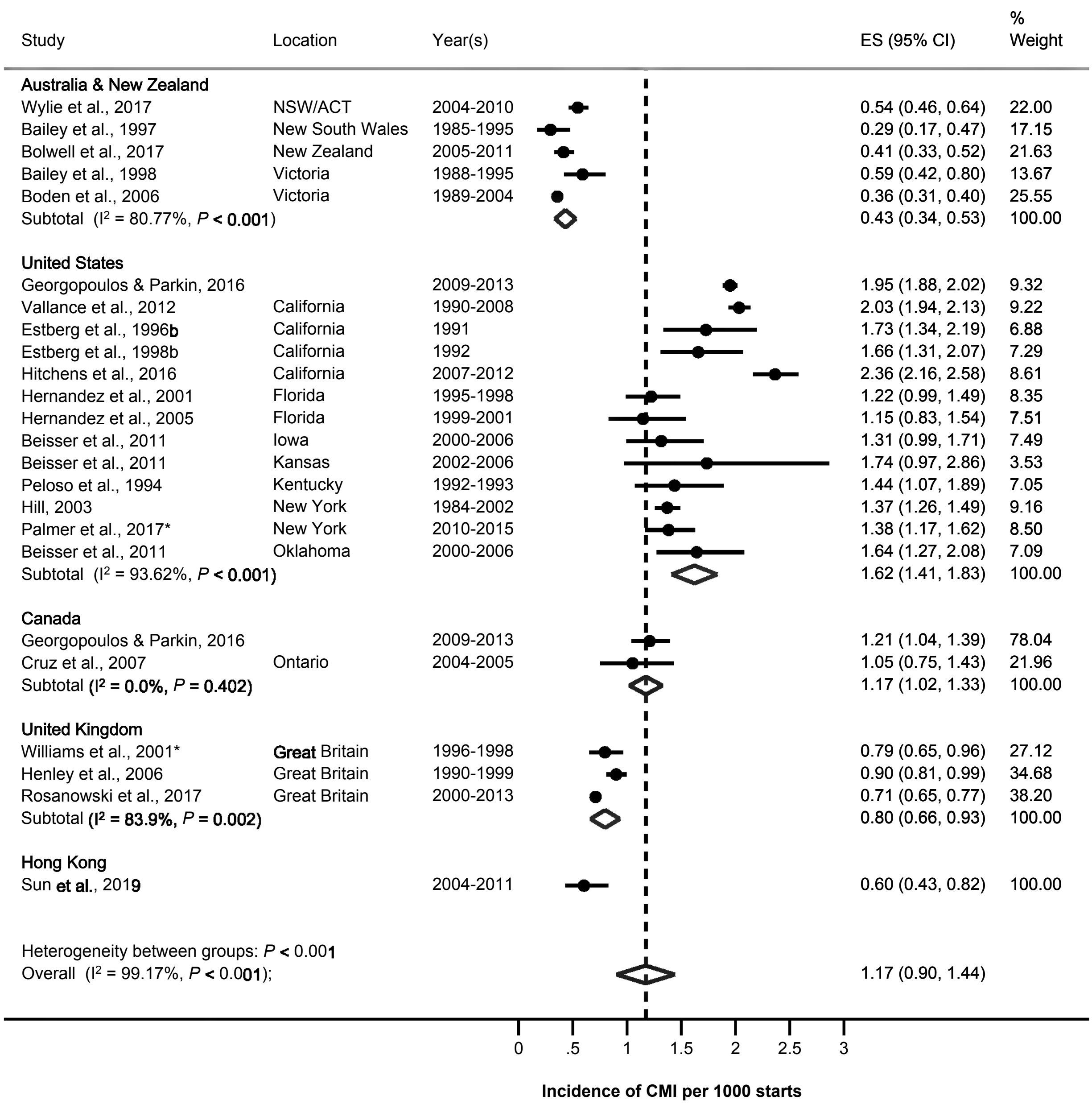


**Fig. 2.** Comparison of reported incidence of racing-related catastrophic musculoskeletal injury (CMI) across studies and countries. NSW/ACT = New South Wales/Australian Capital Territory. ES = effect size (incidence/1000 starts). Estimated incidence of CMI are marked with an asterisk (*). Pooled proportions and tests of heterogeneity ($I^2$) for within sub-groups (countries) and overall are presented. Significant inter-group heterogeneity was observed ($P < 0.001$).

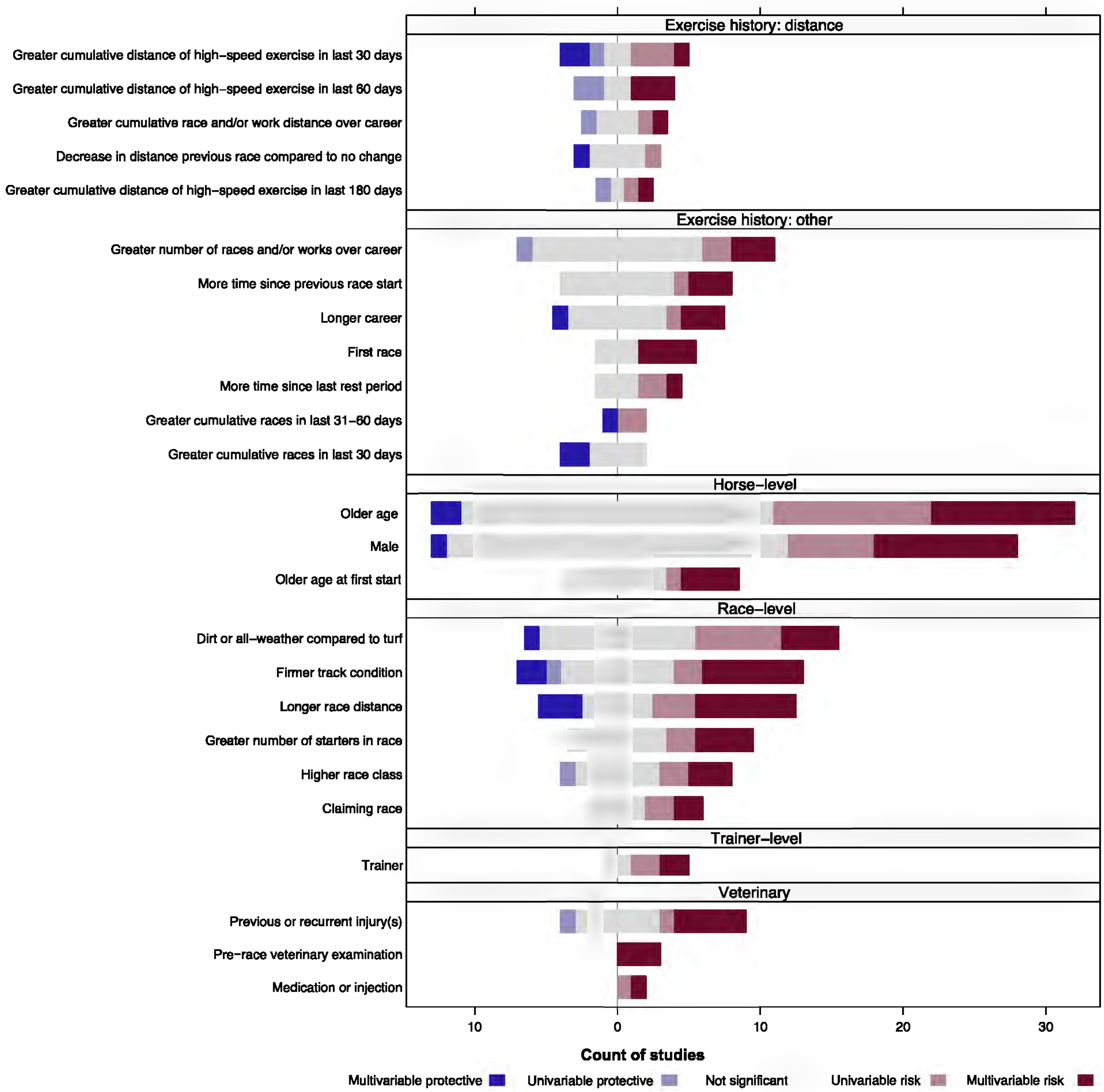


**Fig. 3.** Number of studies investigating potential risk factors for fatal and non-fatal musculoskeletal injury. Evidence of reduced (blue) or increased (red) risk is assumed to be stronger when remaining significant ($P < 0.05$) in multivariable analysis. Factors were included if they were significant in at least two studies and significant in multivariable analysis in at least one study. Some non-modifiable risk factors are not reported (e.g. year, season, racetrack). All factors investigated are reported in the Supplementary Table S3.

Although many factors are likely important, we discuss in detail only those that have consistent evidence for increasing risk and thus may be generalisable to other populations.

## *Horse-level risk factors*

### *Horse age and age at first start*

Older age was associated with greater odds of CMI in pooled analysis of continuous variables ($P = 0.006$; Fig. 4), and with biaxial proximal sesamoid bone (PSB) fracture (Peloso et al., 2015). Several studies reported age was not a risk factor (Estberg et al., 1996a; Kane et al., 1996; Hernandez et al., 2001, 2005; Hill et al., 2004; Parkin et al., 2004a, 2005; Anthenill et al., 2006; Verheyen et al., 2006a,b; Cruz et al., 2007; Vallance et al., 2013; Sun et al., 2018).

Others have reported more complex associations between age and risk of CMI. This includes quadratic associations in some studies, where risk initially increased then either decreased or remained constant after about five years (Estberg et al., 1996b; Rosanowski et al., 2017a), or eight years for all racing types (Henley et al., 2006). Conversely, horses aged two-years and five-years or older were over-represented as cases that had sustained catastrophic scapular fracture compared to the racing population (Vallance et al., 2012). Estberg et al. (1998b) reported an interaction by age and race type with older horses having higher risk of CMI in maiden races, but lower risk in claiming races (races in which participating horses are for sale). On all-weather tracks, horses that started racing as 2-year-olds but were older than 7 years at the time of death had three times the odds of fatality compared to younger horses; but younger horses had almost twice the odds if they started racing at 3 years of age or older (Rosanowski et al., 2017b).

Age was not retained in multivariable analysis in some studies because of multicollinearity with factors indicating career

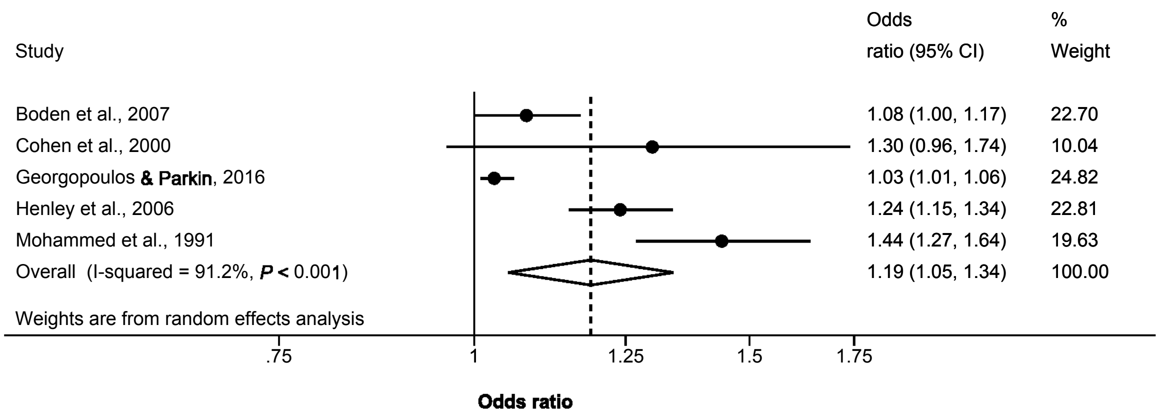


**Fig. 4.** Pooled effect size for racehorse age in years as a risk factor for fatality or catastrophic musculoskeletal injury. Odds ratios for age (in years) expressed as a continuous variable are unadjusted.

progression or exercise history (Anthenill et al., 2007; Georgopoulos and Parkin, 2016). Age was retained over age at first race start in some multivariable models (Bailey et al., 1997, 1998; Henley et al., 2006). Age at first race start analyses could not be pooled because of both categorical and continuous reporting of effect sizes. Horses commencing racing as 2-year-olds compared to those starting as 3-year-olds (Estberg et al., 1998a) or 3-year-olds and older (Boden et al., 2007), or when this variable was analysed as continuous (Estberg et al., 1996a) were not different in risk. Older age at first start was associated with CMI (Georgopoulos and Parkin, 2016), and with distal limb fractures on all-weather surfaces in the UK (Rosanowski et al., 2017b), but not in an earlier study of all UK racetracks (Parkin et al., 2004a). Similarly, in a study of fatal lateral condylar fractures, 2-year-old first starters were at reduced risk compared to 3 and 4-year-olds, but not 5 to 7-year-olds (Parkin et al., 2005). Age at first preparation has also been investigated, but found not to be associated with training related MSI (Cogger et al., 2006).

*Horse sex*

All males (OR 1.48; 95% CI 1.23, 1.79; $P < 0.001$), geldings (OR 1.56; 95% CI 1.25, 1.95; $P < 0.001$) and entires (OR 2.28; 95% CI 1.28, 4.06; $P = 0.005$) had higher odds of CMI compared to females, but there was no difference between geldings and entires in the pooled analysis (OR 1.36; 95% CI 0.71, 2.62; $P = 0.353$; Fig. 5). Peloso et al. (2015) found males and geldings, but not entires alone, were at higher risk of biaxial PSB fracture compared to females. Entires were at higher risk of lateral condylar fracture compared to geldings (Hill et al., 2004). Both entires and geldings were at higher risk of scapular fracture compared to females (Vallance et al., 2012), entires were at higher risk of CMI compared to females in a study of 2-year-olds (Wilson et al., 1996), and males were at higher risk than females for all race types (Henley et al., 2006). Other studies found no differences in CMI risk between sexes (Estberg et al., 1996a, 1998a; Kane et al., 1996; Cohen et al., 1997, 1999, 2000; Parkin et al., 2004a, 2005, 2006; Verheyen and Wood, 2004, 2006a, b; Perkins et al., 2005b; Cogger et al., 2006; Kristoffersen et al., 2010b; Hill et al., 2016; Schweizer et al., 2016; Bolwell et al., 2017; Rosanowski et al., 2017a; Sun et al., 2018).

*Horse performance*

Higher race class was associated with greater CMI risk compared to maiden and/or non-stakes races in our pooled analyses (OR 1.52; 95% CI 1.18, 1.96; $P = 0.001$; Fig. 6). For one study, this remained significant in multivariable analysis (Bailey et al., 1997). An interaction between age and class of race was observed in California. Older horses ( 6 years old) in maiden races had the highest risk, followed by younger horses (2 to 5 years old) in claiming and higher class races (i.e. allowance, stakes races, handicaps), then younger horses in maiden races, and older horses in higher class and claiming races (Estberg et al., 1998b). For our analyses, ORs were recalculated from the raw data allowing comparison of non-claiming with claiming races for three studies (Estberg et al., 1998b; Cohen et al., 1999; Hernandez et al., 2001). Only horses starting in a claiming races worth equal or less than USD 25,000 were at higher risk (OR 3.69; 95% CI 1.43, 9.52; $P = 0.007$) (Hernandez et al., 2001). Claiming races were excluded from the pooled analysis as they presented a generally higher risk profile and are not present in Australasian or European racing.

*Exercise history*

*First race*

In our pooled analyses, horses were at higher risk of fatality or CMI if they had previously raced (OR 0.69; 95% CI 0.60, 0.79; $P < 0.001$; Fig. 7). This effect held true in multivariable analysis performed by Georgopoulos and Parkin (2016, 2017). Horses having their first race start were not at higher risk of sustaining a fatal distal limb fracture (Parkin et al., 2004a) or a fatal lateral condylar fracture (Parkin et al., 2005).

*Career length*

Career length was not a risk factor in the pooled analysis ($P = 0.330$; Fig. 8). In Mohammed et al. (1991), longer career length remained in multivariable analysis as a decreased risk ($P < 0.05$). In Australian studies, greater time since a horse's first start was associated with CMI in Victoria, but not in New South Wales (Bailey et al., 1997, 1998). In studies investigating risk of fatal distal limb fractures and lateral condylar fractures (Parkin et al., 2004a, 2005), risk was highest for horses first year of racing, decreased in the second to fifth year, and gradually increased again for horses that raced for more than 5 years. Longer active career length (days actively racing excluding rest periods) rather than total career length was associated with risk of lateral condylar fracture (Hill et al., 2004), PSB fracture (Anthenill et al., 2007), and scapular fracture (Vallance et al., 2013).

*Cumulative race starts and/or workouts*

Studies investigating association of CMI with cumulative races could not be pooled due to categorical and continuous variable reporting. In a model of horses racing for  6 months, Georgopoulos and Parkin (2016) found CMI to be associated with fewer

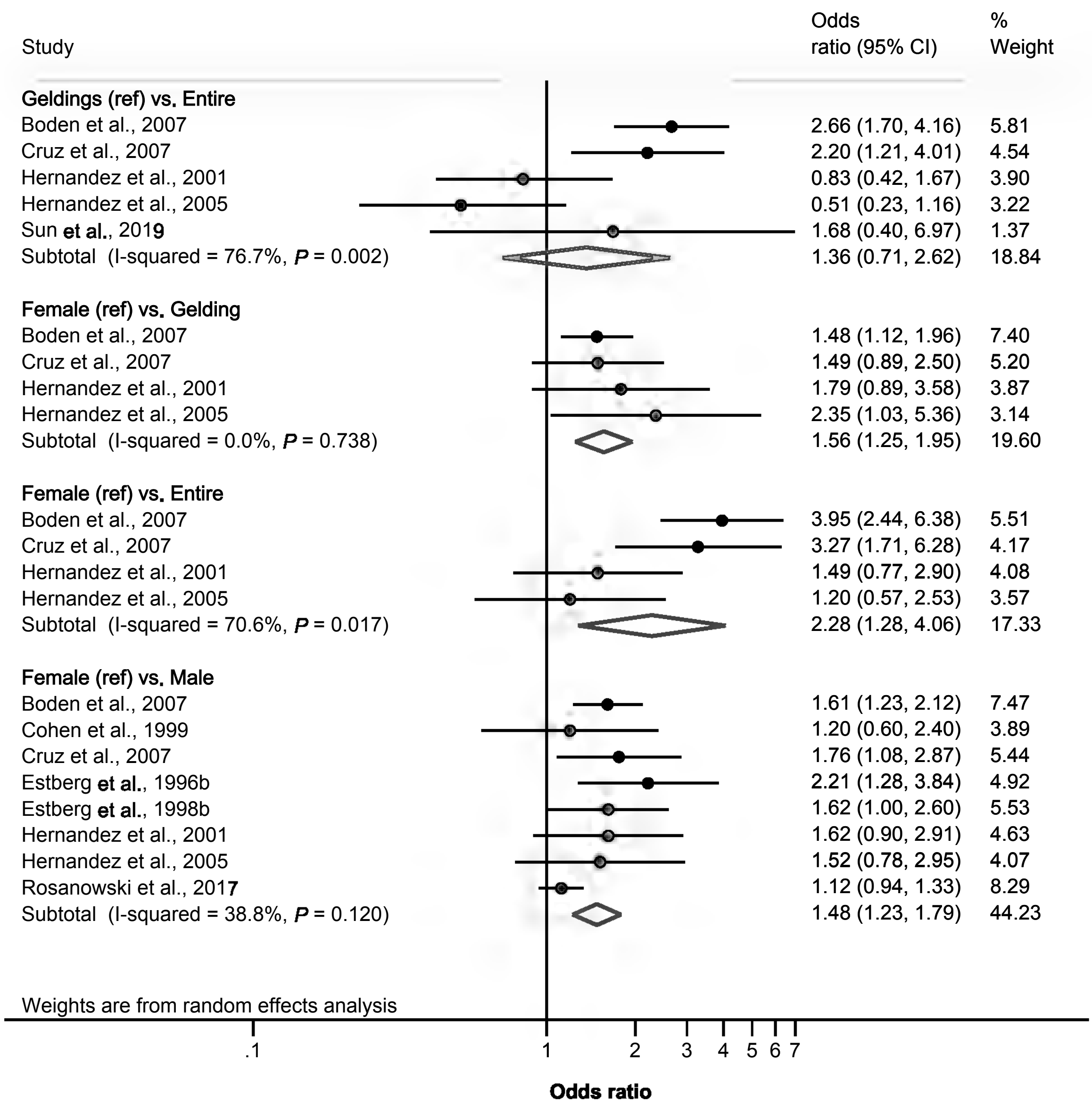


**Fig. 5.** Pooled effect size of comparison between geldings, entires, both geldings and entires combined (males), and female racehorses as a risk factor for fatality or catastrophic musculoskeletal injury. Odds ratios are unadjusted. Ref = Reference value where the OR equals 1.00.

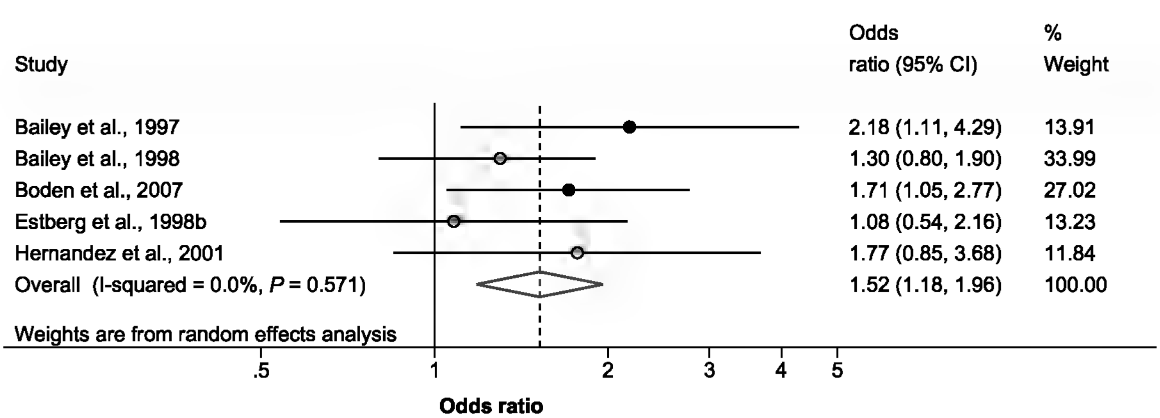


**Fig. 6.** Pooled effect size of comparison between lower class (reference: maiden and non-stakes) and higher class (allowance, stakes and handicap) races as a risk factor for fatality or catastrophic musculoskeletal injury. Odds ratios are unadjusted.

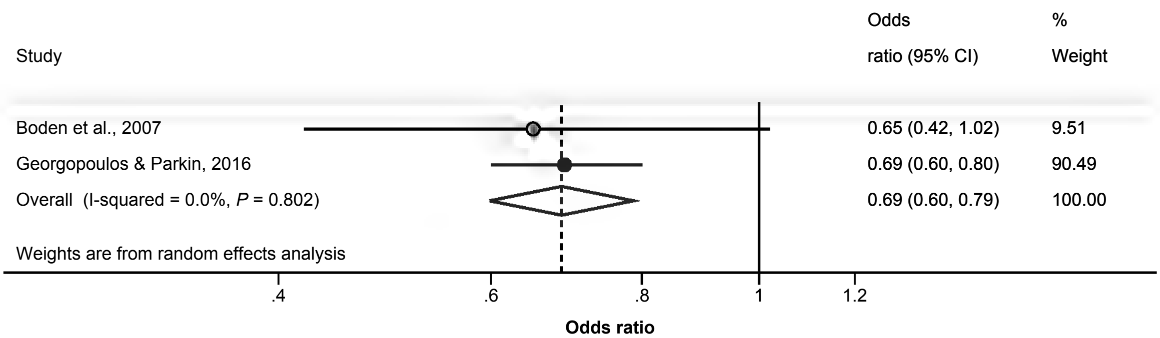


**Fig. 7.** Pooled effect size of comparison between horses in their first race compared to those in subsequent race starts as a risk factor for fatality or catastrophic musculoskeletal injury. Odds ratios are unadjusted.

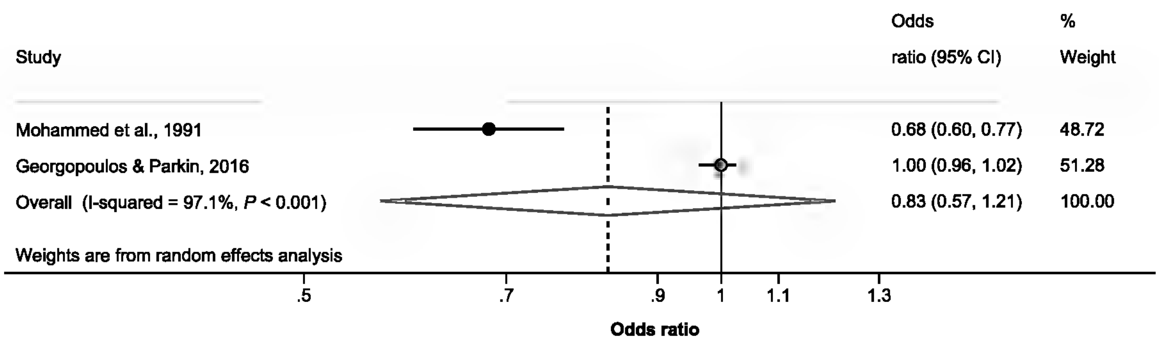


**Fig. 8.** Pooled effect size for career length in years as a risk factor for catastrophic musculoskeletal injury. Odds ratios are unadjusted.

cumulative races less than 30 days, but greater cumulative starts 61–90 days and 91–180 days prior to the race in which the CMI occurred. Conversely, cumulative race starts 30 days prior was not associated with CMI in Kentucky (Cohen et al., 2000), or with fatal distal limb or lateral condylar fracture (Parkin et al., 2004a, 2005). Greater cumulative number of races between 30 to 60 days (Georgopoulos and Parkin, 2016) and horses with at least one start in the 31–60 days prior to fatality (Boden et al., 2007) was significant only univariably. Other indicators of racing intensity not associated with CMI were cumulative races at 60, 90 and 180 days prior to injury (Cohen et al., 2000).

Fewer races in the previous year was associated with CMI for all race types (Henley et al., 2006), but not with CMI at two flat racing racetracks in Florida (Hernandez et al., 2001), or with fatal distal limb or lateral condylar fracture (Parkin et al., 2004a, 2005).

CMI was associated with a greater number of career starts in an Australian study of all race types (Bailey et al., 1998), and with biaxial PSB fractures (Peloso et al., 2015), but with fewer career starts and fewer races per career year in a US study (Mohammed et al., 1991). Horses sustaining PSB fractures had a greater number of races per career year and per active career year (Anthenill et al., 2007). But unraced horses were more likely to have sustained a fatal scapular fracture (Vallance et al., 2013). Career starts was not a risk factor for all CMI or MSI in other studies (Bailey et al., 1997; Cohen et al., 1997, 1999, 2000; Hernandez et al., 2001, 2005), or in studies of fatal PSB, distal limb or lateral condylar fracture (Hill et al., 2004; Parkin et al., 2004a, 2005; Anthenill et al., 2007).

A greater number of officially timed workouts and events were associated with fatal PSB fracture (Anthenill et al., 2007), but fewer workouts and events with fatal scapular fracture (Vallance et al., 2013). Number of workouts was not associated with catastrophic metacarpal lateral condylar fracture (Hill et al., 2004).

*Cumulative distance raced and/or worked*

Risk of cumulative high-speed exercise distance has been investigated with mixed results; both decreased and increased cumulative distance presented as risk factors. Greater distance of high-speed exercise accumulated during a 1 or 2 month period prior to injury was associated with reduced risk of CMI (Hernandez et al., 2005), of all injuries, but not CMI (Cohen et al., 2000), and 1–12 months prior as well as raced and/or worked over their career for catastrophic scapular fracture (Vallance et al., 2013). For fatal distal limb and lateral condylar fracture a quadratic and piecewise linear relationship was observed, with the risk highest for those doing no gallop work in training (Parkin et al., 2004a, 2005). Conversely, higher risk was reported for greater cumulative high-speed exercise distance 1, 2, 4 and 6 months prior to fatal fracture, with only distance in the last 2 months being retained in multivariable analyses (Estberg et al., 1996a); 1–12 months and over their career in univariable analysis, and 2 and 6 months prior in multivariable analysis, for fatal PSB fracture (Anthenill et al., 2007); 1 and 2 months and over their career in univariable analyses, and 2 months in multivariable analyses for catastrophic metacarpal condylar fracture (Hill et al., 2004); and greater career flat race cumulative distances for fatalities univariably, but this was replaced with less cumulative jumps race distance in the multivariable model (Boden et al., 2007). Recent cumulative distance was not found to be associated with fatal and non-fatal pelvic and tibial fracture (Verheyen et al., 2006b).

Recent studies have acknowledged a more complex relationship between cumulative distance, speed and CMI. Where other epidemiological studies have access to only race and/or official workout history, Verheyen et al. (2006a) conducted a large-scale study with daily distances of canter and gallop exercise recorded finding horses exercising over greater distances at highest risk (i.e. critical risk distance of >44 km at the canter and >6 km at the gallop over 30 days).

*Rest periods (lay-ups)*

Horses were more likely to sustain a CMI with greater time since their previous race start (Hernandez et al., 2001, 2005), but this was not significant in other studies (Estberg et al., 1996a; Bailey et al., 1997, 1998; Cohen et al., 1999; Parkin et al., 2004a, 2005; Georgopoulos and Parkin, 2016).

Over their entire career (including and excluding rest periods), greater average time between events, but not workouts or races, was associated with catastrophic scapular fracture (Vallance et al., 2013). Average time between races, works, and events was not associated with fatal PSB fracture (Anthenill et al., 2007), or metacarpal condylar fracture (Hill et al., 2004).

Greater time since last rest period was associated with catastrophic metacarpal condylar fracture (Hill et al., 2004) and PSB fracture (Anthenill et al., 2007), but not with fatal fracture (Estberg et al., 1996a), or scapular fracture (Vallance et al., 2013). Recent return from rest was strongly associated with humeral, but not pelvic fractures (Carrier et al., 1998), and with MSI, but not CMI or career-ending MSI (Cohen et al., 1997). Number of rest periods, mean and total time in rest, and/or percentage of their career in rest was not an important risk factor for CMI; MSI and CMI (Cohen et al., 1997), breakdown (Bailey et al., 1997), fatal fracture (Estberg et al., 1996a), PSB fracture (Anthenill et al., 2007), catastrophic metacarpal condylar fracture (Hill et al., 2004), and scapular fracture (Vallance et al., 2013).

*Race-level risk factors*

Race-level characteristics commonly reported as associated with fatality or catastrophic injury in flat racing include track surface type and track condition, race distance, and field size (number of starters).

*Track surface and condition*

There were no differences in risk of CMI in pooled analysis between turf and all-weather or synthetic tracks ($P = 0.991$), or turf and dirt tracks ($P = 0.138$), but off dirt (i.e. muddy or sloppy; track saturated with water) conditions were higher risk than turf ($P < 0.001$; Fig. 9). Hernandez et al. (2001) speculated that their results differed to others because turf races are typically more competitive in Florida than dirt races; they are run with larger fields, over longer distances, and for more prize money. Not reported in the pooled analysis because of potential overlap of case horses and starts with their previous study, Georgopoulos and Parkin (2017) found that turf and dirt tracks were higher risk for fatal and non-fatal fracture compared to synthetic. All-weather tracks were higher risk than turf tracks for biaxial PSB fracture (Kristoffersen et al., 2010b), fatal distal limb fracture (Parkin et al., 2004c; Reardon et al., 2014), lateral condylar fracture (Parkin et al., 2006), and lower limb injuries (Williams et al., 2001). Other studies found no differences between turf and dirt surfaces (Estberg et al., 1998b; Cohen et al., 1999, 2000).

However, track surface is not independent of track condition. Studies on the effects of track condition could not be pooled because track condition, particularly for turf, is reported on different scales in different countries. Racehorses racing on muddy and/or sloppy dirt tracks were more likely to sustain CMI compared to faster dirt tracks (Wilson et al., 1996; Hernandez et al., 2001; Oikawa and Kusunose, 2005). Faster turf tracks were higher risk for fatal and non-fatal fracture and MSI (Williams et al., 2001; Oikawa and Kusunose, 2005; Bolwell et al., 2017; Rosanowski et al., 2017a), CMI and fatality (Bailey et al., 1998; Henley et al., 2006; Boden et al., 2007), fatal distal limb fracture (Parkin et al., 2004b), and fatal lateral condylar fracture (Parkin et al., 2005). Several studies found no difference between turf track conditions (Mohammed et al., 1991; Bailey et al., 1997; Estberg et al., 1998b; Hernandez et al., 2001), but two US studies had few observations on good, yielding or soft rated tracks (Mohammed et al., 1991; Hernandez et al., 2001).

*Race distance*

Longer race distance was associated with CMI in Florida, US (Hernandez et al., 2001), MSI, CMI and fatality in Australia (Bailey et al., 1998; Boden et al., 2007), failure to finish a race due to MSI in New Zealand (Bolwell et al., 2017), CMI in a study of all race types in the UK (Henley et al., 2006), fatal distal limb fracture (Parkin et al., 2004b), and fatal lateral condylar fracture (Parkin et al., 2005). In other US studies, shorter race distance has been found to be higher risk for MSI and CMI (Cohen et al., 1999; Georgopoulos and Parkin, 2016), fatal and non-fatal fractures (Georgopoulos and Parkin, 2017), and complete scapular fracture (Vallance et al., 2012). Some studies found race distance to be either a confounder (Schweizer et al., 2016) or not a risk factor (Wilson et al., 1996; Bailey et al., 1997; Estberg et al., 1998b; Cohen et al., 2000).

*Field size*

A greater number of race starters (field size) was associated with MSI and CMI, fatal distal limb fracture, and fatal lateral condylar fracture in some studies (Bailey et al., 1997; Hernandez et al., 2001; Parkin et al., 2004b, 2005), but not others (Bailey et al., 1998; Cohen et al., 1999, 2000; Henley et al., 2006; Georgopoulos and Parkin, 2016, 2017; Bolwell et al., 2017).

*Management factors*

Management factors previously identified as associated with MSI or CMI included adverse pre-race inspection findings by regulatory veterinarians, i.e. the horse was assessed to have an increase in severity score from previous inspections, database records or clinical experience indicated higher risk, or substantial palpable abnormalities were identified (Cohen et al., 1997, 1999, 2000). Similarly identified factors are the number of times a horse had been withdrawn from a race previously, being on the vet list (i.e. not cleared to race until passed by a veterinarian) (Georgopoulos and Parkin, 2016, 2017), previous injuries (Hill, 2003; Perkins et al., 2005a; Georgopoulos and Parkin, 2016, 2017), and horseshoe characteristics (Kane et al., 1996).

Administration of medication prior to racing has been associated with CMI. Levels of nonsteroidal anti-inflammatory agents (NSAIDs), phenylbutazone and flunixin, were higher in horses that sustained a CMI in Kentucky (Dirikolu et al., 2009). In an Australian study, the hazard of MSI was greater for horses administered a local corticosteroid injection within a median of 17.5 (range 2–398) days prior to racing compared to untreated horses, and greater still in those that received subsequent injections (Whitton et al., 2014).

Both trainer and recent change in trainer were associated with CMI, indicating the importance of management and changes in those practices (Georgopoulos and Parkin, 2016, 2017). Several

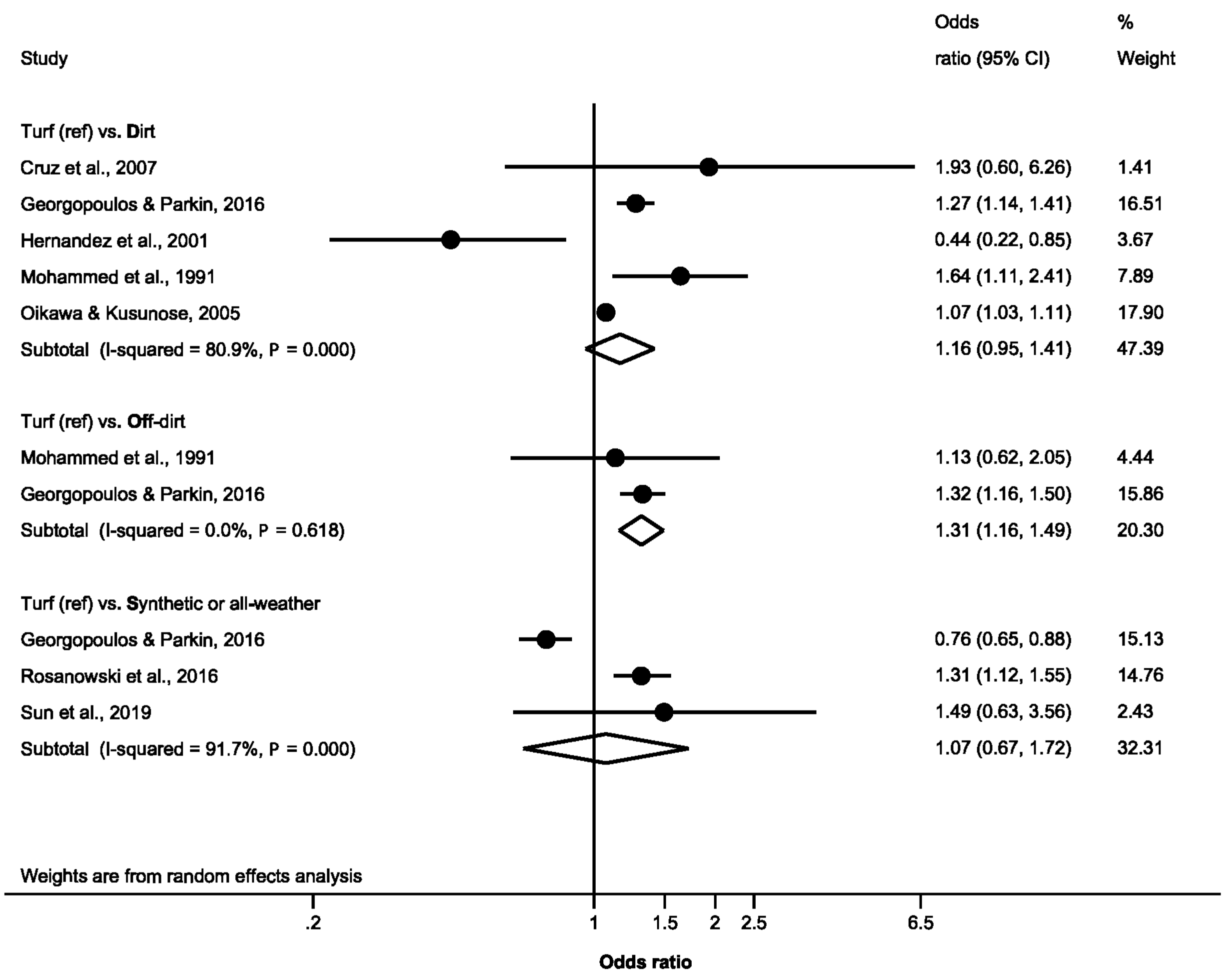


**Fig. 9.** Pooled effect size of comparison between turf tracks (reference) and dirt, off-dirt (non-fast, sloppy or muddy conditions) and synthetic or all-weather tracks as a risk factor for catastrophic musculoskeletal injury. Odds ratios (OR) are unadjusted. Ref = Reference value where the OR equals 1.00.

studies identified variation in injury risk by trainer. This was addressed by fitting trainer as either a fixed-effect (Verheyen and Wood, 2004; Verheyen and Wood, 2004, 2006b; Cogger et al., 2006, 2008; Sun et al., 2018), or random-effect term (Verheyen and Wood, 2004; Perkins et al., 2005b; Whitton et al., 2014). Verheyen et al. (2006a) did not find a significant association between trainer and fracture risk.

*Pre-existing injury or pathology*

Several studies found evidence that fractures are commonly preceded by changes suggestive of pre-existing injury. Bone modelling is a consistent finding in the form of trabecular bone densification or callus formation associated with cortical bone (Entwistle et al., 2009; Anthenill et al., 2010; Whitton et al., 2010; Vallance et al., 2011). Additionally, horses sustaining a fracture of the PSB were more likely to have radiographic evidence of osteophytes or large vascular channels (Anthenill et al., 2006). Evidence of moderate ligamentous suspensory apparatus injury at post-mortem was a strong risk factor for metacarpal condylar fracture (Hill et al., 2004, 2016).

## Discussion

Almost 300 factors have been investigated in epidemiological studies of CMI. Factors found to have consistent evidence of increasing risk are horse-level factors including older horse age and age at first start, male sex (particularly entires), and factors indicating the horse's quality such as higher race class or lower claiming price; race-level factors including firmer track conditions on turf and sloppier conditions on dirt, longer race distance, and a greater number of starters; and factors related to management including issues identified at pre-race examination, previous or pre-existing injury, and recent medication administration. Studies investigating racing and training intensity had conflicting outcomes.

Differences in incidence may be explained by differences in horse-level, race-level or management and environmental factors specific to each country or jurisdiction. For example, the highest rates occur in the US where medication rules are generally less stringent, claiming races are available, and dirt tracks are commonly used. Additionally, a proportion of the differences between studies may be explained by varying definitions of CMI, though most US studies were based on necropsy diagnosis and race-day fatalities. Definitions range from horses that died or were subjected to euthanasia at the track immediately post-race, to those euthanised within 24 h, 3, 5, 30 or 60 days, up to those horses that failed to race or trial for 3 or 6 months from the date of the injury or that were permanently retired. The review by Parkin (2008) presented a list of case definitions from 1982 to 2007 and showed early definitions tended to be more inclusive, whereas later studies focussed on specific injury types or anatomic locations. Although improvement to routine data collection has also allowed refinement of case definitions, these still tend to differ vastly between jurisdictions. Methods of diagnoses of CMI may also explain incidence rate differences. These included clinical examination without further diagnostic investigation (presumptive diagnosis), confirmed by diagnostic imaging reports (radiographic, ultrasonography or nuclear scintigraphy images), and/or confirmed by a pathologist at post-mortem examination (see Supplementary Table S2 in the online version at DOI: 10.1016/j.tvjl.2018.11.014).

Although limited in number, there were modifiable risk factors for which good evidence of an association with CMI was identified. Our findings support the prevention of older horses racing, however due to grouping of older horses together in many studies, further investigation of the age of enforced retirement from racing is required. In jurisdictions where an upper age limit has been implemented, the number of horses affected is so small the benefits are likely marginal. While age at first start was associated with CMI, it is unknown whether this is driven by trainers having difficulty getting horses with underlying problems to their first race or the result of failing to take advantage of the young skeleton's enhanced ability to adapt to training and racing. Encouraging trainers to start horses at a younger age may have unforeseen consequences. Limiting field size and avoiding fast track conditions seem logical interventions that racing authorities can achieve now. The conflicting exercise history risk factors highlight the limitations of epidemiological investigation of complex biological processes. Catastrophic injury is the end result of a process that occurs over time and in some circumstances may be prolonged or in others occur rapidly. Therefore reduced training volume as a result of the injury process may be observed in some cases but not in others. Additionally, based on our current knowledge there are at least two pathways to injury: (1) Bone fatigue in well adapted bone caused by accumulation of micro-damage that is unable to repair is likely to occur following a period of intense training; whereas (2) Bone fatigue injuries caused by loading of unadapted or de-adapted bone is likely to occur early in a training period at relatively low levels of training intensity (Martig et al., 2014). Regardless of the multiple potential pathogenic pathways, most epidemiological studies record only one clinical outcome (e.g. fracture) (Parkin, 2008). More, though relatively small scale studies, have reported on bone material properties that might point to the most likely pathogenic pathway (Anthenill et al., 2010; Kristoffersen et al., 2010a; Whitton et al., 2010; Peloso et al., 2015; Loughridge et al., 2017; Pinilla et al., 2017).

More recently, predictive models aimed at identifying horses at risk have been attempted, with models reporting area under the curve (AUC) of 65–67%, with 100% being perfect predictability and 50% being no better than chance (Georgopoulos and Parkin, 2017; Rosanowski et al., 2017b). With such inadequate predictive capability from such large datasets, there is still more to be done to refine these epidemiological models. The main problem lies with difficulty obtaining data related to previous veterinary history, comprehensive training data, or potential unknown variables (Georgopoulos and Parkin, 2017), thus we need to focus on developing more efficient data recording and retrieval systems (Parkin, 2008). Multicollinearity was also observed in some studies between factors indicating horse age, career progression, and exercise history (Anthenill et al., 2007; Georgopoulos and Parkin, 2016). Multicollinearity can make it difficult to identify study factors that may be causative rather than just predictive (Shmueli, 2010).

The various types of studies, case definitions, and multiple countries involved result in high study design heterogeneity. There is publication bias present, primarily due to the non-reporting of effect sizes for non-significant results. Pooled effect sizes in this analysis may therefore be biased, however an attempt was made to report such non-significant results in Fig. 3. Information provided in our summary of significant risk factors may also only be a reflection of the size of the study, as a risk factor is more likely to be identified as significant if the study is large. Many of these limitations are highlighted in a report of the Havemeyer Workshop (Parkin, 2007), and here we continue the call for standardising case definitions to enable meaningful comparisons between studies conducted across different racing jurisdictions.

The findings from this meta-analysis should be interpreted with caution. Although there is evidence to support the risk factors reported in detail, there are many other studies that do not report these same factors as significant. Development of more advanced methods to model interactions and multi-collinearity between risk factors in multivariable models is required, and this necessitates large datasets. Epidemiological modelling can still be helpful in monitoring changes in incidence rates and investigating whether strategies to reduce the occurrence of injuries are successful. However, research that addresses the causal relationship between CMI and identified risk factors is also required. These consolidated findings could be used in future simulations aimed at predicting the effects of interventions on racehorse injury.

## Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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