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Brief Online Cognitive Behavioural Intervention for Dysfunctional Worry Related to the COVID-19 Pandemic: A Randomised Controlled Trial

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Abstract
Introduction: Worries about the immediate and long-term consequences of the COVID-19 pandemic may for some individuals develop into pervasive worry that is disproportionate in its intensity or duration and significantly interferes with everyday life. ***Objective:*** The aim of this study was to investigate if a brief self-guided, online psychological intervention can reduce the degree of dysfunctional worry related to the COVID-19 pandemic and associated symptoms. ***Methods:*** 670 adults from the Swedish general population reporting daily uncontrollable worry about COVID-19 and its possible consequences (e.g., illness, death, the economy, one's family) were randomised (1:1 ratio) to a 3-week self-guided, online cognitive behavioural intervention targeting dysfunctional COVID-19 worry and associated symptoms, or a waiting list of equal duration. The primary outcome measure was a COVID-19 adapted version of the Generalised Anxiety Disorder 7-item scale administered at baseline and weeks 1–3 (primary endpoint). Follow-up assessments were conducted 1 month after treatment completion. The trial was registered on ClinicalTrials.gov (NCT04341922) before inclusion of the first participant. ***Results:*** The main pre-specified intention-to-treat analysis indicated significant reductions in COVID-19-related worry for the intervention group compared to the waiting list ($\beta = 1.14$, $Z = 9.27$, $p < 0.001$), corresponding to a medium effect size (bootstrapped $d = 0.74$ [95% CI: 0.58–0.90]). Improvements were also seen on all secondary measures, including mood, daily functioning, insomnia, and intolerance of uncertainty. Participant satisfaction was high. No serious adverse events were recorded. ***Conclusions:*** A brief digital and easily scalable self-guided psychological intervention can significantly reduce dysfunctional worry and associated behavioural symptoms related to the COVID-19 pandemic.

Introduction

The COVID-19 outbreak has had a profound impact worldwide since the WHO announced its pandemic status on March 11, 2020. Recent surveys have indicated substantial negative impact of the pandemic on the population's mental health, with increased levels of anxiety, depression, insomnia, irritability, and alcohol consump-

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tion [1–3]. In the current climate of uncertainty, worries about the immediate and long-term consequences of the pandemic for one's health, family, or economy are largely expected and justified. However, pervasive worry that is disproportionate in its intensity or duration, and that significantly interferes with everyday problem-solving or goal-oriented behaviours, is clearly dysfunctional and counterproductive for the individual and society at large. For example, excessive worry about one's health can lead to inappropriate healthcare seeking behaviour that may, in turn, add further pressure to the already burdened healthcare system [4, 5].

One way to improve the psychological health of the population during the current exceptional circumstances could be to provide brief digital, easily scalable, psychological interventions for individuals who worry excessively about COVID-19 and its consequences. Unfortunately, many digital mental health programs and applications are not evaluated before being implemented or procured by public health services. Our research group has previous experience in developing and rigorously evaluating the efficacy and cost-effectiveness of online treatments for excessive worry [6, 7]. In light of the current health emergency, we developed a brief online, self-guided, psychological intervention that specifically targets dysfunctional COVID-19 worry and related behavioural manifestations (e.g., excessive checking of social media for COVID-19 news), and designed a randomised waiting list controlled trial to rapidly evaluate its efficacy.

Materials and Methods

Trial Design

Full details of the trial design, procedures, outcome measures, analysis plans, and Stata code are publicly available at the Open Science Framework (https://osf.io/exh47/). The trial was conducted at a single site (Karolinska Institutet, Stockholm, Sweden) with nationwide inclusion of participants. Participants were randomised to the online intervention or to a waiting list (1:1 ratio). The waiting list controls for the passage of time and spontaneous worry fluctuations, which is crucial given the rapidly changing landscape of COVID-19. The primary endpoint was set to week 3 (post-treatment). Participants randomised to the waiting list were crossed over to the intervention after the controlled study period (week 3). Uncontrolled follow-ups were conducted 1 month post-treatment for the treatment group. The national ethical review board in Sweden approved the study (registration ID: 2020-01719), and the trial was registered on ClinicalTrials.gov on April 10, 2020, before participant enrolment (registration ID: NCT04341922). The study is reported in accordance to the CONSORT statement for nonpharmacological treatment trials.

In order to fast-track implementation of the intervention in the Region Stockholm healthcare services, we conducted a pre-specified interim analysis of the first 300 participants which included a series of a priori stop/go rules to guide decisions regarding implementation and, potentially, termination of the trial. The results from the interim analysis were positive and did not indicate that the trial needed to be terminated prematurely [8].

Participants

The study was open to all adults in Sweden who had daily access to the internet and who self-identified as being excessively worried about the COVID-19 pandemic and its consequences. We operationalised dysfunctional COVID-19 worry as follows:

1 Two mandatory inclusion criteria:
   a. Worry about COVID-19 and its possible consequences (e.g., illness, death, the economy, one's family) every day, often several times a day.
   b. The worry about COVID-19 is perceived as difficult to control.
2 At least one of the following negative consequences of worrying:
   a. Difficulties concentrating on anything else (e.g., work, family, hobbies) because worry about COVID-19 takes so much time and energy.
   b. Trouble sleeping due to worry about COVID-19.
   c. Constantly checking the news and social media to follow developments about COVID-19.
   d. Marked loss of work productivity due to worry about COVID-19.
   e. Difficulties finding joy in everyday situations due to worry about COVID-19.

Exclusion criteria were the following: (a) moderate to severe depression defined as >28 on the Montgomery Åsberg Depression Rating Scale – Self rated (MADRS-S) [9], (b) suicidal risk defined as ≥5 points on item 9 on the MADRS-S, (c) non-Swedish speaking, (d) not resident in Sweden, and (e) having a family member in the same household already included in the study.

Recruitment and Determination of Eligibility

The first participant was included on May 8, 2020, and the full sample was recruited within 39 days. The study was widely advertised on national television, newspapers, and social media. Applicants could self-refer to the trial on the study's secure website (www.coronaoro.se) where they first read information about the study and relevant data protection legislation before consenting to participation using a digital verification app ("BankID"). Contact details to study personnel were provided in case participants had any further questions about the study procedures.

After providing informed consent, participants completed an online screening battery consisting of general sociodemographic questions, a checklist of inclusion and exclusion criteria (described under Participants above), the MADRS-S, and the Coronavirus Health Impact Survey (CRISIS) [10]. The CRISIS assesses the daily impact of the COVID-19 pandemic on mental health and behaviours. Applicants who either did not fulfil all inclusion criteria or fulfilled at least one exclusion criteria, were notified via text message that they could not be included in the study. They also received an encrypted link which they could visit to read more about the reason for exclusion and a phone number to study personnel in case of further questions. Eligible participants received a text message inviting them to continue their study application by log-

ging in to the study website and completing the baseline assessment (including primary and secondary outcome measures, described below). When the baseline assessment was completed, the participant was included in the trial.

Randomisation and Masking

Participants were randomised on a 1:1 ratio to intervention or waiting list without any constraints. A researcher inputted the participant's unique identification code in a password-protected online system (www.randomize.net). Each consecutive participant was subsequently allocated to one of the two groups (intervention or waiting list). The intervention started within 12 h of randomisation. In order to eliminate allocation bias, the randomisation list was created by the independent party Karolinska Trial Alliance (KTA; www.karolinskatrialalliance.se) and randomisation blocks came in different sizes, unknown to the research team. Thus, the researcher had no influence on the group allocation. The research team received a detailed report from KTA each week with the unique identification code, randomisation number, and group allocation of all new participants. This report was crosschecked weekly to ensure that there were no errors in the randomisation procedures.

Outcomes and Assessment Points

The primary outcome was the Generalised Anxiety Disorder 7-items scale (GAD-7) [11] adapted to assess worry related to the COVID-19 pandemic (available at https://osf.io/exh47/). The internal consistency of the modified scale in the current sample was high (Cronbach's alpha = 0.83).

Secondary outcomes were the COVID-19-adapted version of the Work and Social Adjustment Scale (WSAS) [12], a brief measure of functional impairment (available at https://osf.io/exh47/), the MADRS-S, a widely used measure of depressive symptoms [9], the Intolerance of Uncertainty Scale short version (IUS-12), which measures intolerance of uncertainty (a key aspect of worry) [13], and the Insomnia Severity Index (ISI) as a measure of insomnia [14].

Participants filled in the GAD-7 and WSAS at baseline, week 1, week 2, and week 3 (primary endpoint). The other secondary outcomes were administered at baseline and week 3. Adverse events were self-reported at week 3 in both groups. All reported adverse events were assessed by a member of the research team. An adapted version of the Client Satisfaction Questionnaire was administered to the intervention group at week 3 [15]. Follow-up assessments were conducted for the intervention group 1 month after treatment completion.

Intervention

The 3-week intervention is a completely self-guided program, provided via a secure, encrypted study website and organised in five brief modules. The treatment consists of established cognitive behavioural interventions for worry-related problems that have been adapted specifically for dysfunctional COVID-19 worry [16] and additional modules that target related behavioural manifestations of worry. Each module includes a text segment (maximum 8 pages) and one or a few tasks for the participants to practice during at least a couple of days. The participants are encouraged to report on their progress in digital worksheets in the online platform.

The first module covers worry and the evolutionary function of worrisome thoughts (i.e., why worry can be helpful at times, and unhelpful at times). The participant is encouraged to keep a worry diary for a few days and label each worry thought as helpful or unhelpful, using the following instructions: "Does this worry thought help you solve problems or take relevant precautions? If yes, please label it as a helpful worry thought; otherwise, please label it as an unhelpful thought." The aim of the first module is to help the participant become more aware of their worry and be able to discriminate between functional and dysfunctional worries.

The second module focuses on problem solving techniques for solvable problems. Here, the participant is encouraged to identify worry thoughts about solvable problems and work actively to solve them (e.g., "When you get a worrisome thought that is solvable, please schedule a time slot the same or the following day to work on this thought") and to apply simple problem solving techniques (e.g., "Start off by defining the nature of the problem and then come up with as many solutions to the problem as you can think of. Choose a solution that you think is the most reasonable, try it and evaluate if it actually solved the problem. If not, go back to the drawing board and test another solution").

Previous research has indicated that excessive checking is a central mechanism in worry-related problems [17, 18]. Module 3 therefore encourages the participant to first identify and register any unhelpful checking or reassurance-seeking behaviours (e.g., taking one's temperature several times a day without having any symptoms of fever, or repeatedly checking news for COVID-19 death rates). The next step in module 3 is to refrain from unhelpful checking and reassurance-seeking behaviours by either decreasing them (e.g., measuring one's temperature only once or twice per day) or postponing them (e.g., when getting a push notification about COVID-19 on your smartphone, wait at least 60 min and then ask yourself if you really need to read this news). After having tested these techniques for a couple of days, the participant is invited to make an overall assessment of whether decreasing or postponing checking behaviours was helpful in reducing COVID-19 related worry.

Module four contains techniques for detaching oneself from unhelpful worrisome thoughts. More specifically, participants do an exercise called the "flight controller" [19] where they are instructed to first be "on call" for a couple of hours and respond to every worrisome thought that comes to mind. The worrier thereafter explores how it feels to be "off duty," i.e. to not respond to worrisome thoughts but just leave them as "cognitive noise" that does not need any further attention. The data from these two periods are subsequently compared, and the participant is invited to draw conclusions about how these different strategies impacted the level of worry.

The main aim of the fifth and last module is to encourage the participants to engage in competing focus-shifting behaviours, which allow less room for worrying (e.g., cooking, engaging in hobbies, exercising which is compatible with current restrictions, asking for help from others, and helping others). This module also includes a brief summary of the previous modules and relapse prevention strategies.

Control Group

Participants randomised to the waiting list were informed that they would be given access to the intervention after the 3-week waiting period and were provided with a phone number to the study personnel. Control group participants were free to seek other kinds of help for their symptoms if needed (e.g., psychological- or pharmacological treatments). Individuals who experienced significant worsening of symptoms during the waiting period were recommended to contact their regular healthcare providers.

Power Calculation

The study was designed to test the clinical effects of the treatment on self-rated worry and compare the outcomes for the treatment and the waiting list control groups. As it is a novel intervention that is considerably shorter than previous psychological interventions for worry problems [6, 7, 20], and does not involve clinician support, we anticipated a small between-group effect size (Cohen's $d = 0.3$). With 90% power to detect such a difference, using a two-tailed test with an alpha level of 0.05 and allowing for a 30% drop-out rate, we estimated that a sample size of 670 participants would be sufficient to detect a statistically significant difference between the two groups. In order to further increase statistical power through multiple measurement points, the primary outcome measure was also administered weekly during the trial (see statistical analyses below).

Statistical Analyses

Primary analyses were conducted according to the intention-to-treat principle. The efficacy of the intervention was evaluated using linear mixed models with maximum likelihood estimations. The model included fixed effects of group (intervention vs. waiting list), time (baseline, week 1, week 2 and week 3), and group × time interaction as well as random intercepts and slopes. As we did an interim analysis after 300 included participants [8], the statistical significance thresholds were adjusted to $p < 0.0295$ on all outcome measures in order to account for repeated testing in the final analyses, according to Pocock's boundary [21]. Secondary outcomes were analysed identically to the primary outcome with the exception that we did not incorporate random slopes for assessments that were only administered at baseline and post-treatment. The maintenance of the therapeutic gains was evaluated by testing the effect of time from post-treatment to the 1-month follow-up assessment (intervention group only).

The magnitude of the treatment effects was estimated using the m_effectsize command in Stata. This command makes an estimation of the effect sizes by dividing the estimated change score in a mixed effects regression analysis (the estimated group × time interaction based on data from all weekly measures) by the pooled standard deviation at baseline. One advantage of this command is that it uses all available data to estimate the treatment effects instead of completers only and thus provides a more conservative estimate. One thousand bootstrap replications were used in order to construct a 95% confidence interval (CI) around the estimated effect size. The m_effectsize command can be installed in Stata by using the command "net install m_effectsize, from(http://www.imm.ki.se/biostatistics/stata) replace".

Patient and Public Involvement

The project was a close collaboration between the medical university Karolinska Institutet and Region Stockholm public healthcare services. The collaboration aimed to fast-track the development, evaluation, and implementation of the intervention in regular healthcare. As the pre-specified interim analyses were positive [8], Region Stockholm immediately implemented the intervention during the summer of 2020 and made it accessible free of charge to all its citizens via the region's main portal (https://www.1177.se/Stockholm/). Members of the public were not involved in the study design. Five individuals with lived experience of excessive worry reviewed the content of the intervention and provided useful feedback which was incorporated in the treatment before the start of the trial.

Table 1. Sociodemographic and clinical characteristics of the sample ($N = 670$)

Variable		Intervention ($n = 335$)	Waiting list ($n = 335$)
Gender	Women	277 (83%)	270 (77%)
	Men	58 (17%)	65 (19%)
Age	Mean age (SD)	45 (13)	47 (14)
	Min-max	18–81	19–79
Highest education	Primary school	2 (1%)	10 (3%)
	Vocational school	14 (4%)	25 (7%)
	Secondary school	34 (10%)	42 (13%)
	College/university	206 (61%)	199 (59%)
	Other education	68 (20%)	51 (15%)
	Doctorate	11 (3%)	8 (2%)
Occupational status	Working full time	175 (52%)	163 (49%)
	Working part time	75 (22%)	70 (21%)
	Retired	31 (9%)	46 (14%)
	Student	28 (8%)	28 (8%)
	Unemployed	15 (4%)	17 (5 %)
	Sick leave	26 (8%)	30 (9%)
	Disability pension	7 (2%)	8 (2%)
Self-reported psychiatric comorbidity	None	202 (60%)	186 (56%)
	Anxiety disorder	88 (26%)	100 (30%)
	Depressive disorder	54 (16%)	58 (17%)
	Stress-related disorder	22 (7%)	21 (6%)
	Eating disorder	2 (1%)	3 (1%)
	Sleep disorder	21 (6%)	26 (8%)
	Neuropsychiatric disorder	16 (5%)	22 (7%)
	Substance abuse disorder	1 (0%)	2 (1%)
	Other	0 (0%)	4 (1%)
Self-reported somatic disorders	None	212 (63%)	218 (65%)
	Pain disorders	15 (4%)	20 (6%)
	Respiratory disorders	39 (12%)	37 (11%)
	Gastro-intestinal disorders	20 (6%)	33 (10%)
	Rheumatic disorders	6 (2%)	13 (4%)
	Cardiovascular disorders	25 (7%)	28 (8%)
	Endocrine disorders	22 (7%)	21 (6%)
	Cancer	6 (2%)	7 (2%)
	Neurological disorders	15 (4%)	8 (2%)
	Dermatological disorders	9 (3%)	5 (1%)
	Other	21 (6%)	18 (5%)

Results

Table 1 presents baseline characteristics of the 670 included participants. The majority of participants were women in their mid-40s with a college or university degree, and about half of the sample worked full time. Two hundred and eighty-two participants (42%) reported having a previous psychiatric diagnosis, and 240 (36%) reported previous somatic conditions.

Table 2. Endorsement of core and additional inclusion criteria at baseline ($N = 670$)

	Intervention ($n = 335$)	Waiting list ($n = 335$)
Core inclusion criteria (both required for inclusion)		
Daily worry about COVID-19	335 (100%)	335 (100%)
Uncontrollable worry	335 (100%)	335 (100%)
Additional inclusion criteria (at least one required for inclusion)[a]		
Impaired concentration	298 (89%)	289 (86%)
Sleep problems	239 (71%)	229 (68%)
Excessive news and social media usage	234 (70%)	244 (73%)
Impaired work capacity	224 (67%)	224 (67%)
Difficulties enjoying everyday activities	288 (86%)	295 (88%)

[a] Due to an administrative error, one participant who was randomised to the intervention was included in the trial despite not endorsing any of the additional inclusion criteria.

Twenty-seven participants (4%) had a confirmed COVID-19 diagnosis, and another 302 (45%) reported symptoms of the disease without a confirmed diagnosis. About half of the sample ($n = 341$; 51%) reported no symptoms of COVID-19. Seventy-seven participants (11%) had a family member who had been diagnosed with COVID-19 and 10 (1%) had lost a family member due to COVID-19 (online suppl. eTable 1; for all online suppl. material, see www.karger.com/doi/10.1159/000512843).

Table 2 displays the number and proportion of individuals endorsing the mandatory and additional inclusion criteria. To be included in the trial, participants had to report at least one negative consequence of the worrying, and a majority reported experiencing impairment in several domains. Two hundred and six participants (31%) reported all five negative consequences of worrying about the pandemic, 244 (36%) reported four negative consequences, 141 (21%) reported three negative consequences, 57 (9%) reported two negative consequences, and only 21 (3%) reported a single negative consequence.

The main themes and content of the worry thoughts as reported in the CRISIS questionnaire at baseline are summarised in online supplementary eTable 1. Briefly, 495 (74%) participants were very or extremely worried about being infected by COVID-19, and 539 (80%) were also worried about friends or family members being infected. Four hundred and sixty-nine (70%) participants responded they were very or extremely worried about their own mental/emotional health due to COVID-19. Five hundred and sixty-six participants (84%) reported frequently talking or reading about the pandemic. One hundred and seventy-nine (27%) reported at least a moderate financial impact of the pandemic on their or their family members' economy.

Figure 1 displays the participant flow through the study. Data loss at the primary endpoint (week 3) was 11%, which was substantially lower than the worst-case scenario in our power analysis (30%).

The primary intention-to-treat mixed effects regression model showed that both groups improved significantly over time ($\beta = 0.74–1.89$, $Z = 9.36–19.84$, $p < 0.001$) but the intervention group had a larger reduction in COVID-19-related worry than the control group ($\beta = 1.14$, $Z = 9.27$, $p < 0.001$; estimated means and CIs are shown in Fig. 2). The intervention group had on average a 40% reduction in COVID-19-related worry whereas the corresponding reduction of worry in the control group was 17%. The between-group effect size from baseline to post-treatment was in the medium range (bootstrapped $d = 0.74$ [95% CI: 0.58–0.90]). The intervention group had a further reduction on the GAD-7 from post-treatment to the1-month follow-up ($\beta = 1.78$, $Z = 8.06$, $p < 0.001$).

As shown in Table 3, the intervention was associated with significant improvements on all secondary outcome measures, including daily functioning, depressive symptoms, insomnia, and intolerance of uncertainty. There were further improvements on all secondary outcomes from post-treatment to the 1-month follow-up ($\beta = 1.67–0.99$, $Z = 4.76–2.64$, $ps < 0.01$ to <0.001), except for insomnia ($\beta = 0.02$, $Z = 0.08$, $p = 0.94$).

No serious adverse events were reported. There were 35 self-reported adverse events in the intervention group and 7 in the control group (online suppl. eTable 2). These adverse events were mild and expected, i.e. typi-

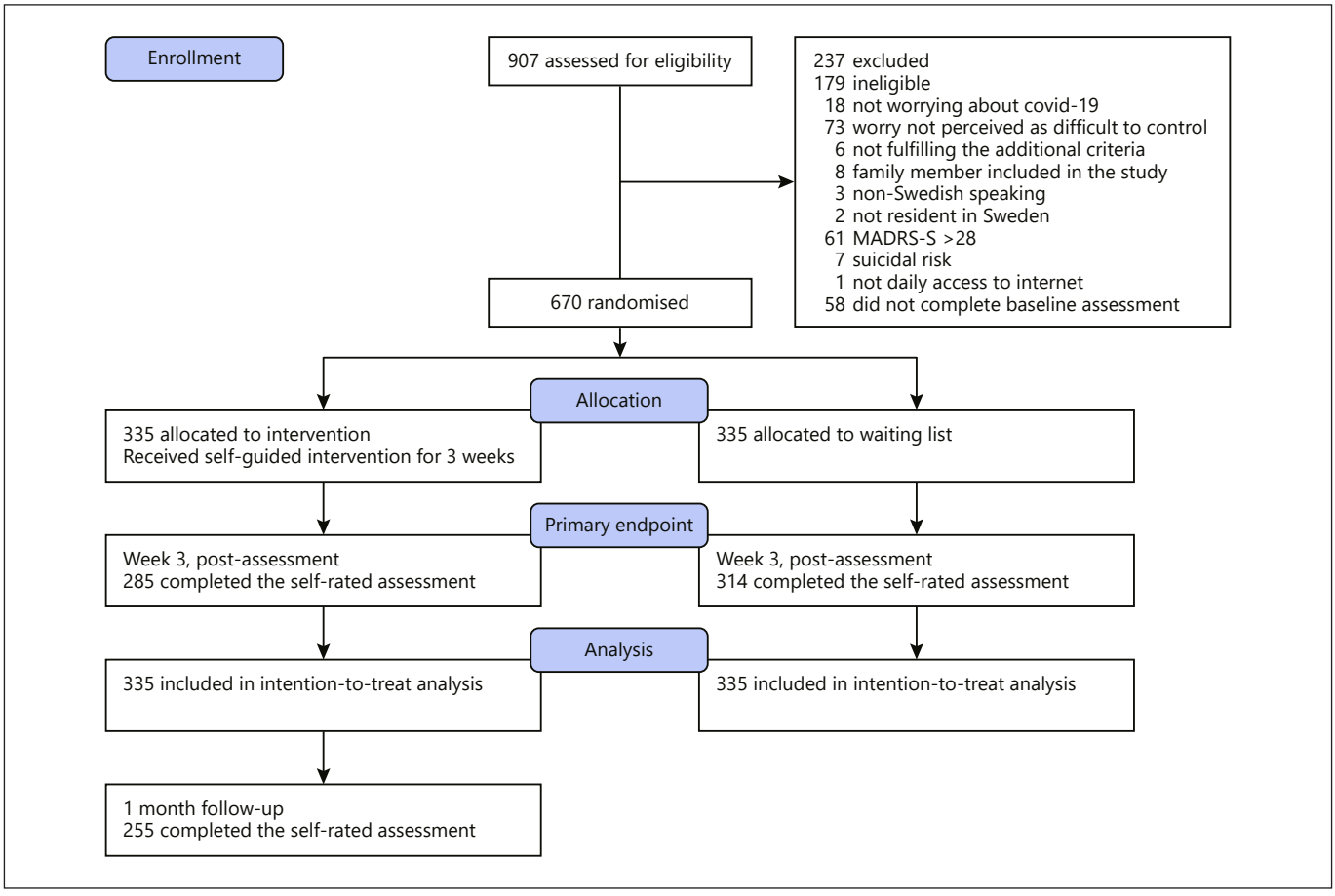

Fig. 1. Participant flow throughout the trial. MADRS-S, Montgomery Åsberg Depression Rating Scale – Self report.

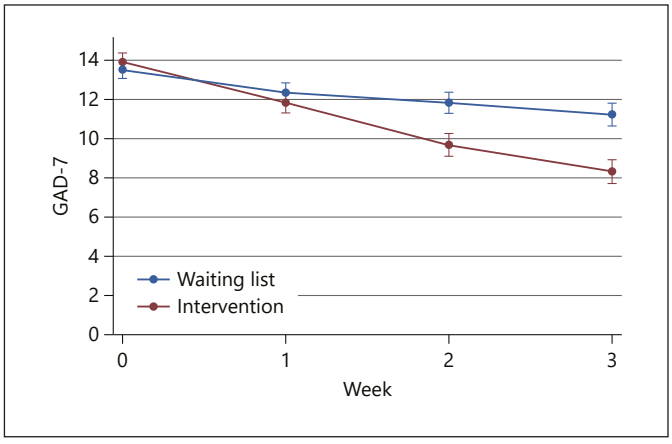

Fig. 2. Estimated means with 95% confidence intervals on the primary outcome measure (intention-to-treat; N = 670). GAD-7, Generalized Anxiety Disorder 7-item scale (scale 0–21).

cally reported in psychological treatment trials (e.g., increased stress and worry when working with the treatment modules).

The number of completed modules and worksheets for participants in the treatment group are shown in online supplementary eTable 4 and eTable 5. Briefly, 201 of 335 (60%) participants completed at least three modules and 123 (37%) completed all five modules. Similarly, 262 of 335 (79%) participants completed at least one worksheet, and 109 (33%) completed at least six worksheets.

Two hundred and nine participants (78%) in the intervention group rated the quality of the intervention as "excellent" or "good," and 197 individuals (74%) thought the intervention had provided them with useful skills to effectively tackle worry thoughts. Two hundred and fourteen participants (80%) said they would recommend the intervention to a friend and/or would come back to the program if needed in the future (online suppl. eTable 3).

Table 3. Impact of the intervention on the primary and secondary outcome measures

Variable	Intervention		Control		Group × time interaction effect		Between group effect size
	mean	SD	mean	SD	*Z* value	*p* value	bootstrapped *d* (95% CI)
GAD-7							
Week 0	13·93	4.10	13.54	4.34			
Week 1	11.84	4.71	12.31	4.74			
Week 2	9.80	4.95	11.83	4.97			
Week 3	8.40	4.95	11.25	5.10	9.27	<0.001	0.74 (0.58–0.90)
1MFUP	6.59	4.83					
WSAS							
Week 0	16.28	7.38	16.21	7.27			
Week 1	14.60	7.87	15.15	7.59			
Week 2	12.89	7.91	15.23	8.47			
Week 3	11.38	8.30	14.78	8.22	6.41	<0.001	0.44 (0.31–0.58)
1MFUP	9.83	8.52					
MADRS-S							
Week 0	19.83	6.20	19.73	6.10			
Week 3	15.44	7.42	18.03	6.98	4.84	<0.001	0.38 (0.22–0.55)
1MFUP	14.09	7.84					
IUS-12							
Week 0	37.07	8.93	35.81	9.40			
Week 3	33.24	9.23	34.58	9.82	4.65	<0.001	0.26 (0.15–0.37)
1MFUP	32.59	9.70					
ISI							
Week 0	11.96	6.18	11.80	5.88			
Week 3	9.56	5.75	10.83	5.95	4.00	<0.001	0.23 (0.11–0.34)
1MFUP	9.65	6.39					

1MFUP, 1-month follow-up; GAD-7, Generalized Anxiety Disorder 7-item scale; ISI, Insomnia Severity Index; IUS-12, Intolerance of Uncertainty 12 items; MADRS-S, Montgomery Åsberg Depression Rating Scale – Self report; WSAS, the Work and Social Adjustment Scale.

Discussion

This trial evaluated if a brief and easily scalable self-administered psychological intervention could significantly reduce dysfunctional COVID-19-related worry and associated symptoms in individuals from the general population. While both the intervention and the waiting list groups improved over time, the intervention group had significantly larger reductions in COVID-19-related worry with a medium between-group effect size at the primary endpoint. The intervention also resulted in significant improvements in secondary outcomes (mood, daily functioning, insomnia, and intolerance of uncertainty) compared to the waiting list. The intervention was highly acceptable, and no serious adverse events were reported. A small number of participants reported mild adverse events that are typical of psychological treatment trials. Results also indicated further symptom reductions during the uncontrolled follow-up (from post-treatment to the 1-month follow-up). Altogether, this brief online, self-guided psychological intervention effectively reduced dysfunctional worry about the COVID-19 pandemic and associated symptoms, and thus has substantial potential to improve public health.

The results were in line with our previous work showing that internet-based interventions can be efficacious for excessive worry about everyday problems [6, 7]. However, the current trial is the first to systematically evaluate a psychological intervention for dysfunctional worry related specifically to the COVID-19 pandemic. Unlike our previous internet-based worry treatments [6, 7], the current intervention was short (3 vs. 10 weeks) and entirely

self-guided. This means that there is no need for a supporting clinician, scheduled appointments, or travel to a clinic, making the intervention highly flexible and potentially very cost-effective. The fixed structure of the online, self-guided format eliminates the risk of therapist drift, and ensures consistent delivery of the treatment content. The intervention is therefore easily scalable and can be made available to the general population via secure digital platforms widely used in most advanced healthcare systems. The intervention is already available free of charge to all citizens in Region Stockholm via the region's secure portal (https://www.1177.se/Stockholm/).

The main strengths of the study were the randomised controlled design, the use of repeated measures, the well-powered sample size and the relatively limited data loss (only 11% of the participants did not provide post-treatment measures, a substantially lower proportion than we expected and that is typically observed in other entirely self-guided psychological interventions) [22–25]. One possible threat to the external validity of the trial was the use of a waiting list control group. Waiting list control groups have been shown to produce higher between-group effect sizes than active controls [26], and future trials should therefore include an active comparator. However, in the rapidly evolving landscape of the COVID-19 pandemic, controlling for the passage of time is particularly important as worry is likely to fluctuate alongside changes in the spread of the virus, societal restrictions, and news coverage of the pandemic. While the majority of participants did not self-report pre-existing psychiatric disorders, many may have met diagnostic criteria for adjustment disorder. However, we developed a public health intervention which was intended to be delivered to individuals from the general population, regardless of their psychiatric status. Another potential limitation of the current study is that self-administered outcome measures of worry symptoms tend to show smaller effects than clinician-rated instruments [20]. It is therefore possible that the between-group effect sizes in this study were in fact underestimated. It is also likely that the primary outcome measure (GAD-7) captures a broader anxious construct than just worry. Finally, the study was conducted in Sweden, a country with high internet access and usage. It will therefore be important to investigate how well this treatment format performs in other contexts and countries.

Despite these limitations, we believe that the current findings are of particular interest for public health. The COVID-19 pandemic seems to be far from over [27] and will likely continue to have a profound impact on the health and economy of citizens around the world. Societies thus need flexible and easily scalable solutions to maintain the psychological health of the population. A myriad of digital tools (e.g., health "apps") have been made available for this purpose. However, these have rarely been rigorously evaluated and often come at high cost for public healthcare providers [28].

We foresee several important research questions for the future. First, are the results from this trial generalisable to other contexts? Our intervention is currently being translated into English and will be made available free of charge to researchers who want to evaluate it in other countries. Second, who benefits the most from the intervention? Analysis of predictor variables could help inform for whom the treatment is most suitable and indicate which aspects of the treatment require further treatment refinement. Third, how will the treatment work in regular public healthcare? This question will be answered during the second half of 2020 as the intervention was recently rolled out in Region Stockholm, and the effect will be evaluated continuously. Finally, can the skills learned during the treatment "psychologically inoculate" individuals and improve psychological resilience in the face of future public health crises, e.g. are individuals who experience significant improvements in tolerance for uncertainty better equipped to tackle future sudden societal changes? The latter question is more difficult to answer but our planned 1-year follow-up analyses will at least shed some light on the long-term maintenance of the therapeutic gains.

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Statement of Ethics

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Conflict of Interest Statement

Dr. Andersson, Dr. Wahlund, Dr. Mataix-Cols, Dr. De Schipper, and Ms Olofsdotter Lauri received financial support from VINNOVA for the submitted work; Dr. Ljótsson reports personal fees from

Pear Therapeutics Inc., outside the submitted work; In addition, Dr. Ljótsson has copyright to an IBS self-help manual with royalties paid from Pear Therapeutics Inc.; Dr. Mataix-Cols reports personal fees from Elsevier and UpToDate Inc., outside the submitted work. The authors have no additional conflicts of interest to declare.

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The funding organisation (VINNOVA) had no role in the conception of the study design, or in the collection, analysis or interpretation of the data, in the writing of the report, or in the decision to submit the paper.

Author Contributions

E.A. was the principal investigator for the trial. T.W., E.A., B.L., and D.M.C. designed the trial. T.W. and E.A. took the main responsibility for drafting the study report. K.A. and E.A. did the analyses of the trial outcome. T.W., E.A., K.O.L., E.D.S., and K.A. collected all trial data. B.L. was responsible for the treatment platform. All authors contributed to, read, and approved the final report. The lead author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data.

References

1 González-Sanguino C, Ausín B, Castellanos MA, Saiz J, López-Gómez A, Ugidos C, et al. Mental health consequences during the initial stage of the 2020 Coronavirus pandemic (COVID-19) in Spain. Brain Behav Immun. 2020 Jul;87:172–6.
2 Voitsidis P, Gliatas I, Bairachtari V, Papadopoulou K, Papageorgiou G, Parlapani E, et al. Insomnia during the COVID-19 pandemic in a Greek population. Psychiatry Res. 2020 Jul; 289:113076.
3 Wang C, Pan R, Wan X, Tan Y, Xu L, Ho CS, et al. Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China. Int J Environ Res Public Health. 2020 Mar;17(5):E1729.
4 Asmundson GJ, Taylor S. Coronaphobia: fear and the 2019-nCoV outbreak. J Anxiety Disord. 2020 Mar;70:102196.
5 Garfin DR, Silver RC, Holman EA. The novel coronavirus (COVID-2019) outbreak: amplification of public health consequences by media exposure. Health Psychol. 2020 May; 39(5):355–7.
6 Andersson E, Hedman E, Wadström O, Boberg J, Andersson EY, Axelsson E, et al. Internet-based extinction therapy for worry: a randomized controlled trial. Behav Ther. 2017 May;48(3):391–402.
7 Andersson E, Ljótsson B, Hedman-Lagerlöf M, Nygren L, Persson M, Rosengren K, et al. Targeting excessive worry with internet-based extinction therapy: a randomised controlled trial with mediation analysis and economical evaluation. Psychol Med. 2020 Apr; 1–11.
8 Wahlund T, Mataix-Col D, Olofsdotter Lauri K, Dias E, Ljótsson B, Aspvall K, et al. Brief online cognitive behavioural intervention for dysfunctionalworry related to the covid-19 pandemic: Pre-specified interim results from a randomised trial. PsyArXiv. 2020.
9 Svanborg P, Åsberg M. A comparison between the Beck Depression Inventory (BDI) and the self-rating version of the Montgomery Asberg Depression Rating Scale (MADRS). J Affect Disord. 2001 May;64(2-3): 203–16.
10 Merikangas KR, Milham M, Stringaris A. The CoRonavIruS Health Impact Survey (CRISIS). 2020.
11 Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006 May;166(10):1092–7.
12 Mundt JC, Marks IM, Shear MK, Greist JH. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. Br J Psychiatry. 2002 May;180(5):461–4.
13 Carleton RN, Norton MA, Asmundson GJ. Fearing the unknown: a short version of the Intolerance of Uncertainty Scale. J Anxiety Disord. 2007;21(1):105–17.
14 Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med. 2001 Jul;2(4):297–307.
15 Larsen DL, Attkisson CC, Hargreaves WA, Nguyen TD. Assessment of client/patient satisfaction: development of a general scale. Eval Program Plann. 1979;2(3):197–207.
16 Behar E, DiMarco ID, Hekler EB, Mohlman J, Staples AM. Current theoretical models of generalized anxiety disorder (GAD): conceptual review and treatment implications. J Anxiety Disord. 2009 Dec;23(8):1011–23.
17 Deacon B, Maack DJ. The effects of safety behaviors on the fear of contamination: An experimental investigation. Behav Res Ther. 2008;46(4):537-47.
18 Olatunji BO, Etzel EN, Tomarken AJ, Ciesielski BG, Deacon B. The effects of safety behaviors on health anxiety: An experimental investigation. Behav Res Ther. 2011;49(11):719-28.
19 Rachman S. The treatment of obsessions. Oxford: Oxford University Press; 2003. https://doi.org/10.1093/med:psych/9780198515371.001.0001.
20 Cuijpers P, Sijbrandij M, Koole S, Huibers M, Berking M, Andersson G. Psychological treatment of generalized anxiety disorder: a meta-analysis. Clin Psychol Rev. 2014 Mar;34(2): 130–40.
21 Pocock SJ. Group sequential methods in the design and analysis of clinical trials. Biometrika. 1977;64(2):191–9.
22 Farvolden P, Denisoff E, Selby P, Bagby RM, Rudy L. Usage and longitudinal effectiveness of a Web-based self-help cognitive behavioral therapy program for panic disorder. J Med Internet Res. 2005 Mar;7(1):e7.
23 Melville KM, Casey LM, Kavanagh DJ. Dropout from Internet-based treatment for psychological disorders. Br J Clin Psychol. 2010 Nov;49(Pt 4):455–71.
24 Twomey C, O'Reilly G, Byrne M, Bury M, White A, Kissane S, et al. A randomized controlled trial of the computerized CBT programme, MoodGYM, for public mental health service users waiting for interventions. Br J Clin Psychol. 2014 Nov;53(4):433–50.
25 Richards D, Richardson T, Timulak L, McElvaney J. The efficacy of internet-delivered treatment for generalized anxiety disorder: A systematic review and meta-analysis. Internet Interv. 2015;2(3):272–82.
26 Gold SM, Enck P, Hasselmann H, Friede T, Hegerl U, Mohr DC, et al. Control conditions for randomised trials of behavioural interventions in psychiatry: a decision framework. Lancet Psychiatry. 2017 Sep;4(9):725–32.
27 Adhanom Ghebreyesus T. WHO Director-General's opening remarks at the media briefing on COVID-19. Geneva. World Health Organization; 2020.
28 Hollis C, Morriss R, Martin J, Amani S, Cotton R, Denis M, et al. Technological innovations in mental healthcare: harnessing the digital revolution. Br J Psychiatry. 2015 Apr; 206(4):263–5.