

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Effectiveness and feasibility of internet- and mobile-based interventions for individuals experiencing bereavement: A systematic review protocol

| | |
|-------------------------------|---|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2019-036034 |
| Article Type: | Protocol |
| Date Submitted by the Author: | 02-Dec-2019 |
| Complete List of Authors: | Luppa, Melanie; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health Loebner, Margrit; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health Pabst, Alexander Schlapke, Christiane; University of Leipzig Faculty of Medicine Stein, Janine; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health Riedel-Heller, Steffi; University of Leipzig, Institute of Social Medicine, Occupational Health and Public Health (ISAP), Medical Faculty |
| Keywords: | MENTAL HEALTH, Depression & mood disorders < PSYCHIATRY, PREVENTIVE MEDICINE |
| | |

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 1 **Effectiveness and feasibility of internet- and mobile-based interventions for individuals**
4
5 2 **experiencing bereavement: A systematic review protocol**
6

7 3

8 4

9
10 5 Luppá, Melanie; Loebner, Margrit; Pabst, Alexander; Schlapke, Christine, Stein, Janine;
11
12 6 Riedel-Heller, Steffi G.
13

14 7

15 8

16 9

17
18 10

19 11

20 12

21 13

22 14

23 15 Corresponding author:

24 16 Melanie Luppá, PhD

25 17 Institute of Social Medicine, Occupational Health and Public Health, University of Leipzig,
26 18 Faculty of Medicine

27 19 Philipp-Rosenthal-StraÙe 55

28 20 04103 Leipzig

29 21 Germany

30 22 Email: melanie.luppa@medizin-uni-leipzig.de

31 23 Phone: +49 341 9715406

32 24 Word count: 3,678
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

25 ABSTRACT

26 Introduction: Internet- and mobile-based interventions (IMIs) provide an innovative and
27 efficient self-management tool for mental health problems. This systematic review aims to
28 summarise and critically evaluate studies addressing the effectiveness and feasibility of IMIs
29 for normal and complicated grief in bereaved adults.

30 Methods and Analysis: The databases MEDLINE, Cochrane Library, PsycINFO, EMBASE and
31 Web of Science and Google Scholar (for “grey” literature) will be systematically searched for
32 feasibility studies or randomized controlled trials of IMIs for bereaved adults who were
33 experiencing normal/complicated grief. Data will be extracted and evaluated independently
34 by two reviewers from studies eligible for inclusion. Quality of evidence will be assessed, and
35 results will be synthesized qualitatively and pooled meta-analytically, if sufficient outcome
36 data are available. PRISMA standards and GRADE methodology will be used.

37 Ethics and Dissemination: No primary data will be collected; thus, ethical approval is not
38 required. The results will be disseminated through a peer-reviewed publication and
39 conference presentations.

40 PROSPERO registration number: CRD42019131428

41 Keywords: grief, bereavement, systematic review, internet- and mobile-based, effectiveness,
42 feasibility

44 Strengths and limitations of this study

- 45 - first study which provides a comprehensive summary of studies investigating
46 effectiveness and feasibility of internet- and mobile-based interventions (IMIs) for
47 normal and complicated grief in bereaved adults
- 48 - possibility of usage of these IMIs in healthcare as additional intervention tools as well
49 as low-threshold treatment options
- 50 - application with the necessary caution of these IMIs seems to be required not to
51 interfere with natural grief processes

56 Background

57
58 Self-management is an widely used approach within the medical health care system for
59 improving patients' knowledge, capabilities and skills in managing their health problems.
60 Internet- and mobile-based interventions (IMIs) provide an innovative and efficient self-
61 management tool for mental health problems. In recent years, web-based self-management
62 interventions have gained increasing attention as effective supplementary treatment
63 elements to standard mental health treatment [1].

64 The effectiveness of IMIs has been shown for treating depression (e.g. [2-4]), anxiety (e.g.
65 [5,6]), post-traumatic stress disorder (PTSD; e.g. [7-9]), and other mental health problems
66 [1]. However, less is currently known about IMIs for individuals experiencing normal or
67 complicated grief.

68 In general, grief is defined as a typical reaction to the loss of a significant other [10] , and is
69 associated with symptoms such as intense subjective distress, loneliness, and somatic
70 symptoms, e.g. tightness of the throat or need for sighing [11,12]. Recently, the concept of
71 an abnormal reaction to loss has been proposed and is included as a disorder in the
72 *Diagnostic Statistical Manual of Mental Disorders*, 5th Edition (*DSM-V*) and is expected to be
73 included in the *International Statistical Classification of Diseases and Related Health*
74 *Problems*, 11th Revision (*ICD-11*) as a new diagnosis. The disorders Complicated, Traumatic,
75 or Prolonged Grief (subsequently summarized under complicated grief) and Complicated
76 Grief are described as "a syndrome of prolonged and intense grief that is accompanied by
77 complications that derail the progress of grief" [13]. In contrast to uncomplicated grief,
78 clinically significant impairment in social, occupational, or other important areas of
79 functioning must be present [13,14]. The diagnosis of complicated grief is given only after a
80 period of six months following the index loss event if the person is still suffering from
81 separation stress as well as cognitive, emotional, and behavioral symptoms [14].

82 Because grief can affect many areas of life [15,16] and is one of the major contributors to
83 the development of mental health disorders, providing IMIs as a low-threshold treatment
84 option may enable more people to receive treatment than through face-to-face
85 interventions alone [17] to prevent the development of mental health disorders. Major
86 Depression, Generalized Anxiety Disorder, and Post-Traumatic Stress Disorder are
87 particularly closely related to the symptoms of complicated grief, but differences between
88 the disorders have also been reported [14,18].

1
2
3 89 To date, a number of IMIs for bereavement problems exist in the international research
4
5 90 literature. Internet-based Cognitive Behavioral Therapy (CBT) interventions were reported to
6
7 91 be effective in treating patients with complicated grief [19] but not for those with
8
9 92 uncomplicated grief [20]. Some researchers have urged caution in implementing
10
11 93 interventions too early or across a wide range of bereavement-related distress so as to not
12
13 94 interfere with natural grief processes [21,22]. One study showed that IMIs for PTSD improve
14
15 95 symptoms of complicated grief [23]. To our knowledge, there are no previous systematic
16
17 96 reviews summarizing the effectiveness and feasibility of IMIs for bereaved individuals – for
18
19 97 normal as well as complicated grief. The results of this review and meta-analysis will
20
21 98 therefore address this gap in the literature. This protocol describes the rationale and design
22
23 99 of the planned systematic review and meta-analysis.

100

101 OBJECTIVES

102 The planned review aims to systematically evaluate and synthesize the evidence base of
103
104 randomized controlled-trials (RCT)s reporting, the effectiveness of IMIs (i.e. improvement of
105
106 objective parameters), and the feasibility of IMIs (e.g. usability, satisfaction, acceptability,
107
108 understandability and usefulness) for individuals aged 18 years and older who experienced
109
110 the death of a significant other. Depending on the number of eligible studies, assessment
111
112 tools, and quality of the studies reported, we will also combine data across RCTs to estimate
113
114 pooled effect sizes for the considered outcomes.

109

110

111 METHODS AND ANALYSIS

112 This protocol outlines the strategies for conducting a systematic review and meta-analysis of
113
114 RCTs which examined the effectiveness of IMIs for bereavement. It is based on the Preferred
115
116 Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) for systematic review
117
118 protocols (PRISMA-P) guidelines [24,25]. The protocol describes the planned strategy to
119
120 systematically evaluate and synthesize data from randomized controlled trials and feasibility
121
122 studies on IMIs for bereaved individuals. We will apply the four-phase PRISMA flow diagram
(figure 1) for our study selection process.

119

120

121

122 Eligibility criteria

1
2
3 123 The systematic review will be divided into two parts: effectiveness studies and feasibility
4
5 124 studies on IMIs (study design criteria) which include adults (18 years and older), who
6
7 125 experienced the death of a significant other and were suffering from normal or complicated
8
9 126 grief (participant criteria). Any measures of effectiveness (i.e. improvement of objective
10
11 127 parameters) and feasibility (e.g. usability, satisfaction, acceptability, understandability and
12
13 128 usefulness) (outcome criteria) of IMIs related to bereavement will be included. Onset data
14
15 129 from clinician-rated scales will be prioritized over self-report questionnaires. The
16
17 130 intervention must have been a psychological intervention according to Kampling et al. [26]
18
19 131 criteria: cognitive behavioral therapy (CBT), psychodynamic psychotherapy, behavior
20
21 132 therapy or behavior modification, systemic therapy, third wave cognitive behavioral therapy,
22
23 133 humanistic therapy, integrative therapy or to other psychological-orientated interventions
24
25 134 and must have been provided in an online setting (intervention criteria). In RCTs, the
26
27 135 comparison group must be either 'treatment as usual', 'waiting list', 'attention placebo'
28
29 136 (inactivity on the part of both researchers and participants), or 'psychological placebo'
30
31 137 (activity on the part of participants and inactivity of researchers). We will consider articles
32
33 138 that are written in either English or German (language criteria). The literature search will not
34
35 139 be restricted by publication date.

35 140 Information sources and search strategy

36
37 141 Systematic literature searches will be conducted in the databases MEDLINE (PubMed
38
39 142 interface), Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central
40
41 143 Register of Controlled Trials (CENTRAL), Cochrane Methodology Register), PsycINFO,
42
43 144 EMBASE, Web of Science (Science and Social Science Citation Index) and Google Scholar (for
44
45 145 "grey" literature) by ML and CS independently. A combination of the following search terms
46
47 146 will be used: (1) bereavement or widowhood or grief; and (2) online or web or computer or
48
49 147 mobile or e-health or internet; and (3) intervention or psychotherapy or cognitive
50
51 148 behavioural therapy or CBT. If feasible, medical subject headings (MeSH) will be used as
52
53 149 search terms. The finalized MEDLINE search strategy will be adapted to the syntax and
54
55 150 subject headings specifications of the other databases. We will initially screen titles and
56
57 151 abstracts for eligibility. Full texts will then be assessed for criteria, and the reference lists of
58
59 152 included articles and systematic reviews will be hand searched to identify further potentially
60
153 relevant studies. Finally, we will conduct a grey literature search for unpublished studies
154
using Google and Google Scholar with the above-named search terms. If applicable and

1
2
3 155 necessary, we will contact researchers directly to gather further relevant non-published
4
5 156 data. The searches will be re-run just before the final analyses so that more recent studies
6
7 157 can be retrieved.

8
9 158
10 159 Data management

11
12 160 References and data will be managed using the Review Manager (RevMan) software package
13
14 161 version 5.3 (by the Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen,
15
16 162 Denmark, 2014). RevMan is specifically designed for managing and analyzing systematic
17
18 163 review data from bibliographical management to data synthesis. If feasible, additional data
19
20 164 analyses and meta-analysis will be conducted using Stata 13.1 SE (StataCorp LP, College
21
22 165 Station, Texas, USA).

23 166
24
25 167 Selection process

26
27 168 All titles and abstracts of articles will be screened independently by two reviewers (ML, CS).
28
29 169 At this stage, articles will be divided into potentially relevant, irrelevant or uncertain.
30
31 170 Reasons for exclusion of irrelevant articles will be given. Potentially relevant and uncertain
32
33 171 articles will be read in full text independently by ML and CS, and study eligibility based on
34
35 172 the established criteria specified above will be assessed. At each stage of the selection
36
37 173 process, any discrepancies will be discussed between the two reviewers. When discrepancies
38
39 174 cannot be resolved, input from a third senior researcher (SRH) will be obtained.

40 175
41 176 Data collection process and data items

42
43 177 A standardized data extraction form will be used to extract data from included studies.
44
45 178 Extracted data will include study characteristics, participant characteristics, methodological
46
47 179 factors and outcome data. A pilot version of the data extraction form will be tested
48
49 180 independently by the two reviewers (ML, CS) on a subsample of relevant studies to ensure
50
51 181 correct extraction of all relevant data. Difficulties with data extraction will be discussed and
52
53 182 the form will be adopted accordingly. Data from each study will be extracted by both
54
55 183 reviewers (ML, CS) independently, and reliability of data extraction will be checked in a
56
57 184 random sample of studies. Discrepancies between the two reviewers will be discussed with a
58
59 185 senior researcher (SRH). Missing data will be requested from study authors.

60 186

1
2
3 187 The following data will be extracted:
4

5 188 (1) Study identification items: e.g. first author, year of publication, country
6

7 189 (2) Study design characteristics: e.g. sample size, recruitment strategy, interventions
8 design/type, control group, type of assessment, inclusion/exclusion criteria, duration
9 190 of intervention, length of follow-up assessments
10 191

11 192 (3) Participants characteristics: e.g. mean age, age range, gender
12

13 193 (4) Methodological aspects: risk of bias, study limitations
14

15 194 (5) Outcomes: effectiveness (i.e. improvement of objective parameters) and feasibility
16 (e.g. usability, satisfaction, acceptability, understandability and usefulness); (serious)
17 adverse events (e. g. disability, hospitalization, death); onset data from clinician-
18 195 rated scales will be prioritized over self-report questionnaires. All different time
19 196 frames of follow-up assessments will be included.
20 197
21 198
22 199

23 199 24 25 200 Quality assessment 26

27 200
28 201 The methodological quality of included studies will be assessed by two researchers (ML, CS)
29 202 independently using the Cochrane Collaboration Tool for Assessing Risk of Bias in RCTs [27].
30

31 203 As recommended, each study will be assessed in the following domains: (1) selection bias,
32 204 i.e. descriptions of the (1a) method of randomisation and (1b) concealment of allocation; (2)
33 205 performance bias, i.e. description of the methods of blinding participants and researchers;
34 206 (3) detection bias, i.e. description of the methods of blinding outcome assessment; (4)
35 207 attrition bias, i.e. description of incomplete outcome data; (5) reporting bias, i.e. description
36 208 of selective outcome reporting; and (6) other bias, i.e. description of important concerns
37 209 about other biases. Studies will be rated as 'high', 'low', or 'unclear'. These assessments will
38 210 be used to inform the corresponding GRADE assessment of study limitations (see table 5.6 of
39 211 the Grades of Recommendation, Assessment, Development and Evaluation (GRADE)
40 212 handbook [28]. Specifically, 'low risk of bias' would indicate 'no limitation'; 'unclear risk of
41 213 bias' would indicate either 'no limitation' or 'serious limitation'; and 'high risk of bias' would
42 214 indicate either 'serious limitation' or 'very serious limitation' in the GRADE approach. Any
43 215 disagreement between the two reviewers will be resolved by discussions with involvement
44 216 of a third review author where necessary. Study authors will be contacted for further
45 217 methodological information if needed. In the risk of bias table, results of the judgements will
46 218 be shown for each domain.
47
48
49
50
51
52
53
54
55
56
57
58
59
60

219

220 Data synthesis and presentation

221 A detailed description of the results for all included studies will be provided in text and
222 tables. Characteristics of selected studies will be listed and qualitatively described (see listed
223 parameter in “data collection process”). Characteristics of the study, sample, intervention
224 and control condition will be presented first, followed by outcome measurements, effect
225 sizes, and overall results. We will provide a narrative synthesis and if appropriate, a
226 quantitative meta-analysis using funnel and forest plots and pooled statistics. If feasible,
227 results of pooled age- and gender-specific outcomes will be reported.

228 Data analyses will be performed using Review Manager 5.3 software from the Cochrane
229 Collaboration Tool for Implementing the Characteristics of Studies (Review Manager
230 (RevMan) [Computer program], 2014).

231

232 Meta-analysis

233 Meta-analysis of pooled data will be based on the assessment of clinical, methodological and
234 statistical heterogeneity. According Cochrane standards, meta-analysis will not be
235 performed if high levels of heterogeneity and/or variation in the effects of the interventions
236 are present.

237 Heterogeneity in study characteristics will be evaluated using forest plots and I^2 statistics. An
238 I^2 of >60% indicates substantial heterogeneity and requires exploration of the sources of
239 heterogeneity in subgroups of studies (Higgins et al. 2011). Depending on the level of
240 observed heterogeneity, fixed-effect, random-effect or mixed-effect models will be used to
241 estimate the pooled effects on outcomes and to quantify the uncertainty of these estimates.
242 If sufficient data are available, subgroup analyses based on the content and form of
243 intervention will be performed. Finally, in order to evaluate the association of
244 sociodemographic variables with pooled effect sizes, meta-regression models will be fitted.
245 We will follow the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011)
246 to deal with missing data.

247

248

249

250 Discussion

1
2
3 251 The planned systematic review will provide a comprehensive summary of the effectiveness
4
5 252 and feasibility of internet- and mobile-based interventions for adults who suffer from
6
7 253 bereavement.

8
9 254 If treatment programs for bereavement which utilize either the Internet or mobile phone
10
11 255 technology show effectiveness and feasibility, this therapeutic delivery method has the
12
13 256 potential to become an additional intervention tool. Internet-based interventions can reach
14
15 257 more people than face-to-face interventions (Muñoz 2010). Their cost-effectiveness for
16
17 258 depression [29] and anxiety disorders [30,31] have also been demonstrated. Because of a
18
19 259 prevalence rate of 3.7% for complicated grief in Germany [32], a low-threshold treatment
20
21 260 option would enable the provision of adequate care to more bereaved adults.

22
23 261 If there are an insufficient number of studies that have examined gender and age
24
25 262 differences, this will be discussed in terms of a need for future research. Second, this review
26
27 263 could motivate other researchers to construct and test in randomized trials new or modified
28
29 264 internet- or mobile-based interventions for bereaved adults.

30
31 265

32
33 266

34
35 267

36 268 Amendments

37 269 In the event of protocol amendments, we will provide the date, a description of and
38
39 270 rationale for of each amendment.

40
41 271

42 272 Abbreviations

43 273 CBT – cognitive behavioural therapy

44 274 CENTRAL - Cochrane Central Register of Controlled Trials

45 275 GRADE - Grades of Recommendation, Assessment, Development and Evaluation

46 276 IMI - Internet- and mobile-based interventions

47 277 PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analysis

48 278 PTSD - post-traumatic stress disorder

49 279 RCT - randomized controlled-trials

50
51 280

52 281 Declarations section

53 282 Ethics Approval and Consent to Participate

1
2
3 283 Ethical approval and consent to participate are not required as no primary data will be
4
5 284 collected. The results of this systematic review are intended to be published in an
6
7 285 international peer-reviewed journal. Results may also be presented at relevant professional
8
9 286 conferences and meetings.

10
11 287
12 288 Availability of supporting data

13
14 289 Not applicable

15
16 290

17
18 291 Competing interest

19
20 292 None declared

21
22 293

23
24 294 Funding

25 295 This publication is part of the AgE-health-study and was funded by the German Federal
26
27 296 Ministry of Education and Research (reference number: 01GY1613). The funding source had no
28
29 297 role in the design of the study and will not have any role in its execution, analyses, interpretation of the
30
31 298 data, or decision to submit results

32
33 299

34
35 300

36 301 Author Contributions

37
38 302 ML and CS are the guarantors of the systematic review. ML and CS drafted the manuscript.

39
40 303 All authors contributed to the conception and design of the review. ML, MLö and CS

41
42 304 developed the search strategy. ML, MLö, AP and CS developed the methodological

43
44 305 approach. ML, MLö and SRH critically revised the protocol for important intellectual content.

45
46 306

47 307 Acknowledgement

48
49 308 Not applicable

50
51 309

52
53 310 Author's information

54
55 311 All authors approved the final version of the manuscript.

56
57 312

58
59 313

60
314

1
2
3 315
4
5 316
6
7 317
8
9 318
10
11 319
12
13 320
14
15 321
16
17 322
18
19 323
20
21 324
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

325 References

326 Brand D, Morgan D, et al. Measuring injury risk factors: question reliability in a statewide
327 sample. *Inj Prev* 2000;6:148–50.

328
329 [1] Stein J, Röhr S, Luck T, et al. Indikationen und Evidenz von international entwickelten
330 Online-Coaches zur Intervention bei psychischen Erkrankungen – ein Meta-Review. *Psychiat
331 Prax* 2018;45:7–15.

332 [2] Richards D, Duffy D, Burke J, et al. Supported Internet-Delivered Cognitive Behavior
333 Treatment for Adults with Severe Depressive Symptoms: A Secondary Analysis. *JMIR Ment
334 Health* 2018;5:e10204.

335 [3] Twomey C, O'Reilly G, Meyer B. Effectiveness of an individually-tailored computerised
336 CBT programme (Deprexis) for depression: A meta-analysis. *Psychiat res* 2017;256:371–7.

337 [4] Karyotaki E, Ebert DD, Donkin L, et al. Do guided internet-based interventions result in
338 clinically relevant changes for patients with depression? An individual participant data meta-
339 analysis. *Clin Psychol Rev* 2018;63:80–92.

340 [5] Morgan C, Mason E, Newby JM, et al. The effectiveness of unguided internet cognitive
341 behavioural therapy for mixed anxiety and depression. *Internet Interv* 2017;10: 47–53.

342 [6] Morris J, Firkins A, Millings A, et al. Internet-delivered cognitive behavior therapy for
343 anxiety and insomnia in a higher education context. *Anxiety, stress, and coping*
344 2016;29:415–31.

345 [7] Lange A, van de Ven J, Schrieken B. Interapy: treatment of post-traumatic stress via the
346 internet. *Cogn Behav Ther* 2003;32:110–24.

347 [8] Sijbrandij M, Kunovski I, Cuijpers P. Effectiveness of internet-delivered cognitive
348 behavioral therapy for posttraumatic stress disorder: A systematic review and meta-analysis.
349 *Dep Anx* 2016;33:783–91.

350 [9] Spence J, Titov N, Dear BF, et al. Randomized controlled trial of Internet-delivered
351 cognitive behavioral therapy for posttraumatic stress disorder. *Dep Anx* 2011;28:541–50.

352 [10] Lammer K. Trauer verstehen. Formen, Erklärungen, Hilfen. 4. Aufl. Berlin: Springer 2014.
353 Online verfügbar unter <http://dx.doi.org/10.1007/978-3-642-41667-5>.

354 [11] Jackson EN. Understanding grief. *Pastoral Psychol* 1957;8:41–8.

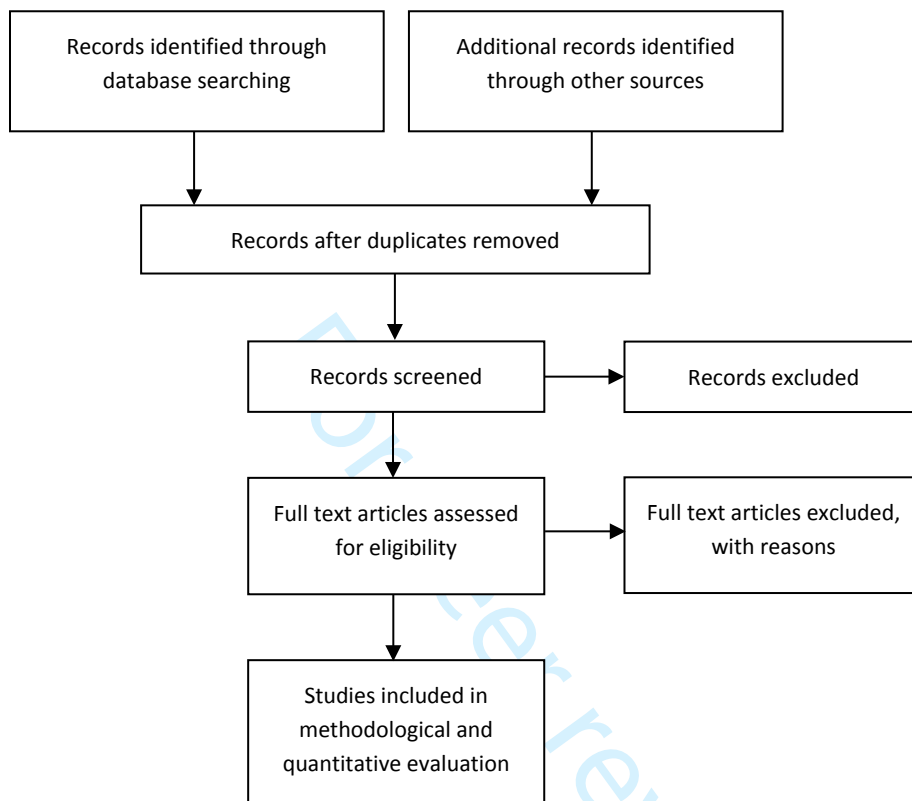
355 [12] Lindemann E. Symptomatology and management of acute grief. *Am J Psychiat*
356 1944;101:141–8.

- 1
2
3 357 [13] Zisook S, Simon NM, Reynolds CF, et al. Bereavement, complicated grief, and DSM, part
4 358 2: complicated grief. *J Clin Psychiat* 2010;71:1097–8.
- 6 359 [14] Prigerson HG, Horowitz MJ, Jacobs SC, et al. Prolonged grief disorder: Psychometric
8 360 validation of criteria proposed for DSM-V and ICD-11. *PLoS Med* 2009;6:e1000121.
- 10 361 [15] Huttu MH, Armstrong DS, Myers JA, et al. Grief intensity, psychological well-being, and
12 362 the intimate partner relationship in the subsequent pregnancy after a perinatal loss. *JOGNN*
14 363 2015;44:42–50.
- 16 364 [16] O'Connor M, Nickerson A, Aderka IM, et al. The temporal relationship between change
17 365 in symptoms of prolonged grief and posttraumatic stress following old age spousal
19 366 bereavement. *Dep Anx* 2015;32:335–40.
- 21 367 [17] Muñoz RF. Using evidence-based internet interventions to reduce health disparities
23 368 worldwide. *J Med Internet Res* 2010;12:e60.
- 25 369 [18] Boelen PA, van de Schoot R, van den Hout MA, et al. Prolonged grief disorder,
27 370 depression, and posttraumatic stress disorder are distinguishable syndromes. *J Aff Dis*
29 371 2010;125: 374-8.
- 31 372 [19] Wagner B, Knaevelsrud C, Maercker A. Internet-based cognitive-behavioral therapy for
33 373 complicated grief: a randomized controlled trial. *Death studies* 2006;30:429–453.
- 35 374 [20] van der Houwen K, Schut H, van den Bout J, et al. The efficacy
37 375 of a brief internet-based self-help intervention for the bereaved. *Behav Res*
39 376 *Ther* 2010;48:359-67.
- 41 377 [21] Kleinman A. Culture, bereavement, and psychiatry. *Lancet* 2012;379:608–9.
- 43 378 [22] Schut H, Stroebe MS, Van den Bout J, et al. The efficacy of bereavement interventions:
45 379 Determining who benefits. 2001. In: Stroebe MS, Hansson RO, Stroebe W, Schut H
47 380 (Eds.), *Handbook of bereavement research: Consequences, coping, and care* (pp. 705-737).
49 381 Washington, DC, US: American Psychological Association.
- 51 382 [23] Kersting A, Dölemeyer R, Steinig J, et al.
53 383 Brief Internet-based intervention reduces posttraumatic stress and prolonged
55 384 grief in parents after the loss of a child during pregnancy: a randomized
57 385 controlled trial. *Psychother Psychosom* 2013;82:372-81.
- 59 386 [24] Moher D, Liberati A, Tetzlaff J. Preferred reporting items for systematic reviews and
61 387 meta-analysis: the PRISMA statement. *BMJ* 2009;339:b2535.

- 1
2
3 388 [25] Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review
4
5 389 and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ (Clin Res*
6
7 390 *ed.)* 2015;350:g7647.
- 8
9 391 [26] Kampling H, Baumeister H, Jaeckel WH, et al. Prevention of depression in chronically
10
11 392 physically ill adults. Cochrane Systematic Review - Intervention – Protocol.
12
13 393 <https://doi.org/10.1002/14651858.CD011246>
- 14
15 394 [27] Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for
16
17 395 assessing risk of bias in randomised trials. *BMJ (Clin Res ed.)* 2011;343: d5928.
- 18
19 396 [28] Guyatt GH, Oxman AD D, Vist GE, et al. GRADE: an emerging consensus on rating quality
20
21 397 of evidence and strength of recommendations. *BMJ (Clin Res ed.)* 2008;336:924–6.
- 22
23 398 [29] Gerhards SAH, de Graaf LE, Jacobs LE, et al. Economic evaluation of online computerised
24
25 399 cognitive behavioural therapy without support for depression in primary care: a randomised
26
27 400 trial. *British J Psych* 2010; 196:310–318.
- 28
29 401 [30] Hedman E, Andersson E, Lindefors N, et al. Cost-effectiveness and long-term
30
31 402 effectiveness of internet-based cognitive behaviour therapy for severe health anxiety.
32
33 403 *Psychol Med* 2013; 43:363–74.
- 34
35 404 [31] Hedman E, Andersson E, Ljótsson B, et al. Cost-effectiveness of Internet-based cognitive
36
37 405 behavior therapy vs. cognitive behavioral group therapy for social anxiety disorder: results
38
39 406 from a randomized controlled trial. *Behav Res Ther* 2011;49:729–36.
- 40
41 407 [32] Kersting, A., Braehler, E., Glaesmer, H., et al. Prevalence of complicated grief in a
42
43 408 representative population-based sample. *J Affect Disord.* 2011; 339–343.
44
45 409
46 410
47 411
48 412
49 413
50 414
51 415
52 416
53 417
54 418
55 419

420

421



422

423

424 Figure 1. Flow diagram of the planned study selection process adapted from the Preferred
425 Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.

426

427

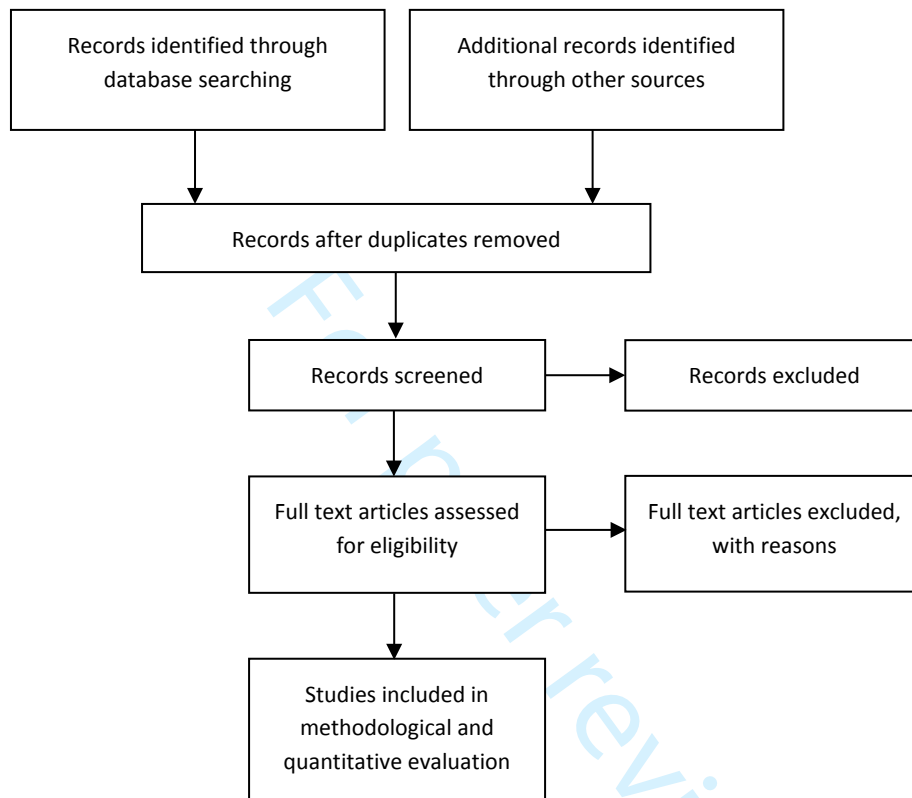


Figure 1. Flow diagram of the planned study selection process adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.

PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|-----------------------------------|----|---|--------------------------|--------------------------|----------------|
| | | | Yes | No | |
| ADMINISTRATIVE INFORMATION | | | | | |
| Title | | | | | |
| Identification | 1a | Identify the report as a protocol of a systematic review | x | <input type="checkbox"/> | 2 |
| Update | 1b | If the protocol is for an update of a previous systematic review, identify as such | <input type="checkbox"/> | <input type="checkbox"/> | n/a |
| Registration | 2 | If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract | x | <input type="checkbox"/> | 41 |
| Authors | | | | | |
| Contact | 3a | Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author | x | <input type="checkbox"/> | 15-22 |
| Contributions | 3b | Describe contributions of protocol authors and identify the guarantor of the review | x | <input type="checkbox"/> | 392-396 |
| 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 | <input type="checkbox"/> | <input type="checkbox"/> | n/a |
| Support | | | | | |
| Sources | 5a | Indicate sources of financial or other support for the review | x | <input type="checkbox"/> | 386-389 |
| Sponsor | 5b | Provide name for the review funder and/or sponsor | x | <input type="checkbox"/> | 386-389 |
| Role of sponsor/funder | 5c | Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol | x | <input type="checkbox"/> | 386-389 |
| INTRODUCTION | | | | | |
| Rationale | 6 | Describe the rationale for the review in the context of what is already known | x | <input type="checkbox"/> | 83-94 |
| Objectives | 7 | Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) | x | <input type="checkbox"/> | 97-103 |
| METHODS | | | | | |

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|---|-----|---|----------------------|--------------------------|----------------|
| | | | Yes | No | |
| Eligibility criteria | 8 | Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review | x | <input type="checkbox"/> | 128-145 |
| Information sources | 9 | Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage | x | <input type="checkbox"/> | 146-203 |
| Search strategy | 10 | Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated | x | <input type="checkbox"/> | 146-203 |
| STUDY RECORDS | | | | | |
| Data management | 11a | Describe the mechanism(s) that will be used to manage records and data throughout the review | x | <input type="checkbox"/> | 206-212 |
| Selection process | 11b | State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis) | x | <input type="checkbox"/> | 214-221 |
| Data collection process | 11c | Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators | x | <input type="checkbox"/> | 223-245 |
| Data items | 12 | List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications | x | <input type="checkbox"/> | 247-258 |
| Outcomes and prioritization | 13 | List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale | x | <input type="checkbox"/> | 254-258 |
| Risk of bias in individual studies | 14 | 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 | x | <input type="checkbox"/> | 260-286 |
| DATA | | | | | |
| Synthesis | 15a | Describe criteria under which study data will be quantitatively synthesized | x | <input type="checkbox"/> | 288-298 |
| | 15b | 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 (e.g., I^2 , Kendall's tau) | x | <input type="checkbox"/> | 288-298 |
| | 15c | Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression) | x | <input type="checkbox"/> | 294-295 |
| | 15d | If quantitative synthesis is not appropriate, describe the type of summary planned | x | <input type="checkbox"/> | 288-298 |
| Meta-bias(es) | 16 | Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies) | x | <input type="checkbox"/> | 305-328 |
| Confidence in cumulative evidence | 17 | Describe how the strength of the body of evidence will be assessed (e.g., GRADE) | x | <input type="checkbox"/> | 260-286 |

BMJ Open

Effectiveness and feasibility of internet- and mobile-based interventions for individuals experiencing bereavement: A systematic review protocol

| | |
|---------------------------------|--|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2019-036034.R1 |
| Article Type: | Protocol |
| Date Submitted by the Author: | 28-Feb-2020 |
| Complete List of Authors: | Luppa, Melanie; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health Loebner, Margrit; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health Pabst, Alexander; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health Schlapke, Christiane; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health Stein, Janine; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health Riedel-Heller, Steffi; University of Leipzig Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health |
| Primary Subject Heading: | Mental health |
| Secondary Subject Heading: | Public health, Health services research |
| Keywords: | MENTAL HEALTH, Depression & mood disorders < PSYCHIATRY, PREVENTIVE MEDICINE |
| | |

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 1 **Effectiveness and feasibility of internet- and mobile-based interventions for individuals**
4
5 2 **experiencing bereavement: A systematic review protocol**
6

7 3

8 4

9
10 5 Luppá, Melanie¹; Loebner, Margrit¹; Pabst, Alexander¹; Schlapke, Christiane¹, Stein, Janine¹;

11
12 6 Riedel-Heller, Steffi G. ¹
13

14 7

15
16 8 ¹ Institute of Social Medicine, Occupational Health and Public Health, Faculty of Medicine,
17 9 University of Leipzig
18

19 10

20 11

21 12

22 13

23 14

24 15

25 16

26 17 Corresponding author:

27 18 Melanie Luppá, PhD

28 19 Institute of Social Medicine, Occupational Health and Public Health, Faculty of Medicine,
29 20 University of Leipzig

30 21 Philipp-Rosenthal-Straße 55

31 22 04103 Leipzig

32 23 Germany

33 24 Email: Melanie.Luppá@medizin.uni-leipzig.de

34 25 Phone: +49 341 9715406

35 26 Word count: 3,678
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

27 ABSTRACT

28 Introduction: Internet- and mobile-based interventions (IMIs) provide an innovative and
29 efficient self-management tool for mental health problems. This systematic review aims to
30 summarise and critically evaluate studies addressing the effectiveness and feasibility of IMIs
31 for normal and complicated grief in bereaved adults.

32 Methods and Analysis: The databases MEDLINE, Cochrane Library, PsycINFO, EMBASE and
33 Web of Science and Google Scholar (for “grey” literature) will be systematically searched for
34 feasibility studies or randomized controlled trials of IMIs for bereaved adults who were
35 experiencing normal/complicated grief. Data will be extracted and evaluated independently
36 by two reviewers from studies eligible for inclusion. Quality of evidence will be assessed, and
37 results will be synthesized qualitatively and pooled meta-analytically, if sufficient outcome
38 data are available. PRISMA standards and GRADE methodology will be used.

39 Ethics and Dissemination: No primary data will be collected; thus, ethical approval is not
40 required. The results will be disseminated through a peer-reviewed publication and
41 conference presentations.

42 PROSPERO registration number: CRD42019131428

43 Keywords: grief, bereavement, systematic review, internet- and mobile-based, effectiveness,
44 feasibility

46 Strengths and limitations of this study

- 47 - first study which provides a comprehensive summary of studies investigating
48 effectiveness and feasibility of internet- and mobile-based interventions (IMIs) for
49 normal and complicated grief in bereaved adults
- 50 - possibility of usage of these IMIs in healthcare as additional intervention tools as well
51 as low-threshold treatment options
- 52 - application with the necessary caution of these IMIs seems to be required not to
53 interfere with natural grief processes

58 Background

59
60 Self-management is a widely used approach within the medical health care system for
61 improving patients' knowledge, capabilities and skills in managing their health problems.
62 Internet- and mobile-based interventions (IMIs) provide an innovative and efficient self-
63 management tool for mental health problems. In recent years, web-based self-management
64 interventions have gained increasing attention as effective supplementary treatment
65 elements to standard mental health treatment[1].

66 The effectiveness of IMIs has been shown for treating depression (e.g.[2-4]), anxiety
67 (e.g.[5,6]), post-traumatic stress disorder (PTSD; e.g.[7-9]), and other mental health
68 problems[1]. However, less is currently known about IMIs for individuals experiencing
69 normal or complicated grief.

70 In general, grief is defined as a typical reaction to the loss of a significant other[10] , and is
71 associated with symptoms such as intense subjective distress, loneliness, and somatic
72 symptoms, e.g. tightness of the throat or need for sighing[11,12]. Recently, the concept of
73 an abnormal reaction to loss has been proposed and is included as a disorder in the
74 *Diagnostic Statistical Manual of Mental Disorders, 5th Edition (DSM-V)* and is expected to be
75 included in the *International Statistical Classification of Diseases and Related Health*
76 *Problems, 11th Revision (ICD-11)* as a new diagnosis. The disorders Complicated, Traumatic,
77 or Prolonged Grief (subsequently summarized under complicated grief) and Complicated
78 Grief are described as "a syndrome of prolonged and intense grief that is accompanied by
79 complications that derail the progress of grief"[13]. In contrast to uncomplicated grief,
80 clinically significant impairment in social, occupational, or other important areas of
81 functioning must be present[13,14]. The diagnosis of complicated grief is given only after a
82 period of six months following the index loss event if the person is still suffering from
83 separation stress as well as cognitive, emotional, and behavioral symptoms[14].

84 Because grief can affect many areas of life[15,16] and is one of the major contributors to the
85 development of mental health disorders, providing IMIs as a low-threshold treatment option
86 may enable more people to receive treatment than through face-to-face interventions
87 alone[17] to prevent the development of mental health disorders. Major Depression,
88 Generalized Anxiety Disorder, and Post-Traumatic Stress Disorder are particularly closely
89 related to the symptoms of complicated grief, but differences between the disorders have
90 also been reported[14,18].

1
2
3 91 To date, a number of IMIs for bereavement problems exist in the international research
4
5 92 literature. Internet-based Cognitive Behavioral Therapy (CBT) interventions were reported to
6
7 93 be effective in treating patients with complicated grief[19] but not for those with
8
9 94 uncomplicated grief[20]. Some researchers have urged caution in implementing
10
11 95 interventions too early or across a wide range of bereavement-related distress so as to not
12
13 96 interfere with natural grief processes[21,22]. One study showed that IMIs for PTSD improve
14
15 97 symptoms of complicated grief[23]. To our knowledge, there are no previous systematic
16
17 98 reviews summarizing the effectiveness and feasibility of IMIs for bereaved individuals – for
18
19 99 normal as well as complicated grief. The results of this review and meta-analysis will
20
21 100 therefore address this gap in the literature. This protocol describes the rationale and design
22
23 101 of the planned systematic review and meta-analysis.

102 103 OBJECTIVES

104 The planned review aims to systematically evaluate and synthesize the evidence base of
105
106 randomized controlled-trials (RCT)s reporting, the effectiveness of IMIs (i.e. improvement of
107
108 objective parameters), and the feasibility of IMIs (e.g. usability, satisfaction, acceptability,
109
110 understandability and usefulness) for individuals aged 18 years and older who experienced
111
112 the death of a significant other. Depending on the number of eligible studies, assessment
113
114 tools, and quality of the studies reported, we will also combine data across RCTs to estimate
115
116 pooled effect sizes for the considered outcomes.

117 118 119 120 121 122 123 METHODS AND ANALYSIS

124 This protocol outlines the strategies for conducting a systematic review and meta-analysis of
125
126 RCTs which examined the effectiveness of IMIs for bereavement. It is based on the Preferred
127
128 Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) for systematic review
129
130 protocols (PRISMA-P) guidelines[24,25]. The protocol describes the planned strategy to
131
132 systematically evaluate and synthesize data from randomized controlled trials and feasibility
133
134 studies on IMIs for bereaved individuals. We will apply the four-phase PRISMA flow diagram
135
136 (figure 1) for our study selection process.

137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 Eligibility criteria

1
2
3 125 The systematic review will be divided into two parts: effectiveness studies and feasibility
4
5 126 studies on IMIs (study design criteria) which include adults (18 years and older), who
6
7 127 experienced the death of a significant other and were suffering from normal or complicated
8
9 128 grief (participant criteria). Any measures of effectiveness (i.e. improvement of objective
10
11 129 parameters) and feasibility (e.g. usability, satisfaction, acceptability, understandability and
12
13 130 usefulness) (outcome criteria) of IMIs related to bereavement will be included. Onset data
14
15 131 from clinician-rated scales will be prioritized over self-report questionnaires. The
16
17 132 intervention must have been a psychological intervention according to Kampling et al.[26]
18
19 133 criteria: cognitive behavioral therapy (CBT), psychodynamic psychotherapy, behavior
20
21 134 therapy or behavior modification, systemic therapy, third wave cognitive behavioral therapy,
22
23 135 humanistic therapy, integrative therapy or to other psychological-orientated interventions
24
25 136 and must have been provided in an online setting (intervention criteria). In RCTs, the
26
27 137 comparison group must be either 'treatment as usual', 'waiting list', 'attention placebo'
28
29 138 (inactivity on the part of both researchers and participants), or 'psychological placebo'
30
31 139 (activity on the part of participants and inactivity of researchers). We will consider articles
32
33 140 that are written in either English or German (language criteria). The literature search will not
34
35 141 be restricted by publication date.

35 142 Information sources and search strategy

36
37 143 Systematic literature searches will be conducted in the databases MEDLINE (PubMed
38
39 144 interface), Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central
40
41 145 Register of Controlled Trials (CENTRAL), Cochrane Methodology Register), PsycINFO,
42
43 146 EMBASE, Web of Science (Science and Social Science Citation Index) and Google Scholar (for
44
45 147 "grey" literature) by ML and CS independently. A combination of the following search terms
46
47 148 will be used: (1) bereavement or widowhood or grief; and (2) online or web or computer or
48
49 149 mobile or e-health or internet; and (3) intervention or psychotherapy or cognitive
50
51 150 behavioural therapy or CBT. The draft of the full MEDLINE search strategy is available in
52
53 151 online supplementary appendix 1. If feasible, medical subject headings (MeSH) will be used
54
55 152 as search terms. The finalized MEDLINE search strategy will be adapted to the syntax and
56
57 153 subject headings specifications of the other databases. We will initially screen titles and
58
59 154 abstracts for eligibility. Full texts will then be assessed for criteria, and the reference lists of
60
155 included articles and systematic reviews will be hand searched to identify further potentially
156 relevant studies. Finally, we will conduct a grey literature search for unpublished studies

1
2
3 157 using Google and Google Scholar with the above-named search terms. If applicable and
4
5 158 necessary, we will contact researchers directly to gather further relevant non-published
6
7 159 data. The searches will be re-run just before the final analyses so that more recent studies
8
9 160 can be retrieved.

10 161

12 162 Data management

14 163 References and data will be managed using the Review Manager (RevMan) software package
15
16 164 version 5.3 (by the Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen,
17
18 165 Denmark, 2014). RevMan is specifically designed for managing and analyzing systematic
19
20 166 review data from bibliographical management to data synthesis. If feasible, additional data
21
22 167 analyses and meta-analysis will be conducted using Stata 13.1 SE (StataCorp LP, College
23
24 168 Station, Texas, USA).

25 169

27 170 Selection process

29 171 All titles and abstracts of articles will be screened independently by two reviewers (ML, CS).
30
31 172 At this stage, articles will be divided into potentially relevant, irrelevant or uncertain.
32
33 173 Reasons for exclusion of irrelevant articles will be given. Potentially relevant and uncertain
34
35 174 articles will be read in full text independently by ML and CS, and study eligibility based on
36
37 175 the established criteria specified above will be assessed. At each stage of the selection
38
39 176 process, any discrepancies will be discussed between the two reviewers. When discrepancies
40
41 177 cannot be resolved, input from a third senior researcher (SRH) will be obtained.

42 178

43 179 Data collection process and data items

45 180 A standardized data extraction form will be used to extract data from included studies.
46
47 181 Extracted data will include study characteristics, participant characteristics, methodological
48
49 182 factors and outcome data. A pilot version of the data extraction form will be tested
50
51 183 independently by the two reviewers (ML, CS) on a subsample of relevant studies to ensure
52
53 184 correct extraction of all relevant data. Difficulties with data extraction will be discussed and
54
55 185 the form will be adopted accordingly. Data from each study will be extracted by both
56
57 186 reviewers (ML, CS) independently, and reliability of data extraction will be checked in a
58
59 187 random sample of studies. Discrepancies between the two reviewers will be discussed with a
60
188 senior researcher (SRH). Missing data will be requested from study authors.

189

The following data will be extracted:

(1) Study identification items: e.g. first author, year of publication, country

(2) Study design characteristics: e.g. sample size, recruitment strategy, inclusion/exclusion criteria, circumstances of the loss (e.g. violent death, suicide), control group, diagnostic criteria/assessment of normal/prolonged/complicated grief, assessment of co-occurring conditions (e. g. Major Depression, Posttraumatic stress disorder, concurrent pharmaco-/psychotherapy), assessment of suicidal ideation or behaviour, interventions design/type, duration of intervention, length of follow-up assessments

(3) Participants characteristics: e.g. mean age, age range, gender

(4) Methodological aspects: risk of bias, study limitations

(5) Outcomes: (a) Effectiveness: Primary outcome measures: reduction of grief symptoms; Secondary outcome measures: reduction of depression, anxiety, somatization or PTS symptoms or suicidal ideation or behaviour) and (b) feasibility: usability, satisfaction, acceptability, understandability and usefulness;; onset data from clinician-rated scales will be prioritized over self-report questionnaires. All different time frames of follow-up assessments will be included.

Quality assessment

The methodological quality of included studies will be assessed by two researchers (ML, CS) independently using the Cochrane Collaboration Tool for Assessing Risk of Bias in RCTs[27]. As recommended, each study will be assessed in the following domains: (1) selection bias, i.e. descriptions of the (1a) method of randomisation and (1b) concealment of allocation; (2) performance bias, i.e. description of the methods of blinding participants and researchers; (3) detection bias, i.e. description of the methods of blinding outcome assessment; (4) attrition bias, i.e. description of incomplete outcome data; (5) reporting bias, i.e. description of selective outcome reporting; and (6) other bias, i.e. description of important concerns about other biases. Studies will be rated as 'high', 'low', or 'unclear'. These assessments will be used to inform the corresponding GRADE assessment of study limitations (see table 5.6 of the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) handbook[28]. Specifically, 'low risk of bias' would indicate 'no limitation'; 'unclear risk of

1
2
3 221 bias' would indicate either 'no limitation' or 'serious limitation'; and 'high risk of bias' would
4
5 222 indicate either 'serious limitation' or 'very serious limitation' in the GRADE approach. Any
6
7 223 disagreement between the two reviewers will be resolved by discussions with involvement
8
9 224 of a third review author where necessary. Study authors will be contacted for further
10
11 225 methodological information if needed. In the risk of bias table, results of the judgements will
12
13 226 be shown for each domain.
14

15 227

16 228 Data synthesis and presentation

17
18 229 A narrative synthesis for all included studies and relevant characteristics listed under 'data
19
20 230 collection process' will be provided in text and 'summary of findings' tables. Characteristics
21
22 231 of the study, sample, intervention and control condition will be presented first, followed by
23
24 232 outcome measurements, effect sizes, and overall results.

25
26 233 Only studies that provide a quantitative measure of grief symptoms will be included in the meta-
27
28 234 analysis. We will analyze heterogeneity by providing I^2 statistics and funnel and forest plots.
29
30 235 According to the Cochrane standards, we suppose a moderate level of heterogeneity
31
32 236 between studies for I^2 values ranging from 30% to 60%[29]. If studies fail to show sufficient
33
34 237 heterogeneity ($I^2 < 60\%$) in at least two trials[30], meta-analytic pooling will not be undertaken.
35
36 238 However, inconsistency may occur from differences in study characteristics[29]. Therefore, we will
37
38 239 explore sources of heterogeneity in subgroups of studies in terms of type of grief or
39
40 240 intervention type. A random effects model will be applied. We will estimate standardized mean
41
42 241 difference values and the respective 95% confidence intervals. We will follow the Cochrane
43
44 242 Handbook for Systematic Reviews of Interventions[27] to deal with missing data.

45
46 243 Data analyses will be performed using Review Manager 5.3 software from the Cochrane
47
48 244 Collaboration Tool for Implementing the Characteristics of Studies (Review Manager
49
50 245 (RevMan) [Computer program], 2014).

51 246

52 247

53 248 Patient and Public Involvement

54
55 249 No patient involved. Discussion

56
57 250 The planned systematic review will provide a comprehensive summary of the effectiveness
58
59 251 and feasibility of internet- and mobile-based interventions for adults who suffer from
60
252 bereavement.

1
2
3 253 If treatment programs for bereavement which utilize either the Internet or mobile phone
4
5 254 technology show effectiveness and feasibility, this therapeutic delivery method has the
6
7 255 potential to become an additional intervention tool. Internet-based interventions can reach
8
9 256 more people than face-to-face interventions[17] . Their cost-effectiveness for depression[31]
10
11 257 and anxiety disorders[32,33] have also been demonstrated. Because of a prevalence rate of
12
13 258 3.7% for complicated grief in Germany[34], a low-threshold treatment option would enable
14
15 259 the provision of adequate care to more bereaved adults.

16 260 If there are an insufficient number of studies that have examined gender and age
17
18 261 differences, this will be discussed in terms of a need for future research. Second, this review
19
20 262 could motivate other researchers to construct and test in randomized trials new or modified
21
22 263 internet- or mobile-based interventions for bereaved adults.

23 264

24 265

25 266

26 267 Amendments

27 268 In the event of protocol amendments, we will provide the date, a description of and
28
29 269 rationale for of each amendment.

30 270

31 271 Abbreviations

32 272 CBT – cognitive behavioural therapy

33 273 CENTRAL - Cochrane Central Register of Controlled Trials

34 274 GRADE - Grades of Recommendation, Assessment, Development and Evaluation

35 275 IMI - Internet- and mobile-based interventions

36 276 PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analysis

37 277 PTSD - post-traumatic stress disorder

38 278 RCT - randomized controlled-trials

39 279

40 280 Declarations section

41 281 Ethics Approval and Consent to Participate

42 282 Ethical approval and consent to participate are not required as no primary data will be
43
44 283 collected. The results of this systematic review are intended to be published in an
45
46 284 international peer-reviewed journal. Results may also be presented at relevant professional
47
48 285 conferences and meetings.

1
2
3 286
4

5 287 Availability of supporting data

6
7 288 Not applicable
8
9 289

10 290 Competing interest

11
12 291 None declared
13
14 292

15
16 293 Funding

17
18 294 This publication is part of the AgE-health-study and was funded by the German Federal
19
20 295 Ministry of Education and Research (reference number: 01GY1613). The funding source had
21
22 296 no role in the design of the study and will not have any role in its execution, analyses,
23
24 297 interpretation of the data, or decision to submit results
25

26 298

27
28 299 Author Contributions

29
30 300 ML, CS, AP, MLö, JS, SRH contributed substantially to the conception of the work; ML and CS
31
32 301 drafted the manuscript; AP, MLö, JS, SRH revised the manuscript critically for important
33
34 302 intellectual content; ML, CS, AP, MLö, JS, SRH finally approved the version to be published.
35
36 303 ML, CS, AP, MLö, JS, SRH gave agreement to be accountable for all aspects of the work.

37 304

38
39 305 Acknowledgement

40
41 306 Not applicable
42
43 307

44 308 Author's information

45
46 309 All authors approved the final version of the manuscript.
47
48 310

49
50 311 Figure legend

51
52 312 Figure 1. Flow diagram of the planned study selection process adapted from the Preferred
53
54 313 Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement
55

56 314

57 315

58
59 316
60

317

318

319 References

- 320 [1] Stein J, Röhr S, Luck T, et al. Indikationen und Evidenz von international entwickelten
321 Online-Coaches zur Intervention bei psychischen Erkrankungen – ein Meta-Review. *Psychiat*
322 *Prax* 2018;45:7–15.
- 323 [2] Richards D, Duffy D, Burke J, et al. Supported Internet-Delivered Cognitive Behavior
324 Treatment for Adults with Severe Depressive Symptoms: A Secondary Analysis. *JMIR Ment*
325 *Health* 2018;5:e10204.
- 326 [3] Twomey C, O'Reilly G, Meyer B. Effectiveness of an individually-tailored computerised
327 CBT programme (Deprexis) for depression: A meta-analysis. *Psychiat res* 2017;256:371–7.
- 328 [4] Karyotaki E, Ebert DD, Donkin L, et al. Do guided internet-based interventions result in
329 clinically relevant changes for patients with depression? An individual participant data meta-
330 analysis. *Clin Psychol Rev* 2018;63:80–92.
- 331 [5] Morgan C, Mason E, Newby JM, et al. The effectiveness of unguided internet cognitive
332 behavioural therapy for mixed anxiety and depression. *Internet Interv* 2017;10: 47–53.
- 333 [6] Morris J, Firkins A, Millings A, et al. Internet-delivered cognitive behavior therapy for
334 anxiety and insomnia in a higher education context. *Anxiety, stress, and coping*
335 2016;29:415–31.
- 336 [7] Lange A, van de Ven J, Schrieken B. Interapy: treatment of post-traumatic stress via the
337 internet. *Cogn Behav Ther* 2003;32:110–24.
- 338 [8] Sijbrandij M, Kunovski I, Cuijpers P. Effectiveness of internet-delivered cognitive
339 behavioral therapy for posttraumatic stress disorder: A systematic review and meta-analysis.
340 *Dep Anx* 2016;33:783–91.
- 341 [9] Spence J, Titov N, Dear BF, et al. Randomized controlled trial of Internet-delivered
342 cognitive behavioral therapy for posttraumatic stress disorder. *Dep Anx* 2011;28:541–50.
- 343 [10] Lammer K. Trauer verstehen. Formen, Erklärungen, Hilfen. 4. Aufl. Berlin: Springer 2014.
344 Online verfügbar unter <http://dx.doi.org/10.1007/978-3-642-41667-5>.
- 345 [11] Jackson EN. Understanding grief. *Pastoral Psychol* 1957;8:41–8.
- 346 [12] Lindemann E. Symptomatology and management of acute grief. *Am J Psychiat*
347 1944;101:141–8.
- 348 [13] Zisook S, Simon NM, Reynolds CF, et al. Bereavement, complicated grief, and DSM, part
349 2: complicated grief. *J Clin Psychiat* 2010;71:1097–8.

- 1
2
3 350 [14] Prigerson HG, Horowitz MJ, Jacobs SC, et al. Prolonged grief disorder: Psychometric
4 351 validation of criteria proposed for DSM-V and ICD-11. *PLoS Med* 2009;6:e1000121.
5
6 352 [15] Huttu MH, Armstrong DS, Myers JA, et al. Grief intensity, psychological well-being, and
7 353 the intimate partner relationship in the subsequent pregnancy after a perinatal loss. *JOGNN*
8 354 2015;44:42–50.
9
10 355 [16] O'Connor M, Nickerson A, Aderka IM, et al. The temporal relationship between change
11 356 in symptoms of prolonged grief and posttraumatic stress following old age spousal
12 357 bereavement. *Dep Anx* 2015;32:335–40.
13
14 358 [17] Muñoz RF. Using evidence-based internet interventions to reduce health disparities
15 359 worldwide. *J Med Internet Res* 2010;12:e60.
16
17 360 [18] Boelen PA, van de Schoot R, van den Hout MA, et al. Prolonged grief disorder,
18 361 depression, and posttraumatic stress disorder are distinguishable syndromes. *J Affect Dis*
19 362 2010;125: 374-8.
20
21 363 [19] Wagner B, Knaevelsrud C, Maercker A. Internet-based cognitive-behavioral therapy for
22 364 complicated grief: a randomized controlled trial. *Death studies* 2006;30:429–453.
23
24 365 [20] van der Houwen K, Schut H, van den Bout J, et al. The efficacy
25 366 of a brief internet-based self-help intervention for the bereaved. *Behav Res*
26 367 *Ther* 2010;48:359-67.
27
28 368 [21] Kleinman A. Culture, bereavement, and psychiatry. *Lancet* 2012;379:608–9.
29
30 369 [22] Schut H, Stroebe MS, Van den Bout J, et al. The efficacy of bereavement interventions:
31 370 Determining who benefits. In: Stroebe MS, Hansson RO, Stroebe W, Schut H
32 371 (Eds.), *Handbook of bereavement research: Consequences, coping, and care* Washington,
33 372 DC, US: American Psychological Association 2001:705-37.
34
35 373 [23] Kersting A, Dölemeyer R, Steinig J, et al. Brief Internet-based intervention reduces
36 374 posttraumatic stress and prolonged grief in parents after the loss of a child during
37 375 pregnancy: a randomized controlled trial. *Psychother Psychosom* 2013;82:372-81.
38
39 376 [24] Moher D, Liberati A, Tetzlaff J. Preferred reporting items for systematic reviews and
40 377 meta-analysis: the PRISMA statement. *BMJ* 2009;339:b2535.
41
42 378 [25] Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review
43 379 and meta-analysis protocols (PRISMA-P): elaboration and explanation. *BMJ (Clin Res ed.)*
44 380 2015;350:g7647.
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 381 [26] Kampling H, Baumeister H, Jaeckel WH, et al. Prevention of depression in chronically
4 382 physically ill adults. Cochrane Systematic Review - Intervention – Protocol.
5
6 383 <https://doi.org/10.1002/14651858.CD011246>
7
8 384 [27] Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for
9 385 assessing risk of bias in randomised trials. *BMJ (Clin Res ed.)* 2011;343: d5928.
10
11 386 [28] Guyatt GH, Oxman AD D, Vist GE, et al. GRADE: an emerging consensus on rating quality
12 387 of evidence and strength of recommendations. *BMJ (Clin Res ed.)* 2008;336:924–6.
13
14 388 [29] Schünemann H, Brożek J, Guyatt G, et al. GRADEpro GDT. 2013. GRADE Handbook
15 389 <https://gdt.grade.org/app/handbook/handbook.html#h.svwngs6pm0f2>.
16
17 390 [30] Valentine JC, Pigott TD, Rothstein HR. How many studies do you need? A primer on
18 391 statistical power for meta-analysis. *J Educ Behav Stat.* 2010;35:215–47.
19
20 392 [31] Gerhards SAH, de Graaf LE, Jacobs LE, et al. Economic evaluation of online computerised
21 393 cognitive behavioural therapy without support for depression in primary care: a randomised
22 394 trial. *British J Psych* 2010;196:310–318.
23
24 395 [32] Hedman E, Andersson E, Lindefors N, et al. Cost-effectiveness and long-term
25 396 effectiveness of internet-based cognitive behaviour therapy for severe health anxiety.
26 397 *Psychol Med* 2013;43:363–74.
27
28 398 [33] Hedman E, Andersson E, Ljótsson B, et al. Cost-effectiveness of Internet-based cognitive
29 399 behavior therapy vs. cognitive behavioral group therapy for social anxiety disorder: results
30 400 from a randomized controlled trial. *Behav Res Ther* 2011;49:729–36.
31
32 401 [34] Kersting, A, Braehler, E, Glaesmer, H, et al. Prevalence of complicated grief in a
33 402 representative population-based sample. *J Affect Disord* 2011;131:339–43.
34
35 403
36 404
37 405
38 406
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

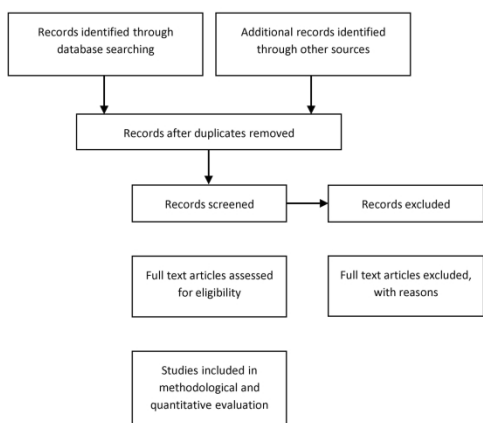


Figure 1. Flow diagram of the planned study selection process adapted from the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement

254x190mm (300 x 300 DPI)

PubMed.gov
US National Library of Medicine National Institutes of Health

PubMed | health OR internet) AND (intervention OR psychotherapy OR cognitive behavioural therapy OR CBT) | Search | Help

Advanced

Search Details

Query Translation:

```
((("bereavement"[MeSH Terms] OR "bereavement"[All Fields]) OR ("widowhood"[MeSH Terms] OR "widowhood"[All Fields]) OR ("grief"[MeSH Terms] OR "grief"[All Fields])) AND (online[All Fields] OR web[All Fields] OR ("computers"[MeSH Terms] OR "computers"[All Fields] OR "computer"[All Fields]) OR mobile[All Fields] OR e-health[All Fields] OR ("internet"[MeSH Terms] OR "internet"[All Fields])) AND (("methods"[MeSH Terms] OR "methods"[All Fields] OR "intervention"[All Fields]) OR ("psychotherapy"[MeSH Terms] OR "psychotherapy"[All Fields]) OR ("cognitive behavioral therapy"[MeSH Terms] OR ("cognitive"[All Fields] AND "behavioral"[All Fields]) AND "therapy"[All Fields]))
```

Search | URL

Result:
273

Translations:

| | |
|---------------|--|
| bereavement | "bereavement"[MeSH Terms] OR "bereavement"[All Fields] |
| widowhood | "widowhood"[MeSH Terms] OR "widowhood"[All Fields] |
| grief | "grief"[MeSH Terms] OR "grief"[All Fields] |
| computer | "computers"[MeSH Terms] OR "computers"[All Fields] OR "computer"[All Fields] |
| internet | "internet"[MeSH Terms] OR "internet"[All Fields] |
| intervention | "methods"[MeSH Terms] OR "methods"[All Fields] OR "intervention"[All Fields] |
| psychotherapy | "psychotherapy"[MeSH Terms] OR "psychotherapy"[All Fields] |
| cognitive | "cognitive behavioral therapy"[MeSH Terms] OR ("cognitive"[All Fields] AND "behavioral"[All Fields] AND "therapy"[All Fields]) OR |
| behavioural | "cognitive behavioral therapy"[All Fields] OR ("cognitive"[All Fields] AND "behavioural"[All Fields] AND "therapy"[All Fields]) OR |
| therapy | "cognitive behavioural therapy"[All Fields] |

Database:
PubMed

User query:
(bereavement OR widowhood OR grief) AND (online OR web OR computer OR mobile OR e-health OR internet) AND (intervention OR psychotherapy OR cognitive behavioural therapy OR CBT)

PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|-----------------------------------|----|---|--------------------------|--------------------------|----------------|
| | | | Yes | No | |
| ADMINISTRATIVE INFORMATION | | | | | |
| Title | | | | | |
| Identification | 1a | Identify the report as a protocol of a systematic review | x | <input type="checkbox"/> | 2 |
| Update | 1b | If the protocol is for an update of a previous systematic review, identify as such | <input type="checkbox"/> | <input type="checkbox"/> | n/a |
| Registration | 2 | If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract | x | <input type="checkbox"/> | 41 |
| Authors | | | | | |
| Contact | 3a | Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author | x | <input type="checkbox"/> | 15-22 |
| Contributions | 3b | Describe contributions of protocol authors and identify the guarantor of the review | x | <input type="checkbox"/> | 392-396 |
| 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 | <input type="checkbox"/> | <input type="checkbox"/> | n/a |
| Support | | | | | |
| Sources | 5a | Indicate sources of financial or other support for the review | x | <input type="checkbox"/> | 386-389 |
| Sponsor | 5b | Provide name for the review funder and/or sponsor | x | <input type="checkbox"/> | 386-389 |
| Role of sponsor/funder | 5c | Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol | x | <input type="checkbox"/> | 386-389 |
| INTRODUCTION | | | | | |
| Rationale | 6 | Describe the rationale for the review in the context of what is already known | x | <input type="checkbox"/> | 83-94 |
| Objectives | 7 | Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) | x | <input type="checkbox"/> | 97-103 |
| METHODS | | | | | |

| Section/topic | # | Checklist item | Information reported | | Line number(s) |
|---|-----|---|----------------------|--------------------------|----------------|
| | | | Yes | No | |
| Eligibility criteria | 8 | Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review | x | <input type="checkbox"/> | 128-145 |
| Information sources | 9 | Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage | x | <input type="checkbox"/> | 146-203 |
| Search strategy | 10 | Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated | x | <input type="checkbox"/> | 146-203 |
| STUDY RECORDS | | | | | |
| Data management | 11a | Describe the mechanism(s) that will be used to manage records and data throughout the review | x | <input type="checkbox"/> | 206-212 |
| Selection process | 11b | State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis) | x | <input type="checkbox"/> | 214-221 |
| Data collection process | 11c | Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators | x | <input type="checkbox"/> | 223-245 |
| Data items | 12 | List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications | x | <input type="checkbox"/> | 247-258 |
| Outcomes and prioritization | 13 | List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale | x | <input type="checkbox"/> | 254-258 |
| Risk of bias in individual studies | 14 | 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 | x | <input type="checkbox"/> | 260-286 |
| DATA | | | | | |
| Synthesis | 15a | Describe criteria under which study data will be quantitatively synthesized | x | <input type="checkbox"/> | 288-298 |
| | 15b | 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 (e.g., I^2 , Kendall's tau) | x | <input type="checkbox"/> | 288-298 |
| | 15c | Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression) | x | <input type="checkbox"/> | 294-295 |
| | 15d | If quantitative synthesis is not appropriate, describe the type of summary planned | x | <input type="checkbox"/> | 288-298 |
| Meta-bias(es) | 16 | Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies) | x | <input type="checkbox"/> | 305-328 |
| Confidence in cumulative evidence | 17 | Describe how the strength of the body of evidence will be assessed (e.g., GRADE) | x | <input type="checkbox"/> | 260-286 |