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#### Psychiatric-Medical Comorbidity

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# Posttraumatic stress disorder in organ transplant recipients: a systematic review\*



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#### ARTICLE INFO

Article history: Received 3 April 2015 Revised 15 May 2015 Accepted 19 May 2015

Keywords:
Posttraumatic stress disorder
Organ transplantation
Quality of life
Outcome assessment (health care)

#### ABSTRACT

Objective: To summarize and critically review the existing literature on the prevalence of posttraumatic stress disorder (PTSD) following organ transplantation, risk factors for posttransplantation PTSD and the relationship of posttransplant PTSD to other clinical outcomes including health-related quality of life (HRQOL) and mortality. *Methods*: We conducted a systematic literature review using PubMed, CINAHL Plus, the Cochrane Library and PsycInfo and a search of the online contents of 18 journals.

Results: Twenty-three studies were included. Posttransplant, the point prevalence of clinician-ascertained PTSD ranged from 1% to 16% (n=738), the point prevalence of questionnaire-assessed substantial PTSD symptoms ranged from 0% to 46% (n=1024) and the cumulative incidence of clinician-ascertained transplant-specific PTSD ranged from 10% to 17% (n=482). Consistent predictors of posttransplant PTSD included history of psychiatric illness prior to transplantation and poor social support posttransplantation. Posttransplant PTSD was consistently associated with worse mental HRQOL and potentially associated with worse physical HRQOL.

Conclusions: PTSD may impact a substantial proportion of organ transplant recipients. Future studies should focus on transplant-specific PTSD and clarify potential risk factors for, and adverse outcomes related to, posttransplant PTSD.

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#### 1. Introduction

Over 100,000 organ transplantations are performed annually worldwide [1]. While graft survival has generally improved across organ types [2], there is interest in identifying modifiable risk factors for adverse outcomes following organ transplantation. Though a growing number of studies have identified that depression is substantially more common in organ transplant recipients than the general population and is associated with increased risk of posttransplant treatment nonadherence and mortality [3–6], relatively little is known about the prevalence and potential health impacts of other psychiatric disorders in this population.

Organ transplant recipients are exposed to extreme physiological and psychological stressors, including life-threatening illness, transplant surgery, pain and intensive care unit (ICU) stays with mechanical ventilation and possible delirium, all of which make posttraumatic stress disorder (PTSD) a reasonable concern for this population [7,8]. PTSD has been estimated to affect 3.5% of the US population [9] and has been found to be especially prevalent in other medically ill populations and associated with both worse health-related quality of life (HRQOL) and increased

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healthcare utilization [7,8,10,11]. Therefore, understanding the epidemiology of PTSD in organ transplant recipients is important, especially since PTSD is amenable to treatment and could represent a modifiable risk factor for adverse outcomes posttransplantation.

The current report details the results of a systematic review of studies examining PTSD in adult organ transplant recipients. The authors' objectives were to (1) determine the prevalence of PTSD posttransplant, (2) identify potential risk factors for posttransplantation PTSD and (3) examine the relationship of PTSD symptoms following organ transplantation to other posttransplantation outcomes such as HRQOL and mortality.

#### 2. Materials and methods

#### 2.1. Approach and search strategy

We conducted a systematic review of the literature utilizing electronic databases and online journal content. We searched PubMed (1966–2014), CINAHL Plus (1969–2014), the Cochrane Library (2014, Issue 12) and PsycInfo (1967–2014) as of January 21, 2015. Our search strategy utilized the following terms mapped to the appropriate MeSH subject headings and "exploded": "mental disorders" AND ("transplants" OR "transplantation"). The following terms were also included as text words: ("depress\*" OR "stress" OR "anxi\*") (see Supplementary Appendix A). In addition, we searched the online contents of 18

 $<sup>\,\</sup>dot{\,}^{}_{}$  Disclosures: The authors have no relevant conflicts of interest to disclose.

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transplantation and psychiatry journals (see Supplementary Appendix B) using the search terms ("posttraumatic" OR "PTSD") AND "transplantation". The search was limited to English language articles.

#### 2.2. Study selection

We sequentially reviewed citations, abstracts and full-text articles in order to select eligible studies. Articles were selected for review if they met the following a priori eligibility criteria: (1) the population was composed of solid organ transplantation survivors  $\geq 18$  years of age; (2) PTSD assessments were conducted using validated measures (e.g., self-report questionnaires or structured/semistructured diagnostic interviews)  $\geq 1$  month following transplantation; and (3) the study size was  $\geq 15$  participants. Abstracts, case reports/case series and review articles were excluded.

#### 2.3. Data abstraction and assessment of study quality

For each eligible study, we abstracted information on study cohorts, PTSD measures, potential risk factors for posttransplant PTSD and associations between PTSD following organ transplantation and posttransplant health outcomes (e.g., HRQOL, mortality, treatment nonadherence, graft rejection) using a data abstraction tool (see Supplementary Appendix C). Authors of eligible studies were contacted for additional information when necessary.

We assessed study quality regarding assessment of potential risk factors for posttransplant PTSD using the following five criteria adapted from the US Preventive Services Task Force and prior systematic reviews

of heterogeneous outcome data [12–14]: (1) enrollment of consecutive participants; (2) no loss to follow-up of > 10% prior to first PTSD symptom assessment; (3) description of participants lost to follow-up; (4) at least one statistical comparison of participants lost to follow-up vs. those completing the study; and (5) adjustment for confounding by stratification, statistical adjustment, randomization or comparison with a matched population. Study quality criteria were not used in decisions on study inclusion or exclusion.

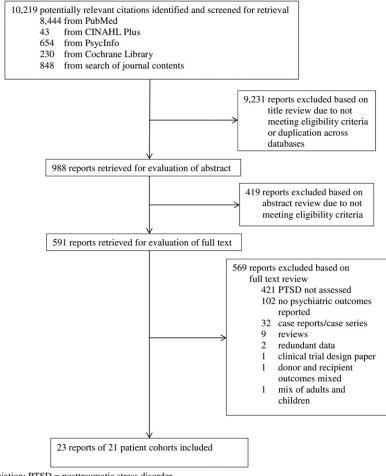
#### 3. Results

#### 3.1. Search results, study characteristics and quality

We reviewed 10,219 citations, 988 abstracts and 591 full-text articles (Fig. 1). Twenty-three articles describing 21 cohorts of organ transplant recipients were eligible for data abstraction (Table 1) [15–37].

Table 1 presents the study designs and baseline descriptive data for the 23 studies, ordered by follow-up timing. Follow-up ranged from 1 month posttransplant [15] to 10.2 years posttransplant [37]. The studies enrolled 2833 participants.

Only slightly over one quarter of studies enrolled consecutive transplant patients (see Supplementary Table) [18,19,21,29,34]. Among cohort studies, more than half had over 10% of participants lost to follow-up [18,19,21,28]. All of these studies provided descriptions of participants lost to follow-up and conducted analyses to compare those lost to follow-up to study completers. Only 6 of the 16 studies that examined potential risk factors for posttransplant PTSD adjusted for confounding in their analyses of these risk associations [18,21,26,28–30].



<u>Abbreviation</u>: PTSD = posttraumatic stress disorder.

Fig. 1. Flow diagram of literature search results.

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