

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	What work-related exposures are associated with post-traumatic stress disorder? A systematic review with meta-analysis
AUTHORS	Coenen, Pieter; van der Molen, Henk

VERSION 1 – REVIEW

REVIEWER	Siegrist, Johannes University of Dusseldorf, Faculty of Medicine
REVIEW RETURNED	10-Mar-2021

GENERAL COMMENTS	<p>This contribution provides a systematic review and meta-analysis of - mainly prospective - studies on occupational factors associated with PTSD. The majority of included investigations concerns armed forces and first responders. Based on pooled data, findings demonstrate elevated risks of PTSD in exposures to combat, army deployment, and confrontation with death. Moreover, in qualitative studies each one of the DSM-5 criteria of PTSD is associated with a significantly elevated disease risk. In summary, a solid body of knowledge documents a moderately increased PTSD risk associated with exposure to a number of stressful work features.</p> <p>This systematic review has been conducted with high methodological quality, meeting all standards of reporting, analysing and interpreting data. Particular strengths relate to the sensitivity analyses exploring risk of bias, the stratification of analyses according to DSM-5 criteria, and the calculation of population-attributable fractions. The presentation and discussion of results is clear and detailed, substantiated by rich supplementary information. The Discussion also emphasizes a protective role of social support. Given this impressive quality of reporting, the manuscript clearly meets the standards of publication, and my comments for revision are minor:</p> <ol style="list-style-type: none">1. Applying GRADE for evaluation of strength of evidence is correct. Maybe the issue of evaluating the causality of reported associations needs some more discussion as data on causal biological pathways are lacking. Here, reference to the Bradford Hill criteria of causality would be instructive. See also Schünemann H et al. (2011) The GRADE approach and Bradford Hill's criteria for causality. <i>J Epidemiol Community Health</i> 65,392.2. While the authors' conclusion of strengthening prevention is well taken, it should also be mentioned that many disasters are not preventable. Therefore, implementing successful treatment approaches to PTSD victims should also be included in policy implications of the study findings.
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	3. A minor detail: Could the name of the Reference source 22 and 25 be fully written?
REVIEWER	Candura, Stefano University of Pavia, Occupational Medicine Unit, Department of Public Health, Experimental and Forensic Sciences
REVIEW RETURNED	04-Jun-2021
GENERAL COMMENTS	The background and aims of the study are clearly defined. Methodology is appropriate. Results are clearly presented and discussed. Typos: in references 1 and 2, "ed." is written twice.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

This contribution provides a systematic review and meta-analysis of - mainly prospective - studies on occupational factors associated with PTSD. The majority of included investigations concerns armed forces and first responders. Based on pooled data, findings demonstrate elevated risks of PTSD in exposures to combat, army deployment, and confrontation with death. Moreover, in qualitative studies each one of the DSM-5 criteria of PTSD is associated with a significantly elevated disease risk. In summary, a solid body of knowledge documents a moderately increased PTSD risk associated with exposure to a number of stressful work features.

This systematic review has been conducted with high methodological quality, meeting all standards of reporting, analysing and interpreting data. Particular strengths relate to the sensitivity analyses exploring risk of bias, the stratification of analyses according to DSM-5 criteria, and the calculation of population-attributable fractions. The presentation and discussion of results is clear and, detailed, substantiated by rich supplementary information. The Discussion also emphasizes a protective role of social support. Given this impressive quality of reporting, the manuscript clearly meets the standards of publication.

My comments for revision are minor:

1. Applying GRADE for evaluation of strength of evidence is correct. Maybe the issue of evaluating the causality of reported associations needs some more discussion as data on causal biological pathways are lacking. Here, reference to the Bradford Hill criteria of causality would be instructive. See also Schünemann H et al. (2011) The GRADE approach and Bradford Hill's criteria for causality.

Response: Thank you for this suggestion. We have now elaborated on this topic in the discussion section of our manuscript. This part on page 11 now read:

'While our use of the GRADE framework provides an adequate way to assess quality of the evidence, it does not necessarily provide insights into causation of the association of work-related exposures and PTSD, for which other approaches such as the Bradford Hill criteria⁶³ could be used. It has been argued that the majority of the Bradford Hill criteria are to some extent incorporated in GRADE, such as the strength and consistency of the association⁶⁴. Other criteria, such as that of the biological plausibility are not well covered nor are they in the current review evidence regarding work-related PTSD. Future studies should therefore aim at providing more insights into this, to further build the evidence base around work-related PTSD and the biology of risk for PTSD⁶⁵.'

2. While the authors' conclusion of strengthening prevention is well taken, it should also be mentioned that many disasters are not preventable. Therefore, implementing successful treatment approaches to PTSD victims should also be included in policy implications of the study findings.

Response: Thank you for this good suggestion. We have now elaborated on this in the discussion section (page 10), where we write:

'Although the prevention of occupational diseases, including PTSD, is preferable, not all risks can be fully eliminated as witnessing traumatic events, disasters and war situations are likely to remain present in our working situations. In the working environment it is also important to attenuate the

impact of exposures on workers or to treat them when having developed work-related PTSD. In the current review we also identified work-related factors that can reduce the risk of PTSD, which can be helpful to attenuate the impact of stressful exposures. For instance, among highly exposed occupational groups, a high level of preparedness (OR[95%CI]: 0.6[0.4 0.9])³, unit support (OR[95%CI]: 0.5[0.3 0.8])³, post-deployment support (OR[95%CI]: 0.3[0.2 0.4])³ and social support (OR[95%CI]: 0.96[0.93 0.98])⁴ were all found to be associated with a reduced risk of PTSD. These elements can be used in the development of interventions, especially for those in occupations that involve high PTSD risks.'

3. A minor detail: Could the name of the Reference source 22 and 25 be fully written?

Response: According to the journal's guideline, we are using abbreviations of the journal titles. For this particular journal, Medical Surveillance Monthly Report, the abbreviation is MSMR. We have not made any changes to the manuscript.

Reviewer 2

The background and aims of the study are clearly defined. Methodology is appropriate. Results are clearly presented and discussed.

4. Typos: in references 1 and 2, "ed." is written twice.

Response: Thank you for your suggestion. We corrected this.