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## Internet- and mobile-based aftercare and follow-up for the tertiary prevention of mental disorders: Protocol of a systematic review and meta-analysis

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3 **Internet- and mobile-based aftercare and follow-up for the tertiary prevention of mental disor-**  
4 **ders: Protocol of a systematic review and meta-analysis**  
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## ABSTRACT

**Introduction:** Mental disorders are characterized by a high likelihood of symptom recurrence or chronicity. Tertiary prevention thus aims at promoting functionality and preventing relapse or readmission (e.g. rehabilitation, aftercare, follow-up, maintenance treatment). Internet- and mobile-based interventions may represent low-threshold and effective extensions to tertiary prevention measures.

**Objectives:** The planned systematic review and meta-analysis aims to synthesize and analyze existing evidence on the effectiveness of Internet- and mobile-based aftercare or follow-up in maintaining treatment effects and/or preventing recurrence in adults with mental disorders.

**Methods and analysis:** Electronic databases (PsycInfo, MEDLINE and CENTRAL) will be searched systematically, complemented by a hand-search of ongoing trials and reference lists of selected studies. Data extraction and evaluation will be conducted by two independent reviewers and quality will be assessed with the Cochrane Risk of Bias tool. Eligibility criteria for selecting studies will be: Randomized controlled trials of Internet- and mobile-based, psychological interventions for the tertiary prevention of mental disorders in an adult population. Primary outcome will be symptom severity. Secondary outcomes will be symptom recurrence rate and incidence rate of mental disorder. Further data items to be extracted will be: Study design characteristics (sample size, intervention design/type, control group, amount of human guidance, assessments, duration of intervention, lengths of follow-up assessment, study drop-out), type of mental disorder, target population items (e.g. age, gender), setting (e.g. country, environment), treatment engagement (e.g. treatment-drop-out rate, treatment fidelity) and assessment of additional outcome variables. Meta-analytic pooling will be conducted when data of included studies are comparable in terms of endpoints, assessments, and target mental disorder. Cumulative Evidence will be evaluated according to the GRADE framework.

**Ethics and dissemination:** Ethics approval is not required. Results from this review will be published in peer-reviewed journals and presented at international conferences.

**Systematic review registration:** PROSPERO CRD420170552289

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- This review will investigate modern technologies in tertiary prevention and will be the first to evaluate the effectiveness of Internet- and mobile-based interventions in maintaining treatment effects or preventing recurrence in adults with mental disorders.
- The differentiated findings will provide clinicians and public health policymakers with a valuable overview of the possibilities of IMIs in tertiary prevention.
- We will perform a sensitive search in electronic databases, complimented by hand-search of ongoing trials to allow for an optimal coverage of innovative developments.
- The present protocol follows the PRISMA-P guidelines.
- We plan to assess the confidence in the cumulative evidence with the GRADE system.

## INTRODUCTION

Mental disorders are not only highly prevalent[1] but are also characterized by frequent recurrence during lifetime or chronic courses[2–5]. Adverse effects of recurrence or chronicity can be severe and include elevated readmission rates[6], early retirement[7], reduced quality of life[8] and increased mortality[9].

Within all areas of health care, tertiary prevention is paramount to monitor and manage symptoms, prevent relapse and promote health and functioning in persons with mental disorders[10]. In terms of continuous care, tertiary prevention may therefore comprise psychosocial, pharmacological or vocational rehabilitation, aftercare, follow-up or maintenance treatment. In particular, the transition after inpatient treatment can be considered a vulnerable phase, in which convalescents have to transfer and maintain health behavior, initiate change and are confronted with various individual, social or occupational challenges[11].

Meta-analytic evidence suggests the efficacy of cognitive behavioral therapy (CBT)[12, 13], psychosocial interventions[14, 15], pharmacological maintenance treatment[16] or psychosomatic rehabilitation[17] in reducing symptom severity or relapse in mental disorders following acute treatment.

However, implementation strategies of tertiary prevention are very heterogeneous and vary between different health care systems, mental disorders and treatment modalities. In this regard, studies in psychiatric or chronic pain patients indicate an insufficient prescription of aftercare by clinicians[18, 19]. Other studies suggest a limited uptake or adherence of psychosocial or medical maintenance treatment in convalescents[20–23]. Reasons for non-participation in psychosocial aftercare may include long waiting-times[24], pessimistic treatment expectancies[21] or various organizational barriers[19]. On the other hand, insufficient resources of health care systems and medical costs may further limit an extensive implementation and lead to gaps in continuity of care[25].

In an effort to overcome these limitations, Internet-delivered health promotion and treatment options for mental disorders have been developed particularly in the last decade. Internet- and mobile-based Interventions (IMIs) can be administered cost-effectively and without local or temporal boundaries[26, 27]. Since Internet access and use are growing constantly across countries and age groups[28], IMIs are also a widely accessible instruments.

A growing amount of evidence suggests efficacy of web-based psychotherapeutic interventions for a wide range of mental conditions[29, 30]. With regard to the implementation of IMIs in different contexts of health care, a recent review by Sander and colleagues[31] found small to medium cross-diagnostic effect sizes ( $d = 0.11 - 0.76$ ) of IMIs in the primary prevention of mental disorders. Furthermore, a review by Niuwenhuijsen et al.[32] suggests efficacy of remote interventions (internet- or telephone-based) on return-to-work of depressed patients.

Previous studies on Internet- or mobile-based aftercare focused on guided, web-based self-help including psychoeducation as well as modular, interactive treatment elements and a certain amount of asynchronous therapist contact[33, 34]. Other approaches comprise mobile based[35] or synchronous, chat-

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3 or video-based aftercare[36, 37]. First evidence suggests the efficacy of IMIs in relapse prevention or  
4 reduction of symptom severity[33, 37].

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6 However, to the best of our knowledge, no previous systematic review has investigated comprehensive  
7 evidence on IMIs as tertiary prevention for adults with mental disorders. Thus, the results of this re-  
8 view will give an overview of this field of research and identify potentials of IMIs for public health  
9 policy makers and health care providers. The present protocol describes the rationale and design of the  
10 systematic review and planned meta-analysis according to the 'Preferred reporting items for systemat-  
11 ic review and meta-analysis protocols (PRISMA-P)'[38].  
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## 14 15 **Objectives**

16  
17 The aim of this systematic review and meta-analysis is to give a comprehensive overview of random-  
18 ized controlled trials (RCTs) investigating the effectiveness of psychological Internet- and mobile-  
19 based tertiary prevention (e.g. rehabilitation, aftercare, follow-up interventions) in maintaining treat-  
20 ment effects or in preventing symptom or disorder recurrence in adults who received treatment for  
21 mental disorders.  
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## 24 25 **METHODS**

### 26 27 **Eligibility criteria**

#### 28 29 **Population**

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31 Studies will be included if they (a) focus on an adult population (> 18 years) who (b) have received  
32 treatment for a mental disorder or have been diagnosed with a mental disorder in somatic treatment.  
33 Preceding treatment of mental disorder may consist of inpatient or outpatient psychotherapy, psychiat-  
34 ric treatment or medical treatment, delivered by physicians or psychotherapists. Mental disorders must  
35 (c) be assessed by a standardized or validated instrument, including standardized interviews (e.g.  
36 SCID, CIDI), validated self-reports (e.g. BDI, BAI, EDI), clinician-rated scales (e.g. HAMD, GAF) or  
37 diagnosis by health care professionals.  
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#### 40 41 **Study design and interventions**

42  
43 (e) Only randomized controlled trials that are available in full text (RCT) will be considered. Manu-  
44 scripts must be published in English or German. Treatment groups should receive a psychological  
45 aftercare or follow-up intervention. Following the definition by Kampling et al.[39], psychological  
46 interventions (f) may include elements of evidence-based therapy forms (cognitive behavioral therapy,  
47 psychodynamic therapies, behavior therapy or behavior modification, systemic therapies, third wave  
48 cognitive behavioral therapies, humanistic therapies, integrative therapies). Interventions may contain  
49 psychoeducation, reinforcement/feedback mechanisms as well as interactive elements or comprise  
50 guided/unguided self-help or comprehensive psychotherapeutic programs. Treatments not clearly de-  
51 scribed will be excluded.  
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(g) Aftercare and follow-up will be defined as interventions for convalescent patients designed to monitor and stabilize symptoms, identify and manage warning signs of symptom recurrence or enhance coping strategies to prevent recurrence, relapse or readmission[40], support transition and adoption of acquired health behavior and to promote or preserve health status, thereby reducing the impact of the illness on functioning or quality of life.

(h) Interventions have to be delivered predominantly in an online setting, via Internet (web-/online) or mobile applications. Interventions may vary in the amount of human support, ranging from unguided self-help, over asynchronous minimal guidance to synchronous therapist contact[41].

Studies must (i) report a minimum follow-up assessment of the main outcome of three months after the end of preceding treatment. Follow-up period of 3-6 months will be categorized as 'short', 6-12 months as 'medium' and above as 'long-term'.

#### Comparators

(i) Control groups may receive either no intervention or comprise a waiting list (inactive control group) or include treatment as usual, another form of treatment (e.g. face-to-face psychotherapy, phone-delivered-, pharmacological/placebo treatment, other forms of psychological interventions) where Internet or mobile applications are not the predominant methods (active control group).

#### Exclusion criteria

Studies will be excluded, if they focus on the prevention of the first onset of a mental disorder or if no distinguishable treatment preceded the intervention under study (stand-alone interventions). Substance-related and addictive disorders will not be included, as this represents another specific research area[42, 43] and treatment rationales are predominantly socio-educational or follow a health behavior change model rather than psychotherapeutic intervention models.

#### Information sources and search strategy

Electronic databases that will be included are Medline, PsycInfo and the Cochrane Central Register of Controlled trials (CENTRAL). A sensitive search strategy will be applied (see supplementary file 1). The WHO International Clinical Trials Registry Platform (ICTRP) will be hand searched to identify ongoing trials. To assure literature saturation, reference lists of included studies will be perused. In case of unclear eligibility or indication of missing or unpublished data, we will contact the principal investigators (PIs) of studies for clarification. Also, when study protocols without a succeeding publication of results are identified, we attempt to contact PI to obtain unpublished results and determine eligibility for inclusion.

#### Study records

In a first step, two independent reviewers (SF, SH) will screen titles and abstracts of the database search to identify qualified studies. Records will be managed in CITAVI®. In a second step, these reviewers will examine full texts in terms of the eligibility criteria. Likewise, the reference lists will be

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3 screened against eligibility criteria. In case of disagreement on eligibility, a third reviewer (LS) will be  
4 consulted. Inter-rater-reliability will be analyzed to illustrate the consistency of study selection. To  
5 illustrate the search and selection process, a flow-chart according to the PRISMA-protocol[38] will be  
6 provided. Criteria for the exclusion of studies will be reported.

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9 Extracted data of eligible studies will be verified by a second reviewer to assure accuracy. Disagree-  
10 ment will be solved by discussion or by consulting a third reviewer in case of unresolved disagree-  
11 ments. Data extraction forms will be developed and piloted. In case of overlapping or multiple re-  
12 ports, we plan to compare studies with regard to list of authors, sample sizes, treatments or outcomes.  
13 In case of unclear or missing information, we will contact PIs with a request to provide these data.  
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### 16 17 **Data items**

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19 The following data items will be extracted for each study: (a) study identification items (first author,  
20 year of publication), (b) study design characteristics (e.g. sample size, intervention design/type, tech-  
21 nical implementation, control group, pre-treatment, amount of human guidance, assessments, duration  
22 of intervention, lengths of follow-up assessment, study drop-out), (c) type of mental disorder or clini-  
23 cal symptom to be treated, (d) target population items (e.g. age, gender), (e) setting (e.g. recruitment  
24 strategy, nationality, environment), (f) treatment engagement (e.g. treatment-drop-out rate, treatment  
25 fidelity), (g) assessment of additional outcome variables, (h) clinical outcome (symptom severi-  
26 ty/recurrence).  
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### 31 32 **Outcomes and prioritization**

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34 Primary outcome will be symptom severity assessed via validated instruments (standardized inter-  
35 views, self- or clinician-rated scales) or clinical diagnosis as an indicator of maintenance of treatment  
36 effects.  
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39 Secondary outcomes will be defined as (a) symptom recurrence rate or (b) incidence rate of mental  
40 disorder under study from post-treatment to latest available follow-up.

41  
42 In the likely case of multiple assessment instruments for primary or secondary outcome, we will pri-  
43 oritize data as follows: (1) Data from structured interviews will be prioritized. (2) Clinician-rated  
44 scales will be preferred over self-report instruments. (3) Self-report questionnaires will be prioritized  
45 over diagnosis by health professionals.  
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48 When several assessment instruments are used within one study that can be assigned to the same hier-  
49 archy level, we will (1) extract outcome of the most frequently used instrument according to eligible  
50 studies or (2) if not evident, select randomly. To control for an investigator bias, a second reviewer  
51 (SH) will cross-check the extraction process.  
52

### 53 54 **Risk of bias in individual studies**

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56 The quality of evidence of each study will be evaluated following the Cochrane Risk of Bias tool[44].  
57 The domains to be analyzed will be: (a) random sequence generation, (b) allocation concealment, (c)  
58

blinding of participants and personnel, (d) blinding of outcome assessment, (e) incomplete outcome data, (f) selective outcome reporting and (g) other threats to validity (e.g. treatment fidelity, parallelism of measurement, variance homogeneity at baseline, co-interventions).

As a distinctive feature of psychological interventions, blinding of health care providers (in guided Internet- or mobile-based intervention studies) or patients regarding treatment is not warranted, resulting in a high risk of bias rating of criterion (c). However, outcome assessors can remain unaware of participant's treatment allocation (criterion (d)).

### **Data synthesis**

#### **Qualitative synthesis**

A narrative synthesis will be reported on all included studies and relevant characteristics listed under 'data items' will be qualitatively described. A detailed description of their results on relevant domains will be provided in text and 'summary of findings' tables (comparison against control groups) following the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P)[38].

#### **Meta-Analysis**

Meta-analytic pooling will be conducted, if comparability of included studies in terms of endpoints, assessments, and target mental disorder is met in at least three studies. The Cochrane Collaborations' Review Manager<sup>®</sup> will be used. By separating analyses in terms of mental disorders, we plan to reduce heterogeneity of pooled estimates. A random-effects model will be used. Only studies with less than substantial statistical heterogeneity will be pooled. If possible, heterogeneity of study results will be analyzed through forest plots and calculating  $I^2$  statistics. The degree of heterogeneity will then be categorized according to the guidelines of the Risk of Bias tool[45].

For continuous data, we will calculate the standardized mean difference (SMD) and 95% confidence intervals. For dichotomous data, we will transform findings into risk ratios (RR). We aim to calculate the number needed to treat (NNT) to further illustrate clinical relevance of the interventions.

Outcome variables (e.g. symptom severity scores) will be pooled and further differentiated in terms of 'short', 'medium' or 'long-term' effectiveness when follow-up assessment is reported. Subject to sufficient group size and comparability of assessment, we plan to analyze study level covariates (e.g. type of mental disorder, type of Internet- or mobile-based intervention, amount of guidance).

#### **Meta-biases - confidence in cumulative evidence**

We will retrieve study protocols or trial registrations to identify reporting biases. Thereby, we will evaluate whether selective reporting of outcomes is present. A possible small sample bias will be assessed by using a random-effect-model. Provided the number of studies is sufficient, we plan to examine a possible publication bias of significant-only studies in funnel plots. We will also search for unpublished or non-significant studies.



We plan to rate the cumulative evidence according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE)[46] in terms of study limitations, inconsistency of results, indirectness of evidence, imprecision of effect estimates reporting bias. Quality of evidence will be categorized into ‘very low’, ‘low’, ‘moderate’, or ‘high’.

## **CONCLUSION**

This systematic review and meta-analysis will complement the evidence base of IMIs and allow for an evaluation of their potential in tertiary prevention as a significant component of mental health care. The findings will extend previous literature on the effectiveness of IMIs in different areas of health care like prevention[31] or as an alternative to face-to-face therapy[47]. Furthermore, the results will provide clinicians and public health policymakers with a valuable overview of the possibilities of IMIs in monitoring and managing patients after regular treatment and in preventing relapse or readmission.

## **ABBREVIATIONS**

BAI: Beck Anxiety Inventory

BDI: Beck Depression Inventory

CBT: Cognitive Behavioral Therapy

CENTRAL: Cochrane Central Register of Controlled trials

CIDI: Composite International Diagnostic Interview

EDI: Eating Disorder Inventory

GAF: Global Assessment of Functioning

HAMD: Hamilton Depression Scale

ICTRP: WHO International Clinical Trials Registry Platform

IMIs: Internet- and mobile-based interventions

PI: Principal investigator

PRISMA-P: Preferred reporting items for systematic review and meta-analysis protocols

RCT: Randomized controlled trials

RR: Risk ratios

SCID: Structured Clinical Interview for DSM Disorders

SMD: Standardized mean difference

NNT: Number needed to treat

## **CONTRIBUTORSHIP STATEMENT**

All authors were involved in the concept and review design of the study and data analysis plan. SH and SF wrote the draft of this manuscript. LS provided valuable revisions. All authors contributed to the further writing and approved the final version of the manuscript.

## **COMPETING INTERESTS**

None declared.

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## DATA SHARING STATEMENT

No additional unpublished data available.

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29 tobacco use: a meta-analysis. *Addiction* 2010;105(8):1381–90. doi:10.1111/j.1360-  
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33 risk of bias in randomised trials. *BMJ* 2011;343:d5928. doi:10.1136/bmj.d5928.  
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36 risk of bias in randomised trials. *BMJ* 2011;343:d5928. doi:10.1136/bmj.d5928.  
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**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Page No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	1	Identify the report as a protocol of a systematic review
Update	1b	--	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:			
Contact	3a	1	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	8	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	--	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:			
Sources	5a	9	Indicate sources of financial or other support for the review
Sponsor	5b	9	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	9	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>			
Rationale	6	3-4	Describe the rationale for the review in the context of what is already known
Objectives	7	4	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
<b>METHODS</b>			
Eligibility criteria	8	4-5	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	5	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	5	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated

Study records:			
Data management	11a	5	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	5-6	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	6	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	6	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	6	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	6-7	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	7	Describe criteria under which study data will be quantitatively synthesised
	15b	7	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )
	15c	7	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	7	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	7-8	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	7-8	Describe how the strength of the body of evidence will be assessed (such as GRADE)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

	<b>MEDLINE via PuPubMed</b>	<b>PsycINFO via Ebsco®</b>	<b>CENTRAL</b>
S1	Aftercare[Mesh]	MA "Aftercare"	MeSH descriptor: [Aftercare] explode all trees
S2	Recurrence[Mesh]	MA "Recurrence"	MeSH descriptor: [Recurrence] explode all trees
S3	Relapse Prevention[Mesh]	MA "Relapse prevention"	MeSH descriptor: [Relapse prevention] explode all trees
S4	Tertiary Prevention[Mesh]	MA "Tertiary Prevention"	MeSH descriptor: [Tertiary Prevention] explode all trees
S5	Convalescence[Mesh]	MA "Convalescence"	MeSH descriptor: [Convalescence] explode all trees
S6	(aftercare[tiab] OR after-care [tiab])	TI,AB aftercare	aftercare:ti,ab,kw in Trials
S7	(after-treatment*[tiab] OR "after treatment" [tiab])	(TI,AB after-treatment* OR TI,AB "after treatment*")	(after-treatment*:ti,ab,kw OR "after treatment*":ti,ab,kw in Trials)
S8	relaps*[tiab]	TI,AB relaps*	relaps*:ti,ab,kw in Trials
S9	follow-up[tiab]	TI,AB follow-up	follow-up:ti,ab,kw in Trials
S10	"intervention following*" [tiab]	TI,AB "intervention following*"	"intervention following*":ti,ab,kw in Trials
S11	rehabilitation*[tiab]	TI,AB rehabilitation*	rehabilitation*:ti,ab,kw in Trials
S12	(tele-rehabilitation*[tiab] OR Telerehabilitation*[tiab])	(TI,AB tele-rehabilitation* OR TI,AB telerehabilitation*)	(tele-rehabilitation*:ti,ab,kw OR telerehabilitation*:ti,ab,kw in Trials)
S13	(post-treatment*[tiab] OR "post treatment*" [tiab])	(TI,AB post-treatment* OR TI,AB "post treatment*")	(post-treatment*:ti,ab,kw OR "post treatment*":ti,ab,kw in Trials)
S14	"treatment after inpatient"[tiab]	TI,AB "treatment after inpatient"	"treatment after inpatient":ti,ab,kw in Trials
S15	recovery[tiab]	TI,AB recovery	recovery:ti,ab,kw in Trials
S16	"maintenance treatment"[tiab]	TI,AB "maintenance treatment"	"maintenance treatment":ti,ab,kw in Trials
S17	"continuation treatment"[tiab]	TI,AB "continuation treatment"	"continuation treatment":ti,ab,kw in Trials
S18	continuation-phase[tiab]	TI,AB continuation-phase	continuation-phase:ti,ab,kw in Trials
S19	"tertiary prevention"[tiab]	TI,AB "tertiary prevention"	"tertiary prevention":ti,ab,kw in Trials
S20	"continuous care"[tiab]	TI,AB "continuous care"	"continuous care":ti,ab,kw in Trials
S21	"disease management*" [tiab]	TI,AB "disease management*"	"disease management*":ti,ab,kw in Trials
S22	recurrence[tiab]	TI,AB recurrence	recurrence:ti,ab,kw in Trials
S23	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
S24	Telemedicine[Mesh]	MA "Telemedicine+"	MeSH descriptor: [Telemedicine] explode all trees
S25	Computer Assisted Instruction[Mesh]	MA "Computer Assisted Instruction"	MeSH descriptor: [Computer Assisted Instruction] explode all trees



	MEDLINE via PuPubMed	PsycINFO via Ebsco®	CENTRAL
S26	Mobile Health Units[Mesh]	MA "Mobile Health Units"	MeSH descriptor: [Mobile Health Units] explode all trees
S27	Therapy, Computer-Assisted[Mesh]	MA "Therapy, Computer-Assisted+"	MeSH descriptor: [Therapy, Computer-Assisted] explode all trees
S28	Mobile Applications[Mesh]	MA "Mobile Applications"	MeSH descriptor: [Mobile Applications] explode all trees
S29	Internet[Mesh]	MA "Internet+"	MeSH descriptor: [Internet ] explode all trees
S30	"computer applications"[tiab]	TI,AB "computer applications"	"computer applications":ti,ab,kw in Trials
S31	ICBT[tiab]	TI,AB ICBT	ICBT:ti,ab,kw in Trials
S32	telemental[tiab]	TI,AB telemental	telemental:ti,ab,kw in Trials
S33	e-therapy[tiab]	TI,AB e-therapy	e-therapy:ti,ab,kw in Trials
S34	CD-ROM[tiab]	TI,AB CD-ROM	CD-ROM:ti,ab,kw in Trials
S35	mhealth[tiab]	TI,AB mhealth	mhealth:ti,ab,kw in Trials
S36	(e-mail [tiab] OR email [tiab])	(TI,AB e-mail OR TI,AB email)	(e-mail:ti,ab,kw OR email:ti,ab,kw in Trials)
S37	SMS[tiab]	TI,AB SMS	SMS:ti,ab,kw in Trials
S38	app[tiab]	TI,AB app	app:ti,ab,kw in Trials
S39	ICT[tiab]	TI,AB ICT	ICT:ti,ab,kw in Trials
S40	online[tiab]	TI,AB online	online:ti,ab,kw in Trials
S41	mobile[tiab]	TI,AB mobile	mobile:ti,ab,kw in Trials
S42	eHealth[tiab]	TI,AB eHealth	eHealth:ti,ab,kw in Trials
S43	(web-based[tiab] OR "web based" [tiab])	(TI,AB web-based OR "web based" TI,AB)	(web-based:ti,ab,kw OR "web based":ti,ab,kw in Trials)
S44	(computer-based[tiab] OR "computer based"[tiab])	(TI,AB computer-based OR TI,AB "computer based")	(computer-based:ti,ab,kw in Trials OR "computer based":ti,ab,kw in Trials)
S45	computerized[tiab]	TI,AB computerized	computerized:ti,ab,kw in Trials
S46	"world wide web"[tiab]	TI,AB "world wide web"	"world wide web":ti,ab,kw in Trials
S47	cyber[tiab]	TI,AB cyber	cyber:ti,ab,kw in Trials
S48	ccbt[tiab]	TI,AB ccbt	ccbt:ti,ab,kw in Trials
S49	(mobile-based [tiab] OR "mobile based"[tiab])	(TI,AB "mobile based" OR TI,AB mobile-based)	(mobile-based:ti,ab,kw OR "mobile based":ti,ab,kw in Trials)
S50	internet[tiab]	TI,AB internet	internet:ti,ab,kw in Trials
S51	(computer-assisted[tiab] OR "computer assisted"[tiab])	(TI,AB computer assisted OR TI,AB "computer assisted")	(computer-assisted:ti,ab,kw OR "computer assisted":ti,ab,kw in Trials)
S52	S24 OR S25 OR S26 Or S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51	S24 OR S25 OR S26 Or S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51	24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51
S53	Mental Disorders[Mesh]	MA "Mental Disorders+"	MeSH descriptor: [Mental Disorders] explode all trees
S54	Mental health[Mesh]	MA "Mental health+"	MeSH descriptor: [Mental health] explode all trees
S55	Mentally Ill Persons[Mesh]	MA "Mentally Ill Persons"	MeSH descriptor: [Mentally Ill Persons] explode all trees

	<b>MEDLINE via PuPMed</b>	<b>PsycINFO via Ebsco®</b>	<b>CENTRAL</b>
S56	"mental distress"[tiab]	TI,AB "mental distress"	"mental distress":ti,ab,kw in Trials
S57	"psychiatric disorder*"[tiab]	TI,AB "psychiatric disorder*"	"psychiatric disorder*":ti,ab,kw in Trials
S58	"psychological disorder*"[tiab]	TI,AB "psychological disorder*"	"psychological disorder*":ti,ab,kw in Trials
S59	"mental illness*"[tiab]	TI,AB "mental illness*"	"mental illness*":ti,ab,kw in Trials
S60	"Mental disorder*" [tiab]	TI,AB "mental disorder*"	"mental disorder*":ti,ab,kw in Trials
S61	Substance-Related Disorders[Mesh]	MA "Substance-Related Disorders+"	MeSH descriptor: [Substance-Related Disorders] explode all trees
S62	Alcohol-Related Disorders[Mesh]	MA "Alcohol-Related Disorders+"	MeSH descriptor: [Alcohol-Related Disorders] explode all trees
S63	"alcohol dependence"[tiab]	TI,AB "alcohol dependence"	"alcohol dependence":ti,ab,kw in Trials
S64	"alcohol abuse"[tiab]	TI,AB "alcohol abuse"	"alcohol abuse":ti,ab,kw in Trials
S65	"substance abuse"[tiab]	TI,AB "substance abuse"	"substance abuse":ti,ab,kw in Trials
S66	"substance-related disorder*"[tiab]	TI,AB "substance-related disorder*"	"substance-related disorder*":ti,ab,kw in Trials
S67	"alcohol-related disorder*"[tiab]	TI,AB "alcohol-related disorder*"	"alcohol-related disorder*":ti,ab,kw in Trials
S68	Psychotic Disorders[Mesh]	MA "Psychotic Disorders+"	MeSH descriptor:[Psychotic Disorders] explode all trees
S69	Schizophrenia[Mesh]	MA "Schizophrenia+"	MeSH descriptor:[Schizophrenia] explode all trees
S70	psychotic[tiab]	TI,AB psychotic	psychotic:ti,ab,kw in Trials
S71	schizophren*[tiab]	TI,AB schizophren *	schizophren*:ti,ab,kw in Trials
S72	Affective Disorders, Psychotic[Mesh]	MA "Affective Disorders, Psychotic+"	MeSH descriptor: [Affective Disorders, Psychotic] explode all trees
S73	Mood Disorders[Mesh]	MA "Mood Disorders+"	MeSH descriptor: [Mood Disorders] explode all trees
S74	Depression[Mesh]	MA "Depression"	MeSH descriptor: [Depression] explode all trees
S75	Bipolar Disorder[Mesh]	MA "Bipolar Disorder+"	MeSH descriptor: [Bipolar Disorder] explode all trees
S76	Dysthymic Disorder[Mesh]	MA "Dysthymic Disorder"	MeSH descriptor: [Dysthymic Disorder] explode all trees
S77	Depressive Disorder[Mesh]	MA "Depressive Disorder+"	MeSH descriptor: [Depressive Disorder] explode all trees
S78	Depressive Disorder, Major[Mesh]	MA "Depressive Disorder, Major+"	MeSH descriptor: [Depressive Disorder, Major]
S79	"affective disorder*"[tiab]	TI,AB "affective disorder*"	"affective disorder*":ti,ab,kw in Trials
S80	depressive[tiab]	TI,AB depressive	depressive:ti,ab,kw in Trials
S81	depression[tiab]	TI,AB depression	depression:ti,ab,kw in Trials
S82	"mood disorder*"[tiab]	TI,AB "mood disorder*"	"mood disorder*":ti,ab,kw in Trials
S83	bipolar*[tiab]	TI,AB bipolar*	bipolar*:ti,ab,kw in Trials

	MEDLINE via PuPMed	PsycINFO via Ebsco®	CENTRAL
S84	dysthymi*[tiab]	TI,AB dysthymic	dysthymic:ti,ab,kw in Trials
S85	cyclothymi * [tiab]	TI,AB cyclothymi*	cyclothymi* Title/Abstract]
S86	Anxiety Disorders[Mesh]	MA "Anxiety Disorders+"	MeSH descriptor: [Anxiety Disorders] explode all trees
S87	Panic[Mesh]	MA "Panic"	MeSH descriptor: [Panic] explode all trees
S88	Panic Disorder[Mesh]	MA "Panic Disorder"	MeSH descriptor: [Panic Disorder] explode all trees
S89	Phobic Disorders[Mesh]	MA "Phobic Disorders"	MeSH descriptor: [Phobic Disorders] explode all trees
S90	Socia Phobia[Mesh]	MA "Social Phobia"	MeSH descriptor: [Social Phobia] explode all trees
S91	Agoraphobia[Mesh]	MA "Agoraphobia"	MeSH descriptor: [Agoraphobia] explode all trees
S92	"anxiety disorder*" [tiab]	TI,AB "anxiety disorder*"	"anxiety disorder*":ti,ab,kw in Trials
S93	panic[tiab]	TI,AB panic	panic:ti,ab,kw in Trials
S94	phobi*[tiab]	TI,AB phobi*	phobi*:ti,ab,kw in Trials
S95	agoraphobi*[tiab]	TI,AB agoraphobi*	agoraphobi*:ti,ab,kw in Trials
S96	"social anxiety" [tiab]	TI,AB "social anxiety"	"social anxiety:ti,ab,kw in Trials
S97	"generalized anxiety disorder" [tiab]	TI,AB "generalized anxiety disorder"	"generalized anxiety disorder":ti,ab,kw in Trials
S98	Obsessive-Compulsive Disorder[Mesh]	MA "Obsessive-Compulsive Disorder+"	MeSH descriptor: [Obsessive-Compulsive Disorder] explode all trees
S99	Disruptive, Impulse Control, and Conduct Disorders[Mesh]	MA "Disruptive, Impulse Control, and Conduct Disorders+"	MeSH descriptor: [Disruptive, Impulse Control, and Conduct Disorders] explode all trees
S100	Stress Disorders, Post-Traumatic[Mesh]	MA "Stress Disorders, Post-Traumatic"	MeSH descriptor: [Stress Disorders, Post-Traumatic] explode all trees
S101	Stress Disorders, Traumatic[Mesh]	MA "Stress Disorders, Traumatic+"	MeSH descriptor: [Stress Disorders, Traumatic] explode all trees
S102	Adjustment Disorders[Mesh]	MA "Adjustment Disorders"	MeSH descriptor: [Adjustment Disorders] explode all trees
S103	PTSD[tiab]	TI,AB PTSD	PTSD:ti,ab,kw in Trials
S104	"posttraumatic stress disorder*" [tiab]	TI,AB "posttraumatic stress disorder*"	"posttraumatic stress disorder*":ti,ab,kw in Trials
S105	"obsessive-compulsive disorder*" [tiab]	TI,AB "obsessive-compulsive disorder*"	"obsessive-compulsive disorder*":ti,ab,kw in Trials
S106	"impulse control disorder*" [tiab]	TI,AB "impulse control disorder*"	"impulse control disorder*":ti,ab,kw in Trials
S107	"stress disorder*, post-traumatic" [tiab]	TI,AB "stress disorder*, post-traumatic"	"stress disorder*, post-traumatic":ti,ab,kw in Trials
S108	"stress disorder*, traumatic" [tiab]	TI,AB "stress disorder*, traumatic"	"stress disorder*, traumatic":ti,ab,kw in Trials
S109	"adjustment disorder*" [tiab]	TI,AB "adjustment disorder*"	"adjustment disorder*":ti,ab,kw in Trials
S110	"Somatoform Disorders"[Mesh]	MA "Somatoform Disorders+"	MeSH descriptor: [Somatoform Disorders] explode all trees

	MEDLINE via PuPubMed	PsycINFO via Ebsco®	CENTRAL
S111	"Body Dysmorphic Disorders"[Mesh]	MA "Body Dysmorphic Disorders"	MeSH descriptor: [Body Dysmorphic Disorders]
S112	"Conversion Disorder"[Mesh]	MA "Conversion Disorder+"	MeSH descriptor: [Conversion Disorder ] explode all trees
S113	"Hypochondriasis"[Mesh]	MA "Hypochondriasis"	MeSH descriptor: [Hypochondriasis ] explode all trees
S114	"Medically Unexplained Symptoms"[Mesh]	MA "Medically Unexplained Symptoms"	MeSH descriptor: [Medically Unexplained Symptoms] explode all trees
S115	somatoform[tiab]	TI,AB somatoform	somatoform:ti,ab,kw in Trials
S116	"somatic symptom disorder*" [tiab]	TI,AB "somatic symptom disorder*"	"somatic symptom disorder*":ti,ab,kw in Trials
S117	"body dysmorphic disorders" [tiab]	TI,AB "body dysmorphic disorders"	"body dysmorphic disorders":ti,ab,kw in Trials
S118	"conversion disorder" [tiab]	TI,AB "conversion disorder"	"conversion disorder":ti,ab,kw in Trials
S119	hypochondriasis[tiab]	TI,AB hypochondriasis	hypochondriasis:ti,ab,kw in Trials
S120	"illness anxiety disorder" [tiab]	TI,AB "illness anxiety disorder"	"illness anxiety disorder":ti,ab,kw in Trials
S121	"medically unexplained*" [tiab]	TI,AB "medically unexplained*"	"medically unexplained*":ti,ab,kw in Trials
S122	somatization[tiab]	TI,AB somatization	somatization:ti,ab,kw in Trials
S123	"pain disorder" [tiab]	TI,AB "pain disorder"	"pain disorder":ti,ab,kw in Trials
S124	"chronic pain" [tiab]	TI,AB "chronic pain"	"chronic pain":ti,ab,kw in Trials
S125	("premenstrual syndrome" [tiab] OR "pre-menstrual syndrome" [tiab])	(TI,AB "premenstrual syndrome" OR TI,AB OR "pre-menstrual syndrome")	("premenstrual syndrome":ti,ab,kw OR "pre-menstrual syndrome":ti,ab,kw in Trials)
S126	"irritable bowel syndrome" [tiab]	TI,AB "irritable bowel syndrome"	"irritable bowel syndrome":ti,ab,kw in Trials
S127	fibromyalgia[tiab]	TI,AB fibromyalgia	fibromyalgia:ti,ab,kw in Trials
S128	"chronic fatigue" [tiab]	TI,AB "chronic fatigue"	"chronic fatigue":ti,ab,kw in Trials
S129	"tension headache" [tiab]	TI,AB "tension headache"	"tension headache":ti,ab,kw in Trials
S130	Dissociative Disorders[Mesh]	MA "Dissociative Disorders+"	MeSH descriptor: [Dissociative Disorders] explode all trees
S131	Depersonalization"[Mesh]	MA "Depersonalization"	MeSH descriptor: [Depersonalization] explode all trees
S132	"dissociative disorder*" [tiab]	TI,AB "dissociative disorder*"	"dissociative disorder*":ti,ab,kw in Trials
S133	depersonalization[tiab]	TI,AB depersonalization	depersonalization:ti,ab,kw in Trials
S134	derealization[tiab]	TI,AB derealization	derealization:ti,ab,kw in Trials
S135	Feeding and Eating Disorders[Mesh]	MA "Feeding and Eating Disorders+"	MeSH descriptor: [Feeding and Eating Disorders] explode all trees
S136	Anorexia[Mesh]	MA "Anorexia"	MeSH descriptor: [Anorexia] explode all trees
S137	Anorexia Nervosa[Mesh]	MA "Anorexia Nervosa"	MeSH descriptor: [Anorexia Nervosa] explode all trees

	MEDLINE via PuPMed	PsycINFO via Ebsco®	CENTRAL
S138	Bulimia[Mesh]	MA "Bulimia"	MeSH descriptor: [Bulimia] explode all trees
S139	Bulimia Nervosa[Mesh]	MA "Bulimia Nervosa"	MeSH descriptor: [Bulimia Nervosa] explode all trees
S140	Binge-Eating Disorder[Mesh]	MA "Binge-Eating Disorder"	MeSH descriptor: [Binge-Eating Disorder] explode all trees
S141	anorexia[tiab]	TI,AB anorexia	anorexia:ti,ab,kw in Trials
S142	bulimia[tiab]	MA "bulimia"	bulimia:ti,ab,kw in Trials
S143	"eating disorder*" [tiab]	TI,AB "eating disorder*"	"eating disorder*":ti,ab,kw in Trials
S144	("binge eating"[tiab] OR binge-eating[tiab])	(TI,Ab "binge eating" OR TI,Ab binge-eating)	(binge-eating:ti,ab,kw in Trials OR "binge-eating":ti,ab,kw in Trials)
S145	"Sexual Dysfunctions, Psychological"[Mesh]	MA "Sexual Dysfunctions, Psychological"	MeSH descriptor: [Sexual Dysfunctions, Psychological] explode all trees
S146	"gender dysphoria"[tiab]	TI,AB "gender dysphoria"	"gender dysphoria":ti,ab,kw in Trials
S147	"sexual dysfunction*" [tiab]	TI,AB "sexual dysfunction*"	"sexual dysfunction*":ti,ab,kw in Trials
S148	"sexual pain disorder*" [tiab]	TI,AB "sexual pain disorder*"	"sexual pain disorder*":ti,ab,kw in Trials
S149	"orgasmic disorder*" [tiab]	TI,AB "orgasmic disorder*"	"orgasmic disorder*":ti,ab,kw in Trials
S150	"sexual arousal disorder*" [tiab]	TI,AB "sexual arousal disorder*"	"sexual arousal disorder*":ti,ab,kw in Trials
S151	"gender identity disorder*" [tiab]	TI,AB "gender identity disorder*"	"gender identity disorder*":ti,ab,kw in Trials
S152	"disorders of sexual preference" [tiab]	TI,AB "disorders of sexual preference"	"disorders of sexual preference":ti,ab,kw in Trials
S153	"Sleep Wake Disorders"[Mesh]	MA "Sleep Wake Disorders+"	MeSH descriptor: [Sleep Wake Disorders] explode all trees
S154	"Sleep Initiation and Maintenance Disorders"[Mesh]	MA "Sleep Initiation and Maintenance Disorders"	MeSH descriptor: [Sleep Initiation and Maintenance Disorders] explode all trees
S155	insomnia[tiab]	TI,AB insomnia	insomnia:ti,ab,kw in Trials
S156	"sleep disorder*" [tiab]	TI,AB "sleep disorder*"	"sleep disorder*":ti,ab,kw in Trials
S157	Attention Deficit Disorder [Mesh]	MA "Attention Deficit Disorder+"	MeSH descriptor: [Attention Deficit Disorder] explode all trees
S158	Attention Deficit Disorder with Hyperactivity[Mesh]	MA "Attention Deficit Disorder with Hyperactivity"	MeSH descriptor: [Attention Deficit Disorder with Hyperactivity] explode all trees
S159	"attention-deficit disorder" [tiab]	TI,AB "attention-deficit disorder"	"attention-deficit disorder":ti,ab,kw in Trials
S160	"attention deficit hyperactivity disorder" [tiab]	TI,AB "attention deficit hyperactivity disorder"	"attention deficit hyperactivity disorder":ti,ab,kw in Trials
S161	Personality Disorders[Mesh]	MA "Personality Disorders+"	MeSH descriptor: [Personality Disorders] explode all trees
S162	"personality disorder*" [tiab]	TI,AB "personality disorder*"	MeSH descriptor: [personality disorder*]:ti,ab,kw in Trials
S163	Antisocial Personality Disorder[Mesh]	MA "Antisocial Personality Disorder"	MeSH descriptor: [Antisocial Personality Disorder] explode all trees

	<b>MEDLINE via PuPMed</b>	<b>PsycINFO via Ebsco®</b>	<b>CENTRAL</b>
S164	Borderline Personality Disorder[Mesh]	MA "Borderline Personality Disorder"	MeSH descriptor: [Borderline Personality Disorder] explode all trees
S165	Compulsive Personality Disorder[Mesh]	MA "Compulsive Personality Disorder"	MeSH descriptor: [Compulsive Personality Disorder] explode all trees
S166	Dependent Personality Disorder[Mesh]	MA "Dependent Personality Disorder"	MeSH descriptor: [Dependent Personality Disorder] explode all trees
S167	Histrionic Personality Disorder[Mesh]	MA "Histrionic Personality Disorder"	MeSH descriptor: [Histrionic Personality Disorder] explode all trees
S168	Paranoid Personality Disorder[Mesh]	MA "Paranoid Personality Disorder"	MeSH descriptor: [Paranoid Personality Disorder] explode all trees
S169	Schizoid Personality Disorder[Mesh]	MA "Schizoid Personality Disorder"	MeSH descriptor: [Schizoid Personality Disorder] explode all trees
S170	Schizotypal Personality Disorder[Mesh]	MA "Schizotypal Personality Disorder"	MeSH descriptor: [Schizotypal Personality Disorder] explode all trees
S171	Narcissistic Personality Disorder[Mesh]	MA "Narcissistic Personality Disorder"	MeSH descriptor: [Narcissistic Personality Disorder] explode all trees
S172	"antisocial personality disorder"[tiab]	TI,AB "antisocial personality disorder"	"antisocial personality disorder":ti,ab,kw in Trials
S173	"borderline personality disorder"[tiab]	TI,AB "borderline personality disorder"	"borderline personality disorder":ti,ab,kw in Trials
S174	"compulsive personality disorder"[tiab]	TI,AB "compulsive personality disorder"	"compulsive personality disorder":ti,ab,kw in Trials
S175	"dependent personality disorder"[tiab]	TI,AB "dependent personality disorder"	"dependent personality disorder":ti,ab,kw in Trials
S176	"histrionic personality disorder"[tiab]	TI,AB "histrionic personality disorder"	"histrionic personality disorder":ti,ab,kw in Trials
S177	"paranoid personality disorder"[tiab]	TI,AB "paranoid personality disorder"	"paranoid personality disorder":ti,ab,kw in Trials
S178	"Schizoid personality disorder"[tiab]	TI,AB "Schizoid personality disorder"	"Schizoid personality disorder":ti,ab,kw in Trials
S179	"Schizotypal personality disorder"[tiab]	TI,AB "Schizotypal personality disorder"	"Schizotypal personality disorder":ti,ab,kw in Trials
S180	"dissocial personality disorder"[tiab]	TI,AB "dissocial personality disorder"	"dissocial personality disorder":ti,ab,kw in Trials
S181	"emotionally unstable personality disorder"[tiab]	TI,AB "emotionally unstable personality disorder"	"emotionally unstable personality disorder":ti,ab,kw in Trials
S182	"anankastic personality disorder"[tiab]	TI,AB "anankastic personality disorder"	"anankastic personality disorder":ti,ab,kw in Trials
S183	"anxious avoidant personality disorder"[tiab]	TI,AB "anxious avoidant personality disorder"	"anxious avoidant personality disorder":ti,ab,kw in Trials
S184	"dependent personality disorder"[tiab]	TI,AB "dependent personality disorder"	"dependent personality disorder":ti,ab,kw in Trials
S185	"narcissistic personality disorder"[tiab]	TI,AB "narcissistic personality disorder"	"narcissistic personality disorder":ti,ab,kw in Trials
S186	"enduring personality change"[tiab]	TI,AB "enduring personality change"	"enduring personality change":ti,ab,kw in Trials

	MEDLINE via PuPubMed	PsycINFO via Ebsco®	CENTRAL
S187	Paraphilic Disorders"[Mesh]	MA "Paraphilic Disorders+"	MeSH descriptor: [Paraphilic Disorders] explode all trees
S188	"paraphilic disorder*"[tiab]	TI,AB "paraphilic disorder*"	"paraphilic disorder*":ti,ab,kw in Trials
S189	Psychosomatic Medicine[mesh]	MA "Psychosomatic Medicine"	MeSH descriptor: [Psychosomatic Medicine] explode all trees
S190	Psychiatry[mesh]	MA "Psychiatry+"	MeSH descriptor: [Psychiatry] explode all trees
S191	Psychotherapy[mesh]	MA "Psychotherapy+"	MeSH descriptor: [Psychotherapy] explode all trees
S192	psychosomatic[tiab]	TI,AB psychosomatic	psychosomatic:ti,ab,kw in Trials
S193	psychiatric[tiab]	TI,AB psychiatric	psychiatric:ti,ab,kw in Trials
S194	psychotherapy[tiab]	TI,AB psychotherapy	"psychotherapy:ti,ab,kw in Trials
S195	S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131 OR S132 OR S133 OR S134 OR S135 OR S136 OR S137 OR S138 OR S139 OR S140 OR S141 OR S142 OR S143 OR S144 OR S145 OR S146 OR S147 OR S148 OR S149 OR S150 OR S151 OR S152 OR S153 OR S154 OR S155 OR S156 OR S157 OR S158 OR S159 OR S160 OR S161 OR S162 OR S163 OR S164 OR S165 OR S166 OR S167 OR S168 OR S169 OR S170 OR S171 OR S172 OR S173 OR S174 OR S175 OR S176 OR S177 OR S178 OR S179 OR S180 OR S181 OR S182 OR S183 OR S184 OR S185 OR S186 OR S187 OR S188 OR S189 OR S190 OR S191 OR S192 OR S193 OR S194	S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131 OR S132 OR S133 OR S134 OR S135 OR S136 OR S137 OR S138 OR S139 OR S140 OR S141 OR S142 OR S143 OR S144 OR S145 OR S146 OR S147 OR S148 OR S149 OR S150 OR S151 OR S152 OR S153 OR S154 OR S155 OR S156 OR S157 OR S158 OR S159 OR S160 OR S161 OR S162 OR S163 OR S164 OR S165 OR S166 OR S167 OR S168 OR S169 OR S170 OR S171 OR S172 OR S173 OR S174 OR S175 OR S176 OR S177 OR S178 OR S179 OR S180 OR S181 OR S182 OR S183 OR S184 OR S185 OR S186 OR S187 OR S188 OR S189 OR S190 OR S191 OR S192 OR S193 OR S194	#53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120 OR #121 OR #122 OR #123 OR #124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133 OR #134 OR #135 OR #136 OR #137 OR #138 OR #139 OR #140 OR #141 OR #142 OR #143 OR #144 OR #145 OR #146 OR #147 OR #148 OR #149 OR #150 OR #151 OR #152 OR #153 OR #154 OR #155 OR #156 OR #157 OR #158 OR #159 OR #160 OR #161 OR #162 OR #163 OR #164 OR #165 OR #166 OR #167 OR #168 OR #169 OR #170 OR #171 OR #172 OR #173 OR #174 OR #175 OR #176 OR #177 OR #178 OR #179 OR #180 OR #181 OR #182 OR #183 OR #184 OR #185 OR #186 OR #187 OR #188 OR #189 OR #190 OR #191 OR #192 OR #193 OR #194
S196	clinical trials as topic[MeSH Terms:noexp]	MA"clinical trials as topic"	MeSH descriptor: [Clinical Trials as Topic] this term only

	<b>MEDLINE via PuPubMed</b>	<b>PsycINFO via Ebsco®</b>	<b>CENTRAL</b>
S197	randomized controlled trial[pt]	PT randomized controlled trial	"randomized controlled trial":pt
S198	"controlled clinical trial"[pt]	PT controlled clinical trial	"controlled clinical trial":pt
S199	clinical trial[pt]	PT clinical trial	"clinical trial":pt
S200	trial[tiab]	TI,AB trial	trial:ti,ab,kw in Trials
S201	randomly[tiab]	TI,AB randomly	"randomly:ti,ab,kw in Trials
S202	random*[tw]	TX random*	random*: tx
S203	"randomized controlled trial"[tw]	TX "randomized controlled trial"	"randomized controlled trial":tx
S204	"controlled clinical trial"[tw]	TX "controlled clinical trial"	"controlled clinical trial":tx
S205	RCT[tw]	TX RCT	RCT:tx
S206	"clinical trial"[tw]	TX "clinical trial"	"clinical trial":tx
S207	S196 S197 S198 OR S199 OR S200 OR S201 OR S202 OR S203 OR S204 OR S205 OR S206	S196 S197 S198 OR S199 OR S200 OR S201 OR S202 OR S203 OR S204 OR S205 OR S206	#196 #197 #198 OR #199 OR #200 OR #201 OR #202 OR #203 OR #204 OR #205 OR #206
S208	S23 AND S52 AND S195 AND S207	S23 AND S52 AND S195 AND S207	#23 AND #52 AND #195 AND #207

Note. mesh = MeSH Term; tiab / ti, ab = Title/Abstract; pt = Publication Type; tw / tx = Text Word; kw = keywords



# BMJ Open

## Internet- and mobile-based aftercare and follow-up for mental disorders: Protocol of a systematic review and meta-analysis

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3 **Internet- and mobile-based aftercare and follow-up for mental disorders: Protocol of a systemat-**  
4 **ic review and meta-analysis**  
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45 **Word count:** 2540  
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## ABSTRACT

**Introduction:** Mental disorders are characterized by a high likelihood of symptom recurrence or chronicity. Thus in the vulnerable post-discharge phase, aftercare (e.g. rehabilitation, follow-up, maintenance treatment) aims at stabilizing treatment effects, promoting functionality and preventing relapse or readmission. Internet- and mobile-based interventions may represent low-threshold and effective extensions to aftercare in tertiary prevention of mental disorders.

**Objectives:** The planned systematic review and meta-analysis aims to synthesize and analyze existing evidence on the effectiveness of psychological Internet- and mobile-based aftercare or follow-up in maintaining treatment effects and/or preventing recurrence in adults with mental disorders.

**Methods and analysis:** Electronic databases (PsycInfo, MEDLINE and CENTRAL) will be searched systematically, complemented by a hand-search of ongoing trials and reference lists of selected studies. Data extraction and evaluation will be conducted by two independent reviewers and quality will be assessed with the Cochrane Risk of Bias tool. Eligibility criteria for selecting studies will be: Randomized controlled trials of Internet- and mobile-based, psychological aftercare for the tertiary prevention of mental disorders in an adult population. Primary outcome will be symptom severity. Secondary outcomes will be symptom/disorder recurrence rate, rehospitalization rate, functionality, quality of life or adherence to primary treatment. Further data items to be extracted will be: Study design-, intervention- or technical characteristics, type of mental disorder or clinical symptom to be treated, target population items, setting, treatment engagement and assessment of additional outcome variables. Meta-analytic pooling will be conducted when data of included studies are comparable in terms of study design, intervention type, endpoints, assessments, and target mental disorder. Cumulative Evidence will be evaluated according to the GRADE framework.

**Ethics and dissemination:** Ethics approval is not required. Results from this review will be published in peer-reviewed journals and presented at international conferences.

**Systematic review registration:** PROSPERO CRD42017055289

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- This review performs a sensitive search in electronic databases on modern technologies in tertiary prevention and will be the first to evaluate the effectiveness of Internet- and mobile-based aftercare in maintaining treatment effects or preventing recurrence in adults with mental disorders.
- Heterogeneity of studies in terms of clinical, methodological or statistical aspects will be considered carefully.
- The differentiated findings will provide clinicians and public health policymakers with a valuable overview of the feasibility of IMIs in tertiary prevention of mental disorders.
- The present protocol follows the PRISMA-P guidelines.

- We plan to assess the confidence in the cumulative evidence with the GRADE system.

## INTRODUCTION

Mental disorders are not only highly prevalent[1] but are also characterized by frequent recurrence during lifetime or chronic courses[2–5]. Adverse effects of recurrence or chronicity can be severe and include elevated readmission rates[6], early retirement[7], reduced quality of life[8] and increased mortality[9].

Within all areas of health care, tertiary prevention is paramount to monitor and manage symptoms, prevent relapse and promote health and functioning in persons with mental disorders[10]. In terms of continuous care, tertiary prevention may therefore comprise psychosocial, pharmacological or vocational rehabilitation, aftercare, follow-up or maintenance treatment. In particular, the transition after inpatient treatment can be considered a vulnerable phase, in which convalescents have to transfer and maintain health behavior, initiate change and are confronted with various individual, social or occupational challenges[11].

Meta-analytic evidence suggests the efficacy of cognitive behavioral therapy (CBT)[12, 13], psychosocial interventions[14, 15], pharmacological maintenance treatment[16] or psychosomatic rehabilitation[17] in reducing symptom severity, relapse rates and promoting functionality or medication adherence[18, 19] in mental disorders following acute treatment.

However, implementation strategies of aftercare are very heterogeneous and vary between different health care systems, mental disorders and treatment modalities. In this regard, studies in psychiatric or chronic pain patients indicate an insufficient prescription of aftercare by clinicians[20, 21]. Other studies suggest a limited uptake or adherence of psychosocial or medical maintenance treatment in convalescents[22–25]. Reasons for non-participation in psychosocial aftercare may include long waiting-times[26], pessimistic treatment expectancies[23] or various organizational barriers[21]. On the other hand, insufficient resources of health care systems and medical costs may further limit an extensive implementation and lead to gaps in continuity of care[27].

In an effort to overcome these limitations, Internet-delivered health promotion and treatment options for mental disorders have been developed particularly in the last decade. Internet- and mobile-based Interventions (IMIs) can be defined as “health related services and systems, carried out over a distance by means of information and communications technologies, for the purpose of global health promotion, disease control and health care” (p. 1)[28]. IMIs can be categorized by technical implementation (e.g. PC, smartphone, wearables), content (e.g. education, monitoring, behavior-change), localization in the health care process (e.g. prevention, stand-alone, aftercare), amount of human support (self-administered/automatized, self-help with minimal guidance, online-therapy) or therapeutic contact (e.g. E-Mail, SMS, Live-Chat/Video)[29]. IMIs be administered cost-effectively and without local or temporal boundaries[30, 31]. Since Internet access and use are growing constantly across countries and age groups[32], IMIs are also a widely accessible instruments.

1  
2  
3 A growing amount of evidence suggests efficacy of web-based psychotherapeutic interventions for a  
4 wide range of mental conditions[33, 34]. One of the first transdiagnostic reviews by Barak and col-  
5 leagues[33] found small to large effect sizes of IMIs ranging from  $d = 0.32$  (depression) to  $d = 0.88$   
6 (PTSD). Further reviews focused on IMIs as ‘stand-alone’ interventions, including meta-analytic evi-  
7 dence of efficacy in depression (SMD = 0.56,  $n = 19$ )[35], anxiety disorders (panic disorder: SMD =  
8 0.83,  $n = 6$ )[36] or post-traumatic-stress disorder (SMD = 0.95,  $n = 8$ )[37]. However, IMIs in psychiat-  
9 ric disorders are less studied, albeit first RCTs show promising results[38]. With regard to the imple-  
10 mentation of IMIs in different contexts of health care, a recent review by Sander and colleagues[39]  
11 found small to medium cross-diagnostic effect sizes ( $d = 0.11 - 0.76$ ) of IMIs in the primary preven-  
12 tion of mental disorders. Furthermore, a review by Niuwenhuijsen et al.[40] suggests efficacy of re-  
13 mote interventions (internet- or telephone-based) on return-to-work of depressed patients.

14  
15  
16 Previous studies on Internet- or mobile-based aftercare focused on guided, web-based self-help includ-  
17 ing psychoeducation as well as modular, interactive treatment elements and a certain amount of asyn-  
18 chronous therapist contact[41, 42]. Other approaches comprise mobile based[43] or synchronous, chat-  
19 or video-based aftercare[44, 45]. First evidence suggests the efficacy of IMIs in relapse prevention or  
20 reduction of symptom severity[41, 45].

21  
22  
23 However, to the best of our knowledge, no previous systematic review has investigated comprehensive  
24 evidence on IMIs as aftercare instruments for adults with mental disorders. Thus, the results of this  
25 review will give an overview of this field of research and identify potentials of IMIs for public health  
26 policy makers and health care providers. The present protocol describes the rationale and design of the  
27 systematic review and planned meta-analysis according to the ‘Preferred reporting items for systemat-  
28 ic review and meta-analysis protocols (PRISMA-P)’[46].

## 29 30 31 32 33 34 35 36 37 **Objectives**

38  
39 The aim of this systematic review and meta-analysis is to give a comprehensive overview of random-  
40 ized controlled trials (RCTs) investigating the effectiveness of Internet- and mobile-based psychologi-  
41 cal aftercare (e.g. rehabilitation, follow-up-, maintenance treatment) in maintaining treatment effects  
42 or in preventing symptom or disorder recurrence of mental disorders in adults.

## 43 44 45 46 **METHODS**

### 47 48 **Eligibility criteria**

#### 49 50 **Population**

51  
52 Studies will be included if they (a) focus on an adult population ( $\geq 18$  years) who (b) have received  
53 treatment for a mental disorder or a somatic condition within the previous six months. Preceding  
54 treatment of mental disorder may consist of inpatient or outpatient psychotherapy, psychiatric treat-  
55 ment or medical treatment, delivered by physicians or psychotherapists. Mental disorders must (c) be  
56 assessed by a standardized or validated instrument, including standardized interviews (e.g. SCID,  
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3 CIDI), validated self-reports (e.g. BDI, BAI, EDI), clinician-rated scales (e.g. HAMD, GAF) or diag-  
4 nosis by health care professionals.  
5

#### 6 Study design and interventions

7  
8 (e) Only randomized controlled trials that are available in full text (RCT) will be considered. Manu-  
9 scripts must be published in English or German. Treatment groups should receive a psychological  
10 aftercare or follow-up intervention. Following the definition by Kampling et al.[47], psychological  
11 interventions (f) may include elements of evidence-based therapy forms (e.g. cognitive behavioral  
12 therapy, psychodynamic therapies, behavior therapy or behavior modification, systemic therapies,  
13 third wave cognitive behavioral therapies, humanistic therapies, integrative therapies). Interventions  
14 may contain symptom monitoring, promotion of adherence to primary treatment (e.g. medication  
15 compliance), psychoeducation, reinforcement/feedback mechanisms as well as interactive elements or  
16 comprise guided/unguided self-help or comprehensive psychotherapeutic programs. If symptom moni-  
17 toring or reminders to treatment adherence are the predominant intervention modality, studies will  
18 only be included, if accompanied by a distinguishable psychological intervention element. Treatments  
19 not clearly described will be excluded.  
20

21  
22 (g) Aftercare and follow-up will be defined as interventions following acute treatment designed to  
23 monitor or stabilize mental symptoms, identify or manage warning signs of symptom/disorder recur-  
24 rence or enhance coping strategies to prevent recurrence, relapse or readmission[48], support transition  
25 and adoption of acquired health behavior and to promote or preserve health status, thereby reducing  
26 the impact of the illness on functioning or quality of life.  
27

28 (h) Interventions have to be delivered predominantly in an online setting, via Internet (web-/online) or  
29 mobile applications. Interventions may vary in the amount of human support, ranging from unguided  
30 self-help, over asynchronous minimal guidance to synchronous therapist contact[49].  
31

32 Studies must (i) report a minimum follow-up assessment of the main outcome of three months after  
33 the end of preceding treatment. Follow-up period of 3-6 months will be categorized as 'short', 6-12  
34 months as 'medium' and above as 'long-term'.  
35

#### 36 Comparators

37 (i) Control groups may receive either no intervention or comprise a waiting list (inactive control  
38 group) or include treatment as usual, another form of treatment (e.g. face-to-face psychotherapy,  
39 phone-delivered-, pharmacological/placebo treatment, other forms of psychological interventions) as  
40 active control group.  
41

#### 42 Exclusion criteria

43 Studies will be excluded, if they focus on the prevention of the first onset of a mental disorder or if no  
44 distinguishable treatment preceded the intervention under study (stand-alone interventions). Sub-  
45 stance-related and addictive disorders will not be included, as this represents another specific research  
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3 area[50, 51] and treatment rationales are predominantly socio-educational or follow a health behavior  
4 change model rather than psychotherapeutic intervention models.  
5

### 6 7 **Information sources and search strategy**

8  
9 Electronic databases that will be included are Medline, PsycInfo and the Cochrane Central Register of  
10 Controlled trials (CENTRAL). A sensitive search strategy will be applied (see supplementary file 1).  
11 The WHO International Clinical Trials Registry Platform (ICTRP) will be hand searched to identify  
12 ongoing trials. To assure literature saturation, reference lists of included studies will be perused. In  
13 case of unclear eligibility or indication of missing or unpublished data, we will contact the principal  
14 investigators (PIs) of studies for clarification. Also, when study protocols without a succeeding publi-  
15 cation of results are identified, we attempt to contact PI to obtain unpublished results and determine  
16 eligibility for inclusion.  
17  
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### 21 **Study records**

22  
23 In a first step, two independent reviewers (SF, SH) will screen titles and abstracts of the database  
24 search to identify qualified studies. Records will be managed in CITAVI<sup>®</sup>. In a second step, these re-  
25 viewers will examine full texts in terms of the eligibility criteria. Likewise, the reference lists will be  
26 screened against eligibility criteria. In case of disagreement on eligibility, a third reviewer (LS) will be  
27 consulted. Inter-rater-reliability will be analyzed to illustrate the consistency of study selection. To  
28 illustrate the search and selection process, a flow-chart according to the PRISMA-protocol[46] will be  
29 provided. Criteria for the exclusion of studies will be reported.  
30  
31  
32

33  
34 Extracted data of eligible studies will be verified by a second reviewer to assure accuracy. Disagree-  
35 ment will be solved by discussion or by consulting a third reviewer in case of unresolved disagree-  
36 ments. Data extraction forms will we developed and piloted. In case of overlapping or multiple re-  
37 ports, we plan to compare studies with regard to list of authors, sample sizes, treatments or outcomes.  
38 In case of unclear or missing information, we will contact PIs with a request to provide these data.  
39  
40  
41  
42

### 43 **Data items**

44  
45 The following data items will be extracted for each study: (a) study identification items (first author,  
46 year of publication), (b) study design characteristics (e.g. sample size, control group, pre-treatment,  
47 lengths of follow-up assessment, study drop-out), (c) intervention characteristics (e.g. psychologi-  
48 cal/therapeutic methods, amount of human guidance, synchronicity of contact, duration of interven-  
49 tion), (d) technical characteristics (e.g. Internet-/mobile-based, devices used, technical prerequisites),  
50 (e) type of mental disorder or clinical symptom to be treated, (f) target population items (e.g. age, gen-  
51 der), (g) setting (e.g. recruitment strategy, nationality, environment, language), (h) treatment engage-  
52 ment (e.g. treatment-drop-out rate, treatment fidelity, adoption of outpatient therapy), (i) assessment of  
53 additional outcome variables, (j) clinical outcome (symptom severity, recurrence rate, rehospitaliza-  
54 tion, functionality/quality of life, adherence to primary treatment).  
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## Outcomes and prioritization

Primary outcome will be symptom severity assessed via validated instruments (standardized interviews, self- or clinician-rated scales) or clinical diagnosis as an indicator of maintenance of treatment effects.

Secondary outcomes will be defined as (a) symptom recurrence rate, (b) incidence rate of mental disorder under study from post-treatment to latest available follow-up, (c) rehospitalization rate, (d) indicators of functionality or quality of life and (e) adherence to primary treatment (e.g. medication compliance).

In the likely case of multiple assessment instruments for primary or secondary outcome, we will prioritize data as follows: (1) Data from structured interviews will be prioritized. (2) Clinician-rated scales will be preferred over self-report instruments. (3) Self-report questionnaires will be prioritized over diagnosis by health professionals.

When several assessment instruments are used within one study that can be assigned to the same hierarchy level, we will (1) extract outcome of the most frequently used instrument according to eligible studies or (2) if not evident, select randomly. To control for an investigator bias, a second reviewer (SH) will cross-check the extraction process.

## Risk of bias in individual studies

The quality of evidence of each study will be evaluated following the Cochrane Risk of Bias tool[52]. The domains to be analyzed will be: (a) random sequence generation, (b) allocation concealment, (c) blinding of participants and personnel, (d) blinding of outcome assessment, (e) incomplete outcome data, (f) selective outcome reporting and (g) other threats to validity (e.g. treatment fidelity, parallelism of measurement, variance homogeneity at baseline, co-interventions).

As a distinctive feature of psychological interventions, blinding of health care providers (in guided Internet- or mobile-based intervention studies) or patients regarding treatment is not warranted, resulting in a high risk of bias rating of criterion (criterion c). However, outcome assessors can remain unaware of participant's treatment allocation (criterion (d)).

## Data synthesis

### Qualitative synthesis

A narrative synthesis will be reported on all included studies and relevant characteristics listed under 'data items' will be qualitatively described. A detailed description of their results on relevant domains will be provided in text and 'summary of findings' tables (comparison against control groups) following the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P)[46].

### Meta-Analysis

The expected heterogeneity of studies in terms of clinical (e.g. mental disorder, intervention objective, type of IMI) methodological (comparators, assessment methods) or statistical (e.g. comparability of



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3 outcome measures) will be considered carefully. Thus, meta-analytic pooling will only be conducted,  
4 if comparability of included studies is met in at least three studies. The Cochrane Collaborations' Re-  
5 view Manager<sup>®</sup> will be used. By separating analyses in terms of mental disorders or intervention type,  
6 we plan to reduce heterogeneity of pooled estimates. A random-effects model will be used. Only stud-  
7 ies with less than substantial statistical heterogeneity by will be pooled. If possible, heterogeneity of  
8 study results will be analyzed through forest plots and calculating I<sup>2</sup> statistics. The degree of heteroge-  
9 neity will then be categorized according to the guidelines of the Risk of Bias tool[53].

10  
11 For continuous data, we will calculate the standardized mean difference (SMD) and 95% confidence  
12 intervals. For dichotomous data, we will transform findings into risk ratios (RR). We aim to calculate  
13 the number needed to treat (NNT) to further illustrate clinical relevance of the interventions.

14  
15 Outcome variables (e.g. symptom severity scores) will be pooled and further differentiated in terms of  
16 'short', 'medium' or 'long-term' effectiveness when follow-up assessment is reported. Subject to suf-  
17 ficient group size and comparability of assessment, we plan to analyze study level covariates (e.g. type  
18 of mental disorder, type of Internet- or mobile-based intervention, amount of guidance).

#### 24 25 **Meta-biases - confidence in cumulative evidence**

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27 We will retrieve study protocols or trial registrations to identify reporting biases. Thereby, we will  
28 evaluate whether selective reporting of outcomes is present. A possible small sample bias will be as-  
29 sessed by using a random-effect-model. Provided the number of studies is sufficient, we plan to exam-  
30 ine a possible publication bias of significant-only studies in funnel plots. We will also search for un-  
31 published or non-significant studies.

32  
33 We plan to rate the cumulative evidence according to the Grading of Recommendations Assessment,  
34 Development and Evaluation (GRADE)[54] in terms of study limitations, inconsistency of results,  
35 indirectness of evidence, imprecision of effect estimates reporting bias. Quality of evidence will be  
36 categorized into 'very low', 'low', 'moderate', or 'high'.

#### 40 41 **ETHICS AND DISSEMINATION**

42  
43 A formal ethical approval is not required since no primary data of individuals will be collected. The  
44 status of the planned review will be updated regularly in PROSPERO. Results from this review will be  
45 published in leading peer-reviewed journals in the field of telemedicine and eHealth. Furthermore,  
46 results will be presented at international conferences and workshops to facilitate dissemination into  
47 clinical practice.

#### 48 49 50 **CONCLUSION**

51  
52 This systematic review and meta-analysis will complement the evidence base of IMIs and allow for an  
53 evaluation of their feasibility as aftercare for the tertiary prevention as a significant component of  
54 mental health care. In case of cavities in research areas or unsatisfactory confirmation, we will suggest  
55 future research strategies. The findings will extend previous literature on the effectiveness of IMIs in  
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3 different areas of health care like prevention[39] or as an alternative to face-to-face therapy[55]. Fur-  
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different areas of health care like prevention[39] or as an alternative to face-to-face therapy[55]. Furthermore, the results will provide clinicians and public health policymakers with a valuable overview of the possibilities of IMIs in monitoring and managing patients after regular treatment and in preventing relapse or readmission.

### ABBREVIATIONS

BAI: Beck Anxiety Inventory

BDI: Beck Depression Inventory

CBT: Cognitive Behavioral Therapy

CENTRAL: Cochrane Central Register of Controlled trials

CIDI: Composite International Diagnostic Interview

EDI: Eating Disorder Inventory

GAF: Global Assessment of Functioning

HAMD: Hamilton Depression Scale

ICTRP: WHO International Clinical Trials Registry Platform

IMIs: Internet- and mobile-based interventions

PI: Principal investigator

PRISMA-P: Preferred reporting items for systematic review and meta-analysis protocols

RCT: Randomized controlled trials

RR: Risk ratios

SCID: Structured Clinical Interview for DSM Disorders

SMD: Standardized mean difference

NNT: Number needed to treat

### CONTRIBUTORSHIP STATEMENT

All authors were involved in the concept and review design of the study and data analysis plan. SH and SF wrote the draft of this manuscript. LS provided valuable revisions. All authors contributed to the further writing and approved the final version of the manuscript. The authors thank the reviewers for their constructive feedback.

### COMPETING INTERESTS

None declared.

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### DATA SHARING STATEMENT

No additional unpublished data available.

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**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Page No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	1	Identify the report as a protocol of a systematic review
Update	1b	--	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:			
Contact	3a	1	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	9	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	--	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:			
Sources	5a	9	Indicate sources of financial or other support for the review
Sponsor	5b	9	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	9	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>			
Rationale	6	3-4	Describe the rationale for the review in the context of what is already known
Objectives	7	4	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
<b>METHODS</b>			
Eligibility criteria	8	4-5	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	6	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	6	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated



Study records:			
Data management	11a	6	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	6	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	6	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	6-7	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	7	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	7	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	7-8	Describe criteria under which study data will be quantitatively synthesised
	15b	7-8	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )
	15c	7-8	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	7	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	8	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	8	Describe how the strength of the body of evidence will be assessed (such as GRADE)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

	MEDLINE via PuPubMed	PsycINFO via Ebsco	CENTRAL
S1	Aftercare[mesh]	MA "Aftercare"	MeSH descriptor: [Aftercare] explode all trees
S2	Recurrence[mesh]	MA "Recurrence"	MeSH descriptor: [Recurrence] explode all trees
S3	Relapse Prevention [mesh]	MA "Relapse prevention"	MeSH descriptor: [secondary prevention] explode all trees
S4	Tertiary Prevention[mesh]	MA "Tertiary Prevention"	MeSH descriptor: [Tertiary Prevention] explode all trees
S5	Convalescence[mesh]	MA "Convalescence"	MeSH descriptor: [Convalescence] explode all trees
S6	aftercare[tiab] OR after-care[tiab]	TI,AB aftercare	aftercare:ti,ab,kw in Trials
S7	(after-treatment*[tiab] OR "after treatment" [tiab])	TI,AB after-treatment* OR TI,AB "after treatment*"	after-treatment*:ti,ab,kw OR "after treatment*":ti,ab,kw in Trials
S8	relaps*[tiab]	TI,AB relaps*	relaps*:ti,ab,kw in Trials
S9	follow-up[tiab]	TI,AB follow-up	follow-up:ti,ab,kw in Trials
S10	"intervention following*[tiab]	TI,AB "intervention following*"	"intervention following*":ti,ab,kw in Trials
S11	rehabilitation*[tiab]	TI,AB rehabilitation*	rehabilitation*:ti,ab,kw in Trials
S12	(tele-rehabilitation*[tiab] OR Telerehabilitation*[tiab])	(TI,AB tele-rehabilitation* OR TI,AB telerehabilitation*)	tele-rehabilitation*:ti,ab,kw OR telerehabilitation*:ti,ab,kw in Trials
S13	(post-treatment*[tiab] OR post treatment*[tiab])	(TI,AB post-treatment* OR TI,AB "post treatment*")	(post-treatment*:ti,ab,kw OR post treatment*:ti,ab,kw in Trials)
S14	"treatment after inpatient"[tiab]	TI,AB "treatment after inpatient"	"treatment after inpatient":ti,ab,kw in Trials
S15	recovery[tiab]	TI,AB recovery	recovery:ti,ab,kw in Trials
S16	"maintenance treatment"[tiab]	TI,AB "maintenance treatment"	"maintenance treatment":ti,ab,kw in Trials
S17	"continuation treatment"[tiab]	TI,AB "continuation treatment"	"continuation treatment":ti,ab,kw in Trials
S18	continuation-phase[tiab]	TI,AB continuation-phase	continuation-phase:ti,ab,kw in Trials
S19	"tertiary prevention"[tiab]	TI,AB "tertiary prevention"	"tertiary prevention":ti,ab,kw in Trials
S20	"continuous care"[tiab]	TI,AB "continuous care"	"continuous care":ti,ab,kw in Trials
S21	"disease management*[tiab]	TI,AB "disease management*"	"disease management*":ti,ab,kw in Trials
S22	recurren*[tiab]	TI,AB recurren*	recurren*:ti,ab,kw in Trials
S23	post-discharge [tiab]	TI,AB post-discharge	post-discharge:ti,ab,kw in Trials
S24	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23
S25	Telemedicine[mesh]	MA "Telemedicine+"	MeSH descriptor: [Telemedicine] explode all trees

Supplementary File 1. Table showing the search strings for MEDLINE, PsycINFO and CENTRAL

	MEDLINE via PubMed	PsycINFO via Ebsco	CENTRAL
S26	Computer Assisted Instruction[mesh]	MA "Computer Assisted Instruction"	MeSH descriptor: [Computer Assisted Instruction] explode all trees
S27	Mobile Health Units[mesh]	MA "Mobile Health Units"	MeSH descriptor: [Mobile Health Units] explode all trees
S28	Therapy, Computer-Assisted[mesh]	MA "Therapy, Computer-Assisted+"	MeSH descriptor: [Therapy, Computer-Assisted] explode all trees
S29	Mobile Applications[mesh]	MA "Mobile Applications"	MeSH descriptor: [Mobile Applications] explode all trees
S30	Internet[mesh]	MA "Internet+"	MeSH descriptor: [Internet ] explode all trees
S31	"computer applications"[tiab]	TI,AB "computer applications"	"computer applications":ti,ab,kw in Trials
S32	ICBT [tiab]	TI,AB ICBT	ICBT:ti,ab,kw in Trials
S33	telemental [tiab]	TI,AB telemental	telemental:ti,ab,kw in Trials
S34	e-therapy [tiab]	TI,AB e-therapy	e-therapy:ti,ab,kw in Trials
S35	CD-ROM [tiab]	TI,AB CD-ROM	CD-ROM:ti,ab,kw in Trials
S36	mhealth [tiab]	TI,AB mhealth	mhealth:ti,ab,kw in Trials
S37	(e-mail [tiab] OR email [tiab])	(TI,AB e-mail OR TI,AB email)	(e-mail:ti,ab,kw OR email:ti,ab,kw in Trials)
S38	SMS [tiab]	TI,AB SMS	SMS:ti,ab,kw in Trials
S39	app [tiab]	TI,AB app	app:ti,ab,kw in Trials
S40	ICT [tiab]	TI,AB ICT	ICT:ti,ab,kw in Trials
S41	online[tiab]	TI,AB online	online:ti,ab,kw in Trials
S42	mobile[tiab]	TI,AB mobile	mobile:ti,ab,kw in Trials
S43	eHealth[tiab]	TI,AB eHealth	eHealth:ti,ab,kw in Trials
S44	(web-based[tiab] OR "web based"[tiab])	(TI,AB web-based OR web based TI,AB)	(web-based:ti,ab,kw OR "web based":ti,ab,kw in Trials)
S45	(computer-based[tiab] OR "computer based"[tiab])	(TI,AB computer-based OR TI,AB "computer based")	(computer-based:ti,ab,kw in Trials OR "computer based:ti,ab,kw in Trials)
S46	computerized[tiab]	TI,AB computerized	computerized:ti,ab,kw in Trials
S47	"world wide web"[tiab]	TI,AB "world wide web"	"world wide web":ti,ab,kw in Trials
S48	cyber[tiab]	TI,AB cyber	cyber:ti,ab,kw in Trials
S49	ccbt[tiab]	TI,AB ccbt	ccbt:ti,ab,kw in Trials
S50	mobile-based[tiab] OR "mobile based"[tiab]	TI,AB "mobile based" OR TI,AB mobile-based	mobile-based:ti,ab,kw OR "mobile based":ti,ab,kw in Trials
S51	internet[tiab]	TI,AB internet	internet:ti,ab,kw in Trials
S52	(computer-assisted[tiab] OR "computer assisted"[tiab])	(TI,AB computer assisted OR TI,AB "computer assisted")	(computer-assisted:ti,ab,kw OR "computer assisted":ti,ab,kw in Trials)
S53	"text messaging"[tiab]	TI,AB "text messaging"	"text messaging":ti,ab,kw in Trials
S54	Smartphone*[tiab]	TI,AB smartphone*	smartphone*:ti,ab,kw in Trials

	MEDLINE via PuPMed	PsycINFO via Ebsco	CENTRAL
S55	S25 OR S26 Or S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54	S25 OR S26 Or S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53OR S54	#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53OR #54
S56	Mental Disorders[mesh]	MA "Mental Disorders+"	MeSH descriptor: [Mental Disorders] explode all trees
S57	Mental health[mesh]	MA "Mental health+"	MeSH descriptor: [Mental health] explode all trees
S58	Mentally Ill Persons[mesh]	MA "Mentally Ill Persons"	MeSH descriptor: [Mentally Ill Persons] explode all trees
S59	"mental distress"[tiab]	TI,AB "mental distress"	"mental distress":ti,ab,kw in Trials
S60	"psychiatric disorder*"[tiab]	TI,AB "psychiatric disorder*"	"psychiatric disorder*":ti,ab,kw in Trials
S61	"psychological disorder*"[tiab]	TI,AB "psychological disorder*"	"psychological disorder*":ti,ab,kw in Trials
S62	"mental illness*"[tiab]	TI,AB "mental illness*"	"mental illness*":ti,ab,kw in Trials
S63	"Mental disorder*"[tiab]	TI,AB "mental disorder*"	"mental disorder*":ti,ab,kw in Trials
S64	Substance-Related Disorders[mesh]	MA "Substance-Related Disorders+"	MeSH descriptor: [Substance-Related Disorders] explode all trees
S65	Alcohol-Related Disorders[mesh]	MA "Alcohol-Related Disorders+"	MeSH descriptor: [Alcohol-Related Disorders] explode all trees
S66	"alcohol dependence"[tiab]	TI,AB "alcohol dependence"	"alcohol dependence":ti,ab,kw in Trials
S67	"alcohol abuse"[tiab]	TI,AB "alcohol abuse"	"alcohol abuse":ti,ab,kw in Trials
S68	"substance abuse"[tiab]	TI,AB "substance abuse"	"substance abuse":ti,ab,kw in Trials
S69	"substance-related disorder*"[tiab]	TI,AB "substance-related disorder*"	"substance-related disorder*":ti,ab,kw in Trials
S70	"alcohol-related disorder*"[tiab]	TI,AB "alcohol-related disorder*"	"alcohol-related disorder*":ti,ab,kw in Trials
S71	Psychotic Disorders[mesh]	MA "Psychotic Disorders+"	MeSH descriptor:[Psychotic Disorders] explode all trees
S72	Schizophrenia[mesh]	MA "Schizophrenia+"	MeSH descriptor:[Schizophrenia] explode all trees
S73	psychotic[tiab]	TI,AB psychotic	psychotic:ti,ab,kw in Trials
S74	schizophren*[tiab]	TI,AB schizophren *	schizophren*:ti,ab,kw in Trials
S75	Affective Disorders, Psychotic[mesh]	MA "Affective Disorders, Psychotic+"	MeSH descriptor: [Affective Disorders, Psychotic] explode all trees
S76	Mood Disorders[mesh]	MA "Mood Disorders+"	MeSH descriptor: [Mood Disorders] explode all trees
S77	Depression[mesh]	MA "Depression"	MeSH descriptor: [Depression] explode all trees
S78	Bipolar Disorder[mesh]	MA "Bipolar Disorder+"	MeSH descriptor: [Bipolar Disorder] explode all trees

Supplementary File 1. Table showing the search strings for MEDLINE, PsycINFO and CENTRAL

	MEDLINE via PuPMed	PsycINFO via Ebsco	CENTRAL
S79	Dysthymic Disorder[mesh]	MA "Dysthymic Disorder"	MeSH descriptor: [Dysthymic Disorder] explode all trees
S80	Depressive Disorder[mesh]	MA "Depressive Disorder+"	MeSH descriptor: [Depressive Disorder] explode all trees
S81	Depressive Disorder, Major[mesh]	MA "Depressive Disorder, Major+"	MeSH descriptor: [Depressive Disorder, Major]
S82	"affective disorder*" [tiab]	TI,AB "affective disorder*"	"affective disorder*":ti,ab,kw in Trials
S83	depressive [tiab]	TI,AB depressive	depressive:ti,ab,kw in Trials
S84	depression [tiab]	TI,AB depression	depression:ti,ab,kw in Trials
S85	"mood disorder*" [tiab]	TI,AB "mood disorder*"	"mood disorder*":ti,ab,kw in Trials
S86	bipolar* [tiab]	TI,AB bipolar*	bipolar*:ti,ab,kw in Trials
S87	dysthymi* [tiab]	TI,AB dysthymic	dysthymic:ti,ab,kw in Trials
S88	cyclothymi * [tiab]	TI,AB cyclothymi*	cyclothymi* Title/Abstract]
S89	Anxiety Disorders[mesh]	MA "Anxiety Disorders+"	MeSH descriptor: [Anxiety Disorders] explode all trees
S90	Panic[mesh]	MA "Panic"	MeSH descriptor: [Panic] explode all trees
S91	Panic Disorder[mesh]	MA "Panic Disorder"	MeSH descriptor: [Panic Disorder] explode all trees
S92	Phobic Disorders[mesh]	MA "Phobic Disorders"	MeSH descriptor: [Phobic Disorders] explode all trees
S93	Socia Phobia[mesh]	MA "Social Phobia"	MeSH descriptor: [Social Phobia] explode all trees
S94	Agoraphobia[mesh]	MA "Agoraphobia"	MeSH descriptor: [Agoraphobia] explode all trees
S95	"anxiety disorder*" [tiab]	TI,AB "anxiety disorder*"	"anxiety disorder*":ti,ab,kw in Trials
S96	panic [tiab]	TI,AB panic	panic:ti,ab,kw in Trials
S97	phobi* [tiab]	TI,AB phobi*	phobi*:ti,ab,kw in Trials
S98	agoraphobi* [tiab]	TI,AB agoraphobi*	agoraphobi*:ti,ab,kw in Trials
S99	"social anxiety" [tiab]	TI,AB "social anxiety"	"social anxiety":ti,ab,kw in Trials
S100	"generalized anxiety disorder" [tiab]	TI,AB "generalized anxiety disorder"	"generalized anxiety disorder":ti,ab,kw in Trials
S101	Obsessive-Compulsive Disorder[mesh]	MA "Obsessive-Compulsive Disorder+"	MeSH descriptor: [Obsessive-Compulsive Disorder] explode all trees
S102	Disruptive, Impulse Control, and Conduct Disorders[mesh]	MA "Disruptive, Impulse Control, and Conduct Disorders+"	MeSH descriptor: [Disruptive, Impulse Control, and Conduct Disorders] explode all trees
S103	Stress Disorders, Post-Traumatic[mesh]	MA "Stress Disorders, Post-Traumatic"	MeSH descriptor: [Stress Disorders, Post-Traumatic] explode all trees
S104	Stress Disorders, Traumatic[mesh]	MA "Stress Disorders, Traumatic+"	MeSH descriptor: [Stress Disorders, Traumatic] explode all trees
S105	Adjustment Disorders[mesh]	MA "Adjustment Disorders"	MeSH descriptor: [Adjustment Disorders] explode all trees
S106	PTSD [tiab]	TI,AB PTSD	PTSD:ti,ab,kw in Trials

	MEDLINE via PuPMed	PsycINFO via Ebsco	CENTRAL
S107	"posttraumatic stress disorder*" [tiab]	TI,AB "posttraumatic stress disorder*"	"posttraumatic stress disorder*":ti,ab,kw in Trials
S108	"obsessive-compulsive disorder*" [tiab]	TI,AB "obsessive-compulsive disorder*"	"obsessive-compulsive disorder*":ti,ab,kw in Trials
S109	"impulse control disorder*" [tiab]	TI,AB "impulse control disorder*"	"impulse control disorder*":ti,ab,kw in Trials
S110	"stress disorder*, post-traumatic" [tiab]	TI,AB "stress disorder*, post-traumatic"	"stress disorder*, post-traumatic":ti,ab,kw in Trials
S111	"stress disorder*, traumatic" [tiab]	TI,AB "stress disorder*, traumatic"	"stress disorder*, traumatic":ti,ab,kw in Trials
S112	"adjustment disorder*" [tiab]	TI,AB "adjustment disorder*"	"adjustment disorder*":ti,ab,kw in Trials
S113	"Somatoform Disorders" [mesh]	MA "Somatoform Disorders+"	MeSH descriptor: [Somatoform Disorders] explode all trees
S114	"Body Dysmorphic Disorders" [mesh]	MA "Body Dysmorphic Disorders"	MeSH descriptor: [Body Dysmorphic Disorders]
S115	"Conversion Disorder" [mesh]	MA "Conversion Disorder+"	MeSH descriptor: [Conversion Disorder] explode all trees
S116	"Factitious Disorders" [mesh]	MA "Factitious Disorders+"	MeSH descriptor: [Factitious Disorders] explode all trees
S117	Hypochondriasis" [mesh]	MA "Hypochondriasis"	MeSH descriptor: [Hypochondriasis] explode all trees
S118	Neurasthenia" [mesh]	MA "Neurasthenia"	MeSH descriptor: [Neurasthenia] explode all trees
S119	"Medically Unexplained Symptoms" [mesh]	MA "Medically Unexplained Symptoms"	n.
S120	somatoform [tiab]	TI,AB somatoform	somatoform:ti,ab,kw in Trials
S121	"somatic symptom disorder*" [tiab]	TI,AB "somatic symptom disorder*"	"somatic symptom disorder*":ti,ab,kw in Trials
S122	"body dysmorphic disorders" [tiab]	TI,AB "body dysmorphic disorders"	"body dysmorphic disorders":ti,ab,kw in Trials
S123	"conversion disorder" [tiab]	TI,AB "conversion disorder"	"conversion disorder":ti,ab,kw in Trials
S124	hypochondriasis [tiab]	TI,AB hypochondriasis	hypochondriasis:ti,ab,kw in Trials
S125	"illness anxiety disorder" [tiab]	TI,AB "illness anxiety disorder"	"illness anxiety disorder":ti,ab,kw in Trials
S126	"medically unexplained*" [tiab]	TI,AB "medically unexplained*"	"medically unexplained*":ti,ab,kw in Trials
S127	somatization [tiab]	TI,AB somatization	somatization:ti,ab,kw in Trials
S128	"pain disorder" [tiab]	TI,AB "pain disorder"	"pain disorder":ti,ab,kw in Trials
S129	"chronic pain" [tiab]	TI,AB "chronic pain"	"chronic pain":ti,ab,kw in Trials
S130	"chronic back pain" [tiab]	TI,AB "chronic back pain"	"chronic back pain":ti,ab,kw in Trials
S131	"premenstrual syndrome" [tiab] OR "pre-menstrual syndrome" [tiab]	TI,AB "premenstrual syndrome" OR TI,AB OR "pre-menstrual syndrome"	"premenstrual syndrome":ti,ab,kw OR "pre-menstrual syndrome":ti,ab,kw in Trials
S132	"irritable bowel syndrome" [tiab]	TI,AB "irritable bowel syndrome"	"irritable bowel syndrome":ti,ab,kw in Trials
S133	fibromyalgia [tiab]	TI,AB fibromyalgia	fibromyalgia:ti,ab,kw in Trials
S134	"chronic fatigue" [tiab]	TI,AB "chronic fatigue"	"chronic fatigue":ti,ab,kw in Trials

Supplementary File 1. Table showing the search strings for MEDLINE, PsycINFO and CENTRAL

	MEDLINE via PuPubMed	PsycINFO via Ebsco	CENTRAL
S135	"tension headache"[tiab]	TI,AB "tension headache"	"tension headache":ti,ab,kw in Trials
S136	Dissociative Disorders[mesh]	MA "Dissociative Disorders+"	MeSH descriptor: [Dissociative Disorders] explode all trees
S137	Depersonalization"[mesh]	MA "Depersonalization"	MeSH descriptor: [Depersonalization] explode all trees
S138	"dissociative disorder*"[tiab]	TI,AB "dissociative disorder*"	"dissociative disorder*":ti,ab,kw in Trials
S139	depersonalization[tiab]	TI,AB depersonalization	depersonalization:ti,ab,kw in Trials
S140	derealization[tiab]	TI,AB derealization	derealization:ti,ab,kw in Trials
S141	Feeding and Eating Disorders[mesh]	MA "Feeding and Eating Disorders+"	MeSH descriptor: [Feeding and Eating Disorders] explode all trees
S142	Anorexia[mesh]	MA "Anorexia"	MeSH descriptor: [Anorexia] explode all trees
S143	Anorexia Nervosa[mesh]	MA "Anorexia Nervosa"	MeSH descriptor: [Anorexia Nervosa] explode all trees
S144	Bulimia[mesh]	MA "Bulimia"	MeSH descriptor: [Bulimia] explode all trees
S145	Bulimia Nervosa[mesh]	MA "Bulimia Nervosa"	MeSH descriptor: [Bulimia Nervosa] explode all trees
S146	Binge-Eating Disorder[mesh]	MA "Binge-Eating Disorder"	MeSH descriptor: [Binge-Eating Disorder] explode all trees
S147	anorexia[tiab]	TI,AB anorexia	anorexia:ti,ab,kw in Trials
S148	bulimia[tiab]	MA "bulimia"	bulimia:ti,ab,kw in Trials
S149	"eating disorder*"[tiab]	TI,AB "eating disorder*"	"eating disorder*":ti,ab,kw in Trials
S150	"binge eating"[tiab] OR binge-eating[tiab]	TI,Ab "binge eating" OR TI,Ab binge-eating	binge-eating:ti,ab,kw in Trials OR "binge-eating":ti,ab,kw in Trials
S151	"Sexual Dysfunctions, Psychological"[mesh]	MA "Sexual Dysfunctions, Psychological"	MeSH descriptor: [Sexual Dysfunctions, Psychological] explode all trees
S152	"gender dysphoria"[tiab]	TI,AB "gender dysphoria"	"gender dysphoria":ti,ab,kw in Trials
S153	"sexual dysfunction*"[tiab]	TI,AB "sexual dysfunction*"	"sexual dysfunction*":ti,ab,kw in Trials
S154	"sexual pain disorder*"[tiab]	TI,AB "sexual pain disorder*"	"sexual pain disorder*":ti,ab,kw in Trials
S155	"orgasmic disorder*"[tiab]	TI,AB "orgasmic disorder*"	"orgasmic disorder*":ti,ab,kw in Trials
S156	"sexual arousal disorder*"[tiab]	TI,AB "sexual arousal disorder*"	"sexual arousal disorder*":ti,ab,kw in Trials
S157	"gender identity disorder*"[tiab]	TI,AB "gender identity disorder*"	"gender identity disorder*":ti,ab,kw in Trials
S158	"disorders of sexual preference"[tiab]	TI,AB "disorders of sexual preference"	"disorders of sexual preference":ti,ab,kw in Trials
S159	"Sleep Wake Disorders"[mesh]	MA "Sleep Wake Disorders+"	MeSH descriptor: [Sleep Wake Disorders] explode all trees
S160	"Sleep Initiation and Maintenance Disorders"[mesh]	MA "Sleep Initiation and Maintenance Disorders"	MeSH descriptor: [Sleep Initiation and Maintenance Disorders] explode all trees

	MEDLINE via PuPMed	PsycINFO via Ebsco	CENTRAL
S161	insomnia[tiab]	TI,AB insomnia	insomnia:ti,ab,kw in Trials
S162	"sleep disorder*" [tiab]	TI,AB "sleep disorder*"	"sleep disorder*":ti,ab,kw in Trials
S163	Attention Deficit Disorder [mesh]	MA "Attention Deficit Disorder+"	MeSH descriptor: [Attention Deficit Disorder] explode all trees
S164	Attention Deficit Disorder with Hyperactivity[mesh]	MA "Attention Deficit Disorder with Hyperactivity"	MeSH descriptor: [Attention Deficit Disorder with Hyperactivity] explode all trees
S165	"attention-deficit disorder"[tiab]	TI,AB "attention-deficit disorder"	"attention-deficit disorder":ti,ab,kw in Trials
S166	"attention deficit hyperactivity disorder"[tiab]	TI,AB "attention deficit hyperactivity disorder"	"attention deficit hyperactivity disorder":ti,ab,kw in Trials
S167	Personality Disorders[mesh]	MA "Personality Disorders+"	MeSH descriptor: [Personality Disorders] explode all trees
S168	"personality disorder*" [tiab]	TI,AB "personality disorder*"	MeSH descriptor: [personality disorder*]:ti,ab,kw in Trials
S169	Antisocial Personality Disorder[mesh]	MA "Antisocial Personality Disorder"	MeSH descriptor: [Antisocial Personality Disorder] explode all trees
S170	Borderline Personality Disorder[mesh]	MA "Borderline Personality Disorder"	MeSH descriptor: [Borderline Personality Disorder] explode all trees
S171	Compulsive Personality Disorder[mesh]	MA "Compulsive Personality Disorder"	MeSH descriptor: [Compulsive Personality Disorder] explode all trees
S172	Dependent Personality Disorder[mesh]	MA "Dependent Personality Disorder"	MeSH descriptor: [Dependent Personality Disorder] explode all trees
S173	Histrionic Personality Disorder[mesh]	MA "Histrionic Personality Disorder"	MeSH descriptor: [Histrionic Personality Disorder] explode all trees
S174	Paranoid Personality Disorder[mesh]	MA "Paranoid Personality Disorder"	MeSH descriptor: [Paranoid Personality Disorder] explode all trees
S175	Schizoid Personality Disorder[mesh]	MA "Schizoid Personality Disorder"	MeSH descriptor: [Schizoid Personality Disorder] explode all trees
S176	Schizotypal Personality Disorder[mesh]	MA "Schizotypal Personality Disorder"	MeSH descriptor: [Schizotypal Personality Disorder] explode all trees
S177	Narcissistic Personality Disorder[mesh]	MA "Narcissistic Personality Disorder"	MeSH descriptor: [Narcissistic Personality Disorder] explode all trees
S178	"antisocial personality disorder"[tiab]	TI,AB "antisocial personality disorder"	"antisocial personality disorder":ti,ab,kw in Trials
S179	"borderline personality disorder"[tiab]	TI,AB "borderline personality disorder"	"borderline personality disorder":ti,ab,kw in Trials
S180	"compulsive personality disorder"[tiab]	TI,AB "compulsive personality disorder"	"compulsive personality disorder":ti,ab,kw in Trials
S181	"dependent personality disorder"[tiab]	TI,AB "dependent personality disorder"	"dependent personality disorder":ti,ab,kw in Trials
S182	"histrionic personality disorder"[tiab]	TI,AB "histrionic personality disorder"	"histrionic personality disorder":ti,ab,kw in Trials



Supplementary File 1. Table showing the search strings for MEDLINE, PsycINFO and CENTRAL

	MEDLINE via PuPubMed	PsycINFO via Ebsco	CENTRAL
S183	"paranoid personality disorder"[tiab]	TI,AB "paranoid personality disorder"	"paranoid personality disorder":ti,ab,kw in Trials
S184	"Schizoid personality disorder"[tiab]	TI,AB "Schizoid personality disorder"	"Schizoid personality disorder":ti,ab,kw in Trials
S185	"Schizotypal personality disorder"[tiab]	TI,AB "Schizotypal personality disorder"	"Schizotypal personality disorder":ti,ab,kw in Trials
S186	"dissocial personality disorder"[tiab]	TI,AB "dissocial personality disorder"	"dissocial personality disorder":ti,ab,kw in Trials
S187	"emotionally unstable personality disorder"[tiab]	TI,AB "emotionally unstable personality disorder"	"emotionally unstable personality disorder":ti,ab,kw in Trials
S188	"anankastic personality disorder"[tiab]	TI,AB "anankastic personality disorder"	"anankastic personality disorder":ti,ab,kw in Trials
S189	"anxious avoidant personality disorder"[tiab]	TI,AB "anxious avoidant personality disorder"	"anxious avoidant personality disorder":ti,ab,kw in Trials
S190	"dependent personality disorder"[tiab]	TI,AB "dependent personality disorder"	"dependent personality disorder":ti,ab,kw in Trials
S191	"narcissistic personality disorder"[tiab]	TI,AB "narcissistic personality disorder"	"narcissistic personality disorder":ti,ab,kw in Trials
S192	"enduring personality change"[tiab]	TI,AB "enduring personality change"	"enduring personality change":ti,ab,kw in Trials
S193	Paraphilic Disorders"[mesh]	MA "Paraphilic Disorders+"	MeSH descriptor: [Paraphilic Disorders] explode all trees
S194	"paraphilic disorder*"[tiab]	TI,AB "paraphilic disorder*"	"paraphilic disorder*":ti,ab,kw in Trials
S195	Psychosomatic Medicine[mesh]	MA "Psychosomatic Medicine"	MeSH descriptor: [Psychosomatic Medicine] explode all trees
S196	Psychiatry[mesh]	MA "Psychiatry+"	MeSH descriptor: [Psychiatry] explode all trees
S197	Psychotherapy[mesh]	MA "Psychotherapy+"	MeSH descriptor: [Psychotherapy] explode all trees
S198	psychosomatic[tiab]	TI,AB psychosomatic	psychosomatic:ti,ab,kw in Trials
S199	psychiatric[tiab]	TI,AB psychiatric	psychiatric:ti,ab,kw in Trials
S200	psychotherapy[tiab]	TI,AB psychotherapy	"psychotherapy:ti,ab,kw in Trials
S201	S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131	S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131	#56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120 OR #121 OR #122 OR #123 OR #124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130 OR #131

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S202	clinical trials as topic[MeSH Terms:noexp]	MA"clinical trials as topic"	MeSH descriptor: [Clinical Trials as Topic] this term only
S203	randomized controlled trial[pt]	PT randomized controlled trial	"randomized controlled trial":pt
S204	"controlled clinical trial"[pt]	PT controlled clinical trial	"controlled clinical trial":pt
S205	clinical trial[pt]	PT clinical trial	"clinical trial":pt
S206	trial[tiab]	TI,AB trial	trial:ti,ab,kw in Trials
S207	randomly[tiab]	TI,AB randomly	"randomly:ti,ab,kw in Trials
S208	random*[tw]	TX random*	random*
S209	"randomized controlled trial"[tw]	TX "randomized controlled trial"	"randomized controlled trial"
S210	"controlled clinical trial"[tw]	TX "controlled clinical trial"	"controlled clinical trial"
S211	RCT[tw]	TX RCT	RCT
S212	"clinical trial"[tw]	TX "clinical trial"	"clinical trial"
S213	S202 OR S203 OR S204 OR S205 OR S206 OR S207 OR S208 OR S209 OR S210 OR S211 OR S212	S202 OR S203 OR S204 OR S205 OR S206 OR S207 OR S208 OR S209 OR S210 OR S211 OR S212	#202 OR #203 OR #204 OR #205 OR #206 OR #207 OR #208 OR #209 OR #210 OR #211 OR #212
S214	S23 AND S54 AND S200 AND S213	S23 AND S54 AND S200 AND S213	#23 AND #54 AND #200 AND #213

Note. mesh = MeSH Term; tiab / ti, ab = Title/Abstract; pt = Publication Type; tw / tx = Text Word; kw = keywords, noexp = no explosion.

# BMJ Open

## Internet- and mobile-based aftercare and follow-up for mental disorders: Protocol of a systematic review and meta-analysis

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3 **Internet- and mobile-based aftercare and follow-up for mental disorders: Protocol of a**  
4 **systematic review and meta-analysis**  
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## ABSTRACT

**Introduction:** Mental disorders are characterized by a high likelihood of symptom recurrence or chronicity. Thus in the vulnerable post-discharge phase, aftercare and follow-up aim at stabilizing treatment effects, promoting functionality and preventing relapse or readmission. Internet- and mobile-based interventions may represent low-threshold and effective extensions to aftercare in tertiary prevention of mental disorders.

**Objectives:** The planned systematic review and meta-analysis aims to synthesize and analyze existing evidence on the effectiveness of psychological Internet- and mobile-based aftercare or follow-up in maintaining treatment effects and/or preventing recurrence in adults with mental disorders.

**Methods and analysis:** Electronic databases (PsycInfo, MEDLINE and CENTRAL) will be searched systematically, complemented by a hand-search of ongoing trials and reference lists of selected studies. Data extraction and evaluation will be conducted by two independent reviewers and quality will be assessed with the Cochrane Risk of Bias tool. Eligibility criteria for selecting studies will be: Randomized controlled trials of Internet- and mobile-based, psychological aftercare and follow-up for the tertiary prevention of mental disorders in an adult population. Primary outcome will be symptom severity. Secondary outcomes will be symptom or disorder recurrence rate, rehospitalization rate, functionality, quality of life or adherence to primary treatment. Further data items to be extracted will be: Study design-, intervention- and technical characteristics, type of mental disorder or clinical symptom to be treated, target population items, setting, treatment engagement and assessment of additional outcome variables. Meta-analytic pooling will be conducted when data of included studies are comparable in terms of study design, intervention type, endpoints, assessments, and target mental disorder. Cumulative Evidence will be evaluated according to the GRADE framework.

**Ethics and dissemination:** Ethics approval is not required. Results from this review will be published in peer-reviewed journals and presented at international conferences.

**Systematic review registration:** PROSPERO CRD42017055289

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- This review performs a sensitive search in electronic databases on digital technologies in tertiary prevention and will be the first to evaluate the effectiveness of Internet- and mobile-based aftercare in maintaining treatment effects or preventing recurrence in adults with mental disorders.
- Heterogeneity of studies in terms of clinical, methodological or statistical aspects will be considered carefully.
- The differentiated findings will provide clinicians and public health policymakers with a valuable overview of the feasibility of IMIs in tertiary prevention of mental disorders.
- The present protocol follows the PRISMA-P guidelines.
- We plan to assess the confidence in the cumulative evidence with the GRADE system.

## INTRODUCTION

Mental disorders are not only highly prevalent[1] but are also characterized by frequent recurrence during lifetime or chronic courses[2–5]. Adverse effects of recurrence or chronicity can be severe and include elevated readmission rates[6], early retirement[7], reduced quality of life[8] and increased mortality[9].

Within all areas of health care, tertiary prevention is paramount to monitor and manage symptoms, prevent relapse and promote health and functioning in persons with mental disorders[10]. In terms of continuous care, tertiary prevention may therefore comprise psychosocial, pharmacological or vocational rehabilitation, aftercare, follow-up or maintenance treatment. In particular, the transition after inpatient treatment can be considered a vulnerable phase[11], in which convalescents have to transfer and maintain health behavior, initiate change and are confronted with various individual, social or occupational challenges[12].

Meta-analytic evidence suggests the efficacy of cognitive behavioral therapy (CBT)[13, 14], psychosocial interventions[15, 16], pharmacological maintenance treatment[17] or psychosomatic rehabilitation[18] in reducing symptom severity, relapse rates and promoting functionality or medication adherence[19, 20] in mental disorders following acute treatment.

However, implementation strategies of aftercare are very heterogeneous and vary between different health care systems, mental disorders and treatment modalities. In this regard, studies in psychiatric or chronic pain patients indicate an insufficient prescription of aftercare by clinicians[21, 22]. Other studies suggest a limited uptake or adherence of psychosocial or medical maintenance treatment in convalescents[23–26]. Reasons for non-participation in psychosocial aftercare may include long waiting-times[27], pessimistic treatment expectancies[24] or various organizational barriers[22]. On the other hand, insufficient resources of health care systems and medical costs may further limit an extensive implementation and lead to gaps in continuity of care[28].

In an effort to overcome these limitations, Internet-delivered health promotion and treatment options for mental disorders have been developed particularly in the last decade. Internet- and mobile-based Interventions (IMIs) can be defined as “health related services and systems, carried out over a distance by means of information and communications technologies, for the purpose of global health promotion, disease control and health care” (p. 1)[29]. IMIs can be categorized by technical implementation (e.g. PC, smartphone, wearables), content (e.g. education, monitoring, behavior-change), localization in the health care process (e.g. prevention, stand-alone interventions, blended- or aftercare), amount of human support (self-administered/automatized, self-help with minimal guidance, online-therapy) or therapeutic contact (e.g. E-Mail, SMS, Live-Chat/Video)[30]. IMIs can be administered cost-effectively and without local or temporal boundaries[31, 32]. Since Internet access and use are growing constantly across countries and age groups[33], IMIs are also a widely accessible instruments.

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2  
3 A growing amount of evidence suggests efficacy of web-based psychotherapeutic interventions for a  
4 wide range of mental conditions[34, 35]. One of the first transdiagnostic reviews by Barak and  
5 colleagues[34] found small to large effect sizes of IMIs ranging from standardized mean difference  
6 (SMD) = 0.32 (depression, n = 16) to SMD = 0.88 (post-traumatic-stress disorder, PTSD, n = 3).  
7  
8 Further reviews focused on IMIs as stand-alone interventions, including meta-analytic evidence of  
9 efficacy in depression (SMD = 0.56, n = 19)[36], anxiety disorders (SMD = 1.06, n = 28)[37] or PTSD  
10 (CBT-based interventions, SMD = 0.95, n = 8)[38]. However, IMIs in psychiatric disorders are less  
11 studied, albeit first RCTs show promising results[39]. With regard to the implementation of IMIs in  
12 different contexts of health care, a recent review by Sander and colleagues[40] found small to medium  
13 cross-diagnostic effect sizes (d = 0.11 - 0.76) of IMIs in the primary prevention of mental disorders.  
14 Furthermore, a review by Niuwenhuijsen et al.[41] suggests efficacy of remote interventions (Internet-  
15 or telephone-based) on return-to-work of depressed patients.

16  
17 Previous studies on Internet- or mobile-based aftercare focused on guided, web-based self-help  
18 including psychoeducation as well as modular, interactive treatment elements and a certain amount of  
19 asynchronous therapist contact[42, 43]. Other approaches comprise mobile based[44] or synchronous,  
20 chat- or video-based aftercare[45, 46]. First evidence suggests the efficacy of IMIs in relapse  
21 prevention or reduction of symptom severity[42, 46].

22  
23 However, to the best of our knowledge, no previous systematic review has investigated comprehensive  
24 evidence on IMIs as aftercare instruments for adults with mental disorders. Thus, the results of this  
25 review will give an overview of this field of research and identify potentials of IMIs for public health  
26 policy makers and health care providers. The present protocol describes the rationale and design of the  
27 systematic review and planned meta-analysis according to the 'Preferred reporting items for  
28 systematic review and meta-analysis protocols (PRISMA-P)'[47].

## 29 Objectives

30  
31 The aim of this systematic review and meta-analysis is to give a comprehensive overview of  
32 randomized controlled trials (RCTs) investigating the effectiveness of Internet- and mobile-based  
33 psychological aftercare (e.g. rehabilitation, follow-up-, maintenance treatment) in maintaining  
34 treatment effects or in preventing symptom or disorder recurrence of mental disorders in adults.

## 35 METHODS

### 36 Eligibility criteria

#### 37 Population

38  
39 Studies will be included if they (a) focus on an adult population ( $\geq 18$  years) who (b) have received  
40 treatment for a mental disorder or a somatic condition with comorbid mental symptoms within the  
41 previous six months. Preceding treatment of mental disorder may consist of inpatient or outpatient  
42 psychotherapy, psychiatric treatment or medical treatment, delivered by physicians or  
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3 psychotherapists. Mental disorders must (c) be assessed by a standardized or validated instrument,  
4 including standardized interviews (e.g. SCID, CIDI), validated self-reports (e.g. BDI, BAI, EDI),  
5 clinician-rated scales (e.g. HAMD, GAF) or diagnosis by health care professionals.  
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#### 8 Study design and interventions

9  
10 (d) Only randomized controlled trials that are available in full text (RCT) will be considered.  
11 Manuscripts must be published in English or German. Treatment groups should receive a  
12 psychological aftercare or follow-up intervention. Following the definition by Kampling et al.[48],  
13 psychological interventions (e) may include elements of evidence-based therapy forms (e.g. cognitive  
14 behavioral therapy, psychodynamic therapies, behavior therapy or behavior modification, systemic  
15 therapies, third wave cognitive behavioral therapies, humanistic therapies, integrative therapies).  
16 Interventions may contain symptom monitoring, promotion of adherence to primary treatment (e.g.  
17 medication compliance), psychoeducation, reinforcement/feedback mechanisms as well as interactive  
18 elements or comprise guided/unguided self-help or comprehensive psychotherapeutic programs. If  
19 symptom monitoring or reminders to treatment adherence are the predominant intervention modality,  
20 studies will only be included, if accompanied by a distinguishable psychological intervention element.  
21 Treatments not clearly described will be excluded.  
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24 (f) Aftercare and follow-up will be defined as interventions following acute treatment designed to  
25 monitor or stabilize mental symptoms, identify or manage warning signs of symptom/disorder  
26 recurrence or enhance coping strategies to prevent recurrence, relapse or readmission[49], support  
27 transition and adoption of acquired health behavior and to promote or preserve health status, thereby  
28 reducing the impact of the illness on functioning or quality of life.  
29

30 (g) Interventions have to be delivered predominantly in an online setting, via Internet (web-/online) or  
31 mobile applications. Interventions may vary in the amount of human support, ranging from unguided  
32 self-help, over asynchronous minimal guidance to synchronous therapist contact[50].  
33

34 Studies must (h) report a minimum follow-up assessment of the main outcome of three months after  
35 the end of preceding treatment. Follow-up periods of 3-6 months will be categorized as 'short', 6-12  
36 months as 'medium' and above as 'long-term'.  
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#### 39 Comparators

40 (i) Control groups may receive either no intervention or comprise a waiting list (inactive control  
41 group) or include treatment as usual, another form of treatment (e.g. face-to-face psychotherapy,  
42 phone-delivered-, pharmacological/placebo treatment, other forms of psychological interventions) as  
43 active control group.  
44

#### 45 Exclusion criteria

46 Studies will be excluded, if they focus on the prevention of the first onset of a mental disorder or if no  
47 distinguishable treatment preceded the intervention under study (stand-alone interventions).  
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3 Substance-related and addictive disorders will not be included, as this represents another specific  
4 research area[51, 52] and treatment rationales are predominantly socio-educational or follow a health  
5 behavior change model rather than psychotherapeutic intervention models.  
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### 8 **Information sources and search strategy**

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10 Electronic databases that will be included are Medline, PsycInfo and the Cochrane Central Register of  
11 Controlled trials (CENTRAL). A sensitive search strategy will be applied (see supplementary file 1).  
12 The WHO International Clinical Trials Registry Platform (ICTRP) will be hand searched to identify  
13 ongoing trials. To assure literature saturation, reference lists of included studies will be perused. In  
14 case of unclear eligibility or indication of missing or unpublished data, we will contact the principal  
15 investigators (PIs) of studies for clarification. Also, when study protocols without a succeeding  
16 publication of results are identified, we attempt to contact PI to obtain unpublished results and  
17 determine eligibility for inclusion.  
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### 23 **Study records**

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25 In a first step, two independent reviewers (SF, SH) will screen titles and abstracts of the database  
26 search to identify qualified studies. Records will be managed in CITAVI®. In a second step, these  
27 reviewers will examine full texts in terms of the eligibility criteria. Likewise, the reference lists will be  
28 screened against eligibility criteria. In case of disagreement on eligibility, a third reviewer (LS) will be  
29 consulted. Inter-rater-reliability will be examined to evaluate the consistency of study selection. To  
30 illustrate the search and selection process, a flow-chart according to the PRISMA-protocol[47] will be  
31 provided. Criteria for the exclusion of studies will be reported.  
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36 Extracted data of eligible studies will be verified by a second reviewer to assure accuracy.  
37 Disagreement will be solved by discussion or by consulting a third reviewer in case of unresolved  
38 disagreements. Data extraction forms will we developed and piloted. In case of overlapping or  
39 multiple reports, we plan to compare studies with regard to list of authors, sample sizes, treatments or  
40 outcomes. In case of unclear or missing information, we will contact PIs with a request to provide  
41 these data.  
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### 46 **Data items**

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48 The following data items will be extracted for each study: (a) study identification items (first author,  
49 year of publication), (b) study design characteristics (e.g. sample size, control group, pre-treatment,  
50 lengths of follow-up assessment, study drop-out), (c) intervention characteristics (e.g.  
51 psychological/therapeutic methods, amount of human guidance, synchronicity of contact, duration of  
52 intervention), (d) technical characteristics (e.g. Internet-/mobile-based, devices used, technical  
53 prerequisites), (e) type of mental disorder or clinical symptom to be treated, (f) target population items  
54 (e.g. age, gender), (g) setting (e.g. recruitment strategy, nationality, environment, language), (h)  
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3 treatment engagement (e.g. treatment-drop-out rate, treatment fidelity, adoption of outpatient therapy),  
4 (i) assessment of additional outcome variables, (j) clinical outcome (symptom severity,  
5 recurrence/incidence rate, rehospitalization, functionality/quality of life, adherence to primary  
6 treatment).

### 9 10 **Outcomes and prioritization**

11 Primary outcome will be symptom severity assessed via validated instruments (standardized  
12 interviews, self- or clinician-rated scales) or clinical diagnosis as an indicator of maintenance of  
13 treatment effects.

14 Secondary outcomes will be defined as (a) symptom recurrence rate, (b) incidence rate of mental  
15 disorder under study from post-treatment to latest available follow-up, (c) rehospitalization rate, (d)  
16 indicators of functionality or quality of life and (e) adherence to primary treatment (e.g. medication  
17 compliance).

18 In the likely case of multiple assessment instruments for primary or secondary outcome, we will  
19 prioritize data as follows: (1) Data from structured interviews will be prioritized. (2) Clinician-rated  
20 scales will be preferred over self-report instruments. (3) Self-report questionnaires will be prioritized  
21 over diagnosis by health professionals.

22 When several assessment instruments are used within one study that can be assigned to the same  
23 hierarchy level, we will (1) extract outcome of the most frequently used instrument according to  
24 eligible studies or (2) if not evident, select randomly. To control for an investigator bias, a second  
25 reviewer (SH) will cross-check the extraction process.

### 26 27 28 **Risk of bias in individual studies**

29 The quality of evidence of each study will be evaluated following the Cochrane Risk of Bias tool[53].  
30 The domains to be analyzed will be: (a) random sequence generation, (b) allocation concealment, (c)  
31 blinding of participants and personnel, (d) blinding of outcome assessment, (e) incomplete outcome  
32 data, (f) selective outcome reporting and (g) other threats to validity (e.g. treatment fidelity,  
33 parallelism of measurement, variance homogeneity at baseline, co-interventions).

34 As a distinctive feature of psychological interventions, blinding of health care providers (in guided  
35 Internet- or mobile-based intervention studies) or patients regarding treatment is not warranted,  
36 resulting in a high risk of bias rating of criterion (criterion c). However, outcome assessors can remain  
37 unaware of participant's treatment allocation (criterion (d)).

### 38 39 40 **Data synthesis**

#### 41 42 43 Qualitative synthesis

44 A narrative synthesis will be reported on all included studies and relevant characteristics listed under  
45 'data items' will be qualitatively described. A detailed description of their results on relevant domains  
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3 will be provided in text and ‘summary of findings’ tables (comparison against control groups)  
4 following the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-  
5 P)[47].  
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#### 7 8 Meta-Analysis

9  
10 The expected heterogeneity of studies in terms of clinical (e.g. mental disorder), intervention-related  
11 (e.g. objective, type of IMI), methodological (e.g. comparators, assessment methods) or statistical (e.g.  
12 comparability of outcome measures) aspects will be considered carefully. Thus, meta-analytic pooling  
13 will only be conducted, if comparability of included studies is met in at least three studies. The  
14 Cochrane Collaborations’ Review Manager® will be used. By separating analyses in terms of mental  
15 disorders or intervention type, we plan to reduce heterogeneity of pooled estimates. A random-effects  
16 model will be used. Only studies with less than substantial statistical heterogeneity by will be pooled.  
17 If possible, heterogeneity of study results will be analyzed through forest plots and calculating  $I^2$   
18 statistics. The degree of heterogeneity will then be categorized according to the guidelines of the Risk  
19 of Bias tool[53].  
20

21  
22 For continuous data, we will calculate SMD and 95% confidence intervals. For dichotomous data, we  
23 will transform findings into risk ratios (RR). We aim to calculate the number needed to treat (NNT) to  
24 further illustrate clinical relevance of the interventions.  
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27 Outcome variables (e.g. symptom severity scores) will be pooled and further differentiated in terms of  
28 ‘short’, ‘medium’ or ‘long-term’ effectiveness when follow-up assessment is reported. Subject to  
29 sufficient group size and comparability of assessments, we plan to analyze study level covariates (e.g.  
30 type of mental disorder, type of Internet- or mobile-based intervention, amount of guidance).  
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#### 36 **Meta-biases - confidence in cumulative evidence**

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38 We will retrieve study protocols or trial registrations to identify reporting biases. Thereby, we will  
39 evaluate whether selective reporting of outcomes is present. A possible small sample bias will be  
40 assessed by using a random-effects model. Provided the number of studies is sufficient, we plan to  
41 examine a possible publication bias of significant-only studies in funnel plots. We will also search for  
42 unpublished or non-significant studies.  
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44  
45 We plan to rate the cumulative evidence according to the Grading of Recommendations Assessment,  
46 Development and Evaluation (GRADE)[54] in terms of study limitations, inconsistency of results,  
47 indirectness of evidence, imprecision of effect estimates reporting bias. Quality of evidence will be  
48 categorized into ‘very low’, ‘low’, ‘moderate’, or ‘high’.  
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#### 52 **ETHICS AND DISSEMINATION**

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54 A formal ethical approval is not required since no primary data of individuals will be collected. The  
55 status of the planned review will be updated regularly in PROSPERO. Results from this review will be  
56 published in leading peer-reviewed journals in the field of telemedicine and eHealth. Furthermore,  
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3 results will be presented at international conferences and workshops to facilitate dissemination into  
4 clinical practice.  
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## 8 9 **CONCLUSION**

10 This systematic review and meta-analysis will complement the evidence base of IMIs and allow for an  
11 evaluation of their feasibility as aftercare for the tertiary prevention as a significant component of  
12 mental health care. In case of cavities in research areas or unsatisfactory confirmation, we will suggest  
13 future research strategies. The findings will extend previous literature on the effectiveness of IMIs in  
14 different areas of health care like prevention[40] or as an alternative to face-to-face therapy[55].  
15 Furthermore, the results will provide clinicians and public health policymakers with a valuable  
16 overview of the possibilities of IMIs in monitoring and managing patients after regular treatment and  
17 in preventing relapse or readmission.  
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## 24 25 **ABBREVIATIONS**

26 BAI: Beck Anxiety Inventory

27 BDI: Beck Depression Inventory

28 CBT: Cognitive Behavioral Therapy

29 CENTRAL: Cochrane Central Register of Controlled trials

30 CIDI: Composite International Diagnostic Interview

31 EDI: Eating Disorder Inventory

32 GAF: Global Assessment of Functioning

33 GRADE: Grading of Recommendations Assessment, Development and Evaluation

34 HAMD: Hamilton Depression Scale

35 ICTRP: WHO International Clinical Trials Registry Platform

36 IMIs: Internet- and mobile-based interventions

37 MEDLINE: Medical Literature Analysis and Retrieval System Online

38 PI: Principal investigator

39 PRISMA-P: Preferred reporting items for systematic review and meta-analysis protocols

40 PTSD: post-traumatic-stress disorder

41 RCT: Randomized controlled trials

42 RR: Risk ratios

43 SCID: Structured Clinical Interview for DSM Disorders

44 SMD: Standardized mean difference (Cohens' d/Hedges' g)

45 NNT: Number needed to treat  
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## CONTRIBUTORSHIP STATEMENT

All authors were involved in the concept and review design of the study and data analysis plan. SH and SF wrote the draft of this manuscript. LS provided valuable revisions. All authors contributed to the further writing and approved the final version of the manuscript. The authors thank the reviewers for their constructive feedback.

## COMPETING INTERESTS

None declared.

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## DATA SHARING STATEMENT

No additional unpublished data available.

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	MEDLINE via PuPubMed	PsycINFO via Ebsco	CENTRAL
S1	Aftercare[mesh]	MA "Aftercare"	MeSH descriptor: [Aftercare] explode all trees
S2	Recurrence[mesh]	MA "Recurrence"	MeSH descriptor: [Recurrence] explode all trees
S3	Relapse Prevention [mesh]	MA "Relapse prevention"	MeSH descriptor: [secondary prevention] explode all trees
S4	Tertiary Prevention[mesh]	MA "Tertiary Prevention"	MeSH descriptor: [Tertiary Prevention] explode all trees
S5	Convalescence[mesh]	MA "Convalescence"	MeSH descriptor: [Convalescence] explode all trees
S6	aftercare[tiab] OR after-care[tiab]	TI,AB aftercare	aftercare:ti,ab,kw in Trials
S7	(after-treatment*[tiab] OR "after treatment" [tiab])	TI,AB after-treatment* OR TI,AB "after treatment*"	after-treatment*:ti,ab,kw OR "after treatment*":ti,ab,kw in Trials
S8	relaps*[tiab]	TI,AB relaps*	relaps*:ti,ab,kw in Trials
S9	follow-up[tiab]	TI,AB follow-up	follow-up:ti,ab,kw in Trials
S10	"intervention following*[tiab]	TI,AB "intervention following*"	"intervention following*":ti,ab,kw in Trials
S11	rehabilitation*[tiab]	TI,AB rehabilitation*	rehabilitation*:ti,ab,kw in Trials
S12	(tele-rehabilitation*[tiab] OR Telerehabilitation*[tiab])	(TI,AB tele-rehabilitation* OR TI,AB telerehabilitation*)	tele-rehabilitation*:ti,ab,kw OR telerehabilitation*:ti,ab,kw in Trials
S13	(post-treatment*[tiab] OR post treatment*[tiab])	(TI,AB post-treatment* OR TI,AB "post treatment*")	(post-treatment*:ti,ab,kw OR post treatment*:ti,ab,kw in Trials)
S14	"treatment after inpatient"[tiab]	TI,AB "treatment after inpatient"	"treatment after inpatient":ti,ab,kw in Trials
S15	recovery[tiab]	TI,AB recovery	recovery:ti,ab,kw in Trials
S16	"maintenance treatment"[tiab]	TI,AB "maintenance treatment"	"maintenance treatment":ti,ab,kw in Trials
S17	"continuation treatment"[tiab]	TI,AB "continuation treatment"	"continuation treatment":ti,ab,kw in Trials
S18	continuation-phase[tiab]	TI,AB continuation-phase	continuation-phase:ti,ab,kw in Trials
S19	"tertiary prevention"[tiab]	TI,AB "tertiary prevention"	"tertiary prevention":ti,ab,kw in Trials
S20	"continuous care"[tiab]	TI,AB "continuous care"	"continuous care":ti,ab,kw in Trials
S21	"disease management*[tiab]	TI,AB "disease management*"	"disease management*":ti,ab,kw in Trials
S22	recurren*[tiab]	TI,AB recurren*	recurren*:ti,ab,kw in Trials
S23	post-discharge [tiab]	TI,AB post-discharge	post-discharge:ti,ab,kw in Trials
S24	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23
S25	Telemedicine[mesh]	MA "Telemedicine+"	MeSH descriptor: [Telemedicine] explode all trees

Supplementary File 1. Table showing the search strings for MEDLINE, PsycINFO and CENTRAL

	MEDLINE via PubMed	PsycINFO via Ebsco	CENTRAL
S26	Computer Assisted Instruction[mesh]	MA "Computer Assisted Instruction"	MeSH descriptor: [Computer Assisted Instruction] explode all trees
S27	Mobile Health Units[mesh]	MA "Mobile Health Units"	MeSH descriptor: [Mobile Health Units] explode all trees
S28	Therapy, Computer-Assisted[mesh]	MA "Therapy, Computer-Assisted+"	MeSH descriptor: [Therapy, Computer-Assisted] explode all trees
S29	Mobile Applications[mesh]	MA "Mobile Applications"	MeSH descriptor: [Mobile Applications] explode all trees
S30	Internet[mesh]	MA "Internet+"	MeSH descriptor: [Internet ] explode all trees
S31	"computer applications"[tiab]	TI,AB "computer applications"	"computer applications":ti,ab,kw in Trials
S32	ICBT [tiab]	TI,AB ICBT	ICBT:ti,ab,kw in Trials
S33	telemental [tiab]	TI,AB telemental	telemental:ti,ab,kw in Trials
S34	e-therapy [tiab]	TI,AB e-therapy	e-therapy:ti,ab,kw in Trials
S35	CD-ROM [tiab]	TI,AB CD-ROM	CD-ROM:ti,ab,kw in Trials
S36	mhealth [tiab]	TI,AB mhealth	mhealth:ti,ab,kw in Trials
S37	(e-mail [tiab] OR email [tiab])	(TI,AB e-mail OR TI,AB email)	(e-mail:ti,ab,kw OR email:ti,ab,kw in Trials)
S38	SMS [tiab]	TI,AB SMS	SMS:ti,ab,kw in Trials
S39	app [tiab]	TI,AB app	app:ti,ab,kw in Trials
S40	ICT [tiab]	TI,AB ICT	ICT:ti,ab,kw in Trials
S41	online[tiab]	TI,AB online	online:ti,ab,kw in Trials
S42	mobile[tiab]	TI,AB mobile	mobile:ti,ab,kw in Trials
S43	eHealth[tiab]	TI,AB eHealth	eHealth:ti,ab,kw in Trials
S44	(web-based[tiab] OR "web based"[tiab])	(TI,AB web-based OR web based TI,AB)	(web-based:ti,ab,kw OR "web based":ti,ab,kw in Trials)
S45	(computer-based[tiab] OR "computer based"[tiab])	(TI,AB computer-based OR TI,AB "computer based")	(computer-based:ti,ab,kw in Trials OR "computer based:ti,ab,kw in Trials)
S46	computerized[tiab]	TI,AB computerized	computerized:ti,ab,kw in Trials
S47	"world wide web"[tiab]	TI,AB "world wide web"	"world wide web":ti,ab,kw in Trials
S48	cyber[tiab]	TI,AB cyber	cyber:ti,ab,kw in Trials
S49	ccbt[tiab]	TI,AB ccbt	ccbt:ti,ab,kw in Trials
S50	mobile-based[tiab] OR "mobile based"[tiab]	TI,AB "mobile based" OR TI,AB mobile-based	mobile-based:ti,ab,kw OR "mobile based":ti,ab,kw in Trials
S51	internet[tiab]	TI,AB internet	internet:ti,ab,kw in Trials
S52	(computer-assisted[tiab] OR "computer assisted"[tiab])	(TI,AB computer assisted OR TI,AB "computer assisted")	(computer-assisted:ti,ab,kw OR "computer assisted":ti,ab,kw in Trials)
S53	"text messaging"[tiab]	TI,AB "text messaging"	"text messaging":ti,ab,kw in Trials
S54	Smartphone*[tiab]	TI,AB smartphone*	smartphone*:ti,ab,kw in Trials

	MEDLINE via PuPubMed	PsycINFO via Ebsco	CENTRAL
S55	S25 OR S26 Or S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54	S25 OR S26 Or S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53OR S54	#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53OR #54
S56	Mental Disorders[mesh]	MA "Mental Disorders+"	MeSH descriptor: [Mental Disorders] explode all trees
S57	Mental health[mesh]	MA "Mental health+"	MeSH descriptor: [Mental health] explode all trees
S58	Mentally Ill Persons[mesh]	MA "Mentally Ill Persons"	MeSH descriptor: [Mentally Ill Persons] explode all trees
S59	"mental distress"[tiab]	TI,AB "mental distress"	"mental distress":ti,ab,kw in Trials
S60	"psychiatric disorder*"[tiab]	TI,AB "psychiatric disorder*"	"psychiatric disorder*":ti,ab,kw in Trials
S61	"psychological disorder*"[tiab]	TI,AB "psychological disorder*"	"psychological disorder*":ti,ab,kw in Trials
S62	"mental illness*"[tiab]	TI,AB "mental illness*"	"mental illness*":ti,ab,kw in Trials
S63	"Mental disorder*"[tiab]	TI,AB "mental disorder*"	"mental disorder*":ti,ab,kw in Trials
S64	Substance-Related Disorders[mesh]	MA "Substance-Related Disorders+"	MeSH descriptor: [Substance-Related Disorders] explode all trees
S65	Alcohol-Related Disorders[mesh]	MA "Alcohol-Related Disorders+"	MeSH descriptor: [Alcohol-Related Disorders] explode all trees
S66	"alcohol dependence"[tiab]	TI,AB "alcohol dependence"	"alcohol dependence":ti,ab,kw in Trials
S67	"alcohol abuse"[tiab]	TI,AB "alcohol abuse"	"alcohol abuse":ti,ab,kw in Trials
S68	"substance abuse"[tiab]	TI,AB "substance abuse"	"substance abuse":ti,ab,kw in Trials
S69	"substance-related disorder*"[tiab]	TI,AB "substance-related disorder*"	"substance-related disorder*":ti,ab,kw in Trials
S70	"alcohol-related disorder*"[tiab]	TI,AB "alcohol-related disorder*"	"alcohol-related disorder*":ti,ab,kw in Trials
S71	Psychotic Disorders[mesh]	MA "Psychotic Disorders+"	MeSH descriptor:[Psychotic Disorders] explode all trees
S72	Schizophrenia[mesh]	MA "Schizophrenia+"	MeSH descriptor:[Schizophrenia] explode all trees
S73	psychotic[tiab]	TI,AB psychotic	psychotic:ti,ab,kw in Trials
S74	schizophren*[tiab]	TI,AB schizophren *	schizophren*:ti,ab,kw in Trials
S75	Affective Disorders, Psychotic[mesh]	MA "Affective Disorders, Psychotic+"	MeSH descriptor: [Affective Disorders, Psychotic] explode all trees
S76	Mood Disorders[mesh]	MA "Mood Disorders+"	MeSH descriptor: [Mood Disorders] explode all trees
S77	Depression[mesh]	MA "Depression"	MeSH descriptor: [Depression] explode all trees
S78	Bipolar Disorder[mesh]	MA "Bipolar Disorder+"	MeSH descriptor: [Bipolar Disorder] explode all trees

Supplementary File 1. Table showing the search strings for MEDLINE, PsycINFO and CENTRAL

	MEDLINE via PuPMed	PsycINFO via Ebsco	CENTRAL
S79	Dysthymic Disorder[mesh]	MA "Dysthymic Disorder"	MeSH descriptor: [Dysthymic Disorder] explode all trees
S80	Depressive Disorder[mesh]	MA "Depressive Disorder+"	MeSH descriptor: [Depressive Disorder] explode all trees
S81	Depressive Disorder, Major[mesh]	MA "Depressive Disorder, Major+"	MeSH descriptor: [Depressive Disorder, Major]
S82	"affective disorder*" [tiab]	TI,AB "affective disorder*"	"affective disorder*":ti,ab,kw in Trials
S83	depressive [tiab]	TI,AB depressive	depressive:ti,ab,kw in Trials
S84	depression [tiab]	TI,AB depression	depression:ti,ab,kw in Trials
S85	"mood disorder*" [tiab]	TI,AB "mood disorder*"	"mood disorder*":ti,ab,kw in Trials
S86	bipolar* [tiab]	TI,AB bipolar*	bipolar*:ti,ab,kw in Trials
S87	dysthymi* [tiab]	TI,AB dysthymic	dysthymic:ti,ab,kw in Trials
S88	cyclothymi * [tiab]	TI,AB cyclothymi*	cyclothymi* Title/Abstract]
S89	Anxiety Disorders[mesh]	MA "Anxiety Disorders+"	MeSH descriptor: [Anxiety Disorders] explode all trees
S90	Panic[mesh]	MA "Panic"	MeSH descriptor: [Panic] explode all trees
S91	Panic Disorder[mesh]	MA "Panic Disorder"	MeSH descriptor: [Panic Disorder] explode all trees
S92	Phobic Disorders[mesh]	MA "Phobic Disorders"	MeSH descriptor: [Phobic Disorders] explode all trees
S93	Socia Phobia[mesh]	MA "Social Phobia"	MeSH descriptor: [Social Phobia] explode all trees
S94	Agoraphobia[mesh]	MA "Agoraphobia"	MeSH descriptor: [Agoraphobia] explode all trees
S95	"anxiety disorder*" [tiab]	TI,AB "anxiety disorder*"	"anxiety disorder*":ti,ab,kw in Trials
S96	panic [tiab]	TI,AB panic	panic:ti,ab,kw in Trials
S97	phobi* [tiab]	TI,AB phobi*	phobi*:ti,ab,kw in Trials
S98	agoraphobi* [tiab]	TI,AB agoraphobi*	agoraphobi*:ti,ab,kw in Trials
S99	"social anxiety" [tiab]	TI,AB "social anxiety"	"social anxiety":ti,ab,kw in Trials
S100	"generalized anxiety disorder" [tiab]	TI,AB "generalized anxiety disorder"	"generalized anxiety disorder":ti,ab,kw in Trials
S101	Obsessive-Compulsive Disorder[mesh]	MA "Obsessive-Compulsive Disorder+"	MeSH descriptor: [Obsessive-Compulsive Disorder] explode all trees
S102	Disruptive, Impulse Control, and Conduct Disorders[mesh]	MA "Disruptive, Impulse Control, and Conduct Disorders+"	MeSH descriptor: [Disruptive, Impulse Control, and Conduct Disorders] explode all trees
S103	Stress Disorders, Post-Traumatic[mesh]	MA "Stress Disorders, Post-Traumatic"	MeSH descriptor: [Stress Disorders, Post-Traumatic] explode all trees
S104	Stress Disorders, Traumatic[mesh]	MA "Stress Disorders, Traumatic+"	MeSH descriptor: [Stress Disorders, Traumatic] explode all trees
S105	Adjustment Disorders[mesh]	MA "Adjustment Disorders"	MeSH descriptor: [Adjustment Disorders] explode all trees
S106	PTSD [tiab]	TI,AB PTSD	PTSD:ti,ab,kw in Trials

	MEDLINE via PuPMed	PsycINFO via Ebsco	CENTRAL
S107	"posttraumatic stress disorder*" [tiab]	TI,AB "posttraumatic stress disorder*"	"posttraumatic stress disorder*":ti,ab,kw in Trials
S108	"obsessive-compulsive disorder*" [tiab]	TI,AB "obsessive-compulsive disorder*"	"obsessive-compulsive disorder*":ti,ab,kw in Trials
S109	"impulse control disorder*" [tiab]	TI,AB "impulse control disorder*"	"impulse control disorder*":ti,ab,kw in Trials
S110	"stress disorder*, post-traumatic" [tiab]	TI,AB "stress disorder*, post-traumatic"	"stress disorder*, post-traumatic":ti,ab,kw in Trials
S111	"stress disorder*, traumatic" [tiab]	TI,AB "stress disorder*, traumatic"	"stress disorder*, traumatic":ti,ab,kw in Trials
S112	"adjustment disorder*" [tiab]	TI,AB "adjustment disorder*"	"adjustment disorder*":ti,ab,kw in Trials
S113	"Somatoform Disorders" [mesh]	MA "Somatoform Disorders+"	MeSH descriptor: [Somatoform Disorders] explode all trees
S114	"Body Dysmorphic Disorders" [mesh]	MA "Body Dysmorphic Disorders"	MeSH descriptor: [Body Dysmorphic Disorders]
S115	"Conversion Disorder" [mesh]	MA "Conversion Disorder+"	MeSH descriptor: [Conversion Disorder] explode all trees
S116	"Factitious Disorders" [mesh]	MA "Factitious Disorders+"	MeSH descriptor: [Factitious Disorders] explode all trees
S117	Hypochondriasis" [mesh]	MA "Hypochondriasis"	MeSH descriptor: [Hypochondriasis] explode all trees
S118	Neurasthenia" [mesh]	MA "Neurasthenia"	MeSH descriptor: [Neurasthenia] explode all trees
S119	"Medically Unexplained Symptoms" [mesh]	MA "Medically Unexplained Symptoms"	n.
S120	somatoform [tiab]	TI,AB somatoform	somatoform:ti,ab,kw in Trials
S121	"somatic symptom disorder*" [tiab]	TI,AB "somatic symptom disorder*"	"somatic symptom disorder*":ti,ab,kw in Trials
S122	"body dysmorphic disorders" [tiab]	TI,AB "body dysmorphic disorders"	"body dysmorphic disorders":ti,ab,kw in Trials
S123	"conversion disorder" [tiab]	TI,AB "conversion disorder"	"conversion disorder":ti,ab,kw in Trials
S124	hypochondriasis [tiab]	TI,AB hypochondriasis	hypochondriasis:ti,ab,kw in Trials
S125	"illness anxiety disorder" [tiab]	TI,AB "illness anxiety disorder"	"illness anxiety disorder":ti,ab,kw in Trials
S126	"medically unexplained*" [tiab]	TI,AB "medically unexplained*"	"medically unexplained*":ti,ab,kw in Trials
S127	somatization [tiab]	TI,AB somatization	somatization:ti,ab,kw in Trials
S128	"pain disorder" [tiab]	TI,AB "pain disorder"	"pain disorder":ti,ab,kw in Trials
S129	"chronic pain" [tiab]	TI,AB "chronic pain"	"chronic pain":ti,ab,kw in Trials
S130	"chronic back pain" [tiab]	TI,AB "chronic back pain"	"chronic back pain":ti,ab,kw in Trials
S131	"premenstrual syndrome" [tiab] OR "pre-menstrual syndrome" [tiab]	TI,AB "premenstrual syndrome" OR TI,AB OR "pre-menstrual syndrome"	"premenstrual syndrome":ti,ab,kw OR "pre-menstrual syndrome":ti,ab,kw in Trials
S132	"irritable bowel syndrome" [tiab]	TI,AB "irritable bowel syndrome"	"irritable bowel syndrome":ti,ab,kw in Trials
S133	fibromyalgia [tiab]	TI,AB fibromyalgia	fibromyalgia:ti,ab,kw in Trials
S134	"chronic fatigue" [tiab]	TI,AB "chronic fatigue"	"chronic fatigue":ti,ab,kw in Trials

Supplementary File 1. Table showing the search strings for MEDLINE, PsycINFO and CENTRAL

	MEDLINE via PuPubMed	PsycINFO via Ebsco	CENTRAL
S135	"tension headache"[tiab]	TI,AB "tension headache"	"tension headache":ti,ab,kw in Trials
S136	Dissociative Disorders[mesh]	MA "Dissociative Disorders+"	MeSH descriptor: [Dissociative Disorders] explode all trees
S137	Depersonalization"[mesh]	MA "Depersonalization"	MeSH descriptor: [Depersonalization] explode all trees
S138	"dissociative disorder*"[tiab]	TI,AB "dissociative disorder*"	"dissociative disorder*":ti,ab,kw in Trials
S139	depersonalization[tiab]	TI,AB depersonalization	depersonalization:ti,ab,kw in Trials
S140	derealization[tiab]	TI,AB derealization	derealization:ti,ab,kw in Trials
S141	Feeding and Eating Disorders[mesh]	MA "Feeding and Eating Disorders+"	MeSH descriptor: [Feeding and Eating Disorders] explode all trees
S142	Anorexia[mesh]	MA "Anorexia"	MeSH descriptor: [Anorexia] explode all trees
S143	Anorexia Nervosa[mesh]	MA "Anorexia Nervosa"	MeSH descriptor: [Anorexia Nervosa] explode all trees
S144	Bulimia[mesh]	MA "Bulimia"	MeSH descriptor: [Bulimia] explode all trees
S145	Bulimia Nervosa[mesh]	MA "Bulimia Nervosa"	MeSH descriptor: [Bulimia Nervosa] explode all trees
S146	Binge-Eating Disorder[mesh]	MA "Binge-Eating Disorder"	MeSH descriptor: [Binge-Eating Disorder] explode all trees
S147	anorexia[tiab]	TI,AB anorexia	anorexia:ti,ab,kw in Trials
S148	bulimia[tiab]	MA "bulimia"	bulimia:ti,ab,kw in Trials
S149	"eating disorder*"[tiab]	TI,AB "eating disorder*"	"eating disorder*":ti,ab,kw in Trials
S150	"binge eating"[tiab] OR binge-eating[tiab]	TI,Ab "binge eating" OR TI,Ab binge-eating	binge-eating:ti,ab,kw in Trials OR "binge-eating":ti,ab,kw in Trials
S151	"Sexual Dysfunctions, Psychological"[mesh]	MA "Sexual Dysfunctions, Psychological"	MeSH descriptor: [Sexual Dysfunctions, Psychological] explode all trees
S152	"gender dysphoria"[tiab]	TI,AB "gender dysphoria"	"gender dysphoria":ti,ab,kw in Trials
S153	"sexual dysfunction*"[tiab]	TI,AB "sexual dysfunction*"	"sexual dysfunction*":ti,ab,kw in Trials
S154	"sexual pain disorder*"[tiab]	TI,AB "sexual pain disorder*"	"sexual pain disorder*":ti,ab,kw in Trials
S155	"orgasmic disorder*"[tiab]	TI,AB "orgasmic disorder*"	"orgasmic disorder*":ti,ab,kw in Trials
S156	"sexual arousal disorder*"[tiab]	TI,AB "sexual arousal disorder*"	"sexual arousal disorder*":ti,ab,kw in Trials
S157	"gender identity disorder*"[tiab]	TI,AB "gender identity disorder*"	"gender identity disorder*":ti,ab,kw in Trials
S158	"disorders of sexual preference"[tiab]	TI,AB "disorders of sexual preference"	"disorders of sexual preference":ti,ab,kw in Trials
S159	"Sleep Wake Disorders"[mesh]	MA "Sleep Wake Disorders+"	MeSH descriptor: [Sleep Wake Disorders] explode all trees
S160	"Sleep Initiation and Maintenance Disorders"[mesh]	MA "Sleep Initiation and Maintenance Disorders"	MeSH descriptor: [Sleep Initiation and Maintenance Disorders] explode all trees

	MEDLINE via PuPMed	PsycINFO via Ebsco	CENTRAL
S161	insomnia[tiab]	TI,AB insomnia	insomnia:ti,ab,kw in Trials
S162	"sleep disorder*" [tiab]	TI,AB "sleep disorder*"	"sleep disorder*":ti,ab,kw in Trials
S163	Attention Deficit Disorder [mesh]	MA "Attention Deficit Disorder+"	MeSH descriptor: [Attention Deficit Disorder] explode all trees
S164	Attention Deficit Disorder with Hyperactivity[mesh]	MA "Attention Deficit Disorder with Hyperactivity"	MeSH descriptor: [Attention Deficit Disorder with Hyperactivity] explode all trees
S165	"attention-deficit disorder"[tiab]	TI,AB "attention-deficit disorder"	"attention-deficit disorder":ti,ab,kw in Trials
S166	"attention deficit hyperactivity disorder"[tiab]	TI,AB "attention deficit hyperactivity disorder"	"attention deficit hyperactivity disorder":ti,ab,kw in Trials
S167	Personality Disorders[mesh]	MA "Personality Disorders+"	MeSH descriptor: [Personality Disorders] explode all trees
S168	"personality disorder*" [tiab]	TI,AB "personality disorder*"	MeSH descriptor: [personality disorder*]:ti,ab,kw in Trials
S169	Antisocial Personality Disorder[mesh]	MA "Antisocial Personality Disorder"	MeSH descriptor: [Antisocial Personality Disorder] explode all trees
S170	Borderline Personality Disorder[mesh]	MA "Borderline Personality Disorder"	MeSH descriptor: [Borderline Personality Disorder] explode all trees
S171	Compulsive Personality Disorder[mesh]	MA "Compulsive Personality Disorder"	MeSH descriptor: [Compulsive Personality Disorder] explode all trees
S172	Dependent Personality Disorder[mesh]	MA "Dependent Personality Disorder"	MeSH descriptor: [Dependent Personality Disorder] explode all trees
S173	Histrionic Personality Disorder[mesh]	MA "Histrionic Personality Disorder"	MeSH descriptor: [Histrionic Personality Disorder] explode all trees
S174	Paranoid Personality Disorder[mesh]	MA "Paranoid Personality Disorder"	MeSH descriptor: [Paranoid Personality Disorder] explode all trees
S175	Schizoid Personality Disorder[mesh]	MA "Schizoid Personality Disorder"	MeSH descriptor: [Schizoid Personality Disorder] explode all trees
S176	Schizotypal Personality Disorder[mesh]	MA "Schizotypal Personality Disorder"	MeSH descriptor: [Schizotypal Personality Disorder] explode all trees
S177	Narcissistic Personality Disorder[mesh]	MA "Narcissistic Personality Disorder"	MeSH descriptor: [Narcissistic Personality Disorder] explode all trees
S178	"antisocial personality disorder"[tiab]	TI,AB "antisocial personality disorder"	"antisocial personality disorder":ti,ab,kw in Trials
S179	"borderline personality disorder"[tiab]	TI,AB "borderline personality disorder"	"borderline personality disorder":ti,ab,kw in Trials
S180	"compulsive personality disorder"[tiab]	TI,AB "compulsive personality disorder"	"compulsive personality disorder":ti,ab,kw in Trials
S181	"dependent personality disorder"[tiab]	TI,AB "dependent personality disorder"	"dependent personality disorder":ti,ab,kw in Trials
S182	"histrionic personality disorder"[tiab]	TI,AB "histrionic personality disorder"	"histrionic personality disorder":ti,ab,kw in Trials



Supplementary File 1. Table showing the search strings for MEDLINE, PsycINFO and CENTRAL

	MEDLINE via PuPubMed	PsycINFO via Ebsco	CENTRAL
S183	"paranoid personality disorder"[tiab]	TI,AB "paranoid personality disorder"	"paranoid personality disorder":ti,ab,kw in Trials
S184	"Schizoid personality disorder"[tiab]	TI,AB "Schizoid personality disorder"	"Schizoid personality disorder":ti,ab,kw in Trials
S185	"Schizotypal personality disorder"[tiab]	TI,AB "Schizotypal personality disorder"	"Schizotypal personality disorder":ti,ab,kw in Trials
S186	"dissocial personality disorder"[tiab]	TI,AB "dissocial personality disorder"	"dissocial personality disorder":ti,ab,kw in Trials
S187	"emotionally unstable personality disorder"[tiab]	TI,AB "emotionally unstable personality disorder"	"emotionally unstable personality disorder":ti,ab,kw in Trials
S188	"anankastic personality disorder"[tiab]	TI,AB "anankastic personality disorder"	"anankastic personality disorder":ti,ab,kw in Trials
S189	"anxious avoidant personality disorder"[tiab]	TI,AB "anxious avoidant personality disorder"	"anxious avoidant personality disorder":ti,ab,kw in Trials
S190	"dependent personality disorder"[tiab]	TI,AB "dependent personality disorder"	"dependent personality disorder":ti,ab,kw in Trials
S191	"narcissistic personality disorder"[tiab]	TI,AB "narcissistic personality disorder"	"narcissistic personality disorder":ti,ab,kw in Trials
S192	"enduring personality change"[tiab]	TI,AB "enduring personality change"	"enduring personality change":ti,ab,kw in Trials
S193	Paraphilic Disorders"[mesh]	MA "Paraphilic Disorders+"	MeSH descriptor: [Paraphilic Disorders] explode all trees
S194	"paraphilic disorder*"[tiab]	TI,AB "paraphilic disorder*"	"paraphilic disorder*":ti,ab,kw in Trials
S195	Psychosomatic Medicine[mesh]	MA "Psychosomatic Medicine"	MeSH descriptor: [Psychosomatic Medicine] explode all trees
S196	Psychiatry[mesh]	MA "Psychiatry+"	MeSH descriptor: [Psychiatry] explode all trees
S197	Psychotherapy[mesh]	MA "Psychotherapy+"	MeSH descriptor: [Psychotherapy] explode all trees
S198	psychosomatic[tiab]	TI,AB psychosomatic	psychosomatic:ti,ab,kw in Trials
S199	psychiatric[tiab]	TI,AB psychiatric	psychiatric:ti,ab,kw in Trials
S200	psychotherapy[tiab]	TI,AB psychotherapy	"psychotherapy:ti,ab,kw in Trials
S201	S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131	S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119 OR S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131	#56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120 OR #121 OR #122 OR #123 OR #124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130 OR #131

	MEDLINE via PuPubMed	PsycINFO via Ebsco	CENTRAL
	OR S132 OR S133 OR S134 OR S135 OR S136 OR S137 OR S138 OR S139 OR S140 OR S141 OR S142 OR S143 OR S144 OR S145 OR S146 OR S147 OR S148 OR S149 OR S150 OR S151 OR S152 OR S153 OR S154 OR S155 OR S156 OR S157 OR S158 OR S159 OR S160 OR S161 OR S162 OR S163 OR S164 OR S165 OR S166 OR S167 OR S168 OR S169 OR S170 OR S171 OR S172 OR S173 OR S174 OR S175 OR S176 OR S177 OR S178 OR S179 OR S180 OR S181 OR S182 OR S183 OR S184 OR S185 OR S186 OR S187 OR S188 OR S189 OR S190 OR S191 OR S192 OR S193 OR S194 OR S195 OR S196 OR S197 OR S198 OR S199 OR S200	OR S132 OR S133 OR S134 OR S135 OR S136 OR S137 OR S138 OR S139 OR S140 OR S141 OR S142 OR S143 OR S144 OR S145 OR S146 OR S147 OR S148 OR S149 OR S150 OR S151 OR S152 OR S153 OR S154 OR S155 OR S156 OR S157 OR S158 OR S159 OR S160 OR S161 OR S162 OR S163 OR S164 OR S165 OR S166 OR S167 OR S168 OR S169 OR S170 OR S171 OR S172 OR S173 OR S174 OR S175 OR S176 OR S177 OR S178 OR S179 OR S180 OR S181 OR S182 OR S183 OR S184 OR S185 OR S186 OR S187 OR S188 OR S189 OR S190 OR S191 OR S192 OR S193 OR S194 OR S195 OR S196 OR S197 OR S198 OR S199 OR S200	OR #132 OR #133 OR #134 OR #135 OR #136 OR #137 OR #138 OR #139 OR #140 OR #141 OR #142 OR #143 OR #144 OR #145 OR #146 OR #147 OR #148 OR #149 OR #150 OR #151 OR #152 OR #153 OR #154 OR #155 OR #156 OR #157 OR #158 OR #159 OR #160 OR #161 OR #162 OR #163 OR #164 OR #165 OR #166 OR #167 OR #168 OR #169 OR #170 OR #171 OR #172 OR #173 OR #174 OR #175 OR #176 OR #177 OR #178 OR #179 OR #180 OR #181 OR #182 OR #183 OR #184 OR #185 OR #186 OR #187 OR #188 OR #189 OR #190 OR #191 OR #192 OR #193 OR #194 OR #195 OR #196 OR #197 OR #198 OR #199 OR #200
S202	clinical trials as topic[MeSH Terms:noexp]	MA"clinical trials as topic"	MeSH descriptor: [Clinical Trials as Topic] this term only
S203	randomized controlled trial[pt]	PT randomized controlled trial	"randomized controlled trial":pt
S204	"controlled clinical trial"[pt]	PT controlled clinical trial	"controlled clinical trial":pt
S205	clinical trial[pt]	PT clinical trial	"clinical trial":pt
S206	trial[tiab]	TI,AB trial	trial:ti,ab,kw in Trials
S207	randomly[tiab]	TI,AB randomly	"randomly:ti,ab,kw in Trials
S208	random*[tw]	TX random*	random*
S209	"randomized controlled trial"[tw]	TX "randomized controlled trial"	"randomized controlled trial"
S210	"controlled clinical trial"[tw]	TX "controlled clinical trial"	"controlled clinical trial"
S211	RCT[tw]	TX RCT	RCT
S212	"clinical trial"[tw]	TX "clinical trial"	"clinical trial"
S213	S202 OR S203 OR S204 OR S205 OR S206 OR S207 OR S208 OR S209 OR S210 OR S211 OR S212	S202 OR S203 OR S204 OR S205 OR S206 OR S207 OR S208 OR S209 OR S210 OR S211 OR S212	#202 OR #203 OR #204 OR #205 OR #206 OR #207 OR #208 OR #209 OR #210 OR #211 OR #212
S214	S23 AND S54 AND S200 AND S213	S23 AND S54 AND S200 AND S213	#23 AND #54 AND #200 AND #213

Note. mesh = MeSH Term; tiab / ti, ab = Title/Abstract; pt = Publication Type; tw / tx = Text Word; kw = keywords, noexp = no explosion.

**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Page No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	1	Identify the report as a protocol of a systematic review
Update	1b	--	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:			
Contact	3a	1	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	8	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	--	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:			
Sources	5a	9	Indicate sources of financial or other support for the review
Sponsor	5b	9	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	9	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>			
Rationale	6	3-4	Describe the rationale for the review in the context of what is already known
Objectives	7	4	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
<b>METHODS</b>			
Eligibility criteria	8	4-5	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	5	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	5	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated

Study records:			
Data management	11a	5	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	5-6	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	6	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	6	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	6	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	6-7	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	7	Describe criteria under which study data will be quantitatively synthesised
	15b	7	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )
	15c	7	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	7	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	7-8	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	7-8	Describe how the strength of the body of evidence will be assessed (such as GRADE)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*