The course of PTSD in naturalistic long-term studies: High variability of outcomes. A systematic review

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Background: With a lifetime prevalence of 8% posttraumatic stress disorder (PTSD) is one of the most common mental disorders; nevertheless, its longitudinal course is largely unknown. Aims: Our aim was to conduct a systematic review summarizing available findings on the prospective, naturalistic long-term course of PTSD and its predictors. Methods: Databases MEDLINE and PsycINFO were searched. Main selection criteria were: 1) naturalistic cohort study with a follow-up period of at least 3 years, 2) adult participants with observer-rated or probable PTSD at baseline. Results: Twenty-four cohorts (25 studies) were retrieved (14 with observer-assessed, 10 with probable PTSD). In total, they comprised about 10,500 participants with PTSD at baseline that were included in the long-term follow-ups. Studies investigating patient populations with observer-assessed PTSD found that between 18% and 50% of patients experienced a stable recovery within 3–7 years; the remaining subjects either facing a recurrent or a more chronic course. Outcomes of community studies and studies investigating probable PTSD varied considerably (remission rates 6–92%). Social factors (e.g. support) as well as comorbid physical or mental health problems seem to be salient predictors of PTSD long-term course and special focus should be laid on these factors in clinical settings. Conclusions: Included studies differed notably with regard to applied methodologies. The resulting large variability of findings is discussed. More standardized systematic follow-up research and more uniformed criteria for remission and chronicity are needed to gain a better insight into the long-term course of PTSD.

Course, Posttraumatic stress disorder, Predictors, PTSD, Recovery, Remission.

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Traumatic experiences are common. Lifetime exposure rates range between about 50% and 70% in the general population (1–3). Posttraumatic stress disorder (PTSD) presumably is the core psychopathology in the aftermath of traumatic events (4, 5) and while it is one of the most frequent mental disorders with a lifetime prevalence of about 8% (6), its long-term course is largely unknown (7).

The course of PTSD has been examined in retrospective and prospective longitudinal studies that differed notably with regard to applied methods, research objectives and assessed outcomes (8, 9). Prospective studies investigating various samples of traumatized populations reported PTSD remission rates that ranged between 35% and 66% after 3–36 months (10–15). These findings suggested that a considerable percentage of subjects with PTSD remitted as time passed, while in others PTSD was a chronic condition, lasting several years.

A recent meta-analysis quantitatively summarized remission rates from PTSD that had been reported in 42 naturalistic long-term outcome studies of more than 81,000 untreated subjects with PTSD (9). The authors included studies with a minimum follow-up period of 10 months and found that on average 44% of participants with PTSD at baseline were non-cases at follow-up. There was a very large amount of variation in remission rates over all samples (8–89%), accordingly heterogeneity was found to be extremely high ($I^2 = 97\%$). Findings of this meta-analysis show that participants with PTSD have been extensively studied but knowledge about the course of PTSD is still scarce.

One of the reasons why findings on remission from PTSD vary enormously from study to study might be related to the problem that its assessment or more generally speaking the definitional problem of what defines
remission in PTSD and how it can be assessed properly has yet not been solved. This issue has recently been broadly and critically discussed by North & Oliver (15).

Two main approaches for defining remission exist: 1) a symptom-based definition (i.e. no more symptoms of the disorder are present) and 2) a threshold-based definition (i.e. some symptoms remain, but they have fallen beneath a diagnostic threshold). According to DSM-IV-TR (16), for a full remission the first definition applies while for partial remission the second one applies. The assessment instrument that is used in a study usually determines the definition of outcome that has to be applied which in turn influences reporting of findings. Moreover, studies applying a threshold-based definition usually also refer to the term remission, which in truth can be misleading and adds to the observed heterogeneity of findings. Consequently, more uniform definitions are needed to enhance the field. Nevertheless, North & Oliver (15) also state that regardless of the definition used, prior studies demonstrated substantial PTSD chronicity (p. 1194).

Various predictors of PTSD onset have been identified, such as early childhood trauma, lower education, female gender, belonging to an ethnic minority and pre-existing psychiatric psychopathology (17–21). It has also been suggested that the severity of the traumatic event itself, initial reactions in the face of a trauma as well as peritraumatic dissociation or early hyperarousal play a role in PTSD onset (17–19, 22–24). In contrast, only a few factors predictive of the PTSD course have been described so far. Among them are early postdisaster symptoms (e.g. acute stress symptoms), which have been suggested to be predictive of a more chronic long-term course (25–27). The same seems to be the case for posttraumatic circumstances like occupational, financial, health or family problems as well as a lack of social support in the aftermath of a trauma (17, 28, 29).

Methods

Identification of relevant literature

To identify relevant literature, electronic databases Medline and PsycINFO were searched up to October 1, 2014 for English language articles. Manual searches of reference lists of included studies and relevant reviews were also performed. Search terms were “PTSD”, “posttraumatic stress disorder”, “course”, “trajectory”, “remission”, “remit”, “recover” and “follow-up” (see Appendix).

Selection criteria

The following selection criteria were applied: 1) naturalistic cohort study with a follow-up period of at least 3 years, 2) adult participants diagnosed with PTSD at baseline, 3) study presenting at least one follow-up assessment of participants with PTSD at baseline, 4) PTSD diagnosed via interview (observer rating) or a self-report scale with a defined cut-off score or algorithm for establishment of diagnosis, 5) baseline assessment taking place in 1980 or later, and 6) minimum of three participants in long-term follow-up.

An important factor that might hamper comparability of PTSD rates across different studies is the use of self-rated vs. observer-rated PTSD assessments. The former often apply a cut-off score to assess PTSD caseness or simply refer to PTSD symptoms, while the latter apply (structured) interviews that are administered by trained staff members or experienced clinicians. An advantage of studies using self-rating scales is that they usually comprise much larger samples as diagnostic assessment is less time and cost-intensive. On the other hand, the sole use of self-report scales may carry a
higher probability of over- or underestimating PTSD caseness. We decided to include both types of studies and report results separately.

For reporting long-term outcome, we used the percentages of recovery, remission, recurrence and chronic course as provided by included studies. As mentioned above, defining remission in PTSD can be problematic with regard to symptom versus threshold-based criteria. Furthermore, the terms recovery and remission also imply different outcomes but are sometimes used synonymously to describe improvement. Thus, for our review, we decided to apply the following definitions of outcome: in order to be classified as recovered or fully remitted participants had to be described as (nearly) symptom-free over a certain time span (i.e. symptom-based definition). In contrast, participants were classified as remitted if they were free of a PTSD diagnosis at a certain point in time. In this definition, remission implies a reduced PTSD symptomatology, which could, however, merely reflect a momentary shift in PTSD severity (i.e. a threshold-based definition). Recurrence was defined as the comeback of full PTSD symptoms after recovery had been achieved. A chronic course was defined as either fulfilling the diagnostic criteria or screening positive for PTSD at both or all diagnostic assessments, or by still showing considerable residual symptoms. The term “partial remission” was dropped for the present review.

**Data extraction and review process**

After completing literature searches as outlined in Table A1 (see Appendix to be found online at http://informahealthcare.com/doi/abs/10.3109/08039488.2015.1005023), all hits \( n = 331 \pm 12 \) were saved in EndNote. Two researchers (CS, MH) independently screened titles and abstracts according to the predefined selection criteria. All potentially relevant articles were then retrieved for full-text review \( n = 106 \). Uncertainties regarding inclusion were discussed. A flow chart showing the process of study selection and reasons for exclusion is given in Fig. 1.

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### IDENTIFICATION

Potentially relevant articles identified through electronic searches in Medline and PsycINFO: 331

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### SCREENING

Articles screened on basis of title and abstract \( n = 343 \)

236 articles excluded based on review of titles and/or abstracts

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### ELIGIBILITY

106 articles retrieved for full-text review

81 articles excluded. Reasons for exclusion \( n \):

- No long-term follow-up \( \geq 36 \) months (18)
- Cross-sectional data (14)
- Diagnostic assessment unclear (3)
- No baseline PTSD assessment (3)
- Assessment of lifetime PTSD (1)
- Retrospective design (2)
- Different outcome (e.g. change of brain anatomy, incident CHD, cortisol level change; or same sample as an already included partner study but different outcome) (17)
- Case study (1)
- Treatment trial (1)
- Children and adolescents (6)
- No sufficient data on long-term course (7)
- Assessment of symptoms only, no cut-off for probable PTSD reported (3)
- <3 participants with PTSD at baseline (1)
- Baseline assessment prior 1980 (4)

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### INCLUDED

24 cohorts (25 articles) met inclusion criteria and were included in the systematic review

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Fig. 1. Selection process of studies.
Results
In all, we found 25 studies (investigating 24 different cohorts) that had been published between 1988 and 2014. Fourteen studies used observer-rated diagnostic assessments (Table 1), 10 studies used self-reports and therefore assessed probable PTSD (Table 2).

Studies with observer-rated PTSD
Characteristics of included studies
Studies with observer-assessed PTSD included about 703 subjects in their long-term follow-ups. Follow-up times ranged between 3 and 10 years, the number of assessments (including the baseline assessment) ranged between 2 and 8. Four of the 14 studies included patients (clinical or primary care setting), while 10 studies investigated subjects from the community.

We will report results separately with regard to where subjects were recruited, as participants from primary, secondary or tertiary care settings might have a different long-term prognosis than participants recruited in the community (34). Additionally, three of the four studies investigating patients (35–37) applied a different research design than the other studies, a fact that is worth mentioning: firstly because they included patients who reported various kinds of traumatic events (e.g. rape, assault, serious accidents, witnessing violence) as opposed to subjects who had all undergone the same traumatic event and were then followed for a certain time span. Secondly, due to sample composition, the time between the individual trauma and baseline assessment differed for each patient. Thirdly, they assessed recovery/full remission as described above. Also, in studies comprising patient samples most subjects received some kind of treatment (psychosocial and/or pharmacological, generally referred to as “psychiatric” by the authors)—which was, however, not systematically recorded, as all studies were observational in nature.

Generally, the time spans between the traumatic events and the baseline assessments for PTSD varied over all studies. In one study, the time that had passed since the traumatic event was approximately 50 years (38). In most of the other studies, the time span between the traumatic event and the baseline PTSD assessment was much shorter and took place within a maximum of 2 years.

Clinical patients
Three studies (35, 37, 40) investigated PTSD patients (of whom all had comorbid disorders, i.e. personality disorders, major depression or other anxiety disorders). Recovery rates varied considerably between 18% over 5 years (35) and 77% over 7 years (37). Both of these studies used the Longitudinal Interval Follow-up Evaluation (LIFE), which defines recovery as a Psychiatric Status Rating (PSR) ≤ 2 (no or only minimal symptoms) over a time span of 8 consecutive weeks. The low recovery rate of 18% in the study by Zlotnick et al. (35) might be explained by two circumstances: all patients had a comorbid anxiety disorder and additionally all patients had chronic PTSD, i.e. PTSD with a duration of at least 1 year (assessed retrospectively) before study intake. Therefore, this sample possibly represented a group of more severely affected patients. Furthermore, Ansell et al. (37) reported a recurrence rate of 34%, which means that more than one third of the 77% who had recovered at some stage during the 7-year follow-up did experience a further episode of full PTSD symptomatology. Together with those patients who did not experience recovery at all over the 7-year period (23%), this adds up to about 50% of patients who either encountered a more chronic or a recurrent course, while the remaining 50% experienced a stable recovery with no relapse.

Primary care patients
One study examined the long-term course in primary care patients (again by the use of LIFE) and found a recovery rate of 38% after 5 years (36). However, nearly 30% of those who had recovered experienced at least one recurrence. Therefore, based on the total sample, about 27% of patients experienced a stable recovery, while the remaining 73% had either a recurrent or a more chronic course.

Participants from the community
The remaining 10 community studies found PTSD remission rates that ranged considerably between 12.5% and 92% after 3–10 years.

The worst long-term result could be seen in the only study examining the consequences of a natural disaster (41). Here, a sample of eight firefighters with PTSD at baseline was followed after a serious bushfire and only 12.5% were found to be remitted after 3 years, while 87.5% still had PTSD. This finding might partly be explained by the “extreme” (p. 23) nature of trauma exposure: the author refers to the bushfire as “unusually intense and uncontrollable” (p. 23).

The most favorable outcomes were seen in a sample of 11 motor-vehicle accident survivors (42) with a remis-
Table 1. Characteristics of included studies with observer-rated posttraumatic stress disorder (PTSD).

| Study, country (ref.) | Diagnosis/assessment instrument | Number of participants (total sample) in long-term follow-up/mean age, gender (male %) | Number of subjects with PTSD at baseline in long-term follow-ups (% of total sample in long-term follow-up) | Main outcome instrument(s) | Follow-up length/number of main assessments | Main outcome |
|-----------------------|---------------------------------|-------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|---------------------------|-------------------------------------------|---------------|
| **Clinical setting**  |                                 |                                                                                     |                                                                                                    |                           |                                           |               |
| Ansell et al., 2011, USA (37) | PTSD (DSM-IV) with comorbid PD or MDD/SCID | 142 patients (traumatic events not reported)/32.5, 35% (referring to total sample of patients, i.e. all 499 followed up patients of the CLPS) | < 142 * | Observer rating (LIFE) 7 years/10 (baseline, 6 months, 1, 2, 3, 4, 5, 6, 7 years after intake) | Recovery rate 77%† by year 7; recurrence rate 34%‡ by year 7 |               |
| Zlotnick et al., 1999, USA (35) | Chronic (> 1 year) PTSD (DSM-III-R) with comorbid anxiety disorder(s)/SCID/RDC | 32 (of originally 54) patients reporting various traumatic events (the most frequently reported being: sexual or physical abuse in childhood, rape, assault, accidents, witnessing violence, and war)/36 years, 24% (referring to total sample of 54) | 32 || Observer rating (LIFE/LIFE-UP) 5 years/8 (baseline, 6 months, 1, 1.5, 2 years, yearly thereafter) | Recovery rate† † 18% by year 5 |               |
| Kivling-Boden & Sundbom, 2001, Former Yugoslavia/Sweden (40) | PTSD (DSM-III-R)/Clinical Interview and HTQ | 27 (of originally 35) psychiatric outpatients; refugees from the former Yugoslavia/41, 59% (referring to total sample of 27) | 16 (Interview)/17 (HTQ) (59.3%) | Self-rating questionnaire (HTQ) 3 years/2 (baseline, 3 years after study intake) | Chronic course ‡: 70.6%; remission**: 29.4% |               |
| Perez Benitez et al., 2012, USA (36) | PTSD (DSM-IV)/SCID | 199 PTSD patients reporting various traumatic events (i.e. unwanted sex, rape, assault, witnessing someone being injured or killed, serious accident, fear of being killed or injured)?, 20% | 134 (199)† | Observer rating (LIFE-UP) 5 years/6 (baseline, 1, 2, 3, 4, 5 years after study intake) | Recovery rate 38%† by year 5; recurrence rate 29.5%‡ over 5 years |               |
| **Primary care setting** |                                 |                                                                                     |                                                                                                    |                           |                                           |               |
| Eytan et al., 2011, Kosovo (48) | PTSD (DSM-IV)/MINI | 551 (of originally 996) war exposed civilians?, 43.4% | 128 (23%) | Observer rating (MINI) 6 years/2 (2 and 8 years after the end of the conflict) | Chronic course‡: 23%; remission**: 77% |               |
| McFarlane, 1988, Australia (10) | PTSD (DSM-III)/Interview | 44 (of originally 50) firefighters with intense exposure to a natural disaster? | 8 (18.2%) | Observer rating (DIS) 3 years/2 (8 and 42 months after disaster) | Chronic course‡: 87.5%; remission**: 12.5% |               |
| Hauff & Vaglum, 1994, Norway (46) | PTSD (DSM-III)/Interview and questionnaire | 129 (of originally 145) Vietnamese refugees/26, 79% (referring to total sample of 145) | 10 (7.7%) | Observer rating (PSE) 3 years/2 (6–8 weeks and 3 years after arrival) | Chronic course‡: 20%; remission**: 80% |               |
| Jeon et al., 2013, Korea (43) | PTSD (DSM-IV)/SCID | 106 (of originally 200) North Korean defectors/35, 59% (referring to total sample of 106) | 26 (24.5%) | Observer rating (SCID) 7 years/2 (1–12 month and about 7 years after defection) | Chronic course‡: 7.7%; remission**: 92.3% |               |

(Continued)
### Table 1. Continued

| Study, country (ref.) | Diagnosis/assessment instrument | Number of participants (total sample in long-term follow-up/ mean age, gender (male %)) | Number of subjects with PTSD at baseline in long-term follow-ups (% of total sample in long-term follow-up) | Main outcome instrument(s) | Follow-up length/number of main assessments | Main outcome |
|----------------------|----------------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------------|----------------------------|---------------------------------------------|-------------|
| Jeon et al., 2013, Korea (43) | PTSD (DSM-IV)/SCID | 106 (of originally 200) North Korean defectors/35, 59% (referring to total sample of 106) | 26 (24.5%) | Observer rating (SCID) | 7 years/2 (1–12 month and about 7 years after defection) | Chronic course: 7.7%; remission**: 92.3% |
| Johnson et al., 2002, USA (44) | PTSD (DSM-III)/DIS/DS | 77 (of originally 80) victims of a mass shooting incidence/39, 35% (referring to total sample of 77) | 4 (5.2%) | Observer rating (DIS/DS) | 3 years/3 (6–8 weeks, 1 and 3 years after the incidence) | Chronic course: 25%; remission**: 75% |
| Mayou et al., 1997, UK (42) | PTSD (DSM-III-R)/PSE | 111 (of originally 188) motor vehicle accident victims/31, 67% (referring to total sample of 111) | 11 (9.9%) | Self-rating questionnaires; telephone interviews in 66 subjects who claimed compensations | 5 years/4 (baseline, 3 months, 1 and 5 years after the accident) | Chronic course: 9%; remission** at year 1: 27%; remission** at year 5: 81% |
| Mollica et al., 2001, Croatia/ Bosnia-Herzegovina (47) | PTSD (DSM-III-R/DSM-IV) or comorbid PTSD&MDD/HTQ (Interview, caseness defined via algorithm method) | 376 (of originally 528) Bosnian refugees/?, 60.8% (referring to total sample of 376) | 98 (26.1%) | HTQ (Interview, caseness defined via algorithm method) | 3 years/2 (about 1 year and 4 years after the war) | 37% asymptomatic, 33% PTSD or comorbid PTSD/MD, 30% MD alone |
| North et al., 2002, USA (45) | PTSD (DSM-III-R)/DIS/DS | 116 (of originally 136) survivors of a mass shooting incidence/39.5 years, 48% (referring to total sample of 116) | 28 (24.1%) | Observer rating (DIS) | 3 years/3 (4–8 weeks, 1 and 3 years after shooting) | Remission**: 43% |
| North et al., 2011, USA (7) | PTSD (DSM-IV-TR)/DIS/DS | 113 (of originally 182 survivors of the Oklahoma City bombing/?, ? | 46 (40.7%) | Observer rating (DIS) | 6.5 years/2 (6 months and 7 years after the bombing) | 37% free of PTSD diagnosis at follow-up and fully remitted according to DSM-IV-TR (i.e. no symptoms of the disorder left) |
| Yehuda et al., 2009, USA (38) | PTSD (DSM-III-R/IV)/SCID, CAPS | 40 (of originally 63) holocaust survivors/66, 32.5% (referring to total sample of 40) | 20 (50%) | Observer rating (SCID, CAPS) | 10 years/2 (about 50 and 60 years after the holocaust) | Chronic course: 70%; remission**: 30% |

CAPS, Clinician-administered PTSD Scale; CLPS, Collaborative Longitudinal Personality Disorders Study; DIS, Diagnostic Interview Schedule; DIS/DS, Diagnostic Interview Schedule for DSM-III-R/Disaster supplement; HTQ, Harvard Trauma Questionnaire; LIFE, Longitudinal Interval Follow-up Evaluation; LIFE-UP, Longitudinal Interval Follow-up Evaluation-Upjohn; MINI, Mini Neuropsychiatric Interview; MDD, major depression; PD, personality disorder; PSE, Present State Examination; PSR, Psychiatric Status Rating; RDC, Research Diagnostic Criteria; SCID, Structured Clinical Interview for DSM-III-R/DSM-IV.

*No information on attrition available for this group.
†PSR level of ≥ 2 for 8 consecutive weeks.
††PSR level of ≥ 5 for 2 consecutive weeks following a recovery period.
‡3-year follow-up data available for 32 patients.
||PTSD diagnosis at both (or all) time points.
||Free of PTSD diagnosis at (last) follow-up.
||3-year follow-up data available for 32 patients.
‡‡199 PTSD subjects analyzed with life table analysis, at least 3 years of data available for 134 PTSD subjects.
Table 2. Characteristics of included studies with self-report/probable posttraumatic stress disorder (PTSD).

| Study, country (ref.) | Diagnosis/outcome instrument | Number of participants (total sample) in long term follow-up/mean age, gender (% male) | Number of subjects with “probable PTSD” at baseline in long-term follow-ups (% of total sample in long-term follow-up) | Follow-up length/number of main assessments | Main outcome |
|-----------------------|--------------------------------|--------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|---------------------------------------------|-------------|
| **War veterans**      |                                |                                                                                      |                                                                                                  |                                             |             |
| Dirkzwager et al., 2001, Netherlands (49) | Probable PTSD (DSM-IV)/SRIP/PTSD diagnosis determined according to DSM-IV rules | Group 1: 576 WWII veterans with military disability pension, Group 2: 198 WWII veterans from the community/Group 1: 73, 100%, Group 2: 73, 98% | Group 1: 200 (34.7%), Group 2: 17 (8.6%) | 6 years/2 (about 47 and 53 years after WWII) | Chronic course*: 68% (Group 1) resp. 59% (Group 2); remission†: 32% (Group 1) resp. 41% (Group 2) |
| Koenen et al., 2003, USA (50) | Probable PTSD (DSM-III/DSM-III-R)/PTSD Symptom Frequency Scale/diagnosis determined according to DSM-III-R rules | 1377 Vietnam veterans/39, 100% | 162 (11.8%) | 14 years/2 (about 9 and 23 years after the Vietnam war) | Chronic course*: 45.7%; remission†: 54.3% |
| Port et al., 2001, USA (32) | Probable PTSD (DSM-III)/Mississippi Scale for Combat Related PTSD, Cut-off score: 91 | 177 veterans and ex-POWs (mostly WW II)/75.5, 100% | 47 (26.5%) | 4 years/2 (about 51 and 55 years after WW II) | Chronic course*: 87.2%; remission†: 12.8% |
| Solomon & Mikulincer, 2006, Israel (51) | Probable PTSD (DSM-III and DSM-IV)/PTSD Inventory/PTSD diagnosis determined according to DSM-III/DSM-IV rules* | Group 1: 131 war veterans with combat stress reaction (psychiatric casualties), Group 2: 83 war veterans without combat stress reaction (comparison group)/26 (at baseline), 100% | Group 1: 84 (64.1%), Group 2: 12 (14.5%) | 20 years/4 (1, 2, 3 and 20 years after the Lebanon war) | Group 1: Chronic course*: 31%, positive screen result only at first assessment (stable remission): 6%; positive screening at first assessment, negative result at third or fourth assessment (remission): 61.9%. Group 2: chronic course*: 25%, stable remission: 25%; remission: 25%, missing percentages: fluctuating course |
| Solomon et al., 2005, 2012, Israel (33, 52) | Probable PTSD (DSM-III-R and DSM-IV)/PTSD Inventory/PTSD diagnosis determined according to DSM-III-R/DSM-IV rules† | Group 1: 106 combat veterans (ex-POWs), Group 2: 64 combat veterans (comparison group)/?, ? | Group 1: 7 (6.6%), Group 2: 4 (4%) | 17 years/3 (18, 30 and 35 years after release) | Group 1: Chronic course (PTSD at all 3 waves): 85.7%; remission (PTSD at 1st or 2nd wave): 14.3%. Group 2: Chronic course (PTSD at all 3 waves): 50%; remission (PTSD at 1st or 2nd wave): 50% |

(Continued)
Table 2. Continued

| Study, country | Diagnosis/outcome instrument | Number of participants (total sample) in long term follow-up/mean age, gender (% male) | Number of subjects with “probable PTSD” at baseline in long-term follow-ups (% of total sample in long-term follow-up) | Follow-up length/number of main assessments | Main outcome |
|----------------|------------------------------|------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------------------------|-------------|
| Rona et al., 2012, UK (53) | Probable PTSD (DSM-III and DSM-IV)/PCL-C ≥ 50 | 6123 participants, service personnel deployed to Iraq?, about 90% | 230 (3.8%) | 3.3 years/2 (1–3 and 4–6 years after deployment to Iraq) | Chronic course*: 33%; remission**: 32%; partial remission (positive screen result at wave 1, lower score [30–49] at wave 2: 36% |
| 9/11 | Brackbill et al., 2009, USA (54) | Probable PTSD (DSM-IV)/PCL ≥44 | 46322 participants (including rescue workers, residents, office workers, and passersby)>42000 aged between 25 and 64, 61.2% | 6141 (13.3%) | About 3 years/2 (about 2 and 5 years after 9/11) | Chronic course*: 66.9%; remission**: 33.1% |
| Neria et al., 2010, USA (57) | Probable PTSD (DSM-IV)/PCL-C ≥ 44 | 455 NYC primary care patients/52, 26% | 47 (10.3%) | 3 years/2 (1 and 4 years after 9/11) | Chronic course*: 10.6%; remission**: 89% |
| Niles et al., 2011, USA (55) | Probable PTSD (DSM-IV-TR)/PCL-m/PTSD algorithm based on DMS-IV-TR criteria | 5363 firefighters exposed to 9/11 rescue work/>5200 aged between 25 and 54, 100% | 458 (8.5%) | About 3–4 years/2 (0–1 and 4–5 years after 9/11) | Chronic course*: 44.8%; remission**: 55.2% |
| Pietrzak et al., 2014, USA (56) | Probable PTSD (DSM-IV)/PCL-S ≥ 44 | Group 1: 4035 police responders, Group 2: 6800 non-traditional responders (both groups) exposed to 9/11 rescue work/Group 1: 41, 87%, Group 2: 45, 85% | Group 1: 535 (13.7%), Group 2: 1904 (28%) | 5 years/3 (3, 5 and 8 years after 9/11) | Group 1: Severe chronic course: 38.7%; remitting course: 61.3%. Group 2: Severe chronic course: 33.9%, moderate chronic course: 22.1%, Remitting course: 43.9% |

Note. IES, Impact of Event Scale; PCL, PTSD-Checklist; PCL-C, PTSD-Checklist-Civilian Version; PCL-m, FDNY-modified PCL; PCL-S, Specific-Stressor Version; POW, prisoner of war; SRIP, Self-Rating Inventory for PTSD.

*DSM-III outcome reported in detail in study.
†DSM-IV outcome reported in detail in study.
‡Positive screen result at wave 1 and wave 2.
§Positive screen result at wave 1, negative result at wave 2.
sion rate of 81% 5 years after baseline PTSD assessment as well as in a sample of 26 North Korean defectors with a 92% remission rate after 7 years (43).

One study, investigating holocaust survivors, methodologically stands out from the others as the trauma happened about 50 years prior to baseline assessment (38). The authors found that 30% of their participants were remitted from PTSD after 10 years.

The remaining five studies found remission rates that ranged between 37% and 77% over 3–6.5 years: Two studies followed victims of a mass shooting incident over a course of 3 years and found that 75% and 43%, respectively, were free of a PTSD diagnosis at follow-up (44, 45). Three studies followed refugees or war exposed civilians that stayed in their home country over a course of 3–6 years and found that between 80% and 67% were free of a PTSD diagnosis at follow-up (46–48). However, of those 67%, only 37% were asymptomatic while 30% still suffered from depression. Finally, in a study with survivors of the Oklahoma City bombing, 37% were recovered 6.5 years after baseline PTSD assessment (7).

Studies with self-report/probable PTSD

Characteristics of included studies
The total number of participants in studies with self-report PTSD was considerably higher \( n = 9848 \) than in studies with observer-rated PTSD. Follow-up times ranged between 3 and 20 years, and the number of assessments (including the baseline assessment) ranged between two and four (Table 2). Five studies investigated war veterans, four studies followed subjects exposed to the 9/11 terrorist attacks in Manhattan and one study included service personnel deployed to Iraq.

Studies with war veterans

Five studies included war veterans, i.e. veterans from WWII, the Vietnam, the Yom Kippur or the Lebanon war (32, 49–52). Time that had passed between (the end of the) war and the first PTSD assessment varied between 1 and about 50 years, which means that some men were investigated immediately others not until several decades later. Overall, between 13% and 75% of veterans remitted over the course of follow-up; thus outcomes were again hugely variable. Studies in which more than four decades had passed between the war and the baseline PTSD assessment found the lowest remission rates (13% and 32%) with a majority of veterans still having probable PTSD at follow-up 4 and 6 years later, respectively (32, 49).

One study with four assessments 1, 2, 3 and 20 years after the Lebanon war and two subsamples (veterans with or without combat stress reaction, CSR) provided more detailed course data (51). Here, only 6% (with CSR) and 25% (without CSR), respectively, showed a stable remission (i.e. were free of PTSD at all later assessments). The remaining veterans showed either a fluctuating course or a remission at one of the later assessments. Koenen et al. (50), who studied Vietnam veterans about 9 and 23 years after the war, found that 54% were remitted at the second assessment. Solomon et al. (52) found that remission rates depended on whether the combat veterans had also been prisoners of war (14.3% vs. 50%), but again this finding has to be interpreted with caution, as this study consisted of only 11 veterans with PTSD at baseline.

Finally, in a study following a sample of service personnel deployed to Iraq, 32% were remitted after 3 years, while 33% had probable PTSD at both times (53). The remaining 36% showed some symptomatic improvement.

Studies relating to 9/11

Three of the four long-term studies investigating PTSD in relation to the 9/11 terrorist attacks in Manhattan found remission rates that were quite similar (54–56). Each of these three studies comprised large samples, ranging from 458 to 6141 participants and similar lengths of follow-up (3–5 years). Baseline assessments in these studies either took place within the first year post-9/11 or 2–3 years after the attacks. Between 38.7% and 66.9% of study participants experienced a chronic or severe chronic course, while one-third to two-thirds had a remitting course. Meanwhile, Neria et al. (57) found a remission rate of 89% in 47 primary care patients investigated 1 and 4 years after 9/11. The difference in remission rates might be because participants in the former studies had a high probability of having been more severely affected by the attacks (i.e. rescue and recovery workers, lower Manhattan residents and office workers, as well as passersby).

Factors associated with the long-term course of PTSD

Ten studies reported factors that were associated with the long-term course of PTSD. As can be seen in Table 3, the most prominent negative course predictors were (comorbid) mental health problems (found by five studies) as well as social factors (e.g. feeling unsupported) as found by four studies.

Discussion

As far as we know, this is one of only two studies systematically reviewing findings on the prospective long-term course of PTSD in adults (9). Overall it can be said that considering the frequency and associated disease burden of PTSD (58), the number of studies eligible for inclusion was relatively small, especially as the number of subjects with PTSD included in five of the 24 long-term follow-ups was quite limited (4–11 participants). On
the other hand, a notable portion of studies was based on larger samples, with the largest comprising more than 6000 participants screening positive for PTSD at baseline (54).

**Methodological factors and their possible impact on findings**

A majority of studies investigated man-made disasters (e.g. war, terrorist attacks, mass-shootings), while one focused on a natural disaster (41) and one on traffic accident victims (42); thus the generalizability of our findings is limited with respect to natural and accidental traumas.

Results show that there is considerable variation in the percentages of participants who do or do not remit. Surprisingly, and contrary to our expectations, outcomes are equally heterogeneous irrespective of PTSD status, i.e. PTSD diagnosis determined by an interview versus probable PTSD established through self-reports. Therefore, other methodological aspects might have played a role, as studies varied notably regarding the following factors:

- Follow-up length (3–20 years);
- Time between the traumatic event and the baseline PTSD assessment (4–8 weeks up to about 50 years);
- Kind of trauma/kind of traumatized population;
- Number of PTSD assessments (2–10);
- Sample types (clinical, primary care, community);
- Definition of remission/recovery (symptom based versus threshold-based).

As mentioned above, studies reviewed in the present article varied with regard to symptom-based versus threshold-based definitions of outcome: five of the studies included in our review (7, 36, 37, 47, 59) used a more symptom-based outcome definition (e.g. a PSR-
level of ≤ 2 [no or very mild symptoms only] over several weeks), while the remaining studies provided threshold-based rates of remission and chronicity (or failed to make it clear which criteria were applied). We investigated whether this difference could explain some of the heterogeneity in outcome rates. When only looking at outcomes of these five studies, recovery rates (i.e. being free of symptoms) were 18%, 37%, 37%, 38% [27%] and 77% [50%]. Some of the rates decrease, when recurrences are taken into account (see figures in square brackets). As can be seen, there is still some variability, but also a tendency towards uniformly low values of stable recoveries (below 50%). This confirms our assumption that the high variability of findings is partly due to heterogeneous definitions of outcome.

Taken together, the methodological differences listed above impede comparability between studies and likely account for (some or most of) the found variability regarding long-term PTSD outcome. Nevertheless, despite this methodological diverseness some conclusions may be drawn:

1. Participants whose traumatic experiences happened up to several decades prior to the baseline PTSD assessment (which was the case in five studies) and who were followed up over some years in later life, often showed a chronic course (46–87%). While it remains unclear whether participants in these studies were new cases in the sense of a delayed PTSD onset or had suffered PTSD or PTSD symptoms throughout the years, the results reported here suggest that PTSD occurring in older age is rather chronic. Consistent with our findings, previous research pointed towards a U-shaped curve of PTSD in long-term survivors of trauma, with symptoms being elevated shortly after a traumatic experience, declining thereafter and increasing again in older age, when age-related problems and age-related threshold-situations appear (32).

2. Three studies following patient samples applied quite uniformed methods, as they used at least six observer-based assessments and well-defined outcome criteria. Interestingly, they provided less heterogeneous data on the long-term course of PTSD suggesting that methodological aspects play an important role in investigating long-term outcome. These studies found that the long-term PTSD prognosis is favorable in only 18–50% of patients and that PTSD can be quite fluctuating in its course with recurrence rates ranging between 29.5% and 34%. As these studies investigated consecutive patients with (comorbid) PTSD, we have no information on the time that had elapsed between first PTSD occurrence and baseline assessment.

3. Studies with patient samples are limited in their generalizability. When studying the long-term course of an illness it is important to consider that samples consisting of treatment-seeking participants (i.e. patients) might be subjected to bias (34), as it is likely that they are experiencing a more severe illness course, which led them to seek treatment in the first place. Consequently, this might result in an overestimation of chronicity. Thus, it is of note that results from these studies may not generalize to non-treatment-seeking subjects.

4. Recent studies conducted in the aftermath of 9/11 provided us with valuable information on the longitudinal course of PTSD. They found that chronic courses could be seen in about one third to two-thirds of subjects with PTSD.

Predictors of the long-term course

Several predictors of PTSD onset have been identified while factors predicting the long-term course of PTSD are lesser known. Based on findings reviewed here, it can be seen that some factors related to a more chronic PTSD course resemble predictors of PTSD onset, which was the case for female gender, belonging to a minority race, childhood trauma, trauma severity and severe initial reactions to trauma.

Furthermore, some studies reviewed here support earlier research, suggesting that the amount of early postdisaster symptoms as well as negative posttraumatic events, such as adverse life events, a lack of social support or health related problems, psychological or physical in nature, might play a role in the long-term course of PTSD (17, 24, 29, 60). More specifically, four studies found social factors predictive of PTSD course. Social support, in many of its connotations—be it the acknowledgement in the community, the possibility to disclose one’s thoughts and feelings to a near person, living in a partnership, or the availability of friends—seems to be an integrative part in the long-term development of PTSD (17, 18). However, the factor marital status has to be viewed with caution in this context: while being separate, widowed or divorced was found to be a risk factor for a negative course in two studies (36, 56), prior research found that being married could also be a risk factor for an unfavorable development in the aftermath of a trauma, especially for women, while the opposite may be true for men (19). Accordingly, the same study who reported being separate, widowed or divorced could be a risk factor found that being married or cohabiting was also a negative predictor (56).

The findings on course predictors have some implications for clinical practice where it is vital to identify those subjects who are at risk for an unfavorable course and supply them with suited treatments or other interventions. On the one hand the findings suggest that subjects with PTSD who are embedded in supportive social structures and do not suffer from posttraumatic physical impairments or comorbid mental problems might be at
lesser risk for the development of a chronic PTSD course. Those, on the other hand who are socially isolated or do not feel supported and are physically or mentally impaired seem to be at higher risk for non-remission and should therefore be identified early on to prevent chronicity. Consequently, a thorough examination of individuals with PTSD should always comprise an assessment of possible comorbid mental and physical disorders as well as an evaluation of the psychosocial situation a patient lives in (60, 61).

Limitations
This review has some limitations:

- We designed the review to present a wide range of articles published in the research area in focus. Consequently, the selection criteria we used were broad which led to the inclusion of heterogeneous studies and findings that are difficult to compare. Considering the large heterogeneity in studies and findings, the performance of a meta-analytic evaluation did not seem suitable and therefore conclusions are based on a merely descriptive synthesis.

- There is the possibility that some studies were missed because of the way our search strategy was designed. In an attempt to attenuate this, we did not rely solely on electronic searches but manually searched the reference lists of included studies. Additionally, as we limited our search to English language articles, there is the risk of having missed some relevant studies.

- Moreover, as we focused on information about recovery and remission rates from the same individuals at baseline and follow-up(s), we have—with one exception who provided a mixed approach (56)—neglected data regarding varying symptom levels over time. Studies assessing PTSD severity over time by using symptom-profiles (24, 38, 62) generally suggested that the PTSD course is better characterized by gradual levels of severity and changes within the core symptoms (i.e. hyperarousal, avoidance and intrusions) than by examination of the diagnostic status, or as Solomon et al. (62) put it, “PTSD is not a monolithic disorder” (p. 837), a view that supports the varying long-term course found in some studies reviewed here. Also, as most reviewed studies relied on two assessments only (i.e. one baseline and one follow-up measurement), they only allowed a limited view into the multiannual course of PTSD. Studies including patient samples generally applied a higher number of assessments than community studies (on average 5.6 versus 2.3) and consequently especially the latter might have missed important course information, such as recurrences.

- Generally, information on whether subjects of included studies received treatment (and if they did, what kind of treatment) was sparse or non-existent; thus we do not know what role treatment might have played in the outcome of PTSD as it is reported here.

Summing up, the results presented here give some insight into the naturalistic long-term course of PTSD in different samples. In order to further enlighten this issue, future research should apply more than one follow-up examination as well as enhanced definitions of outcome.

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References
1. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1995;52:1048–60.
2. Resnick HS, Kilpatrick DG, Dansky BS, Saunders BE, Best CL. Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. J Consult Clin Psychol 1993;61:984–91.
3. Norris FH. Epidemiology of trauma: Frequency and impact of different potentially traumatic events on different demographic groups. J Consult Clin Psychol 1992;60:409–18.
4. Breslau N, Chase GA, Anthony JC. The uniqueness of the DSM definition of post-traumatic stress disorder: Implications for research. Psychol Med 2002;32:573–6.
5. Neria Y, Nandi A, Galea S. Post-traumatic stress disorder following disasters: A systematic review. Psychol Med 2008;38:467–80.
6. Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen HU. Twelve-month and lifetime prevalence and lifetime morbidity risk of anxiety and mood disorders in the United States. International Journal of Methods in Psychiatric Research 2012;21:169–84.
7. North CS, Pfefferbaum B, Kawasaki A, Lee S, Spitznagel EL. Psychosocial adjustment of directly exposed survivors 7 years after the Oklahoma City bombing. Compr Psychiatry 2011; 52:1–8.
8. Peleg T, Shalev AY. Longitudinal studies of PTSD: Overview of findings and methods. CNS Spectr 2006;11:589–602.
9. Morina N, Wicherts JM, Lobbrecht J, Priebe S. Remission from post-traumatic stress disorder in adults: A systematic review and meta-analysis of long term outcome studies. Clin Psychol Rev 2014;34:249–55.
10. McFarlane AC. The longitudinal course of posttraumatic morbidity. The range of outcomes and their predictors. J Nerv Ment Dis 1988;176:30–9.
11. Rothbaum BO, Foa EB. Subtypes of post-traumatic stress disorder and duration of symptoms. In: Davidson JRT, Foa EB, editors. Post-traumatic stress disorder: DSM-IV and beyond. Washington, DC: American Psychiatric Press; 1993. p. 23–35.
12. Mayou R, Bryant R, Duthie R. Psychiatric consequences of road traffic accidents. BMJ 1993;307:647–51.
13. Feinstein A, Dolan R. Predictors of post-traumatic stress disorder following physical trauma: An examination of the stressor criterion. Psychol Med 1991;21:85–91.
14. Blanchard EB, Hickling EJ, Barton KA, Taylor AE, Loos WR, Jones-Alexander J. One-year prospective follow-up of motor vehicle accident victims. Behav Res Ther 1996;34:775–86.
15. North CS, Oliver J. Analysis of the longitudinal course of PTSD in 716 survivors of 10 disasters. Soc Psychiatry Psychiatr Epidemiol 2013;48:1189–97.

16. American Psychological Association. Diagnostic and statistical manual of mental disorders. 4th ed, text revision ed. Washington, DC: APA; 2000.

17. Brewin CR, Andrews B, Valentine JD. Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. J Consult Clin Psychol 2000;68:748–66.

18. Maercker A, editor. Posttraumatische Belastungsstörungen [Posttraumatic stress disorders]. Heidelberg: Springer; 2009.

19. Norris FH, Friedman MJ, Watson PJ, Byrne CM, Diaz E, Kaniasty K. 60,000 disaster victims speak: Part I. An empirical review of the empirical literature, 1981–2001. Psychiatry 2002;65:207–39.

20. Maercker A. Lifespan psychological aspects of trauma and PTSD: Symptoms and psychological impairments. In: Maercker A, Schützwohl M, Solomon Z, editors. Posttraumatic stress disorder. A lifespan developmental perspective. Seattle, WA: Hogrefe & Huber; 1999.

21. North CS, Nixon SJ, Shariat S, Mallonee S, McMillen JC, Spitznagel EL, et al. Psychiatric disorders among survivors of the Oklahoma City bombing. JAMA 1999;282:755–62.

22. Maercker A, Beauducel A, Schützwohl M. Trauma severity and initial reactions as precipitating factors for posttraumatic stress disorder and chronic dissociation in former political prisoners. J Trauma Stress 2000;13:651–60.

23. Delahanty DL, Herberman HB, Craig KJ, Hayward MC, Fullerton CS, Ursano RJ, et al. Acute and chronic distress and posttraumatic stress disorder as a function of responsibility for serious motor vehicle accidents. J Consult Clin Psychol 1997;65:560–7.

24. Schell TL, Marshall GN, Jaycox LH. All symptoms are not created equal: The prominent role of hyperarousal in the natural course of posttraumatic psychological distress. J Abnorm Psychol 2004;113:189–97.

25. Bui E, Tremblay L, Brunet A, Rodgers R, Jehel L, Very E, et al. Course of posttraumatic stress symptoms over the 5 years following an industrial disaster: A structural equation modeling study. J Trauma Stress 2010;23:759–66.

26. Koren D, Arnon I, Klein E. Long term course of chronic posttraumatic stress disorder in traffic accident victims: A three-year prospective follow-up study. Behav Res Ther 2001;39:1449–58.

27. Mayou R, Ehlers A, Bryant B. Posttraumatic stress disorder after motor vehicle accidents: 3-year follow-up of a prospective longitudinal study. Behav Res Ther 2002;40:665–75.

28. Carlier IV, Lamberts RD, Gersons BP. Risk factors for posttraumatic stress symptomatology in police officers: A prospective analysis. J Nerv Ment Dis 1997;185:498–506.

29. King DW, King LA, Foy DW, Keane TM, Fairbank JA. Posttraumatic stress disorder in a national sample of female and male Vietnam veterans: Risk factors, war-zone exposures, and resilience-recovery variables. J Abnorm Psychol 1999;108:164–70.

30. Goldstein G, van Kammen W, Shelly C, Miller DJ, van Kammen DP. Survivors of imprisonment in the Pacific theater during World War II. Am J Psychiatry 1987;144:1210–3.

31. Marshall GN, Schell TL, Elliott MN, Berthold SM, Chun CA. Mental health of Cambodian refugees 2 decades after resettlement in the United States. JAMA 2005;294:571–9.

32. Port CL, Engdahl B, Frazier P. A longitudinal and retrospective study of PTSD among older prisoners of war. Am J Psychiatry 2001;158:1474–9.

33. Solomon Z, Dekel R. Posttraumatic stress disorder among Israeli ex-prisoners of war 18 and 30 years after release. J Clin Psychiatry 2005;66:1031–7.

34. Berkson J. Limitations of the application of fourfold table analysis to hospital data. Biometrics 1946;2:47–53.

35. Zlotnick C, Warshaw M, Shea MT, Allsworth J, Pearlstein T, Keller MB. Chronicity in posttraumatic stress disorder (PTSD) and predictors of course of comorbid PTSD in patients with anxiety disorders. J Trauma Stress 1999;12:89–100.

36. Perez Benitez CL, Zlotnick C, Stout RJ, Lou F, Dyck I, Weisberg R, et al. A 5-year longitudinal study of posttraumatic stress disorder in primary care patients. Psychopathology 2012;45:286–93.

37. Ansell EB, Pinto A, Edelen MO, Markowitz JC, Sanislow CA, Yen S, et al. The association of personality disorders with the prospective 7-year course of anxiety disorders. Psychiat Med 2011;41:1019–28.

38. Yehuda R, Schmeidler J, Labinsky E, Bell A, Morris A, Zemelman S, et al. Ten-year follow-up study of PTSD diagnosis, symptom severity and psychosocial indices in aging holocaust survivors. Acta Psychiatr Scand 2009;119:25–34.

39. Perez Benitez CL, Zlotnick C, Dyck I, Stout R, Angert E, Weisberg R, et al. Predictors of the long-term course of comorbid PTSD: A naturalistic prospective study. Int J Psychiatry Clin Pract 2013;17:232–7.

40. Kivling-Boden G, Sundbom E. Life situation and posttraumatic symptoms: A follow-up study of refugees from the former Yugoslavia living in Sweden. Nord J Psychiatry 2001;55:401–8.

41. McFarlane AC. The phenomenology of posttraumatic stress disorders following a natural disaster. J Nerv Ment Dis 1988;176:22–9.

42. Mayou R, Tynel S, Bryant B. Long-term outcome of motor vehicle accident injury. Psychosom Med 1997;59:578–84.

43. Jön WT, Eom JS, Min SK. A 7-year follow-up study on the mental health of North Korean defectors in South Korea. J Trauma Stress 2013;26:158–64.

44. Johnson SD, North CS, Smith EM. Psychiatric disorders among victims of a courthouse shooting spree: A three-year follow-up study. Community Ment Health J 2002;38:181–94; discussion 95–7.

45. North CS, McCutcheon V, Spitznagel EL, Smith EM. Three-year follow-up of survivors of a mass shooting episode. J Urban Health 2002;79:383–91.

46. Haufl E, Vaglum P. Chronic posttraumatic stress disorder in Vietnamese refugees: A prospective community study of prevalence, course, psychopathology, and stressors. J Nerv Ment Dis 1994;182:85–90.

47. Mollica RF, Sarajlic N, Chernoff M, Lavelle J, Vukovic IS, Massagli MP. Longitudinal study of psychiatric symptoms, disability, mortality, and emigration among Bosnian refugees. JAMA 2001;286:546–54.

48. Eytan A, Guthmiller A, Durieux-Paillard S, Loutan L, Gex-Fabry M. Mental and physical health of Kosovar Albanians in their place of origin: A post-war 6-year follow-up study. Soc Psychiatry Psychiatr Epidemiol 2011;46:953–63.

49. Dirkwazer AJ, Bransen I, van der Ploeg HM. The longitudinal course of posttraumatic stress disorder symptoms among aging military veterans. J Nerv Ment Dis 2001;189:846–53.

50. Koenen KC, Stellman JM, Stellman SD, Sommer JF. Jr. Risk factors for course of posttraumatic stress disorder among Vietnam veterans: A 14-year follow-up of American Legionnaires. J Consult Clin Psychol 2003;71:980–6.

51. Solomon Z, Mikulincer M. Trajectories of PTSD: A 20-year longitudinal study. Am J Psychiatry 2006;163:659–66.

52. Solomon Z, Horesh D, Ein-Dor T, Ohry A. Predictors of PTSD trajectories following captivity: A 35-year longitudinal study. Psychiatry Res 2012;199:188–94.

53. Rona RJ, Jones M, Sundin J, Goodwin L, Hull L, Wessely S, et al. Predicting persistent posttraumatic stress disorder (PTSD) in UK military personnel who served in Iraq: A longitudinal study. J Psychiatr Res 2012;46:1191–8.

54. Brackbill RM, Hadler JL, DiGrande L, Ekenga CC, Farfel MR, Friedman S, et al. Asthma and posttraumatic stress symptoms 5 to 6 years following exposure to the World Trade Center terrorist attack. JAMA 2009;302:502–16.

55. Niles JK, Webber MP, Gustave J, Cohen HW, Zeig-Owens R, Kelly KJ, et al. Comorbid trends in World Trade Center cough syndrome and probable posttraumatic stress disorder in firefighters. Chest 2011;140:1146–54.

56. Pietrzak RH, Feder A, Singh R, Schechter CB, Bremet EJ, Katz CL, et al. Trajectories of PTSD risk and resilience in World Trade Center responders: An 8-year prospective cohort study. Psychol Med 2014;44:205–19.

57. Neria Y, Olfsen M, Gamaner O, Djibril DR, Wickramaratne P, Gross R, et al. Long-term course of probable PTSD after the 9/11 attacks: A study in urban primary care. J Trauma Stress 2010;23:474–82.
58. Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jonsson B, et al. The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharmacol 2011;21:655–79.

59. Zlotnick C, Warshaw M, Shea MT, Allsworth J, Pearlstein T, Keller MB. Chronicity in posttraumatic stress disorder (PTSD) and predictors of course of comorbid PTSD in patients with anxiety disorders. J Trauma Stress 1999;12:89–100.

60. McFarlane AC. Posttraumatic stress disorder: A model of the longitudinal course and the role of risk factors. J Clin Psychiatry 2000;61 Suppl 5:15–20; discussion 1–3.

61. Brady KT. Posttraumatic stress disorder and comorbidity: Recognizing the many faces of PTSD. J Clin Psychiatry 1997;58 Suppl 9:12–5.

62. Solomon Z, Horesh D, Ein-Dor T. The longitudinal course of posttraumatic stress disorder symptom clusters among war veterans. J Clin Psychiatry 2009;70:837–43.

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Supplementary material available online
Supplementary Appendix Table 1. Search terms and search strategy, searched up to October 1, 2014.