





# BMJ Open Efficacy of high-intensity versus low-intensity psychoanalytically oriented long-term treatments and determinants of outcome: individual participant data Meta-analysis of Long-term Analytic treatment Studies (MeLAS)

Lina Krakau <sup>1</sup>, Marianne Leuzinger-Bohleber,<sup>1</sup> Elmar Brähler,<sup>1,2</sup> Peter Schmidt,<sup>1</sup> Felicitas Rost,<sup>3,4</sup> Dorothea Huber,<sup>5</sup> Guenther Klug,<sup>6</sup> Henriette Löffler-Stastka <sup>7</sup>, Hemma Rössler-Schüle,<sup>8</sup> Falk Leichsenring <sup>9</sup>, Simone Salzer,<sup>10</sup> Josef Brockmann,<sup>11</sup> Thorsten Jakobsen,<sup>12</sup> Mareike Ernst <sup>13</sup>, Manfred E Beutel<sup>1</sup>

**To cite:** Krakau L, Leuzinger-Bohleber M, Brähler E, *et al*. Efficacy of high-intensity versus low-intensity psychoanalytically oriented long-term treatments and determinants of outcome: individual participant data Meta-analysis of Long-term Analytic treatment Studies (MeLAS). *BMJ Open* 2023;**13**:e069332. doi:10.1136/bmjopen-2022-069332

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-069332>).

Received 19 October 2022

Accepted 04 June 2023



© Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

## Correspondence to

Dr Lina Krakau;  
lina.krakau@unimedizin-mainz.de

## ABSTRACT

**Introduction** Long-term psychodynamic/psychoanalytic psychotherapy (LTPP) is a prevalent treatment option for complex mental disorders. Yet, little is known about the role of treatment intensity in LTPP. We present a study protocol for a systematic review and individual participant data (IPD) meta-analysis aggregating and analysing individual data from randomised and quasi-experimental trials by meta-analysis. The purpose is to (1) determine the treatment effectiveness of LTPP with low versus high intensity (up to 2 weekly sessions vs three or more), (2) compare their joint effectiveness to shorter therapies and treatments as usual, (3) identify predictors and moderators of treatment outcomes and (4) determine reciprocal relationships between different outcome domains (symptomatic and structural/personality change) over the courses of LTPP.

**Methods and analysis** We include studies from (randomised controlled trial, RCT) and quasi-experimental trials, where at least one condition was LTPP of high or low frequency. Long-term treatment is defined as ≥1 year or ≥50 sessions. To be eligible studies must include a standardised outcome measure of symptoms (global or disorder specific) with at least one proof of reliability. The primary outcome is symptom reduction (global or specific), secondary outcome criteria are reliable change, remission, functional capacities, personality, personality functioning and interpersonal pathology. Relevant studies will mainly be identified by searching relevant databases: PubMed, PsycINFO (via EBSCO), Web of Science (via Elsevier), Cochrane's Central Register of Controlled Trials (via Wiley). Risk of bias will be evaluated in line with the Cochrane assessments tools for quasi-experimental trials and RCTs, respectively.

**Ethics and dissemination** Aggregation of data from primary trials collected based on ethics votes. Dissemination into clinical practice via open access publications of findings.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Individual participant data (IPD) meta-analysis has increased power to detect differences between treatment groups and to examine prognostic and prescriptive factors associated with outcome.
- ⇒ The inclusion of quasi-experimental trials and the examination of non-randomised conditions (high vs low treatment intensity) lowers the quality of the evidence according to gold standard.
- ⇒ In IPD meta-analysis, bias may be introduced as not all relevant studies identified can be included, for example, non-response of the authors, difficulties with data sharing.

**PROSPERO registration number** CRD42022304982; Pre-results.

## INTRODUCTION

Short-term psychodynamic psychotherapy (STPP) has demonstrated comparable efficacy to cognitive-behavioural therapy (CBT) and other bona fide psychotherapies.<sup>1–3</sup> However, common mental disorders often take a chronic course<sup>4,5</sup> and short-term treatments might be insufficient for patients with complex mental disorders.<sup>5,6</sup> Complex mental disorders have been defined as mental disorders characterised by rigidity or inflexibility, for example, personality disorders (PDs), chronic mental disorders (eg, chronic depression).<sup>7</sup> They show high comorbidity with other mental and physical health conditions<sup>8</sup> and are associated with considerable functional impairments.<sup>9</sup> Regardless of a categorical diagnosis of PD, lower levels

of personality organisation are typically found in more severe mental disorders.<sup>10</sup> Previous data on dose–effect relations have indicated that patients with such disorders need longer treatments.<sup>11 12</sup> Nevertheless, most evidence for psychotherapy is based on short-term treatments and short-term outcomes, the latter usually assessed at treatment termination.<sup>13</sup> Only a few trials report 1-year follow-up, and longer-term follow-ups of 2 and more years are scarce.<sup>2 14</sup> To our best knowledge, long-term remission rates of bona fide short-term psychotherapies are often unsatisfactory<sup>14</sup> and up to half of the study, patients have been found to seek auxiliary psychotherapy during follow-up.<sup>15</sup> Naturalistic trials further indicate that many patients require and receive long-term treatments up to several years.<sup>16</sup>

A basic claim of long-term psychoanalytic psychotherapies (LTPP), comprising psychoanalysis and long-term psychoanalytic/psychodynamic psychotherapy, has been to improve structural capacities related to the personality organisation<sup>17–19</sup> in addition to symptoms. Structural integration (ie, personality functioning) comprises different domains of psychological functioning, for example, identity, affect differentiation and tolerance, and self-other regulation which relate to core developmental tasks of attachment/relatedness and individuation/self-definition.<sup>20–22</sup> Conceptualised by the term personality functioning, the alternative model of PDs has introduced a similar<sup>23 24</sup> model to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).<sup>25 26</sup> Here, impairment in personality functioning is described along the dimensions of self (identity perception, self-regulation) and interpersonal (empathy, intimacy) functioning as shared characteristic of all PDs. In the psychoanalytic literature, improvements in these domains have been described as structural change<sup>17–19</sup> and have been related to treatments with higher frequency promoting greater capacity for self-analysis.<sup>27</sup> In line with the traditionally transdiagnostic scope of psychoanalysis, LTPP studies have focused on global or disorder-specific symptom improvement, and social and personality functioning with long-term outcomes up to 10 years.<sup>15</sup> However, the number of available trials on LTPP with long-term follow-up is comparably small, as they pose special methodological challenges of recruitment, study design, duration and funding. For ethical reasons, placebo or waiting-list control conditions are not feasible over extended periods, and it would be difficult to conceptualise plausible interventions with similar frequency and duration of intervention. Studies that included long-term follow-ups have shown that LTPP indeed led to lasting changes at the level of symptoms and other domains of functioning.<sup>15 28–32</sup> In the long run, several studies indicated LTPP to be more effective than treatment as usual (TAU)<sup>29</sup> or short-term treatments.<sup>15 33</sup>

Huber *et al*<sup>30</sup> found psychoanalytic treatment to be more effective than CBT at long-term follow-up, while others reported a comparable reduction of symptoms in psychoanalytic therapy and CBT,<sup>34 35</sup> but stronger

evidence for restructuring in psychoanalytic treatment groups.<sup>32 35</sup> Other studies have focused on the comparison of psychodynamic psychotherapy with more intensive and longer psychoanalytic treatment and found the latter to be more effective at 1-year<sup>36</sup> or 3-year follow-up.<sup>37</sup> Town *et al*<sup>38</sup> found that therapy effects were maintained and continued to improve following termination of psychodynamic therapies of different frequencies and lengths. To our knowledge, only four conventional meta-analyses have focused on the effectiveness of LTPP specifically. Focusing on randomised controlled trials (RCTs) and quasi-experimental observational studies, Leichsenring and Rabung<sup>6 7 39</sup> found LTPP to be more effective than short term psychotherapies with medium to large effect sizes in terms of symptom reduction and social and personality functioning. Using different inclusion criteria, the meta-analysis of Smit *et al*<sup>40</sup> questioned the effectiveness of LTPP, as they found it more effective only in comparison to control conditions that were no specialised forms of therapy. Exploratory analyses indicated that a greater difference in treatment intensity between LTPP and the control group was related to the effect size. The seemingly conflicting findings between Leichsenring and Rabung's<sup>6 7</sup> and Smit *et al*'s<sup>40</sup> meta-analyses have been discussed elsewhere.<sup>39 41</sup> More recently, Woll and Schönbrodt aimed to replicate and update Leichsenring *et al*'s<sup>39</sup> meta-analysis, but only found small additional gains for LTPP in comparison to other forms of psychotherapy, regarding symptoms and social functioning. No significant differences were found with respect to personality functioning. Restricting their meta-analysis to psychoanalysis proper, defined as the patient lying on the couch with at least two sessions, one research group found large within-group effect sizes regarding symptomatic improvement and personality characteristics. Yet, most of the trials they examined were naturalistic and did not have control groups.<sup>42</sup>

Beyond efficacy studies, psychotherapy research, in general, has identified numerous patient, psychotherapist and relational prognostic factors (predictors) for psychotherapy outcome, for example, racial or social minority status, high symptom load or high self-criticism.<sup>43</sup> However, less is known about prescriptive variables (moderators) associated with different outcomes depending on the type of treatment, for example, maladaptive defenses or rigid relationship patterns for psychodynamic treatments.<sup>1 44 45</sup> Identifying prescriptive variables that reliably predict differential treatment outcomes has become the main target of personalised treatment approaches.<sup>43 46</sup> To our knowledge, no meta-analysis has examined prognostic or prescriptive variables in LTPP.

Given the evidence outlined above, we presume that LTPP facilitates changes in intrapsychic, structural processes underlying mental disorders in addition to improving symptoms. Yet, it remains unclear whether this is due to the effects of psychoanalytic technique or its treatment frequency and duration.<sup>12 40</sup> Changes in structural functioning have been posited as a mechanism of change

in psychotherapy and LTPP specifically, with a stronger focus on insight and self-understanding.<sup>47</sup> Several studies found greater changes, eg, in personality or reflective functioning associated with greater<sup>32 48</sup> and sustained<sup>49 50</sup> symptom reduction. However, the studies mostly focused on between-person (BP) effects and did not apply lagged analysis over multiple time points to investigate if changes in structural capacities were associated with a decrease in symptoms at subsequent assessment.

Due to the limitations of the individual trials, empirical evidence on the role of treatment intensity for the efficacy of LTPP and the identification of prescriptive variables has been limited. Small samples and unequal group sizes as well as decreasing case numbers throughout therapy and follow-up have led to methodological problems in data analysis of individual trials, including a lack of statistical power. Hence, small differences between different treatment approaches cannot be identified and testing for subgroups with differential outcome is prohibited.<sup>51</sup> Additional problems include the utilisation of different designs (RCT vs quasi-experimental), varying definitions of LTPP (eg, ranging from 42 to over 300 sessions), varying frequency of measurements, definition and timing of follow-ups, and the comparability of measures of relevant variables (eg, sociodemographic and clinical characteristics) and different outcome measures.

The current study aims to conduct a systematic review and individual participant data (IPD) meta-analysis concerning the efficacy of LTPP treatments of different intensities and associated prognostic and prescriptive factors in common mental disorders. IPD meta-analysis is a technique to examine treatment effects by combining participant-level data of multiple trials collected from the original data and is currently considered the gold standard in evidence synthesis.<sup>52 53</sup> A one-stage approach is favoured, especially when the original trials have small samples.<sup>54</sup> It has increased statistical power to detect differences between treatment conditions and to examine prognostic and prescriptive variables associated with treatment efficacy.<sup>46</sup> Compared with conventional meta-analyses that rely on the aggregated level data extracted from published reports, with IDP the same statistical methods can be applied across all studies involved. This allows for the application of newer statistical modelling techniques and similar handling of missing data, thus increasing comparability.<sup>55</sup> The use of the original data may further circumvent bias related to the publication of positive results or the removal of patients before analysis in published trials.<sup>56</sup>

In summary, the current project aims to:

1. Compare treatment effectiveness of LTPP of low versus high intensity (based on average weekly sessions).
  - a. At treatment termination.
  - b. At long-term follow-up (stability of outcome).
  - c. Compare their joint efficacy to shorter therapies and TAU as included as control groups in the trials.

2. Identify individual characteristics that reliably predict or moderate differential treatment outcomes of low-intensity and high-intensity LTPP.
3. Examine the reciprocal relationship of symptoms and personality functioning over time.

## METHODS AND ANALYSIS

The study is an IPD meta-analysis, registered on the International prospective register of systematic reviews (PROSPERO; CRD42022304982) before conducting the main search and soliciting any data. Amendments will be documented here. Eligible studies will be identified through systematic literature research. Study results will be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for IPD.<sup>57</sup> Project planning and preliminary literature research have started in June 2022, and we expect the completion of the project within 3 years.

### Selection of studies

The aim of the study is the examination of the efficacy of LTPP with different intensity in adult outpatient populations with common mental disorders. Low-intensity treatments are defined as treatments with on average 1 weekly session, and high-intensity treatments are treatments with two or more weekly sessions. We will include randomised and quasi-experimental clinical trials on LTPP. We will include trials that directly compared high-intensity versus low-intensity LTPP, and trials that compared high-intensity and/or low-intensity LTPP to shorter treatments or TAU). In our main analysis, we will compare high-intensity versus low-intensity LTPP as defined above. A sensitivity analysis will be conducted to contrast 1 weekly session with three or more (instead of up to two). In a second analysis, we will compare high-intensity and-low intensity LTPP (combined) to shorter treatments and TAU (combined). We will conduct a sensitivity analysis excluding TAU. Due to randomisation difficulties for LTPP, especially psychoanalysis, we include quasi-experimental cohort studies along with prospective RCTs. Eligible studies must contain LTPP. LTPP is defined according to Leichsenring and Rabung's<sup>6</sup> criteria for LTPP by (1) studies of psychodynamic therapy; (2) working with transference and resistance and (3) duration of at least 50 sessions or at least 1 year. Moreover, we will include psychoanalysis proper, meaning up to five sessions per week in a supine position. Control conditions are psychodynamic treatments of shorter duration (fewer than 50 sessions), other treatments (eg, CBT) from various psychotherapeutic backgrounds, or TAU. Treatment must be individual therapy for common mental disorders (eg, depression, anxiety or PDs) in adults. The exact inclusion and exclusion criteria can be found in [table 1](#). We will apply a three-step selection process. During the first step, two independent raters (one postdoc and one doctoral candidate) will apply the outlined selection criteria to the titles and abstracts of the references retrieved from the systematic literature

**Table 1** Selection criteria

Inclusion	Prospective RCT or quasi-experimental cohort study
	Baseline assessment and post/follow-up assessment that exceeds at least 1 year
	Outpatient individual treatment
	Participants ( $\geq 18$ –65 Jahre)
	One treatment is LTPP (psychodynamic or -analytic long-term psychotherapy, psychoanalysis)
	Long-term is defined as $\geq 1$ year or $\geq 50$ sessions
	Standardised outcome measure of symptoms (global or specific) with at least one empirical proof of reliability
	Data on frequency of sessions are available
	Treatment is carried out by licensed psychotherapists
Exclusion	Focus on psychotic disorders
	Focus on organic disorders
	Single-case studies
	Serial case studies
	Qualitative studies
	Information on session frequency and therapy duration is not available
Outcomes	Primary:
	Standardised symptom assessment (global symptom level or disorder-specific)
	Secondary:
	Reliable change, no change and deterioration, calculated based on the primary outcome measure; serious adverse events, standardised assessments of personality/personality functioning, functional capacities or relationship pathology
LTPP, long-term psychoanalytic psychotherapy.	

research. In case of disagreement, consensus will be reached through discussion. If a study is considered as potentially fulfilling inclusion criteria, we will request full texts. Next, full texts will be rated according to the selection criteria by two independent raters. Disagreements will be resolved through discussion or the involvement of a third rater. Finally, selected studies will be rated by experts (full professors with analytical training) to confirm that the treatment investigated is LTPP.

### Search strategy

To identify as many relevant studies as possible, different search strategies will be used. First, we will conduct a systematic literature review using the following databases: PubMed, PsycINFO (via EBSCO), Web of Science (via Elsevier) and the Cochrane's Central Register of Controlled Trials (via Wiley). We define five categories of search strings

**Table 2** Systematic literature search

Data banks	PubMed PsycINFO Web of Science Cochrane Central Register of Controlled Trials
<b>Category</b>	<b>Search terms</b>
Treatment	Emotion focused OR mentalization OR mentalization OR self-psychology OR transference-focused OR insight-oriented OR interpretativ* OR psychodynamic* OR psychoanalys* OR psychoanalytic* OR "psychotherapy, psychodynamic" OR "psychoanalytic therapy"
	AND
Long-term	"follow-up studies" OR follow OR long-term OR longer-term OR open-ended
	AND
Study	study OR studies OR trial*
	AND
Effectiveness	treatment outcome OR outcome OR effect* OR efficacy OR result* OR change*
	AND
Common mental disorder	mental disorder*OR psychiatric illness*OR psychiatric disease*OR mental illness*OR psychiatric disorder* OR behavior disorder*OR behaviour disorder* OR psychiatric diagnos* OR anxiet*OR mood disorder* OR affective disorder* OR personality disorder*OR borderline personalit* OR depress*OR post-traumatic stress disorder* OR post-traumatic neuros* OR PTSD

(1) treatment, (2) long-term (3) study, (4) effectiveness and (5) common mental disorders, with synonyms that will be searched as index and free text terms. The Boolean combination of search strings is depicted in [table 2](#). We will not apply language or date restrictions for the searches, however, the included studies must be published in English, French or German for our team to conduct risk of bias (RoB) assessments. Second, we will search the controlled-trial register to identify ongoing and unpublished studies <https://www.isrctn.com/search?q=&filters=conditionCategory%3AMental+and+Behavioural+Disorders> and the Open Door Review of Clinical, Conceptual, Process and Outcome Studies in Psychoanalysis, third edition [https://www.ipa.world/en/Psychoanalytic\\_Theory/Research/open\\_door.aspx](https://www.ipa.world/en/Psychoanalytic_Theory/Research/open_door.aspx); accessed on 10 July 2023. Third, we will handsearch published meta-analyses<sup>40–42</sup> and the citations of the included trials to identify other possibly eligible trials. We will contact experts in the field through a list-serv of related societies (eg, Society for Psychotherapy Research, Psychoanalytic Research Society, International Psychoanalytic Society) to ask for yet unpublished trials or studies we have missed.

### Data collection and management

Named corresponding authors will be contacted via email. They will be provided with all necessary information



(including a link to the project's PROSPERO registration and the protocol) and asked whether they would be willing to participate/collaborate. Contact information will be retrieved from the relevant publications or if unavailable or outdated through online searches. Authors will be offered coauthorship on the published paper in return for sharing the studies' deidentified IPD. Following Driessen *et al.*<sup>58</sup> authors who do not respond will be contacted three times by mail. If we do not get a response, we will try to establish contact by phone, next send up to three letters by post. This procedure will be repeated first with the corresponding author, then the PI, and then sequentially with all other authors of the study. If we still do not get a response, we will contact colleagues or other persons who may help to establish contact. If we do not succeed in contacting the authors with the above-outlined efforts, or if authors respond that the IPD cannot be shared or has been deleted, study data are considered unavailable. If authors choose to share their data, data-sharing agreements between all parties will need to be drawn up. The procedures are country-dependent and will need to be taken into consideration. Once data-sharing agreements in line with General Data Protection Rules (GDPR) ethical standards are arranged, authors will be asked to transfer deidentified individual-level data sets encrypted using a save cloud service, procedures will be provided by the University Medical Center Mainz. Authors will be asked to send item-based data sets if available and to provide a description of how the data was coded (codebook). Datasets will contain deidentified participant-level data comprising sociodemographic data, prognostic and prescriptive variables assessed at baseline, outcome variables assessed at baseline, during and after treatment, therapy duration and session frequency, additional treatment, and case status (intention to treat/according to protocol, ITT/ATP). Study-level data, for example, requirements of therapists' professional experience (eg, years of licensed practice), supervision, treatment integrity and adherence, and inter-rater reliability for diagnostic assessment of primary outcome measures will be retrieved from the publication or requested, if unavailable. Example code for analyses, detailed RoB ratings, list of studies excluded at full-text stage including reasons for exclusion will be shared via the Open Science Framework.

## Measures

The primary outcome is treatment effectiveness of low-intensity versus high-intensity LTPP as assessed by a global measure of symptomology, most commonly the Symptom Checklist-90,<sup>59</sup> or disorder-specific measures at treatment termination and follow-up. Secondary outcomes are: (1) Remission, reliable change, no change and deterioration,<sup>60</sup> calculated based on the primary outcome measure. (2) Changes in functional capacities, personality, personality functioning or relationship pathology, most commonly the Inventory of Interpersonal Problems,<sup>61</sup> at treatment termination and long-term follow-up. (3) Serious adverse

events defined according to the definition of the International Conference on Harmonisation of pharmaceuticals for the human use-Good Clinical Practice as a medical occurrence resulting in death, being life-threatening, requiring any form of hospitalisation or resulting in persistent or significant disability of the patient.<sup>62</sup> As original trials may not have applied this definition, we will also evaluate their definition of adverse events. If possible, additional subgroup analyses will be performed for specific mental disorders (major depression, anxiety, PDs). To identify potential prognostic and prescriptive factors for treatment response, we include patient-specific characteristics at baseline: sociodemographic data (eg, gender, education, employment, income, migration background, clinical characteristics, (diagnosis given by the trial, previous treatments including psychopharmacological treatments) and continuous measures of symptom severity, personality and personality functioning, relationships, functional capacities and life events (eg, social occupational functioning, comorbid disorders, childhood adversity). Patient characteristics will be included when they are consistently reported among trials and can be standardised in a coherent way (eg, by collapsing categories). We will include a variable referring to the original trial design (predetermined length vs open-ended treatment) and a variable indicating whether cases were treated (ATP vs drop-out).

## Data integrity and preparation

Received data sets will be thoroughly examined to identify out-of-range items or invalid scoring and will be compared with the original publication (sample size, missing data, gender, age, mean pretreatment scores in the primary outcome as defined by the study, and mean post-treatment scores in the primary outcome as defined by the study). In case of deviations, we will contact the authors to resolve the issue (eg, cases dropped from the analysis, imputation method used for computing mean scores of the questionnaires received). Next, all variables relevant for the IPD meta-analysis will be extracted from each study including prognostic and prescriptive variables, treatment information received, the diagnoses given within the original trial, and primary and secondary outcomes at baseline, intermediate and follow-up assessment. The resulting variables will be copied into a new data set and study-level criteria (study type, treatment integrity, RoB assessment) and a participant ID containing numeric ID and an abbreviation of the study will be added. A copy of this file containing a study's raw data relevant to IPD will be standardised to the variable names and coding used in the IPD database. A variable will be created indicating the participants' group membership (high intensity LTPP, low intensity LTPP, shorter treatment/TAU). For the planned sensitivity analyses, we will create different grouping variables (1 weekly session vs 3 or more and separating shorter treatment from TAU). All studies will be integrated into the database structured by the created ID. RoB will be evaluated in line with the

Cochrane assessments tools for quasi-experimental trials<sup>63</sup> and RCTs<sup>64</sup> respectively. The results of the RoB ratings will be presented in tables listing each original study. They will be used for an overall appraisal for the quality of evidence of the IPD-MA, which is carried out following Tierney *et al.*<sup>65</sup> As the type of measures applied by individual studies will likely vary, individual scores will be standardised (using z-transformation or a common metric approach<sup>66</sup>) for continuous measures. Centring will be applied within individual trials. Data screening, data extraction and risk of bias assessment will be performed independently by two researchers (one postdoctoral researcher and one doctoral candidate).

### Missing data

We intend to conduct an ITT analysis. Missing data will be assessed in each study received, including the amount of missing data per participant and variable and possible reasons for missingness. We will compare subsamples of participants without missing data to those with missing data per study and summarise distributions per variable. Missing data will be handled using multilevel multiple imputation, an approach that handles sporadically (missing data on variables for some but not all participants) and systematically (variables that have not been assessed by a specific study) missing values and can adequately preserve between-study heterogeneity. As we expect some of the included studies to have a small sample size and the overall number of studies to be rather low, we will use a full conditional specification approach (FCS; also multiple imputation by chained equations).<sup>67–70</sup> We will follow White's *et al.*<sup>71</sup> rule of thumb and impute one data set per per cent of participants with one or more missing variables. We will include all variables and interactions relevant to our analysis model and variables potentially predictive for missing data. Specifically, we will use the R-packages mice and its extension micemd.<sup>68</sup>

### Data analysis

To address research questions 1 and 2, we will carry out a one-stage IPD meta-analysis. To analyse effectiveness, we will statistically predict symptom severity (global if available, otherwise specific) and remission (binary) controlling for baseline severity. To predict symptom severity over time, we will use a generalised linear mixed model framework, as participants are clustered in trials and treatment groups. Following Riley *et al.*'s<sup>72</sup> recommendations for IPD-meta-analysis, we will use restricted maximum likelihood estimation and obtain 95% CIs for treatment effects using the Kenward-Roger approach. We will specify a random treatment effect to account for heterogeneity in study populations (intercept) and treatment effects (slope). To account for clustering within trials, we will fit a random intercept for each trial. Separate models will be estimated to compare LTTP of low versus high intensity, and to compare joint LTTP against control groups as provided by the trials. The estimation procedure will be repeated using our secondary outcome

measures based on the trials providing these additional measures. Reliable response, no change and deterioration will be analysed for symptom outcome only using multilevel logistic regression.<sup>60</sup> We intend to perform subgroup analysis by repeating analysis steps in subgroups with different mental disorders (A) depressive disorders, (B) anxiety disorders and (c) PDs. The primary diagnosis given in the original trial will define group membership. Next, we will analyse prognostic factors by adding available participant-level and study-level variables as predictors to the specified models. If possible, continuous variables will be kept on a continuous scale to avoid loss of power. We will analyse prescriptive variables by adding interaction terms between the predictor and treatment groups. The third research question will be addressed by a two-stage IPD meta-analysis approach. We will first, estimate multigroup random intercept cross-lagged panel models<sup>73 74</sup> to examine the respective lagged and cross-lagged effects of personality functioning and symptoms on BP and within-person (WP) level per study. We will consider every study providing data on personality functioning and symptoms for baseline, treatment termination and follow-up. We will use WP centring<sup>75 76</sup> of scores prior to analyses to derive standardised coefficients for lagged and cross-lagged effects. Next, findings will be meta-analysed using random effects meta-analytical structural equation modelling, a technique to meta-analyse path or structural equation models. Analyses will be carried out in R-lavaan<sup>77</sup> and R-metaSEM.<sup>78</sup> Sensitivity analyses for all research questions will be carried out based on complete cases. If enough studies have used the same instrument, we will rerun analysis for research question 1 and 2 based on these studies without standardising the variables.

### Patient and public involvement

No patient and public involvement.

### ETHICS AND DISSEMINATION

Given that all studies obtained ethical approval from the relevant ethics boards, further ethical approval is not necessary but requirements for data-sharing need to be met. A data-sharing agreement based according to principles of the GDPR of the European Union will be signed between the University Medical Center Mainz and all parties involved (shared responsibility). All parties sharing their data are responsible to ensure that data sharing is in line with their institutional, local and international requirements, which they confirm by signing the agreement on shared responsibility. All data transferred will be deidentified. The results of the study will be presented at international conferences for clinician scientists and practitioners. Scientific reports of the study results will be submitted for publication in international, preferably open-access journals.

## DISCUSSION

This study protocol describes a systematic review with meta-analysis of IPD to determine the effectiveness of low vs high intensity LTPP at the end of treatment and long-term follow-up. Additionally, we aim to identify associated prognostic and prescriptive variables and the interaction of different outcome domains over time.

### Clinical and scientific relevance

The evidence base of effectiveness for psychotherapy in general but also for psychodynamic treatments has been predominantly based on short-term therapies and short-term outcomes.<sup>13</sup> Previous research found a potential benefit of LTPP over short-term treatments for complex mental disorders.<sup>6 7 39 41</sup> Yet, little is known about the role of treatment intensity in LTPP, including psychoanalysis and psychoanalytic/psychodynamic long-term psychotherapy. Given unsatisfactory response rates, for example, about 41% for (short-term) psychotherapy<sup>79</sup> but high additional costs of extensive treatment, the effectiveness of LTPP at long-term follow-up represents a health outcome of public interest. Individual studies lack sufficient power to reliably examine prognostic and prescriptive variables, however, identifying factors associated with benefits from (specific) treatments is an important step towards optimised treatment planning.<sup>46</sup> The project serves to close this gap, by consolidating the evidence base for LTPP for the major common mental disorders (eg, depression, anxiety and PDs). As LTPP treatments strive to achieve structural and personality changes, outcomes will go beyond symptom change and cover relevant outcome domains, such as personality, interpersonal and social-occupational functioning. This is consistent with the recommendations for updating the criteria of evidence-based therapies.<sup>80</sup> The stability of therapeutic gains during long-term follow-up is of particular interest, as psychoanalytic theory posits that change does not necessarily cease at the end of treatment. Rather, insights gained during therapy are understood to promote further development during follow-up, when autonomy and greater capacity for self-analysis evolve.<sup>81</sup> Hence, changing underlying structural capacities should enable patients to gain further benefits in the follow-up phase.<sup>38 49 50</sup>

### Limitations

Limitations of data aggregation and analyses include different designs regarding the assessment of process and follow-up. Moreover, definitions of LTPP differ between studies regarding the frequency of sessions and setting. We cannot conduct a conventional meta-analysis to compare our results with trials not providing original data as some original studies will have analysed low-and-high intensity LTPP together. If enough trials provide separate analyses, we will conduct a conventional meta-analysis based on these trials. The study includes RCTs and quasi-experimental cohort studies, lowering the quality of evidence according to gold standards. Yet, the inclusion of quasi-experimental trials in diverse settings, where

patients self-select their treatment, enhances the external validity of the results as treatment length and techniques in practice are individually adapted. An important limitation of IPD meta-analysis is that some trials may not be integrated due to non-response, problems with data sharing, or the deletion of the original data. Thus, even if IPD meta-analyses are considered the gold standard in evidence synthesis, bias cannot be precluded, and information obtained by IPD should be used in addition to conventional meta-analyses and reviews. Identifying, collecting and aggregating relevant data will require a certain time, and newly published trials cannot easily be incorporated. Even though IPD meta-analysis will likely have enough power to examine prognostic and prescriptive treatment variables, the choice of variables examined depends on the variables included in the original trials. Moreover, results may be restricted to individuals who choose to participate in treatment trials. Akin to previous work including high frequent LTPP, we excluded trials on schizophrenia.<sup>42</sup> We have specified secondary outcomes, however, our analyses will not be controlled for type I and type II errors.

### Author affiliations

<sup>1</sup>Psychosomatic Medicine and Psychotherapy, University Medical Center of The Johannes Gutenberg University, Mainz, Germany

<sup>2</sup>Department of Psychiatry and Psychotherapy Leipzig, Leipzig University Medical Center, Leipzig, Germany

<sup>3</sup>Tavistock and Portman NHS Foundation Trust, London, UK

<sup>4</sup>School of Psychology and Psychotherapy, Faculty of Arts and Social Sciences, The Open University, Milton Keynes, UK

<sup>5</sup>Department of Clinical Psychology and Psychosomatics, International Psychoanalytic University, Berlin, Germany

<sup>6</sup>Technical University of Munich, Munchen, Germany

<sup>7</sup>Department of Psychoanalysis and Psychotherapy, Medical University Vienna, Vienna, Austria

<sup>8</sup>Vienna Psychoanalytic Society, Vienna, Austria

<sup>9</sup>Department of Psychosomatics and Psychotherapy, University of Giessen, Giessen, Germany

<sup>10</sup>Clinical Psychology and Psychoanalysis, International Psychoanalytic University, Berlin, Germany

<sup>11</sup>Private Outpatient Clinic, Frankfurt, Germany

<sup>12</sup>Private Outpatient Clinic, Basel, Switzerland

<sup>13</sup>Department of Clinical Psychology, University of Klagenfurt, Klagenfurt am Wörthersee, Austria

**Twitter** Mareike Ernst @ernst\_mareike

**Acknowledgements** We would like to thank Lorena Cascant Ortolano for helping with the development and critical review of the search strings and Anouk Olivia Bonay for support in coordinating and preliminary literature research. Moreover, we are grateful to all patients, therapists and former staff involved in carrying out the original trials.

**Contributors** MEB, ML-B and EB conceived the original idea. LK wrote the first draft of the manuscript reviewed and edited by MEB, ML-B and EB. LK and PS developed the analysis plan. HL-S, JB, DH, GK, TJ, HR-S, FR, SS, FL and ME revised the manuscript for important intellectual content. All authors have reviewed the final version of the manuscript, agree with its submission and are responsible for all aspects of the work. This work is part of the PhD of LK.

**Funding** This work was supported by the DGPT (German Society for Psychoanalysis, Psychotherapy, Psychosomatics and Psychodynamic Psychology). No grant number is associated with this project.

**Disclaimer** The funder had no role in the development of this study protocol, nor was there editorial direction or censorship from the sponsor in this manuscript.



**Competing interests** MEB, FL, ML-B and HL-S are state-licensed psychoanalysts, involved in the training of psychodynamic therapists/psychoanalysts. JB, DH, GK, TJ, HR-S, FR and SS are state-licensed psychoanalysts/psychodynamic psychotherapists. ME and LK are training as a psychodynamic/psychoanalytic psychotherapists. They have conceived and/or performed trials that will serve as a data source for the proposed study (FH Study, JB; Göttingen Study, FL; HB Study, TJ; Munich Psychotherapy Study, DH, GK; LAC Study, ML-B, MEB, ME; Tavistock Adult Depression Study, FR; Viennese Psychoanalytic Process and Outcome Study, HL-S and HR-S).

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

#### ORCID iDs

Lina Krakau <http://orcid.org/0000-0001-7727-9773>

Henriette Löffler-Stastka <http://orcid.org/0000-0001-8785-0435>

Falk Leichsenring <http://orcid.org/0000-0002-3808-0072>

Mareike Ernst <http://orcid.org/0000-0003-4952-9717>

## REFERENCES

- Barber JP, Muran JC, McCarthy KS. Research on dynamic therapies. In: Barkham M, Lutz W, Castonguay LG, eds. *Handbook of Psychotherapy and Behavior Change*. Hoboken, NJ: Wiley, 2021: 387–419.
- Cuijpers P, Quero S, Noma H, et al. Psychotherapies for depression: a network Meta-Analysis covering efficacy, acceptability and Long-Term outcomes of all main treatment types. *World Psychiatry* 2021;20:283–93.
- Steinert C, Munder T, Rabung S, et al. Psychodynamic therapy: as efficacious as other empirically supported treatments? A meta-analysis testing equivalence of outcomes. *Am J Psychiatry* 2017;174:943–53.
- Bruce SE, Yonkers KA, Otto MW, et al. Influence of psychiatric Comorbidity on recovery and recurrence in generalized anxiety disorder, social Phobia, and panic disorder: A 12-year prospective study. *Am J Psychiatry* 2005;162:1179–87.
- Maj M, Stein DJ, Parker G, et al. The clinical characterization of the adult patient with depression aimed at personalization of management. *World Psychiatry* 2020;19:269–93. Available <https://onlinelibrary.wiley.com/doi/10.1111/wps.12545>
- Leichsenring F, Rabung S. Long-term Psychodynamic psychotherapy in complex mental disorders: update of a meta-analysis. *Br J Psychiatry* 2011;199:15–22.
- Leichsenring F, Rabung S. Effectiveness of long-term Psychodynamic psychotherapy: A meta-analysis. *JAMA* 2008;300:1551–65.
- Saxena S, Maj M. Physical health of people with severe mental disorders: leave no one behind. *World Psychiatry* 2017;16:1–2.
- Jacobi F, Grafiadeli R, Volkmann H, et al. Krankheitslast Der Borderline-Persönlichkeitsstörung: Krankheitskosten, somatische Komorbidität und Mortalität. *Nervenarzt* 2021;92:660–9.
- Luyten P, Fonagy P. Integrating and differentiating personality and psychopathology: A Psychodynamic perspective. *J Pers* 2022;90:75–88.
- Kopta SM, Howard KI, Lowry JL, et al. Patterns of symptomatic recovery in psychotherapy. *J Consult Clin Psychol* 1994;62:1009–16.
- Zimmermann J, Löffler-Stastka H, Huber D, et al. Is it all about the higher dose? Why psychoanalytic therapy is an effective treatment for major depression: Is it all about the higher dose? *Clin Psychol Psychother* 2015;22:469–87.
- Leichsenring F, Steinert C, Rabung S, et al. The efficacy of Psychotherapies and Pharmacotherapies for mental disorders in adults: an umbrella review and meta-analytic evaluation of recent meta-analyses. *World Psychiatry* 2022;21:133–45.
- Steinert C, Hofmann M, Kruse J, et al. Relapse rates after psychotherapy for depression - stable long-term effects? A meta-analysis. *J Affect Disord* 2014;168:107–18.
- Knekt P, Virtala E, Härkänen T, et al. The outcome of Short- and long-term psychotherapy 10 years after start of treatment. *Psychol Med* 2016;46:1175–88.
- Leuzinger-Bohleber M, Stuh U, Rüger B, et al. How to study the 'quality of psychoanalytic treatments' and their Long-Term effects on patients' Well-Being: A representative, Multi-Perspective Follow-Up study. *Int J Psychoanal* 2003;84(Pt 2):263–90.
- Kernberg OF. *Object relations theory and clinical psychoanalysis*. Northvale, NJ: Jason Aronson, 1984.
- Kernberg OF. Psychic structure and structural change: an ego psychology-object relations theory viewpoint. *J Am Psychoanal Assoc* 1988;36:315–37.
- Wallerstein RS. Assessment of structural change in psychoanalytic therapy and research. *J Am Psychoanal Assoc* 1988;36:241–61.
- Blatt SJ. Levels of object representation in Anaclitic and Introjective depression. *Psychoanal Study Child* 1974;29:107–57.
- Blatt SJ. A fundamental polarity in psychoanalysis: implications for personality development, psychopathology, and the therapeutic process. *Psychoanalytic Inquiry* 2007;26:494–520.
- Ehrenthal JC, Benecke C. Tailored treatment planning for individuals with personality disorders. In: *Case Formulation for Personality Disorders*. Elsevier, 2019: 291–314.
- Zimmermann J, Brakemeier E-L, Benecke C. The DSM-5 alternative model for the classification of personality disorders: references to Psychodynamic and behavioral diagnostics. *Psychotherapeut* 2015;60:269–79.
- Zimmermann J, Ehrenthal JC, Cierpka M, et al. Assessing the level of structural integration using Operationalized Psychodynamic diagnosis (OPD): implications for DSM-5. *J Pers Assess* 2012;94:522–32.
- Bach B, Kerber A, Aluja A, et al. International assessment of DSM-5 and ICD-11 personality disorder traits: toward a common Nosology in DSM-5.1. *Psychopathology* 2020;53:179–88.
- Bender DS, Morey LC, Skodol AE. Toward a model for assessing level of personality functioning in DSM-5, part I: a review of theory and methods. *J Pers Assess* 2011;93:332–46.
- Falkenström F, Grant J, Broberg J, et al. Self-analysis and post-termination improvement after psychoanalysis and long-term psychotherapy. *J Am Psychoanal Assoc* 2007;55:629–74.
- Brockmann J, Schlüter T, Eckert J. Long-term effects of long-term psychoanalytic and long-term behavior therapy. A comparative study from the general practices of psychotherapists. *Psychotherapeut* 2006;51:15–25.
- Fonagy P, Rost F, Carlyle J-A, et al. Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock adult depression study (TADS). *World Psychiatry* 2015;14:312–21.
- Huber D, Zimmermann J, Henrich G, et al. Comparison of cognitive-behaviour therapy with psychoanalytic and Psychodynamic therapy for depressed patients – a three-year follow-up study. *Z Psychosom Med Psychother* 2012;58:299–316.
- Leichsenring F, Biskup J, Kreische R, et al. The Göttingen study of psychoanalytic therapy: first results. *Int J Psychoanal* 2005;86(Pt 2):433–55.
- Leuzinger-Bohleber M, Kauffhold J, Kallenbach L, et al. How to measure sustained psychic transformations in long-term treatments of chronically depressed patients: symptomatic and structural changes in the LAC depression study of the outcome of cognitive-behavioural and psychoanalytic long-term treatments. *Int J Psychoanal* 2019;100:99–127.
- Knekt P, Lindfors O, Laaksonen MA, et al. Quasi-experimental study on the effectiveness of psychoanalysis, long-term and short-term psychotherapy on psychiatric symptoms, work ability and functional capacity during a 5-year follow-up. *J Affect Disord* 2011;132:37–47.
- Leuzinger-Bohleber M, Hautzinger M, Fiedler G, et al. Outcome of psychoanalytic and cognitive-behavioural long-term therapy with chronically depressed patients: A controlled trial with preferential and randomized allocation. *Can J Psychiatry* 2019;64:47–58.
- Beutel M, Krakau L, Kauffhold J, et al. Recovery from chronic depression and structural change: 5-year outcomes after psychoanalytic and cognitive-behavioural long-term treatments (LAC depression study). *Clinical Psychology & Psychotherapy* 2023;30:188–201.
- Jakobsen T, Rudolf G, Brockmann J, et al. Results of psychoanalytic long-term therapy in specific diagnostic groups: improvement in symptoms and interpersonal relationships. *Z Psychosom Med Psychother* 2007;53:87–110.
- Huber D, Henrich G, Clarkin J, et al. Psychoanalytic versus Psychodynamic therapy for depression: a three-year follow-up study. *Psychiatry* 2013;76:132–49.



- 38 Town JM, Diener MJ, Abbass A, *et al.* A meta-analysis of Psychodynamic psychotherapy outcomes: evaluating the effects of research-specific procedures. *Psychotherapy (Chic)* 2012;49:276–90.
- 39 Leichsenring F, Abbass A, Luyten P, *et al.* The emerging evidence for long-term Psychodynamic therapy. *Psychodyn Psychiatry* 2013;41:361–84.
- 40 Smit Y, Huibers MJH, Ioannidis JPA, *et al.* The effectiveness of long-term psychoanalytic psychotherapy—A meta-analysis of randomized controlled trials. *Clin Psychol Rev* 2012;32:81–92.
- 41 Woll CFJ, Schönbrodt FD. A series of meta-analytic tests of the efficacy of long-term psychoanalytic psychotherapy. *European Psychologist* 2020;25:51–72.
- 42 de Maat S, de Jonghe F, de Kraker R, *et al.* The current state of the empirical evidence for psychoanalysis: A meta-analytic approach. *Harv Rev Psychiatry* 2013;21:107–37.
- 43 Constantino MJ, Boswell JF, Coyne AE. Patient, therapist, and relational factors. In: Barkham M, Lutz W, Castonguay LG, eds. *Handbook of psychotherapy and behavior change*. Hoboken, NJ: Wiley, 2021: 225–62.
- 44 Löffler-Stastka H, Rössler-Schülein H, Skale E. Predictors of therapy discontinuation in psychoanalytic treatment of patients with personality disorders. *J Psychother Psychosom* 2008;54:63–76.
- 45 Löffler-Stastka H, Bluemel V, Boes C. Exploration of personality factors and their predictive impact on therapy utilization: the Externalizing mode of functioning. *Psychother Res* 2010;20:295–308.
- 46 Cuijpers P, Ciharova M, Quero S, *et al.* The contribution of "individual participant data" meta-analyses of Psychotherapies for depression to the development of personalized treatments: A systematic review. *J Pers Med* 2022;12:93.
- 47 Crits-Christoph P, Connolly Gibbons MB. Psychotherapy process-outcome research: advances in understanding causal connections. In: Barkham M, Lutz W, Castonguay LG, eds. *Handbook of psychotherapy and behavior change*. Hoboken, NJ: Wiley, 2021: 263–97.
- 48 De Meulemeester C, Vansteelandt K, Luyten P, *et al.* Mentalizing as a mechanism of change in the treatment of patients with borderline personality disorder: A parallel process growth modeling approach. *Personal Disord* 2018;9:22–9.
- 49 Grande T, Dilg R, Jakobsen T, *et al.* Structural change as a Predictor of long-term follow-up outcome. *Psychother Res* 2009;19:344–57.
- 50 Huber D, Zimmermann J, Klug G. Change in personality functioning during psychotherapy for depression predicts long-term outcome. *Psychoanalytic Psychology* 2017;34:434–45.
- 51 Brookes ST, Whitely E, Egger M, *et al.* Subgroup analyses in randomized trials: risks of subgroup-specific analyses. *Journal of Clinical Epidemiology* 2004;57:229–36.
- 52 Thomas CL, Cassady JC, Heller ML. The influence of emotional intelligence, cognitive test anxiety, and coping strategies on undergraduate academic performance. *Learning and Individual Differences* 2017;55:40–8.
- 53 Tierney JF, Stewart LA, Clarke M. Individual participant data Cochrane Handbook for systematic reviews of interventions. Wiley, 2019: 643–58.
- 54 Burke RM, Killerby ME, Newton S, *et al.* Symptom profiles of a convenience sample of patients with COVID-19 — United States, January–April 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:904–8.
- 55 Riley RD, Lambert PC, Abo-Zaid G. Meta-analysis of individual participant data: rationale, conduct, and reporting. *BMJ* 2010;340.
- 56 Stewart LA, Parmar MKB. Meta-analysis of the literature or of individual patient data: is there a difference? *Lancet* 1993;341:418–22.
- 57 Stewart LA, Clarke M, Rovers M, *et al.* Preferred reporting items for systematic review and meta-analyses of individual participant data: the PRISMA-IPD statement. *JAMA* 2015;313:1657–65.
- 58 Driessen E, Abbass AA, Barber JP, *et al.* Which patients benefit specifically from short-term Psychodynamic psychotherapy (STPP) for depression? study protocol of a systematic review and meta-analysis of individual participant data. *BMJ Open* 2018;8.
- 59 Weiner IB, Craighead WE. The Corsini encyclopedia of psychology. In: Weiner IB, Craighead WE, eds. *Symptom Checklist-90-Revised*. Hoboken, NJ, USA: John Wiley & Sons, Inc, 2010.
- 60 Jacobson NS, Truax P. Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *J Consult Clin Psychol* 1991;59:12–9.
- 61 Horowitz LM, Alden LE, Wiggins JS. Inventory of interpersonal problems manual. In: *Menlo Park*. Ca. Mind Garden Inc, 2003.
- 62 International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised guideline: integrated Addendum to ICH E6(R1): guideline for good clinical practice (ICH- GCP). 2016.
- 63 Sterne JA, Hernán MA, Reeves BC, *et al.* ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;355:i4919.
- 64 Sterne JAC, Savović J, Page MJ, *et al.* Rob 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366.
- 65 Tierney JF, Vale C, Riley R, *et al.* Individual participant data (IPD) meta-analyses of randomised controlled trials: guidance on their use. *PLOS Med* 2015;12.
- 66 Wahl I, Löwe B, Björner JB, *et al.* Standardization of depression measurement: a common metric was developed for 11 self-report depression measures. *J Clin Epidemiol* 2014;67:73–86.
- 67 Audigier V, White IR, Jolani S, *et al.* Multiple imputation for Multilevel data with continuous and binary variables. *Statist Sci* 2018;33.
- 68 BuurenS van, Groothuis-OudshoornK mice. Multivariate imputation by chained equations in R. *J Stat Softw* 2011;45.
- 69 Jolani S, Debray TPA, Koffijberg H, *et al.* Imputation of systematically missing predictors in an individual participant data meta-analysis: a generalized approach using MICE. *Stat Med* 2015;34:1841–63.
- 70 Kunkel D, Kaizar EE. A comparison of existing methods for multiple imputation in individual participant data meta-analysis. *Stat Med* 2017;36:3507–32.
- 71 White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 2011;30:377–99.
- 72 Riley RD, Tierney JF, Stewart LA, *et al.* Individual participant data Meta-Analysis. Hoboken, NJ: Wiley, 2021.
- 73 Hamaker EL, Kuiper RM, Grasman RPPP. A critique of the cross-lagged panel model. *Psychol Methods* 2015;20:102–16.
- 74 Mulder JD, Hamaker EL. Three extensions of the random intercept cross-lagged panel model. *Structural Equation Modeling: A Multidisciplinary Journal* 2021;28:638–48.
- 75 Schuurman NK, Ferrer E, de Boer-Sonnenschein M, *et al.* How to compare cross-lagged associations in a Multilevel Autoregressive model. *Psychol Methods* 2016;21:206–21.
- 76 Wang L, Zhang Q, Maxwell SE, *et al.* On standardizing within-person effects: potential problems of global standardization. *Multivariate Behav Res* 2019;54:382–403.
- 77 Rosseel Y. Lavaan: R package for structural equation modeling. *J Stat Softw* 2012;48.
- 78 Cheung M-L. metaSEM: an R package for meta-analysis using structural equation modeling. *Front Psychol* 2014;5:1521.
- 79 Cuijpers P, Karyotaki E, Ciharova M, *et al.* The effects of Psychotherapies for depression on response, remission, reliable change, and deterioration: A Meta-Analysis. *Acta Psychiatr Scand* 2021;144:288–99.
- 80 Tolin DF, McKay D, Forman EM. Empirically supported treatment: recommendations for a new model. *Clinical Psychology: Science and Practice* 2015;22:317–38.
- 81 Thomä H, Kächele H, Bilger A. *Psychoanalytic therapy: 1 principles*. Germany: Psychosozial-Verlag, 2020.