Interpersonal psychotherapy or antidepressant medication for adult depression? A systematic review and individual participant data meta analysis of treatment outcome moderators

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Abstract

Background: Interpersonal psychotherapy (IPT) and antidepressant medication (ADM) are recommended treatments for adult depression, but which individuals benefit more from one intervention than the other remains largely unclear. Individual participant data (IPD) meta-analysis constitutes a reliable method to examine treatment-covariate interactions with increased statistical power.

Aims: This IPD meta-analysis examined participant baseline characteristics as moderators of outcome in IPT versus ADM.

Method: A systematic literature search conducted January 1, 2024 identified randomized clinical trials comparing IPT and ADM in adults with acute-phase depression. Anonymized IPD were requested and analyzed using mixed-effects models. Primary outcome was post-treatment Hamilton Rating Scale for Depression (HRSD) score.

Results: IPD were obtained for 9 of 15 eligible studies (N = 1613/2025, 79.6%; mean age = 42.36 years (SD = 13.39); 70.2% female). No participant baseline characteristic was significantly associated with differential outcome at treatment completion. Between-study heterogeneity ranged from 1.81% to 29.31%.

Conclusions: We found no indication that one of these interventions can be preferred over the other based on participant demographic and clinical characteristics.

Keywords: interpersonal psychotherapy, antidepressant medication, depression, moderators, individual participant data meta-analysis

Introduction

Depression, affecting millions of people worldwide, has been characterized as the leading contributor to global disability (World Health Organization, 2017). The high burden of depression along with the increasing prevalence rates over time (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018; Moreno-Agostino et al., 2021) emphasize the need for effective treatment plans.

Pharmacotherapy and psychotherapy are both recommended for the treatment of adult depression (National Institute for Health and Care Excellence [NICE], 2022). Despite that antidepressant medication (ADM) is efficacious and well-tolerated, potential risks and side effects may arise (Möller et al., 2012) and some individuals indicate a preference for psychological treatments rather than ADM (McHugh, Whitton, Peckham, Welge, & Otto, 2013). Among the range of psychotherapies for depression, interpersonal psychotherapy (IPT) is an evidence-based intervention included as a treatment of choice in practice guidelines (NICE, 2022). IPT was originally developed for the treatment of depression, and it is a structured, time-limited intervention based on the premise that stressful interpersonal experiences contribute to the onset and maintenance of depressive symptoms (Klerman, Weissman, Rounsaville, & Chevron, 1984; Weissman, Markowitz, & Klerman, 2018). IPT consists of three phases (beginning, middle, ending). During the beginning phase, the therapist identifies through assessment the interpersonal context, which is thought to be closely linked to current depressive symptoms (e.g. grief, relational disputes, role transitions, interpersonal deficits). Specific strategies adapted to the focal area identified are taught, aiming to improve relationships and interpersonal experiences, which are considered important in the alleviation of depressive symptoms (Ravitz et al., 2019).

The comparative efficacy of IPT and ADM at treatment completion has been examined in several meta-analyses either with no statistically significant differences found between the two interventions (Cuijpers, Donker, Weissman, Ravitz, & Cristea, 2016; Cohen et al., in press; de Mello, de Jesus Mari, Bacaltchuk, Verdeli, & Neugebauer, 2005) or with small effect sizes favoring ADM (Cuijpers et al., 2011; van Hees, Rotter, Ellermann, & Evers, 2013). However, individuals do not respond equally to depression treatments (Kaiser et al., 2022), which indicates that despite no large differences in effects being found on average, individuals might benefit more from one

treatment than the other. Therefore, identifying pre-treatment individual characteristics that are associated with differential response, holds promise for a more personalized approach in depression treatment selection and consequently, improvement of outcomes (Cohen & DeRubeis, 2018).

Research on moderators of outcome in IPT versus ADM is limited. To the best of our knowledge, moderators were assessed in two randomized clinical trials (RCTs). Menchetti et al. (2014) found that low depression severity and absence of comorbid anxiety disorder predicted better response to IPT than ADM, whereas this was not found in another study (Frank et al., 2011). Low functional impairment, no history of depressive episodes and smoking were associated with better response to IPT than ADM in one RCT (Menchetti et al, 2014), awaiting further replication. Demographic characteristics including gender, age, education, marital status, and occupation were not found to moderate treatment outcome (Frank et al., 2011; Menchetti et al., 2014). However, RCT sample sizes might have been too small to identify smaller effects, for the identification of which increased statistical power is required (Brookes et al., 2004; Fisher, Carpenter, Morris, Freeman, & Tierney, 2017). Thus, which individuals benefit more from one intervention than the other remains largely unclear.

To overcome the aforementioned limitations, we aim to conduct an IPD meta-analysis examining participant baseline characteristics as potential moderators of post-treatment Hamilton Rating Scale for Depression (HRSD) score in IPT versus ADM for acute-phase depression in adults. IPD meta-analysis differs from conventional meta-analysis as participant-level data from the studies' raw datasets are synthesized and analyzed instead of aggregate study-level data from publications (Riley, Lambert, & Abo-Zaid, 2010). IPD meta-analysis constitutes a reliable approach to examine treatment covariate interactions, as it increases statistical power compared to both single RCTs and conventional meta-analyses, to detect differential effects across individuals (Riley et al., 2020). Moreover, IPD meta-analysis contrary to conventional meta-analysis avoids ecological bias, namely associations found not being representative for individuals due to directly assessing participant-level information (Debray et al., 2015). Additionally, the standardization of data-analysis across studies is facilitated, and the examination of variables collected but not reported in publications becomes possible (Riley et al., 2010), rendering IPD meta-analysis an appropriate method to examine our research question.

Methods

Design

This systematic review and IPD meta-analysis is part of a larger project for which the protocols have been published (PROSPERO: CRD42020219891, Driessen et al., 2021; Driessen et al., 2023), and the current study has been pre-registered (https://doi.org/10.17605/OSF.IO/CJFBU).

Search strategy and study selection

Studies were identified by searching the METAPSY database, which includes RCTs examining the efficacy and effectiveness of psychological treatments for depression (www.metapsy.org) (Driessen et al., 2021; Driessen et al., 2023). The METAPSY database was developed through comprehensive literature searches in PubMed, PsychINFO, Embase.com, and the Cochrane Library and is updated every four months. The search strings use a combination of index terms and free-text words indicative of depression and psychotherapies, with filters for randomized clinical trials. The exact terms for the searches can be found at https://osf.io/nv3ea/. Searches were performed January 1, 2024. Two independent raters screened all records, assessed full-text papers for METAPSY database eligibility and categorized the treatment comparison(s) examined. Then, two raters assessed all full-text papers of studies marked as comparing a psychotherapy monotreatment condition against another active monotreatment condition for meeting the inclusion criteria for this study. Disagreement was resolved through consensus. In addition, reference lists of included studies and prior reviews were inspected for studies that were missed. A listserv of members of the International Society of Interpersonal Psychotherapy was contacted for ongoing or unpublished studies (Driessen et al., 2021; Driessen et al., 2023).

Eligible studies were RCTs that directly compared IPT and ADM in adults with acute-phase depression. No restrictions were placed regarding the language, date, and status of publication, or time of study. IPT was considered an intervention that was a psychotherapy based on the manuals developed by Klerman and Weissman for IPT (Klerman et al., 1984; Weissman, Markowitz, & Klerman, 2000, 2007; Weissman et al., 2018) or the briefer version called interpersonal counselling (IPC) (Weissman et al.,

2014). No restrictions were placed on the number of sessions, the duration of follow-up, the delivery format and the setting as long as the therapy was administered by a clinician (Driessen et al., 2021; Driessen et al., 2023). ADM was considered the oral administration of any type of standard antidepressant medication within the therapeutic dose range (e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs)). Participants needed to be at least 18 years old and were considered depressed if they met the diagnostic criteria for major depressive disorder or another unipolar mood disorder assessed by a semi-structured interview or a clinician's assessment, or if they presented a score at or above a validated cut-off for clinically significant depressive symptoms on an evaluator-assessed, clinician-assessed, or self-reported measure of depression. Comorbid psychiatric and somatic illnesses were allowed. Eligibility criteria were assessed at study level (Driessen et al., 2021; Driessen et al., 2023).

Data collection

Authors of identified studies were contacted using a multi-step protocol (Driessen et al., 2021; Driessen et al., 2023) and were invited to share the anonymized participant-level data of their studies. Collected IPD relevant to the current study included randomized treatment condition, depression outcome measures assessed prior to and after treatment, and all potential moderator variables assessed in the study. Only data from the acute-phase treatment with IPT or ADM were used for analysis (e.g., only depression outcomes measured before augmentation following non-response to monotherapy). Study-level characteristics, consisting of country, recruitment method, target group, depression inclusion criteria, number of IPT sessions, IPT format, and ADM type were extracted from the study publications. Data received were checked for matching the data reported in the publications, for including all variables reported and for invalid, out-of-range, and inconsistent values. Discrepancies were discussed with the authors (Driessen et al., 2021; Driessen et al., 2023). Risk of bias assessments were performed at outcome level using the Cochrane risk of bias tool for RCTs (Higgins, Savović, Page, Elbers, & Sterne, 2023) by two independent raters. Disagreements were resolved through consensus or with the consultation of a third rater, if consensus could not be reached.

Measures

Depressive symptom level at treatment completion was the primary outcome measure and it was operationalized as a participant's score on the 17-item Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960) at the study's primary post-treatment point as defined by the study authors. If collected data from identified studies did not include scores on the HRSD scale, scores on the Montgomery and Åsberg Depression Rating Scale (MADRS) (Montgomery, 1978; Montgomery & Åsberg, 1979), were converted into HRSD scores using existing conversion algorithms (Leucht, Fennema, Engel, Kaspers-Janssen, & Szegedi, 2018). The transformation table can be found in Appendix Table A.1.

Potential moderator variables were pre-specified as all demographic, clinical, and psychological participant characteristics assessed prior to the beginning of treatment (Driessen et al., 2021; Driessen et al., 2023). A variable was examined as a potential moderator if IPD were available for at least two identified studies. Categorical moderators were recoded into similar categories, if primary studies used different assessment methods and recoding was finalized before data analysis started. Baseline depression severity as a potential moderator was operationalized as a participant's (converted) HRSD score at baseline.

Data analysis

One-stage IPD meta-analyses using mixed-effects models with restricted maximum likelihood estimation were conducted in R (version 4.2.1; R Core Team, 2022) using the lme4 package (version 1.1-27.1; Bates, Mächler, Bolker, & Walker, 2015). Between-study heterogeneity was assessed using the I^2 statistic and normality of the distribution of the residuals using histograms. As far as possible, analyses were based on intention-to-treat samples. Moderators were tested in separate models. The models included a main effect for time (dummy variable), a main effect for treatment condition (categorical variable), a moderator main effect, a time-by-treatment interaction, a time-by-moderator interaction, a treatment-by-moderator interaction, a time-by-moderator-by-treatment three-way interaction, a random intercept for study (to account for participants clustered within studies), a random intercept for participants (to account for clustering of repeated measures within participants), and a random slope with respect to time on study level. A significant moderator effect was indicated by a

significant time-by-moderator-by-treatment three-way interaction after Bonferroni adjustment for multiple testing ($p < .004$, 12 tests).

Results

Included studies

Literature search results are presented in Figure 1. Fifteen studies ($N = 2025$) were identified to meet eligibility criteria for this IPD meta-analysis (for references see Appendix Table A.2). IPD were obtained for 9 studies totaling 1613 (79.6%) participants ($N_{IPT} = 805$, 49.91%; $N_{ADM} = 806$, 49.97%). Six participants had invalid or missing pre- and post-treatment depression scores and were excluded from analysis.

Study characteristics are shown in Table 1. Of the 9 studies for which IPD were obtained, seven studies (77.8%) researched adults in general, one study (11.1%) investigated adults with post-stroke depression and one study (11.1%) recruited adults with type 2 diabetes. Major depressive disorder was the primary depression diagnosis used in six studies (66.7%), while major depressive episode was used as inclusion criterion in two studies (22.2%) and in one other study (11.1%) participants needed to meet criteria for dysthymic disorder. SSRI was used as the ADM type in six studies (66.7%), while TCA, other type and multiple types were used in one study each (11.1%). The majority of studies (seven studies; 77.8%) investigated IPT ranging from 8 to 20 sessions, while two studies (22.2%) examined IPC, ranging from 6 to 8 sessions.

Mean age of participants for which IPD were available was 42.36 years ($SD = 13.39$; $N = 1564$). Female participants represented 70.2% ($N = 1613$) of the total sample and mean of education years was 13.91 ($SD = 3.43$; $N = 1045$). Participants' mean episode duration was 42.62 ($SD = 54.13$ $N = 569$) weeks and baseline HRSD score was 18.7 ($SD = 4.72$ $N = 1584$).

Risk of bias assessment

The risk of bias assessment is presented in Table 2. Overall, no study met criteria to be considered low risk of bias. Six studies (66.7%) were rated with risk of some concern and three studies (33.3%) with high risk. While, eight studies (88.9%) reported an adequate randomization process, and seven studies (77.8%) stated that

interventions were delivered with no deviations, main reason for rating as 'some concern' in these domains was the lack of sufficient information regarding randomization procedure or the delivery of treatments as intended reported in the publication. Seven studies (77.8%) reported an intention-to-treat sample, while eight studies (88.9%) adequately measured the outcome. The majority of studies (88.9%) did not provide a pre-registered analysis plan of their trial, which constituted a main reason for study ratings of 'some concern'.

IPD meta-analyses

Results of the moderator analyses are presented in Table 3. No participant baseline characteristic was found to moderate IPT-ADM comparative efficacy. Specifically, demographics were not significantly related to differential depression outcome, consisting of gender (b = -0.021, 95% CI [-0.211, 0.171], p = .825), age (b = 0.006, 95% CI [-0.006, 0.019], p = .318), years of education (b = 0.045, 95% CI [-0.022, 0.111], p = .193), marital status (b = 1.073, 95% CI [0.082, 2.094], p = .283), living situation (b = -0.183, 95% CI [-0.535, 0.175], p = .336), and employment status (b = -0.794, 95% CI [-1.437, -0.157], p = .165). Clinical characteristics were not found to be associated with differential post-treatment depressive scores, consisting of depression severity (b = -0.006, 95% CI [-0.038, 0.025], p = .687), depression type (b = 0.603, 95% CI [-1.162, 2.335], p = .493), duration of current depressive episode (b = -0.001, 95% CI [-0.006, 0.003], p = .557), previous depressive episode (b = 0.168, 95% CI [-0.036, 0.371], p = .102), age of depression onset (b = 0.004, 95% CI [-0.018, 0.027], p = .725), and comorbid somatic disorder (b = -0.252, 95% CI [-0.033, 0.373], p = .077). Between-study heterogeneity ranged from 1.81% to 29.31%.

Discussion

This systematic review and IPD meta-analysis examined a range of participant baseline characteristics as moderators of depressive symptom level at treatment completion in IPT versus ADM for adult depression. No participant characteristic was found to be associated with differential outcome between the two interventions.

Regarding demographic characteristics, no indication of a moderating effect was found for gender, age, education, marital status, living situation and employment status,

which is in line with previous RCT findings (Frank et al., 2011; Menchetti et al. 2014). Although small sample sizes in RCTs might limit the detection of small treatment covariate effects (Lorenzo-Luaces, Peipert, De Jesús Romero, Rutter & Rodriguez-Quintana, 2021), methodological advantages related to the IPD meta-analytic approach and specifically, the adequate statistical power to examine intervention moderators (Riley et al., 2020) suggests with increased accuracy that individuals across the different levels of these characteristics can expect similar benefit from both interventions.

Symptom-related and clinical indicators, specifically baseline depression severity, history of depressive episodes, duration of the current depressive episode, depression type, age of depression onset and comorbid somatic disorder were not found to be associated with differential outcome in IPT versus ADM. Findings regarding baseline depression severity and depression type are consistent with previous IPD meta-analyses comparing cognitive-behavioral therapy, another widely used intervention for depression, with ADM, which also did not find a moderating effect for these characteristics (Cuijpers et al., 2017; Furukawa et al, 2018; Weitz et al., 2015). In addition, baseline depression severity was not identified as a moderator in a previous conventional meta-analysis comparing ADM with a range of psychotherapies, including IPT (Tröger et al., 2023) and a previous RCT (Frank et al., 2011), although depression severity and history of depressive episodes were found to moderate efficacy in another RCT (Menchetti et al., 2014).

This study was the first to examine a broad range of characteristics as moderators of IPT versus ADM for adult depression using an IPD meta-analytic method. Because of the high statistical power that this approach offers to examine treatment moderators, non-significant findings are of high importance, as they indicate that these characteristics are not relevant as moderators, meaning that individuals across the different levels in demographic and clinical characteristics would similarly benefit from IPT or ADM for depression (Cuijpers et al., 2022).

Strengths and limitations

The current study has several strengths. First, the IPD meta-analytic approach allowed for conducting intention-to-treat analyses for most of the included studies, for standardizing data-analysis methods and for analyzing data collected, but not reported

in original studies. Most importantly, it allowed for studying moderators with increased statistical power, therefore providing more reliable estimates than single RCTs and conventional meta-analyses. Second, between-study variation was low in all statistical models conducted, thus reducing bias (Deeks, Higgins & Altman, 2023). Third, studies were largely comparable regarding target population, depression inclusion criteria, ADM type and mean participant baseline depression score.

Some limitations also need to be mentioned. First, risk of bias of the included studies was rated as of 'some concern' or 'high'. Nevertheless, it should be noted that the risk of bias tool for randomized trials (Higgins et al., 2023) was originally developed for conventional meta-analysis and no adaptation for IPD meta-analysis exists. For this reason, some areas assessed, such as bias arising due to selection of the reported result might be less problematic in this context. Indeed, eight out of nine studies were rated as of 'some concern' in this domain due to lack of a prespecified analysis plan, which is less relevant in an IPD meta-analytic approach, as IPD are synthesized and analyzed. Second, not all moderator variables were assessed in all studies. Therefore, some individual moderator models, such as living situation ($k = 2$, $N = 410$), comorbid somatic disorder ($k = 3$, $N = 512$) and age of depression onset ($k = 3$, $N = 598$) might relate to a subgroup of studies and not be representative of the total sample of studies. Third, data on duration of current depressive episode and age of depression onset were based on individuals' self-reported and retrospective judgment, therefore might be prone to recall bias.

Clinical and research implications

Given that both IPT and ADM are widely used interventions for adult depression, research on moderators of treatment outcome has important implications for clinical practice. This study found that differential treatment effects cannot be predicted based on a range of demographic and clinical participant characteristics. Because of the high statistical power and low between-study heterogeneity of this IPD meta-analysis, non-significant findings suggest that there is no indication that one of these interventions is to be preferred over the other (Cuijpers et al., 2022). Therefore, in order for treatment selection, patients' preference for a psychological or pharmacological intervention, or the availability of these treatments should be taken into consideration.

Given the importance of the research question and the limitations of this study, further research is warranted. First, research would benefit from the consistent collection and reporting of a broad range of variables in RCTs. Second, as differences between IPT and ADM regarding measures of general psychopathology and dysfunctional attitudes for adult depression have been found, favoring ADM (Cohen et al., in press), researching which individuals improve more from which treatment on these areas would contribute to adequately informed decision-making and treatment selection for adult depression.

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Figure 1

The PRISMA Individual Participant Data flow diagram

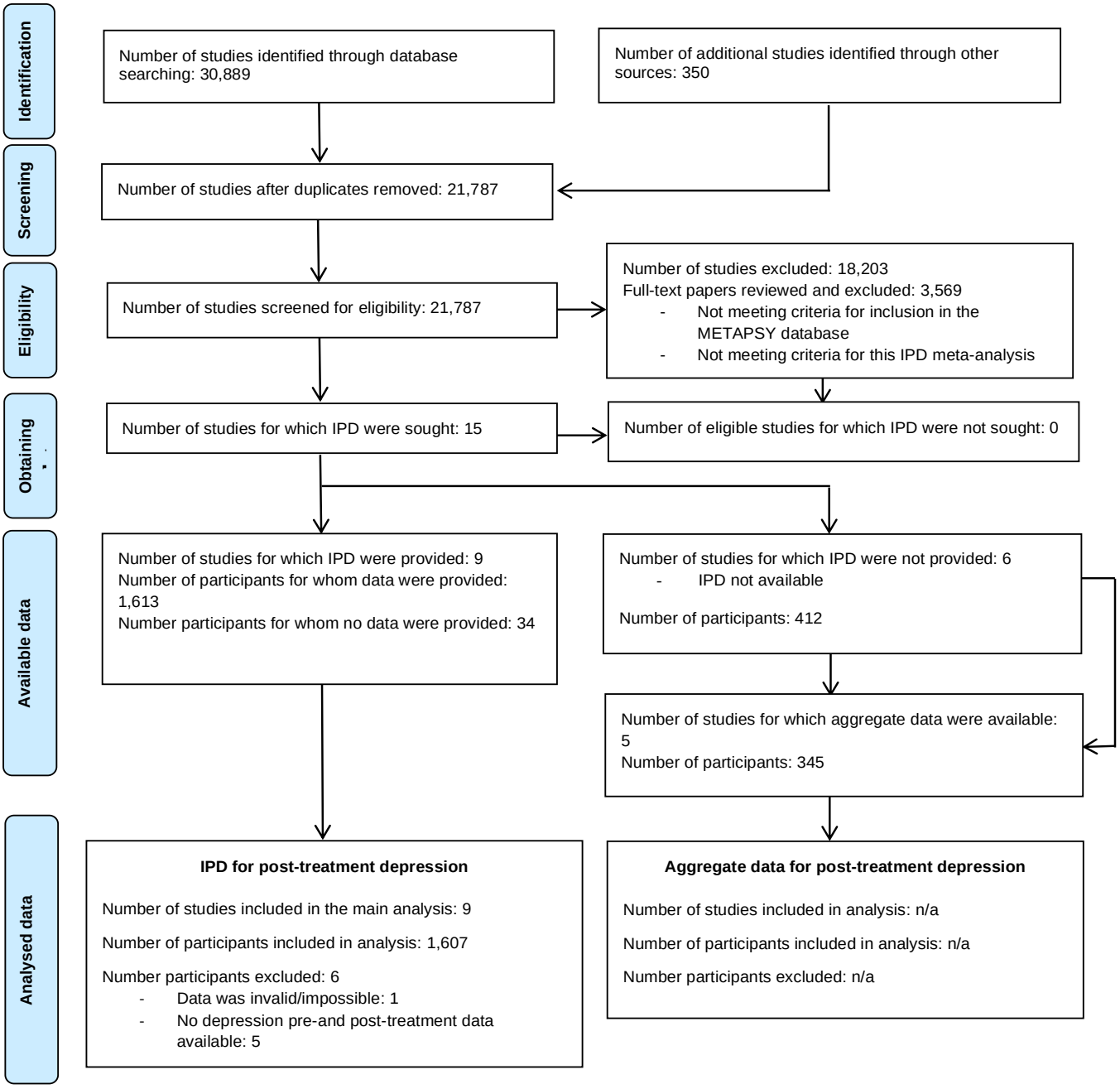

Table 1

Characteristics of Included Studies

Study	Country	Target population	Depression inclusion criteria	ADM type	N_{IPT} sessions	$N_{IPT/ADM}$	% Female	Mean Age	Mean Baseline HRSD-17
			IPD available						
Altamura et al., 2017	Italy	Adults	MDD (DSM-V); HRSD ≥ 8	SSRI	6	27/28	76.3	41.2	12.9
Blom et al., 2007	Netherlands	Adults	MDD (DSM-IV); HRSD ≥ 14	Other	12	50/47	71.1	40.5	21.0
Browne et al., 2002	Canada	Adults	Dysthymic disorder, with or without MDD (DSM-IV)	SSRI	12	231/229	68.7	42.4	19.3
Elkin et al., 1989	USA	Adults	MDD (RDC); HRSD ≥ 14	TCA	16-20	63/63	69	34.8	19.5
Finkenzeller et al., 2009	Germany	Adults with post-stroke depression	Depressive disorder (ICD-10); HADS > 7; HRSD ≥ 14	SSRI	8-16	27/24	54.9	68.5	21.1
Frank et al., 2011	USA/Italy	Adults	MDE (DSM-IV); HRSD ≥ 15	SSRI	12	186/182	71.7	38.9	20.1
Gois et al., 2014	Portugal	Adults with type 2 diabetes	MDD (DSM-4); HADS ≥ 7; MADRS ≥ 17	SSRI	12	17/17	88.2	55.1	18.9

Menchetti et al., 2014	Italy	Adults	MDE (DSM-IV); HRSD ≥ 13	SSRI	6-8	143/144	73.4	45.0	15.7
Quilty et al., 2008	Canada	Adults	MDD (DSM-IV)	SSRI, SNRI, MAOI, Other	16-20	63/72	63.7	41.6	18.1
IPD not available									
Markowitz et al., 2005	USA	Adults	Dysthymic disorder with early onset (DSM-IV); HRSD > 13; GAF < 61	SSRI	16-18	23/24	63[a]	42.3[b]	-
Martin et al., 2001	UK	Adults	MDE (DSM-IV); HRSD ≥ 18	SNRI	6	13/15	71.4	38.9	22.5
O'Hara et al., 2019	USA	Women with post-partum depression	MDE (DSM-IV); HRSD ≥ 15	SSRI	12	53/56	100	27.3	21.8
Schulberg et al., 1996	USA	Adults	Major depression (DSM-III-R); HRSD ≥ 13	TCA	16	93/91	81.5	37.8	23
Sloane et al., 1985	USA	Older adults	MDD (RDC); HRSD ≥ 17	TCA	6	19/18	52.7[a]	64.4[b]	23.4[c]

Weissman et al., 1979	USA	Adults	Major depression (SADS; RDC); Raskin Three Area Depression Scale ≥ 7	TCA	16	25/24	-	-	-

Note: ADM = Antidepressant medication; DSM = Diagnostic and Statistical Manual of Mental Disorders; GAF = Global Assessment of Functioning; HADS = Hospital Anxiety and Depression Scale; HRSD = Hamilton Rating Scale for Depression; ICD = International Classification of Diseases; IPD = Individual Participant Data; MAOI = Monoamine Oxidase Inhibitor; IPT = Interpersonal Psychotherapy; MADRS = Montgomery Åsberg Depression Rating Scale; MDD = Major Depressive Disorder; MDE = Major Depressive Episode; $N_{IPT\ \text{sessions}}$ = Number of sessions in the IPT condition; $N_{\text{IPT/ADM}}$ = Number of participants randomized to IPT and ADM conditions; RDC = Research Diagnostic Criteria; SADS = Schedule for Affective Disorders and Schizophrenia; SNRI = Serotonin Norepinephrine Reuptake Inhibitor; SSRI = Selective Serotonin Reuptake Inhibitor; TCA = Tricyclic Antidepressant; - = Not specified.

[a] Percentage of female participants includes also participants randomized in other treatment conditions examined in the study.

[b] Mean age also includes participants of other treatment conditions examined in the study, since it was not reported separately for the IPT and ADM groups.

[c] Mean baseline HRSD-17 is reported only for completers ($N_{\text{IPT/ADM}}$ = 19/10).

Table 2

Risk of Bias Assessments at Depression Outcome Level of Included Studies with Available IPD

Study	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Altamura et al., 2017	+	+	+	+	+/-	+/-
Blom et al., 2007	+	+	-	+	+/-	-
Browne et al., 2002	+	+	+	+	+/-	+/-
Elkin et al., 1989	+	+/-	+	+	+/-	+/-
Finkenzeller et al., 2009	+	+	+	+	+/-	+/-
Frank et al., 2011	+	+	-	+	+/-	-
Gois et al., 2014	+	+	+	+	+/-	+/-
Menchetti et al., 2014	+	+/-	+	+	+	+/-
Quilty et al., 2008	+/-	+	+	-	+/-	-

Note: + = low risk of bias; +/- = some concerns; - = high risk of bias

Table 3

Participant Baseline Characteristics as Moderators of Post-Treatment Depressive Symptom Level in IPT versus ADM

Moderator	*k*	*N*	*b*	95% CI	*p*	I^2
Gender	9	1607	-0.021	-0.211, 0.171	.825	18.51%
Age	9	1564	0.006	-0.006, 0.019	.318	18.43%
Years of education	6	1045	0.045	-0.022, 0.111	.193	1.81%
Marital status	7	1398	1.073	0.082, 2.094	.283	18.51%
Living situation	2	410	-0.183	-0.535, 0.175	.336	17.28%
Employment status	6	1275	-0.794	-1.437, -0.157	.165	11.53%
Depression severity	9	1584	-0.006	-0.038, 0.025	.687	7.34%
Depression type	6	1275	0.603	-1.162, 2.335	.493	24.65%
Current episode duration (weeks)	4	569	-0.001	-0.006, 0.003	.557	23.74%
Previous depressive episode	7	998	0.168	-0.036, 0.371	.102	23.34%
Age of onset	3	598	0.004	-0.018, 0.027	.725	1.57%
Comorbid somatic disorder	3	512	-0.252	-0.033, 0.373	.077	29.31%

Note: IPT = Interpersonal psychotherapy; *ADM* = Antidepressant medication; *k* = number of studies; *N* = number of participants; I^2 = between-study heterogeneity. Continuous variables were centered before being entered in the model. Depression severity is represented by baseline Hamilton Rating Scale for Depression (HRSD) scores. Levels of the categorical variables are: gender (0 = male, 1 = female); marital status (0 = single, 1 = married, 2 = separated/divorced, 3 = widowed, 4 = living together); living situation (0 = living alone, 1 = living with others), employment status (0 = employed, 1 = unemployed, 2 = student, 3 = retired, 4 = unable to work, 5 = caregiver/homemaker, 6 = other); depression type (0 = unspecified, 1 = melancholic, 2 = atypical, 3 = catatonic); previous depressive episode (0 = no, 1 = yes); comorbid somatic disorder (0 = no, 1 = yes).

Appendix

Table A.1

Transformation of MADRS Total Scores to HRSD Total Scores

MADRS	HRSD	MADRS	HRSD
3	3	29	23
4	4	30	23
5	4	31	24
6	5	32	25
7	6	33	25
8	7	34	26
9	7	35	27
10	8	36	28
11	9	37	29
12	9	38	29
13	10	39	30
14	11	40	31
15	12	41	32
16	12	42	33
17	13	43	34
18	14	44	35
19	15	45	35
20	16	46	36
21	16	47	37
22	17	48	37
23	18	49	38
24	19	50	38
25	19	51	39
26	20	52	40
27	21	53	40
28	22		

Note: MADRS = Montgomery and Åsberg Depression Rating Scale; HRSD = Hamilton Rating Scale for Depression.

Table A.2

References of Identified Studies

Study	Reference
	IPD available
Altamura et al., 2017	Altamura, M., Iuso, S., Terrone, G., Balzotti, A., Carnevale, R., Malerba, S., … Petito, A. (2017). Comparing interpersonal counseling and antidepressant treatment in primary care patients with anxious and nonanxious major depression disorder: A randomized control trial. *Clinical Neuropsychiatry, 14*, 257–262.
Blom et al., 2007	Blom, M. B., Jonker, K., Dusseldorp, E., Spinhoven, P., Hoencamp, E., Haffmans, J., & van Dyck, R. (2007). Combination treatment for acute depression is superior only when psychotherapy is added to medication. *Psychotherapy and Psychosomatics*, *76*(5), 289–297. https://doi.org/10.1159/000104705
Browne et al., 2002	Browne, G., Steiner, M., Roberts, J., Gafni, A., Byrne, C., Dunn, E., … Kraemer, J. (2002). Sertraline and/or interpersonal psychotherapy for patients with dysthymic disorder in primary care: 6-month comparison with longitudinal 2-year follow-up of effectiveness and costs. *Journal of Affective Disorders*, *68*(2-3), 317–330. https://doi.org/10.1016/s0165-0327(01)00343-3
Elkin et al., 1989	Elkin, I., Shea, M. T., Watkins, J. T., Imber, S. D., Sotsky, S. M., Collins, J. F., … Docherty, J. P. (1989). National Institute of Mental Health Treatment of Depression Collaborative Research Program. General effectiveness of treatments. *Archives of General Psychiatry*, *46*(11), 971–983. https://doi.org/10.1001/archpsyc.1989.01810110013002
Finkenzeller et al., 2009	Finkenzeller, W., Zobel, I., Rietz, S., Schramm, E., & Berger, M. (2009). Interpersonelle psychotherapie und pharmakotherapie bei post-stroke-depression. Machbarkeit und effektivität [Interpersonal psychotherapy and pharmacotherapy for post-stroke depression. Feasibility and effectiveness]. *Der Nervenarzt*, *80*(7), 805–812. https://doi.org/10.1007/s00115-008-2649-1

Frank et al., 2011	Frank, E., Cassano, G. B., Rucci, P., Thompson, W. K., Kraemer, H. C., Fagiolini, A., … Forgione, R. N. (2011). Predictors and moderators of time to remission of major depression with interpersonal psychotherapy and SSRI pharmacotherapy. *Psychological Medicine*, *41*(1), 151–162. https://doi.org/10.1017/S0033291710000553
Gois et al., 2014	Gois, C., Dias, V. V., Carmo, I., Duarte, R., Ferro, A., Santos, A. L., … Barbosa, A. (2014). Treatment response in type 2 diabetes patients with major depression. *Clinical Psychology & Psychotherapy*, *21*(1), 39–48. https://doi.org/10.1002/cpp.1817
Menchetti et al., 2014	Menchetti, M., Rucci, P., Bortolotti, B., Bombi, A., Scocco, P., Kraemer, H. C., & Berardi, D. (2014). Moderators of remission with interpersonal counselling or drug treatment in primary care patients with depression: randomised controlled trial. *British Journal of Psychiatry*, *204*(2), 144–150. https://doi.org/10.1192/bjp.bp.112.122663
Quilty et al., 2008	Quilty, L. C., McBride, C., & Bagby, R. M. (2008). Evidence for the cognitive mediational model of cognitive behavioural therapy for depression. *Psychological Medicine*, *38*(11), 1531–1541. https://doi.org/10.1017/S0033291708003772
IPD not available	
Markowitz et al., 2005	Markowitz, J. C., Kocsis, J. H., Bleiberg, K. L., Christos, P. J., & Sacks, M. (2005). A comparative trial of psychotherapy and pharmacotherapy for "pure" dysthymic patients. *Journal of Affective Disorders*, *89*(1-3), 167–175. https://doi.org/10.1016/j.jad.2005.10.001
Martin et al., 2001	Martin, S. D., Martin, E., Rai, S. S., Richardson, M. A., & Royall, R. (2001). Brain blood flow changes in depressed patients treated with interpersonal psychotherapy or venlafaxine hydrochloride: preliminary findings. *Archives of General Psychiatry*, *58*(7), 641–648. https://doi.org/10.1001/archpsyc.58.7.641
O'Hara et al., 2019	O'Hara, M. W., Pearlstein, T., Stuart, S., Long, J. D., Mills, J. A., & Zlotnick, C. (2019). A placebo controlled treatment trial of sertraline and interpersonal psychotherapy for postpartum depression. *Journal of Affective Disorders*, *245*, 524–532. https://doi.org/10.1016/j.jad.2018.10.361

Schulberg et al., 1996	Schulberg, H. C., Block, M. R., Madonia, M. J., Scott, C. P., Rodriguez, E., Imber, S. D., … Coulehan, J. L. (1996). Treating major depression in primary care practice. Eight-month clinical outcomes. *Archives of General Psychiatry*, *53*(10), 913–919. https://doi.org/10.1001/archpsyc.1996.01830100061008
Sloane et al., 1985	Sloane, B. R., Staples, F. R., & Schneider, L. S. (1985). Interpersonal therapy versus nortriptyline for depression in the elderly. *Clinical and Pharmacological Studies in Psychiatric Disorders,* 344-346.
Weissman et al., 1979	Weissman, M. M., Prusoff, B. A., Dimascio, A., Neu, C., Goklaney, M., & Klerman, G. L. (1979). The efficacy of drugs and psychotherapy in the treatment of acute depressive episodes. *The American Journal of Psychiatry*, *136*(4B), 555–558. https://doi.org/10.1176/ajp.1979.136.4b.555

Note: IPD = Individual Participant Data.