SYSTEMATIC REVIEW

The use of eHealth to promote physical activity in patients with mental health conditions: a systematic review [version 1; peer review: 3 approved with reservations]

Jonathan Moran,1 Gráinne Kelly,1 Ciarán Haberlin,1 David Mockler,2 Julie Broderick1

1Discipline of Physiotherapy, Trinity College, University of Dublin, Dublin, D08 W9RT, Ireland
2John Stearne Medical Library, Trinity Centre for Health Sciences, St James’ Hospital, Dublin, D08 W9RT, Ireland

Abstract

Background: Achieving adequate amounts of physical activity (PA) confers important physical and mental health benefits. Despite this, individuals with mental health conditions often do not meet recommended levels of PA. eHealth, the delivery of health information through internet and mobile technologies, is an emerging concept in healthcare which presents opportunities to improve PA in people with mental conditions. The aim of this systematic review is to explore if eHealth interventions increase PA levels among individuals with mental health conditions.

Methods: Databases searched included OVID Medline, EMBASE, PsychInfo and Web of Science using a combination of key-words and medical subject headings. Articles were included if they described an eHealth intervention designed to improve PA in individuals with mental health conditions. Two reviewers screened articles for inclusion.

Results: In total 2,994 articles were identified. Seven studies met the eligibility criteria. A variety of eHealth platforms designed to increase PA were described in these studies; web-based (n=4), web and mobile application (n=3) and e-mail-based (n=1), one study used both a web-based and mobile application. Three studies reported eHealth intervention significantly increased PA levels. Four studies reported that higher levels of PA resulted in improvements in mental health outcomes.

Conclusion: eHealth interventions may be an innovative low cost method to increase PA levels which may have knock-on effects on mental health outcomes. Although some of the included studies in this review demonstrated promising results, methodological restrictions and potential biases from using subjective measures of PA limit the interpretability of these results. Future research should evaluate this nascent technology using well designed trials.

Keywords
eHealth, technology, mental health, physical activity
Corresponding authors: Jonathan Moran (moranj2@tcd.ie), Julie Broderick (julie.broderick@tcd.ie)

Author roles: Moran J: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Kelly G: Data Curation, Formal Analysis, Investigation, Software, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Haberlin C: Conceptualization, Data Curation, Formal Analysis, Methodology, Supervision, Validation, Writing – Review & Editing; Mockler D: Conceptualization, Data Curation, Investigation, Resources, Validation, Writing – Review & Editing; Broderick J: Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing

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Introduction

Physical activity (PA) is associated with a number of health related benefits such as improved cardiovascular health, bone strength, and a reduced risk of developing chronic conditions such as colorectal and breast cancers, cardiovascular disease, and Type II diabetes[12]. In addition, the benefits of PA among individuals with mental health conditions extend beyond physical health benefits and include improved mood and sleep, reduced stress, and enhanced self-esteem[14]. Despite the numerous physical and mental benefits of PA, insufficient levels are prevalent among individuals with mental health conditions[5,6]. The low levels of PA among this population and potential mental and physical health gains make a strong case to explore innovative and effective ways to improve PA levels.

eHealth is a relatively new concept in healthcare which may present unique opportunities to improve PA levels. The World Health Organisation (WHO) defines eHealth as the transfer of health resources and health care by electronic means, including, but not limited to the delivery of health information through the internet and mobile technologies. The implementation of internet technology in health-care provides a number of benefits such as convenience for users, easy storage of large amounts of information, ease of updating information, and ability to provide personalized feedback[2]. eHealth interventions have been extensively studied in a number of populations ranging from cancer survivors to community dwelling adults[8,12]. Systematic review evidence has consistently supported the effectiveness of eHealth interventions to increase PA levels.

To our knowledge, no systematic review has synthesised the literature on eHealth interventions to increase PA for people with mental health conditions. To address this gap, the objective of this systematic review was to investigate the effectiveness of eHealth interventions to increase PA among individuals with mental health conditions.

Methods

Study design

This systematic review was conducted to identify eHealth interventions with a primary or secondary aim to increase PA in individuals with mental health conditions. The “Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)”[13] and the criteria outlined in “A Measurement Tool to Assess Systematic Reviews (AMSTAR)” guidelines were followed in drafting this review (PRISMA checklist in Supplementary File 1). The protocol outlining the planned search strategy and method of analysis for this review was registered online and is available on PROSPERO, a registry of systematic reviews (CRD42017068834).

Eligibility criteria

Experimental studies and observational studies, with or without controls, were eligible for inclusion if they evaluated an eHealth-based intervention (internet and mobile technologies) delivered to participants with mental health conditions which included PA as a primary or secondary outcome measure. Single eHealth interventions or multi-modal interventions in conjunction with eHealth were included. Studies were excluded if only telephone calls, SMS or conference calls were used, as these are not considered eHealth interventions. Review articles, case studies and letters to the editor were also excluded.

PA is a complex multi-dimensional construct measured through objective (e.g. indirect calorimetry, accelerometers, pedometers) or self-report methods (e.g. questionnaire, log)[15]. Domains of PA can be considered on a continuum from light activity (e.g. slow walking) through to moderate level activity (e.g. brisk walking) and vigorous activity (e.g. jogging). Sedentary behaviour consists of low levels of activity, similar to resting (e.g. sitting or lying down)[16]. There are many different ways of quantifying PA. We included the following methods of measuring PA, but not limited to the following; MET-minutes·week⁻¹, minutes in light, moderate and/or vigorous PA per week, and meeting/not meeting PA guidelines (150 minutes per week of moderate/vigorous activity)[17]. All methods of measuring PA were included e.g. self-report, objective or direct measures.

Data sources & search strategy

An experienced medical librarian was consulted and a comprehensive search strategy was developed with all keywords and subject headings included (DM). The search strategy consisted of a search of four electronic databases: OVID Medline, EMBASE, PsychINFO, and Web of Science. Search terms included keywords and medical subject headings adapted for each database. These related to three categories: 1) the condition (e.g. ‘mental health’ ‘depression’, ‘bipolar disorder’, ‘schizophrenia’ and ‘anxiety disorder’), 2) technology (e.g.’teleHealth’, ‘telerhabilitation’, ‘mobile health’, ‘Mhealth’, ‘eHealth’, ‘e-health’, ‘mobile technology’, ‘smartphone’), and 3) PA (e.g. ‘exercise’, ‘physical activity’, ‘exercise therapy’, ‘physical activity’). There was no limit placed on the year published as it was believed that the search strategy would produce only articles published within the last ten years, due to the relatively novel nature of this technology. Databases were searched until August 2017. The bibliographies of all included studies were examined to identify further studies. The search strategy is available in Supplementary File 2.

Selection of eligible studies

Two researchers (JM and GK), independently screened titles and abstracts to identify studies that met the eligibility criteria. Any disagreements between researchers were discussed and if a consensus could not be reached a third researcher (JB) intervened. All full-texts were retrieved and examined in detail to assess for inclusion in this review.

Risk of bias and classification of intervention type within studies

Two researchers (JM and GK) independently appraised the risk of bias of included studies; any disagreements were resolved through discussion. The Downs and Black checklist was used to assess the risk of bias of all included observational studies[19]. This checklist contains 27 items, with a maximum possible score of 32 points. The final score is variable as some items of the checklist may not be applicable and can be excluded. In addition,
the Cochrane Collaboration’s tool was used to assess risk of bias for each RCT. Risk of bias was assessed in the following six areas; sequence generation (randomisation); allocation concealment; blinding of participants, personnel and investigator; incomplete data (e.g. losses to follow-up, intention-to treat analysis); selective outcome reporting; and other possible sources of bias.

**Data extraction & analysis**

Data was extracted by two researchers (JM and GK) onto standardised data abstraction forms. Any disagreements were discussed, if a consensus could not be reached, a third member of the research team (JB) arbitrated. The standardised data extraction form was piloted on two randomly selected studies and modified accordingly. Data was extracted using the following headings: methods, allocation, blinding, duration, design, setting, participants, diagnosis, age, sex, inclusion criteria, exclusion criteria, intervention, control group, primary outcomes, secondary outcomes, results in PA outcomes, results in secondary outcomes.

A quantitative synthesis of included data was planned, but was deemed inappropriate due to the heterogeneity of study design, participants, interventions and outcomes. Consequently, a qualitative synthesis of study interventions and results was completed. A number of sub-group analyses were planned, including comparing self-report and objectively measured PA and intervention focus such as smart phone applications vs. web-based interventions. Due to insufficient data in included studies these comparisons could not be completed.

**Results**

**Study selection**

The PRISMA flow diagram outlines study selection (Figure 1). A total of 2,994 articles were retrieved and 191 duplicates were removed. Following title and abstract screening, 2,728 articles were excluded leaving 75 full-text articles to be screened. Ultimately, seven articles were included in this review. Types of studies were mixed, including RCTs (n=3) and observational studies (n=4). Table 1 describes the methodological features of included studies.

![Figure 1. PRISMA Flow diagram of study selection.](image-url)
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>Design</th>
<th>Duration</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beiwinkel et al., 2016</td>
<td>Germany</td>
<td>Pilot Observational Study</td>
<td>12 months</td>
<td>Diagnosis of bipolar I or bipolar II disorder according to the criteria in the DSM-IV ≥18 years of age Sufficient knowledge of the German language Basic competence in using mobile devices</td>
<td>The need for inpatient treatment at the time of recruitment Suicidality Diagnosis of schizophrenia or an intellectual disability Alcohol or drug abuse up to 6 months prior to the study</td>
</tr>
<tr>
<td>Glozier et al., 2013</td>
<td>Australia</td>
<td>RCT</td>
<td>12 weeks</td>
<td>Self-reported history of CVD, or risk factors for CVD, defined as any one of the following: receiving treatment for heart attack/angina, other heart disease, hypertension or high blood cholesterol in the past month; taking medications for heart disease, hypertension or high blood cholesterol in the past month; previous doctor's diagnosis of heart disease, stroke or hypertension; previous doctor's diagnosis of diabetes and report taking glucose lowering therapy in the past month; two or more of the following risk factors: current smoker, obese (BMI&gt;30), aged 65 years or more, family history of heart disease or stroke in two or more first degree relatives, all of which are well established risk factors for CVD Psychological distress at recruitment to the health survey, defined with a high sensitivity as a Kessler-10 (K-10) score of greater than or equal to 16. This screening score reflects distress six months to three years prior to trial recruitment Provided an email address established as previously valid through 45 and Up Study checking processes</td>
<td>N/R</td>
</tr>
<tr>
<td>Kerr et al., 2008</td>
<td>USA</td>
<td>Pilot Study</td>
<td>12 weeks</td>
<td>English speaking men and women, aged 25–65 years, with newly diagnosed or recurrent mild-to-moderate depression (PHQ-9 score 15 or greater at screening) Doctor approved prescription of escitalopram (Lexapro) Telephone and internet access at home Ability to participate in mild- to moderate-intensity physical activity (PAR-Q) Willingness to participate in all study components</td>
<td>Individuals currently receiving psychotherapy for their depression from a psychiatrist or psychologist and those at high risk for suicide as assessed by the PHQ-9 suicide item.</td>
</tr>
<tr>
<td>Mailey et al., 2010</td>
<td>USA</td>
<td>Pilot RCT</td>
<td>10 weeks</td>
<td>Be registered for and receiving mental health counselling services A student at the university Able to participate in physical activity without exacerbating a pre-existing condition Access to a personal computer with internet connection.</td>
<td>N/R</td>
</tr>
<tr>
<td>Author, Year</td>
<td>Country</td>
<td>Design</td>
<td>Inclusion Criteria</td>
<td>Exclusion Criteria</td>
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<td>------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Naslund et al., 2016</td>
<td>USA</td>
<td>Observational Cohort Study</td>
<td>Serious mental illness defined by an axis I diagnosis of schizophrenia, schizoaffective disorder, major depressive disorder, or bipolar disorder. Spoke English. On stable pharmacological treatment defined as receiving the same psychiatric medications over the prior 2 months. Obesity (BMI ≥ 30).</td>
<td>Participants were excluded if they had any medical contraindication to weight loss. Pregnant or planning to become pregnant within the next 6 months. Current diagnosis of an active alcohol-use or substance-use disorder.</td>
<td></td>
</tr>
<tr>
<td>Shin et al., 2016</td>
<td>South Korea</td>
<td>Observational Cohort Study</td>
<td>Patient had to be hospitalized with chronic schizophrenia in a closed ward. Be involved in ordinary activity in a regular psychiatric treatment program. Agree to wear an activity tracker and keep it continuously for a week.</td>
<td>Patients who were restricted from outdoor activity. Patients with severe medical conditions affecting physical activity. Patients who lacked an understanding of this study due to psychiatric symptoms or moderate intellectual disability. Patients with conditions such as akathisia, delirium, tic, or drug induced Parkinsonism or epilepsy.</td>
<td></td>
</tr>
<tr>
<td>Ström et al., 2013</td>
<td>Sweden</td>
<td>RCT</td>
<td>Mild to moderate major depression diagnosis. A sedentary lifestyle. High levels of physical activity prior to treatment. Recent changes in medication.</td>
<td>Subclinical depressive symptoms, depressive symptoms, dysthymia as a primary diagnosis. Elevated suicide risk. Somatic illness making physical exercise inappropriate.</td>
<td></td>
</tr>
</tbody>
</table>

Participant characteristics
Participant characteristics are summarised in Table 2. A total of 811 participants were recruited with 102 dropping out. Ultimately, 709 participants were analysed across seven studies. The majority of participants analysed had depression (n=588). The remaining mental health conditions included; schizophrenia or schizophrenia spectrum disorders (n=69) and bipolar disorders (n=22). One study did not report the specific diagnoses of mental health conditions included.

Risk of bias of included studies
Risk of bias of all included studies is noted in Table 3. The Cochrane Collaboration’s tool was used to evaluate the risk of bias of the three included RCTs. Two studies were ranked as having an unclear risk of bias, while the remaining RCT had a low risk of bias. The Downs and Black checklist assessed the risk of bias of the remaining observational studies (n=4).

Study design
Included studies were varied in design, likely reflecting this emerging research field. Three studies compared an eHealth intervention to a control group. The remaining studies (n=4) used an eHealth intervention to measure physical activity in participants with mental health conditions. Mobile technologies such as smartphones and the Fitbit were used to measure physical activity levels and predict clinical signs and symptoms of mental health conditions such as mood. The length of interventions ranged from 9 days to 12 months, with the majority of studies not assessing physical activity post-study completion. Only one study assessed maintenance at 6 months post-baseline.

Physical activity assessment
Objective methods of measuring physical activity included smartphones (GPS, cell tower movement and accelerometer data), wearable technologies (Fitbit), accelerometers and

Table 2. Participant characteristics.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Participants</th>
<th>Age: Mean (SD) years</th>
<th>Sex (Baseline)</th>
<th>Mental Health Conditions: Number of participants (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beiwinkel et al., 2016</td>
<td>14 (0 drop-outs)</td>
<td>47.2 (3.8)</td>
<td>Male: 8 Female: 5</td>
<td>Bipolar disorder: 13 (100%)</td>
</tr>
<tr>
<td>Glozier et al., 2013</td>
<td>562 (75 drop-outs)</td>
<td>IG: 57.5 (6.6)</td>
<td>IG: Female, 173 61.8%</td>
<td>Mild-moderate depression: 487 (100%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG: 58.4 (6.6)</td>
<td>CG: Female, 172 61.0%</td>
<td></td>
</tr>
<tr>
<td>Kerr et al., 2008</td>
<td>36 (13 drop-outs)</td>
<td>44.1 (9.8)</td>
<td>Males: 9 (25%) Female: 27 (75%)</td>
<td>Depression: 36 (100%)</td>
</tr>
<tr>
<td>Mailay et al., 2010</td>
<td>47 (4 drop-outs)</td>
<td>25 (range 18–52)</td>
<td>Females: 32 (68.1%) Males: 15 (32%)</td>
<td>N/R</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not separated by groups</td>
<td>Not separated by groups</td>
<td></td>
</tr>
<tr>
<td>Naslund et al., 2016</td>
<td>43 (9 drop-outs)</td>
<td>50.2 (11.0)</td>
<td>Female: 21 (61.8%) Male: 13 (38.2%)</td>
<td>Schizophrenia spectrum disorders: 8 (23.5%) Major depressive disorder: 17 (50.0%) Bipolar disorder: 9 (26.5%)</td>
</tr>
<tr>
<td>Shin et al., 2016</td>
<td>61 (0 drop-outs)</td>
<td>46.59 (8.40)</td>
<td>Males: 35 (52.4%) Women: 26 (42.6%)</td>
<td>Schizophrenia: 61 (100%)</td>
</tr>
<tr>
<td>Ström et al., 2013</td>
<td>48 (0 drop-outs)</td>
<td>Total: 49.2 (10.7)</td>
<td>Total: Female = 40; Male = 8</td>
<td>Mild to moderate depression: 48 (100%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IG: 48.8 (12.7)</td>
<td>IG: Female = 20; Male = 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG: 49.6 (8.7)</td>
<td>C: Female = 20; Male = 4</td>
<td></td>
</tr>
</tbody>
</table>

CG: Control group, IG: Intervention group, N/R: Not reported
Table 3. Risk of Bias of included studies.

<table>
<thead>
<tr>
<th>Author</th>
<th>Cochrane Risk of Bias</th>
<th>Downs and Black Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beiwinkel et al., 2016</td>
<td>-</td>
<td>11/18</td>
</tr>
<tr>
<td>Glozier et al., 2013</td>
<td>Low</td>
<td>-</td>
</tr>
<tr>
<td>Kerr et al., 2008</td>
<td>-</td>
<td>17/20</td>
</tr>
<tr>
<td>Mailey et al., 2010</td>
<td>Unclear</td>
<td>-</td>
</tr>
<tr>
<td>Naslund et al., 2016</td>
<td>-</td>
<td>19/20</td>
</tr>
<tr>
<td>Shin et al., 2016</td>
<td>-</td>
<td>16/17</td>
</tr>
<tr>
<td>Ström et al., 2013</td>
<td>Unclear</td>
<td>-</td>
</tr>
</tbody>
</table>

pedometers26. The remaining studies (n=2) used the IPAQ to subjectively measure PA21,22.

Four studies used eHealth interventions to measure physical activity in participants with mental health conditions23-26. Higher levels of PA as measured using eHealth are associated with less manic symptoms as measured using the Young Mania Rating Scale (YMRS) in participants with bipolar disorder (YMRS: beta=-.37, p<0.001)24. In addition, a decline in physical activity participation was reported to be predictive of an increase in depressive symptoms. In participants with schizophrenia, daily PA levels as measured by an eHealth device (Fitbit Flex®), showed a significant association with positive (steps per day: -0.508, p<0.001), general (steps per day: -0.39, p=0.002) and total (steps per day: -0.459, p<0.001) scores measured using the Positive and Negative Syndrome Scale (PANSS)21.

eHealth interventions were shown to increase physical activity participation in participants with depression26. Kerr and colleagues reported daily step count significantly increased from baseline (Mean: 6604.1 (SE: 883.6)) to 12 weeks (Mean: 9053.3 (SE: 818.1)) in 36 participants with depression. In addition, sedentary behaviour reduced from baseline to 12 weeks, however, this did not reach significance (Table 4). Naslund and colleagues reported a significant association between participants’ average daily step count and weight loss25. For every 1000 step increase in daily average step count, participants experienced a decrease in weight of 1.78 pounds (F=5.07; df=1, 32; p=0.0314).

Discussion

All experimental studies (n=3) reported eHealth interventions significantly increased PA levels from baseline, however, it is unclear if eHealth interventions are superior to traditional mental health services at increasing PA. Glozier and colleagues reported a greater proportion of participants with mild-moderate depression (n=487) engaging in the recommended levels of physical activity (≥150 mins a week) who performed internet based cognitive behavioural therapy (ICBT) compared to the control group (67% in ICBT vs 61% in control group, Odds Ratio: 1.91, 95% CI: 1.01–3.61). In contrast two studies reported that there was no significant differences in physical activity levels between eHealth interventions and control treatments. Mailey and colleagues noted an increase in PA in both the intervention and control group, however, there was a larger increase in mean PA in the intervention group (Pre: 243421.81 vs. Post: 299791.57, d=0.68) compared to the control group (Pre: 247753.55 vs. Post: 251625.04, d=0.05) as measured using the Actigraph accelerometer. Furthermore, Ström and colleagues noted PA significantly increased in both the intervention and control groups, however, there was no significant difference between the eHealth and waiting list control group.

This systematic review comprehensively searched and evaluated the effect of eHealth interventions on PA levels in participants with a range of mental health conditions. Overall, eHealth interventions appear to be feasible to use, although consistent increases in PA were not demonstrated across all studies. Importantly perhaps, higher levels of physical activity were associated with improvements in clinical signs and symptoms of mental health conditions (e.g. mood) in two studies23,24. Although beneficial in increasing PA levels, it is currently unclear if eHealth interventions are superior to traditional care at increasing physical activity as results are inconsistent.

Importantly perhaps, higher levels of physical activity were associated with improvements in clinical signs and symptoms of mental health conditions (e.g. mood) in two studies23,24. Although beneficial in increasing PA levels, it is currently unclear if eHealth interventions are superior to traditional care at increasing physical activity as results are inconsistent.

Glozier and colleagues noted a greater proportion of participants achieved the recommended levels of physical activity (≥150 mins a week) in favour of the e-health intervention compared to the control group (67% in ICBT vs 61% in control group, Odds Ratio: 1.91, 95% CI: 1.01–3.61). The risk of bias as measured using the Cochrane collaboration tool ranked this study as low. In contrast, two studies comparing eHealth interventions to control treatments reported no significant differences between the intervention and control arms in terms of PA, however both of these studies had an unclear risk of bias25. In addition, both of these studies had much smaller sample sizes compared to the study by Glozier and colleagues which was notably much larger in size (n=487) compared to other studies included in this review. It should be noted however that Glozier and colleagues employed a subjective measure of physical activity, the IPAQ, compared to the more reliable objective measure of PA, the Actigraph accelerometer used by Mailey and colleagues. This limits the interpretability of these results and raises the likelihood of results being influenced by bias.

Discussion

This systematic review comprehensively searched and evaluated the effect of eHealth interventions on PA levels in participants with a range of mental health conditions. Overall, eHealth interventions appear to be feasible to use, although consistent increases in PA were not demonstrated across all studies. Importantly perhaps, higher levels of physical activity were associated with improvements in clinical signs and symptoms of mental health conditions (e.g. mood) in two studies23,24. Although beneficial in increasing PA levels, it is currently unclear if eHealth interventions are superior to traditional care at increasing physical activity as results are inconsistent.
<table>
<thead>
<tr>
<th>Author, year</th>
<th>Intervention (IG) and control group (CG)</th>
<th>Physical activity outcomes and result</th>
<th>How PA recorded</th>
<th>Method of PA quantification</th>
<th>Baseline and end-intervention PA results: Mean (Standard Deviation) unless otherwise stated.</th>
</tr>
</thead>
</table>
| Beiwinkel et al., 2016 | IG: Physical activity recorded over 12 months in 13 participants with bipolar disorder  
CG: N/A | | Smartphone. Three smartphone sensors were used to measure physical activity.  
**GPS** for the distance travelled per day, **cell tower movement** as an indicator of location changes, and **accelerometer** to measure the users’ device activity | GPS, distance travelled (km)  
Cell tower changes  
Device activity, % of day | **Mean levels**  
Distance travelled (km): 10.5 (41.5)  
Cell tower changes: 10.5 (17.0)  
Device activity, % of day: 7.3 (8.2)  
**Between-patient analysis**  
Distance travelled as measured by the GPS signal had a significant negative relationship with clinical manic symptoms (YMRS: beta=-.37, *P*<.001).  
**Within-patient analysis**  
An increase in cell tower movement was negatively related to both manic symptoms (YMRS: beta=-.17, *P*<.001) and depressive symptoms (HAMD: beta=-.11, *P*=.03) |
| Glozier et al., 2013 | IG: 12 weeks of internet delivered cognitive behavioural therapy  
CG: 12-week online programme that delivers health information on topics including nutrition, stroke, physical activity, medicines in the home, blood pressure and cholesterol, and heart health | IPAQ | The average time spent walking per day and a composite measure of undertaking enough exercise to provide a health benefit (defined as at least 150 mins of activity over 5 or more occasions each week) | **Post-intervention**  
Activity sufficient to confer a health benefit post intervention (150 mins over 5 occasions/week)  
IG: N=136 (67%)  
CG: N=165 (61%) (**Odds Ratio 1.91, 95%CI: 1.01–3.61**)  
**Average walking time per day**  
0-14 mins per day, IG: N=78 (38%), CG: N=116 (43%)  
15-29 mins per day, IG: N=47 (23%), CG: N=64 (23%)  
30+ mins per day, IG: N=79 (39%), CG: N=92 (34%) (**Odds ratio = 1.46, 95% CI: 0.81–2.62**) |
<table>
<thead>
<tr>
<th>Author, year</th>
<th>Intervention (IG) and control group (CG)</th>
<th>Physical activity outcomes and result</th>
<th>Baseline and end-intervention PA results: Mean (Standard Deviation) unless otherwise stated.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kerr et al., 2008</td>
<td>IG: A community based physical activity intervention (involving internet, telephone, and pedometer support), integrated with medication and mood management for depressed patients&lt;br&gt;CG: N/A</td>
<td>Pedometer&lt;br&gt;Steps per day</td>
<td>All participants (n=36)&lt;br&gt;Daily step count: Mean (SE)&lt;br&gt;Baseline: 6604.1 (883.6)&lt;br&gt;6 weeks: 8558.8 (868.8)&lt;br&gt;12 weeks: 9053.3 (818.1)&lt;br&gt;Sedentary behavior: Mean (SE)&lt;br&gt;Baseline: 62.2 (5.0)&lt;br&gt;6 weeks: 58.9 (4.2)&lt;br&gt;12 weeks: 57.6 (4.2)&lt;br&gt;Completers only (n=23)&lt;br&gt;Daily step count: Mean (SE)&lt;br&gt;Baseline: 6656.2 (1618.7)&lt;br&gt;6 weeks: 8903.2 (1665.2)&lt;br&gt;12 weeks: 8550.0 (1374.4)&lt;br&gt;Sedentary behavior: Mean (SE)&lt;br&gt;Baseline: 63.4 (6.3)&lt;br&gt;6 weeks: 58.9 (4.3)&lt;br&gt;12 weeks: 56.8 (4.4)</td>
</tr>
<tr>
<td>Mailey et al., 2010</td>
<td>IG: An internet-based physical activity intervention on physical activity, self-efficacy, depression, and anxiety in college students (n=23) receiving mental health counselling&lt;br&gt;CG: Standard mental health care (n=24)</td>
<td>Actigraph accelerometer&lt;br&gt;Total daily activity score&lt;br&gt;Daily totals were averaged across five days of continuous activity</td>
<td>Physical activity pre-intervention&lt;br&gt;IG: 243421.81 (62414.56)&lt;br&gt;CG: 247753.55 (69613.96)&lt;br&gt;Physical activity post-intervention&lt;br&gt;IG: 299791.57 (102800.00)&lt;br&gt;CG: 251625.04 (83080.77)&lt;br&gt;A significant main effect for time with both conditions increasing their physical activity levels across the 10-week period, p=0.04.</td>
</tr>
<tr>
<td>Author, year</td>
<td>Intervention (IG) and control group (CG)</td>
<td>Physical activity outcomes and result</td>
<td>Method of PA quantification</td>
</tr>
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</table>
| Naslund et al., 2016 | IG: Daily step count measured using Fitbit wearable devices to improve weight loss and fitness among individuals with serious mental illness enrolled in a 6-month lifestyle programme  
   CG: N/A                             | How PA recorded: Fitbit               | Method of PA quantification: Steps per day | Participants achieved an average of 4453.5 (SD = 2707.4) steps each day.  
   Average daily step counts ranged from 1037.6 (SD = 767.9) steps to 11,366.3 (SD = 3416.9) steps.  
   21 (61.8%) participants achieved 10,000 steps or more on at least one day.  
   There was a significant association between participants’ average daily step count and weight loss.  
   For every 1000 step increase in participants’ daily average step count, they experienced a decrease in weight of 1.78 pounds ($F = 5.07; \text{df} = 1, 32; \ p = 0.0314$) |
| Shin et al., 2016  | IG: Measure physical activity using an mHealth device correlations with psychopathology in participants with chronic schizophrenia  
   CG: N/A                             | How PA recorded: Fitbit               | Method of PA quantification: Steps per day | Mean daily activity: 12,649.21 ± 5883.99 steps/day.  
   Range: 3612 – 29,663 steps/day  
   Significant correlations were found between daily activity and PANSS positive, general and total subscale.  
   **Activity levels (steps per day)**  
   PANSS-positive: -0.508 (p<0.001)  
   PANSS-negative: -0.356 (p=0.005)  
   PANSS-general: -0.39 (p=0.002)  
   PANSS-total: -0.459 (p<0.001)  
   PANSS 5-factor positive: -0.495 (p<0.001)  
   PANSS 5-factor negative: -0.445 (p<0.001)  
   PANSS 5-factor disorganisation: - 0.362 (p=0.004) |
| Ström et al., 2013 | IG: Internet based therapist delivered self-help programme  
   CG: Waiting list                      | How PA recorded: IPAQ                | Method of PA quantification: Total MET (Metabolic equivalent of task) per week | IPAQ  
   IG:  
   - Pre: 778 (695)  
   - Post: 1331 (990)  
   - 6-months: 1282 (1255)  
   CG:  
   - Pre: 953 (670)  
   - Post: 1143 (918)  
   - 6-months: N/a  
   Physical activity increased in both groups, no significant difference between two groups |
Subjective methods of measuring PA are more prone to error compared to objective measures such as pedometers and accelerometers\textsuperscript{37}. Subjective measures of PA raise the likelihood of self-report bias influencing results as participants are instructed to think about PA. Furthermore, subjective measures are liable to recall bias, further limiting the interpretability of these results. eHealth technologies such as smartphones and wearable technology (i.e. Fitbit) demonstrate good validity and reliability at measuring physical activity and have been noted to improve patient motivation to partake in physical activity\textsuperscript{28-30}. The use of such tools may limit the influence of bias and other factors associated with subjective measures of PA\textsuperscript{33}.

eHealth technologies are rapid and constantly evolving through continuous software and hardware updates that regularly outpace medical research. The RCT is widely regarded the gold-standard of experimental research, however the mean duration from enrolment to publication is 5.5 years\textsuperscript{31}. eHealth technologies are likely to become obsolete within this time-frame. A call has been made for medical research to evolve and adapt to maintain pace with developments in eHealth\textsuperscript{32}. The Continuous Evaluation of Evolving Behavioural Intervention Technologies (CEEBIT) methodological framework has been proposed as an alternative to the conventional RCT design\textsuperscript{33}. It is statistically powered to continuously valuate eHealth applications throughout the study duration while accounting for updates to the application. Therefore, future eHealth interventions should consider using this novel methodological framework specific to the ever evolving eHealth technologies.

Further research is required to make a judgement of the ability of eHealth interventions to increase physical activity in people with mental health conditions. A recent systematic review showed that drop-out rates from exercise trials in people with depression are lower when delivered by a health professional with specific training in exercise prescription\textsuperscript{34}. The need for qualified personnel to supervise PA programmes for people with schizophrenia was also echoed in a review by Vancampfort (2016)\textsuperscript{35}. Drop-out rates of the PA arm of randomised controlled trials in people with schizophrenia was reported to be 26.7%\textsuperscript{35}. Amalgamated drop-out rates for the current review show a lower drop-out rate of 12.5% but this may be reflective of the mixed mental health population with the majority having mild-moderate depression. It is not known whether the remotely delivered nature of eHealth interventions may result in less or more efficacious outcomes than traditionally delivered programmes. Head-to-head comparisons between these intervention mediums are necessary to elucidate the relative benefits of each.

Previous reviews in other clinical populations such as cancer survivors have reported that the initial results of eHealth technologies to increase physical activity in the cancer rehabilitation setting are promising\textsuperscript{36}. However, similar to this review, weaknesses in methodological quality and uses of subjective measures of PA limit the interpretability of these findings.

Table 5. Features of E-Health intervention.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Platform for intervention</th>
<th>App / software</th>
<th>Personalisation</th>
<th>Behaviour change theory</th>
<th>PA Reporting by user</th>
<th>Interaction</th>
<th>Feedback</th>
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<tr>
<td></td>
<td>Web app</td>
<td>Mobile app</td>
<td>Email</td>
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<td>No</td>
<td>SGT</td>
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<td>Automated reminders</td>
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<td>SMS</td>
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</table>

CBT; Cognitive Behavioural Therapy; IPACS; Internet Physical Activity for College Students; SIMBA; Social Information Monitoring for Patients with Bipolar Affective Disorder; SCT-Social Cognitive Theory; TTM-Trans Theoretical Model
studies examining eHealth interventions and physical activity participation among mental health populations. Future studies should use objective measures of physical activity, including but not limited to pedometers, accelerometers and wearable technology. In addition, eHealth interventions should adhere to improved reporting of interventions, to ensure that such interventions can be repeated. Follow-up times in this review have varied from 9 days-12 months, with the majority of studies not recording PA levels in the maintenance phase. Therefore, the long-term implications of eHealth technologies to increase PA in a mental health population should be explored.

Conclusion

eHealth interventions appear feasible for people with mental health conditions and may improve PA levels and mental health symptoms. Even though some of the included studies in this review demonstrated promising results, methodological restrictions and potential biases from using subjective measures of PA limit the interpretability of these results. Currently, it is unclear if eHealth interventions are superior compared to traditional interventions methods to increase PA. Larger well designed studies are needed to extensively evaluate the true potential of this medium.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Competing interests

No competing interest were disclosed.

Grant information

Health Research Board Ireland [CFT-2014-880].

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Supplementary material

Supplementary File 1: PRISMA Checklist.
Click here to access the data.

Supplementary File 2: Search strategies for all databases.
Click here to access the data.

References

Open Peer Review

Current Peer Review Status:  ?  ?  ?

Version 1

Reviewer Report 05 April 2018

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Helen P. French
School of Physiotherapy, Royal College of Surgeons in Ireland, Dublin, Ireland

Thank you for the opportunity to review this review on a topical and relevant issue. The review appears to have been well conducted but there are some flaws which should be addressed. My comments below are designed to enhance the quality of the manuscript.

Abstract
- Background: change ‘mental conditions’ to ‘mental health conditions’
- In the methods section can you provide some information on the methodological quality evaluation of the review
- In the conclusion section, the word nascent is not very common, so I would suggest changing it to another term that would be more familiar to non-native English readers.

Methods
- In the ‘eligibility criteria’ section, was a full-text version of a study an inclusion criterion?
- Please provide full word for SMS
- In the data analysis section, suggest changing the word ‘abstraction’ to ‘extraction’
- In Figure 1: please add in the box for number of duplicates removed in line with PRISMA flowchart.

Results
- The results section is quite confusing to read, generally because of the way the information is presented in the different tables.
- The presentation of the results in the different tables could be clearer. I suggest merging the content of Tables 1-3 into 2 tables. Please also check the abbreviations in the tables are explained in the legends e.g. CVD, PAR-Q not explained currently.
- Review text in each table thoroughly to ensure information is presented more succinctly
- In table 2, in the column (sex baseline), suggest changing to ‘Gender’. I am unclear why gender is reported for non-missing data and why the word ‘baseline’ is there. In relation to the Mailey study, if the mental health condition was not reported, how did you determine it was eligible for inclusion.
- In relation to Table 3: it would be more useful to provide information on risk of bias for individual items, as overall risk of bias is somewhat meaningless. Issues such as randomisation, baseline
comparability, intention-to-treat analysis and drop-out rates are important to report to allow the reader to interpret results in the context of study methodology.

- Table 4:
  - Row on Belwinkel study: results presented in the last column are confusing. I do not think that the between-patient analysis and between-patient analysis is relevant. The results should focus on pre-post intervention results.
  - Row on Naslund study: in the last column, were these results related to post 6-month lifestyle programme?
  - Row on Shin study 2016- please review wording in the first column to ensure clarity.
  - Row on Strom study, please provide the units of measure for IPAQ in the last column

- In the paragraph on ‘Participant Characteristics’ is there a typing error here ‘709 participants 7 were analysed’. Please review this sentence.
- Pg 8, 3rd paragraph, please clarify that ‘significance’ relates to ‘statistical significance’
- Pg 8, 5th paragraph change ‘there was no significant differences’ to ‘that no significant differences’
  
In the same paragraph, what does the ‘d’ refer to in relation to the results presented- should this be p?

**Discussion**

- The discussion section is well written and raises some interesting points.
- Please add a section outlining the limitations of this review

**Are the rationale for, and objectives of, the Systematic Review clearly stated?**

Yes

**Are sufficient details of the methods and analysis provided to allow replication by others?**

Yes

**Is the statistical analysis and its interpretation appropriate?**

Partly

**Are the conclusions drawn adequately supported by the results presented in the review?**

Partly

**Competing Interests:** No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 15 March 2018

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Jennifer M. Ryan

1 Department of Epidemiology and Public Health Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland
2 Department of Clinical Sciences, Brunel University London, Uxbridge, UK

This systematic review aims to investigate the effectiveness of eHealth to increase physical activity (PA) among individuals with mental health conditions. This review is on an important topic and the authors provide a timely summary of the evidence.

The introduction provides a brief but coherent justification of the need for this review by summarising the benefits of physical activity and describing eHealth. Further information on the benefits of using eHealth for people with mental health conditions, over other modes of service delivery, would strengthen the rationale for this review.

Appropriate methods were used to address the objective of the review. In particular, study eligibility was assessed independently by two reviewers, data were extracted by two reviewers using a standardised data extraction form, and risk of bias was assessed. The methods and results of this review are strengthened by the use of the PRISMA checklist and by registering the protocol in advance of conducting the review.

However, the review would be improved if there was better alignment between the objective, methods and results. There is discrepancy between the objective of the review, the types of study included in the review, and the results. The description of the types of study included in the review could be clearer. Study designs are often considered as “intervention” studies and “observational” studies. An intervention study may be randomised or non-randomised. Critically, the inclusion of studies that include an intervention but are termed observational studies seems contradictory. This may be improved if the use of eHealth is considered an exposure and studies were therefore classified as cohort studies, but if this is the case it could be explained more clearly. The lack of clarity over study design is compounded by the description of study design in Table 1. For example, Beiwinkel et al. is reported as a pilot observational study, but the type of observational design is not reported (e.g. cohort, case-control, cross-sectional), while this detail is provide for Naslund (i.e. “observational cohort study”). Perhaps of more importance is that Kerr et al. is reported as a pilot study but it is not clear if it is an intervention study or observational study.

The authors identify only a small number of studies examining the effect of eHealth on physical activity in people with mental health conditions (n=7), and only three of these are randomised controlled trials (n=3). The results of the randomised controlled trials provide inconsistent evidence that eHealth results in an increase in physical activity. However, it is difficult to determine if the content of the intervention (e.g. CBT) or the fact that it’s delivered electronically is responsible for the change in the PA. It would help the reader to understand the causal pathway if the content of the comparator was described when reporting the results of the study. For example, if the control group received the same intervention (e.g. CBT) as the intervention group but delivered in person rather than electronically it is more plausible than any change in PA is due to eHealth rather than the content of the intervention. If there is no difference in PA between groups eHealth may offer additional benefits such as being more feasible and cost-effective to deliver.

It is not clear, based on the objective and eligibility criteria, why studies that used an eHealth intervention to measure physical activity were included. If monitoring physical activity was considered an intervention, and physical activity was measured pre- and post-introduction of PA monitoring then these studies should be considered intervention studies, and the outcome reported should be change in PA. Monitoring PA is a
behaviour-change technique, and as such is very likely an intervention. The authors do report change in PA following PA monitoring for some studies but not all.

The results include findings relating to associations between physical activity/change in physical activity and symptoms and weight loss. While this is of interest it goes beyond the objectives of the review. If an objective of the review is to explore associations between PA and other variables in people with mental health conditions it should be stated under the study objective and the eligibility criteria should be amended accordingly.

Further information on how each domain on the risk of bias tools were assessed and how the overall risk of bias was determined for RCTs should be provided to allow the reader to understand the quality of the studies and justify areas for future research. It is stated in the discussion that Glozier et al. used a self-report measure of physical activity and this may introduce bias. This should be captured under detection bias when assessing risk of bias. However, despite this, Glozier et al. is rated as low risk of bias. It would be beneficial to understand how the authors determined the study was at low risk of bias despite the outcome assessor not being blinded (as a self-report measure was used).

The authors provide a summary of the findings of the review and discuss a number of pertinent points including the potential to introduce bias by using self-report measure of PA and the need for studies to directly compare eHealth with physical activity interventions delivered in person. The discussion suggests that eHealth is feasible. However, examining the feasibility of eHealth is not a specific objective and the presentation of results do not support this conclusion. If this is of interest, and studies examine feasibility, this should be an objective and results reported accordingly.

The authors reach a sound conclusion based on the findings of the review, acknowledging the limitations with previous studies. However, given that Glozier et al. was a large study (n=562) and it was rated low risk of bias, the statement that larger well designed studies are needed is not justified. Specific information about the limitations of Glozier et al., which a future trial needs to address, should be provided.

Further points for consideration:
To improve consistency throughout the review, the title and objective should align (i.e. the title states to “promote physical activity in patients with mental health conditions” and the objective states “to increase physical activity in individuals with mental health conditions”.

The results section of the abstract is misleading and suggests different conclusions than those presented in the main text. Although three studies reported that eHealth increased PA, the change in PA over time is not of interest when a control group is included, as is the case in these studies. Where a control group is included the effect of interest is whether a larger change in PA is observed in the intervention group in comparison to the control group.

A definition of eHealth could be provided under “eligibility criteria” to further explain decisions regarding exclusion of studies. The description of eHealth in the introduction, as “…the transfer of health resources and health care by electronic means, including but not limited to the delivery of health information through the internet and mobile technologies” suggests that interventions that use only telephone calls, SMS or conference calls, are eHealth. These studies were however excluded.

A definition of mental health conditions and/or examples of mental health conditions of interest included in the section on eligibility criteria would be beneficial in order to describe the participants of interest.
Under eligibility criteria it states that “we included the following methods of measuring PA...”. These, however, are ways of quantifying rather than measuring PA. As the sentence after this correctly states, methods of measuring PA are self-report measures e.g. questionnaires, and objective measures, e.g. accelerometers, indirect calorimetry.

For clarity, it would be helpful if the authors stated if data were extracted independently by two researchers.

The authors describe where they were not able to conduct the review as planned e.g. quantitative synthesis. However, it would be helpful for the reader to have a section summarising the differences between the protocol and review.

It would make the results easier to read if subsections were ordered as follows: results of the search, description of included studies (design, participants, settings, interventions, comparator, physical activity assessment), risk of bias, effect of interventions.

Authors were unable to obtain full text for 6 articles. If full texts were obtained this may nearly double the number of included articles. Further explanation of why these full texts were not found or the potential limitation of not including this data should be provided.

Data are plural (i.e. “data were”).

It would be helpful for the reader if the authors stated the full name of the IPAQ before abbreviating and stated if the short or long form was used.

When reporting studies by author in text and tables e.g. Glozier, it would be helpful to cite the reference number (e.g. 22) to allow cross-referencing with different sections of the text.

It is stated in the discussion that the Actigraph accelerometer is more reliable than the IPAQ; this statement should be supported.

**Are the rationale for, and objectives of, the Systematic Review clearly stated?**  
Yes

**Are sufficient details of the methods and analysis provided to allow replication by others?**  
Partly

**Is the statistical analysis and its interpretation appropriate?**  
Not applicable

**Are the conclusions drawn adequately supported by the results presented in the review?**  
Partly

**Competing Interests:** No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
We would like to very much thank the reviewer for her insightful comments.

**Competing Interests:** No competing interests were disclosed.
intervention for promoting PA. While the results of this study are narratively reported in the review synthesis, it is not clear whether this was a pre stated objective in the methodology.

To address these issues, the reviewers suggest that the title and objectives should reflect broader objectives

e.g. The use of eHealth to promote or monitor physical activity in individuals with mental health conditions: a systematic review

In addition, given the complexity in study types and interventions considered in this review, the reviewers recommend the authors state their objectives as clinically relevant questions and that the results reported follow this outline and conclude with a best evidence synthesis summary for each question.

e.g. Can eHealth technology as a stand-alone or component of a multimodal intervention improve PA in individuals with a mental health condition?
Do eHealth interventions designed to promote PA improve general or mental health profiles in individuals with a mental health condition?
Are eHealth captured PA levels, of individuals with a mental health condition, associated with severity of clinical signs and symptoms of the mental health condition?

Results of the review can then be narratively synthesised and a best evidence synthesis summary provided. An example of what is suggested as summary is provided below but should be in table format:

**Question:**
Can ehealth technology as a stand-alone or component of a multimodal intervention improve PA in individuals with a mental health condition?

**Best available evidence**
Evidence from one high quality RCT supports the use of ehealth technology as part of a multimodal intervention in individuals with psychological distress and concomitant CVD in increasing the likelihood of achieving PA guidelines for adults (Odds Ratio 1.91, 95%CI: 1.01–3.61)

**Question:**
Do ehealth interventions designed to promote physical activity improve general or mental health profiles in individuals with a mental health condition?

**Best available evidence.....**

Other comments the peer reviews raise for consideration are summarised below:

**Title:**
The reviewers recommend that the authors change the wording patients with mental health conditions to individuals with mental health conditions and continue this throughout the text.

**Abstract:**
In the results, it is not correct to say that four studies reported that higher levels of PA resulted in improvements in mental health outcomes. We suggest this should read as ... four studies reported that higher levels of PA are associated with better mental or general health profiles.

**Manuscript:**
**Methods:** In the data extraction and analysis section, the authors provide results with reference to heterogeneity in study design, participants etc. These should be reported in the results section. In the methods section only the proposed analysis should be stated.
Similarly with respect to subgroup analyses, only the proposed analyses should be reported in the methodology section. Results of the data presented from the review that prohibited this analysis should not be presented in this section.

**Tables:** The reviewers recommend collapsing a number of the study summary and quality review tables and include the reference number with the study identified to allow the reader to better consider multiple study aspects together and reference back and forth more easily to the narrative summary provided.

In the results section of table 4 the reviewers advise the following:
- Beiwinel et al., remove the between patient and within patient analysis labels as these are not relevant to the analysis and results provided
- Kerr et al., please report were within group changes statistically significant and provide p values
- Mailey et al., please report the results of the main effect analysis.
- Naslund et al., please detail whether within group change scores over the intervention period were reported and their significance
- Sin et al., please provide a reference correlation coefficient (r or rho) used in the analysis conducted and comment on the strength of the association identified (moderate to strong) before addressing whether these were significant associations
- Strom et al., please provide the results of the within and between group analysis conducted

Table 5: please reconsider the label: Features of eHealth Interventions. Given the inclusion of the Shin et al. study this would be better labelled as Features of eHealth technologies and interventions employed in included studies.

**Results:**
The peer reviewers request further clarity with respect to the Glozier study in the participant characteristics section of the text. Here the Kessler-10 screening tool for psychological distress was used to identify individuals with CVD and a mental health condition identified as a K-10 >=16. As this tool screens for both symptoms of depression and anxiety, please justify the inclusion of this group under the summary of included participants with a depressive disorder.

In the risk of bias section in the text, please provide a summary of the quality of the observation studies. Results are difficult to interpret from the table provided. Please indicate whether the results generated indicate high or low quality in the included studies. This detail becomes more relevant when readers consider the best available evidence, in the absence of RCTs in the area.

**Discussion:**
The discussion section considers the findings of this review well and with broad consideration of the contemporary literature. As the primary finding of this review lies in a population of individuals with high psychological distress and concomitant CVD, the discussion would benefit from considering what is known with respect to eHealth technologies for promoting PA in CVD. Similarly where the association between higher levels of PA and clinical signs and symptoms is discussed, it would be worth exploring the broader PA in mental health literature to strengthen discussion in this area. Here the peer reviewers reiterate concerns in stating that increased PA levels are associated with improved clinical signs and symptoms. This is only possible where the studies have looked at the linear association between changes in clinical signs and symptoms and changes in PA levels and we believe the studies cited have not clearly addressed this.

In conclusion this systematic review was conducted with scientific rigour and makes a valuable
contribution to the scientific literature in the area. The authors, as a result of this review, provide valuable recommendations for future research with respect to PA measurement and intervention reporting that will enable better standardisation and data synthesis at a future date.

**Are the rationale for, and objectives of, the Systematic Review clearly stated?**
Partly

**Are sufficient details of the methods and analysis provided to allow replication by others?**
Yes

**Is the statistical analysis and its interpretation appropriate?**
Yes

**Are the conclusions drawn adequately supported by the results presented in the review?**
Partly

**Competing Interests:** No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

**Julie Broderick**, Trinity College Dublin, University of Dublin, Dublin, Ireland

We would very much like to thank the reviewers for their insightful comments

**Competing Interests:** No competing interests were disclosed.