Eksplorerende review om sammenhængen mellem belastende og længerevarende stresspåvirkninger på arbejdspladsen og udvikling af belastningsreaktion (fraset posttraumatisk belastningsreaktion)

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Forord

Arbejdsmarkedets Erhvervssikring og Erhvervssygdomsudvalget har ønsket en udredning af, om der er tilstrækkelig lægevidenskabelig evidens for en årsagsmæssig sammenhæng mellem belastende og længerevarende stress-eksponering på arbejdspladsen og udvikling af belastningsreaktion (fraset posttraumatisk belastningsreaktion (PTSD)). Det blev understreget, at belastende og længerevarende stress-eksponering på arbejdspladsen skulle forstås som eksponeringer, der med hensyn til alvorlighedsgrad, er lavere end krævet for PTSD.

Projektet er udført på opdrag af Arbejdsmiljøforskningsfonden efter særligt opslag med ansøgningsfrist 3. september 2018 og tilsagn om bevilling 18. december 2018 (projektnr 45-2018-09). Arbejdet med rapporten blev påbegyndt i januar 2019 og afsluttet 15. januar 2020.

Lægevidenskabelig evidens om årsagssammenhænge, hvor evidensen væsentligst baseres på epidemiologiske undersøgelser, forudsætter, at eksponering og udfald er målt uafhængigt af hinanden. Dette forhold indebærer i høj grad udfordringer for stress-relaterede lidelser, hvor eksponeringen er en forudsætning for at stille diagnosen belastningsreaktion. Vores bedste bud på, hvor der måske kunne foreligge relevante epidemiologiske undersøgelser med den forudsatte uafhængighed mellem eksponering og udfald, har været gentagne belastende hændelser af mindre alvorlig karakter end svarende til PTSD. I vores projektansøgning foreslog vi derfor at opgaven blev løst med et eksplorerende litteraturstudie vedrørende denne problemstilling.

Projektet er udført i et samarbejde mellem de på forsiden anførte forfattere og institutioner. David Coggon og Patricia Casey var fra projektstart tilknyttet som eksterne konsulenter, men har deltaget i projektet i et omfang, der gør det naturligt, at de er medforfattere. Reviewet er udarbejdet på engelsk og suppleres med et mere letlæst dansk resumé.

Vi ønsker at takke professor, overlæge, dr.med. Lars Vedel Kessing, Psykiatrisk Center København, Afdeling O, Region Hovedstadens Psykiatri, og overlæge, docent, PhD Gunnar Ahlborg, Instutet for Stress Medicin, Göteborg Universitet for deres bedømmelser af manuskriptet.

København, januar 2020

Forfattergruppen

Indholdsfortegnelse

Dansk Resumé

Baggrund og afgrænsning

Opslaget til dette review har ønsket en vurdering af den årsagsmæssige sammenhæng mellem belastende og længerevarende stress-eksponering på arbejdspladsen og udviklingen belastningsreaktion (fraset posttraumatisk belastningsreaktion (PTSD)). Det blev understreget, at belastende og længerevarende stress-eksponering på arbejdspladsen skulle forstås som eksponeringer, der med hensyn til alvorlighedsgrad, var lavere end krævet for PTSD.

I WHO's sygdomsklassifikationer (ICD-10 og ICD-11) forudsætter diagnosen PTSD, at traumet, der kan være kortere eller længerevarende, er så ekstremt svært at næsten alle, der udsættes for det vil udvikle symptomer på lidelsen. Symptomerne centrerer sig omkring 1) genoplevelse af traumet (flashbacks, mareridt), 2) undgåelse af omstændigheder, der minder om traumet, og 3) en vedvarende fornemmelse af overfølsomhed og alarmberedskab. Symptomerne varer adskillige uger og skal ledsages af en betydelig funktionssvækkelse på det personlige og sociale plan.

Belastende længerevarende eksponeringer, der ikke har tilstrækkelig sværhedsgrad til at opfylde kravene for en PTSD-diagnose, kunne være mindre traumatiske og stressende hændelser gentaget med en vis hyppighed eller andre definerbare psykosociale eksponeringer på arbejde. En undersøgelse af en årsagsmæssig sammenhæng mellem sådanne påvirkninger og en psykisk lidelse forudsætter, at sygdomsbilledet er rimeligt veldefineret. Det behøver ikke nødvendigvis at ligne PTSD-symptomer selv om belastningen kunne være gentagne mindre traumer og stressende hændelser.

For sygdomsbilleder, der svarer til tilpasningsreaktioner (adjustment disorders) i forbindelse med fx konflikter på arbejde og lignende belastninger, anses årsagssammenhængen allerede som etableret gennem en overbevisende sygehistorie.

Ifølge AES-retningslinjer for vurderingen af graden af evidens for en årsagssammenhæng mellem udsættelse for en specifik risikofaktor og et specifikt udfald er nøglekriteriet den epidemiologiske evidens. En årsagsvurdering baseret på epidemiologisk evidens forudsætter at eksponering og udfald er målt uafhængigt af hinanden. Epidemiologiske undersøgelser af kausale relationer mellem arbejdsrelaterede psykosociale faktorer og ICD-definerede stress-relaterede lidelser, hvor den formodede årsag er en del af diagnosekriteriet, er ikke mulig.

På ovenstående baggrund har vi afgrænset opgaven til en eksplorerende undersøgelse af kohorte og case-kontrolundersøgelser af længerevarende gentagne belastende hændelser på arbejde, der har en mindre sværhedsgrad en krævet til diagnosen PTSD, med henblik på om de var risikofaktorer for udvikling bestemte symptombilleder forenelige med en stress-lidelse, hvor eksponeringen ikke er en del af diagnosen. Vi formodede, at sådanne lidelser relateret til stressende hændelser ofte ville blive publiceret som 'subthreshold' eller 'subclinical' PTSD-tilfælde, altså tilfælde, hvor stressende hændelser og symptomer ikke lever op til kravene for PTSD og hvor man i princippet ville kunne designe studiet således at information om sygdomstilstanden (symptomer og adfærd) ikke var betinget af udsættelse for bestemte formodede risikofaktorer (stressorer).

Eksplorerende litteratursøgning

Vi lavede to litteratursøgninger I PubMed. Den første søgte i titler og abstracts på søgeord relateret til traumer og vold i kombination med 'stress disorder' eller 'mental disorder', afgrænset til longitudinelle

undersøgelser og case-kontrol undersøgelser. Denne søgning gav 52 hits, men ved gennemlæsning af titler og abstract var der ingen af dem, der var relevante i forhold til dette review. Den anden søgning søgte titler og abstracts med på søgeordene 'subthreshold' or 'subclinical' i kombination med 'PTSD' eller 'post traumatic stress' og gav 393 hits, som efter afgrænsning til longitudinelle og case-kontrol undersøgelser blev til 62 hits.

Læsning af titel og abstracts, evt. suppleret med gennemlæsning af hele artiklen og gennemgang af deres referencelister resulterede i nogle få longitudinelle studier af interesse i sammenhængen. Det drejede sig om studier af politi, buschauffører, militært personel og socialpædagoger.

Det sidste studie er et dansk studie og det eneste studie baseret på en veldefineret studiegruppe med gentagne potentielt stressende hændelser over en længere periode og en mindre sværhedsgrad af symptomer end krævet til diagnosen PTSD. Dette studie viste en sammenhæng mellem de anførte hændelser og PTSD-lignende symptomer, men var udelukkende baseret på spørgeskema-oplysninger fra de undersøgte personer, og en diagnose, der ikke var registreret uafhængigt af eksponeringen. Sammenhængen kan derfor forklares ved common method bias.

Resume og konklusion

Denne eksplorerende litteratursøgning viste, at kohortestudier af gentagne stressende hændelser som risikofaktorer for udvikling af stress-lidelser formentlig er ganske få. Den viste også at begrebet 'subthreshold' PTSD er veletableret, men definitionerne varierede og var ofte baseret på mindre krav til symptomer end til eksponeringer i forhold til kravene til en PTSD-diagnose. Der er en vis evidens for at 'subthreshold' PTSD er forbundet med funktionsnedsættelse, brug af sundhedssystemet og udvikling af PTSD. Vi fandt ingen undersøgelser af erhvervsmæssig eksponering for gentagne stressende hændelser som risikofaktor for udvikling af stress-lidelser under follow-up, hvor udfald og eksponering var registret uafhængigt af hinanden.

Anbefalinger vedrørende fremtidig forskning

Vi anbefaler, at fremtidige studier bruger metoder, der sikrer en uafhængig vurdering af eksponering og psykiske lidelser. Psykiske lidelser bør vurderes på basis af semi-strukturerede kliniske interviews, blindet i forhold til eventuelle stressende hændelser. Rapportering af sådanne hændelser bør udføres med validerede rutine-metoder ledsaget af systematiske oplysninger om hvordan de håndteres, fx vedr. gruppe-debriefing og individuelle behandlingstilbud. Klinisk vurdering af symptomer bør undgå at forbinde symptomer med formodede risikofaktorer (stressende hændelser og andre stressorer). For eksempel bør oplysninger om mareridt og undvige-adfærd baseres på en første neutral udspørgen uden relation til stressende hændelser, og først hvis der angives sådanne symptomer bør der udspørges neutralt om indholdet af mareridt og undvigeadfærd.

Vi anerkender, at det kan være vanskeligt at konstruere en epidemiologisk studie protokol, der tager højde for mulig bias. Men hvis det ikke er muligt, vil studiet kun have begrænset værdi mhp at vurdere den årsagsmæssige sammenhæng mellem eksponering og udsættelse.

Review

English

Exploratory review of the relationship between work-related straining and long-lasting psychosocial exposures and stress disorders (other than PTSD)

Background

The call for this review specified that it should assess the causal relationship of straining and long-lasting stressful exposures in the workplace to the development of mental disease in the form of stress disorders (other than posttraumatic stress disorder (PTSD)). It was emphasized that straining and long-lasting, stressful exposures in the workplace are to be understood as exposures which, with regard to severity, are below what is required for the diagnosis of PTSD.

In the ICD-10 classification of mental disorders, a diagnosis of PTSD requires that the patient has been exposed to a stressful event or situation (either short or long-lasting) of exceptionally threatening or catastrophic nature, which would be likely to cause pervasive distress in almost anyone.

In the ICD-11 classification PTSD is defined as a disorder that may develop following exposure to an extremely threatening or horrific event or series of events.

Neither definition of PTSD requires the triggering stressful exposure to have been long-lasting.

Key PTSD-symptoms in the two classification systems overlap. This review applies the description in ICD-11 because this system will be the standard from 2022. According to ICD-11 PTSD is characterized by all of the following symptoms:

> 1) re-experiencing the traumatic event or events in the present in the form of vivid intrusive memories, flashbacks, or nightmares. These are typically accompanied by strong or overwhelming emotions, particularly fear or horror, and strong physical sensations;
>
> 2) avoidance of thoughts and memories of the event or events, or avoidance of activities, situations, or people reminiscent of the event or events; and
>
> 3) persistent perceptions of heightened current threat, for example as indicated by hypervigilance or an enhanced startle reaction to stimuli such as unexpected noises.
>
> The symptoms persist for at least several weeks and cause significant impairment in personal, family, social, educational, occupational or other important areas of functioning.

Stressful exposures insufficient for a diagnosis of PTSD could be less severe stressful events or other identifiable psychosocial stressors at work.

Since the terms of reference for the current review specified that exposure had to be long-lasting, mental symptoms related to *single* stressful exposures were not considered. Exposure to frequent but less severe stressful events was included if they were considered to be stressful and occurred over a sustained period. It is not clear, however, how severe events should be to be assessed as stressful and how frequently and

over how long time they should occur too be assessed as long-lasting. Furthermore, if frequent exposure to less severe stressful events is suspected of causing mental disorders, those disorders must be clearly defined. Since stressful events do not have the severity required for PTSD, the resultant symptoms may not be the same as those of PTSD. Thus, re-experiences, avoidance behavior and perceptions of constant threat should not necessarily be required to define a mental disorder caused by frequent exposure to less severe stressful events.

As stated above, stressful exposures below the threshold of severity that is required for a diagnosis of PTSD could be identifiable non-traumatic psychological stressors as exemplified in the ICD-11-definition of adjustment disorders:

> Adjustment disorder is a maladaptive reaction to an identifiable psychosocial stressor or multiple stressors (e.g., divorce, illness or disability, socio-economic problems, conflicts at home or work) that usually emerges within a month of the stressor. The disorder is characterized by preoccupation with the stressor or its consequences, including excessive worry, recurrent and distressing thoughts about the stressor, or constant rumination about its implications, as well as by failure to adapt to the stressor that causes significant impairment in personal, family, social, educational, occupational or other important areas of functioning. The symptoms are not of sufficient specificity or severity to justify the diagnosis of another Mental and Behavioural Disorder and typically resolve within 6 months, unless the stressor persists for a longer duration.

This definition mentions conflicts at work, but no other work-related exposures. Maladaptive reactions to, for example, conflicts with superiors or colleagues could be classified as an adjustment disorder if symptoms were in accordance with the ICD-11 description. heThe ICD-11-definitiion describes criteria to discriminate these disorders from normal adaptive reactions to stress but not from depressive episodes (1), and there is no guidance on assessment of any lower level of intensity or duration of the stressor.

Against the background outlined above, we decided that this part of the review should examine whether there is evidence of a causal relation between repeated occupational stressful eventsover a longer period and of lower intensity than would be required for a diagnosis of PTSD, and the development of mental symptoms and disorders.

A causal relation requires that the exposure is present before the outcome occurs. If the exposure is well-defined and unusual, and the outcome is well-defined, unusual, and a plausible consequence of the exposure, then a consistently close time-relation between exposure and outcome may be sufficient to establish causation - for example falling and breaking a leg. PTSD-diagnoses are to some extent modelled on that situation, considering a close time-relation between symptoms specifically related to the event (re-experience and avoidance behaviour). When exposures and outcomes are more common and less well-defined, establishing causality between a risk factor and a mental disorder depends mainly on inference from epidemiological studies. In the epidemiological context it is preferable that exposures and outcome be ascertained by independent methods, to avoid common method bias. Moreover, it must be established that the exposure preceded the outcome. This is often done by using a cohort study design with exclusion of individuals in whom the outcome of interest is already present at baseline, and then studying exposure at baseline as a predictor for the outcome at follow-up. Exposures should be clearly described, and mental health outcomes should be diagnosed by experienced clinicians using a semi-structured clinical interview, rather than simply by questionnaires. As an alternative, case-control studies may be used if outcomes can be clearly defined and if exposures can be assessed by methods that are independent of the outcome.

In general, epidemiological studies addressing causal relations between work-related psychosocial exposures and ICD defined stress-related disorders are not feasible because the assumed cause is part of

the diagnostic criteria of the latter. However, as repeated stressful events at the workplace can be objectively ascertained and sub-threshold PTSD seems a rather well established entity (although not a ICD diagnosis) that may be defined without including the supposed triggering event(s) – it was decided to limit the review to an exploration of work-related repetitive trauma (stressful events) and sub-threshold PTSD (as specified in the application study protocol for this call).

We therefore looked for cohort and case-control studies fulfilling these conditions and dealing with repetitive stressful events of lower intensity than required for a diagnosis of PTSD, experienced over a longer period, and analysed as a predictor of stress disorders. We assumed that such stress disorders would often be published as 'subthreshold' or 'subclinical' PTSD cases.

Subthreshold PTSD has been associated with functional impairment (2), help-seeking (2, 3) and as a predictor of PTSD (4). A narrative review from 2010 presented results from a number of very different studies suggesting that repeated minor trauma could lead to symptoms resembling PTSD (5).

Exploratory literature search

We made two literature searches in PubMed (October 8th, 2019). The first searched titles and abstracts for terms indicating repeated trauma or violence in combination with a stress disorder or a mental disorder in the context of a study that was tagged as 'longitudinal', 'cohort', 'prospective' or 'case-control'. We excluded studies with the terms 'treatment' or 'therapy' in the title (PubMed Search string: ((((((((((repeated[Title/Abstract] OR repetitive[Title/Abstract])) AND (trauma[Title/Abstract] OR violence[Title/Abstract] OR violent[Title/Abstract]))) AND ((stress disorder[Title/Abstract]) OR mental disorder[Title/Abstract]))) AND ((longitudinal[Title/Abstract] OR cohort[Title/Abstract] OR prospective[Title/Abstract] OR case-control[Title/Abstract] OR case-referent[Title/Abstract]))))) NOT (therapy[Title] OR treatment[Title]))).
This search gave 52 hits. Scrutiny of titles and abstracts revealed no studies of interest for the present review.

The other search in PubMed first assessed the extent of the literature on subthreshold PTSD. We searched titles and abstracts for the terms 'subthreshold' or 'subclinical' in combination with 'PTSD' or 'post-traumatic stress', excluding studies on treatment (in PubMed defined by the search string: (((((((subthreshold) OR sub-threshold)) OR ((sub-clinical[Title/Abstract]) OR subclinical))) AND (((PTSD[Title/Abstract]) OR posttraumatic stress) OR posttraumatic stress))) NOT ((treatment[Title]) OR psychotherapy[Title]))). We did not include the term "PTSD-symptoms" as we deemed this concept insufficiently specific as a marker of subthreshold caseness.
This search resulted in 393 hits, indicating that the concept of subthreshold PTSD-caseness is not uncommon in research on mental symptoms related to exposure to violence or threats of violence.

We examined how many of these studies were longitudinal or case-control investigations by adding the search terms 'longitudinal' or 'cohort' or 'prospective' or 'case-control' or 'case-referent' to the search string applied to titles and abstracts. This gave 62 hits, indicating that the large majority of the 393 studies were cross-sectional or that the design of the study was not considered in its PubMed indexing.

Reading titles and abstracts for these studies, scrutiny of full text for selected articles and "snowballing" from the latter, revealed a few longitudinal studies (but no case-control studies) that included cases of

subthreshold PTSD as an outcome in occupational groups such as police officers (3, 6), bus drivers (7), military personnel (4), and social educators working with disabled adults (8). Only two of these were identified from the literature search (6, 8), indicating that more studies could probably be found by expanding and refining the search terms. However, the representativeness of participants exposed to stressful events in the studies of Carlier (6), Marchand (3) and Zhou (7) was unclear. Furthermore, the stressful events in studies of Marchand (3) and Fink (4) were single events consistent with requirement for PTSD. In the studies of Zhou (7) and Carlier (6) the stressful events were single events of mixed severity.

Pihl-Tingvad et al. (8) examined the effects of the frequency (defined by respondents) and severity (defined by researchers) of a broader range of stressful events on PTSD-symptoms in a cohort of 1763 social educators working with disabled adults. At follow-up 3.5% of participants had symptoms corresponding to subclinical or clinical PTSD as defined by questionnaire responses. The incidence increased with frequency and severity of violent events in the workplace. This study supports a link between repeated work-place violence of lower severity than is required for a diagnosis of PTDS, and mental illness with symptoms that fall short of the criteria for PTSD. However, all information was based on questionnaires. The exposure assessment was not validated against objective data, and the questionnaire outcome measure had not been validated against a semi-structured clinical interview. The outcome was based on self-report of symptoms specifically linked to their previously reported stressful events, and common method bias may therefore have influenced the results. Also, the exposure-response relationship to severity of symptoms seems questionable, being based on a group with only one outcome and a dubious ordering of the lowest exposure groups.

The study did not report on consequences of subclinical PTSD or clinical PTSD in terms of functional impairment or help-seeking (primary care, referral to psychiatrist or psychologist, treatment with psychotropic drugs etc.).

Summary and conclusion

This exploratory literature search showed that cohort studies of work-related repetitive low-level stressful events as a predictor of incident stress disorders are probably very few. It also shows that the concept of subthreshold PTSD is well established within research. However, definitions vary across studies and are often based on relaxation of symptom requirements rather than the exposure requirements for a full PTSD-diagnosis. There is some evidence that subthreshold PTSD is associated with functional impairment, help-seeking and future PTSD. We found no studies of occupational exposure to repeated low-level traumas as a risk factor for incident stress disorders during follow-up, assessed by a method independent of exposure. Thus, there is insufficient epidemiological evidence to determine whether there is a causal relationship between exposure and outcome.

Suggestions for additional research

We suggest that future studies use methods that ensure independent assessment of exposure and mental disorders. Mental disorders should be assessed by semi-structured clinical interviews blind to any exposure to stressful events. The reporting of such events should be made by routine validated methods and a record should be made of how it was handled, e.g. by group debriefing or individual treatment schedules. Clinical assessment of symptoms should not link a symptom to any stressful evemt. For example, nightmare

re-experience of stressful events and avoidance behaviour related to stressful events may be assessed in a neutral way by asking about nightmares and avoidance behaviour without mentioning any events, and if reported, the participant could then be asked about the content of nightmares and specific aspects of avoidance behaviour.

We acknowledge that it may be difficult to construct an epidemiological study protocol with no biases inherent in the methods of assessing exposures and outcomes. However, if that cannot be done, the study will be of only limited value in assessing a *causal* relation between exposure and outcome.

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Eksterne bedømmelser

Externe bedømmelser med besvarelser

Reviewer #1:

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Exploratory review of the correlation between straining and long-lasting, stressful exposures in the workplace and the development of mental disease in the form stress disorders (apart from posttraumatic stress disorder)

The call for this review specified that it should include the relationship of straining and long-lasting stress exposures in the workplace and the development of mental disease in the form of stress disorder (apart from posttraumatic stress disorder (PTSD)). It was emphasized that straining and long-lasting, stressful exposures in the workplace are to be understood as exposures which, with regard to severity, are below what is required for the diagnosis of PTSD.

The search included cohort and case-control studies fulfilling these conditions and dealing with repetitive trauma of lower intensity than required for a diagnosis of PTSD, experienced over a longer period, and analysed as a predictor of stress disorders. It was assumed that such trauma-related disorders would often be published as 'subthreshold' or 'subclinical' PTSD cases.

The Exploratory literature search seems well conducted although importantly only searches from PubMed were included.

The exploratory literature search showed that cohort studies of repetitive low-level trauma as a predictor of incident stress disorders are probably very few. It also shows that the concept of subthreshold PTSD is well established within research. The authors identified no longitudinal or case-control studies of occupational exposure to repeated low-level traumas as risk factors for incident stress disorders during follow-up, assessed by a method independent of exposure. It seems correctly concluded that there is insufficient epidemiological evidence to determine whether there is a causal relationship between exposure and outcome.

The authors acknowledge that it may be difficult to construct an epidemiological study protocol with no biases inherent in the methods of assessing exposures and outcomes but also correctly that if this cannot be done, the study will be of only limited value in assessing a *causal* relation between exposure and outcome.

The explorative review seems well conducted although it is recommended to include searches from other databases than PubMed alone.

Response: The review is exploratory. We are confident that further searches would not have produced a number of studies which would have changed the conclusion.

Reviewer #2:

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Institute of Stress

Review of the manuscript *" Exploratory review of the correlation between straining and long-lasting, stressful exposures in the workplace and the development of mental disease in the form stress disorders (apart from posttraumatic stress disorder)"* by Mikkelsen et.al.

Background and aim

The scope and aim of this paper are to me somewhat confusing, when comparing the title, the first sentence, the authors formulation of what the review should examine, and their assumption about disorders found in the literature (sub-threshold PTSD). In the title the word "correlation" is used but not found in the text where "relationship" and "causal relation" is used. The title use (straining and long-lasting) "stressful exposure", which after the definition of PTSD is defined for the purpose of the review as "less severe traumatic events or identifiable psychosocial stressors". The authors then state that against the background given the focus will be on "repeated occupational traumas" and searched for literature indicating "repeated trauma or violence". Also, the term low-level trauma is used. Finally, the title use "mental disease in the form of stress disorders" (apart from PTSD), as in the first sentence, while the authors decided to examine "mental symptoms and disorders" and searched for mental disorder and stress disorder.
Response: We accept that the relations of the many different concepts referred to above are not completely clear. However, this delimitation of the task was clearly specified in the application protocol for this call.

In order to further clarify the delimitation of the task, we have included this additional explanation in the introduction:

"In general, epidemiological studies addressing causal relations between work-related psychosocial exposures and ICD defined stress-related disorders are not feasible because the assumed cause is part of the diagnostic criteria of the latter. However, as repeated trauma in terms of events at the workplace can be objectively ascertained and sub-threshold PTSD seems a rather well established entity (although not a ICD diagnosis) that may be defined without including the supposed triggering event(s) – it was decided to limit the review to an exploration of work-related repetitive trauma (stressful events) and sub-threshold PTSD (as specified in the application study protocol for this call)."

For belastningsreaktioner udgør de manglende diagnostiske kriterier og den forudbestemte sammenknytning mellem symptomer og årsag et principielt og praktisk problem med hensyn til at vurdere diagnosernes validitet og kriterier for relevante belastninger. Vi foreslår derfor et eksplorerende

litteraturstudie om sammenhænge mellem belastninger og symptom-konstellationer, der ligner, men ikke opfylder de diagnostiske krav til posttraumatisk stress syndrom (PTSD). Der har de senere år inden for PTSD-litteraturen været betydelig interesse for disse sammenhænge, bl.a inden for fag med belastninger i form af vold og trusler og andre former for sværere emotionel belastning (fx politi, akutmodtagelser på hospital og lignende). Litteratur-studiet skal danne baggrund for forslag til forskningsprojekter, der bedre kan belyse de problemstillinger, der er rejst i opslaget, end man kan i dag

As I read it, the review in fact ends up in exploring if the available literature suggests that there is evidence for a causal relationship between workplace exposure to (low-level) repeated/repetitive trauma and subthreshold PTSD. Straining and long-lasting stress exposures in the workplace is a much broader concept, including a range of psychosocial conditions and factors, of which some may be denoted as trauma. Also, mental/stress symptoms and disorders include many diagnoses and clinically relevant illness besides PTSD and sub-threshold PTSD. Among the stress-related conditions F43 in ICD-10 (the ICD-11 classification have not been in use when studies were made) only Adjustment disorder is mentioned (besides PTSD). Since there is a time-limit condition for this diagnosis physicians will use other another diagnosis for patients with incapacitating symptoms as a reaction to long-standing severe stress, e.g. depression and/or anxiety, if such criteria are met, or Other reactions to severe stress (F43.8). The latter is sometimes used when other concepts found in the literature such as “Clinical burnout” or “Exhaustion syndrome” are applied as a description of the long-standing severe illness. These are not generally accepted, but nor is Sub-threshold PTSD. Overlapping of these as clinical conditions is obvious.
Response: We agree with this description of reality. To review and solve these problems is close to impossible. This is why we chose to delimit the task as correctly understood by the reviewer, and as we wrote in the study protocol.

Method and result

This is briefly but sufficiently described for this type of report under the same heading *Exploratory literature search.* There is no flow-chart and no tables presenting the included studies, indicating that the present paper is not intended for publication. The main limitations are clearly indicated.
Response: Correct

Summary and conclusion

Given that the review took PTSD as its starting point and the authors found sub-threshold PTSD to be the only relevant stress condition/disorder in published studies on the matter, and that repetitive low-level trauma was the exposure assessed, the summary and conclusions presented seem well motivated.