

# Digital cognitive—behavioural therapy to reduce suicidal ideation and behaviours: a systematic review and meta-analysis of individual participant data

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**ABSTRACT** 

**Ouestion** Digital interventions based on cognitive behavioural therapy (iCBT) is associated with reductions in suicidal ideation. However, fine-grained analyses of effects and potential effect-moderating variables are missing. This study aimed to investigate the effectiveness of iCBT on suicidal ideation, effect moderators, effects on suicide attempts and predictors of adherence.

Study selection and analysis We systematically searched CENTRAL, PsycINFO, Embase and PubMed for randomised controlled trials that investigated iCBT for suicidal ideation or behaviours. Participants reporting baseline suicidal ideation were eligible. We conducted a one-stage individual participant data (IPD) meta-analysis. Suicidal ideation was the primary outcome, analysed as three indices: severity of suicidal ideation, reliable changes and treatment response.

Findings We included IPD from nine out of ten eligible trials (2037 participants), iCBT showed significant reductions of suicidal ideation compared with control conditions across all indices (severity: b=-0.247, 95% CI −0.322 to −0.173; reliable changes: b=0.633, 95% CI 0.408 to 0.859; treatment response: b=0.606, 95% CI 0.410 to 0.801). In iCBT, the rate of reliable improvement was 40.5% (controls: 27.3%); the deterioration rate was 2.8% (controls: 5.1%). No participant-level moderator effects were identified. The effects on treatment response were higher for trials with waitlist-controls compared with active controls. There were insufficient data on suicide attempts. Human support and female gender predicted treatment adherence. The main source of potential bias was missing outcome data.

**Conclusions** The current evidence indicates that iCBT is effective in reducing suicidal ideation irrespective of age, gender and previous suicide attempts. Future studies should rigorously assess suicidal behaviour and drop-out reasons.

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#### INTRODUCTION

Suicidal ideation and behaviours can have a tremendous impact on those affected, as well as on family members, friends and society as a whole. 12 Suicidal

#### WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Suicidal ideation and behaviours are a major public health challenge and those affected face various barriers to treatment.
- ⇒ Meta-analyses of aggregated data found first indications that digital cognitive-behavioural therapy can reduce suicidal ideation.

#### WHAT THIS STUDY ADDS

- ⇒ This meta-analysis of individual participant data revealed that digital interventions targeting suicidal ideation are effective irrespective or participants' age, gender or history of suicide
- ⇒ Changes in suicidal ideation associated with digital interventions are clinically relevant, with an improvement rate of 40.5% and a deterioration rate of 2.8%.

#### HOW THIS STUDY MIGHT AFFECT RESEARCH. PRACTICE AND/OR POLICY

⇒ Digital cognitive—behavioural therapy can be considered as a low-threshold treatment option to improve healthcare for individuals with suicidal ideation.

ideation is an important risk factor for suicidal behaviours; 60% of individuals who transition from suicidal ideation to suicidal behaviour do so within twelve months of onset.3 A timely reduction of suicidal ideation is of utmost importance as conclusive indicators for who will proceed to suicidal behaviour are lacking.45

Cognitive-behavioural therapy (CBT) and dialectical behavioural therapy have shown to reduce suicidal ideation and behaviours. 6-8 Nevertheless, many individuals at risk of suicide do not seek treatment. 9-11 The wish to solve the problem by oneself, limited access to treatments, low perceived need and stigma have been identified as barriers to treatment.<sup>10</sup> Digital interventions based on CBT (iCBT) might address some of the barriers to treatment: they can be used independently, are highly accessible and flexible and can be offered anonymously. <sup>12</sup> <sup>13</sup> Thus, the low-threshold nature of digital interventions might contribute to increased rates of treatment uptake. Digital interventions have gained additional importance during the COVID-19 pandemic. <sup>14</sup> <sup>15</sup>

Digital interventions are typically delivered through interactive exercises, videos and text elements; moreover, they are usually provided in several modules that can be accessed self-reliantly. 13 These interventions can involve some degree of human support, for example written feedback to homework assignments. 13 In contrast to other mental health conditions such as depression or anxiety, the field of iCBT targeting suicidal ideation is comparably young, with the first randomised controlled trial published less than a decade ago. 16 The self-help intervention investigated in this trial contains components such as psychoeducation, cognitive restructuring, problem solving, elements of dialectical behavioural therapy and relapse prevention.<sup>17</sup> Adapted versions have been implemented in the Netherlands, Belgium and Denmark (https://www.113.nl/heb-je-nu-hulpnodig/zelfhulpcursus-en-testen/zelfhulpcursus; https://thinklife. zelfmoord1813.be/; https://sos.internetbehandling.dk/).

The findings from two recent meta-analyses (MA) of aggregated data suggest that iCBT offered to individuals with suicidal ideation reduces suicidal ideation with effect sizes of -0.23 to -0.29. However, conventional MA cannot investigate differential effects on participant level, as well as clinically relevant improvement and deterioration of symptoms. Those aspects are of utmost importance because nonresponse or harmful effects could be a serious safety threat in this vulnerable group.

Individual participant data MA (IPD-MA) go beyond conventional MA by collecting the IPD from primary trials and analysing them in a multilevel approach. This method allows analyses of clinically relevant changes, as well as participant-level moderator and predictor analyses. Here, IPD-MA contribute to moving the field one step closer to personalised treatment models. <sup>19</sup>

We conducted an IPD-MA to investigate the effectiveness of iCBT on suicidal ideation, to examine clinically relevant improvement and deterioration, and to identify effect moderators on the participant, intervention and study level. Furthermore, we aimed to examine the effectiveness of iCBT on suicide attempts and to assess predictors of treatment adherence.

#### **METHODS**

Detailed methods are displayed in the study protocol<sup>20</sup>; deviations from the protocol are given in online supplemental eMethods1. This report adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement for IPD systematic reviews (online supplemental eMethods2).

#### Eligibility criteria

Participants were eligible if they reported baseline suicidal ideation; there were no restrictions on participants' age. Studies were eligible if they investigated stand-alone iCBT interventions (including third-wave approaches) which directly targeted suicidal ideation or behaviours. We defined iCBT as internet-based or mobile-based programmes that incorporated multiple components of CBT in several modules. Interventions could include additional human support, for example, written feedback. Control groups could consist of treatment as usual, no intervention, other passive or active control conditions (such as a digital attention control programme) or waitlist groups. Studies were eligible if they reported a quantitative measure of suicidal ideation. Eligible measures included validated self-report

instruments, clinician ratings and single items from other scales; we prioritised the measures in this order. We included randomised controlled trials that were published in a peer-reviewed journal in any language with no restrictions on publication dates. Studies were excluded if interventions consisted of blended care, exclusively targeted stigma or help-seeking or were directed at 'gate-keepers' (eg, social workers).

#### Search strategy

For this systematic review and IPD-MA, we systematically searched the databases CENTRAL, PsycINFO, Embase and PubMed from inception to the 31 January 2022 using a specific set of search terms (online supplemental eMethods3). All titles and abstracts were screened by two independent reviewers (RB and HMM) for relevant trials. Next, they screened the full texts of identified studies. Conflicting evaluations were discussed with a third researcher (LS). Reference searches were performed using Web of Science.

#### **Data collection**

Authors of primary trials were asked to provide the anonymised raw IPD. In data checks, IPD were compared with the published data. Two independent reviewers (RB and HMM) extracted data from the raw IPD, transferring them into a combined file. We extracted data on clinical and sociodemographic variables for all available time points. In addition, two independent reviewers (HMM & RB) extracted data items from the published reports. These data items were used for analyses of study-level moderators, an aggregated MA and data integrity checks.

#### Risk of bias

Risk of bias for the primary outcome was evaluated using the revised Cochrane Risk of Bias Tool for randomised controlled trials (RoB 2).<sup>21</sup> In a first step, potential bias was assessed based on the published reports. We did not evaluate bias in measurement of the outcome because blinding of participants is usually not possible in psychological interventions. In a second step, we reassessed the domains based using information from the IPD. We additionally assessed range restrictions, variances and sample composition. Quality of evidence was evaluated using Grading of Recommendations Assessment, Development and Evaluation.<sup>22</sup>

#### Statistical analysis

We conducted a one-stage IPD-MA which combined all included data into a multilevel model with participants nested in trials and the hierarchical structure reflected in a random intercept. Self-reported suicidal ideation was the primary outcome. We accounted for missing data by conducting multiple imputation for each study separately; the imputation was conducted on the level of total scores (for one trial we were only able to obtain imputed data).<sup>23</sup>

We conducted the IPD-MA using three prespecified indices of suicidal ideation: (1) The severity of suicidal ideation based on continuous change scores, (2) the Reliable Change Index (RCI) per person, <sup>24</sup> and (3) the treatment response (50% symptom reduction from baseline). We accounted for multiple testing in the three indices using the Bonferroni correction. For severity of suicidal ideation (1), we performed a multilevel linear regression. Change scores were scaled to the study-specific variance. For the analysis of reliable change (2), participants were categorised into symptom deterioration, no change and improvement based on the RCI. We performed a multilevel ordinal regression with the ordered factor as the dependent variable. For treatment response

#### Systematic review

(3), we performed a logistic multilevel regression. The models were fitted to the pre-post and prefollow-up comparisons. We investigated effects at short-term follow-up (<6 months after baseline); there were insufficient data on long-term follow-up. Based on model comparisons, the treatment effect was modelled as a fixed effect.

Moderator analyses were performed for all three indices of suicidal ideation at postintervention. Participant-level moderators were shifted to the same starting point of scales and scaled to the study-specific variance, if necessary. Continuous moderators were centred across studies. Moderators (variable×treatment interactions) were modelled as fixed effects based on model comparisons, with one exception where model comparisons indicated a random effect.

We conducted a prespecified random-effects MA based on aggregated data from published reports, including data from the trial that could not provide IPD.<sup>25</sup> Hedges' g was calculated based on the pre–post change scores. One trial<sup>26</sup> was excluded as only a subsample of the tailored iCBT condition received eligible modules.

Effectiveness on suicide attempts was investigated by performing a logistic multilevel regression. This exploratory analysis was based on complete datasets because severe attempts will likely lead to missing self-report data, violating the missing-at-random assumption that underlies multiple imputation. The suicide attempt data stemmed from stand-alone single-item measures, single items extracted from suicidality questionnaires and, in one trial, <sup>27</sup> from hospital registers. We combined data from self-reported and hospital-registered data and coded suicide attempt when indicated in at least one data source. For computational reasons, we only included trials with at least one suicide attempt in each condition, leading to the exclusion of two trials. <sup>23</sup> <sup>28</sup>

We examined predictors of treatment adherence by performing a prespecified one-stage IPD-MA. Adherence was defined as the proportion of completed modules; we only included technically assessed data.

The statistical analysis plan (online supplemental eMethods4), R packages used (online supplemental eMethods5) and sensitivity analyses (ie, analyses based on complete cases, participants ≥18 years, excluding interventions targeting youth, two categories of the RCI collapsed into 'no improvement' versus 'improvement' and severity of suicidal ideation controlled for baseline suicidal ideation; online supplemental eMethods6, eResults1) are displayed in the supplement. The analyses were conducted with R V.3.6.1 and RevMan V.5.3. This study was preregistered with the Open Science Framework (OSF; https://osf.io/45tcd). The analysis script will be provided in OSF with publication.

#### **RESULTS**

#### Study selection

The study selection process is displayed in figure 1. The systematic database searches resulted in a total of 4098 unique records. Among these, ten studies were identified as eligible and IPD was obtained from nine studies (90%), <sup>16</sup> <sup>23</sup> <sup>26–32</sup> whereas in one case, data were not available. <sup>25</sup> A total of 2037 participants were included in the IPD-MA, after exclusion of 156 ineligible participants (7.11%); reasons are given in the flowchart (figure 1). A total of 1019 participants (50.0%) were assigned to iCBT and 1018 (50.0%) were assigned to control conditions.

#### Study and participant characteristics

An overview of characteristics of all eligible trials is shown in table 1. In six studies, participants were recruited from the general population; specific target groups included Turkish migrants, <sup>28</sup> Australian Indigenous youth, <sup>23</sup> school students <sup>25</sup> and heavy episodic drinkers. 32 Two trials 25 29 included adolescents and all other trials focused on adults. All studies measured suicidal ideation using self-report questionnaires. The majority of trials used browser-based programmes, while one trial used a mobilebased intervention.<sup>23</sup> In seven studies, the control condition was waitlist 16 23 27-30 32; three studies used active control conditions (digital attention control intervention<sup>26 31</sup> or treatment as usual consisting of contact with school staff and any other side treatments.<sup>25</sup> The number of iCBT modules ranged between 2<sup>29</sup> and  $10^{26}$ ; the maximum time participants were expected to spend in the intervention ranged between  $1^{29}$  and 21 hours.  $^{16\ 27\ 28\ 30\ 31}$ Short-term follow-up assessments were conducted in five trials (four providing  $IPD^{26\ 28-30}$ ; two trials assessed data at long-term follow-up. 27 31 In three trials, there was no relevant follow-up comparison because the control participants received access to the intervention after postintervention. 16 23 32

In this IPD-MA, the mean age of participants was 36.2 years (SD=13.4) and 1383 participants (68.5%) were females. A total of 957 participants (51.9%) reported no history of suicide attempts, whereas 887 (48.1%) reported at least one previous suicide attempt. A total of 927 participants (55.7%) were in parallel psychological or psychiatric treatment. For a detailed overview of the participant characteristics, see online supplemental eTable1.

#### Effects on suicidal ideation

The one-stage IPD-MA (table 2) revealed a reduction of suicidal ideation severity compared with control conditions both at postintervention (b=-0.247; 95% CI -0.322 to -0.173; p<0.001; n=2037; k=9) and short-term follow-up (b=-0.189; 95% CI -0.296 to -0.083; n=891; k=4).

The IPD-MA of reliable changes showed that the probability to be in a favourable category (ie, no change or symptom improvement) was higher in iCBT than in control conditions at postintervention (b=0.633; 95% CI 0.408 to 0.859; p<0.001; n=2037; k=9). The treatment effect was not maintained at follow-up (b=0.441; 95% CI 0.056 to 0.826; n=891; k=4). In iCBT conditions, the rate of reliable deterioration was 2.8% (controls: 5.1%) and the rate of reliable improvement was 40.5% (controls: 27.3%) at postintervention.

The odds of treatment response (ie, symptom reduction by 50%) were higher in the iCBT groups compared with control conditions at postintervention (b=0.606; 95% CI 0.410 to 0.801; p<0.001; n=2037; k=9) and follow-up (b=0.603; 95% CI: 0.295 to 0.911; n=891; k=4). At postintervention, a treatment response occurred in 41.5% of participants in the iCBT condition (controls: 28.2%). The number needed to treat was 7.5. A descriptive overview of the three indices of suicidal ideation (ie, severity of suicidal ideation, reliable changes and treatment response) is displayed in table 3.

#### **Moderator analyses**

The type of control group moderated the effect on response rates (table 2); the effect was smaller for active controls compared with waitlist controls (b=-0.694; 95% CI -1.200 to -0.188; n=2037; k=9). No other moderator effects were identified after correcting for multiple testing in the three indices of suicidal ideation.

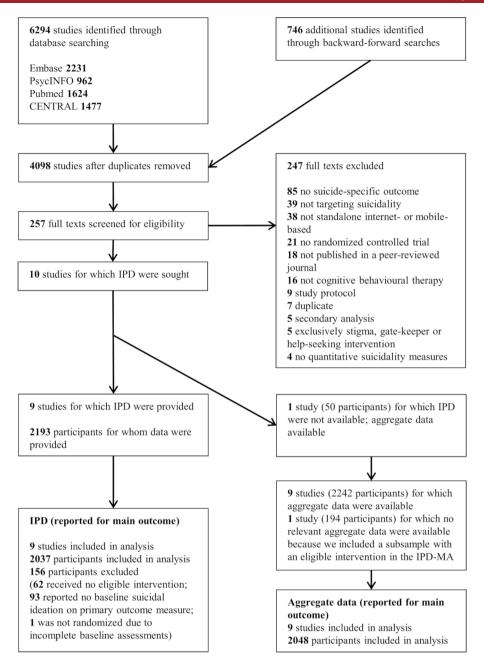


Figure 1 Flowchart. IPD-MA, individual participant data meta-analyses.

#### **Conventional MA**

The MA of aggregated data (online supplemental eFigure1) showed reduced suicidal ideation at postintervention among iCBT participants (g=-0.31; 95% CI -0.40 to -0.22; n=2048; k=9) when compared with those in control conditions. The subgroup analysis showed that the overall effect size did not change when we included the trial by Hetrick *et al*<sup>25</sup> that could not be included in the IPD-MA. The funnel plot did not indicate publication bias (online supplemental eFigure2).

#### Effects on suicide attempts

The IPD-MA did not reveal a significant effect on suicide attempts during the intervention period (b=0.091; 95% CI -0.440 to 0.617; n=864; k=3). A post hoc power analysis indicated that when considering a rate of suicide attempts of 10% in the target population, <sup>27</sup> a total of 2002 participants

per condition would be necessary to detect a 25% reduction of suicide attempts in the iCBT condition ( $\alpha$ =0.05,  $\beta$ =0.80).

#### Adherence

Overall, participants completed 56.8% of assigned iCBT modules; 28.4% of participants completed all assigned modules (n=486 participants in the iCBT condition; k=5). Female gender (b=0.086; 95% CI 0.015 to 0.157; n=483; k=5) and the presence of human support (b=0.228; 95% CI 0.149 to 0.306; n=486; k=5) were associated with increased treatment adherence (table 4).

#### **Drop-out**

At postintervention, 782 participants (38.4%) did not provide primary outcome data. 337 participants (33.1%) dropped out from control conditions and 445 participants (43.7%) from the iCBT condition. At follow-up, 535 participants (60.0%)

**Table 1** Study characteristics

| Study                             | Total n | Target group                                     | Eligible age group    | Co | mparison   | iCBT weeks<br>(no of<br>modules) | Included<br>measure<br>of suicidal<br>ideation | Drop-out iCBT* | Drop-out<br>control* | IPD |
|-----------------------------------|---------|--|-----------------------|----|--|----------------------------------|--|----------------|----------------------|-----|
| Batterham<br>2018 <sup>26</sup>   | 132†    | General<br>population (young<br>adults)          | 18+ (initially 18–25) |    | unguided iCBT<br>(online)<br>active online<br>intervention | 2 (10)                           | SIDAS  | 41 (62.1%)     | 37 (56.1%)           | Yes |
| De Jaegere<br>2019 <sup>30</sup>  | 724     | General<br>population<br>(adults)                | 18+                   |    | unguided iCBT<br>(online)<br>waitlist                      | 6 (6)                            | BSS  | 270 (74.0%)    | 187 (52.1%)          | Yes |
| Eylem 2021 <sup>28</sup>          | 18      | Turkish migrants<br>(adults)                     | 18+                   |    | guided iCBT<br>(online)<br>waitlist                        | 6 (6)                            | BSS  | 0 (0%)         | 2 (25.0%)            | Yes |
| Hetrick 2017 <sup>25</sup>        | 50      | School students (adolescents)                    | 13–19                 |    | guided iCBT<br>(online)+TAU<br>TAU                         | 10 (8)                           | SIQ  | 8 (30.8%)      | 3 (12.5%)            | No  |
| Hill 2019 <sup>29</sup>           | 80      | General<br>population<br>(adolescents)           | 13–19                 |    | unguided iCBT<br>(online)<br>waitlist                      | 2 (2)                            | BSS  | 5 (12.2%)      | 4 (10.0%)            | Yes |
| Mühlmann<br>2021 <sup>27</sup>    | 402     | General<br>population<br>(adults)                | 18+                   |    | guided iCBT<br>(online)<br>waitlist                        | 6 (6)                            | BSS  | 25 (12.8%)     | 24 (11.7%)           | Yes |
| Tighe 2017 <sup>23</sup>          | 61      | Australian<br>Indigenous youth<br>(young adults) | 18+ (initially 18–35) |    | unguided iCBT<br>(App)<br>waitlist                         | 6 (3)                            | DSI-SS   | 2 (6.5%)       | 0 (0%)               | Yes |
| Van Spijker<br>2014 <sup>16</sup> | 236     | General<br>population<br>(adults)                | 18+                   |    | unguided iCBT<br>(online)<br>waitlist                      | 6 (6)                            | BSS  | 11 (9.5%)      | 10 (8.3%)            | Yes |
| Van Spijker<br>2018 <sup>31</sup> | 418     | General<br>population<br>(adults)                | 18–65                 |    | unguided iCBT<br>(online)<br>active online<br>intervention | 6 (6)                            | SIDAS  | 98 (47.3%)     | 94 (44.5%)           | Yes |
| Wilks 2018 <sup>32</sup>          | 59      | Heavy episodic<br>drinkers (adults)              | 18+                   |    | guided iCBT<br>(online)<br>waitlist                        | 8 (8)                            | BSS  | 8 (26.7%)      | 1 (3.4%)             | Yes |

<sup>\*</sup>This refers to drop-out at postintervention as reported in the original trials.

†The total number of participants does not include the ineligible static intervention condition (third intervention arm with an additional n=62, excluded from our analyses). BSS, Beck Scale for Suicidal Ideation; DSI-SS, Depressive Symptom Inventory-Suicidality Subscale; iCBT, interventions based on cognitive—behavioural therapy; SIDAS, Suicidal Ideation Attributes Scale: SIO. Suicidal Ideation Ouestionnaire.

dropped out; 222 (50.7%) dropped out from controls and 313 (69.1%) from iCBT. Exploratory analyses of baseline characteristics of participants who dropped out versus those who provided outcome data are displayed in online supplemental eTable2.

#### Risk of bias

Taking information from IPD into account, the main source of potential bias was bias due to missing outcome data. In five out of nine included trials, the drop-out rates were >30% or the differences in drop-out rates between conditions were >10%. Reasons for drop-out were only reported in two out of nine trials, <sup>16 27</sup> which had comparably low drop-out rates (<15%). Risk of bias related to the randomisation process was low. Also, few deviations from intended interventions were noted; in two trials, technical issues in the iCBT interventions led to high-risk ratings. Bias related to the selection of the outcome was low, reflecting that data were analysed according to a prespecified analysis in this IPD-MA. Additional inspections of the IPD concerning range restrictions, high or low variances and sample composition did not suggest other sources of bias (see online supplemental eResults2 for detailed ratings).

#### **Quality of evidence**

The quality of evidence (online supplemental eResults3) for the effectiveness on suicidal ideation at postintervention was judged to be low due to missing outcome data (38.4%) and differing drop-out rates between conditions. Furthermore, seven out of nine trials were waitlist-controlled, which might lead to an overestimated effect size. <sup>33</sup> At follow-up, the quality of evidence for a reduction of suicidal ideation was judged to be very low. Reasons for downgrading the rating at follow-up included risk of bias (60.0% drop-out), indirectness of evidence (only four trials were included and one trial accounted for 80% of the included follow-up data, <sup>30</sup> leading to a less representative IPD sample) and imprecision of the effect estimate. Quality of evidence for suicide attempts during the intervention period was rated very low due to sources of potential bias and a highly imprecise effect estimate.

#### DISCUSSION

This is the first IPD-MA focusing on digital interventions for suicidal ideation and behaviours. The study moves beyond previous MA by providing insights into differential effects on participant level, investigating clinically relevant changes and by

|  |          | Severity of suicidal ideati | al ideation    |         | Reliable changes (RCI)+ | (RCI)†        |         | Treatment response | Treatment response (50% symptom reduction) | ction)  |
|--|----------|-----------------------------|----------------|---------|-------------------------|---------------|---------|--------------------|--|---------|
|  | n (k)*   | b (SE)                      | 95% CI         | P value | b (SE)                  | 95% CI        | P value | b (SE)             | 95% CI                                     | P value |
| Effects on severity of suicidal ideation |          |                             |                |         |                         |               |         |                    |  |         |
| Treatment effect at postintervention     | 2037 (9) | -0.247 (0.038)              | -0.322; -0.173 | <0.001  | 0.633 (0.115)           | 0.408; 0.859  | <0.001  | 0.606 (0.100)      | 0.410; 0.801                               | <0.001  |
| Treatment effect at follow-up            | 891 (4)  | -0.189 (0.054)              | -0.296; -0.083 | 0.001   | 0.441 (0.195)           | 0.056; 0.826  | 0.075   | 0.603 (0.157)      | 0.295; 0.911                               | <0.001  |
| Moderator analyses                       |          |                             |                |         |                         |               |         |                    |  |         |
| Suicidal ideation#                       | 2037 (9) | -0.202 (0.099)              | -0.396; -0.008 | 0.125   | 0.220 (0.293)           | -0.355; 0.795 | 1.000   | 0.196 (0.294)      | -0.380; 0.771                              | 1.000   |
| History of suicide attempts#             | 1850 (6) | -0.123 (0.080)              | -0.279; 0.033  | 0.370   | 0.184 (0.224)           | -0.255; 0.624 | 1.000   | 0.023 (0.222)      | -0.411; 0.457                              | 1.000   |
| Depressiveness#                          | 1980 (8) | -0.008 (0.034)              | -0.074; 0.058  | 1.000   | -0.011 (0.100)          | -0.207; 0.184 | 1.000   | -0.105 (0.091)§    | -0.283; 0.074                              | 0.750   |
| Hopelessness#                            | 1785 (5) | -0.055 (0.034)              | -0.121; 0.011  | 0.303   | 0.146 (0.097)           | -0.044; 0.337 | 0.395   | 0.182 (0.091)      | 0.004; 0.360                               | 0.135   |
| Anxiety#                                 | 1516 (5) | -0.069 (0.040)              | -0.148; 0.009  | 0.249   | 0.151 (0.117)           | -0.079; 0.380 | 0.595   | 0.152 (0.103)      | -0.051; 0.355                              | 0.426   |
| Worrying                                 | 1369 (4) | 0.000 (0.003)               | -0.007; 0.007  | 1.000   | 0.003 (0.010)           | -0.016; 0.023 | 1.000   | -0.008 (0.009)     | -0.026; 0.010                              | 1.000   |
| Age‡                                     | 1907 (7) | -0.001 (0.003)              | -0.007; 0.004  | 1.000   | 0.003 (0.008)           | -0.013; 0.019 | 1.000   | -0.007 (0.007)     | -0.021; 0.008                              | 1.000   |
| Female gender‡                           | 2019 (9) | -0.034 (0.082)              | -0.195; 0.127  | 1.000   | 0.056 (0.240)           | -0.414; 0.527 | 1.000   | -0.031 (0.223)     | -0.468; 0.406                              | 1.000   |
| Secondary education or higher‡           | 1872 (7) | 0.025 (0.140)               | -0.248; 0.299  | 1.000   | -0.026 (0.425)          | -0.862; 0.809 | 1.000   | -0.072 (0.422)     | -0.898; 0.755                              | 1.000   |
| Married/living with partner‡             | 1616 (5) | -0.043 (0.096)              | -0.231; 0.144  | 1.000   | 0.124 (0.268)           | -0.402; 0.649 | 1.000   | -0.020 (0.263)     | -0.535; 0.495                              | 1.000   |
| Employed#                                | 710 (6)  | 0.151 (0.135)               | -0.112; 0.415  | 0.782   | -0.702 (0.407)          | -1.502; 0.098 | 0.256   | -0.470 (0.371)     | -1.198; 0.258                              | 0.616   |
| Current treatment                        | 1829 (6) | 0.082 (0.081)               | -0.076; 0.241  | 0.929   | -0.105 (0.236)          | -0.569; 0.358 | 1.000   | -0.415 (0.223)     | -0.852; 0.022                              | 0.187   |
| Alcohol use                              | 558 (3)  | -0.022 (0.026)              | -0.073; 0.029  | 1.000   | 0.038 (0.090)           | -0.139; 0.214 | 1.000   | -0.012 (0.070)     | -0.149; 0.124                              | 1.000   |
| Human support during intervention        | 2037 (9) | 0.002 (0.090)               | -0.173; 0.178  | 1.000   | 0.137 (0.244)           | -0.342; 0.617 | 1.000   | 0.212 (0.234)      | -0.246; 0.670                              | 1.000   |
| Treatment dose (No of modules)#          | 2037 (9) | 0.014 (0.031)               | -0.046; 0.074  | 1.000   | -0.088 (0.083)          | -0.250; 0.075 | 0.868   | -0.048 (0.078)     | -0.201; 0.104                              | 1.000   |
| Treatment dose (weeks)#                  | 2037 (9) | -0.042 (0.034)              | -0.108; 0.025  | 0.661   | 0.082 (0.092)           | -0.098; 0.263 | 1.000   | -0.020 (0.087)     | -0.190; 0.150                              | 1.000   |
| Type of control group#                   | (6) 2500 | 0.182 (0.091)               | 0.003.0360     | 0 1 20  | (020 0) 023 0           | 1 10E. O.0E1  | 1000    | (010 // 700        | 1 200. 0 100                               | 1000    |

Note: These analyses are based on imputed data. P values have been corrected for multiple testing across the three indices of suicidal ideation using the Bonferroni correction term; corrected p>1.000 have been rounded to 1.000. The CIs have not been corrected. For moderators, the treatment×moderator interaction is displayed.

<sup>\*</sup>n (k): total number of participants included in the respective analyses (number of studies).

<sup>†</sup>RCI: categorised RCI per person (improvement, no change, deterioration).

<sup>#</sup>These moderator variables were prespecified in the study protocol.

<sup>§</sup>The moderator depressiveness in the response rate model was modelled as a random effect as indicated in model comparisons; all other moderators were modelled as fixed effects. iCBT, interventions based on cognitive—behavioural therapy; RCJ, Reliable Change Index.

 Table 3
 Descriptive values of suicidal ideation at baseline, postintervention and follow-up

|  | •   |  |   |
|--|---|--|---|
|  | iCBT conditions<br>(n <sub>Post</sub> =1019; n <sub>Follow-up</sub> =453) | Control conditions<br>(n <sub>Post</sub> =1018; n <sub>Follow-up</sub> =438) | Total sample (n <sub>Post</sub> =2037; n <sub>Follow-up</sub> =891) |
|  | M (SD)* or n (%)†   | M (SD)* or n (%)†  | M (SD)* or n (%)†   |
| Severity of suicidal ideation‡             |   |  |   |
| Baseline                                   | 0.922 (0.375)   | 0.915 (0.371)  | 0.918 (0.373)   |
| Postintervention                           | 0.718 (0.583)   | 0.862 (0.594)  | 0.790 (0.593)   |
| Follow-up                                  | 0.650 (0.619)   | 0.839 (0.657)  | 0.743 (0.645)   |
| RCI improvement§                           |   |  |   |
| Postintervention                           | 413 (40.5%)   | 278 (27.3%)  | 691 (33.9%)   |
| Follow-up                                  | 231 (51.0%)   | 184 (42.1%)  | 415 (46.6%)   |
| RCI no change§                             |   |  |   |
| Postintervention                           | 577 (56.7%)   | 688 (67.6%)  | 1266 (62.1%)  |
| Follow-up                                  | 211 (46.6%)   | 236 (53.8%)  | 447 (50.2%)   |
| RCI deterioration§                         |   |  |   |
| Postintervention                           | 29 (2.8%)   | 51 (5.1%)  | 80 (4.0%)   |
| Follow-up                                  | 11 (2.4%)   | 18 (4.1%)  | 29 (3.2%)   |
| Treatment response (50% symptom reduction) |   |  |   |
| Postintervention                           | 423 (41.5%)   | 287 (28.2%)  | 710 (34.9%)   |
| Follow-up                                  | 228 (50.4%)   | 158 (36.0%)  | 386 (43.3%)   |

Note: These analyses are based on the imputed data.

conducting standardised analyses across trials of a high methodological rigour. The results indicate that iCBT is associated with clinically relevant reductions in suicidal ideation and might be effective irrespective of participants' age, gender or history of suicide attempts. This review identified a lack of evidence on suicidal behaviour.

We found a postintervention reduction of suicidal ideation compared with control conditions (b=-0.247; 95% CI -0.322 to -0.173). The analyses of treatment response and reliable changes showed an increased probability for a favourable outcome in the iCBT condition; symptom improvements were more frequent and deteriorations were less frequent than in control conditions. It remains unclear whether the effects can be maintained at follow-up. The effects on response rates were higher for waitlist-controlled trials compared with active controls.

The effect sizes on suicidal ideation at postintervention 17 18 and higher effects for waitlist controlled trials<sup>17</sup> are in line with previous MA on digital interventions for suicidal ideation. Furthermore, a recent MA on various intervention approaches (eg, face-to-face psychotherapy, medication, means restriction) found that all intervention types were associated with small reductions in suicidal ideation and behaviours.<sup>34</sup> Given that digital interventions are highly scalable and accessible, even small changes can make an important contribution at the population level. 12 When interpreting the identified effect sizes, it is important to note that research participants with suicidal ideation typically receive psychological or psychiatric side treatments for ethical reasons 35 36; in our IPD-MA, this was the case for 55.7% of all participants. This might partly explain the response rates in control conditions and is likely to contribute to reduced effect sizes compared with more restrictive efficacy

|                                   | n (k)*  | b      | SE    | 95% CI        | P value |
|-----------------------------------|---------|--------|-------|---------------|---------|
| Suicidal ideation                 | 486 (5) | 0.034  | 0.042 | -0.047; 0.116 | 0.410   |
| History of suicide attempts       | 411 (3) | -0.020 | 0.034 | -0.086; 0.046 | 0.556   |
| Depressiveness                    | 457 (4) | 0.002  | 0.016 | -0.030; 0.034 | 0.885   |
| Hopelessness                      | 411 (3) | -0.002 | 0.017 | -0.035; 0.032 | 0.917   |
| Anxiety                           | 252 (2) | -0.019 | 0.022 | -0.062; 0.024 | 0.382   |
| Age                               | 440 (4) | -0.001 | 0.001 | -0.003; 0.002 | 0.561   |
| Female gender                     | 483 (5) | 0.086  | 0.036 | 0.015; 0.157  | 0.017   |
| Secondary education or higher     | 465 (5) | 0.038  | 0.057 | -0.073; 0.149 | 0.498   |
| Married/living with partner       | 440 (4) | 0.047  | 0.036 | -0.024; 0.117 | 0.193   |
| Employed                          | 222 (5) | -0.017 | 0.055 | -0.124; 0.091 | 0.760   |
| Current treatment                 | 433 (4) | 0.014  | 0.035 | -0.054; 0.083 | 0.682   |
| Human support during intervention | 486 (5) | 0.228  | 0.040 | 0.149; 0.306  | < 0.001 |

<sup>\*</sup>Means (m) and SD are displayed for severity of suicidal ideation.

tFor the RCI and reponse rates, the number of participants in the respective category (n) and corresponding percentages (%) are displayed.

<sup>‡</sup>Scaled to the study-specific variance as different measures were used.

<sup>§</sup>RCI: categorised RCI per person.

iCBT, interventions based on cognitive—behavioural therapy; RCI, Reliable Change Index.

trials.<sup>13</sup> The treatment response rate of 41.5% is substantial, especially when considering the self-help format of the interventions.

We did not find differential effects of iCBT for specific subgroups based on the available participant-level data. Our findings provide considerable evidence that iCBT works irrespective of participants' age, gender and history of suicide attempts. These variables were assessed in >1800 participants, were highly comparable across trials and different subgroups were well represented across the IPD sample. This is encouraging in light of the urgent need for low-threshold treatment options for the undertreated group of suicidal men.<sup>37</sup> However, younger individuals and males did tend to drop out from studies more frequently and male gender was associated with lower treatment adherence. Lower adherence in individuals with a younger age and male gender was also found in digital interventions for depression.<sup>38</sup> It remains unclear why younger individuals tend to drop out more frequently. Males might have had lower usage rates because the design features of investigated interventions may have been less acceptable to them. For example, a survey study on e-health found a higher preference for a video game format in men, and a lower preference for exercises or self-help materials.<sup>39</sup> For both young participants and males, participatory research could contribute substantially to the development of more suitable interventions, tailored to the needs of these specific target groups.40

Nevertheless, the overall treatment adherence was comparable to digital interventions for other mental health conditions. The mean percentage of completed iCBT modules was 56.8% and 28.4% of participants completed all assigned modules. This is a substantial proportion, considering that adherence is a major challenge in digital interventions<sup>13</sup> and individuals with suicidal ideation tend to drop out frequently even from face-to-face treatment.<sup>41</sup> We found that iCBT with human support was associated with increased adherence, which is a typical finding in digital intervention research. <sup>13</sup> <sup>42</sup>

Finally, the effect of iCBT on suicide attempts remains unclear. Most assessments of suicide attempts relied on self-report in single items and the analysis was underpowered, resulting in a very low quality of evidence. Mühlmann *et al*<sup>27</sup> included register-based data on suicide attempts and suicide deaths. They found that two out of 402 participants died by suicide and 44 participants attempted suicide during the study period; attempts and suicides were equally distributed across conditions.

Some limitations need to be taken into account. First, the quality of evidence for the effects on suicidal ideation is limited by a high rate of study drop-out (38.4% at postintervention), especially in the iCBT condition. If drop-out is associated with the true outcome (eg, someone dropped out because they got worse), the missing-at-random assumption underlying the method used for the handling of missing data is violated, potentially leading to biased results. Three trials 16.25.27 reported reasons for drop-out. Unfavourable reasons included feeling unwell, hospitalisation, suicide attempts or plans and not finding iCBT useful. However, there were also positive or neutral reasons such as getting help elsewhere, feeling better, no internet connection or lack of time. Drop-out might be lower in control conditions because filling in the questionnaire was linked to getting access to the intervention afterwards.

Second, the potential to identify effects might be reduced for some moderator variables because they were assessed in few trials, the treatment effect on suicidal ideation was small and because some categorical variables might lack comparability across trials. Third, we were not able to include IPD from one eligible trial, <sup>25</sup> leading to a coverage rate of 90%. However, the conventional MA including this trial showed an effect size that is comparable to the IPD-MA.

Fourth, for one trial only imputed IPD were available<sup>23</sup>; however, only two participants had missing outcome data at postintervention in this trial, so the imputation method is unlikely to have affected the analyses.

Fifth, it remains unclear whether the findings generalise to specific subpopulations such as adolescents, migrants or ethnic minorities. Fortunately, first trials have been conducted for these target groups. <sup>23</sup> <sup>25</sup> <sup>28</sup> <sup>29</sup>

Sixth, we were not able to investigate which intervention components make the largest contribution to the treatment effect due to the limited number of available trials. It is likely that treatment components have differential effects, potentially leading to different effect sizes between interventions. With a substantially larger number of trials, a network IPD-MA on intervention components as recently conducted in the field of depression 43 could be a fruitful approach in the future.

#### Conclusions

The findings of this IPD-MA indicate that iCBT for suicidal ideation or behaviours is a promising approach. This is encouraging because iCBT, especially unguided interventions, might represent a scalable low-threshold option for those who might not seek treatment otherwise. In clinical practice, guidance could be offered on demand in order to increase adherence, but also to connect with individuals who report deteriorations or non-response. This allows alternative treatment options to be offered in a stepped care model.

Our study identified several recommendations for future research. Given the vulnerable target group of suicidal individuals and methodological limitations due to high drop-out rates, it is imperative that future trials prioritise rigorous and valid assessment of harmful effects and drop-out reasons, despite the ethical and practical challenges that are inherent in these assessments. 35 36 Å future large-scaled multicentre trial with long-term follow-up and a valid assessment strategy of suicide attempts (eg, register-based data or rigorous investigation of lost cases) could unveil potential effects on suicide attempts. In addition, greater effort in the assessment of potential moderators and mediators may stimulate the development of evidence-based treatment decision models. Furthermore, it is imperative to refine existing interventions and develop new intervention formats. Promising approaches could be the integration of adherence-fostering elements such as reminders or a higher level of human support, momentary assessment strategies or digital sensing responding to the high fluctuations of suicidal ideation, 44 45 or machine learning algorithms to provide just-in-time adaptive interventions. 12 46

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