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## Article:

Littlewood, Liz orcid.org/0000-0002-4606-4590, McMillan, Dean orcid.org/0000-0002-2901-8410, Chew-Graham, Carolyn A et al. (29 more authors) (Accepted: 2022) Can we mitigate the psychological impacts of social isolation using behavioural activation? Long-term results of the UK BASIL Urgent Public Health COVID-19 pilot randomised controlled trial and living systematic review. Evidence-Based Mental Health. ISSN 1468-960X (In Press)

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1 **TITLE: Can we mitigate the psychological impacts of social isolation using**  
2 **behavioural activation? Long-term results of the UK BASIL Urgent Public**  
3 **Health COVID-19 pilot randomised controlled trial and living systematic**  
4 **review**

6 **Authors from the BASIL trials and living meta-analysis collective**

7 Elizabeth Littlewood<sup>1</sup>, Dean McMillan<sup>1,2</sup>, Carolyn A. Chew-Graham<sup>3</sup>, Della Bailey,<sup>1</sup> Samantha  
8 Gascoyne,<sup>1</sup> Claire Sloan,<sup>1</sup> Lauren Burke<sup>1</sup>, Peter Coventry,<sup>1,10</sup> Suzanne Crosland<sup>1</sup>, Caroline Fairhurst<sup>1</sup>,  
9 Andrew Henry<sup>1,4</sup>, Catherine Hewitt<sup>1</sup>, Kalpita Baird<sup>1</sup>, Eloise Ryde<sup>1,4</sup>, Leanne Shearsmith<sup>5</sup>, Gemma  
10 Traviss-Turner<sup>5</sup>, Rebecca Woodhouse<sup>1</sup>, Judith Webster<sup>8</sup>, Nick Meader<sup>9</sup>, Rachel Churchill,<sup>9</sup> Elizabeth  
11 Eddy<sup>1</sup>, Paul Heron,<sup>1</sup> Nisha Hickin,<sup>12</sup> Roz Shafran<sup>13</sup>, Osvaldo P. Almeida<sup>11</sup>, Andrew Clegg<sup>5</sup>, Tom Gentry<sup>6</sup>,  
12 Andrew Hill<sup>5</sup>, Karina Lovell<sup>7</sup>, Sarah Dexter Smith<sup>4</sup>, David Ekers,<sup>1,4</sup> Simon Gilbody<sup>1,2\*</sup>

14 *\*Corresponding author, e-mail: [simon.gilbody@york.ac.uk](mailto:simon.gilbody@york.ac.uk) Telephone number: 01904 321370*

15 *Declared competing interests of authors: none*

- 18 1. Department of Health Sciences, University of York, York, YO10 5DD, UK  
19 2. Hull York Medical School, University of York, York, YO10 5DD, UK  
20 3. School of Medicine, Keele University, Staffordshire, ST5 5BG, UK  
21 4. Tees, Esk and Wear Valleys NHS FT, Research & Development, Flatts Lane Centre, Middlesbrough,  
22 TS6 0SZ, UK  
23 5. Leeds Institute of Health Sciences, University of Leeds, Leeds, LS2 9NL, UK  
24 6. Age UK, 7th Floor, One America Square, 17 Crosswall, London, EC3N 2LB  
25 7. Division of Nursing, Midwifery & Social Work, University of Manchester, Oxford Road,  
26 Manchester, M13 9PL  
27 8. Patient and Public Representative, UK  
28 9. Centre for Reviews and Dissemination, University of York, UK.  
29 10. York Environmental Sustainability Institute, University of York, YO10 5NG  
30 11. Medical School, University of Western Australia, Perth, Australia.  
31 12. Department of Psychology, Royal Holloway, University of London, Egham, UK  
32 13. UCL Great Ormond Street Institute of Child Health, 30 Guilford Street, London, UK

36 **Abstract [250 words]**

37 **Background**

38 Behavioural and cognitive interventions remain credible approaches in addressing loneliness and  
39 depression. There was a need to rapidly generate and assimilate trial-based data during COVID-19.

40 **Objectives**

41 We undertook a parallel pilot RCT of behavioural activation [a brief behavioural intervention] for  
42 depression and loneliness [the BASIL-C19 trial ISRCTN94091479]. We also assimilate these data in a  
43 living systematic review [PROSPERO CRD42021298788] of cognitive and/or behavioural  
44 interventions.

45 **Methods**

46 Participants ( $\geq 65$  years) with long-term conditions were computer randomised to Behavioural  
47 Activation ( $n=47$ ) versus care-as-usual ( $n=49$ ). Primary outcome was PHQ-9. Secondary outcomes  
48 included loneliness (De Jong Scale). Data from the BASIL-C19 trial were included in a metaanalysis of  
49 depression and loneliness.

50 **Findings**

51 The 12 months adjusted mean difference for PHQ-9 was -0.70 (95% CI -2.61 to 1.20) and for  
52 loneliness was -0.39 (95% CI -1.43 to 0.65).

53 The BASIL-C19 living systematic review (12 trials) found short-term reductions in depression  
54 (standardised mean difference [SMD]=-0.31, 95%CI -0.51 to -0.11) and loneliness (SMD=-0.48, 95%CI  
55 -0.70 to -0.27). There were few long-term trials, but there was evidence of some benefit (loneliness  
56 SMD=-0.20, 95%CI -0.40 to -0.01; depression SMD=-0.20, 95%CI -0.47 to 0.07).

57 **Discussion**

58 We delivered a pilot trial of a behavioural intervention targeting loneliness and depression;  
59 achieving long term follow-up. Living meta-analysis provides strong evidence of short-term benefit  
60 for loneliness and depression for cognitive and/or behavioural approaches. A fully-powered BASIL  
61 trial is underway.

62 **Clinical implications**

63 Scalable behavioural and cognitive approaches should be considered as population-level strategies  
64 for depression and loneliness on the basis of a living systematic review.

65 **Funding**

66 This study was funded by National Institute for Health and Care Research (NIHR) Programme Grants  
67 for Applied Research (PGfAR) RP-PG-0217-20006.

68

69

70 **Author summary**

71 **Why was this study done?**

- 72 ● Older people with long-term conditions have been impacted by COVID-19 pandemic  
73 restrictions and have experienced social isolation. In turn, this puts them at risk for  
74 depression and loneliness, and these are bad for health and wellbeing. Psychosocial  
75 approaches, such as behavioural activation, could be helpful.
- 76 ● Trial-based evidence is needed to demonstrate if it is possible to address the onset, or  
77 mitigate the impact, of loneliness and depression.
- 78 ● There are few studies of brief psychosocial interventions to mitigate depression and  
79 loneliness, and it is important to know how emerging trial-based data adds to existing  
80 evidence.

81 **What did the researchers do and find?**

- 82 ● There was preliminary evidence that levels of loneliness were reduced at 3 months when  
83 behavioural activation was offered.
- 84 ● At longer term (12-month) follow-up there was a potential positive impact.
- 85 ● When BASIL-C19 data were assimilated into a living systematic review there is clear  
86 evidence of impact of brief psychological interventions on depression and loneliness in the  
87 short-term. More research into the longer-term impact is needed.

88 **What does all this mean?**

- 89 ● Cognitive and/or behavioural interventions show evidence of benefit which will be useful for  
90 policy makers in offering support to people who are socially isolated.
- 91 ● This research knowledge will be useful once the COVID-19 pandemic has passed, since  
92 loneliness is common in older populations and effective scalable solutions will be needed to  
93 tackle this problem.
- 94 ● As new trial-based data emerges, our living meta-analysis will be updated since this is an  
95 area of active research.

96

97

98 **Introduction**

99 The mental health of the population deteriorated during the COVID-19 pandemic<sup>1</sup>. Many people  
100 reported social isolation, and the incidence of depression and anxiety particularly increased for  
101 older people and those with medical vulnerabilities<sup>2</sup>. A plausible mechanism for this deterioration  
102 was that COVID-19 restrictions led to disruption of daily routines, loss of social contact and  
103 heightened isolation and increased loneliness, which are each powerful precipitants of mental ill  
104 health<sup>3</sup>.

105 Social isolation, social disconnectedness, perceived isolation and loneliness are known to be linked  
106 to common mental health problems, such as depression in older people<sup>3 4</sup>. Loneliness is a risk  
107 factor for depression and seems detrimental to physical health and life expectancy<sup>5</sup>. It is  
108 recognised that strategies that, for instance, maintain social connectedness could be important in  
109 ensuring the mental health of older people<sup>6</sup>, particularly during the pandemic<sup>3</sup> and in the planning  
110 for post-pandemic recovery<sup>7</sup>.

111 The need for research to mitigate the psychological impacts of COVID-19, particularly loneliness,  
112 was highlighted as a priority<sup>8</sup>, and we responded by designing and delivering one of a small number  
113 of psychotherapy trials programmes<sup>9</sup>.

114 Behavioural activation (BA) is an evidence-based psychological treatment that explores how physical  
115 inactivity, avoidance and low mood are linked and result in a reduction of valued activity<sup>10</sup>. Small  
116 scale trials of BA delivered to socially-isolated older people have produced encouraging preliminary  
117 results<sup>11</sup>, but there is not yet sufficient research evidence to support whole-scale adoption, or to  
118 inform the population response to COVID-19 or in planning for post-pandemic recovery. We  
119 therefore adapted an ongoing work programme into the role of BA in multiple long-term conditions  
120 in early-2020 to answer the following overarching question: **‘Can we prevent or ameliorate  
121 depression and loneliness in older people with long-term conditions during isolation?’**.

122 In this paper we present the long-term (12-month) results of the BASIL-C19 trial (**B**ehavioural  
123 **A**ctivation in **S**ocial **I**solation): a pilot randomised controlled trial (RCT) of manualised BA, adapted  
124 specifically to be delivered at scale and remotely (via the telephone or video call) for older adults  
125 who became socially isolated as a consequence of COVID-19. The long-term (12-month outcomes)  
126 complement the already-published short-term (up to 3 months) outcomes of the BASIL-C19 trial<sup>12</sup>.  
127 In the short-term BASIL-C19 results, we demonstrated our ability to recruit to a trial during COVID  
128 and found a statistically significant effect in reducing levels of loneliness in a vulnerable older  
129 population.

130 Research into loneliness is a rapidly evolving area, and we therefore present the short- and long-  
131 term results of the BASIL-C19 trial alongside all available randomised data in a prospective evidence  
132 synthesis and cumulative meta-analysis. We adopted the method of a ‘living systematic review’

133 which is a form of evidence synthesis that is continually updated, incorporating relevant new  
134 evidence as it becomes available <sup>13</sup>.

135 Existing reviews in this area are conventional systematic reviews <sup>14 15,16</sup> and will not incorporate new  
136 emerging evidence until their next update; which for most reviews is unplanned or does not happen  
137 and is not responsive to new emerging evidence. The adoption of living systematic reviews, as a  
138 method, was accelerated during the COVID pandemic to facilitate the rapid assimilation and  
139 mobilisation of trial-based evidence as soon as it becomes available and is our chosen method of  
140 evidence synthesis.<sup>17</sup>

141

142

143 **Trial methods**

144 ***Study design and participants***

145 The BASIL-C19 pilot RCT was the first and only mental health trial adopted by the National Institute  
146 for Health and Care Research (NIHR) Urgent Public Health programme (adopted on 28<sup>th</sup> May 2020)  
147 <sup>18</sup>. The BASIL-C19 pilot was designed to provide key information on methods of recruitment and  
148 training for intervention practitioners (hereafter BASIL Support Workers [BSWs]). The trial was  
149 registered on 9<sup>th</sup> June 2020 (ISRCTN94091479) and participants were recruited between 23<sup>rd</sup> June  
150 and 15<sup>th</sup> October 2020. Older adults with long-term conditions were identified as being a ‘high risk  
151 group’ for loneliness and depression as a consequence of social isolation under COVID-19  
152 restrictions. They were recruited from primary care registers in the North East of England. Eligible  
153 and consenting participants were randomised to receive either usual primary care (with signposting  
154 to resources to support mental health during COVID) from their general practice or Behavioural  
155 Activation intervention in addition to usual care. Methods, recruitment, intervention uptake,  
156 retention, experience of the BA intervention for our target population, and acceptability of the  
157 intervention are described in full in the short-term results paper <sup>12</sup>.

158 *Inclusion criteria:* Based on the Academy of Medical Sciences definition of multimorbidity <sup>19</sup> we  
159 recruited older adults (65 years or over) with two or more physical long-term conditions (LTCs) on  
160 primary care registers in two general practices in the North East of England. Participants included  
161 those subject to English Government guidelines regarding COVID-19 self-isolation, social distancing  
162 and shielding as relevant to their health conditions and age (though this was not a requirement and  
163 these requirements changed during the study period).

164 *Exclusion criteria:* Older adults who had cognitive impairment [ascertained on clinical grounds by the  
165 GP], bipolar disorder /psychosis/ psychotic symptoms, alcohol or drug dependence, in the palliative  
166 phase of illness, had active suicidal ideation, were currently receiving psychological therapy, or are  
167 unable to speak or understand English.

168 Potentially eligible participants were telephoned and those who expressed an interest in the study  
169 were contacted by a member of the research team to determine eligibility, obtain consent and  
170 collect baseline data. Interested patients could also complete an online consent form or contact the  
171 study team directly.

172 ***Randomisation, concealment of allocation and masking***

173 Eligible and consenting participants were randomised 1:1 to BA intervention or usual care using  
174 simple randomisation via an automated computer data entry system, administered remotely by the  
175 York Trials Unit, University of York. Participants, general practices, study clinicians, or BSWs were

176 not blinded to treatment allocation. Outcome assessment was by self-report, and study researchers  
177 facilitating the telephone-based outcome assessment were blind to treatment allocation.

178 **Intervention (Behavioural Activation):**

179 The intervention (BA within a collaborative care framework) has been described elsewhere <sup>20</sup> and  
180 was adapted for the purposes of the BASIL-C19 trial. The main adaptation was the use of telephone  
181 delivery, and the use of functional equivalence to maintain social interactions.

182 Behavioural Activation pays particular attention to the function the behaviour holds for an individual  
183 and that reinforcement is determined functionally. An important consequence of this view is the  
184 idea of functional equivalence. A specific form of a behaviour may have served a particular function  
185 for a person. However, that behaviour may no longer be possible due to physical health problems  
186 or COVID lockdown. In this situation an aim of treatment was to identify a functionally equivalent  
187 behaviour that is different and therefore still possible despite physical changes or shielding, but  
188 which may serve the same function for a person.

189 Intervention participants were offered up to eight sessions over a 4 to 6 week period delivered by  
190 trained BSWs, accompanied by a BASIL Behavioural Activation booklet.

191 Sessions were delivered by BSWs remotely via telephone or video call, according to participant  
192 preference. The first session was scheduled to last approximately one hour, with subsequent  
193 sessions lasting approximately 30 minutes.

194 **Comparator (usual GP care with signposting):** Participants in the control group received usual care  
195 as provided by their current NHS and/or third sector providers. In addition, control participants  
196 were 'signposted' to reputable sources of self-help and information, including advice on how to  
197 keep mentally and physically well (e.g., Public Health England (PHE) 'Guidance for the public on the  
198 mental health and wellbeing aspects of coronavirus (COVID-19)' <sup>21</sup> and Age UK <sup>22</sup>).

199 ***Outcome measures***

200 Demographic information obtained at baseline included: age, sex, long-term condition type, socio-  
201 economic status, ethnicity, education, marital status, and number of children.

202 The overarching aim of the BASIL-C19 pilot trial was to test the feasibility of the intervention and the  
203 methods of recruitment, randomisation and follow-up <sup>23</sup>. The primary clinical outcome was self-  
204 reported symptoms of depression, assessed by the PHQ-9 <sup>24</sup>, where higher scores indicate greater  
205 levels of depressive symptomatology. The PHQ-9 was administered at baseline, one, three and 12  
206 months post-randomisation by research staff blind to treatment allocation. Other secondary clinical  
207 outcomes measured at baseline, one, three and 12 months were health related quality of life (SF-  
208 12v2 mental component scale (MCS) and physical component scale (PCS)) <sup>25</sup>, anxiety (GAD-7) <sup>26</sup>,



209 perceived social and emotional loneliness (De Jong Gierveld Scale - 11 items loneliness scale) and  
210 questions relating to COVID-19 circumstances and adherence to government guidelines<sup>27</sup>. Findings  
211 from one- and three-month outcomes have been presented elsewhere<sup>12</sup>, along with information on  
212 intervention compliance.

### 213 ***Sample size & statistical analysis***

214 **Sample size:** Sample size calculations were based on estimating attrition and standard deviation  
215 (SD) of the primary outcome. We aimed to recruit 100 participants. The intervention was delivered  
216 by BSWs and allowed for potential clustering by BSWs assuming an inter-cluster correlation (ICC) of  
217 0.01 and mean cluster size of 15 based upon previous studies<sup>20</sup>. The effective sample size was  
218 therefore 88. Anticipating 15-20% of participants would be lost to follow-up (17% in the CASPER  
219 trial of older adults<sup>20</sup>), this would result in an effective sample size of at least 70 participants, which  
220 is sufficient to allow reasonably robust estimates of the SD of the primary outcome measure to  
221 inform the sample size calculation for a definitive trial<sup>28</sup>.

222 **Statistical analysis:** This study is reported as per the Consolidated Standards of Reporting Trials  
223 (CONSORT) guideline. The flow of participants through the pilot trial is shown in a CONSORT flow  
224 diagram [Figure 1]. Differences in the clinical outcomes between the two groups were compared at  
225 12 months. This was done using a covariance pattern, mixed-effect linear regression model  
226 incorporating all post-randomisation time points. Treatment group, time point, a treatment-by-time  
227 interaction and the baseline score of the outcome of interest were included as fixed effects, and  
228 participant as a random effect (to account for the repeated observations per participant).

229 Different covariance structures were applied to the model. An unstructured covariance pattern for  
230 the correlation between the observations for a participant over time was specified in the final model  
231 based on Akaike's Information Criterion (AIC) (smaller value preferred).

232 An estimate of the difference between treatment groups in all outcome measures was extracted  
233 from the models for the 12-month time point, and overall, with a 95% confidence interval (CI) as  
234 preliminary estimates of effect, but this pilot trial was not powered to show efficacy. Model  
235 assumptions were checked as follows: the normality of the standardised residuals was visually  
236 assessed using a QQ plot, and homoscedasticity by means of a scatter plot of the standardised  
237 residuals against fitted values. No concerning deviations were noted.

### 238 ***Prospective meta-analysis of trial-based data***

239 Using all available trial data to February 2022 we incorporated studies from an earlier Cochrane<sup>16</sup>  
240 and non-Cochrane<sup>15</sup> meta-analyses of cognitive and/or behavioural interventions to prevent or  
241 mitigate loneliness and depression in adult populations in light of the BASIL-C19 results. The

242 planned living meta-analysis protocol was registered on the PROSPERO database (review protocol  
243 CRD42021298788).

244 We searched PubMed, EMBASE, PsycINFO from inception to February 2022 using the MetaPsy  
245 database, and also scrutinised the bibliography of two recent systematic reviews in this area to  
246 identify additional studies (a Cochrane review <sup>16</sup> and a 2021 systematic review <sup>15</sup> by the current  
247 authors). Eligible interventions included first, second, or third wave cognitive or behavioural  
248 therapies (CBT) seeking to improve or prevent loneliness, as well as other CBT interventions where  
249 the focus is on improving common mental health problems but in which loneliness or a related  
250 construct is measured as an outcome. We studied depression and/or loneliness as the main  
251 outcomes of interest, under the advice of the BASIL Lived Experience Advisory Panel. We calculated  
252 a standardised mean difference (SMD) with 95% CI. SMD represents the size of the intervention  
253 effect of each study compared with the between-participant variability in outcome measurements  
254 recorded in each individual study. We categorised the post-intervention outcomes into short-term  
255 outcomes (< 6 months, including end of treatment time points), medium-term (≥6 to <12 months),  
256 and long-term outcomes (≥12 months). If a study reported follow-up outcomes at more than one  
257 time point within one of these time frames, we selected the outcome at the latest point within the  
258 time frame. We conducted a random effects meta-analysis, and included the BASIL-C19 study  
259 evidence. We tested for small study bias using Egger's approach and test <sup>29</sup>.

#### 260 ***Role of Funding Source***

261 BASIL C-19 was funded by the NIHR Programme Grants for Applied Research (PGfAR) programme  
262 (RP-PG-0217-20006). The scope of our pre-existing research into multi-morbidity in older people  
263 was extended at the outset of the COVID-19 pandemic with the agreement of the funder to consider  
264 loneliness and depression in this vulnerable group. The NIHR PGfAR programme had no role in the  
265 writing of this manuscript or the decision to submit it for publication.

#### 266 ***Ethical approval***

267 Ethical approval for the BASIL-C19 study was granted by Yorkshire & The Humber - Leeds West  
268 Research Ethics Committee on 23/04/2020 (The Old Chapel, Royal Standard Place, Nottingham, NG1  
269 6FS, UK; +44 (0)207 104 8018; leedswest.rec@hra.nhs.uk), ref: 18/YH/0380 (approved as substantial  
270 amendment 02 under existing NIHR IRAS249030 research programme).

271

272 **Results**

273 ***Participant recruitment, characteristics and follow-up***

274 Ninety-six participants were randomised (47 to the BA intervention group; and 49 to usual care with  
275 signposting group), of which 80 (83.3%) completed the 12-month follow-up and valid scores were  
276 available for 79 (82.3%). See Figure 1 [CONSORT flow diagram].

277 **<Figure 1> consort diagram**

278 The mean age of randomised participants was 74 years (SD 5.5) and most were White (n=92, 95.8%).  
279 Nearly two-thirds of the sample were female (n=59, 61.5%) (Table 1), and the most common long-  
280 term health problems were cardiovascular conditions. Mean depression scores were indicative of  
281 mild depression (BA mean = 7.5, SD 6.2; usual care mean = 6.0, SD 5.6). There was reasonable  
282 balance in baseline characteristics at randomisation between the two groups.

283 ***Outcome data and between-group comparisons at 12 months***

284 Eighty randomised participants (83.3%) completed the 12-month follow-up and valid primary and  
285 secondary outcome data were available for 79 (82.3%) participants (one participant commenced the  
286 questionnaire but then felt too unwell to continue and did not complete any of the outcome  
287 measures). At 12 months, unadjusted between-group mean differences was in the direction of the  
288 intervention for the PHQ-9, GAD-7, De Jong Social Loneliness and the SF-12 MCS, and usual care for  
289 De Jong total and the Emotional Loneliness subscale, and the SF-12 PCS. The point estimate  
290 adjusted mean difference between groups in the PHQ-9 indicated lower severity in the intervention  
291 group at 12 months (-0.70, 95% CI -2.61 to 1.20), with an overall difference of -0.41 (95% CI -1.65 to  
292 0.83) across all time points. The width of confidence intervals included benefit, harm and no overall  
293 effect. The adjusted mean difference for the total De Jong Gierveld score indicated lower severity in  
294 the intervention group at 12 months (-0.39, 95% CI -1.43 to 0.65), with an overall difference of -0.32  
295 (95% CI -0.97 to 0.34) across all time points. The direction of effect in long-term follow up was  
296 consistent, though the majority were non-significant (Table 1) and the width of confidence intervals  
297 included benefit, harm and no overall effect. For mental health-related quality of life (the SF12  
298 mental component score) there was an overall benefit across all time points (3.22, 95% CI 0.22 to  
299 6.21). There were no adverse events attributed to the trial intervention or participation in the pilot  
300 trial.

301 **Table 1. Unadjusted and adjusted mean differences between the BA and usual care groups by**  
 302 **time point**

| Mean difference (95% CI)  | 1-month             |                             | 3-month              |                             | 12-month            |                             | Over 12 months              |
|---|---------------------|-----------------------------|----------------------|-----------------------------|---------------------|-----------------------------|-----------------------------|
|   | <i>Unadjusted</i>   | <i>Adjusted<sup>a</sup></i> | <i>Unadjusted</i>    | <i>Adjusted<sup>a</sup></i> | <i>Unadjusted</i>   | <i>Adjusted<sup>a</sup></i> | <i>Adjusted<sup>a</sup></i> |
| <b>PHQ-9 [primary outcome]</b>  | -1.44 (-3.66, 0.77) | -0.50 (-2.01, 1.01)         | -0.39 (-2.70, 1.91)  | 0.19 (-1.36, 1.75)          | -0.59 (-2.92, 1.74) | -0.70 (-2.61, 1.20)         | -0.41 (-1.65, 0.83)         |
| <b>GAD-7</b>  | -0.54 (-2.52, 1.44) | 0.20 (-1.33, 1.73)          | -0.16 (-2.09, 1.78)  | 0.31 (-1.08, 1.70)          | -0.97 (-2.93, 0.99) | -0.67 (-2.31, 0.97)         | -0.18 (-1.35, 0.98)         |
| <b>De Jong Gierveld scale (total)</b>   | 0.13 (-1.14, 1.41)  | 0.28 (-0.51, 1.06)          | -0.86 (-2.14, 0.43)  | -0.87 (-1.56, -0.18)        | 0.07 (-1.31, 1.45)  | -0.39 (-1.43, 0.65)         | -0.32 (-0.97, 0.34)         |
| <b>De Jong Gierveld Emotional Loneliness Subscale</b>   | 0.07 (-0.68, 0.81)  | 0.14 (-0.39, 0.67)          | -0.36 (-1.09, 0.36)  | -0.37 (-0.85, 0.11)         | 0.19 (-0.70, 1.08)  | -0.05 (-0.74, 0.65)         | -0.16 (-0.57, 0.26)         |
| <b>De Jong Gierveld Social Loneliness Subscale</b>  | 0.07 (-0.68, 0.81)  | 0.14 (-0.42, 0.69)          | -0.50 (-1.22, -0.23) | -0.50 (-1.00, -0.01)        | -0.12 (-0.84, 0.60) | -0.33 (-0.88, 0.22)         | -0.14 (-0.55, 0.26)         |
| <b>SF-12v2 (Physical Component Score)<sup>b</sup></b>   | 1.40 (-3.42, 6.22)  | 0.34 (-4.17, 4.85)          | 0.81 (-4.16, 5.77)   | 0.11 (-4.46, 4.67)          | -0.04 (-5.39, 5.30) | -0.53 (-4.15, 3.09)         | -0.27 (-2.73, 2.18)         |
| <b>SF-12v2 (Mental Component Score)<sup>b</sup></b>   | 3.60 (-1.17, 8.37)  | 1.91 (-2.64, 5.15)          | 2.09 (-2.48, 6.65)   | 1.26 (-2.64, 5.15)          | 2.17 (-2.54, 6.89)  | 3.61 (-0.22, 7.44)          | 3.22 (0.22, 6.21)           |
| <sup>a</sup> adjusted for the baseline score of the outcome; <sup>b</sup> positive difference indicates better health in intervention group |                     |                             |                      |                             |                     |                             |                             |

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306 **Living systematic review, incorporating BASIL-C19 data with all available trials data**

307 We identified 12 studies (including BASIL-C19) that evaluated cognitive or behavioural interventions  
308 and reported either loneliness or depression outcomes (or both) (Gilbody-BASIL 2021<sup>12</sup>, Choi- Pepin  
309 2021-<sup>11,30</sup>, Kall 2020<sup>31 32</sup>, Kall 2021<sup>33</sup>, Soucy 2019<sup>34</sup>, Williams 2004<sup>35</sup>, Zhang 2018<sup>36</sup>, Cohen-  
310 Mansfield 2018<sup>37</sup>, Cresswell 2012<sup>38</sup>, Jarvis 2019<sup>39</sup>, Theeke 2016<sup>40</sup> and Almeida 2022<sup>41</sup>. The details  
311 of these trails are summarised in [supplementary table 1](#).

312 When we applied the Cochrane Risk of Bias (RoB) tool<sup>42</sup> to the 12 included studies, all were judged  
313 at some risk of bias. For most individual RoB domains, the majority of studies were judged to have  
314 some concerns or a higher risk of bias. For the first domain, bias arising from the randomisation  
315 process, five studies were judged to have some concerns and one study to be at high risk. For the  
316 second domain, bias due to deviations from the intended protocol, the picture was more mixed,  
317 with five at low risk, five having some concerns and two at high risk. For the third domain, bias due  
318 to missing outcome data, just under half were judged at high risk and three had some concerns. For  
319 the fourth domain, bias in measurement of the outcome, the majority [seven studies] judged to be  
320 at high risk or to have some concerns. For the final domain, bias in selection of reported outcomes,  
321 majority [eight studies] were judged to have some concerns.

322 When we pooled data for cognitive and/or behavioural interventions, all twelve studies assessed  
323 loneliness in the short-term ( $\geq 6$  months) and there was strong evidence of benefit for cognitive  
324 and/or behavioural interventions (986 participants, SMD=-0.48, 95%CI -0.70 to -0.27,  $I^2=64.3\%$ ).  
325 Four studies assessed loneliness in the long-term ( $\geq 12$  months) and there was some evidence of  
326 benefit (321 participants, SMD=-0.20, 95%CI -0.40 to -0.01,  $I^2 = 0\%$ ). Nine studies assessed  
327 depression in the short-term, and there was strong evidence of benefit (775 participants, SMD=-  
328 0.31, 95%CI -0.51 to -0.11,  $I^2 = 38.0\%$ ). Four studies assessed depression in the long-term, at 12+  
329 months, and although favouring cognitive and/or behavioural interventions the 95% CI was wider  
330 due to fewer studies reporting at this time point (324 participants, SMD=-0.20, 95%CI -0.47 to 0.07,  
331  $I^2 = 35.7\%$ ). No studies reported medium term ( $\geq 6$  to  $<12$  month) data. In all analyses the level of  
332 between-study heterogeneity was low to moderate.

333 There were sufficient short term outcome data to allow subgroup analyses according to whether the  
334 intervention was a generic psychological therapy versus therapy that focuses specifically on  
335 loneliness. We were also able to compare the effects in working age adults compared to older adult

336 populations. There were insufficient studies to allow us to compare the effects of purely  
337 behavioural intervention with those that focussed on or included cognitive elements.

338 For loneliness as an outcome, we found that although the effect estimate was larger in working age  
339 adults (SMD -0.57, 95% CI -0.84 to -0.30, n=5 studies) than in studies in older adult populations  
340 (SMD -0.46, 95%CI -0.83 to -0.11, n=7 studies), differences between subgroups were not statistically  
341 significant ( $\chi^2=0.24$ ,  $df=1$ ,  $p=0.62$ ). The effect estimate for loneliness was larger in studies using  
342 loneliness-specific intervention (SMD -0.61, 95%CI -0.87 to -0.34, No. trials=9) compared with  
343 interventions using generic interventions (SMD -0.19, 95%CI -0.45 to 0.08, No. trials=3) and the  
344 difference between subgroups was statistically significant ( $\chi^2=4.81$ ,  $df=1$ ,  $p=0.03$ ).

345 For depression as an outcome, we found that the effect estimates were similar in working age adults  
346 (SMD -0.37, 95% CI -0.69 to -0.06, n=4 studies) compared to studies in older adult populations (SMD  
347 -0.26, 95%CI -0.55 to 0.03, n=5 studies), and differences between subgroups were not statistically  
348 significant ( $\chi^2=0.26$ ,  $df=1$ ,  $p=0.61$ ). The effect estimate for depression was also larger in studies  
349 using loneliness-specific intervention (SMD -0.41, 95%CI -0.68 to -0.13, No. trials=6) compared with  
350 interventions using generic interventions (SMD -0.15, 95%CI -0.36 to 0.07, No. trials=3), but the  
351 difference between subgroups was not statistically significant ( $\chi^2= 2.10$ ,  $df=1$ ,  $p=0.15$ ).

352 Where it was possible to test for small study and publication bias, there was evidence of funnel plot  
353 asymmetry for short term loneliness (Egger test  $p<0.05$ ), but not for short term depression (Egger  
354 test  $p= 0.76$ ).

355 <Figure 2: meta-analysis here>

356 <Figure 3: meta-analysis here>

357

## 358 **Discussion**

359 The BASIL-C19 trial is an external pilot trial, designed to test an adapted behavioural intervention  
360 and to refine trial procedures before undertaking a full-scale trial. To our knowledge, this is one of  
361 only a small number of trials undertaken during COVID-19 to mitigate the psychological impact of  
362 the pandemic and its restrictions<sup>9</sup>. We demonstrate that it was possible to trial a scalable  
363 intervention, and achieve good long term follow-up rates under pandemic conditions. The pilot  
364 study was not deigned to have sufficient statistical power to test the effectiveness of behavioural  
365 activation and there are wide confidence intervals. However, we were able to judge how the BASIL  
366 results add to existing trial-based evidence by undertaking a living systematic review.

367 We have previously reported the short-term outcomes where there was a statistically-significant  
368 benefit in reducing loneliness<sup>12</sup>, and here we present the 12-month outcomes alongside a 'living  
369 systematic review', undertaken during the pandemic to evaluate accumulating evidence of cognitive  
370 and behavioural approaches in the prevention or mitigation of depression and loneliness. Our main  
371 meta-analytic finding is that the BASIL-C19 pilot trial results add to a growing body of trial-based  
372 research [summarised in a living systematic review] that demonstrates that brief psychological  
373 interventions can potentially offer clinical benefit to address both depression and loneliness. We  
374 also demonstrate the relative absence of long-term follow up data, but note that the BASIL-C19 trial  
375 is one of only four trials to assess longer term outcomes.

376 Research to date has shown behavioural approaches to be highly effective in the treatment of  
377 depression among older people<sup>10,20,43,44</sup> and the preliminary results of the BASIL-C19 trial support  
378 this approach under COVID-19 restrictions and in mitigating loneliness<sup>45</sup> in an at risk population.  
379 On this basis a fully powered trial was planned and has been justified.

380 Our pilot trial was also undertaken rapidly and during the COVID-19 pandemic in early 2020; the  
381 time elapsed between the onset of the pandemic and the recruitment of the first participant was  
382 less than 3 months. We chose to study the impact of a plausible psychosocial intervention to  
383 mitigate depression and loneliness in an at-risk population of older people with multiple long-term  
384 conditions. It is also important that interventions to tackle the higher rates of depression and  
385 loneliness in all age groups are also developed and evaluated.

386 The BASIL-C19 trial was not designed or powered to detect effectiveness, and a fully-powered  
387 pragmatic trial (BASIL+, ISRCTN63034289), is now underway to test for robust effects in important  
388 secondary outcomes such as loneliness with the benefit of greater statistical precision<sup>46</sup>. We note  
389 the potential impacts of small study size in making baseline imbalances more likely to be observed  
390 by chance alone. We were able to adjust for such differences in our planned statistical analysis, but  
391 some anomalous results emerged adding caution to the interpretation of between group  
392 differences. For example, confidence interval for loneliness changed quite substantially in the  
393 adjusted compared with the unadjusted model. We assume this is due to the increase in power and  
394 precision caused by baseline adjustment for the outcome. However, we also note that this pattern  
395 was not observed at any other time-point.

396 The COVID-19 pandemic prompted a number of studies to understand the impacts of COVID-19,<sup>47</sup>  
397 but there have been very few studies to evaluate psychosocial interventions to mitigate  
398 psychological impact<sup>9</sup>. A clinical priority and policy imperative is to identify a brief and scalable

399 intervention to prevent and mitigate loneliness, particularly in older people <sup>48</sup>. The BASIL trials  
400 programme (including the living systematic review) will be informative in improving the mental  
401 health of populations in socially isolated at-risk populations after the pandemic has passed <sup>7</sup>.

402 We also emphasise that we have used, for the first time, the technique of 'living systematic review'  
403 to describe the impact of cognitive and/or behavioural interventions in addressing depression and  
404 loneliness in the face of social isolation. This will be updated in line with future and emerging trial-  
405 based evidence. The use of this technique was accelerated in many domains of health during the  
406 COVID pandemic,<sup>13 17</sup> and here we present novel results in relation to loneliness. The living  
407 systematic review demonstrates that there are now multiple small-scale trials of interventions for  
408 loneliness. The strong meta-analytic signal of effect in reducing loneliness in the short term should  
409 be interpreted with some caution, since there is a potential small study and methodological biases,  
410 and larger well-designed studies are needed. We also note the range of populations included in  
411 trials in terms of age and the specific treatment modality. The living systematic review  
412 demonstrated that psychological approaches are likely to be equally effective in older adult and  
413 working age adult populations. It was also demonstrated that interventions designed to specifically  
414 target loneliness are likely to be more effective than unmodified cognitive and/or behavioural  
415 approaches in reducing levels of loneliness. More trials will be needed to explore this further.  
416 Finally, the living systematic review highlighted common methodological concerns among trials of  
417 brief psychological therapies, including suboptimal randomisation methods and selective reporting  
418 of outcomes.

419 It is not clear on the basis of the living systematic review whether behavioural or cognitive  
420 approaches are equally effective, and more trials-based research is needed to understand this. The  
421 broader literature shows the equivalence, in terms of effectiveness, of behavioural versus cognitive  
422 treatment modalities in treating depression,<sup>49</sup> and it is not yet clear on the basis of the BASIL living  
423 systematic review whether this also applies to loneliness. We anticipate that further updates of the  
424 living systematic review will allow this to be explored further and that there is now a large-scale trial  
425 of a behavioural approach in follow up.<sup>46</sup>

426



427 ***Contributions of the authors***

428 SG, DE, CCG, EL, DMcM, CH, DB and SGa planned the trial, contributed to the trial design and drafted  
429 the trial protocol. EL, SG, DMcM, PC and DE led manuscript writing. EL, SG and DE oversaw the trial  
430 as chief investigators (SG, DE) and trial manager (EL), and critically revised the manuscript. SG, EL,  
431 DMcM, CCG, CH, PC, GTT, AC, TG, AHi, KL, SDS, TO and JW contributed to trial design and trial  
432 management meetings.

433 SG, CCG, DE, DMcM and DB designed the intervention and BSW training materials, and DB, DMcM,  
434 CCG and DE delivered the BSW training. EL led the day-to-day management of the trial, and SGa and  
435 RW were the trial coordinators. DB, SC and DMcM provided BSW clinical supervision. SGa, LB, AH,  
436 ER, LS and RW facilitated participant recruitment and follow-up data collection, and participated in  
437 trial management meetings. ER and LS delivered the BA intervention. CF, KB and CH developed the  
438 statistical analysis plan and analysed the quantitative data.

439 SG, DMcM, EE, PH, RS, RC & NH designed the living systematic review and are guarantors for the  
440 PROSPERO-registered review. OA provided unpublished data for the meta-analysis and is an  
441 international collaborator to the BASIL programme and the evaluation of behavioural interventions  
442 for older people.

443

444 All authors contributed to the drafts of manuscripts and read the final manuscript. The York Trials  
445 Unit act as data custodians for the BASIL-C19 trial and SG and DMcM act as data custodians for the  
446 living meta-analysis.

447

448

449 ***Competing interests***

450 We have read the journal's policy and the authors of this manuscript have the following competing  
451 interests.

452 DE and CCG were committee members for the NICE Depression Guideline (update) Development  
453 Group between 2015 and 2022, and SG was a member between 2015-18. SG, PC and DMcM are  
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462 collaboration.

463

464 ***Data sharing***

465 The BASIL research collective is especially keen that the BASIL data contributes to prospective meta-  
466 analyses and individual patient data meta-analyses. Requests for data sharing will be considered by  
467 the independent trial steering and data monitoring committee. Full underlying (non-aggregated)  
468 data cannot be made publicly available since the ethics approval of this study does not cover openly  
469 publishing non-aggregated data.

470

471 A request to access these data must be made to the legal representative of the University of York  
472 (michael.barber@york.ac.uk). Data requestors will have to provide: i) written description and legally  
473 binding confirmation that their data use is within the scope of the study; ii) detailed written  
474 description and legally binding confirmation of their actions to be taken to protect the data (e.g.  
475 with regard to transfer, storage, back-up, destruction, misuse, and use by other parties), as legally  
476 required and to current national and international standards (data protection concept); and iii)  
477 legally binding and written confirmation and description that their use of this data is in line with all  
478 applicable national and international laws (e.g. the General Data Protection Regulation of the EU).  
479

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608 **Figure 1: BASIL CONSORT flow diagram**

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612 **Figure 2: Living meta-analysis of behavioural and cognitive trials targeting loneliness in socially**  
613 **isolated populations**

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615 **Figure 3: Living meta-analysis of behavioural and cognitive trials targeting depression in socially**  
616 **isolated populations**

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