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

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

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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
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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
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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.

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122 Eligibility criteria

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

140 Information sources and search strategy

141 Systematic literature searches will be conducted in the databases MEDLINE (PubMed
142 interface), Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central
143 Register of Controlled Trials (CENTRAL), Cochrane Methodology Register), PsycINFO,
144 EMBASE, Web of Science (Science and Social Science Citation Index) and Google Scholar (for
145 "grey" literature) by ML and CS independently. A combination of the following search terms
146 will be used: (1) bereavement or widowhood or grief; and (2) online or web or computer or
147 mobile or e-health or internet; and (3) intervention or psychotherapy or cognitive
148 behavioural therapy or CBT. If feasible, medical subject headings (MeSH) will be used as
149 search terms. The finalized MEDLINE search strategy will be adapted to the syntax and
150 subject headings specifications of the other databases. We will initially screen titles and
151 abstracts for eligibility. Full texts will then be assessed for criteria, and the reference lists of
152 included articles and systematic reviews will be hand searched to identify further potentially
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
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3 155 necessary, we will contact researchers directly to gather further relevant non-published
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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.

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10 159 Data management

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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).

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25 167 Selection process

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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:
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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
16 195 (e.g. usability, satisfaction, acceptability, understandability and usefulness); (serious)
17 196 adverse events (e. g. disability, hospitalization, death); onset data from clinician-
18 197 rated scales will be prioritized over self-report questionnaires. All different time
19 198 frames of follow-up assessments will be included.
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27 200 Quality assessment

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

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.
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5 220 Data synthesis and presentation
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7 221 A detailed description of the results for all included studies will be provided in text and
8
9 222 tables. Characteristics of selected studies will be listed and qualitatively described (see listed
10
11 223 parameter in “data collection process”). Characteristics of the study, sample, intervention
12
13 224 and control condition will be presented first, followed by outcome measurements, effect
14
15 225 sizes, and overall results. We will provide a narrative synthesis and if appropriate, a
16
17 226 quantitative meta-analysis using funnel and forest plots and pooled statistics. If feasible,
18
19 227 results of pooled age- and gender-specific outcomes will be reported.

20 228 Data analyses will be performed using Review Manager 5.3 software from the Cochrane
21
22 229 Collaboration Tool for Implementing the Characteristics of Studies (Review Manager
23
24 230 (RevMan) [Computer program], 2014).

25 231

26 232 Meta-analysis

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29 233 Meta-analysis of pooled data will be based on the assessment of clinical, methodological and
30
31 234 statistical heterogeneity. According Cochrane standards, meta-analysis will not be
32
33 235 performed if high levels of heterogeneity and/or variation in the effects of the interventions
34
35 236 are present.

36 237 Heterogeneity in study characteristics will be evaluated using forest plots and I^2 statistics. An
37
38 238 I^2 of >60% indicates substantial heterogeneity and requires exploration of the sources of
39
40 239 heterogeneity in subgroups of studies (Higgins et al. 2011). Depending on the level of
41
42 240 observed heterogeneity, fixed-effect, random-effect or mixed-effect models will be used to
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44 241 estimate the pooled effects on outcomes and to quantify the uncertainty of these estimates.
45
46 242 If sufficient data are available, subgroup analyses based on the content and form of
47
48 243 intervention will be performed. Finally, in order to evaluate the association of
49
50 244 sociodemographic variables with pooled effect sizes, meta-regression models will be fitted.
51
52 245 We will follow the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011)
53
54 246 to deal with missing data.

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60 250 Discussion

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

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9 254 If treatment programs for bereavement which utilize either the Internet or mobile phone
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11 255 technology show effectiveness and feasibility, this therapeutic delivery method has the
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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
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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
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21 260 option would enable the provision of adequate care to more bereaved adults.

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23 261 If there are an insufficient number of studies that have examined gender and age
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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.

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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.

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42 272 Abbreviations

43 273 CBT – cognitive behavioural therapy

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45 274 CENTRAL - Cochrane Central Register of Controlled Trials

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47 275 GRADE - Grades of Recommendation, Assessment, Development and Evaluation

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49 276 IMI - Internet- and mobile-based interventions

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51 277 PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analysis

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53 278 PTSD - post-traumatic stress disorder

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55 279 RCT - randomized controlled-trials

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57 280

58 281 Declarations section

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60 282 Ethics Approval and Consent to Participate

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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.

10 287

11
12 288 Availability of supporting data

13
14 289 Not applicable

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16 290

17
18 291 Competing interest

19
20 292 None declared

21
22 293

23
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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

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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.

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46 306

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49 308 Not applicable

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53 310 Author's information

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

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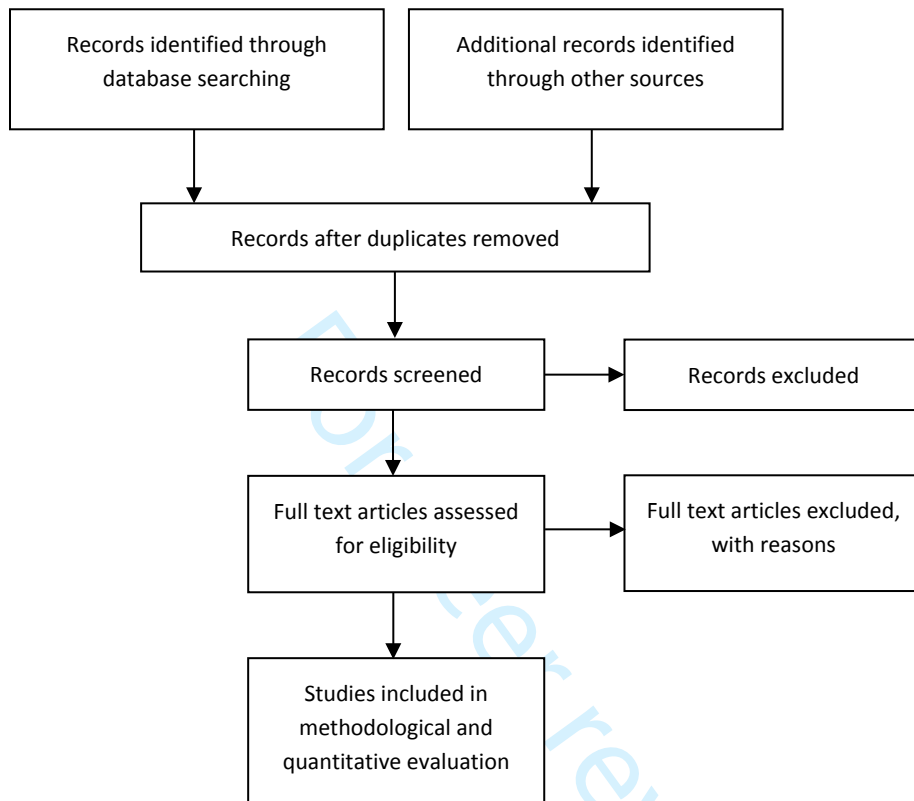
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424 Figure 1. Flow diagram of the planned study selection process adapted from the Preferred
 425 Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.
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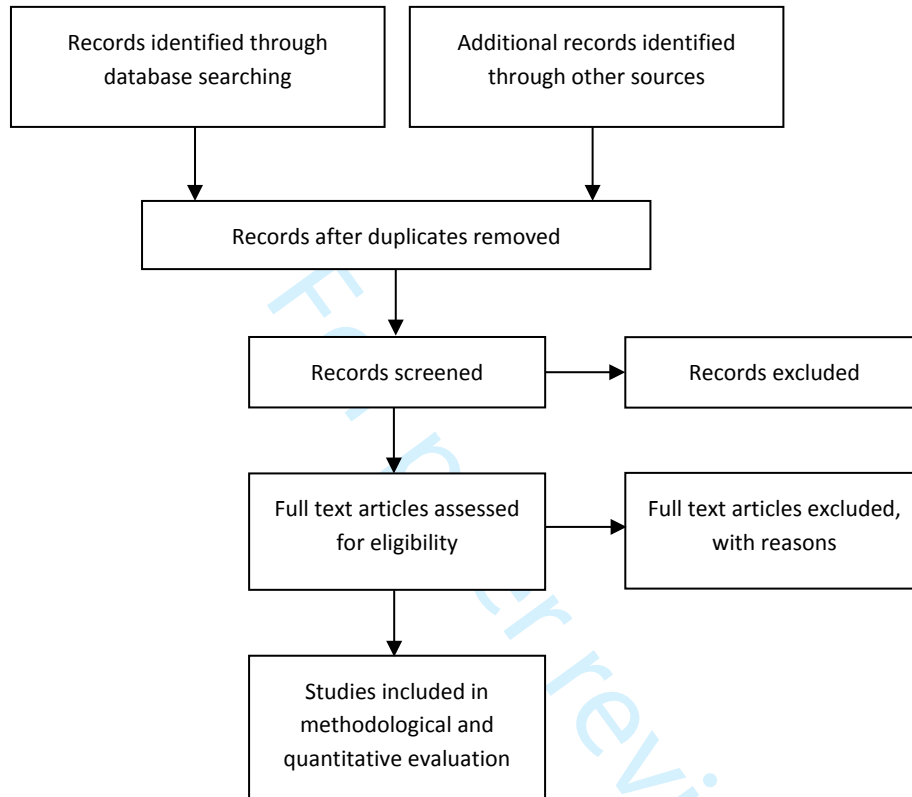


Figure 1. Flow diagram of the planned study selection process adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.

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
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Primary Subject Heading:	Mental health
Secondary Subject Heading:	Public health, Health services research
Keywords:	MENTAL HEALTH, Depression & mood disorders < PSYCHIATRY, PREVENTIVE MEDICINE

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3 1 **Effectiveness and feasibility of internet- and mobile-based interventions for individuals**
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5 2 **experiencing bereavement: A systematic review protocol**
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44 26 Word count: 3,678

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2
3 27 ABSTRACT

4
5 28 Introduction: Internet- and mobile-based interventions (IMIs) provide an innovative and
6
7 29 efficient self-management tool for mental health problems. This systematic review aims to
8
9 30 summarise and critically evaluate studies addressing the effectiveness and feasibility of IMIs
10
11 31 for normal and complicated grief in bereaved adults.

12
13 32 Methods and Analysis: The databases MEDLINE, Cochrane Library, PsycINFO, EMBASE and
14
15 33 Web of Science and Google Scholar (for “grey” literature) will be systematically searched for
16
17 34 feasibility studies or randomized controlled trials of IMIs for bereaved adults who were
18
19 35 experiencing normal/complicated grief. Data will be extracted and evaluated independently
20
21 36 by two reviewers from studies eligible for inclusion. Quality of evidence will be assessed, and
22
23 37 results will be synthesized qualitatively and pooled meta-analytically, if sufficient outcome
24
25 38 data are available. PRISMA standards and GRADE methodology will be used.

26
27 39 Ethics and Dissemination: No primary data will be collected; thus, ethical approval is not
28
29 40 required. The results will be disseminated through a peer-reviewed publication and
30
31 41 conference presentations.

32
33 42 PROSPERO registration number: CRD42019131428

34
35 43 Keywords: grief, bereavement, systematic review, internet- and mobile-based, effectiveness,
36
37 44 feasibility

38 46 Strengths and limitations of this study

- 39
40 47 - first study which provides a comprehensive summary of studies investigating
41
42 48 effectiveness and feasibility of internet- and mobile-based interventions (IMIs) for
43
44 49 normal and complicated grief in bereaved adults
45
46 50 - possibility of usage of these IMIs in healthcare as additional intervention tools as well
47
48 51 as low-threshold treatment options
49
50 52 - application with the necessary caution of these IMIs seems to be required not to
51
52 53 interfere with natural grief processes
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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.

111

112

113 METHODS AND ANALYSIS

114 This protocol outlines the strategies for conducting a systematic review and meta-analysis of
115
116 RCTs which examined the effectiveness of IMIs for bereavement. It is based on the Preferred
117
118 Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) for systematic review
119
120 protocols (PRISMA-P) guidelines[24,25]. The protocol describes the planned strategy to
121
122 systematically evaluate and synthesize data from randomized controlled trials and feasibility
123
124 studies on IMIs for bereaved individuals. We will apply the four-phase PRISMA flow diagram
(figure 1) for our study selection process.

121

122

123

124 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
11 161
12 162 Data management

13
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
26
27 170 Selection process

28
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

44
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.

207

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.

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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
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17
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19
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24 297 interpretation of the data, or decision to submit results
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28 299 Author Contributions

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30 300 ML, CS, AP, MLö, JS, SRH contributed substantially to the conception of the work; ML and CS
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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.
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36 303 ML, CS, AP, MLö, JS, SRH gave agreement to be accountable for all aspects of the work.

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44 308 Author's information

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46 309 All authors approved the final version of the manuscript.
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50 311 Figure legend

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52 312 Figure 1. Flow diagram of the planned study selection process adapted from the Preferred
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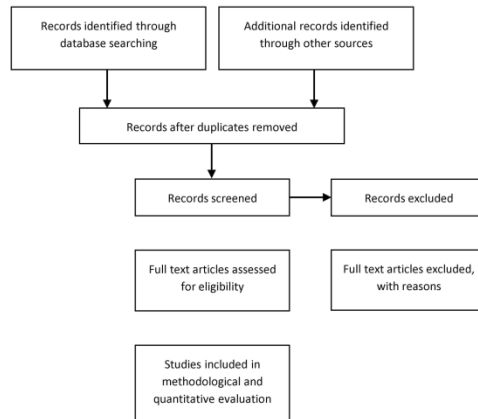


Figure 1. Flow diagram of the planned study selection process adapted from the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement

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PubMed US National Library of Medicine National Institutes of Health

PubMed [Advanced](#) [Help](#)

Search Details

Query Translation:

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((("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]) OR "cognitive behavioural therapy"[All Fields]))
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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 "cognitive behavioural therapy"[All Fields]
behavioural	"cognitive behavioral therapy"[All Fields] OR ("cognitive"[All Fields] AND "behavioural"[All Fields] AND "therapy"[All Fields]) OR "cognitive behavioural therapy"[All Fields]
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