Effectiveness of an online insomnia program (SHUTi) for prevention of depressive episodes (the GoodNight Study): a randomised controlled trial

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Summary

Background In view of the high co-occurrence of depression and insomnia, a novel way to reduce the risk of escalating depression might be to offer an insomnia intervention. We aimed to assess whether an online self-help insomnia program could reduce depression symptoms.

Methods We did this randomised controlled trial at the Australian National University in Canberra, Australia. Internet users (aged 18–64 years) with insomnia and depression symptoms, but who did not meet criteria for major depressive disorder, were randomly assigned (1:1), via computer-generated randomisation, to receive SHUTi, a 6 week, modular, online insomnia program based on cognitive behavioural therapy for insomnia, or HealthWatch, an interactive, attention-matched, internet-based placebo control program. Randomisation was stratified by age and sex. Telephone-based interviewers, statisticians, and chief investigators were masked to group allocation. The primary outcome was depression symptoms at 6 months, as measured with the Patient Health Questionnaire (PHQ-9). The primary analysis was by intention to treat. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12611000121965.

Findings Between April 30, 2013, and June 9, 2014, we randomly assigned 1149 participants to receive SHUTi (n=574) or HealthWatch (n=575), of whom 581 (51%) participants completed the study program assessments at 6 weeks and 504 (44%) participants completed 6 months' follow-up. SHUTi significantly lowered depression symptoms on the PHQ-9 at 6 weeks and 6 months compared with HealthWatch ($F_{[\text{degrees of freedom } 2,640\cdot1]}=37\cdot2$, $p<0\cdot0001$). Major depressive disorder was diagnosed in 22 (4%) participants at 6 months (n=9 in the SHUTi group and n=13 in the HealthWatch group), with no superior effect of SHUTi versus HealthWatch (Fisher's exact test=0·52; p=0·32). No adverse events were reported.

Interpretation Online cognitive behaviour therapy for insomnia treatment is a practical and effective way to reduce depression symptoms and could be capable of reducing depression at the population level by use of a fully automatised system with the potential for wide dissemination.

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Introduction

Major depressive disorder is preventable in 25% of cases with use of cognitive behaviour therapy (CBT).[1] However, prevention of depression is hugely challenging. Most depression cases have an onset in young people unaware that they are at risk;[2] furthermore, the causal pathways are poorly understood and are not associated with any specific biomedical or psychosocial marker, doctors do not routinely detect depression risk, help seeking is low,[3] and CBT can be difficult to access.

One promising strategy to prevent depression in people at risk might be to target insomnia, in view of the high co-occurrence of the two disorders. Evidence suggests that insomnia is associated with, but distinct from, depression, and is also linked to other psychiatric and behavioural disorders, such as schizophrenia, anxiety, and suicide.[4] Nevertheless, depression is the highest comorbid disorder:[5] 35–47% of people with insomnia have clinically significant depression and 60–84% of people with major depressive disorder have significant insomnia symptoms.[6,7] Insomnia is also a strong risk factor for the development of depression, commonly preceding its development.[8] Insomnia complicates depression treatment,[9] does not necessarily remit when depression improves,[8] and increases risk of depression relapse,[10] suggesting that it is an independent problem. Insomnia treatments for people with insomnia can be effective in reducing depressive symptoms independently of their direct effects on sleep symptoms, although the evidence is not conclusive.

To date, there have been four trials[11–14] of CBT for insomnia (CBT-I) interventions targeting insomnia in patients with residual or concurrent depression. The main aim of these trials was to establish whether residual insomnia symptoms could be relieved in individuals with diagnosed depression. Two trials[11,12] reported statistically significant reductions in both insomnia and depression. The other two trials[13,14] had no significant findings, but showed effects in the predicted direction. In a trial[15] of 43 adults that examined the effectiveness of CBT-I versus depression CBT, both delivered via the internet, in patients with a dual diagnosis of major depressive disorder and insomnia, CBT-I was as effective as depression CBT in

Research in context

Evidence before this study

We searched PubMed between Jan 1, 2012, and Aug 12, 2015, for new randomised controlled trials of depression prevention in adults published after Van Zoonen and colleagues' systematic review in 2012. Our search terms were ((((((((((((((depressive disorder[Title]) OR depressive[Title]) AND disorder[Title]) OR depression[Title]) OR depressive)[Title]) AND (prevention[Title]) AND control)[Title]) OR preventive[Title]) OR prevention[Title]) AND randomized controlled trial[Publication Type]) AND clinical trial[Publication Type]) AND ("2012/03/01"[Date - Publication] : "2015/08/12"[Date - Publication])) AND English[Language])) AND depress*[Title]. We also searched for randomised controlled trials in which an insomnia treatment was given to individuals diagnosed with depression from 2012 onwards, to ascertain whether any trials were missed in our original search. Search terms for this additional search were (((((((insomnia[Title]) OR sleep*[Title]) AND depress*[Title]) AND randomized controlled trial[Publication Type]) OR clinical trial[Publication Type]) AND English[Language]) AND depress*[Title]) AND sleep*[Title]) AND ("2012/01/01"[Date - Publication] : "2015/08/12"[Date - Publication]). We identified no trials that focused on an insomnia intervention to prevent depression.

Added value of this study

We have shown for the first time that depression, suicidal ideation, and anxiety symptoms can be reduced in individuals at risk for depression by use of a behavioural online sleep program.

Implications of all the available evidence

An insomnia intervention could be the preferred method to prevent depression in individuals with insomnia because it is effective, has low stigma, and can be disseminated through the internet to the appropriate population. Long-term follow-up results will provide more evidence for any continuation of the preventive effect. Larger trials are needed to establish effects on the incidence of major depressive disorder.

reducing depression symptoms. Despite these findings, the mechanisms by which insomnia treatment might affect depression are unclear. The treatment might act artifactually by simply reducing insomnia symptoms that contribute to measured depression scores, or it might reverse prolonged disruption of 24 h sleep–wake, activity, and neurohormonal and metabolic cycles.

No trial has yet assessed whether depression can be prevented in people with both subclinical depression symptoms and insomnia. Thus, we did the GoodNight Study to establish whether insomnia could be a primary preventive target for individuals with high depression symptomatology, but not meeting criteria for a diagnosis of major depressive disorder. To maximise access and the potential for dissemination, we used an internet-based automated intervention, SHUTi, which focuses on sleep restriction and consolidation, rather than the direct modification of depression, anxiety, or rumination.[16] We speculated that an insomnia intervention would be more acceptable to the public, on the basis of evidence that people frequently seek help from family doctors for insomnia.[17] Although several reasons exist as to why people with insomnia might not seek help, stigma is reported to be the reason in only 17% of cases.[18] By contrast, stigma is the most frequently cited reason for not seeking help for depression.[3]

We recruited adults with depression symptom levels that were elevated but subclinical (indicated sample), who concurrently had insomnia (selective sample). We predicted that people given the SHUTi intervention would have fewer depression symptoms at the end than at the beginning of the intervention, and at 6 weeks and 6 months, and that the intervention would reduce major depressive disorder, suicide risk, and anxiety, and improve disability at these timepoints.

Methods

Study design and participants

We did this randomised controlled trial at the Australian National University in Canberra, Australia. Community-dwelling adults aged 18–64 years were recruited through the internet by use of advertisements on a social networking site (Facebook), websites of sleep or mental health associations, and media releases. Initial inclusion criteria, via online screening, were the presence of subclinical depression, as measured by a score of between 4 and 20 on the Patient Health Questionnaire-9 (PHQ-9),[19] and the presence of insomnia, as measured by a score of 3 or more on at least one of the first four items of the Bergen Insomnia Scale and a score of 3 or more on at least one of the last two items.[20] Absence of a 2 week diagnosis of major depressive disorder or lifetime bipolar disorder, and diagnostic confirmation of insomnia, were established via the telephone-administered Mini International Neuropsychiatric Interview (MINI).[21] In the diagnostic telephone interview, participants had to meet criteria for insomnia on Morin's modified diagnostic insomnia interview.[22]

Exclusion criteria included shift work, pregnancy, or work, family, or other commitments that interfered with regular night-time sleep patterns, and if time of awakening was outside the hours of 0400 h and 1000 h, or bedtime was outside the hours of 2000 h and 0200 h, more than twice a week. Other exclusion criteria were absence of reliable internet access; difficulty reading English; a reported diagnosis of psychosis, schizophrenia, or bipolar disorder by a psychiatrist; or current involvement in a non-medication treatment programme for insomnia with a health professional. We also excluded individuals with an untreated sleep disorder other than

insomnia, medication changes in the past 3 months, a medical disorder accounting for their insomnia, or reported suicidal plans or attempts in the previous 2 weeks identified by the MINI interview. Participants who did not complete ten online sleep diaries within a 14 day period, within 21 days of sleep-diary commencement, could not proceed to randomisation. The study was approved by the Australian National University Human Ethics Committee (protocol number 2011/041). The study protocol has been published elsewhere.[23] All participants provided informed consent.

Randomisation and masking

Immediately after completion of the pre-assessment sleep-diary phase, participants were randomly assigned (1:1), via computer-generated randomisation integrated into the trial management software, to receive either SHUTi, a 6 week, modular, online insomnia program based on CBT-I, or HealthWatch, an interactive, attention-matched, internet-based placebo control program. Randomisation was stratified by age and sex. Telephone-based interviewers, statisticians, and chief investigators were masked to group allocation.

Procedures

Participants visited a web portal that managed screening, consent, randomisation, delivery of the assessment sleep diaries, baseline and endpoint surveys, and delivery of HealthWatch and link to SHUTi. Participants submitted sleep diaries for a period of 2 weeks before randomisation and start of the study program. All assessment surveys were completed online, except for the diagnostic interviews, which were administered via telephone.

SHUTi provides six sequential modules consisting of an overview of insomnia, and two behavioural modules focusing on sleep restriction and stimulus control, cognitive restructuring, sleep hygiene, and relapse prevention. An 11 item daily sleep diary is required to advance from the first to the second module so the system can establish an algorithmically defined sleep window. The HealthWatch program has no specific mental health or sleep-related content and is not associated with therapeutic reductions in depression, and can therefore be regarded as an excellent control condition.[24] Modules contained information about environmental health, nutrition, heart health, activity, medication, oral health, blood pressure and cholesterol, calcium, and back pain, in addition to weekly surveys of these topics. Once a participant was randomly assigned, an email contact regimen was implemented to remind participants about completion of sleep diaries, and availability of program modules and assessments. Manual email reminders were sent to participants who did not complete 6 month follow-up assessments, and a telephone call was made to non-responders at the time of the 6 month follow-up MINI assessment.

Outcomes

The prespecified primary outcome was depression symptoms at 6 months, as measured with the PHQ-9. We tested the effects of the insomnia intervention with inclusion and exclusion of sleep items in the PHQ-9. Secondary outcomes were current major depressive disorder and suicidal ideation at 6 months, as measured with the Psychiatric Symptom Frequency scale (PSF).[25] Additionally, at baseline and 6 month follow-up, we measured the proportion of participants in each group according to PHQ depression category (mild, moderate, moderate to severe, or severe). Other secondary outcomes included insomnia symptoms, generalised anxiety symptoms, disability, cognitive functioning, and help seeking. We assessed insomnia symptoms with the Insomnia Severity Index,[26] a seven item scale with scores ranging from 0 to 28; scores of 15 or more are indicative of clinical insomnia. We measured symptoms of generalised anxiety disorder with the Generalized Anxiety Disorder 7-item scale (GAD-7),[27] with scores ranging from 0 to 21. We measured sleep-related and depression-related disability with the 12 item WHO Disability Assessment Schedule.[28]

Because poor concentration is a key complaint of people with depression and insomnia, we measured cognitive functioning with the Brief Test of Adult Cognition by Telephone,[29] assessed at baseline and 6 months only by trained clinical interviewers. We measured intended and actual help seeking to establish whether participants sought additional professional help for, separately, emotional problems or insomnia. Specifically, intentions to seek professional help were measured with the General Help-Seeking Questionnaire,[30] with scores ranging from 0 to 12 based on intentions to seek help from a family doctor or mental health professional (higher scores indicating greater intentions) for either sleep problems or emotional problems. We assessed help-seeking behaviours with the Actual Help-Seeking Questionnaire,[31] scored as a count of sources reported for help with either sleep problems or emotional problems. Participant preference for the allocated treatment program was also recorded. Participants were asked which of the two conditions they preferred: "Monitoring your sleep activity and then doing online training so that you can change your sleep routine" or "Monitoring your sleep activity, being provided with health information, and being asked your views about the possible causes of your sleep problems", or could choose "No preference". Medication use was based on the Client Service Receipt Inventory.[32]

Statistical analysis

Although our primary outcome variable was depression symptoms assessed with the PHQ-9, we calculated that with 80% power and a 40% reduction in risk in a sample with a baseline incidence of 15%, a total sample size of 972 participants was needed to detect our secondary outcome of major depressive disorder. We reasoned that our technology would allow us to recruit

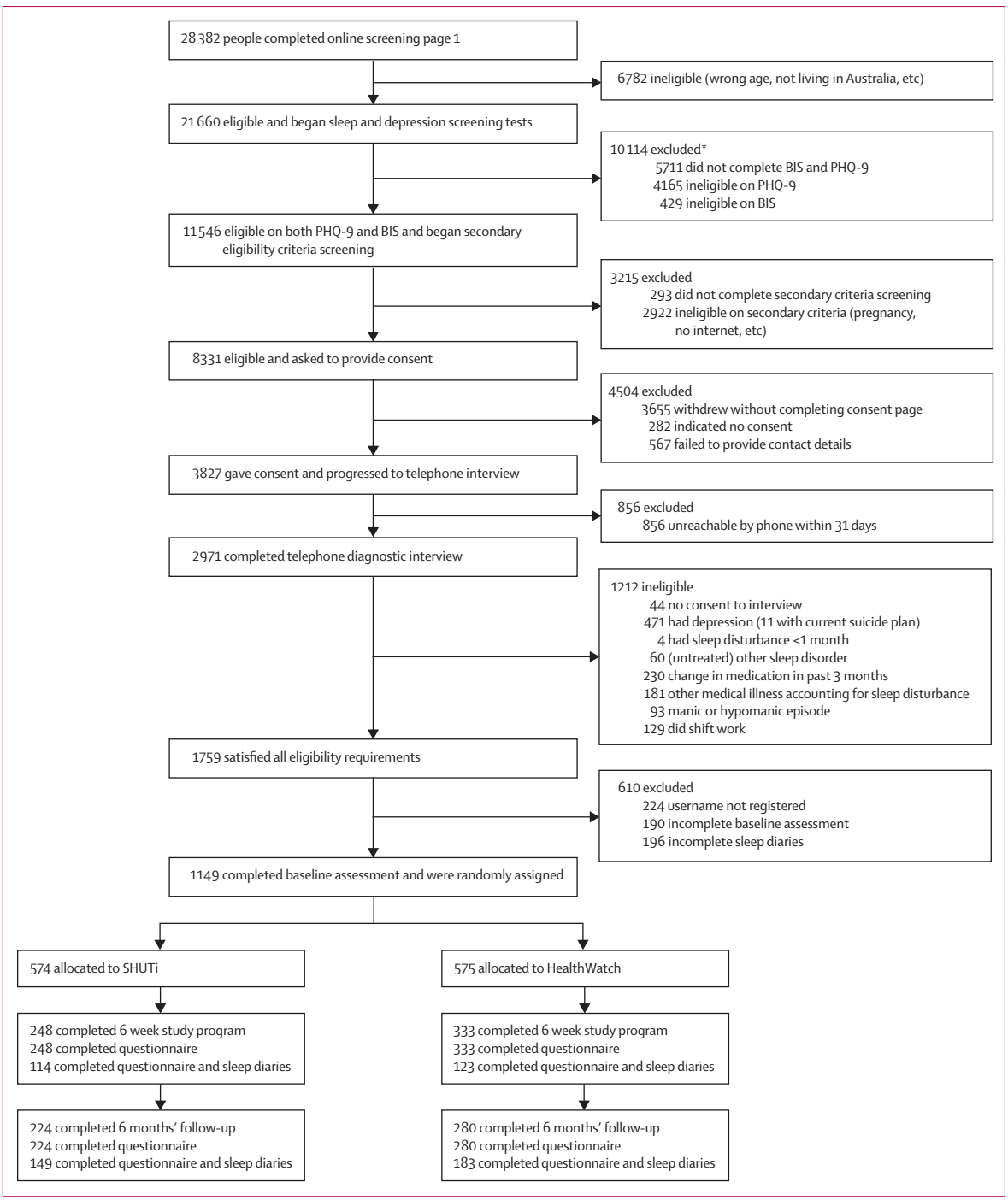

Figure 1: **Trial profile**
PHQ=Patient Health Questionnaire. BIS=Bergen Insomnia Scale. *Overlap of 191 people who were ineligible on both scales.

up to 1600 in the allocated trial delivery window. However, recruitment was restricted by the planned release of new technological developments within our research platform, and the necessity to complete the 18 month follow-up by 2016, when these changes would come into place.

We used mixed model repeated measures ANOVA[33] to account for missing data and to include all available data for participants analysed in the trial. This approach yields unbiased estimates of intervention effects in the assumption that data were missing at random. We used an unstructured matrix, and estimated degrees of freedom

(df) with Satterthwaite's correction. We present df alongside *F*-test statistics and *t* statistics. We did sensitivity analyses with removal of the sleep item from the PHQ-9 to control for reduction of depression symptoms scores arising solely from improved sleep. Additionally, we categorised individuals on the basis of four categories of depression, based on PHQ-9 cutoffs at baseline, 6 weeks, and 6 month follow-up, and examined shifts in categories as a function of severity. The primary analysis was by intention to treat. We did analyses with SPSS (version 20), and used Stata IC (version 10) for categorical analysis. Ordinal mixed models for depression category and suicidal ideation were based on the gllamm procedure in Stata. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12611000121965.

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Figure 1 shows the trial profile. Between April 30, 2013, and June 9, 2014, we randomly assigned 1149 participants to receive SHUTi (n=574) or HealthWatch (n=575), of whom 581 (51%) participants completed the study program assessments at 6 weeks and 504 (44%) participants completed 6 months' follow-up (figure 1). At baseline, levels of employment, education, depression severity, anxiety, or sleep disturbance were similar between groups (table 1). Only six participants reported taking medication related to moods and emotions (depression or anxiety): three (1%) from the SHUTi group and three (1%) from the HealthWatch group. The preferred program was SHUTi (table 1). Mean PHQ-9 scores were in the mild range (table 1), a level of symptoms that is consistent with a clinical approach of watchful waiting. On average, 3·5 (58%) of the six SHUTi modules (SD 2·5) and 4·7 (52%) of the nine HealthWatch modules (3·5) were completed. Attrition from assessment was significantly greater in the SHUTi group at 6 weeks (Fisher's exact test p<0·0001) and 6 months (Fisher's exact test p=0·0015).

Depression symptoms were significantly reduced from baseline in patients in the SHUTi group compared with those in the HealthWatch group (table 2, figure 2), and at both 6 weeks ($t_{[724·5]}$=–8·2; p<0·0001) and 6 months ($t_{[665·6]}$=–10·1; p<0·0001). At 6 weeks and 6 month follow-up, the mean PHQ-9 score for patients receiving the SHUTi intervention was no longer in the depressed range, whereas the score for patients in the HealthWatch group registered in the lower range of mild depression (table 2). Between-group effect sizes (Cohen's d) were 0·69 at 6 weeks and 0·48 at 6 months. Within-group effect sizes for the change from baseline to 6 weeks were 1·34 for SHUTi and 0·41 for HealthWatch, and for the change to 6 months were 1·17 and 0·59, respectively. The depression effects were consistent for participants with few and elevated depression symptoms (PHQ-9 score <10 at baseline: $F_{[2,453·7]}$=25·5, p<0·0001; PHQ-9 ≥10 at baseline: $F_{[2,166·5]}$=15·4, p<0·0001) The effects did not change after omission of item three from the PHQ score: "How much have you been bothered in the last two weeks by trouble falling or staying asleep, or sleeping too much" ($F_{[2,644·71]}$=28·1; p<0·0001). When age and sex

	HealthWatch group (n=575)	SHUTi group (n=574)
Age (years)	42·51 (12·24)	42·95 (12·17)
Sex		
Female	423 (74%)	422 (74%)
Male	152 (26%)	152 (26%)
Relationship status		
Married	260 (45%)	263 (46%)
De facto*	107 (19%)	86 (15%)
Separated	26 (5%)	26 (5%)
Divorced	44 (8%)	52 (9%)
Widowed	6 (1%)	9 (2%)
Never married	131 (23%)	135 (24%)
Educational attainment		
Less than high school	26 (5%)	35 (6%)
Completed high school	40 (7%)	35 (6%)
Certificate, diploma, or trade	215 (37%)	191 (33%)
Bachelor's degree	191 (33%)	177 (31%)
Higher degree	103 (18%)	135 (24%)
Employment status		
Full-time	287 (50%)	306 (53%)
Part-time, seeking full-time	24 (4%)	12 (2%)
Part-time	133 (23%)	134 (23%)
Unemployed (looking for work)	28 (5%)	35 (6%)
Not in the labour force	102 (18%)	82 (14%)
Location		
Rural	119 (21%)	111 (19%)
Urban	456 (79%)	463 (81%)
Preference for condition		
Matched condition	74 (13%)	285 (50%)
Did not match or no preference	501 (87%)	289 (50%)
Suicide ideation in the past 6 months	57 (10%)	46 (8%)
Suicide attempt in the past 6 months	34 (6%)	36 (6%)
PHQ-9 score (depression)	7·84 (3·96)	8·03 (4·20)
GAD-7 score (generalised anxiety)	5·77 (4·33)	5·83 (4·36)
PSF score (suicidality)	0·78 (1·69)	0·74 (1·71)
ISI score (insomnia)	16·23 (4·32)	15·92 (4·18)

Data are mean (SD) or n (%). PHQ=Patient Health Questionnaire. GAD=Generalised Anxiety Disorder. PSF=Psychiatric Symptom Frequency scale. ISI=Insomnia Severity Index. *De facto spouses were partnered but not married.

Table 1: **Baseline characteristics**

	SHUTi group			HealthWatch group			Time × condition interaction		
	Baseline (n=574)	6 weeks (n=248)	6 months (n=224)	Baseline (n=575)	6 weeks (n=333)	6 months (n=280)	*F*	Degrees of freedom	p value
PHQ-9	8·0 (0·2)	3·8 (0·2)	3·8 (0·2)	7·8 (0·2)	6·2 (0·2)	5·5 (0·2)	37·2	2640·1	<0·0001
PHQ-8*	5·8 (0·2)	2·8 (0·2)	2·8 (0·2)	5·6 (0·2)	4·6 (0·2)	3·9 (0·2)	28·1	2644·7	<0·0001
PSF suicidality	0·7 (0·1)	0·5 (0·1)	0·6 (0·1)	0·8 (0·1)	0·8 (0·1)	0·7 (0·1)	3·4	2642·0	0·0356
GAD-7	5·8 (0·2)	3·2 (0·2)	3·1 (0·2)	5·8 (0·2)	5·0 (0·2)	4·2 (0·2)	23·0	2624·5	<0·0001
ISI	15·9 (0·2)	7·3 (0·3)	7·7 (0·3)	16·2 (0·2)	13·2 (0·3)	12·1 (0·3)	111·3	2595·0	<0·0001
WHODAS-12	18·9 (0·3)	16·3 (0·3)	16·1 (0·3)	18·9 (0·3)	18·1 (0·3)	17·2 (0·3)	10·6	2668·3	<0·0001
BTACT†	44·3 (0·5)	..	49·0 (0·8)	43·8 (0·5)	..	48·8 (0·8)	0·1	1854·1	0·7823
GHSQ-sleep	5·5 (0·1)	5·5 (0·1)	5·2 (0·1)	5·3 (0·1)	5·6 (0·1)	5·4 (0·1)	3·4	2627·4	0·0340
GHSQ-emotional	5·6 (0·1)	6·0 (0·1)	5·8 (0·1)	5·3 (0·1)	5·6 (0·1)	5·5 (0·1)	0·3	2638·0	0·7530
AHSQ-sleep	4·2 (0·2)	2·0 (0·1)	1·2 (0·1)	4·1 (0·2)	2·7 (0·1)	1·8 (0·1)	7·6	21147·0	0·0005
AHSQ-emotional	2·8 (0·2)	1·1 (0·1)	0·9 (0·1)	2·4 (0·2)	1·6 (0·1)	1·2 (0·1)	7·7	21147·0	0·0005

Data are mean (SE), unless otherwise specified. PHQ=Patient Health Questionnaire. PSF=Psychiatric Symptom Frequency scale. GAD=Generalised Anxiety Disorder. ISI=Insomnia Severity Index. WHODAS=WHO Disability Assessment Scale. BTACT=Brief Test of Adult Cognition by Telephone. GHSQ=General Help Seeking Questionnaire. AHSQ=Actual Help Seeking Questionnaire. *Excluding sleep item. †Assessed at baseline and 6 months only.

Table 2: **Estimated marginal means and *F* tests of time × condition interactions**

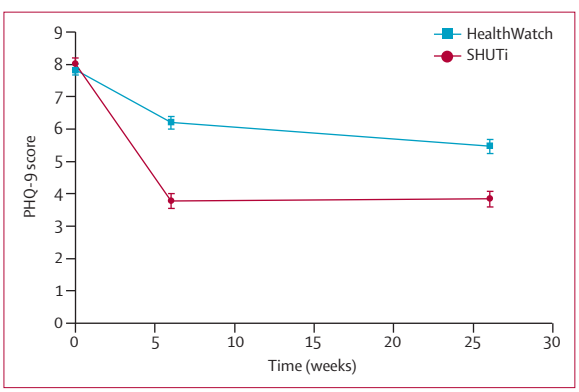

Figure 2: **Comparison of PHQ-9 depression estimated marginal mean scores at baseline, 6 weeks, and 6 months**
Error bars show SEs. PHQ=Patient Health Questionnaire.

were included in the model, the depression effect remained consistent ($F_{[2,641·8]}$=36·2, p<0·0001; at 6 weeks $t_{[745·5]}$=–8·5, p<0·0001; at 6 months $t_{[671·5]}$=–5·1, p<0·0001).

Table 3 describes the severity of depression symptoms as a function of PHQ-9 categories. The overall χ^2 comparing none or mild with moderate to severe was 26·4 (df=2; p<0·0001). In an ordinal mixed model of depression category (none, mild, moderate, moderately severe) with random participant intercept, significant effects were shown in favour of the insomnia intervention on depression category at 6 weeks (*Z*=–7·77; p<0·0001) and 6 months (–4·85; p<0·0001).

Not receiving the preferred condition did not affect outcomes. Among participants who completed four or more cores (modules) of SHUTi (n=310), we recorded a significant effect relative to the complete HealthWatch group (n=575; $F_{[2,594·9]}$=32·6; p<0·0001), reflected in significant differences at 6 weeks ($t_{[685·0]}$=–8·05; p<0·0001) and at 6 months ($t_{[612·4]}$=–4·98; p<0·0001). However, among participants who completed fewer than four modules (n=264), SHUTi had no overall significant effect compared with HealthWatch ($F_{[2,625·4]}$=2·8; p=0·060), but had a significant effect at 6 weeks ($t_{[429·2]}$=–2·33; p=0·020) albeit not at 6 months ($t_{[368·8]}$=–0·8; p=0·411).

On the basis of the MINI assessment at 6 month follow-up, we identified 22 cases of depression: nine (2%) in the SHUTi group and 13 (2%) in the HealthWatch group. SHUTi had no superior effect on diagnosis of major depressive disorder (Fisher's exact test 0·52; p=0·32). Suicidal ideation was reduced at 6 weeks ($t_{[69·3]}$=–2·5, Cohen's d=0·14; p=0·012), but not at 6 months (Cohen's d=0·08; p=0·390; figure 3). Because the PSF was skewed, we also examined outcomes with an ordinal mixed model. The effect of the SHUTi intervention on PSF score remained significant at 6 weeks (Z=–3·11; p=0·002), but not 6 months (–1·45; p=0·148).

We recorded significant effects of the SHUTi intervention on all other secondary outcomes, except for help-seeking intentions for emotional problems. Specifically, generalised anxiety disorder and insomnia symptoms were reduced at 6 weeks (Cohen's d=0·50 and 1·10, respectively; p<0·0001 for both) and 6 months (0·36 and 0·83, respectively; p<0·0001 for both), and disability was reduced at 6 weeks (Cohen's d=0·33; p<0·0001) and 6 months (0·23; p=0·0071) with SHUTi versus HealthWatch. SHUTi had no significant effect on cognition (table 2). Intentions to seek professional help for insomnia decreased more in the SHUTi group than in the HealthWatch group at 6 months (Cohen's d=0·10; p=0·013), but not at 6 weeks (p=0·064), whereas intentions to seek professional help for emotional problems did not differ significantly. The number of sources of help used also decreased more in the SHUTi group than in the HealthWatch group, both for sleep problems (Cohen's d=0·24, p=0·0002 at 6 weeks; 0·23,

	No depression (score 0–4)		Mild (score 5–9)		Moderate (10–14)		Moderately severe (≥15)	
	SHUTi group	HealthWatch group	SHUTi group	HealthWatch group	SHUTi group	HealthWatch group	SHUTi group	HealthWatch group
Baseline	128/574 (22%)	124/575 (22%)	257/574 (45%)	273/575 (47%)	141/574 (25%)	143/575 (25%)	48/574 (8%)	35/575 (6%)
6 weeks	183/256 (71%)	150/358 (42%)	57/256 (22%)	132/358 (37%)	12/256 (5%)	61/358 (17%)	4/256 (2%)	15/358 (4%)
6 months	169/231 (73%)	151/290 (52%)	47/231 (20%)	98/290 (34%)	8/231 (3%)	29/290 (10%)	7/231 (3%)	12/290 (4%)

Data are n/N (%).

Table 3: **Proportion of participants in each Patient Health Questionnaire category at baseline, 6 weeks, and 6 months**

p=0·0015 at 6 months) and emotional problems (0·26, p=0·0001 at 6 weeks; 0·20, p=0·0113 at 6 months).

In dropout analysis, participants who completed the 6 month assessment were significantly more likely to be married (χ^2=16·6, df=5; p=0·0052), and were older ($F_{[1,1147]}$=29·5; p<0·0001), less depressed ($F_{[1,1147]}$=9·7; p=0·0019), less anxious ($F_{[1147]}$=14·0; p=0·0004), and had less severe insomnia ($F_{[1147]}$=10·0; p=0·0016) than did those who remained in the study. Participants in the SHUTi group were significantly less likely to complete the 6 month assessment than were those in the HealthWatch group (χ^2=10·1, df=1; p=0·001). However, completers of the 6 month assessment did not differ significantly from non-completers on the basis of sex, education, employment status, location (rural *vs* urban), suicidal ideation, suicidal behaviours, or condition preference. The effects on PHQ-9 (and PHQ-8 and all other significant outcomes) remained after adjustment for characteristics that were differentially associated with dropout. That is, after adjustment for relationship status, age, anxiety symptoms, and insomnia symptoms at baseline, the effect of SHUTi on reducing depression symptoms remained significant ($F_{[2,635·7]}$=34·5; p<0·0001), with significant differences at 6 weeks ($t_{[741·4]}$=–8·29; p<0·0001) and 6 months ($t_{[655·9]}$=–4·86; p<0·0001). No adverse events were reported in either study group.

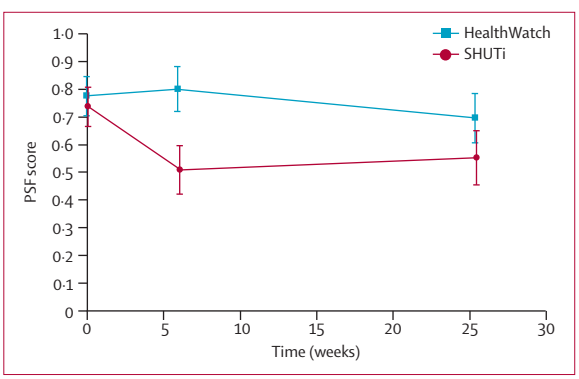

Figure 3: **Comparison of PSF estimated marginal mean scores at baseline, 6 weeks, and 6 months**

Error bars show SEs. PSF=Psychiatric Symptom Frequency scale.

Discussion

Our findings show that an internet-based intervention for insomnia effectively reduced symptoms of depression in people with insomnia and subclinical depression at the end of the intervention and at 6 months' follow-up, taking participants in the SHUTi group from a status of mild depression to one of no depression, according to PHQ-9 categories. This effect persisted even after elimination of the insomnia item on the PHQ-9, taking account of differential dropout and participant preference. The effect was present in participants with both higher and lower depression symptoms at baseline, in line with findings reported by Bower and colleagues,[34] who recorded effects at all levels of depression in an analysis of 16 datasets of low intensity interventions. The SHUTi intervention was delivered by an automated platform, with human contact occurring only during assessment to obtain telephone-based diagnoses and cognitive functioning at baseline and 6 month follow-up. Anxiety, insomnia, and disability all improved in participants in the SHUTi group, and participants were significantly less likely to intend to seek help (for insomnia) than were those in the HealthWatch group, and reported fewer contacts with professionals for emotional or sleep problems. The lower level of contact with professionals in the SHUTi group might be due to the actual benefit they gained from the intervention.

The size of the effect on depression symptoms was similar in magnitude to internet-based psychological interventions designed specifically to lower depression symptoms or major depressive disorder. For example, electronic health interventions of all types have been found to achieve an average endpoint effect of 0·72 (95% CI 0·55–0·90)[35] in children and young people up to the age of 25 years, similar to our reported level of 0·69. In adults, automated or unsupported depression interventions, such as ours, normally report effect sizes of about 0·25. The effect size of 0·69 approaches the size of that reported for face-to-face transdiagnostic interventions in adults with depression (0·80).[36] It is difficult to interpret the relative magnitude of these effect sizes because the samples are likely to be very different and the purposes of the studies differ. Nevertheless, the effect sizes achieved are substantial and clinically meaningful. Indeed, the effect of SHUTi on depression seems to be stronger than that of non-supported internet-based CBT program for depression in adolescents and adults.

A clear secondary goal was to establish whether cases of major depressive disorder would be fewer in participants in the SHUTi group than in those in the HealthWatch group. We did not record a significant effect; however, few cases of major depressive disorder developed over the 6 month period, nine (2%) in the SHUTi group and 13 (2%) in the HealthWatch group. This result was despite our prediction of at least 86 (15%) cases in the HealthWatch group, an estimate based on data from a subsample of participants in the PATH Through Life study,[23] with similar initial depression scores, adjusting for the length of observation (6 months for the present study *vs* 4 years for PATH). However, if a less robust assessment of major depressive disorder is used, the PHQ cutoffs suggest that cases of depression were fewer in the SHUTi group, with fewer SHUTi participants experiencing less moderate, or moderate to severe, depression at 6 weeks and 6 months compared with HealthWatch participants. The incidence of depression was 13·5% lower with SHUTi than with HealthWatch at 6 months (4·6% *vs* 4·0%). These figures were similar to, albeit lower than, the overall percentage reduction of 21% in a meta-analysis of 32 depression prevention trials of psychological interventions.[1] Long-term follow-up results at 12 months and 18 months will provide more evidence for any continuation of the preventive effect.

Suicidal ideation at 6 weeks was reduced in the SHUTi group. This is a notable finding, particularly because participants had relatively low levels of suicidal ideation because individuals were excluded from the trial if they reported any suicide plans or attempts in the previous 2 weeks or met criteria for major depressive disorder. We did not identify any prevention studies that used an insomnia treatment alone to address suicidal ideation, although studies have reported a link between suicidal ideation and insomnia.[37] Our finding of reduced effects on suicide at 6 weeks but not 6 months is unclear, but the effects were in the same direction, suggesting that the effect dissipated rather than ceased. The findings reinforce observations that, although suicidal ideation and depression can both respond to an intervention, they represent different conditions with different trajectories. Suicidal ideation is clearly also linked to insomnia and, if not mediated directly by depression, might be mediated by stress, hyperarousal, or broader circadian disruptions.

We recorded an increase of less than 2% in development of major depressive disorder overall, but were expecting a conversion rate of about 15% on the basis of our epidemiological data. We did not recruit 1600 participants as per the protocol, reducing power to detect new cases of major depressive disorder. Nevertheless, our trial size of 1149 represents the largest randomised controlled trial of an internet-based insomnia program to date. The lower than expected rate of major depressive disorder diagnosis might indicate a difference in sample characteristics between study participants, unmeasured factors associated with good prognosis, dropout, or that our participants had a lower severity of symptoms than those in other studies and might have had some remission from symptoms before randomisation.

Although we had current diagnostic data, we did not have data for previous depression diagnosis. Consequently, participants might have included a mix of those experiencing depression for the first time, those seeking help for persistent subclinical symptoms, and those in remission. Very few participants reported taking medication for moods or emotions before recruitment, suggesting that our sample was relatively naive to medication and, perhaps, largely medically untreated for depression. This population represents individuals either with depression who might not seek treatment, or those who prefer not to take medication.

Although the dropout rate was about 50%, and higher in the SHUTi group, the findings were significant, even when accounting for differential dropout. Differential dropout is often greater in active conditions than control conditions in treatment trials, and can be interpreted as due to the additional psychological effort required in the active group or to attainment of treatment goals.

It is increasingly recognised that prevention will reduce the prevalence of depression. Many people have both insomnia and depressive symptoms. If delivered widely, insomnia interventions might offer non-stigmatised assistance that could revolutionise public health depression efforts. To our knowledge, the present study is the first to show that depression symptoms can be prevented in people with depression and insomnia by use of an insomnia intervention. This finding is notable given that the intervention used was a fully automated system involving no human support.

Contributors

HC is lead investigator, designed the study, oversaw trial implementation and data interpretation, is the principal writer of the manuscript, and is lead investigator on the grant. PJB was responsible for trial implementation, supervision of the trial manager, design of trial instruments, primary data analysis, and critical review of the manuscript. JAG was the trial manager; designed the study, particularly regarding anxiety outcomes; implemented design protocols; designed analysis of anxiety and other outcomes; critically reviewed the manuscript; implemented all trial details; and wrote the trial protocol. LMR designed the trial, particularly sleep interventions and sleep outcomes; implemented the trial; oversaw the SHUTi design and measures; and critically reviewed the manuscript. KMG designed the study, oversaw the trial and its implementation, and critically revised the paper. FPT designed the trial design, particularly sleep interventions and sleep outcomes; implemented the trial and the SHUTi intervention; and critically reviewed the manuscript. NG designed the trial, particularly sleep interventions and sleep outcomes; implemented the trial; and critically reviewed the manuscript. BO'D did the literature search and conceptualisation, and wrote and critically reviewed the manuscript. IBH designed and conceptualised the trial, particularly regarding depression and sleep, and contributed to manuscript writing and critical review of manuscript. AJM designed the trial, oversaw statistical analyses and psychometrics, produced the figures, wrote the manuscript, interpreted the data, and critically reviewed the manuscript.

Declaration of interests

HC has received grants from the National Health and Medical Research Council (NHMRC) and the Australian Research Council, during the conduct of the study. LMR receives research funding from the National

Institute of Health (NIH) that, in part, focuses on insomnia. LMR and FPT have equity ownership in BeHealth Solutions (Charlottesville, VA, USA), a company that develops and makes available products related to the research reported in this manuscript. Specifically, BeHealth Solutions has licensed the SHUTi program and the software platform on which it was built from the University of Virginia. The terms of this arrangement have been reviewed and approved by the University of Virginia in accordance with its conflict of interest policy. NG has received grants from the National Health and Medical Research Council during the conduct of the study, and personal fees from Lundbeck, Servier, and Janssen outside the submitted work. IBH has received grants from the NHMRC, NSW Health, and Drinkwise during the conduct of the study, and personal fees from Servier, Janssen, AstraZeneca, and Pfizer outside the submitted work; has previously served on the advisory boards member of Headspace Australia, Psychosis Australia Trust, Australian National Council on Drugs, and Bupa Australia Medical Advisory Board; and is currently a co-director of the Brain and Mind Centre, University of Sydney, and is serving on the National Mental Health Commission and the Medibank Clinic Reference Group. PJB, KMG, AJM, JAG, and BO'D declare no competing interests.

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