


# BMJ Open Integrative-interpersonal dynamic therapy for poststroke depression (INID): study protocol of a randomised controlled pilot trial

Matthias Volz <sup>1</sup>, Sibumundiyanapurath,<sup>2</sup> Henning Schauenburg,<sup>3</sup> Sven Guenther Meuth,<sup>4</sup> Beate Wild,<sup>3</sup> Katja Werheid,<sup>5</sup> Jacques P Barber,<sup>6</sup> Ralf Schäfer,<sup>7</sup> Luisa Beerbaum,<sup>7</sup> Ulrike Dinger<sup>7</sup>

**Tocite:** VolzM, Mundiyanapurath S, Schauenburg H, *et al*. Integrative-interpersonal dynamic therapy for poststroke depression (INID): study protocol of a randomised controlled pilot trial. *BMJ Open* 2023;13:e077656. doi:10.1136/bmjopen-2023-077656

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2023-077656>).

Received 11 July 2023  
Accepted 25 July 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 Matthias Volz;  
Matthias.Volz@uni-kassel.de and  
Professor Ulrike Dinger;  
Ulrike.Dinger-Ehrenthal@lvr.de

## ABSTRACT

**Introduction** Depression is the most frequent psychiatric disorder following stroke, affecting about one-third of stroke survivors. Patients experience poorer recovery, lower quality of life and higher mortality compared with stroke survivors without depression. Despite these well-known malign consequences, poststroke depression (PSD) is regarded underdiagnosed and undertreated. Evidence of beneficial effects of psychotherapy to treat PSD remains scarce and inconclusive and is limited by heterogeneity in design, content and timing of the intervention. This pilot study aims to assess the feasibility of a newly developed integrative-interpersonal PSD intervention in an outpatient setting and provide a first estimation of the potential effect size as basis for the sample size estimation for a subsequent definite trial.

**Method and analysis** Patients will be recruited from two German stroke units. After discharge from inpatient rehabilitation, depressed stroke survivors will be randomised to short-term psychotherapy (12 weeks, ≤16 sessions) or enhanced treatment as usual. The manualised psychotherapy integrates key features of the Unified Psychodynamic and Cognitive-Behavioural Unified Protocol for emotional disorders and was adapted for PSD. Primary endpoints are recruitment feasibility and treatment acceptability, defined as a recruitment rate of ≥20% for eligible patients consenting to randomisation and ≥70% completion-rate of patients participating in the treatment condition. A preliminary estimation of the treatment effect based on the mean difference in Patient Health Questionnaire-9 (PHQ-9) scores between intervention and control group six months poststroke is calculated. Secondary endpoints include changes in depression (PHQ-9/Hamilton Depression Scale) and anxiety (Generalised Anxiety Disorder 7) of all participants across all follow-ups during the first year poststroke.

**Ethics and dissemination** The INID pilot study received full ethical approval (S-321/2019; 2022-2286\_1). Trial results will be published in a peer-reviewed journal in the first half of 2025. One-year follow-ups are planned to be carried out until summer 2025.

**Trial registration number** DRKS00030378.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This pilot study aims to provide a high-quality design to assess the feasibility and acceptability of a newly developed short-term intervention for stroke survivors suffering from poststroke depression.
- ⇒ Key aspects are the use of established manualised modules from psychodynamic and cognitive-behavioural psychotherapy, regular training and supervision of therapists, and an evidence-derived timing of the planned intervention.
- ⇒ Limitations are the unknown feasibility of recruitment rate and acceptability of the treatment modules, which have not yet been tested in this patient group.

## INTRODUCTION

Depression is the most frequent psychiatric condition after stroke, affecting about one in three stroke survivors.<sup>1-3</sup> Poststroke depression (PSD) occurs most frequently during the first two years after stroke, with a tendency of peaking prevalence about six months after stroke,<sup>4-7</sup> when stroke survivors usually have returned home after inpatient rehabilitation and must readapt to their lives in their familiar environment. Depressed stroke survivors experience malign long-term consequences including poorer functional outcomes, longer hospitalisation, lower quality of life as well as higher mortality and reinfarction rates compared with stroke survivors without depression.<sup>8-11</sup> Moreover, stroke recovery may also be hampered by depressed stroke survivors' tendency to retreat from social participation.<sup>12</sup> Lastly, the burden of PSD also affects spousal and significant relationships.<sup>13 14</sup>

Despite these well-known negative consequences, PSD is regarded as both underdiagnosed and undertreated.<sup>4 15 16</sup> When PSD is diagnosed, less than 50% of depressed stroke

survivors receive antidepressant drug treatment, and less than 10% receive psychotherapy treatment.<sup>17–19</sup> This striking gap is exacerbated by missing treatment guidelines and scarce evidence for standardised psychotherapy treatments for PSD.<sup>11</sup> Moreover, psychotherapists might be reluctant to treat PSD due to an uncertainty how to address stroke-specific challenges, handle medication and often complex comorbid somatic symptoms.<sup>17 20</sup> Taken together, evidence-based, effective and standardised psychotherapeutic interventions are crucial to address the need of adequate treatment for the growing number of stroke survivors experiencing PSD. Moreover, treatment strategies for PSD should address the time-sensitive prevalence after stroke<sup>6 11 21</sup> and bridge the crucial gap between inpatient rehabilitation and the difficult reintegration in survivors' familiar environment<sup>22</sup> after discharge.

Interventions aiming at the treatment of PSD can be broadly grouped into two categories: pharmacological and non-pharmacological treatments. Recent meta-analytical evidence showed that antidepressant medication is by far the most frequent treatment strategy.<sup>18 19 23</sup> Pharmacological interventions using antidepressants mainly include selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, monoamine oxidase inhibitors and tricyclic antidepressants and are associated with greater reduction of both prevalence and levels of PSD compared with control treatments.<sup>19 23</sup> However, pharmacological interventions were also found to increase the risk of bone fractures and adverse central nervous system and gastrointestinal effects.<sup>19 24 25</sup>

Regarding non-pharmacological treatments of PSD, psychological (talking) therapies must be differentiated from other treatments such as acupuncture,<sup>26</sup> or non-invasive brain stimulation.<sup>27</sup> Psychotherapy is recommended as first-line treatment for mild and moderate depression, and in combination with antidepressants for severe depression by the German National Treatment Guidelines for Unipolar depression<sup>28</sup> and is associated with lower relapse rates than (only) pharmacotherapy and control treatments.<sup>29</sup>

Studies focusing on prevention of PSD suggest that brief and low-threshold psychological interventions may decrease PSD prevalence after stroke.<sup>30 31</sup> However, these trials did not focus on treatments of stroke survivors with clinical depression levels and/or diagnosed PSD. Recent meta-analytical evidence on treatments focusing on clinical levels of PSD found that psychological interventions were associated with a reduction of both prevalence and levels of PSD compared with control treatments at the end of treatment, but not at follow-up.<sup>19</sup> Although all of these assessed interventions were required to be talking therapies,<sup>19</sup> interventions were characterised by substantial heterogeneity across studies ranging from one session of motivational interviewing via telephone<sup>32</sup> up to weekly psychotherapy sessions over the course of several months.<sup>33</sup> Psychological interventions were mostly compared with a control condition (eg, treatment as usual (TAU) or no treatment) and were mostly based on

short-term cognitive behavioural,<sup>33–37</sup> supportive (psycho-social) counselling,<sup>32 38–41</sup> motivational interviewing<sup>42 43</sup> or problem solving.<sup>44</sup> One pilot trial examined the effect of additional interpersonal psychotherapy during inpatient rehabilitation<sup>45</sup> and another pilot trial examined a new treatment called ecosystem focused therapy.<sup>46</sup> Two of these trials allowed for parallel medication for some patients,<sup>34 47</sup> while another trial prescribed parallel medication for part of the sample<sup>45</sup> and two trials included pharmacotherapy for the full sample.<sup>37 48</sup> Moreover, the majority of trials did not include follow-up assessments<sup>34 38 40 41 43 44 46 47</sup> while other trials which included a single follow-up assessment between 1.5 and 20 months after stroke<sup>32 35–37 39 42</sup> while the time of the baseline assessment after stroke ranged from 1 to 52 weeks after stroke. Regarding the application of treatment, interventions were carried out by trained therapists (including, psychological assistants),<sup>33–37 46</sup> nurses<sup>32 42 43</sup> social workers<sup>44</sup> or trained staff from various professional backgrounds.<sup>40</sup> Only six studies reported if therapists had initial training or regular supervision.<sup>33 35–37 43 46</sup> These limitations might have contributed to the heterogeneity and current level of conclusiveness of evidence for psychotherapy.<sup>19</sup>

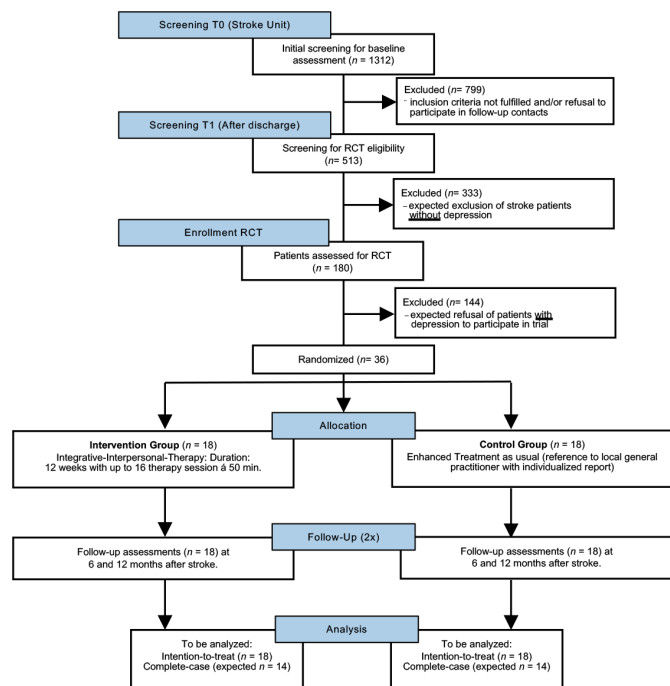
In summary, evidence of the efficacy of psychological treatment of PSD remains fragmented and is limited by substantial heterogeneity across studies regarding the type of treatment, duration, follow-up assessments, time after stroke, administrating personnel, training and supervision. Established recommendations for psychotherapy trials include not only an adequate therapy exposure (ie, duration and dosage), but also sufficient therapist qualification to guarantee an adequate level of clinical expertise.<sup>11 19 49–51</sup> Moreover, the previous trials further differed in setting (inpatient rehabilitation, outpatient, home visits, telephone and face-to-face setting), the use of manualised interventions and the inclusion of caregivers. Moreover, most previous studies did not have or report sufficient statistical power based on an adequate sample size. Thus, previous trials on psychological interventions for PSD might not allow to assess the full potential effect of a manualised, stroke-specific psychotherapy due to their brevity and specific design characteristics outlined above.

Finally, no previous trial has investigated the efficacy of a manualised integrated interpersonal psychotherapy, delivered by trained and supervised therapists drawing on psychodynamic and cognitive-behavioural principles which explicitly considers the dynamic prevalence during the first year after stroke.

## DESIGN AND METHOD

### Overall aim and general framework

The primary aim of the present multicentre pilot (the terms 'pilot' and 'feasibility' study will be used according to<sup>52</sup> where a pilot study is defined as a special case of the feasibility study: A pilot study carries out a feasibility study with the unique feature that the pilot



**Figure 1** Consolidated Standards of Reporting Trials (CONSORT) flow diagram of patient recruitment and participation. Initial screening will take place at baseline (T0) on two stroke units, where stroke survivors will be invited to participate in the study and—given written informed consent—assessed for inclusion criteria (ie, occurrence of stroke and sufficient verbal and German language comprehension for study participation). Second screening will take place after discharge from inpatient rehabilitation. Participants will be randomised based on a cut-off for PSD (ie, a PHQ-9 score  $\geq 11$ ) to either an intervention or control-group (E-TAU) given their informed consent. Follow-up assessments will take place 6 (T2) and 12 (T3) months after stroke. E-TAU, enhanced treatment as usual; PHQ-9, Patient Health Questionnaire; PSD, poststroke depression; RCT, randomised controlled trial.

study will be carried with a design that mirrors the planned main trial on a smaller scale, that is, where the processes and procedures are planned to be applied in the main randomised controlled trial (RCT) if found feasible) study is to assess the feasibility of recruitment and treatment acceptability of a manualised intensive short-term psychotherapy. Moreover, the INID (Integrative-interpersonal dynamic therapy for post-stroke depression)-PILOT aims to provide a preliminary estimation of the effect size including confidence intervals of the new treatment to serve as a basis for sample size calculation for the planned main RCT. Recruitment is planned to be conducted from August 2023 to May 2024 at two German Stroke Units at the Dept. of Neurology at the University Hospital Düsseldorf and the University Hospital Heidelberg. The study was approved by the ethic committees of the Medical Faculties in Heidelberg (registry no: S-321/2019) and Düsseldorf (registry no: 2022-2286\_1).

## Recruitment and assessments

Figure 1 shows the Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the INID-PILOT: First, all stroke survivors will be screened for study eligibility at baseline (T0). Second, participants will be screened shortly after discharge from inpatient rehabilitation (T1) to assess RCT eligibility. After this second screening, patients with PSD will be randomised to either the control or intervention group. Note that this step (ie, the proportion of patients consenting to be randomised) will serve as a basis for the feasibility assessment (see below). Moreover, all participating patients screened at T1, will be assessed after 6 (T2) and 12 (T3) months regardless of their PSD levels to assess the influence and control for known risk factors and relevant outcomes (see below: secondary outcomes description). Randomised participants in the intervention group will have three additional assessments at beginning, mid and end of their 12-week intervention, which are planned to be carried out from November 2023 to November 2024 (ie, 12 weeks after the last patient was discharged from inpatient rehabilitation).

## Feasibility and acceptability hypotheses

The planned psychotherapy intervention will take place at two university hospital departments and will be conducted after patients discharge from inpatient rehabilitation (T1). Given stroke survivors transition during this period,<sup>6 22</sup> it is unclear—and thus necessary to assess—how many patients will consent to randomisation and subsequent treatment and how many patients discontinue treatment participation. Based on available data from other PSD clinical trials,<sup>36 43 44</sup> we derived conservative thresholds for the feasibility of the recruitment rate and acceptability of the treatment in terms of treatment participation. The main aim of this pilot study is to assess the feasibility and acceptability of the study protocol: As primary outcome we define a rate of  $\geq 20\%$  for RCT eligible stroke survivors with clinical levels of depression at T1 consenting to randomisation as feasible. Acceptability is defined as  $\geq 70\%$  of randomised patients participation in  $\geq 66\%$  of therapy sessions, measured at the end of treatment.

## Participants and selection criteria

Participants are patients admitted to the Stroke Unit at the Department of Neurology at the University Hospital Düsseldorf or the University Hospital Heidelberg. Screening will take place during the first week of admittance where stroke survivors will be invited to participate in the INID-PILOT. Participation will depend on participants' written informed consent (see online supplemental ESM1) and the following criteria:

Inclusion criteria at T0: Diagnosed occurrence of ischaemic stroke (International Classification of Diseases (ICD) -Code: I.63) or intracerebral haemorrhage (I.61) in patients admitted to the two Stroke Units. Sufficient verbal comprehension at baseline (T0) as defined by a sum of  $\geq 6$  points of the shortened Aphasia-Schnell-Test



(aphasia (AST)),<sup>53 54</sup> signifying a comparatively low threshold for patients to be included.<sup>53</sup> Sufficient German language comprehension for questionnaire completion and participation in psychotherapy, assessed at baseline (T0).

Inclusion criteria for randomisation at T1: Depression (ie, a Patient Health Questionnaire-9 (PHQ-9) score  $\geq 11$ ) after discharge from inpatient rehabilitation. This cut-off is based on meta-analytical evidence for diagnosing PSD, showing that it offers an optimal trade-off between sensitivity and specificity across several settings and was therefore set over the PHQ-9 manual-recommended (non-stroke-specific) threshold of 10.<sup>55–57</sup> The rationale for choosing this cut-off is to recruit a sample with high enough levels of PSD (in terms of PHQ-9 scores) to expect a clinically relevant effect, yet low enough to include a representative PSD sample.

Exclusion criteria: Patients with diagnosed transitory ischaemic attack (ICD-Code G.45), due to limited comparability between the impact of transitory complications and potentially chronic consequences of stroke on patients' affective well-being. Patients with severe intracerebral haemorrhage, requiring neurosurgical treatment shortly after stroke.

Note that, applying international recommendations,<sup>11 58</sup> we minimised the number of exclusion criteria to allow a representative range of stroke survivors with PSD to be eligible.

### Randomisation

Participating patients will be randomised to either the treatment conditions or E-TAU at T1, which will take place shortly after discharge from inpatient rehabilitation (cf. figure 1). Randomisation will be conducted using R package *blockrand*,<sup>59</sup> ensuring transparent and chance-based group allocation of all eligible participants. Group randomisation will be stratified based on severity of depressive symptoms (PHQ-9  $\geq 15$ , after discharge from inpatient rehabilitation) and stroke severity (National Institute of Health Stroke Scale (NIHSS)  $\geq 6$  (ie, threshold between minor and moderate stroke) at baseline) to increase comparability. To avoid predictable patterns in randomisation, block sizes will be permuted with sizes of 2 or 4.<sup>59</sup>

### Procedure after initial screening

After baseline screening at the university departments of neurology (T0), eligible study participants will be contacted shortly after discharge from inpatient rehabilitation, approximately 3 months after stroke (T1). Randomisation will take place after the T1 screening with patients above the defined cut-off for depression (PHQ-9 score  $\geq 11$ ) given their informed consent. To avoid systematic bias, follow-up interviews will be carried out by blinded interviewers at Kassel University, (ie, psychology B.Sc. and/or M.Sc. students who receive clinical training). In the intervention group, participants will be additionally

assessed at the beginning and end of treatment, and every fifth therapy session (cf. table 1).

### Treatment

The proposed manualised treatment integrates key aspects of psychodynamic and cognitive-behavioural psychotherapy for depressed stroke patients. The focus is on the interpersonal dynamic after stroke using the psychodynamic Core-Conflictual-Relationship-Theme (CCRT)<sup>60</sup> in addition to structured elements for behavioural activation and fostering of patients' agency. Furthermore, patients' family members are routinely offered support and can be included in the treatment. Study treatment will consist of manualised integrative-interpersonal dynamic therapy over a period of 12 weeks. Patients will receive two diagnostic evaluations (see module 1) and up to 16 individual psychotherapy sessions. The treatment will be conducted as individual outpatient therapy. Exceptions to the individual therapy setting are two preplanned sessions, where patients are invited to bring their partner and/or other family members to the therapy (module 2 and 6). In addition, two group sessions for family members are offered during each patient's individual treatment (module 8) to provide psychoeducation and connect caregivers among themselves. In case of immobility of patients, the therapist can also visit at home and conduct therapy sessions there.

The treatment is manualised and integrates key features of the Unified Psychodynamic Protocol (UPP) for depressive disorders<sup>61</sup> as well as the Cognitive-Behavioural Unified Protocol (CB-UP) for emotional disorders.<sup>62</sup> Consistent with the recommendations of both unified protocols, the manual is organised in treatment modules and includes elements on treatment motivation, setting of treatment goals and psychoeducation as well as a relapse prevention module. Following the UPP, the therapy focuses on raising patients' self-understanding of their CCRT<sup>60</sup> and the connection between the interpersonal dynamics, the experience of stroke and depressive symptoms. In accordance with the CB-UP, the therapy includes tools and exercises aimed at raising emotional awareness, reducing behavioural avoidance and facilitating cognitive reappraisal. A specific focus on supportive interventions is intended to facilitate a positive therapeutic alliance. The modules are: (1) diagnostics using (semi)structured interviews (two sessions), (2) psychoeducation and treatment rationale (two therapy sessions), (3) motivation and individual treatment goals (two therapy sessions), (4) emotional awareness (two therapy sessions), (5) maladaptive interpersonal pattern in everyday life (six therapy sessions), (6) termination and relapse prevention (four therapy sessions), (7) supportive alliance interventions (across entire treatment) and an optional module (8) for family members and caregivers (invitation to two patient sessions and two separate and specific sessions for caregivers).

### Control condition

Patients randomised to the control condition will receive enhanced TAU (E-TAU). E-TAU consists of the standard

**Table 1** Overview of measures, type of rating, source and measurement occasions of the INID pilot trial

	Type/source	Measurement occasion
<i>Measures for all participants</i>		
Structured Clinical Interview for DSM-5 (SCID I)	Observer based	T0, T1*, T2*, T3*
Patient Health Questionnaire (PHQ-9)	Self-assessment	T0, T1, T2, T3
Hamilton Depression Scale (HAMD-D)	Observer based	T0, T1, T2, T3
Generalised Anxiety Disorder 7 (GAD-7)	Self-assessment	T0, T1, T2, T3
Social Support Questionnaire (F-SozU-K6)	Self-assessment	T0, T1, T2, T3
European Quality of Life 5 Dimensions (EQ-5D)	Self-assessment	T0, T1, T2, T3
OPD Structure Questionnaire Short Form (OPD-SQS)	Self-assessment	T0, T1, T2, T3
Modified Ranking Scale (mRS)	Observer based	T0, T1, T2, T3
Self-Compassion Scale-Short Form	Self-assessment	T0, T1, T2, T3
Montreal Cognitive Assessment (MoCA)	Observer based	T0
Barthel-Index (BI)	Observer based	T0
Mod. National Inst. of Health Stroke Scale	Observer based	T0
Aphasia-Schnell-Test (AST)	Observer based	T0
Post-Stroke-Depression Risk Scale (PoStDeRis)	Observer based	T0
Signs of Depression Scale (SODS)	Observer based	T0
<i>Additional measures for the intervention group</i>		
Operationalised Psychodynamic Diagnostic (OPD-2) Interview	Observer based	DS1
Experience in Close Relationship-Revised (ECR-R)	Self-assessment	DS1, EOT
OPD Structure Questionnaire - Short (OPD-SQS)	Self-assessment	DS1, EOT
Patient Health Questionnaire (PHQ-9)	Self-assessment	Every fifth TS until EOT
Working Alliance Inventory (WAI-SR) (Patient and therapist)	Self-assessment	Every fifth TS until EOT
T0=baseline assessment during the first week after stroke; T1=after discharge from inpatient rehabilitation; T2=6 months after stroke; T3=12 months after stroke; DS prior to treatment; TS (up to 16 over the 12-week long treatment); detailed instrument description is provided below. *During follow-up, SCID-I interviews will be conducted fully for the intervention group and the depression part for all participants. DS, diagnostic session; DSM, Diagnostic and Statistical Manual of Mental Disorders; EOT, end of treatment; TS, therapy session.		

referral of patients after regular discharge from inpatient rehabilitation, mostly to their general practitioner (GP). As enhancement, stroke survivors will receive their individual results of the psychological study assessment (table 1) to complement their standard discharge report. Patients are encouraged to share the results of their psychological assessments with their GP and initiate treatment if indicated. All treatments (antidepressant medication, psychotherapy, speech therapist, etc) initiated by the patient or their GP will be recorded throughout follow-up assessments. In addition, E-TAU participants will receive contact information for local self-help organisations.

### Therapists

Therapists hold a PhD, an M.D. or a master's degree in psychology or equivalent (eg, Dipl.-Psych.). They are required to have at least 2 years of clinical experience. Furthermore, previous outpatient psychotherapy of depressed patients is a prerequisite to be included as therapist. Therapists will receive specific training based on the treatment manual prior to the start of the trial. In addition, they will participate in biweekly group supervision throughout the entire study period. During supervision,

video recordings will be used to continuously monitor adherence throughout the study.

### Medication

Antidepressant medication will be documented at all measurement occasions using half-structured interviews. Because a discontinuation of antidepressant medication shortly after its start during an ongoing depressive episode is potentially harmful and may lead to further symptom aggravation,<sup>63</sup> existing antidepressant medication will not be changed or conditioned for randomised patients, but recorded and used as a covariate (see the 'Statistical analysis' section). With this procedure, the proportion of (pre)medicated patients and changes in regimens<sup>17</sup> can be estimated for a subsequent confirmatory definite trial.

### Patient and public involvement

Patient involvement was secured throughout trial planning by involving key local self-help organisations and integrating their feedback. For example, the specific module for family members and caregivers was newly designed and included based on patient representatives' feedback as well as the reference of patients in the control

condition (E-TAU) to their respective local self-help organisation after T1 screening.

### Outcome measures

**Table 1** lists all outcome measures throughout the INID-PILOT trial.

The Patient Health Questionnaire (PHQ-9) is a self-report instrument for depression according to Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria.<sup>56</sup> Psychometric evaluation showed excellent discrimination between depressed and non-depressed stroke patients (minor and major depression) with specificity of 0.89 and sensitivity of 0.89 for the cut-off of  $\geq 11$ .<sup>57</sup> The PHQ-9 will be the primary outcome measure in this trial.

The Structured Clinical Interview for DSM-5 clinical version represents a semistructured clinical interview to assess and diagnose Axis I mental disorders according to DSM-5 criteria.<sup>64</sup> Psychometric evaluation showed satisfactory inter-rater and retest reliability.<sup>65</sup>

The Hamilton Depression Scale (HAMD-D) is a 21-item standard observer-rated instrument to assess the severity of depression.<sup>66</sup> Psychometric evaluation showed high construct validity and acceptable discrimination between depressed and non-depressed stroke patients with specificity of 0.94 and sensitivity of 0.54 for the recommended cut-off of  $\geq 10$ .<sup>67</sup>

The Generalised Anxiety Disorder 7 (GAD-7) allows the brief self-assessment of anxiety symptoms based on DSM criteria.<sup>68</sup> The seven-item questionnaire is used in primary care and shows favourable psychometric evaluation with specificity of 0.82 and sensitivity of 0.89 for the standard cut-off of  $\geq 10$ .

The Social Support Questionnaire (F-SozU-K6) allows the brief self-assessment of perceived social support. The six-item short version captures patients' perceived social support on a 5-point Likert-Scale. Psychometric evaluation showed excellent characteristics.<sup>69</sup>

The Questionnaire for European Quality of Life 5 Dimensions (EQ-5D) assesses five dimensions of perceived problems in five health domains on a 5-point Likert-scale, next to an overall assessment on a 0–100 Visual Analogue Scale. The EQ-5D is validated in the general population and patient samples including cardiovascular disease and showed satisfactory reliability and validity.<sup>70</sup>

Patients' medication (drug class, dosage and regimen) after acute and inpatient rehabilitation will be obtained from medical files and/or discharge reports or semistructured interviews during the telephone follow-ups.

The Montreal Cognitive Assessment (MoCA) is a brief screening instrument for mild cognitive impairments which was developed to address ceiling effects of comparable measures.<sup>71</sup> Validation in patients who had a stroke showed favourable psychometric properties.<sup>72</sup>

The Barthel-Index (BI) allows standard assessment of functional independence in terms of patients' ability to perform activities of daily living.<sup>73</sup> Scores range from 0 (complete dependence/disability) to

100 (complete independence). The BI is a routinely used and represents the most consistently found predictor for PSD.<sup>11 74</sup>

The modified National Institute of Health Stroke Scale (mNIHSS) allows a graded assessment of patients' stroke severity in terms of neurological deficits<sup>75</sup> including motoric/sensory impairment, level of consciousness, visual field/movement, language and neglect. Psychometric evaluation showed favourable properties in various clinical settings.

The German version of the AST (Aphasia Quick Test) was used in a shortened form according to,<sup>54</sup> which is especially suited the acute setting.<sup>53</sup> The AST captures the ability to comprehend and execute verbal commands. In our study, the cut-off of  $\geq 6$  was used for all ages groups as a relatively low threshold for inclusion.<sup>15 54</sup>

The Post-Stroke Depression Risk Scale is a short observer-based assessment, which allows accurate identification risk patients for PSD.<sup>19</sup> It consists of three items (history of depression, PHQ-2 Items and BI) and was developed for assessments during acute care.<sup>19</sup>

The Signs of Depression Scale (SODS) is one of the few non-language based PSD screening instruments,<sup>76</sup> which was developed for acute care settings. It consists of six items answered on a yes/no scale and can be administered by staff or family members.

The modified Rankin Scale (mRS) represents a standard observer-based measure of functional outcome<sup>77</sup> and is assessed on a 7-point scale ranging from 0 (no symptoms at all) to 6 (death). Psychometric evidence showed excellent reliability and satisfactory validity.<sup>78</sup>

The Self-compassion Scale-Short Form<sup>79</sup> is a self-report measure of self-compassion as the ability to hold one's feelings of suffering with a sense of warmth, connection and concern. It evaluates how often certain actions are used in difficult times by a 5-point scale ranging from 1 (almost never) to 5 (almost always). Psychometric evidence demonstrated good reliability and validity.<sup>79</sup>

The Operationalised Psychodynamic Diagnostic (OPD-2) assesses patients relationship patterns, conflict and structure using a semistructured clinical interview.<sup>80 81</sup> The OPD-2 interview shows satisfactory psychometric properties and represents a standard instrument for psychodynamic diagnostics.<sup>81</sup>

The Experience in Close Relationships-Revised (ECR-R) is a brief self-assessment capturing individual differences in attachment style.<sup>82</sup> This eight-item version assesses patients' perception of current and past relationships on a 7-point Likert scale. Psychometric evaluation showed acceptable model fit.

The short form of the OPD Structure Questionnaire (OPD-SQS) is a 12-item self-assessment capturing three dimensions (self-perception, contact organisation and relationship model and of structural deficits). Psychometric evaluation showed adequate model fit, reliability and validity in therapeutic contexts.<sup>83</sup>



Working Alliance will be assessed using the revised short-form of the Working Alliance Inventory (WAI-SR).<sup>84</sup> This 12-item self-report allows a reliable and brief assessment of Bordin's<sup>85</sup> three-factor model (bond, task, goals). The WAI-SR can be used for patients and therapists and shows excellent psychometric properties.<sup>86</sup>

### Statistical analysis

Feasibility will be assessed by calculating recruitment rates of RTC eligible patients at T1 (see the 'Feasibility and acceptability hypotheses' section). For the preliminary estimation of effect size and sample size calculation, the mean difference in PHQ-9 scores between the intervention and control group at T2 (6 months after stroke) will be used. Effect size calculation will be standardised by using the pooled, bias-corrected (for  $n < 50$ ) SD between the intervention and control group.

As secondary outcome, changes in depression (PHQ-9/HAMD-D) and anxiety (GAD-7) across all follow-ups will be tested using (multivariate) analysis of variances (ANOVA) with repeated measurements. These analyses also encompasses all participants, regardless of randomisation and levels of PSD at T1. Relevant measures, which are known predictors of PSD (eg, BI, MoCA, mNIHSS, F-SozU-K6, QoL, early depressive symptoms (HAMD-D/SODS)) are assessed as described in [table 1](#) to be included as covariates for the analysis of the secondary outcomes.

**Sample size estimation:** For this pilot study, we aim to recruit  $n=18$  patients for each group, the intervention and control group (E-TAU). This sample size calculation is based on CI approach, following the CONSORT recommendations for pilot studies.<sup>52 87 88</sup> The CI approach uses the anticipated larger RCT to estimate the pilot trial's sample size.<sup>87</sup> Specifically, the approach yields a pilot sample size where the expected CI excludes a clinically significant threshold given that the treatment has no (zero) significant effect. Thus, if the CI of the treatment effect in the pilot study reaches (or overcomes) the threshold, it is recommended to move forward with the anticipated main study.<sup>87</sup> In more statistical terms, the sample size calculation is based on a one-sided 80 or 90% CI, where the upper limit excludes a predefined threshold of clinical significance. In this pilot study, this threshold was defined as a medium standardised effect size of  $d=0.50$  for the primary outcome (ie, PHQ-9 at 6-month follow-up). This effect size is drawn from mean effect sizes of other psychotherapies (for a recent meta-analysis, see Leichsenring *et al*<sup>89</sup>) and corresponds to a PHQ-9 reduction of about 3 points when considering the SD of the PHQ-9 in stroke populations.<sup>90 91</sup> For the sample size estimation, a 90% (ie, more conservative than 80%) CI was chosen, yielding a required sample size of  $n=14$  for each group.<sup>87</sup> Notably, this does not account for study drop-out, which was assumed to be about 30%,<sup>36 43 44</sup> resulting in our final sample size of

$n=18$  for each group. Intention-to-treat analysis will be carried out for the effect size calculation.<sup>92</sup>

### ETHICS AND DISSEMINATION

The INID pilot study received ethical approval from both recruitment locations (University Hospital Heidelberg: Reg-Nr.: S-321/2019) and the Heinrich-Heine-University Düsseldorf (Reg-Nr.: 2022-2286\_1) and complies with the Declaration of Helsinki.<sup>64</sup> Adverse events are not expected throughout the trial. Patients in the intervention group will be informed about potential side effects<sup>93</sup> of psychotherapy, in compliance with German professional regulations. Data management was evaluated within the ethics approval process according to the General Data Protection Regulation. Recruitment is planned to commence in August 2023 and last 9 months until May 2024. The intervention is planned to start in November 2023 (ie, about 3 months after the start of recruitment) and last until November 2024 (ie, about 6 months after the last patient was recruited). Publication of trial results is expected during the first half of 2025 after recruitment and subsequent treatment termination. Follow-ups are planned to be carried out until May 2025 (ie, 1 year after the last patient was recruited). The INID pilot study is pre-registered at the German register for clinical studies (Deutsches Register Klinischer Studien: Reg-Nr. DRKS00030378).

### Author affiliations

<sup>1</sup>Psychology, Universität Kassel, Kassel, Germany

<sup>2</sup>Department of Neurology, University Hospital Heidelberg, Heidelberg, Germany

<sup>3</sup>Department of General Internal Medicine and Psychosomatics, Heidelberg University Hospital, Heidelberg, Germany

<sup>4</sup>Department of Neurology, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

<sup>5</sup>Department of Psychology, Clinical Neuropsychology and Psychotherapy, University of Bielefeld, Bielefeld, Germany

<sup>6</sup>Adelphi University, Gordon F Derner School of Psychology, New York City, New York, USA

<sup>7</sup>Department of Psychosomatic Medicine and Psychotherapy, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

**Contributors** UD and MV conceptualised the study design and the new treatment, BW consulted on the methodology. MV wrote the original draft of the manuscript. UD, HS, SGM, BW, KW, JPB, RS, LB and SM contributed to reviewing and editing. Additionally, BW edited the method section. All authors contributed to further revisions and have read and approved the final manuscript.

**Funding** This work is supported by the German Research Foundation (Deutsche Forschungsgemeinschaft (DFG)): Grant number: 451696278.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication** Consent obtained directly from patient(s).

**Provenance and peer review** Not commissioned; peer reviewed for ethical and funding approval prior to submission.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content

includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**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 iD

Matthias Volz <http://orcid.org/0000-0002-0946-1116>

## REFERENCES

- Hackett ML, Pickles K. Part I: frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. *Int J Stroke* 2014;9:1017–25.
- Ayerbe L, Ayis S, Wolfe CDA, et al. Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis. *Br J Psychiatry* 2013;202:14–21.
- De Ryck A, Brouns R, Geurden M, et al. Risk factors for poststroke depression: identification of inconsistencies based on a systematic review. *J Geriatr Psychiatry Neurol* 2014;27:147–58.
- Löck J, Delbari A. Management of depression in elderly stroke patients. *Neuropsychiatr Dis Treat* 2010;6:539–49.
- Volz M, Voelkle MC, Werheid K. General self-efficacy as a driving factor of post-stroke depression: a longitudinal study. *Neuropsychol Rehabil* 2019;29:1426–38.
- Werheid K. A two-phase pathogenetic model of depression after stroke. *Gerontology* 2015;62:33–9.
- Whyte EM, Mulsant BH. Post stroke depression: epidemiology, pathophysiology, and biological treatment. *Biol Psychiatry* 2002;52:253–64.
- Blöchl M, Meissner S, Nestler S. Does depression after stroke negatively influence physical disability? A systematic review and meta-analysis of longitudinal studies. *J Affect Disord* 2019;247:45–56.
- Cai W, Mueller C, Li Y-J, et al. Post stroke depression and risk of stroke recurrence and mortality: a systematic review and meta-analysis. *Ageing Res Rev* 2019;50:102–9.
- Kim E-S, Kim J-W, Kang H-J, et al. Longitudinal impact of depression on quality of life in stroke patients. *Psychiatry Investig* 2018;15:141–6.
- Towfigh A, Ovbiagele B, El Hussein N, et al. Poststroke depression: a scientific statement for Healthcare professionals from the American heart association/American stroke association. *Stroke* 2017;48:e30–43.
- Mast BT. Cerebrovascular disease and late-life depression: a latent-variable analysis of depressive symptoms after stroke. *Am J Geriatr Psychiatry* 2004;12:315–22.
- Opara JA, Jaracz K. Quality of life of post-stroke patients and their Caregivers. *J Med Life* 2010;3:216–20.
- Thompson HS, Ryan A. The impact of stroke consequences on spousal relationships from the perspective of the person with stroke. *J Clin Nurs* 2009;18:1803–11.
- Ladwig S, Ziegler M, Südmeyer M, et al. The post-stroke depression risk scale (Postderis): development of an acute-phase prediction model for depression 6 months after stroke. *J Acad Consult Liaison Psychiatry* 2022;63:144–52.
- Ramasubbu R. Therapy for prevention of post-stroke depression. *Expert Opin Pharmacother* 2011;12:2177–87.
- Werheid K, Volz M, Ladwig S, et al. Too much and too little: antidepressant treatment in stroke survivors during the first year. *J Integr Neurosci* 2022;21:108.
- Ladwig S, Zhou Z, Xu Y, et al. Comparison of treatment rates of depression after stroke versus myocardial infarction. A systematic review and meta-analysis of observational data. *Psychosom Med* 2018;80:754–63.
- Allida S, Cox KL, Hsieh C-F, et al. Pharmacological, psychological and non-invasive brain stimulation interventions for preventing depression after stroke. *Cochrane Database Syst Rev* 2020;5:CD003689.
- Kruse J, Herzog W, Hofmann D-P-S, et al. Zur Ambulanten Psychosomatischen/Psychotherapeutischen Versorgung in der Kassenärztlichen Versorgung in Deutschland—Formen der Versorgung und Ihre Effizienz. In: *Zwischenbericht zum Gutachten, im Auftrag der Kassenärztlichen Bundesvereinigung (KBV). Zugriff am 2012.* 2015: 22.
- Volz M, Möbus J, Letsch C, et al. The influence of early depressive symptoms, social support and decreasing self-efficacy on depression 6 months post-stroke. *J Affect Disord* 2016;206:252–5.
- Wottrich AW, Aström K, Löfgren M. On parallel tracks: newly home from hospital—people with stroke describe their expectations. *Disabil Rehabil* 2012;34:1218–24.
- Deng L, Sun X, Qiu S, et al. Interventions for management of post-stroke depression: a Bayesian network meta-analysis of 23 randomized controlled trials. *Sci Rep* 2017;7:16466.
- Hackam DG, Mrkobrada M. Selective serotonin reuptake inhibitors and brain hemorrhage: a meta-analysis. *Neurology* 2012;79:1862–5.
- Jones JS, Kimata R, Almeida OP, et al. Risk of fractures in stroke patients treated with a selective serotonin reuptake inhibitor: a systematic review and meta-analysis. *Stroke* 2021;52:2802–8.
- Li X-B, Wang J, Xu A-D, et al. Clinical effects and safety of electroacupuncture for the treatment of post-stroke depression: a systematic review and meta-analysis of randomised controlled trials. *Acupunct Med* 2018;36:284–93.
- Bucur M, Papagno C. A systematic review of noninvasive brain stimulation for post-stroke depression. *J Affect Disord* 2018;238:69–78.
- Deutsche Gesellschaft für Psychiatrie, Psychotherapie und Nervenheilkunde, Ärztliches Zentrum für Qualität in der Medizin. S3-Leitlinie/Nationale Versorgungsleitlinie Unipolare Depression - Leitlinienreport, 3. Auflage Deutsche Gesellschaft für Psychiatrie, Psychotherapie und Nervenheilkunde (DGPPN); Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF); 2022.
- 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.
- de Man-van Ginkel JM, Gooskens F, Schuurmans MJ, et al. A systematic review of therapeutic interventions for poststroke depression and the role of nurses. *J Clin Nurs* 2010;19:3274–90.
- Hackett ML, Anderson CS, House AO, et al. Interventions for treating depression after stroke. *Cochrane Database Syst Rev* 2004;2008:CD003437.
- Kirkness CJ, Cain KC, Becker KJ, et al. Randomized trial of telephone versus in-person delivery of a brief psychosocial intervention in post-stroke depression. *BMC Res Notes* 2017;10:500.
- Thomas SA, Walker MF, Macniven JA, et al. Communication and low mood (CALM): a randomized controlled trial of behavioural therapy for stroke patients with aphasia. *Clin Rehabil* 2013;27:398–408.
- Gao J, Lin M, Zhao J, et al. Different interventions for post-ischaemic stroke depression in different time periods: a single-blind randomized controlled trial with stratification by time after stroke. *Clin Rehabil* 2017;31:71–81.
- Hoffmann T, Ownsworth T, Eames S, et al. Evaluation of brief interventions for enhancing early emotional adjustment following stroke: a pilot randomised controlled trial. *Top Stroke Rehabil* 2015;22:117–26.
- Lincoln NB, Flannaghan T. Cognitive behavioral psychotherapy for depression following stroke. *Stroke* 2003;34:111–5.
- Mitchell PH, Veith RC, Becker KJ, et al. Brief psychosocial-behavioral intervention with antidepressant reduces poststroke depression significantly more than usual care with antidepressant: living well with stroke: randomized, controlled trial. *Stroke* 2009;40:3073–8.
- Fang Y, Mpofu E, Athanasou J. Reducing depressive or anxiety symptoms in post-stroke patients: pilot trial of a constructive integrative psychosocial intervention. *Int J Health Sci (Qassim)* 2017;11:53–8.
- Cullen B, Pownall J, Cummings J, et al. Positive psychotherapy in ABI Rehab (Popstar): a pilot randomised controlled trial. *Neuropsychol Rehabil* 2018;28:17–33.
- Zhao HW, Zhou CX, Su XL, et al. Effect of mental intervention on post-stroke depression and rehabilitation of neurological function. *Chinese Journal of Clinical Rehabilitation* 2004;8:2408–9.
- Wang X, Song J, Mu J. The effect of psychotherapy on depression and cognitive function of patients with cerebral stroke. *Chin Ment Health J* 2004:778–81.
- Kerr D, McCann T, Mackey E, et al. Effects of early motivational interviewing on post-stroke depressive symptoms: a pilot randomized study of the good mood intervention program. *Int J Nurs Pract* 2018;24:e12657.
- Watkins CL, Auton MF, Deans CF, et al. Motivational interviewing early after acute stroke. *Stroke* 2007;38:1004–9.
- Towle D, Lincoln NB, Mayfield LM. Service provision and functional independence in depressed stroke patients and the effect of



- social work intervention on these. *J Neurol Neurosurg Psychiatry* 1989;52:519–22.
- 45 Finkenzeller W, Zobel I, Rietz S, et al. Interpersonelle psychotherapie und pharmakotherapie BEI post-stroke-depression. *Nervenarzt* 2009;80:805–12.
- 46 Alexopoulos GS, Wilkins VM, Marino P, et al. Ecosystem focused therapy in Poststroke depression: a preliminary study. *Int J Geriatr Psychiatry* 2012;27:1053–60.
- 47 Cao WW, Yu JM, Sun SY, et al. Group psychotherapy in treatment of post stroke depression. *Chin Ment Health J* 2009;23:100–4.
- 48 Williams LS, Kroenke K, Bakas T, et al. Care management of poststroke depression: a randomized, controlled trial. *Stroke* 2007;38:998–1003.
- 49 Association AP. Evidence-based practice in psychology: APA presidential task force on evidence-based practice. *Am Psychol* 2006;61:271–85.
- 50 Wampold BE, Mondin GW, Moody M, et al. A meta-analysis of outcome studies comparing BONA fide psychotherapies: Empirically, "all must have prizes. *Psychol Bull* 1997;122:203–15.
- 51 Kocsis JH, Gerber AJ, Milrod B, et al. A new scale for assessing the quality of randomized clinical trials of psychotherapy. *Compr Psychiatry* 2010;51:319–24.
- 52 Eldridge SM, Lancaster GA, Campbell MJ, et al. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. *PLoS ONE* 2016;11:e0150205.
- 53 Aphasie-Schnell-Test C. *Aphasie-Schnell-Test (AST). Ein standardisierter Test für die Differentialdiagnose; Aphasie-keine Aphasie-Dysarthrie in der Akutphase*. 2006.
- 54 Hirt J, van Meijeren LCJ, Saal S, et al. Predictive accuracy of the post-stroke depression prediction scale: a prospective Binational observational study<sup>3</sup>. *J Affect Disord* 2020;265:39–44.
- 55 Meader N, Moe-Byrne T, Llewellyn A, et al. Screening for poststroke major depression: a meta-analysis of diagnostic validity studies. *J Neurol Neurosurg Psychiatry* 2014;85:198–206.
- 56 Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. *J Gen Intern Med* 2001;16:606–13.
- 57 Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the patient health questionnaire (PHQ-9): a meta-analysis. *CMAJ* 2012;184:E191–6.
- 58 Casaubon LK, Boulanger J-M, Glasser E, et al. Canadian stroke best practice recommendations: acute inpatient stroke care guidelines, update 2015. *Int J Stroke* 2016;11:239–52.
- 59 Snow G, Snow MG. Package 'Blockrand'. In: *The comprehensive R archive network*. 2013.
- 60 Luborsky L, Mark D, Hole AV, et al. Supportive-expressive dynamic psychotherapy of depression: a time-limited version. (keine Angabe); 1995.
- 61 Leichsenring F, Schauenburg H. Empirically supported methods of short-term psychodynamic therapy in depression - towards an evidence-based unified protocol. *J Affect Disord* 2014;169:128–43.
- 62 Barlow DH, Farchione TJ, Sauer-Zavala S, et al. *Unified protocol for transdiagnostic treatment of emotional disorders: therapist guide*. Oxford University Press, 2017.
- 63 Narushima K, Robinson RG. The effect of early versus late antidepressant treatment on physical impairment associated with poststroke depression: is there a time-related therapeutic window? *J Nerv Ment Dis* 2003;191:645–52.
- 64 Association WM. World medical association declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013;310:2191–4.
- 65 Beesdo-Baum K, Zaudig M, Wittchen H. *Strukturiertes Klinisches Interview für DSM-5-Störungen – Klinische Version [The Structured Clinical Interview for DSM-5 Disorders – Clinical Version]*. Hogrefe, 2019.
- 66 Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56–62.
- 67 Berg A, Lönnqvist J, Palomäki H, et al. Assessment of depression after stroke: a comparison of different screening instruments. *Stroke* 2009;40:523–9.
- 68 Spitzer RL, Kroenke K, Williams JBW, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006;166:1092–7.
- 69 Lin M, Hirschfeld G, Margraf J. Brief form of the perceived social support questionnaire (F-Sozu K-6): validation, norms, and cross-cultural measurement invariance in the USA, Germany, Russia, and China. *Psychol Assess* 2019;31:609–21.
- 70 Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;20:1727–36.
- 71 Nasreddine ZS, Phillips NA, Bédirian V, et al. The montreal cognitive assessment, Moca: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005;53:695–9.
- 72 Burton L-J, Tyson S. Screening for mood disorders after stroke: a systematic review of psychometric properties and clinical utility. *Psychol Med* 2015;45:29–49.
- 73 Mahoney FI, Barthel DW. Functional evaluation: the barthel index. *Md State Med J* 1965;14:61–5.
- 74 Kutlubaev MA, Hackett ML. Part II: predictors of depression after stroke and impact of depression on stroke outcome: an updated systematic review of observational studies. *Int J Stroke* 2014;9:1026–36.
- 75 Brott T, Adams HP Jr, Olinger CP, et al. Measurements of acute cerebral infarction: a clinical examination scale. *Stroke* 1989;20:864–70.
- 76 van Dijk MJ, de Man-van Ginkel JM, Hafsteinsdóttir TB, et al. Psychometric properties of the dutch version of the signs of depression scale. *Clin Nurs Res* 2018;27:617–37.
- 77 RANKIN J. Cerebral vascular accidents in patients over the age of 60: II. *Scott Med J* 1957;2:200–15.
- 78 Wilson JTL, Hareendran A, Grant M, et al. Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin scale. *Stroke* 2002;33:2243–6.
- 79 Raes F, Pommier E, Neff KD, et al. Construction and factorial validation of a short form of the self-compassion scale. *Clin Psychol Psychother* 2011;18:250–5.
- 80 Arbeitskreis OP. Operationalisierte psychodynamische diagnostik OPD-2. In: *Das Manual für Diagnostik und Therapieplanung*. Bern: Huber, 2006.
- 81 Dahlbender RW, Rudolf G, OPD TF. Psychic structure and mental functioning: current research on the reliable measurement and clinical validity of operationalized psychodynamic diagnostics (OPD) system. In: *Psychodynamic Diagnostic Manual*. 2006: 615–62.
- 82 Ehrenthal J, Dinger U, Lamla A, et al. Evaluation der deutschsprachigen version des Bindungsfragebogens "experiences in close relationships--revised. *Psychother Psych Med* 2009;59:215–23.
- 83 Ehrenthal JC, Dinger U, Schauenburg H, et al. Entwicklung Einer Zwölf-item-version des OPD-Strukturfragebogens (OPD-SFK)/Development of a 12-item version of the OPD-structure questionnaire (OPD-SQS). *Zeitschrift Für Psychosomatische Medizin Und Psychotherapie* 2015;61:262–74.
- 84 Wilmers F, Munder T, Leonhart R, et al. Die Deutschsprachige version des working alliance inventory--short revised (WAI-SR)--Ein Schulenbergreifendes, Ökonomisches und Empirisch Validiertes instrument Zur Erfassung der Therapeutischen Allianz. *Klinische Diagnostik Und Evaluation* 2008;1:343–58.
- 85 Bordin ES. The Generalizability of the psychoanalytic concept of the working alliance. *Psychotherapy: Theory, Research & Practice* 1979;16:252–60.
- 86 Munder T, Wilmers F, Leonhart R, et al. Working alliance inventory-short revised (WAI-SR): Psychometric properties in outpatients and inpatients. *Clin Psychol Psychother* 2010;17:231–9.
- 87 Cocks K, Torgerson DJ. Sample size calculations for pilot randomized trials: a confidence interval approach. *J Clin Epidemiol* 2013;66:197–201.
- 88 Thabane L, Ma J, Chu R, et al. A Tutorial on pilot studies: the what, why and how. *BMC Med Res Methodol* 2010;10:1.
- 89 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.
- 90 Turner A, Hambridge J, White J, et al. Depression screening in stroke: a comparison of alternative measures with the structured diagnostic interview for the diagnostic and statistical manual of mental disorders, fourth edition (major depressive episode) as criterion standard. *Stroke* 2012;43:1000–5.
- 91 de Man-van Ginkel JM, Hafsteinsdóttir TB, Lindeman E, et al. Clinical manifestation of depression after stroke is it different from depression in other patient populations? *PLoS ONE* 2015;10:e0144450.
- 92 Unnebrink K, Windeler J. Intention-to-treat: methods for dealing with missing values in clinical trials of progressively deteriorating diseases. *Stat Med* 2001;20:3931–46.
- 93 Klatter R, Strauss B, Flückiger C, et al. Defining and assessing adverse events and harmful effects in psychotherapy study protocols: a systematic review. *Psychotherapy* 2022;60:130–48.