#### Sex



Personal characteristics, such as sex, can influence one's degree of risk for developing PTSD. How such personal characteristics may affect the development of PTSD would be influenced by other personal characteristics as well as differences in the trauma experience itself. This summary table presents the evidence for differences in the risk of PTSD in males and females.

#### Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results separately for people with PTSD. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. When multiple copies of reviews were found, only the most recent version was included. We prioritised reviews with pooled data for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis<sup>1</sup>. Reviews with less than 50% of items checked have been excluded from the library. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from



observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)<sup>2</sup>. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

#### Results

We found 19 systematic reviews that met our inclusion criteria<sup>3-21</sup>.

- Moderate to high quality evidence found a small association between increased PTSD symptoms in female compared to male children and adolescents following any trauma exposure (21% vs. 11%). Risk of PTSD was highest in female children and adolescents exposed to interpersonal trauma (33%).
- Moderate quality evidence found the prevalence of PTSD in adolescent males in detention centres was 8.6%, and 18.2% in adolescent females in detention centres.
- Moderate to high quality evidence found a medium-sized effect of more PTSD symptoms in girls compared to boys following exposure to a death of a parent, sibling, or close friend.
- Moderate to low quality evidence found the prevalence of PTSD in mothers ranged from 23% to 49.1% within 3 months post-loss, from 0.6% to 37% between 3 months and 12 months post-loss, and from 3.3% to 15.2% by 18 years post-loss. In fathers, prevalence of PTSD ranged from 5% to 8.4% between 7 weeks and 18 years post-loss.
- Moderate to high quality evidence found small effects showed both adult and child females had an increased risk of PTSD following earthquakes compared to males.
   Moderate quality evidence found the

### Sex

incidence of PTSD following exposure to earthquakes was 35% in females and 23% in males.

- Moderate quality evidence found the prevalence of PTSD following road traffic accidents was higher in females than males (28% vs. 20%). In children and adolescents exposed to road traffic accidents, rates were also higher in females (34% vs. 22%).
- Moderate quality evidence a small association between increased PTSD symptoms in female than male youth following exposure to any disaster.
- Moderate to low quality evidence found a small association between increased PTSD symptoms in females than males following a burn injury.
- Moderate quality evidence found a mediumsized effect of higher rates of PTSD in females than males after a coronavirus infection (severe acute respiratory syndrome [SARS], Middle East respiratory syndrome [MERS], or coronavirus disease 2019 [COVID-19]).
- Moderate quality evidence found a trend small effect of greater risk of PTSD during the COVID-19 pandemic in females than males in the general population.
- High quality evidence found a small association between increased PTSD symptoms in mothers than fathers of chronically ill children.
- Moderate to high quality evidence found a small effect of an increased risk of PTSD in female than male military personnel and veterans.
- Moderate to high quality evidence found lifetime rates are nearly twice as high in women than in men over 65 years.
- Moderate quality evidence found no differences in rates of PTSD between males and females aged over 65 years after a fall.
- Moderate to high quality evidence found no effect of sex on risk of PTSD following a traumatic brain injury.



 Moderate to high quality evidence found no differences in the rates of PTSD between males and females following exposure to secondary workplace trauma.





Alisic E, Zalta AK, van Wesel F, Larsen SE, Hafstad GS, Hassanpour K, Smid GE

Rates of post-traumatic stress disorder in trauma-exposed children and adolescents: meta-analysis

British Journal of Psychiatry 2014; 204: 335-40

View review abstract online

Comparison	PTSD in children and adolescents at least one month after exposure to trauma.
Summary of evidence	Moderate quality evidence (large sample, inconsistent, direct) found the incidence of PTSD in children and adolescents was higher in females than males (21% vs. 11%) after exposure to trauma, particularly in females exposed to interpersonal trauma (33%).

#### Any trauma

The incidence of PTSD following exposure to any trauma was higher in females than males;

42 studies, N = 3,563

Males: 30 studies, incidence = 11.1%, 95%CI 7.0% to 17.1%

Females: 31 studies, incidence = 20.8%, 95%Cl 13.6% to 30.5%

#### Males

Interpersonal: incidence = 12 studies, incidence = 16.8%, 95%CI 8.8% to 29.6%

Non-interpersonal: incidence = 18 studies, incidence = 8.4%, 95%Cl 4.7% to 14.5%

#### **Females**

Interpersonal: incidence = 13 studies, incidence = 32.9%, 95%Cl 19.8% to 49.3%

Non-interpersonal: incidence = 18 studies, incidence = 13.3%, 95%Cl 7.4% to 22.9%

These differences were statistically significant.

Consistency in results <sup>‡</sup>	Authors report data are inconsistent
Precision in results§	Appears imprecise
Directness of results	Direct

Beaudry G, Yu R, Langstrom N, Fazel FS

An Updated Systematic Review and Meta-regression Analysis: Mental Disorders Among Adolescents in Juvenile Detention and Correctional



### Sex

Facilities		
	cademy of Child and Adolescent Psychiatry 2021; 60(1): 46-60	
View review abstract online		
Comparison	PTSD in adolescents in juvenile detention and correctional facilities.	
Summary of evidence	Moderate quality evidence (large sample, inconsistent, appears imprecise, direct) found the prevalence of PTSD in adolescent males in detention centres was 8.6% and 18.2% in adolescent females in detention centres.	
Juvenile detention		
Prevalence of PTSD was higher in females than males in detention;		
Males: 20 studies, N = 14,260, prevalence = 8.6%, 95%Cl 6.4% to 10.7%, I <sup>2</sup> = 92%		
Females: 11 studies, N = 1,876, prevalence = 18.2%, 95%CI 13.1% to 23.2%, I <sup>2</sup> = 78%		
Consistency in results	Inconsistent	
Precision in results	Appears imprecise	
Directness of results	Direct	

### Bloch F

Literature review and meta-analysis of risk factors for delayed posttraumatic stress disorder in older adults after a fall

International Journal of Geriatric Psychiatry 2017; 32: 136-40

View review abstract online

Comparison	Effect of age on risk of PTSD in older adults (≥65-90 vs. >90 years) after a fall (up to 24 weeks).
Summary of evidence	Moderate quality evidence (small to medium-sized sample, consistent, imprecise, direct) found no differences in rates of PTSD after a fall between males and females aged over 65 years.

#### Falls in the elderly

There were no differences between elderly males and females after a fall; 3 studies, N = 211, OR = 1.72, 95%CI 0.82 to 3.62, p > 0.05,  $I^2 = 0\%$ 



#### Sex

Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct

#### Christiansen DM

Posttraumatic stress disorder in parents following infant death: A systematic review

Clinical Psychology Review 2017; 51: 60-74

View review abstract online

Comparison	PTSD in parents following infant loss.
Summary of evidence	Moderate to low quality evidence (unclear sample size, appears inconsistent and imprecise, direct) found the prevalence of PTSD in mothers ranged from 23% to 49.1% within 3 months post-loss, from 0.6% to 37% between 3 months and 12 months post-loss, and from 3.3% to 15.2% by 18 years post-loss. In fathers, prevalence of PTSD ranged from 5% to 8.4% between 7 weeks and 18 years post-loss.

#### PTSD in parents after infant loss

Incidence of PTSD was higher in mothers than fathers following loss of an infant;

#### **Mothers**

<3 months post-loss: 5 studies, prevalence ranged from 23% to 49.1% 3-12 months post-loss: 6 studies, prevalence ranged from 0.6% to 37% Up to 18 years post-loss: 3 studies, prevalence ranged from 3.3% to 15.2%

#### **Fathers**

7 weeks to 18 years post-loss: 2 studies, prevalence ranged from 5% to 8.4%

There were no moderating effects from whether the death occurred prior to, during, or following birth and nor was gestational age consistently associated with PTSD severity.

Consistency in results	Appears inconsistent
Precision in results	Appears imprecise
Directness of results	Direct



Sex

Cnossen MC, Scholten AC, Lingsma HF, Synnot A, Haagsma J, Steyerberg PEW, Polinder S

Predictors of Major Depression and Posttraumatic Stress Disorder Following Traumatic Brain Injury: A Systematic Review and Meta-Analysis

Journal of Neuropsychiatry and Clinical Neurosciences 2017; 29: 206-24

View review abstract online

Comparison	PTSD following a traumatic brain injury.
Summary of evidence	Moderate to high quality evidence (large sample, consistent, imprecise, direct) found no effect of sex on risk of PTSD following a traumatic brain injury.
Traumatic brain injury	

No difference in rates of PTSD between males and females following a traumatic brain injury; 4 studies, N = 621, OR = 1.27, 95%CI 0.83 to 1.96, p > 0.05,  $I^2 = 0\%$ 

Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct

Dai W, Chen L, Lai Z, Li Y, Wang J, Liu A

The incidence of post-traumatic stress disorder among survivors after earthquakes: a systematic review and meta-analysis

**BMC Psychiatry 2016; 16: 188** 

View review abstract online

Comparison	PTSD after earthquakes.
Summary of evidence	Moderate quality evidence (large sample, imprecise, direct) found the incidence of PTSD following exposure to earthquakes was higher in females than males (35% vs. 23%).

#### **Earthquakes**

The incidence of PTSD following exposure to earthquakes was higher in females than males;



#### Sex

46 studies, N = 76,101	
Males: Incidence = 22.57%, 95%CI 16.53% to 29.23%, I <sup>2</sup> not reported	
Females: Incidence = 34.82%, 95%Cl 26.85% to 43.24%, I <sup>2</sup> not reported	
Consistency in results	No measure of consistency was reported for this subgroup analysis.
Precision in results	Appears imprecise
Directness of results	Direct

Dai W, Liu A, Kaminga AC, Deng J, Lai Z, Wen SW

Prevalence of Posttraumatic Stress Disorder among Children and Adolescents following Road Traffic Accidents: A Meta-Analysis

Canadian Journal of Psychiatry 2018; 63: 798-808

View review abstract online

Comparison	PTSD in children and adolescents after road traffic accidents.
Summary of evidence	Moderate quality evidence (large sample, imprecise, direct) found the prevalence of PTSD following road traffic accidents was higher in female than male children and adolescents (34% vs. 22%).

#### Road traffic accidents

The prevalence of PTSD following road traffic accidents was higher in female than male children and adolescents;

Males: 4 studies, N = 510, prevalence = 22.21%, 95%CI 18.66% to 25.96%,  $I^2$  not reported Females: 4 studies, N = 391, prevalence = 34.45%, 95%CI 21.94% to 48.12%,  $I^2$  not reported

Consistency in results	No measure of consistency was reported for this subgroup analysis.
Precision in results	Appears imprecise
Directness of results	Direct

Furr JM, Comer JS, Edmunds JM, Kendall PC

Disasters and youth: a meta-analytic examination of posttraumatic stress

Journal of Consulting and Clinical Psychology 2010; 78: 765-80



#### Sex

View review abstract online	
Comparison	PTSD symptoms in youth (≤18 years) after disasters.
Summary of evidence	Moderate quality evidence (large sample, direct) found a small association between increased PTSD symptoms in female than male youth following exposure to a disaster.
Disasters	
A small association between increased PTSD symptoms in females than males following disasters; 48 studies, $N = 41,909$ , $r = 0.14$ , $p < 0.001$	
Consistency in results	No measure of between study heterogeneity was reported.
Precision in results	No CIs are reported
Directness of results	Direct

Giannoni-Pastor A, Eiroa-Orosa FJ, Fidel Kinori SG, Arguello JM, Casas M

Prevalence and Predictors of Posttraumatic Stress Symptomatology Among Burn Survivors: A Systematic Review and Meta-Analysis

Journal of Burn Care and Research 2016; 37: e79-89

View review abstract online

	Comparison	Effect of age on risk of PTSD symptoms following a burn injury.
females than males following a burn injury.	Summary of evidence	Moderate to low quality evidence (small samples, direct) found a small association between increased PTSD symptoms in females than males following a burn injury.

#### **Burn injury**

A small association between increased PTSD symptoms in females than males following a burn injury;

4 studies, N = 554, r = 0.20

Consistency in results	No measure of consistency is reported.
Precision in results	No measure of precision is reported.
Directness of results	Direct



#### Sex

Grenier S, Payette MC, Gunther B, Askari S, Desjardins FF, Raymond B, Berbiche D

Association of age and gender with anxiety disorders in older adults: A systematic review and meta-analysis

International Journal of Geriatric Psychiatry 2019; 34: 397-407

View review abstract online

Comparison	PTSD in older adults (≥65 years).
Summary of evidence	Moderate to high quality evidence (large samples, consistent, imprecise, direct) found lifetime rates are nearly twice as high in women than in men over 65 years.
Flacult	

#### **Elderly**

Lifetime prevalence was higher in older females than males;

Lifetime prevalence = 3.42% vs. 1.83%, OR = 1.93, 95%CI 1.24 to 3.03, p = 0.002,  $I^2 = 0$ %

Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct

Hensel JM, Ruiz C, Finney C, Dewa CS

Meta-analysis of risk factors for secondary traumatic stress in therapeutic work with trauma victims

Journal of Traumatic Stress 2015; 28: 83-91

View review abstract online

Comparison	Effect of age on risk of PTSD in professionals indirectly exposed to trauma through their therapeutic work with trauma victims.	
Summary of evidence	Moderate to high quality evidence (large samples, inconsistent, precise, direct) found no differences in the rates of PTSD between males and females following secondary workplace trauma.	
Secondary workplace trauma		



#### Sex

No differences in rates of PTSD between males and females following secondary workplace trauma;

15 studies, N = 3,934, r = 0.05, 95%CI -0.02 to 0.11, p > 0.05,  $I^2$  = 69%

Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Lin W, Gong L, Xia M, Dai W

Prevalence of posttraumatic stress disorder among road traffic accident survivors: A PRISMA-compliant meta-analysis

Medicine 2018; 97: e9693

View review abstract online

Comparison	PTSD in people after road traffic accidents.
Summary of evidence	Moderate quality evidence (large sample, inconsistent, imprecise, direct) found the prevalence of PTSD following road traffic accidents was higher in females than males (28% vs. 20%).

#### Road traffic accidents

15 studies, N = 6,804

The prevalence of PTSD following road traffic accidents was higher in females than males;

Males: prevalence = 20.49%, 95%CI 12.37% to 30.00%, I<sup>2</sup> not reported

Females: prevalence = 27.61%, 95%CI 17.44% to 39.08%, I<sup>2</sup> not reported

Consistency in results	Authors report data are inconsistent.
Precision in results	Appears imprecise
Directness of results	Direct

#### Pinguart M

Posttraumatic Stress Symptoms and Disorders in Parents of Children and Adolescents With Chronic Physical Illnesses: A Meta-Analysis



#### Sex

Journal of Traumatic Stress 2019; 32: 88-96 <u>View review abstract online</u>	
Comparison	PTSD in parents of children with a chronic physical illness (cancer, burns, heart disease, diabetes, epilepsy, and asthma).
Summary of evidence	High quality evidence (large sample, consistent, imprecise, direct) found a small association between increased PTSD symptoms in mothers than fathers of chronically ill children.
Parents of children with chronic physical illness	
184 studies, N = 30,068	
A small association between increased PTSD symptoms in mothers than fathers of chronically ill children;	
75 studies, $r = 0.19$ , 95%Cl 0.15 to 0.23, $p < 0.001$ , $Qp > 0.05$	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, Zandi MS, Lewis G, David AS

Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic

The Lancet Psychiatry 2020; 7: 611-27

View review abstract online

Comparison	PTSD in people post-coronavirus illness (severe acute respiratory syndrome [SARS], Middle East respiratory syndrome [MERS], or coronavirus disease 2019 [COVID-19]). Follow-up time varied between 60 days and 12 years.
Summary of evidence	Moderate quality evidence (large sample, appears inconsistent and imprecise, direct) found a medium-sized effect of higher rates of PTSD in females than males after a coronavirus infection.
	Coronavirus infections



#### Sex

A medium-sized effect showed rates of PTSD were higher in females than males after a coronavirus infection;	
4 studies, N = 402, OR = 3.85, 95%CI 1.18 to 12.54	
Consistency in results	Appears inconsistent
Precision in results	Appears imprecise
Directness of results	Direct

Shulla RM, Toomey RB

Sex differences in behavioral and psychological expression of grief during adolescence: A meta-analysis

Journal of Adolescence 2018; 65: 219-27

View review abstract online

Comparison	Rates of PTSD in adolescents following exposure to a death of a parent, sibling, or close friend.
Summary of evidence	Moderate to high quality evidence (large sample, consistent, unable to assess precision, direct) found a medium-sized effect that girls were more likely to develop PTSD symptoms than males.

#### Sex differences

A medium-sized effect showed girls were more likely to develop PTSD symptoms than males; 4 studies, N = 4,034, d = 0.36, 95%CI not reported,  $I^2 = 0\%$ 

Consistency in results	Consistent
Precision in results	Unable to assess; no CI reported.
Directness of results	Direct

Tang B, Deng Q, Glik D, Dong J, Zhang L

A Meta-Analysis of Risk Factors for Post-Traumatic Stress Disorder (PTSD) in Adults and Children after Earthquakes

International Journal of Environmental Research and Public Health 2017; 14: 1537



#### Sex

<u>View review abstract online</u>		
Comparison	PTSD after earthquakes.	
Summary of evidence	Moderate to high quality evidence (large sample, inconsistent, precise, direct) found small effects showed both adult and child females had an increased risk of PTSD following earthquakes.	
Earthquakes		
15 studies, N = 22,931		
Small effects showed both adult and child females had an increased risk of PTSD following earthquakes;		
Adults: OR = 1.85, 95%CI 1.69 to 2.02, $p < 0.05$ , $I^2 = 51\%$		
Children: OR = 1.45, 95%Cl 1.31 to 1.60, $p < 0.05$ , $l^2$ not reported		
Consistency in results	Inconsistent for adults.	
Precision in results	Precision in results Precise	

Trickey D, Siddaway AP, Meiser-Stedman R, Serpell L, Field AP

Direct

A meta-analysis of risk factors for post-traumatic stress disorder in children and adolescents

Clinical Psychology Review 2012; 32: 122-38

#### View review abstract online

**Directness of results** 

Comparison	PTSD in children and adolescents following any trauma.	
Summary of evidence	Moderate to high quality evidence (unclear sample size, consistent, precise, direct) found a small association between increased PTSD symptoms in female than male children and adolescents following any trauma exposure.	
Any trauma exposure		
A small association bet	ween increased PTSD symptoms in females than males following any trauma exposure;	

29 studies, N not reported, r = 0.15, 95%Cl 0.13 to 0.18, p < 0.001, Qp > 0.05

Consistency in results Consistent



#### Sex

Precision in results	Precise
Directness of results	Direct

Wang Y, Kala MP, Jafar TH

Factors associated with psychological distress during the coronavirus disease 2019 (COVID-19) pandemic on the predominantly general population: A systematic review and meta-analysis

PLOS ONE 2021; 15: e0244630

View review abstract online

Comparison	PTSD during the COVID-19 pandemic.
Summary of evidence	Moderate quality evidence (large samples, consistent, some imprecision, direct) found a trend small effect of greater risk of PTSD during the COVID-19 pandemic in females than males.

#### COVID-19

A trend small effect of greater risk of PTSD during the COVID-19 pandemic in females than males; 4 studies, N = 6,158, OR = 1.82, 95%CI 0.97 to 3.40, I<sup>2</sup> = 93.5%

	Consistency in results	Inconsistent
	Precision in results	Imprecise
	Directness of results	Direct

Xue C, Ge Y, Tang B, Liu Y, Kang P, Wang M, Zhang L

A meta-analysis of risk factors for combat-related PTSD among military personnel and veterans

PLoS ONE 2015; 10: e0120270

View review abstract online

Comparison	PTSD in military personnel and veterans.
Summary of evidence	Moderate to high quality evidence (large samples, inconsistent, precise, direct) found a small effect of an increased risk of PTSD in female than male military personnel and veterans.



#### Sex

Military personnel and veterans	
A small effect of an increased risk of PTSD in female than male military personnel;	
32 studies, N = 413,580, OR = 1.63, 95%CI 1.32 to 2.01, $I^2 = 42\%$	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

### Explanation of acronyms

CI = confidence interval, d = Cohens' d standardised mean difference,  $I^2$  = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, OR = odds ratio, p = statistical probability of obtaining that result, r = correlation coefficient, vs. = versus

### Sex



#### Explanation of technical terms

Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias - selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias - only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small<sup>22</sup>.

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect<sup>22</sup>.

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or <  $0.2^{23}$ . InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not

#### Sex

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confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents а strona association. Unstandardised (b) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in independent variable, statistically controlling the other independent for variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is heterogeneity. considerable |2 calculated from Q (chi-square) for the test of heterogeneity with the following formula<sup>22</sup>;

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also

recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed<sup>24</sup>.

Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a population, intervention, particular comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-tohead comparisons of A and B.

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#### Sex

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