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META-ANALYSIS

A meta-analysis on the incidence of donor-related depression after liver transplant

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SUMMARY

Living donor liver transplantation (LDLT) is increasing, yet gaps exist in the understanding of psychological wellbeing of donors after liver transplant. This meta-analysis seeks to evaluate the incidence and risk factors for donor-related depression after liver transplantation. A search was conducted on Medline and Embase database. Articles assessing incidence of depression in LDLT donors were included. Incidence was pooled after Freeman–Turkey double-arcsine transformation. For risk factors, dichotomous variables were analyzed with generalized linear model, while a conventional meta regression with logit transformation was conducted for continuous variables. Of 1069 abstracts, 40 articles underwent full-text review. Seventeen articles were included. The pooled incidence of depression among 1888 LT donors was 7.66% (CI: 4.47–12.80%). Depression rates were significantly higher in Asian compared to Western studies (RR: 1.73, CI: 1.19–2.52, $P = 0.0039$). Female gender ($P < 0.001$), Caucasian ethnicity ($P = 0.047$), employment status ($P < 0.001$) and lower education levels ($P = 0.044$) were significantly associated with depression. Donor relationship with recipients was not a significant risk factor. LDLT remains a core aspect of the treatment of end-stage liver disease. However, the high depression rates after LT suggest that there remains room for improvement in the care of donors' mental health post-transplant.

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Introduction

Deceased donor liver transplantation has been the predominant organ source for patients waitlisted for liver transplantation. However, the shortage of deceased donors, especially in Asia, has warranted the need to adopt living donor liver transplantation (LDLT) [1,2], resulting in a ten-fold increase in the number of the LDLT performed per year in Asia [3]. Donor-related psychological trauma after LDLT has been reported with depression being a common psychological complication identified after liver transplant hospitalization [4].

The consortium from the adult-to-adult LDLT cohort study (A2ALL) was the first large-scale attempt to study donor psychological wellbeing after liver donation across different countries [5,6] with 12 of 392 donors developing depression amongst other psychiatric complications. In addition, three individuals in the study also experienced severe psychiatric complications (suicide, accidental drug overdose, suicide attempt) [5,6]. Previous reports have also suggested that donors had a higher score for depression compared to healthy controls [7]. The effects of depression on donors include decreased quality of life [8], increased nonadherence and avoidance of medical care, which contribute to poor post donation prognosis and other severe psychiatric complications [5,9]. Understanding the impact of donation on the donor's clinical outcomes and psychological welfare is hence of clinical significance.

Although previous reviews have explored the psychosocial impact of LDLT on donors [6,10–12], none has focused specifically on depression and potential predictors of donor-related depression. Identification of these potential risk factors may aid in early risk stratification of donors vulnerable to post-LDLT depression, allowing transplant centres to monitor and develop targeted treatments for these higher risk donors [6]. Thus, this meta-analysis sought to evaluate the incidence and risk factors for donor-related depression after liver transplantation.

Methods

Search strategy

A search was conducted on Medline and Embase database for articles related to depression diagnosis in liver transplant donors, and this review was registered with PROSPERO (Registration Number: CRD42021234330) [13]. The PRISMA guidelines was adhered to in the synthesis of this review [14]. The search strategy used was '((((liver* OR hepat*) adj3 (transplan* OR graft*)).tw. or exp Liver Transplantation/) and (exp Depression/ or depress*.tw.)))'. No date restriction was applied. Identified abstracts were compiled, and duplicates were removed with Endnote X9 Software. In addition, the screening of references of relevant papers was also conducted to identify further eligible studies not covered by the original database searches. No institutional review board approval is required for meta-analysis.

Selection criteria and extraction

Prospective and retrospective articles assessing the incidence of depression after liver transplantation were included in the study with articles originating from the same database excluded. A predetermined set criterion was implemented to systematically analyze each title and abstract for inclusion. Only original studies and English language articles were included excluding reviews, commentaries, editorials and conference abstracts. The inclusion of an article was evaluated by four independent blinded authors (CHN, WHL, XCL, JLX) with disagreements being resolved by obtaining the consensus of a fourth author (CSH). As with a previous review [15], the diagnosis of depression can be classified into clinical diagnosis, self-rated questionnaire or self-reported depression. A clinician-rated diagnosis was made either through an evaluation by a psychiatrist according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR) or based on the use of antidepressants

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[5,7,16–23]. Self-rated questionnaire included the used of validated depression scales (e.g., patient health questionnaire; PHQ-9 [6,24], Hospital Anxiety and Depression Scale; HADS [25], Korean Center for Epidemiological Studies-Depression Scale; CES-D [8], Brief Symptom Rating Scale; BSRS [26], Primary Care Evaluation of Mental Disorders; PRIME-MD [27]), while self-reported depression referred to patients' self-identification of depressive symptoms post donation [28,29]. Key data was extracted from a predefined set of criteria, which included the background information (e.g., author, year, hospital and country), baseline characteristics (e.g., sample size, mean age, ethnicity, donor relationship and employment status), diagnosis method and incidence of depression. Each article was double-coded blinded by four independent authors in independent pairs (CHN, WHL, XCL, JX) using a structured proforma to ensure accuracy in data extraction.

Statistical analysis and quality assessment

The analysis was conducted in STATA (Statacorp 16.1, StataCorp LLC, College Station, TX, USA) and RStudio (Ver: 4.0.3) [30]. A Freeman–Turkey double-arcsine transformation was used to stabilize the variance before the results were pooled with DerSimonian and Laird random effects model [76,77]. The random effects model was utilized for all analysis [32]. Quantification of heterogeneity was done by the I^2 and Cochran Q test. A I^2 of 25%, 50% and 75% represented low, moderate and high degree of heterogeneity, respectively [33,34]. A Cochran Q test of $P < 0.10$ was significant for heterogeneity. However, traditional tools measuring heterogeneity for single-arm meta-analysis have been found to be inaccurate [35] with several single-arm analyses exceeding $I^2 > 90\%$ [36,37]. Similar to previous reviews [15,38], a subgroup analysis was done to pool the individual rates of depression based on the type of scales used, namely into clinician-rated, self-rated and self-reported depression. Publication bias by funnel plot analysis was not conducted due to inaccurate measures in single-arm meta-analysis [39]. To assess for variables that could affect the rate of depression, a generalized linear model was conducted in the binomial family and logit link with inverse variance weightage where each independent variable represents a 10% increase in odds of events [40]. For continuous variables, a conventional meta regression with logit transformation was conducted with Knapp Hartung variance estimator in the restricted maximum likelihood model [41]. The coefficient was then exponentiated to obtain the odds ratio (OR).

Additionally, a subgroup analysis was conducted to observe incidence based on the region of origin (Western, Asia and Middle Eastern) of the included articles, and a risk ratio was constructed to compare the rates of depression from each region [42]. The individual rates of depression were pooled from the Asia region (p1) and Western region (p2), respectively. Next, the upper and lower bound of the confidence interval (UCI and LCI, respectively) were estimated using the Katz-logarithmic method [43]. The P-value was then calculated from the natural log transformation of the relative risk z-score [44]. Similar applications to compare depression rates were conducted for Asia versus Middle Eastern and Middle Eastern versus Western geographical regions. A P-value of <0.05 denoted significance. Last, quality assessment of the included articles was conducted by two independent authors (CHN, WHL) using Hoy et al.'s tool for prevalence study that assesses risk of bias based on sampling population, validity of data collection and appropriate study instruments across ten domains [45].

$$LCI = RRe^{\left(-1.96\times\sqrt{\frac{1-p_1}{n_1p_1}+\frac{1-p_2}{n_2p_2}}\right)}$$

$$UCI = RRe^{\left(1.96\times\sqrt{\frac{1-p_1}{n_1p_1}+\frac{1-p_2}{n_2p_2}}\right)}$$

$$P\text{value} = e^{\left(-0.717\times\left|\frac{\ln RR}{\frac{\ln UCL-\ln LCL}{2\times1.96}}\right|-0.416\times\left(\frac{\ln RR}{\frac{\ln UCL-\ln LCL}{2\times1.96}}\right)^2\right)}$$

Results

Summary of included articles

In total, 1069 articles were retrieved from the search after the removal of duplicates, with a final of 40 articles undergoing full text review. Of the 40 articles, a final of 17 articles were included in this review (Fig. 1). There were five included studies from United States [6,21,22,28,46], three each from Taiwan [8,25,26] and Germany [7,18,29], two from Egypt [20,23] and one each from Poland [24], Turkey [17], Japan [16] and Canada [19]. The articles included spanned from 2005 to 2020 with more articles using clinical diagnosis ($n = 9$) than self-rated ($n = 6$) or self-reported depression (n = 2). In total, 1888 living donors were assessed for depression after liver transplant, and 205 individuals

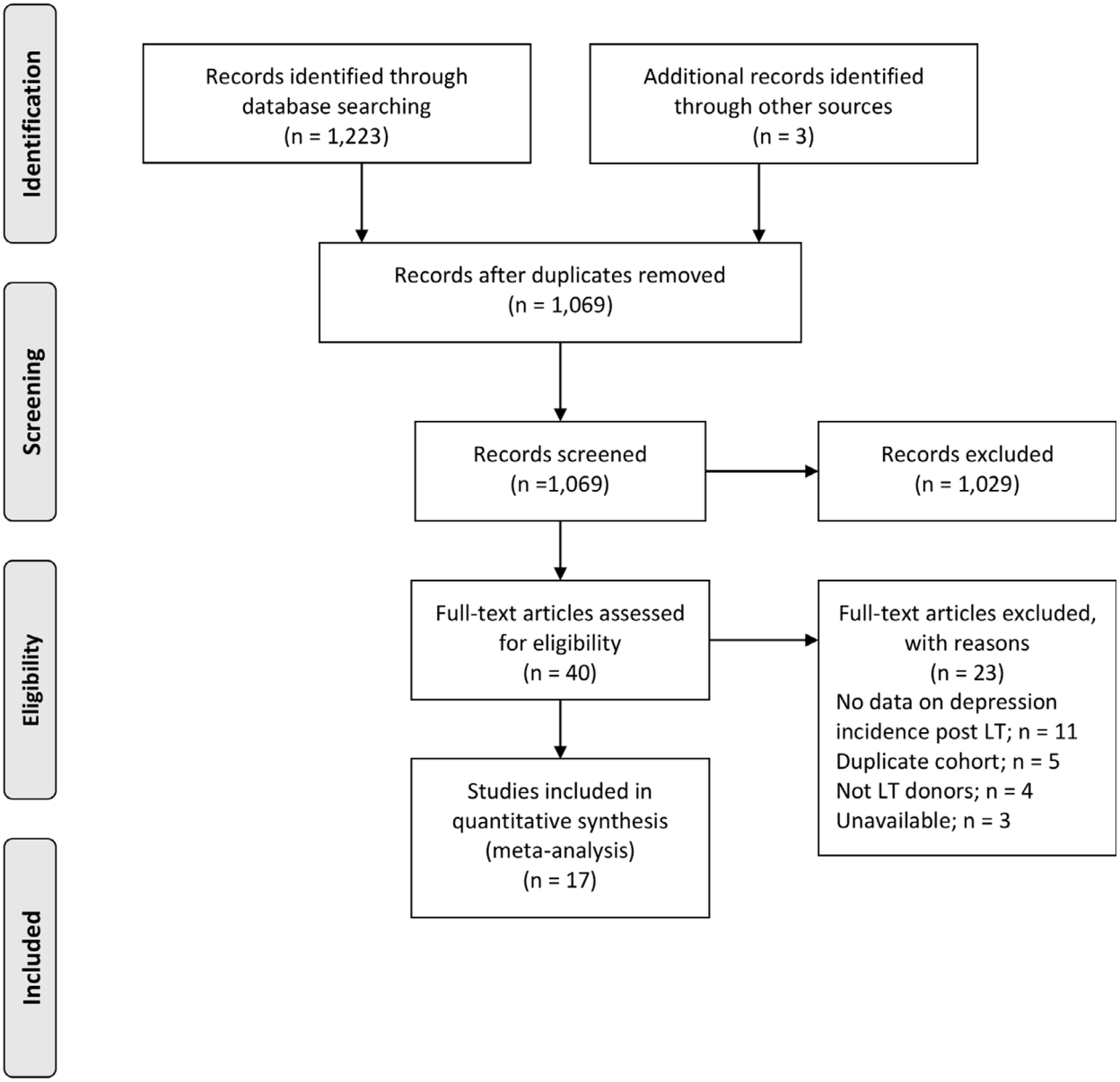

Figure 1 PRISMA flow diagram.

were identified to have depression. The summary of included articles can be found in Table S1. The risk of bias assessment can be found in Table S2, with majority of included studies assessed to have low ($n = 13$, 76.5%) or moderate risk of bias ($n = 4$, 23.5%).

Incidence of depression

The pooled incidence of depression among 1888 donors after liver transplant was 7.66% (CI: 4.47–12.80%, Fig. 2). A subgroup analysis was conducted to compare depression rates among self-rated, self-reported and clinician rated diagnosis. The rate of self-reported depression was 15.49% (CI: 7.04–30.74%) compared to 14.90% (CI: 7.02–28.88%) for self-rated depression in 147 and 914 donors, respectively. The rate of clinician-rated depression among 827 donors was 4.02% (CI: 2.24–7.09%).

Regression analysis was conducted to assess the baseline characteristics that could influence the rates of depression (Table 1). Female gender and Caucasian ethnicity were associated with increase odds of depression (OR: 1.67, 1.35–2.06, $P < 0.001$; OR: 1.88, 1.01–3.49, $P = 0.047$, respectively). A lower education status also resulted in an increase rate of depression (OR: 1.41, CI: 1.11–1.79, $P = 0.004$). Last, being employed was protective against depression (OR: 0.88, CI: 0.81–0.94, $P < 0.001$). Donor relationship with recipient was by

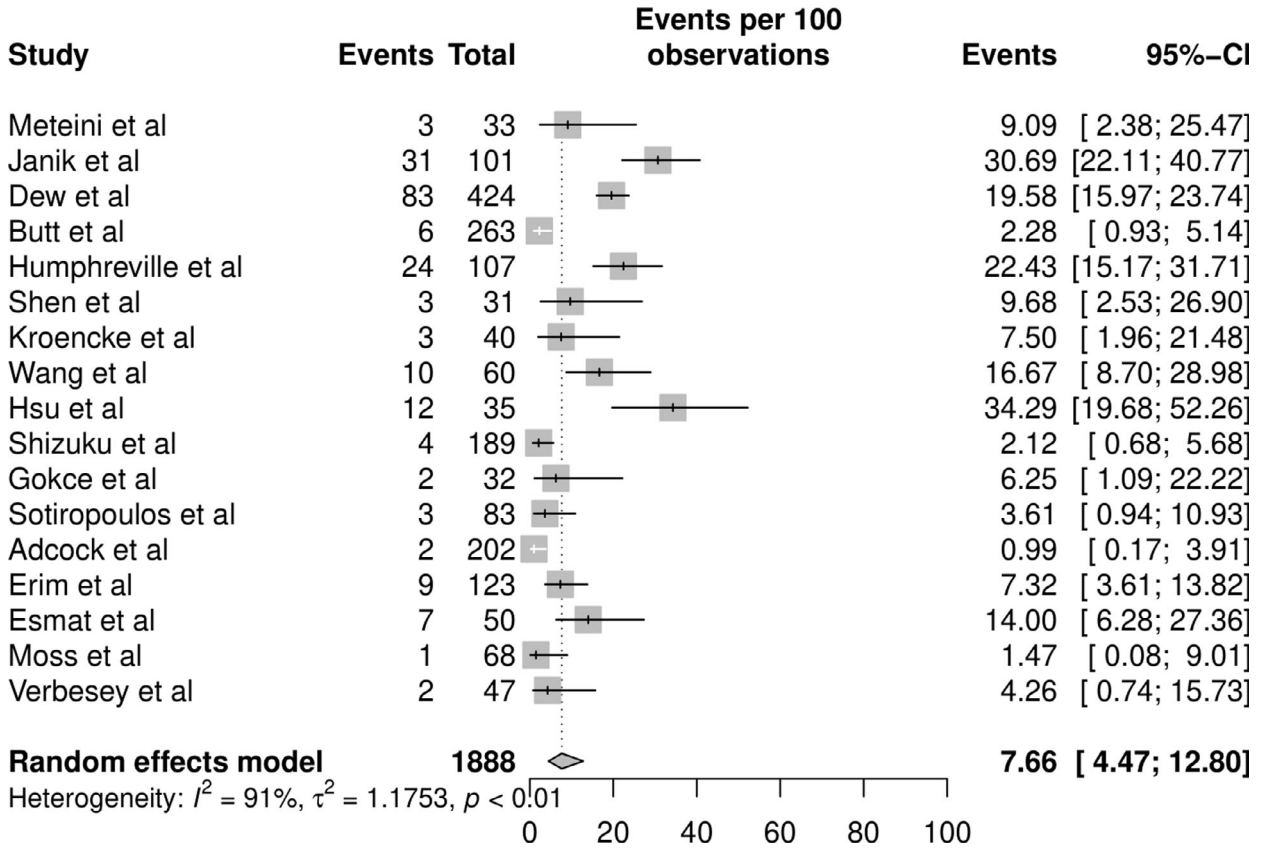

Figure 2 Overall incidence of donor depression.

and large not a significant factor in the development of depression (Table 1). Donors who were non-related to recipients did not have a significant increase in odds of depression (OR: 1.17, CI: 0.89–1.55, $P = 0.27$).

A subsequent subgroup analysis was done to account for rates of depression based on geographical regions (Fig. 3). The incidence of depression was 6.25% (CI: 2.88–13.01%) in Western countries, 10.84% (CI: 3.60–28.36%) in studies originating from Asia and 10.43% (CI: 6.02–17.48%) in Middle Eastern centres. There was a significant increase in risk of depression among donors in Asia compared to Western regions (RR: 1.73, CI: 1.19–2.52, $P = 0.0039$), while risk of donor depression in Asia and the Middle East was comparable (RR: 1.03, CI: 0.56–1.94, $P = 0.91$). Donors from Middle Eastern countries had a borderline non-significant increase in risk of depression compared to those from Western countries (RR: 1.67, CI: 0.94–2.95, $P = 0.079$).

Discussion

Living donor transplantation continues to be a major form of organ donation especially in Asian countries and the wellbeing of donors after LDLT remains a core aspect of transplant programmes internationally. Previous reviews have focused on the general quality of life including physical functioning and mental wellbeing of donors post-donation (Table S3) [10,11,47], while this study presents the first meta-analysis that summarizes the rate and risk factors of depression in LT donors. According to varying diagnosis methods, the rate of self-reported depression was 15.49% (CI: 7.04–30.74%), 14.90% (CI: 7.02–28.88%) for self-rated depression and 4.02% (CI: 2.24–7.09%) for clinician-rated depression. However, depression rates estimated by clinical diagnosis may be falsely low, especially in the Asian setting, due to the stigma associated with seeking consultation for depression. Instead, self-reported and self-rated questionnaires may provide a better estimate on the true rates of depression.

In the analysis of factors linked to depression, gender, ethnicity, education level and employment status of donors were significant factors associated with donor depression. Although the prognosis of transplant recipients may be a major factor affecting the rates of depression in donors, the lack of sufficient studies ($n = 4$) prevented any meaningful regression analysis. Female gender was associated with a significant increase in

Table 1. Summary of variables affecting rates of depression.

	No. of Studies	Odds Ratio	LCI	UCI	*P* Value
Baseline demographics					
Age	15	0.993	0.977	1.001	0.392
Female	17	1.668	1.352	2.057	<0.001*
Caucasian	5	1.876	1.008	3.493	0.047*
Hispanic	5	0.339	0.046	2.476	0.286
High School	6	1.410	1.113	1.785	0.004*
College	8	1.247	0.858	1.813	0.248
University	7	0.948	0.857	1.049	0.305
Employed	8	0.875	0.814	0.940	<0.001*
Married	8	1.255	0.817	1.928	0.300
Donor Relationship					
1st Degree	14	1.124	0.921	1.372	0.250
Parents	12	1.068	0.989	1.153	0.092
Children	11	0.844	0.473	1.505	0.566
Siblings	12	1.256	0.706	2.236	0.438
Spouse	9	0.774	0.378	0.334	0.55
Other Relative	11	0.761	0.312	1.856	0.548
Not Related	7	1.173	0.886	1.554	0.265

*Denotes significance at $P < 0.05$.

depression rates. Previous studies have found females to have a 1.7-fold increase in risk of developing depression, attributable to a myriad of hormonal, environmental and psychological differences between females and their male counterparts [48–51]. Genetic risk may also account for higher rates of depression in females [51]. Caucasian ethnicity was associated with an increased likelihood of depression post-donation. Previous studies have shown that the lifetime risk of depression in Caucasians is 17.9%, whereas other ethnic groups have significantly lower risk [52,53]. Additionally, lower education level resulted in a significant increase in depression rates [54]. Previous estimates suggest a 3% decrease in log OR for developing depression with every year of education [55]. Donors who were employed were also less likely to be depressed, with unemployment being a highly cited, major risk factor for depression [56,57]. Interestingly, donors who did not have a familial relationship with recipients were not at an increased risk of developing depression. This could partly be due to the altruistic nature of organ donation. Previous studies assessing the psychometrics of altruistic donors found that 84% of donors were free from psychiatric disorders and possessed personality traits such as being self-directed, self-confident and interested in others [58].

LDLT accounts for 90% of transplants in Asia but only 10% in Western countries [59]. However, the majority of included studies were from Western countries (58.80%) with only 17.65% from Middle Eastern countries and 23.53% originating from Asian centres. Donors from Asian countries had the highest rates of depression at 10.84% compared to 6.25% and 10.43% from Western and Middle Eastern countries, respectively. Although depression rates in the Middle East and Asia were comparable, there was a 68% increase in risk of depression for donors in Asia compared to the Western countries (RR: 1.68, CI: 1.16–2.42, $P = 0.006$). Yet, the reported rates in Asia may be more optimistic than in reality as traditional screening methods for depression have been demonstrated to be less sensitive in Asians [60]. In addition, stigmatization of mental health issues in Asia can often result in lower utilization of mental health services [61,62]. More original studies involving Asian populations are warranted to further investigate the impact of ethnicity on depression among LDLT patients.

Currently, most transplant centres have adopted a formal psychosocial assessment of donors by clinical psychologists as an integral part of their potential donor evaluation [63]. The International Liver Transplant Society (ILTS) recommends a multi-disciplinary approach for donor psychological assessment [64]. However, there remains no validated disease-specific instruments to measure mental health disorders in the LDLT population to date, and considering the high

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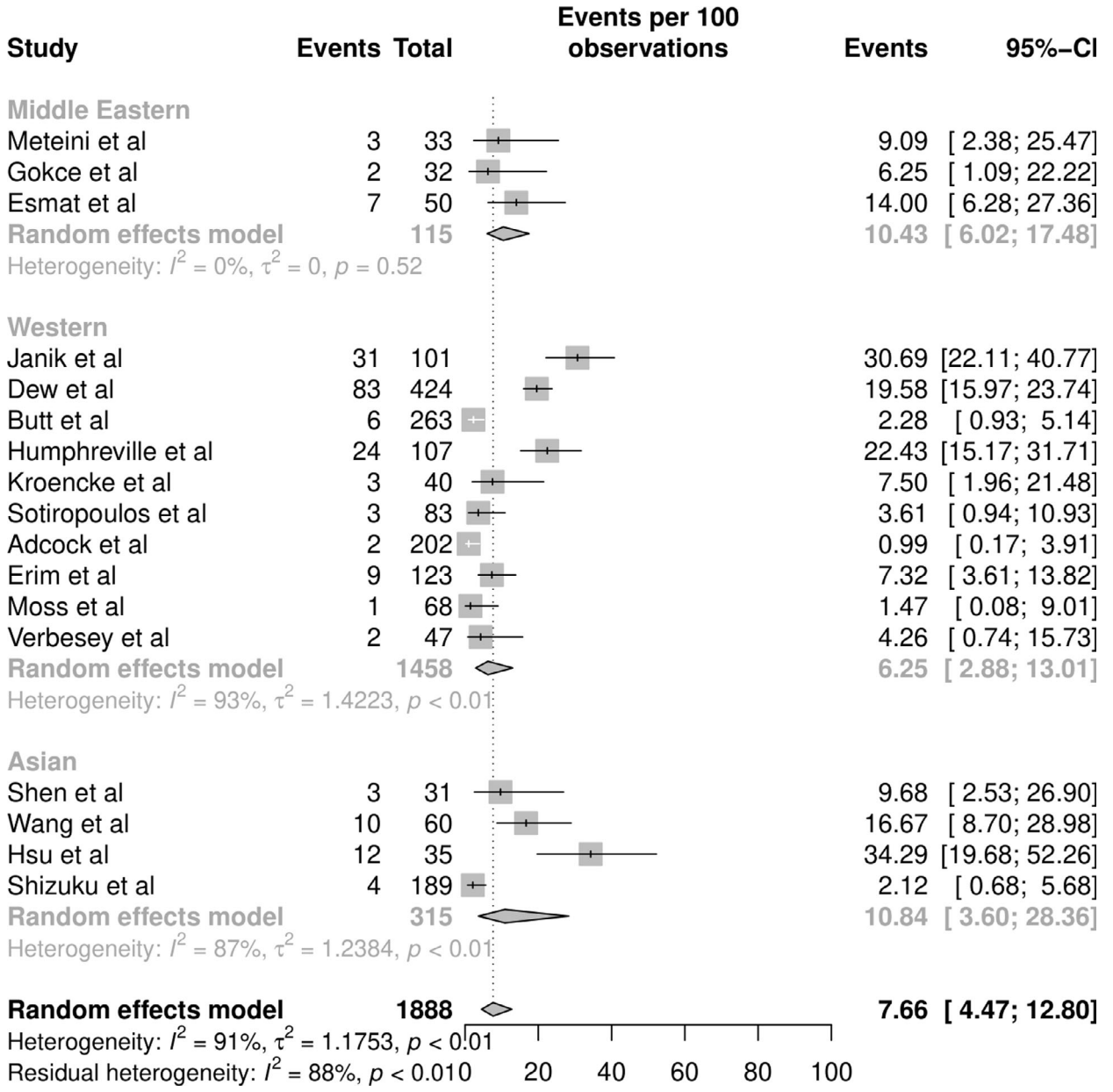

Figure 3 Pooled incidence of donor depression by geographical region.

prevalence of depression among women donors, more considerations should be given to gender-diversified assessment process and follow-up, such as the development of gender-sensitive depression screening tools to assess the mental health among this higher risk population. Psychosocial evaluations to screen for resilience and sense of coherence may also help to objectify donors' mental stability and eligibility [8,65]. The rising importance of donor wellbeing post donation has led to significant progress in areas such as the initiation of pre-donation motivational interviewing [66] to reduce ambivalence towards donations and the commencement of early post-surgery interventions such as supportive counselling, cognitive-behavioural-therapy [67], mindfulness-based resilience training [68] and acceptance and commitment therapy [69]. In addition, instrumental support from social support networks to share the care-taking workload of both recipient and donor during the recovery stages has been shown to exert a protective effect against depression [70].

Strengths and limitations

This study has several strengths. To our knowledge, this is the first meta-analysis that systematically reviews the evidence of depression in living liver donors with a

combined sample size of 1888 living donors. However, there are several limitations. There remains much heterogeneity in the diagnosis method of depression. Although depression disorders can only be validated via a structured psychiatric or psychological interview, it is important to note that self-rated and self-reported questionnaires are indispensable proxies that serve as practical tools and are often used and widely accepted in many well-established, reputable studies [71–73]. Additionally, the I^2, a measure of heterogeneity, is significantly large in the analysis. However, simulation studies have shown that the I^2 can often be an inappropriate measure of heterogeneity despite the ease of interpretation when sample sizes are large [74]. Consequently, such meta-analyses often have a large I^2 of >90% [75,76]. This may suggest that an appropriate tool for reliable assessment of heterogeneity is lacking. In turn, as demonstrated by a previous review [71], multiple subgroup analyses may present the best alternative to address heterogeneity and to test for the robustness of associations. Other limitations include varying follow-up time that may be a potential confounder and sparsity in reporting among included studies that prevented regression analysis of other factors including donor complications, indications for LT and symptoms affecting quality of life after donation, of which await the maturity of future studies on depression in transplant donors. Only English language articles with retrospective or prospective study design were considered, and further analysis could not be conducted on year of publication with limited studies published prior to 2010. Regardless, this meta-analysis provides an overarching picture of the incidence of depression in living donors and serves as a call for more in-depth analysis in future studies.

Conclusion

LDLT remains a critical means for treatment of end-stage liver disease especially in countries where deceased cadaveric liver donors are scarce. Although significant efforts in recent years have paved the way for improvements in quality of life, the systematic assessment of depression and implementation of support infrastructure for donors after transplant remains an unmet need. As evident from the high rates of depression, there is much room for improvement in the care of mental health among donors, and more studies are required to assess the impact of other factors that affect depression in LDLT.

Authorship

CHN, WHL, XCL, JX, DT and NS: contributed to the acquisition of data, analysis and interpretation of data and drafted the article. CSHH, AWCK, EXXT, JF, MDM: aided in revising the article critically for important intellectual content. All authors read and gave final approval of the version to be submitted.

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Conflicts of Interests

None of the authors declare any conflict of interest.

Data availability statement

All articles in this manuscript are available from Medline and Embase.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Summary of included articles.
Table S2. Hoy et al. risk-of-bias assessment.
Table S3. Summary of previous systematic reviews.
Figure S1. PRISMA flow diagram.

REFERENCES

1. Kim PTW, Testa G. Living donor liver transplantation in the USA. *Hepatobiliary Surg Nutr*. 2016; **5**: 133.
2. Chen C-L, Kabiling CS, Concejero AM. Why does living donor liver transplantation flourish in Asia? *Nat Rev Gastroenterol Hepatol* 2013; **10**: 746.
3. Hibi T, Wei Chieh AK, Chi-Yan Chan A, *et al*. Current status of liver transplantation in Asia. *Int J Surg* 2020; **82**: 4.
4. Ghobrial RM, Freise CE, Trotter JF, *et al*. Donor morbidity after living donation for liver transplantation. *Gastroenterology* 2008; **135**: 468.
5. Trotter JF, Hill-Callahan MM, Gillespie BW, *et al*. Severe psychiatric problems in right hepatic lobe donors for living donor liver transplantation. *Transplantation* 2007; **83**: 1506.
6. Butt Z, Dew MA, Liu Q, *et al*. Psychological outcomes of living liver donors

from a multicenter prospective study: results from the adult-to-adult living donor liver transplantation cohort study2 (A2ALL-2). *Am J Transplant* 2017; **17**: 1267.
7. Erim Y, Beckmann M, Kroencke S, *et al*. Psychological strain in urgent indications for living donor liver transplantation. *Liver Transpl* 2007; **13**: 886.
8. Wang S-H, Lin P-Y, Wang J-Y, *et al*. Mental health status after living donor hepatectomy. *Medicine (Baltimore)* 2017; **96**: e6910.
9. Krahn LE, DiMartini A. Psychiatric and psychosocial aspects of liver transplantation. *Liver Transpl* 2005; **11**: 1157.
10. Middleton PF, Duffield M, Lynch SV, *et al*. Living donor liver transplantation–adult donor outcomes: a systematic review. *Liver Transpl* 2006; **12**: 24.
11. Parikh ND, Ladner D, Abecassis M, *et al*. Quality of life for donors after living donor liver transplantation: a review of the literature. *Liver Transpl* 2010; **16**: 1352.
12. Noma S, Hayashi A, Uehara M, *et al*. Comparison between psychosocial long-term outcomes of recipients and donors after adult-to-adult living donor liver transplantation. *Clin Transplant* 2011; **25**: 714.
13. Schiavo JH. PROSPERO: an international register of systematic review protocols. *Med Ref Serv Quart* 2019; **38**: 171.
14. Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; **339**: b2535.
15. Ismail Z, Elbayoumi H, Fischer CE, *et al*. Prevalence of depression in patients with mild cognitive impairment: a systematic review and meta-analysis. *JAMA Psychiatry*. 2017; **74**: 58.
16. Shizuku M, Kamei H, Kimura H, *et al*. Clinical features and long-term outcomes of living donors of liver transplantation who developed psychiatric disorders. *Ann Transplant*. 2020; **25**: e918500.
17. Gökçe S, Durmaz O, Peykerlı Gürsu G, *et al*. Assessment of living donors with respect to pre- and posttransplant psychosocial properties and posttransplant family functioning in pediatric liver transplantation. *Turk J Gastroenterol*. 2011; **22**: 36.
18. Sotiropoulos GC, Radtke A, Molmenti EP, *et al*. Long-term follow-up after right hepatectomy for adult living donation and attitudes toward the procedure. *Ann Surg* 2011; **254**: 694; discussion -1.
19. Adcock L, Macleod C, Dubay D, *et al*. Adult living liver donors have excellent long-term medical outcomes: the University of Toronto liver transplant experience. *Am J Transplant* 2010; **10**: 364.
20. Esmat G, Yosry A, El-Serafi M, *et al*. Donor outcomes in right lobe adult living donor liver transplantation: single-center experience in Egypt. *Transplant Proc*. 2005; **37**: 3147.
21. Moss J, Lapointe-Rudow D, Renz JF, *et al*. Select utilization of obese donors in living donor liver transplantation: implications for the donor pool. *Am J Transplant* 2005; **5**: 2974.
22. Verbesey JE, Simpson MA, Pomposelli JJ, *et al*. Living donor adult liver transplantation: a longitudinal study of the donor's quality of life. *Am J Transplant* 2005; **5**: 2770.
23. El-Meteini M, Shorub E, Mahmoud DAM, *et al*. Psychosocial profile and psychiatric morbidity among Egyptian patients after living donor liver transplantation. *Middle East Curr Psychiatry* 2019; **26**: 3.
24. Janik MK, Księżopolska A, Kostrzewa K, *et al*. Long-term health-related quality of life in living liver donors. *Ann Transplant* 2019; **24**: 45–51.
25. Shen CJ, Huang HL, Chen KH, *et al*. Comparison of liver function, emotional status, and quality of life of living liver donors in Taiwan. *Transplant Proc*. 2016; **48**: 1007.
26. Hsu HT, Hwang SL, Lee PH, *et al*. Impact of liver donation on quality of life and physical and psychological distress. *Transpl Proc* 2006; **38**: 2102.
27. Spitzer RL, Williams JBW, Kroenke K, *et al*. Utility of a new procedure for diagnosing mental disorders in primary care: the PRIME-MD 1000 study. *JAMA* 1994; **272**: 1749.
28. Humphreville VR, Radosevich DM, Humar A, *et al*. Longterm health-related quality of life after living liver donation. *Liver Transpl* 2016; **22**: 53.
29. Kroencke S, Nashan B, Fischer L, *et al*. Donor quality of life up to two years after living donor liver transplantation: a prospective study. *Transplantation* 2014; **97**: 582.
30. RStudio Team (2020). RStudio: Integrated Development for R. RStudio. Boston, MA: PBC. http://www.rstudio.com/
31. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. *Archives Public Health* 2014; **72**: 39.
32. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**: 177.
33. Barili F, Parolari A, Kappetein PA, *et al*. Statistical Primer: heterogeneity, random- or fixed-effects model analyses? *Interact Cardiovasc Thorac Surg* 2018; **27**: 317.
34. Fletcher J. What is heterogeneity and is it important? *BMJ (Clinical research ed)*. 2007; **334**: 94.
35. Higgins JP, Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557.
36. Borges Migliavaca C, Stein C, Colpani V, *et al*. How are systematic reviews of prevalence conducted? A methodological study. *BMC Med Res Methodol* 2020; **20**: 96.
37. Ye Q, Zou B, Yeo YH, *et al*. Global prevalence, incidence, and outcomes of non-obese or lean non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2020; **5**: 739.
38. Huang DQ, Yeo YH, Tan E, *et al*. ALT levels for Asians with metabolic diseases: a meta-analysis of 86 studies with individual patient data validation. *Hepatol Commun* 2020; **4**: 1624.
39. Jieling Xiao LKEL, Ng CH, Tan DJH, *et al*. Is fatty liver associated with depression? A meta-analysis and systematic review on the prevalence, risk factors, and outcomes of depression and non-alcoholic fatty liver disease. *Front Med* 2021; **8**. https://doi.org/10.3389/fmed.2021.691696
40. Hunter JP, Saratzis A, Sutton AJ, *et al*. In meta-analyses of proportion studies, funnel plots were found to be an inaccurate method of assessing publication bias. *J Clin Epidemiol* 2014; **67**: 897.
41. Low CJ, Leow AS, Syn NL, *et al*. Outcomes of left ventricular thrombosis in post-acute myocardial infarction patients stratified by antithrombotic strategies: a meta-analysis with meta-regression. *Int J Cardiol* 2021; **329**: 36.
42. Harbord RM, Higgins JPT. Meta-regression in stata. *Stata J* 2008; **8**: 493.
43. Koo CH, Chang JHE, Syn NL, *et al*. Systematic review and meta-analysis on colorectal cancer findings on colonic evaluation after CT-confirmed acute diverticulitis. *Dis Colon Rectum* 2020; **63**: 701.
44. Neo VSQ, Jain SR, Yeo JW, *et al*. Controversies of colonic stenting in obstructive left colorectal cancer: a critical analysis with meta-analysis and meta-regression. *Int J Colorectal Dis* 2021; **36**: 689.
45. Katz D, Baptista J, Azen SP, *et al*. Obtaining confidence intervals for the risk ratio in cohort studies. *Biometrics* 1978; **34**: 469.
46. Hoy D, Brooks P, Woolf A, *et al*. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012; **65**: 934.

47. Dew MA, Butt Z, Liu Q, *et al*. Prevalence and predictors of patient-reported long-term mental and physical health after donation in the adult-to-adult living-donor liver transplantation cohort study. *Transplantation* 2018; **102**: 105.
48. Dew MA, Butt Z, Humar A, *et al*. Long-term medical and psychosocial outcomes in living liver donors. *Am J Transplant* 2017; **17**: 880.
49. Kendler KS, Gardner CO. Sex differences in the pathways to major depression: a study of opposite-sex twin pairs. *Am J Psychiatry* 2014; **171**: 426.
50. Whiteford HA, Degenhardt L, Rehm J, *et al*. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 2013; **382**: 1575.
51. Baxter AJ, Scott KM, Ferrari AJ, *et al*. Challenging the myth of an "epidemic" of common mental disorders: trends in the global prevalence of anxiety and depression between 1990 and 2010. *Depress Anxiety*. 2014; **31**: 506.
52. Kuehner C. Why is depression more common among women than among men? *Lancet Psychiatry*. 2017; **4**: 146.
53. Williams DR, González HM, Neighbors H, *et al*. Prevalence and distribution of major depressive disorder in African Americans, Caribbean blacks, and non-Hispanic whites: results from the National Survey of American Life. *Arch Gen Psychiatry* 2007; **64**: 305.
54. Woodward AT, Taylor RJ, Abelson JM, *et al*. Major depressive disorder among older African Americans, Caribbean blacks, and non-Hispanic whites: secondary analysis of the National Survey of American Life. *Depress Anxiety* 2013; **30**: 589.
55. Peyrot WJ, Lee SH, Milaneschi Y, *et al*. The association between lower educational attainment and depression owing to shared genetic effects? Results in ˜25 000 subjects. *Mol Psychiatry* 2015; **20**: 735.
56. Lorant V, Deliège D, Eaton W, *et al*. Socioeconomic inequalities in depression: a meta-analysis. *Am J Epidemiol* 2003; **157**: 98.
57. Stankunas M, Kalediene R, Starkuviene S, *et al*. Duration of unemployment and depression: a cross-sectional survey in Lithuania. *BMC Public Health* 2006; **6**: 174.
58. Zuelke AE, Luck T, Schroeter ML, *et al*. The association between unemployment and depression-Results from the population-based LIFE-adult-study. *J Affect Disord* 2018; **235**: 399.
59. Jendrisak MD, Hong B, Shenoy S, *et al*. Altruistic living donors: evaluation for nondirected kidney or liver donation. *Am J Transplant* 2006; **6**: 115.
60. Rela M, Reddy MS. Living donor liver transplant (LDLT) is the way forward in Asia. *Hep Intl* 2017; **11**: 148.
61. Comino E, Silove D, Manicavasagar V, *et al*. Agreement in symptoms of anxiety and depression between patients and GPs: the influence of ethnicity. *Fam Pract* 2001; **18**: 71.
62. Augsberger A, Yeung A, Dougher M, *et al*. Factors influencing the underutilization of mental health services among Asian American women with a history of depression and suicide. *BMC Health Services Res* 2015; **15**: 542.
63. Georg Hsu LK, Wan YM, Chang H, *et al*. Stigma of depression is more severe in Chinese Americans than Caucasian Americans. *Psychiatry* 2008; **71**: 210.
64. Shrestha R. Psychosocial assessment of adult living liver donors. *Liver Transpl* 2003; **9**(10 Suppl 2): S8–S11.
65. Miller CM, Durand F, Heimbach JK, *et al*. The International Liver Transplant Society guideline on living liver donation. *Transplantation* 2016; **100**: 1238.
66. Erim Y, Beckmann M, Kroencke S, *et al*. Sense of coherence and social support predict living liver donors' emotional stress prior to living-donor liver transplantation. *Clin Transplant* 2008; **22**: 273.
67. Dew MA, DiMartini AF, DeVito Dabbs AJ, *et al*. Preventive intervention for living donor psychosocial outcomes: feasibility and efficacy in a randomized controlled trial. *Am J Transplant* 2013; **13**: 2672.
68. Wirken L, van Middendorp H, Hooghof CW, *et al*. Development and feasibility of a guided and tailored internet-based cognitive-behavioural intervention for kidney donors and kidney donor candidates. *BMJ Open* 2018; **8**: e020906.
69. Stonnington CM, Darby B, Santucci A, *et al*. A resilience intervention involving mindfulness training for transplant patients and their caregivers. *Clin Transplant* 2016; **30**: 1466.
70. Azari S, Kiani G, Hejazi M. The effect of acceptance and commitment based group therapy on increasing the quality of life in kidney transplant and hemodialysis patients in Zanjan City: a randomized clinical trial study. *RUMS J* 2020; **19**: 555.
71. Lai Y-C, Lee W-C, Juang Y-Y, *et al*. Effect of social support and donation-related concerns on ambivalence of living liver donor candidates. *Liver Transpl* 2014; **20**: 1365.
72. Barberio B, Zamani M, Black CJ, *et al*. Prevalence of symptoms of anxiety and depression in patients with inflammatory bowel disease: a systematic review and meta-analysis. *Lancet. Gastroenterol Hepatol* 2021; **6**: 359.
73. Fancourt D, Steptoe A, Bu F. Trajectories of anxiety and depressive symptoms during enforced isolation due to COVID-19 in England: a longitudinal observational study. *Lancet Psychiatry* 2021; **8**: 141.
74. Karyotaki E, Efthimiou O, Miguel C, *et al*. Internet-based cognitive behavioral therapy for depression: a systematic review and individual patient data network meta-analysis. *JAMA Psychiatry* 2021; **78**: 361.
75. Rücker G, Schwarzer G, Carpenter JR, *et al*. Undue reliance on I(2) in assessing heterogeneity may mislead. *BMC Med Res Methodol* 2008; **8**: 79.
76. Borenstein M, Higgins JP, Hedges LV, *et al*. Basics of meta-analysis: I(2) is not an absolute measure of heterogeneity. *Res Synth Methods* 2017; **8**: 5.
77. Rücker G, Schwarzer G, Carpenter JR, *et al*. Undue reliance on I2 in assessing heterogeneity may mislead. *BMC Med Res Methodol* 2008; **8**: 79.