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# BMJ Open

## A brief physical activity behaviour change intervention within routine clinical care for young people with depression (the IMPACT study): A cluster randomised controlled trial protocol

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3 **A brief physical activity behaviour change intervention within routine clinical care**  
4 **for young people with depression (the IMPACT study): A cluster randomised**  
5 **controlled trial protocol**  
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10 **Authors:**

11 Alexandra G. Parker<sup>1,2,3</sup>

12 Connie Markulev<sup>2,3</sup>

13 Debra Rickwood<sup>4,5</sup>

14 Andrew Mackinnon<sup>6,7</sup>

15 Rosemary Purcell<sup>2,3</sup>

16 Mario Alvarez-Jimenez<sup>2,3</sup>

17 Alison Yung<sup>2,3,8</sup>

18 Patrick McGorry<sup>2,3</sup>

19 Victoria Rayner<sup>2,3</sup>

20 Sarah E. Hetrick<sup>2,3,9\*</sup>

21 Anthony Jorm<sup>6\*</sup>

22 \* Joint senior authors  
23  
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35  
36 **Correspondence:** Alexandra G. Parker; E: [Alexandra.parker@vu.edu.au](mailto:Alexandra.parker@vu.edu.au); T: +61 3 9919 5874.  
37 Institute for Health and Sport, Victoria University, PO Box 14428, Melbourne, Victoria, 3001,  
38 Australia.  
39  
40  
41  
42

43 **Author affiliations:**

44 <sup>1</sup> Institute for Health and Sport, Victoria University, Melbourne, Australia

45 <sup>2</sup> Centre for Youth Mental Health, University of Melbourne, Melbourne, Australia

46 <sup>3</sup> Orygen, The National Centre of Excellence in Youth Mental Health, Melbourne, Australia

47 <sup>4</sup> University of Canberra, Canberra, Australia

48 <sup>5</sup> headspace National Youth Mental Health Foundation, Melbourne, Australia

49 <sup>6</sup> Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Australia

50 <sup>7</sup> Black Dog Institute, University of New South Wales, Sydney, Australia

51 <sup>8</sup> School of Health Sciences, University of Manchester, Manchester, United Kingdom

52 <sup>9</sup> Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand  
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## ABSTRACT

### Introduction

Depression is highly prevalent and the leading contributor to the burden of disease in young people worldwide, making it an ongoing priority for early intervention. As the current evidence-based interventions of medication and psychological therapy are only modestly effective, there is an urgent need for additional treatment strategies. This paper describes the rationale of the Improving Mood with Physical ACTivity (IMPACT) trial. The primary aim of the IMPACT trial is to test the effectiveness of a physical activity intervention compared with psycho-education, in addition to routine clinical care, on depressive symptoms in young people. Additional aims are to evaluate the intervention effects on anxiety and functional outcomes, and to examine whether changes in physical activity mediate improvements in depressive symptoms.

### Methods and analysis

The study is being conducted in six youth mental health services across Australia and is using a parallel-group, two arm cluster-randomised controlled trial (C-RCT) design, with randomisation occurring at the clinician level. Participants aged between 12 and 25 years with moderate to severe levels of depression are randomised to receive, in addition to routine clinical care, either: 1) a physical activity behaviour change intervention; or 2) psycho-education about physical activity. The primary outcome will be change in the Quick Inventory of Depressive Symptomatology, with assessments occurring at baseline, post-intervention (end-point), and 6-month follow-up from end-point. Secondary outcome measures will address additional clinical outcomes, functioning, and quality of life. IMPACT is to be conducted between 2014 and 2019.

### Ethics and dissemination

Ethical approval was obtained from the University of Melbourne Human Research Ethics Committee on 8 June 2014 (HREC 1442228). Trial findings will be published in peer-reviewed journals and presented at conferences. Key messages will also be disseminated by the youth mental health services organisation (headspace National Youth Mental Health Foundation).

**Trial registration number** ACTRN12614000772640

**Strengths and limitations of the study**

- The study is a cluster randomised controlled trial, which reduces the risk of contamination bias, and uses validated outcome measures
- The study is conducted in real-world clinical services, which increases the likelihood of translation into practice
- A large number of participants needs to be recruited to provide sufficient power to demonstrate a relevant effect size
- Limited capacity to provide ongoing supervision for clinicians in implementing the intervention

## BACKGROUND

Depression is highly prevalent<sup>1</sup> and is the leading cause of disability in young people worldwide<sup>2</sup>. Associated adverse consequences include impairments in academic attainment and achievement<sup>3</sup>, unemployment or underemployment<sup>3</sup>, and increased risk of self-harm and suicide<sup>4</sup>. Effective treatments have the potential to improve the health and functioning of young people and prevent the entrenchment of problems with relationships, education and health<sup>5</sup>. The current international evidence-based clinical practice guideline for treating depression in children and young people recommends cognitive behavioural therapy (CBT) as the first-line treatment for moderate to severe depression, with or without the anti-depressant medication, fluoxetine<sup>6</sup>. Recent evidence from meta-analyses of randomised controlled trials (RCTs) have shown the effect sizes of both CBT and anti-depressant medication are smaller than previously reported<sup>7-9</sup>. This suggests that many young people either fail to respond or do not show a clinically significant change even after receiving the best available guideline-recommended treatment delivered in controlled trials<sup>7 10</sup>.

With such modest effects of first-line treatments, there is a need for additional therapeutic strategies. One such strategy with an emerging evidence-base is exercise or physical activity as an augmentation or adjunct treatment<sup>11</sup>. Large cross-sectional and cohort studies show that less physically active young people are currently more likely to be depressed and are at greater risk of developing future depression<sup>12 13</sup>. Whilst insufficient physical activity places all young people at greater risk of poor physical health, including higher rates of cardiovascular disease, diabetes and premature death<sup>14 15</sup>, young people with depression are far more likely to be physically inactive than the general population, placing them at higher risk of long-term poorer physical health<sup>16 17</sup>. In addition to mental and physical health benefits, physical activity is a low-stigma intervention that has few side effects<sup>18 19</sup>. Both of these factors are important to help-seeking young people<sup>20</sup>.

There is strong evidence from RCTs and meta-analyses that physical activity is an effective intervention for depression in adults (standard mean difference (SMD)=1.135,  $p<.001$ )<sup>21</sup> and reduces the risk of suicidal ideation<sup>22</sup>. Although not as

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3 robust as the evidence base for adults<sup>21</sup>, physical activity interventions for young  
4 people with depression show similar findings<sup>23-25</sup>. A recent meta-analysis, conducted  
5 by members of our investigator team, of RCTs in young people aged 12-25 years  
6 established that physical activity is effective in reducing depression symptoms<sup>26</sup>.  
7 Data from 771 participants across 16 trials showed a large effect of supervised  
8 physical activity interventions on depression symptoms compared to controls in sub-  
9 threshold samples (SMD=-0.82,  $p<0.01$ ). The effect remained robust in 5 trials of  
10 young people with a diagnosis of depression (SMD=-0.72,  $p<0.01$ ). However, clinical  
11 applications are hindered by the majority of studies being of low quality, lack of  
12 longer-term follow-up and inadequate consideration of real-world implementation  
13 factors<sup>26</sup>.  
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25 Our group developed an intervention and evaluated it in the first RCT examining the  
26 potential benefits of low-intensity, simple psychological and unsupervised physical  
27 activity interventions for young people (N=176) with high prevalence mental health  
28 problems<sup>25</sup>, implemented within community-based youth mental health services.  
29 Conducted in two such services in the western region of Melbourne, Australia, the  
30 trial used a factorial design to compare the effects of a psychological intervention  
31 (problem solving therapy versus supportive counselling) and a physical activity  
32 intervention (behavioural change versus psychoeducation) delivered in up to 6 sessions  
33 (an average of 4.3 sessions were completed). Importantly, we recruited males and  
34 females, making this the first physical activity study to be conducted with young  
35 males with depression or anxiety symptoms. The physical activity intervention  
36 focused on addressing barriers to engaging in physical activity and creating  
37 individualised activity plans. Post-intervention data showed the main effect of the  
38 physical activity intervention was significant when compared to the control condition  
39 (psycho-education), resulting in a clinically meaningful reduction in depression  
40 symptoms with a medium effect size ( $d=0.41$ ; (95% CI: 0.07 – 0.76)), measured by  
41 the Beck Depression Inventory<sup>27</sup>. Those in the physical activity intervention group  
42 reported the greatest improvement regardless of the type of psychological  
43 intervention received<sup>25</sup>. However, it is important to note that the physical activity  
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3 intervention was delivered in conjunction with manualised psychological therapies  
4 by research therapists rather than as part of routine clinical care.  
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### 8 **Study Rationale**

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10 Current first-line treatments for depression in young people are, at best, modestly  
11 effective. Augmentation with an additional intervention such as physical activity is a  
12 strong candidate to improve response to treatment. The results from our earlier  
13 study indicate that physical activity in combination with psychological treatment is  
14 effective in reducing depression symptoms in young people<sup>25</sup>. However, as clinicians  
15 do not routinely include physical activity interventions in standard care<sup>28</sup>, the  
16 opportunity to improve depression and functional outcomes and prevent poor  
17 physical health for young people with depression may be missed<sup>13 28</sup>. This lack of  
18 integration likely occurs because clinicians are not aware of the evidence, are unsure  
19 how to implement physical activity interventions, or lack the time and resources<sup>28 29</sup>.  
20 By providing training and clinical resources, the objective of the current study is to  
21 determine the effectiveness of a physical activity behaviour change intervention  
22 when used as an adjunct to routine clinical care, delivered in real-world mental  
23 health contexts.  
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### 38 **METHODS AND ANALYSIS**

#### 39 **Study aims**

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41 The aims of this study are to test the effectiveness of a physical activity behaviour  
42 change intervention, compared to psycho-education about physical activity, in  
43 addition to routine clinical care in improving depressive symptoms [primary  
44 outcome] in young help-seekers with depression. Secondary outcomes include the  
45 effects of the intervention on anxiety symptoms and functioning; and to examine  
46 whether changes in physical activity mediate improvements in depressive symptoms.  
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#### 52 **Study design**

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54 The study will use a parallel group, two arm cluster-randomised controlled trial (C-  
55 RCT) design to test the effect of the physical activity intervention compared to  
56 psycho-education, in addition to routine clinical care, with randomisation occurring  
57 at the clinician level (see figure 1). Randomising clinicians will reduce the  
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3 contamination associated with clinicians concurrently managing intervention and  
4 control participants, as would occur in a standard patient randomised trial<sup>30</sup>.  
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6 Assessment time points will be at baseline, intervention end-point [primary  
7 outcome], and 6-months (follow up). The trial has well-defined objectives and  
8 protocols addressing Good Clinical Practice (GCP)<sup>31</sup> and SPIRIT guidelines<sup>32</sup>. Patients  
9 or the public were not involved in the design, or conduct, or reporting, or  
10 dissemination of our research.  
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18 ***Insert Figure 1 about here***

### 21 **Setting**

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23 *headspace* centres are accessible, community-based mental health services that  
24 support young people aged 12-25 years, funded by the Australian federal  
25 government<sup>33</sup>. Services are delivered in a youth-friendly environment staffed by a  
26 range of service providers, including general practitioners, psychologists,  
27 psychiatrists, youth workers, mental health nurses and other allied health  
28 professionals. *headspace* centres assess approximately 850 new patients per year,  
29 40% presenting with depression<sup>34</sup>. A subset of approximately 6 of the more than 100  
30 *headspace* centres will be involved in this study.  
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### 40 **Participant and recruitment procedures**

#### 41 **Clinicians**

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43 All allied health professionals, including psychologists, social workers and  
44 occupational therapists ('clinicians'), who provide mental health treatments to young  
45 people in the participating *headspace* centres will be invited to participate in the  
46 study and will be randomised to deliver either the intervention group (physical  
47 activity behaviour change) or the control group (psycho-education), in addition to  
48 routine clinical care. Clinicians in predominantly intake and assessment roles will not  
49 be included.  
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#### 56 **Participants**

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58 All help-seeking young people aged 12-25 who present to participating *headspace*  
59 centres will be screened for eligibility. We aim to recruit a total of 960 participants.  
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3 Informed consent will be obtained from all participants; those aged between 15 and  
4 18 years will be assessed for mature minor capacity<sup>35</sup> during the intake assessment  
5 procedure at entry to the service and, if they meet this threshold, will be able to  
6 make the decision whether or not to consent to participate. Those aged 12-14 years  
7 can provide assent to participate but will also require parental/legal guardian  
8 consent. After obtaining informed consent, participants will be screened by research  
9 assistants who will: a) assess the eligibility of the young person; and b) collect  
10 outcome data (interview and self-report) at baseline, post-treatment and 6-month  
11 follow-up assessments.  
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### 22 **Inclusion, exclusion and discontinuation criteria**

#### 23 Inclusion criteria

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25 (i) meeting the requirements for a Mental Health Treatment Plan (MHTP) to access  
26 up to 10 sessions of psychological treatment under the Medicare Benefits Scheme  
27 Better Access program per annum<sup>36</sup>; and (ii) a Quick Inventory of Depressive  
28 Symptomatology-Adolescent (17 item) - Clinician Rated (QIDS-A17-C)<sup>37</sup> score of 11 or  
29 greater, indicating depression levels of moderate or above.  
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#### 34 Exclusion criteria

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36 (i) presence of a psychotic disorder or eating disorder during the intake assessment  
37 upon first presentation to the *headspace* centre<sup>38</sup>; (ii) current physical activity  
38 meeting the Australian Government Guidelines (i.e., for those under 18 years, 60  
39 min of moderate to vigorous activity every day; for those over 18 years, 30 min of  
40 moderate activity at least 5 times for week)<sup>39 40</sup>; (iii) physical illness that contra-  
41 indicates participation in physical activity; iv) organic mental disorder; and (v)  
42 intellectual disability/cognitive impairment that precludes providing informed  
43 consent; as assessed by the *headspace* intake and access team members and the  
44 study's research assistants, and referred for review to the study site's Principal  
45 Investigator or clinical review team. Any young person reporting a prior history of  
46 physical illness that might impede their ability to take part in physical activity will be  
47 required to receive medical clearance from a general practitioner in order to  
48 participate in the trial.  
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#### 60 Discontinuation criteria

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3 (i) incidence of a psychotic disorder or eating disorder meeting diagnostic threshold;  
4 or (ii) physical illness that contra-indicates participation in physical activity, as  
5 assessed by the treating clinicians during the course of the intervention.  
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7 Discontinuation from the active or control interventions can be at the request of the  
8 participant or if any changes in the participant's presentation warrants a referral to  
9 another service, as determined by their treating clinician or clinical review team.  
10 These participants will discontinue their assigned intervention, but will remain  
11 involved in the post-intervention assessment.  
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## 20 **Interventions**

21 The interventions will be integrated into routine clinical care and delivered by a  
22 *headspace* clinician, which may also include probationary psychologists (graduate  
23 trainees) on clinical placement. The current funding rules of the Medicare Benefits  
24 Schedule allow for 6 sessions of psychological treatment (plus an additional 4 if  
25 clinically warranted) per calendar year. We anticipate that the interventions (both  
26 physical activity and control) will be delivered in an average of 4 treatment sessions  
27 across approximately 4-6 weeks, consistent with the average national attendance  
28 rates to *headspace* centres<sup>41</sup>. The intervention will be capped at a maximum of 10  
29 sessions. The active and control interventions have been described to meet the  
30 Template for Intervention Description and Replication (TIDieR) standards<sup>42</sup>. At the  
31 first treatment session, participants will be provided with relevant materials and  
32 resources according to the treatment condition to which their treating clinician has  
33 been assigned.  
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### 48 **Physical activity intervention**

49 Participants who receive treatment from a clinician who has been allocated to this  
50 group will receive a manualised integrated physical activity behaviour change  
51 intervention, as per the training delivered to the clinicians, within their psychological  
52 treatment sessions. Treatment sessions will be delivered face-to-face and onsite at  
53 each participating *headspace* centre. The IMPACT treatment manual includes  
54 evidence-based behaviour change techniques, targeting self-regulation (planning,  
55 organising), motivation, enjoyment and tailoring for individual needs<sup>43 44</sup>.

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3 Participants will be encouraged to set short- and longer-term specific and  
4 measureable goals; monitor progress towards these goals; discuss the benefits of  
5 physical activity; consider factors that may facilitate their participation (e.g., enlisting  
6 support from others, choosing physical activities that are enjoyable<sup>44 45</sup>); and identify  
7 potential barriers and strategies for overcoming these barriers. Clinicians will review  
8 weekly goals, participants' self-monitoring of mood pre- and post-activity,  
9 addressing barriers and enhancing individual facilitators, reinforcing achievements  
10 and revising physical activity plans, in each weekly session of psychological  
11 treatment to facilitate an increase in engagement in physical activity<sup>46</sup>. The  
12 intervention is designed to be delivered within 15-20 minutes to the initial session,  
13 with 5-10 minutes' duration in subsequent sessions. Given the real-world nature of  
14 the intervention context, it is not possible to define the frequency of sessions or  
15 duration of the intervention period *a priori*, due to variation in each of the study  
16 sites in terms of allocation to clinicians, managing service demands and appointment  
17 scheduling.

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33 Participants will receive verbal and written information about the relationship  
34 between depressive symptoms and exercise<sup>47</sup>; access to online resources providing  
35 advice and instructions on physical activities; minimal equipment (resistance band  
36 for resistance activity and skipping rope for cardiovascular physical activity); written  
37 worksheets and resources to enhance motivation, address barriers and provide  
38 physical activity suggestions, including the current Australian national physical  
39 activity and sedentary behaviour guidelines<sup>48 49</sup>; and a weekly planner to discuss and  
40 plan for how and when the physical activity can be completed, and any memory aids  
41 that could be used to aid in completion of this (including mobile technology  
42 applications ('apps')).

#### 51 52 53 Psycho-education intervention

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55 Participants who receive treatment from a clinician who has been allocated to this  
56 group will be provided with the same psycho-education about the relationship  
57 between depressive symptoms and physical activity as the intervention group,  
58 within the first treatment session only. Treatment sessions will be delivered face-to-  
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3 face and onsite at each participating *headspace* centre. The inclusion of the control  
4 group intervention is to examine whether the provision of information about  
5 physical activity for mental health and minimal resources is sufficient for participants  
6 to increase their current levels of physical activity. This will include providing the  
7 same verbal and written information about the relationship between depressive  
8 symptoms and exercise<sup>47</sup>; minimal equipment (resistance band for resistance activity  
9 and skipping rope for cardiovascular physical activity); and physical activity  
10 suggestions, including the current Australian national physical activity and sedentary  
11 behaviour guidelines<sup>48 49</sup>, that will be provided to the intervention group. The  
12 importance of physical activity for depression will be addressed in the first session  
13 but will not be included in ongoing treatment.  
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### 25 **Study hypotheses**

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27 Primary: that the physical activity intervention will lead to greater reductions in  
28 depressive symptoms compared psycho-education on physical activity, in addition to  
29 routine clinical care;  
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32 Secondary: a) that the physical activity intervention will lead to greater reductions in  
33 anxiety symptoms and greater improvements in functioning, when compared to the  
34 control condition; and b) that changes in depressive symptoms will be mediated by  
35 increases in physical activity.  
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### 42 **Primary outcome**

43 The *primary outcome* will be level of depression symptoms post-intervention and at  
44 6 month follow-up, measured by the Quick Inventory of Depressive  
45 Symptomatology-Adolescent (17 item) Clinician Rated (QIDS-A17-C)<sup>37</sup>.  
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### 49 **Secondary outcomes**

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51 *Physical Activity (mediator)*: levels of physical activity measured by the International  
52 Physical Activity Questionnaire<sup>50</sup> and an electronic accelerometer device worn for 5-  
53 7 days;  
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56 *Mental health and substance use*: anxiety symptoms measured by the Overall  
57 Anxiety Severity and Impairment Scale<sup>51</sup>; depression module from the SCID-IV<sup>52</sup>; and  
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3 substance use measured by the WHO Alcohol, Smoking and Substance Involvement  
4 screening test (ASSIST).

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6 *Anthropomorphic and lifestyle variables:* height, weight and hip and waist  
7 measurements to determine Body Mass Index and hip/waist ratio; Pittsburgh Sleep  
8 Quality Index<sup>53</sup>; and the Simple Dietary Questionnaire.

9  
10 *Functioning:* Social and Occupational Functional Assessment Scale<sup>54</sup>; and Australian  
11 Quality of Life scale (AQoL 6d) for adolescents<sup>55</sup>, to facilitate future cost utility and  
12 other economic analyses.

13  
14 *Variables that will be the subject of subsequent exploratory analyses include:* self-  
15 efficacy measured by General Self Efficacy Scale<sup>56</sup> and Barriers Self-Efficacy Scale  
16 (physical activity)<sup>57</sup>; Perceived Social Support Scale; Positive and Negative Affect  
17 Schedule<sup>58</sup>) Cognitive and Behavioural Therapy Skills Questionnaire<sup>59</sup>; Behavioural  
18 Activation for Depression Scale<sup>60</sup>; Montgomery Asberg Depression Rating Scale<sup>61</sup>;  
19 and Working Alliance Inventory (therapeutic alliance)<sup>62</sup>; and the Trail Making Test A  
20 & B<sup>63 64</sup> to assess attention, processing speed and mental flexibility.

21  
22 Assessments and measures will be conducted as per the assessment schedule: i)  
23 screening for eligibility; ii) baseline, post-intervention (end-point) and 6-month  
24 follow-up assessments. Data from participating young people will be entered into a  
25 project-specific secure online database at all assessment time-points, using a  
26 reversible process in which the identifiers are removed and replaced by a code.

## 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 **Process and implementation measures**

### 44 45 Training

46  
47 All participating clinicians will be trained in GCP and IMPACT study procedures,  
48 delivered in a 1.5-hour session in face-to-face format. Additionally, all participating  
49 clinicians will participate in a further 30-minute training session on how to deliver  
50 the psycho-education on physical activity and share resources with participants in  
51 the study. Following this, all clinicians who are randomised to the physical activity  
52 intervention group will take part in an additional 60-minute training session to  
53 integrate the IMPACT intervention into routine clinical care. For the intervention  
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3 group, skills, knowledge and attitudes will be assessed before and after the training  
4 session, measured by the Theoretical Domains Framework questionnaire<sup>65</sup>.  
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9 The face-to-face training will be supported by additional online resources using a  
10 learning management system that will host an electronic version of the intervention  
11 manual, project resources, training videos and case vignettes. The training will  
12 incorporate practice recommendations for delivering physical activity behaviour  
13 change interventions for mental health, including: a) creating individual training  
14 plans to increase adherence and aim to increase physical activity levels and decrease  
15 sedentary behaviours, b) integrating the physical activity intervention into routine  
16 psychoeducation and psychotherapy; c) incorporating evidence-based behaviour  
17 change techniques, targeting self-regulation (planning, organising), motivation,  
18 enjoyment and tailoring for individual needs<sup>43 44</sup>. Clinicians will be provided with a  
19 comprehensive IMPACT treatment manual<sup>66</sup> and the resources required to deliver  
20 the intervention (handouts, worksheets, and access to online materials). Clinicians in  
21 the control condition will not have access to the online support materials.  
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### 34 Fidelity

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36 Fidelity will be assessed using a brief checklist to be completed by clinicians after  
37 each session to estimate time spent on the intervention and the type of  
38 psychological treatment that was delivered as part of routine care (e.g., CBT,  
39 interpersonal therapy, etc). Fidelity will also be assessed by audio recording of all  
40 treatment sessions, with a random subset of 10% of the recordings to be coded by  
41 an independent rater for adherence to the treatment manual and to discriminate  
42 between the intervention and control conditions. Fidelity will be maintained by  
43 offering quarterly online group peer supervision sessions for the clinicians in the  
44 intervention group to allow group discussion and case presentations, in addition to  
45 the face-to-face training at the commencement of the trial. Less frequent peer  
46 supervision (approximately every 6 months) will be offered to the control group  
47 clinicians. Fidelity of the intervention will also be assessed using a checklist of  
48 components of the active and control conditions collected from participants at the  
49 post-intervention assessment. In addition, at the end of the intervention period, a  
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3 subgroup of physical activity intervention group clinicians and young people will be  
4 invited to participate in semi-structured interviews to explore their experiences of  
5 delivering and receiving the intervention, respectively.  
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### 10 **Randomisation and allocation to treatment**

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12 Clinicians will be allocated to the intervention and control groups using a  
13 minimisation procedure commencing with random assignment<sup>67</sup>. The procedure  
14 was devised by the study statistician (AM) and will be carried out by an independent  
15 researcher, following the ICH Guideline<sup>68</sup>, to ensure allocation concealment.  
16 Minimisation factors to be incorporated are gender of clinician (2 level factor,  
17 male/female), background training of clinician (2 level factor, psychologist/non-  
18 psychologist) and *headspace* centre, to ensure equal numbers in each intervention at  
19 each site (6 centres). Participants will be stratified by age ( $\leq 17$ , 18+), gender  
20 (male/female) and QIDS-A17-C score ( $\leq 15$ , 16+). Participants will be assigned to a  
21 clinician based on a randomised list. Due to the nature of the intervention, it will not  
22 be possible to blind the clinicians and participants; however, all pre-, post-  
23 intervention and follow-up assessments will be conducted by research assistants  
24 blinded to treatment allocation. Investigators not involved in the delivery of the  
25 intervention and the trial statistician will be blind to group allocation until the  
26 analysis is completed.  
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### 41 **Statistical analysis**

#### 42 Analysis plan

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44 Primary quantitative analyses will be undertaken on an intent-to-treat basis,  
45 including all participants as randomised, regardless of treatment received or  
46 withdrawal from the study. Linear mixed models will be used to analyse change in  
47 the primary outcome measure (QIDS-A17-C). Models will include a random 'clinician'  
48 factor. Correlation of repeated outcome measures will be accommodated using an  
49 unstructured variance-covariance matrix. An *a priori* planned comparison of change  
50 from baseline to the post-intervention assessment will be used to test the primary  
51 hypothesis. Comparison of change from baseline to follow-up between arms will be  
52 undertaken as a secondary outcome analysis. Factors used in assignment by  
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3 minimisation (clinician gender, discipline, and *headspace* centre) will be introduced  
4 in models as covariates and retained if significant. Variables associated with  
5 participant missingness or found to be substantially imbalanced between groups will  
6 be included in models on an exploratory basis<sup>69</sup>.  
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12 Mathematical transformation or categorisation of raw scores will be undertaken to  
13 meet distributional assumptions and address any violation of assumptions required  
14 in mixed models. When transformations have been undertaken to better meet  
15 distribution assumptions, models using the transformed data will be considered the  
16 main test of the primary hypotheses. Mixed models use all available data and do not  
17 involve any substitution of missing values with supposed or estimated values. The  
18 assumptions underlying mixed modelling allow 'missingness' to be related to  
19 observed variables in the analysis but not to unobserved values (termed 'missing at  
20 random')<sup>70</sup>.  
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31 Similar analyses of scaled secondary measures will assess differential change due to  
32 intervention arm. For dichotomous outcomes such as diagnoses and ordinal or count  
33 outcomes, comparable generalised mixed modelling approach will be used. Relative  
34 and reduction in risk of depression based on SCID diagnostic status will be estimated  
35 at the trial endpoint and follow-up. Numbers needed to treat will be derived from  
36 these values. All analyses will use two-sided tests, with an alpha value set at 0.05. In  
37 the event of substantial missingness, sensitivity analyses based on identified  
38 clinically plausible mechanisms may be undertaken to determine the robustness of  
39 findings.  
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49 Qualitative analyses of the semi-structured interviews included within the process  
50 and implementation measures will be undertaken on audio recorded interviews that  
51 will be transcribed verbatim, with data analysed using thematic analysis<sup>71</sup>.  
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### 56 **Power analysis**

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58 Calculations of required sample size were based on detecting a post-intervention  
59 effect size of 0.34, which is at the lower boundary of utility and also reflects the  
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3 adjunctive status of the intervention. Power was set at .90, alpha = .05 (two-tailed)  
4 and correlation of .5 assumed between pre-treatment and post-treatment scores. To  
5 allow for possible clustering effects (participants with the same therapist having  
6 characteristics and outcomes more alike than between therapists) a design effect<sup>72</sup>  
7 was calculated assuming an intraclass correlation (ICC) of 0.05 and the number of  
8 clients per therapist up to 24. The estimate of the ICC is at the upper range of  
9 therapist effects and is conservative given the prescribed, manualised nature of the  
10 intervention. It is anticipated that 6-8 clinicians per *headspace* centre will be  
11 involved in the study. The resultant design effect of 2.15 reflects the possible non-  
12 independence of cluster-sampled participants and was used to inflate the calculated  
13 sample size, which assumes independence. The estimated required sample size was  
14 784. To accommodate a potential attrition/withdrawal rate of up to 20%, the target  
15 sample size was set at 960, or 480 participants per condition.  
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### 29 **Safety Procedures and Oversight**

30 Each participating *headspace* centre will have a Principal Site Investigator and will  
31 also be required to nominate a lead clinician who will be responsible for the  
32 oversight of participant safety during the course of the trial. Withdrawal from the  
33 study can be at the request of the participant or if the participant meets  
34 discontinuation criteria. Once withdrawn, the young person will be reviewed using  
35 the *headspace* centre's standard clinical review procedure and either maintained in  
36 the *headspace* centre or referred to other services as necessary. Any *adverse*  
37 *incident*, any serious or unanticipated adverse effects of the research on study  
38 participants, and unforeseen events that might affect continued ethical acceptability  
39 of the project, will be captured and reported until resolution, stabilisation or the  
40 participant is lost to follow-up, unless the condition is unlikely to resolve as per the  
41 opinion of the medical practitioner appointed by the study sponsor to monitor  
42 adverse incidents. In the event of an adverse incident or unexpected outcome, the  
43 allied health professional or research personnel will report to the study Sponsor,  
44 Orygen. If necessary, a decision will be made as to whether to withdraw or suspend  
45 participation. The study Sponsor will conduct annual centralised monitoring visits of  
46 the study sites.  
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## DISCUSSION

Depressive disorders are highly prevalent and are the leading cause of disability in young people worldwide. If effective, the physical activity intervention tested in this C-RCT has the potential to improve the immediate outcomes for young people with depression by providing an additive treatment effect in conjunction with routine clinical care. Additional benefits may include improvements in social and vocational functioning, thereby reducing the likelihood of longer-term damage in these domains.

The IMPACT intervention is easily scalable. As it is set within the national network of *headspace* centres, this will increase the likelihood that any benefits are translated into routine clinical practice for the many thousands of young people who access *headspace* services per annum. There is also potential to adapt the intervention for other service delivery models (e.g. primary care, tertiary mental health services) nationally and internationally – including to regional and remote areas – which may be of interest to policy makers and those funding mental health programs or services.

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3 **Author contributions:** AGP led the development of this manuscript. AGP, DR, AM,  
4 RP, MAJ, ARY, PM, SEH and AJ secured the funding for the project and, together with  
5 author CM, devised the research design and measures. AGP, CM, DR, RP, MAJ, AY,  
6 PM, SEH and AJ were involved in devising the intervention content and intervention  
7 implementation strategies, which were based on those established and previously  
8 operated by AGP, RP, ARY, PM, SEH and AJ. AM was primarily responsible for the  
9 sample size and power calculations and development of proposed statistical  
10 analyses. AGP wrote the initial draft of the manuscript. All authors contributed to  
11 and approved the final version of the manuscript.  
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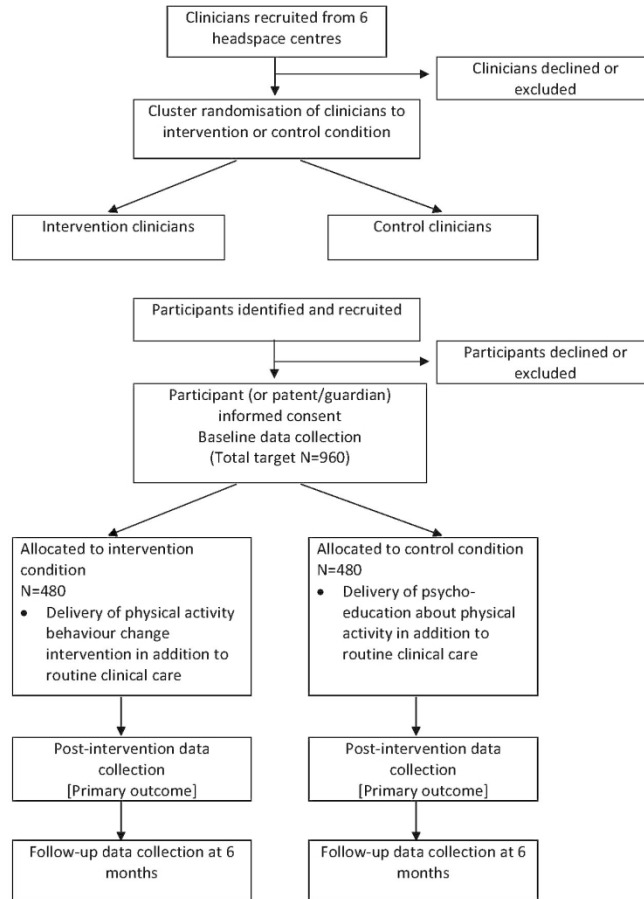
45 **Study sponsor:** The study is sponsored by the Sponsor Operations Department,  
46 Orygen, The National Centre of Excellence in Youth Mental Health. Contact details:  
47 35 Poplar Road, Parkville, Victoria, Australia 3052. The study sponsor has had no role  
48 in the study design or the decision to submit the manuscript for publication. A risk  
49 assessment of the study conducted by the study sponsor determined that a data  
50 monitoring committee was not needed due to the low-risk nature of the  
51 intervention.  
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3 **Ethics approval:** Full ethics clearances have been received for all methods described  
4 in the manuscript from the University of Melbourne's Human Research Ethics  
5 Committee HREC 1442228 (2014-2019) (Protocol Version 1, 22 May 2014). Revisions  
6 to the study protocol will be enacted once approval from the HREC has been  
7 received and reported in the trial registry by the study's clinical trial managers (CM,  
8 VR).

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16 **Competing interests:** The authors have no competing interests to declare.  
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For peer review only



**Figure 1**  
Flow chart of clinician and participant recruitment and study timeline

**Figure 1**  
Flow chart of clinician and participant recruitment and study timeline

209x297mm (200 x 200 DPI)

# BMJ Open

**Protocol of the Improving Mood with Physical ACTivity (IMPACT) trial: A cluster randomised controlled trial to determine the effectiveness of a brief physical activity behaviour change intervention on depressive symptoms in young people, compared to psycho-education, in addition to routine clinical care within youth mental health services**

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Complete List of Authors:	Parker, Alexandra; Victoria University, Institute for Health and Sport; The University of Melbourne, Centre for Youth Mental Health Markulev, Connie; The University of Melbourne, Centre for Youth Mental Health; Orygen The National Centre of Excellence in Youth Mental Health Rickwood, Debra; University of Canberra, Psychology; headspace National Youth Mental Health Foundation Ltd Mackinnon, Andrew; The University of Melbourne School of Population and Global Health; Black Dog Institute, The University of New South Wales Purcell, Rosemary; Orygen The National Centre of Excellence in Youth Mental Health; The University of Melbourne, Centre for Youth Mental Health Alvarez-Jimenez, Mario; Orygen, The National Centre of Excellence in Youth Mental Health; The University of Melbourne, Centre for Youth Mental Health Yung, Alison; Orygen The National Centre of Excellence in Youth Mental Health; The University of Manchester, School of Health Sciences McGorry, Patrick; Orygen, The National Centre of Excellence in Youth Mental Health; University of Melbourne, Centre for Youth Mental Health Hetrick, Sarah; University of Auckland, Department of Psychological Medicine; Orygen The National Centre of Excellence in Youth Mental Health Jorm, A; The University of Melbourne School of Population and Global Health
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3 **Protocol of the Improving Mood with Physical ACTivity (IMPACT) trial: A cluster**  
4 **randomised controlled trial to determine the effectiveness of a brief physical activity**  
5 **behaviour change intervention on depressive symptoms in young people, compared**  
6 **to psycho-education, in addition to routine clinical care within youth mental health**  
7 **services**  
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14 **Authors:**

15  
16 Alexandra G. Parker<sup>1,2,3</sup>

17  
18 Connie Markulev<sup>2,3</sup>

19  
20 Debra Rickwood<sup>4,5</sup>

21  
22 Andrew Mackinnon<sup>6,7</sup>

23  
24 Rosemary Purcell<sup>2,3</sup>

25  
26 Mario Alvarez-Jimenez<sup>2,3</sup>

27  
28 Alison R. Yung<sup>2,3,8</sup>

29  
30 Patrick McGorry<sup>2,3</sup>

31  
32 Sarah E. Hetrick<sup>2,3,9\*</sup>

33  
34 Anthony Jorm<sup>6\*</sup>

35  
36 \* Joint senior authors

37  
38 **Correspondence:** Alexandra G. Parker; E: [Alexandra.parker@vu.edu.au](mailto:Alexandra.parker@vu.edu.au); T: +61 3 9919 5874.  
39  
40 Institute for Health and Sport, Victoria University, PO Box 14428, Melbourne, Victoria, 3001,  
41  
42 Australia.

43  
44 **Author affiliations:**

45  
46 <sup>1</sup> Institute for Health and Sport, Victoria University, Melbourne, Australia

47  
48 <sup>2</sup> Centre for Youth Mental Health, University of Melbourne, Melbourne, Australia

49  
50 <sup>3</sup> Orygen, The National Centre of Excellence in Youth Mental Health, Melbourne, Australia

51  
52 <sup>4</sup> University of Canberra, Canberra, Australia

53  
54 <sup>5</sup> headspace National Youth Mental Health Foundation, Melbourne, Australia

55  
56 <sup>6</sup> Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Australia

57  
58 <sup>7</sup> Black Dog Institute, University of New South Wales, Sydney, Australia

59  
60 <sup>8</sup> School of Health Sciences, University of Manchester, Manchester, United Kingdom

<sup>9</sup> Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

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5 **ABSTRACT**  
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7 **Introduction**  
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9 Depression is highly prevalent and the leading contributor to the burden of disease in  
10 young people worldwide, making it an ongoing priority for early intervention. As the  
11 current evidence-based interventions of medication and psychological therapy are  
12 only modestly effective, there is an urgent need for additional treatment strategies.  
13 This paper describes the rationale of the Improving Mood with Physical ACTivity  
14 (IMPACT) trial. The primary aim of the IMPACT trial is to determine the effectiveness  
15 of a physical activity intervention compared with psycho-education, in addition to  
16 routine clinical care, on depressive symptoms in young people. Additional aims are to  
17 evaluate the intervention effects on anxiety and functional outcomes, and examine  
18 whether changes in physical activity mediate improvements in depressive symptoms.  
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27 **Methods and analysis**  
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29 The study is being conducted in six youth mental health services across Australia and  
30 is using a parallel-group, two arm cluster-randomised controlled trial (C-RCT) design,  
31 with randomisation occurring at the clinician level. Participants aged between 12 and  
32 25 years with moderate to severe levels of depression are randomised to receive, in  
33 addition to routine clinical care, either: 1) a physical activity behaviour change  
34 intervention; or 2) psycho-education about physical activity. The primary outcome will  
35 be change in the Quick Inventory of Depressive Symptomatology, with assessments  
36 occurring at baseline, post-intervention (end-point), and 6-month follow-up from end-  
37 point. Secondary outcome measures will address additional clinical outcomes,  
38 functioning, and quality of life. IMPACT is to be conducted between May 2014 and  
39 December 2019.  
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49 **Ethics and dissemination**  
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51 Ethical approval was obtained from the University of Melbourne Human Research  
52 Ethics Committee on 8 June 2014 (HREC 1442228). Trial findings will be published in  
53 peer-reviewed journals and presented at conferences. Key messages will also be  
54 disseminated by the youth mental health services organisation (headspace National  
55 Youth Mental Health Foundation).  
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60 **Trial registration number** ACTRN12614000772640



### Strengths and limitations of the study

- The study is a cluster randomised controlled trial, which reduces the risk of contamination bias, and uses validated outcome measures
- The study is conducted in real-world clinical services, which increases the likelihood of translation into practice
- A large number of participants needs to be recruited to provide sufficient power to demonstrate a relevant effect size
- Limited capacity to provide ongoing supervision for clinicians in implementing the intervention

## BACKGROUND

Depression is highly prevalent<sup>1</sup> and is the leading cause of disability in young people worldwide<sup>2</sup>. Associated adverse consequences include impairments in academic attainment and achievement<sup>3</sup>, unemployment or underemployment<sup>3</sup>, and increased risk of self-harm and suicide<sup>4</sup>. Effective treatments have the potential to improve the health and functioning of young people and prevent the entrenchment of problems with relationships, education and health<sup>5</sup>. The current international evidence-based clinical practice guideline for treating depression in children and young people recommends cognitive behavioural therapy (CBT) as the first-line treatment for moderate to severe depression, with or without the anti-depressant medication, fluoxetine<sup>6</sup>. Recent evidence from meta-analyses of randomised controlled trials (RCTs) have shown the effect sizes of both CBT and anti-depressant medication are smaller than previously reported<sup>7-9</sup>. This suggests that many young people either fail to respond or do not show a clinically significant change even after receiving the best available guideline-recommended treatment delivered in controlled trials<sup>7 10</sup>.

With such modest effects of first-line treatments, there is a need for additional therapeutic strategies. One such strategy with an emerging evidence-base is exercise or physical activity as an augmentation or adjunct treatment<sup>11</sup>. Large cross-sectional and cohort studies show that less physically active young people are currently more likely to be depressed and are at greater risk of developing future depression<sup>12 13</sup>. Whilst insufficient physical activity places all young people at greater risk of poor physical health, including higher rates of cardiovascular disease, diabetes and premature death<sup>14 15</sup>, young people with depression are far more likely to be physically inactive than the general population, placing them at higher risk of long-term poorer physical health<sup>16 17</sup>. In addition to mental and physical health benefits, physical activity is a low-stigma intervention that has few side effects<sup>18 19</sup>. Both of these factors are important to help-seeking young people<sup>20</sup>.

There is strong evidence from RCTs and meta-analyses that physical activity is an effective intervention for depression in adults (standard mean difference (SMD)=1.135,  $p<.001$ )<sup>21</sup> and reduces the risk of suicidal ideation<sup>22</sup>. Although not as

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3 robust as the evidence base for adults<sup>21</sup>, physical activity interventions for young  
4 people with depression show similar findings<sup>23-25</sup>. A recent meta-analysis, conducted  
5 by members of our investigator team, of RCTs in young people aged 12-25 years  
6 established that physical activity is effective in reducing depression symptoms<sup>26</sup>. Data  
7 from 771 participants across 16 trials showed a large effect of supervised physical  
8 activity interventions on depression symptoms compared to controls in sub-threshold  
9 samples (SMD=-0.82,  $p<0.01$ ). The effect remained robust in 5 trials of young people  
10 with a diagnosis of depression (SMD=-0.72,  $p<0.01$ ). However, clinical applications are  
11 hindered by the majority of studies being of low quality, lack of longer-term follow-up  
12 and inadequate consideration of real-world implementation factors<sup>26</sup>.  
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23 Our group developed an intervention and evaluated it in the first RCT examining the  
24 potential benefits of low-intensity, simple psychological and unsupervised physical  
25 activity interventions for young people (N=176) with high prevalence mental health  
26 problems<sup>25</sup>, implemented within community-based youth mental health services.  
27 Conducted in two such services in the western region of Melbourne, Australia, the trial  
28 used a factorial design to compare the effects of a psychological intervention (problem  
29 solving therapy versus supportive counselling) and a physical activity intervention  
30 (behavioural change versus psychoeducation) delivered in up to 6 sessions (an average  
31 of 4.3 sessions were completed). Importantly, we recruited males and females,  
32 making this the first physical activity study to be conducted with young males with  
33 depression or anxiety symptoms. The physical activity intervention focused on  
34 addressing barriers to engaging in physical activity and creating individualised activity  
35 plans. Post-intervention data showed the main effect of the physical activity  
36 intervention was significant when compared to the control condition (psycho-  
37 education), resulting in a clinically meaningful reduction in depression symptoms with  
38 a medium effect size ( $d=0.41$ ; 95% CI: 0.07 – 0.76), measured by the Beck Depression  
39 Inventory<sup>27</sup>. Those in the physical activity intervention group reported the greatest  
40 improvement regardless of the type of psychological intervention received<sup>25</sup>. However,  
41 it is important to note that the physical activity intervention was delivered in  
42 conjunction with manualised psychological therapies by research therapists rather  
43 than as part of routine clinical care.  
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## Study Rationale

Current first-line treatments for depression in young people are, at best, modestly effective. Augmentation with an additional intervention such as physical activity is a strong candidate to improve response to treatment. The results from our earlier study indicate that physical activity in combination with psychological treatment is effective in reducing depression symptoms in young people<sup>25</sup>. However, as clinicians do not routinely include physical activity interventions in standard care<sup>28</sup>, the opportunity to improve depression and functional outcomes and prevent poor physical health for young people with depression may be missed<sup>13 28</sup>. This lack of integration likely occurs because clinicians are not aware of the evidence, are unsure how to implement physical activity interventions, or lack the time and resources<sup>28 29</sup>. By providing training and clinical resources, the objective of the current study is to determine the effectiveness of a physical activity behaviour change intervention when used as an adjunct to routine clinical care, delivered in real-world mental health contexts.

## METHODS AND ANALYSIS

### Study aims

The aims of this study are to test the effectiveness of a physical activity behaviour change intervention, compared to psycho-education about physical activity, in addition to routine clinical care in improving depressive symptoms [primary outcome] in young help-seekers with depression. Secondary outcomes include the effects of the intervention on anxiety symptoms and functioning; and to examine whether changes in physical activity mediate improvements in depressive symptoms.

### Study design

The study will use a parallel group, two arm cluster-randomised controlled trial (C-RCT) design to test the effect of the physical activity intervention compared to psycho-education, in addition to routine clinical care, with randomisation occurring at the clinician level (see figure 1). Randomising clinicians will reduce the contamination associated with clinicians concurrently managing intervention and control participants, as would occur in a standard patient randomised trial<sup>30</sup>. Assessment time points will be at baseline, intervention end-point [primary outcome], and 6-months (follow up).

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3 The trial has well-defined objectives and protocols addressing Good Clinical Practice  
4 (GCP)<sup>31</sup> and SPIRIT guidelines<sup>32</sup>. Patients or the public were not involved in the design,  
5 or conduct, or reporting, or dissemination of our research.  
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10 ***Insert Figure 1 about here***

### 14 **Setting**

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16 *headspace* centres are accessible, community-based mental health services that  
17 support young people aged 12-25 years, funded by the Australian federal  
18 government<sup>33</sup>. Services are delivered in a youth-friendly environment staffed by a  
19 range of service providers, including general practitioners, psychologists, psychiatrists,  
20 youth workers, mental health nurses and other allied health professionals. *headspace*  
21 centres assess approximately 850 new patients per year, 40% presenting with  
22 depression<sup>34</sup>. A subset of approximately 6 of the more than 100 *headspace* centres  
23 will be involved in this study.  
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### 32 **Participant and recruitment procedures**

#### 34 **Clinicians**

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36 All allied health professionals, including psychologists, social workers and  
37 occupational therapists ('clinicians'), who provide mental health treatments to young  
38 people in the participating *headspace* centres will be invited to participate in the study  
39 and will be randomised to deliver either the intervention group (physical activity  
40 behaviour change) or the control group (psycho-education), in addition to routine  
41 clinical care. Clinicians in predominantly intake and assessment roles will not be  
42 included.  
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#### 49 **Participants**

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51 All help-seeking young people aged 12-25 who present to participating *headspace*  
52 centres will be screened for eligibility. We aim to recruit a total of 960 participants.  
53 Informed consent will be obtained from all participants; those aged between 15 and  
54 18 years will be assessed for mature minor capacity<sup>35</sup> during the intake assessment  
55 procedure at entry to the service and, if they meet this threshold, will be able to make  
56 the decision whether or not to consent to participate. Those aged 12-14 years can  
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3 provide assent to participate but will also require parental/legal guardian consent.  
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5 After obtaining informed consent, participants will be screened by research assistants  
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7 who will: a) assess the eligibility of the young person; and b) collect outcome data  
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9 (interview and self-report) at baseline, post-treatment and 6-month follow-up  
10  
11 assessments.

### 12 13 14 **Patient and public involvement**

15  
16 No patient involved.

### 17 18 19 **Inclusion, exclusion and discontinuation criteria**

#### 20 21 Inclusion criteria

22  
23 (i) meeting the requirements for a Mental Health Treatment Plan (MHTP) to access up  
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25 to 10 sessions of psychological treatment under the Medicare Benefits Scheme Better  
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27 Access program per annum<sup>36</sup>; and (ii) a Quick Inventory of Depressive  
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29 Symptomatology-Adolescent (17 item) - Clinician Rated (QIDS-A17-C)<sup>37</sup> score of 11 or  
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31 greater, indicating depression levels of moderate or above.

#### 32 33 Exclusion criteria

34  
35 (i) presence of a psychotic disorder or eating disorder during the intake assessment  
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37 upon first presentation to the *headspace* centre<sup>38</sup>; (ii) current physical activity meeting  
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39 the Australian Government Guidelines (i.e., for those under 18 years, 60 min of  
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41 moderate to vigorous activity every day; for those over 18 years, 30 min of moderate  
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43 activity at least 5 times for week)<sup>39 40</sup>; (iii) physical illness that contra-indicates  
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45 participation in physical activity; iv) organic mental disorder; and (v) intellectual  
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47 disability/cognitive impairment that precludes providing informed consent; as  
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49 assessed by the *headspace* intake and access team members and the study's research  
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51 assistants, and referred for review to the study site's Principal Investigator or clinical  
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53 review team. Any young person reporting a prior history of physical illness that might  
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55 impede their ability to take part in physical activity will be required to receive medical  
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57 clearance from a general practitioner in order to participate in the trial.

#### 58 59 Discontinuation criteria

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(i) incidence of a psychotic disorder or eating disorder meeting diagnostic threshold;  
or (ii) physical illness that contra-indicates participation in physical activity, as

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3 assessed by the treating clinicians during the course of the intervention.  
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5 Discontinuation from the active or control interventions can be at the request of the  
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7 participant or if any changes in the participant's presentation warrants a referral to  
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9 another service, as determined by their treating clinician or clinical review team. These  
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11 participants will discontinue their assigned intervention, but will remain involved in  
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13 the post-intervention assessment.  
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## 16 **Interventions**

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18 The interventions will be integrated into routine clinical care and delivered by a  
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20 *headspace* clinician, which may also include probationary psychologists (graduate  
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22 trainees) on clinical placement. The current funding rules of the Medicare Benefits  
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24 Schedule allow for 6 sessions of psychological treatment (plus an additional 4 if  
25  
26 clinically warranted) per calendar year. We anticipate that the interventions (both  
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28 physical activity and control) will be delivered in an average of 4 treatment sessions  
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30 across approximately 4-6 weeks, consistent with the average national attendance  
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32 rates to *headspace* centres<sup>41</sup>. The intervention will be capped at a maximum of 10  
33  
34 sessions. The active and control interventions have been described to meet the  
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36 Template for Intervention Description and Replication (TIDieR) standards<sup>42</sup>. At the first  
37  
38 treatment session, participants will be provided with relevant materials and resources  
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40 according to the treatment condition to which their treating clinician has been  
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42 assigned.  
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### 44 **Physical activity intervention**

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46 Participants who receive treatment from a clinician who has been allocated to this  
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48 group will receive a manualised integrated physical activity behaviour change  
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50 intervention, as per the training delivered to the clinicians, within their psychological  
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52 treatment sessions. Treatment sessions will be delivered face-to-face and onsite at  
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54 each participating *headspace* centre. The IMPACT treatment manual includes  
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56 evidence-based behaviour change techniques, targeting self-regulation (planning,  
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58 organising), motivation, enjoyment and tailoring for individual needs<sup>43 44</sup>. Participants  
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60 will be encouraged to set short- and longer-term specific and measurable goals;  
monitor progress towards these goals; discuss the benefits of physical activity;

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3 consider factors that may facilitate their participation (e.g., enlisting support from  
4 others, choosing physical activities that are enjoyable<sup>44 45</sup>); and identify potential  
5 barriers and strategies for overcoming these barriers. Clinicians will review weekly  
6 goals, participants' self-monitoring of mood pre- and post-activity, addressing barriers  
7 and enhancing individual facilitators, reinforcing achievements and revising physical  
8 activity plans, in each weekly session of psychological treatment to facilitate an  
9 increase in engagement in physical activity<sup>46</sup>. The intervention is designed to be  
10 delivered within 15-20 minutes to the initial session, with 5-10 minutes' duration in  
11 subsequent sessions. Given the real-world nature of the intervention context, it is not  
12 possible to define the frequency of sessions or duration of the intervention period *a*  
13 *priori*, due to variation in each of the study sites in terms of allocation to clinicians,  
14 managing service demands and appointment scheduling.  
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27 Participants will receive verbal and written information about the relationship  
28 between depressive symptoms and exercise<sup>47</sup>; access to online resources providing  
29 advice and instructions on physical activities; minimal equipment (resistance band for  
30 resistance activity and skipping rope for cardiovascular physical activity); written  
31 worksheets and resources to enhance motivation, address barriers and provide  
32 physical activity suggestions, including the current Australian national physical activity  
33 and sedentary behaviour guidelines<sup>48 49</sup>; and a weekly planner to discuss and plan for  
34 how and when the physical activity can be completed, and any memory aids that could  
35 be used to aid in completion of this (including mobile technology applications ('apps')).  
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#### 45 Psycho-education intervention

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47 Participants who receive treatment from a clinician who has been allocated to this  
48 group will be provided with the same psycho-education about the relationship  
49 between depressive symptoms and physical activity as the intervention group, within  
50 the first treatment session only. Treatment sessions will be delivered face-to-face and  
51 onsite at each participating *headspace* centre. The inclusion of the control group  
52 intervention is to examine whether the provision of information about physical  
53 activity for mental health and minimal resources is sufficient for participants to  
54 increase their current levels of physical activity. This will include providing the same  
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3 verbal and written information about the relationship between depressive symptoms  
4 and exercise<sup>47</sup>; minimal equipment (resistance band for resistance activity and  
5 skipping rope for cardiovascular physical activity); and physical activity suggestions,  
6 including the current Australian national physical activity and sedentary behaviour  
7 guidelines<sup>48 49</sup>, that will be provided to the intervention group. The importance of  
8 physical activity for depression will be addressed in the first session but will not be  
9 included in ongoing treatment.  
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### 18 **Study hypotheses**

19 Primary: that the physical activity intervention will lead to greater reductions in  
20 depressive symptoms compared psycho-education on physical activity, in addition to  
21 routine clinical care;  
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25 Secondary: a) that the physical activity intervention will lead to greater reductions in  
26 anxiety symptoms and greater improvements in functioning, when compared to the  
27 control condition; and b) that changes in depressive symptoms will be mediated by  
28 increases in physical activity.  
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### 34 **Primary outcome**

35 The *primary outcome* will be level of depression symptoms post-intervention and at 6  
36 month follow-up, measured by the Quick Inventory of Depressive Symptomatology-  
37 Adolescent (17 item) Clinician Rated (QIDS-A17-C)<sup>37</sup>.  
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### 41 **Secondary outcomes**

42 *Physical Activity (mediator)*: levels of physical activity measured by the International  
43 Physical Activity Questionnaire<sup>50</sup> and an electronic accelerometer device worn for 5-7  
44 days;  
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48 *Mental health and substance use*: anxiety symptoms measured by the Overall Anxiety  
49 Severity and Impairment Scale<sup>51</sup>; depression module from the SCID-IV<sup>52</sup>; and  
50 substance use measured by the WHO Alcohol, Smoking and Substance Involvement  
51 screening test (ASSIST).  
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55 *Anthropomorphic and lifestyle variables*: height, weight and hip and waist  
56 measurements to determine Body Mass Index and hip/waist ratio; Pittsburgh Sleep  
57 Quality Index<sup>53</sup>; and the Simple Dietary Questionnaire.  
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3 *Functioning*: Social and Occupational Functional Assessment Scale<sup>54</sup>; and Australian  
4 Quality of Life scale (AQoL 6d) for adolescents<sup>55</sup>, to facilitate future cost utility and  
5 other economic analyses.  
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8 *Variables that will be the subject of subsequent exploratory analyses include*: self-  
9 efficacy measured by General Self Efficacy Scale<sup>56</sup> and Barriers Self-Efficacy Scale  
10 (physical activity)<sup>57</sup>; Perceived Social Support Scale; Positive and Negative Affect  
11 Schedule<sup>58</sup>) Cognitive and Behavioural Therapy Skills Questionnaire<sup>59</sup>; Behavioural  
12 Activation for Depression Scale<sup>60</sup>; Montgomery Asberg Depression Rating Scale<sup>61</sup>; and  
13 Working Alliance Inventory (therapeutic alliance)<sup>62</sup>; and the Trail Making Test A & B<sup>63</sup>  
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64 to assess attention, processing speed and mental flexibility.

Assessments and measures will be conducted as per the assessment schedule: i) screening for eligibility; ii) baseline, post-intervention (end-point) and 6-month follow-up assessments. Data from participating young people will be entered into a project-specific secure online database at all assessment time-points, using a reversible process in which the identifiers are removed and replaced by a code.

### **Process and implementation measures**

#### **Training**

All participating clinicians will be trained in GCP and IMPACT study procedures, delivered in a 1.5-hour session in face-to-face format. Additionally, all participating clinicians will participate in a further 30-minute training session on how to deliver the psycho-education on physical activity and share resources with participants in the study. Following this, all clinicians who are randomised to the physical activity intervention group will take part in an additional 60-minute training session to integrate the IMPACT intervention into routine clinical care. For the intervention group, skills, knowledge and attitudes will be assessed before and after the training session, measured by the Theoretical Domains Framework questionnaire<sup>65</sup>.

The face-to-face training will be supported by additional online resources using a learning management system that will host an electronic version of the intervention manual, project resources, training videos and case vignettes. The training will

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3 incorporate practice recommendations for delivering physical activity behaviour  
4 change interventions for mental health, including: a) creating individual training plans  
5 to increase adherence and aim to increase physical activity levels and decrease  
6 sedentary behaviours, b) integrating the physical activity intervention into routine  
7 psychoeducation and psychotherapy; c) incorporating evidence-based behaviour  
8 change techniques, targeting self-regulation (planning, organising), motivation,  
9 enjoyment and tailoring for individual needs<sup>43 44</sup>. Clinicians will be provided with a  
10 comprehensive IMPACT treatment manual<sup>66</sup> and the resources required to deliver the  
11 intervention (handouts, worksheets, and access to online materials). Clinicians in the  
12 control condition will not have access to the online support materials.  
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### 23 Fidelity

24 Fidelity will be assessed using a brief checklist to be completed by clinicians after each  
25 session to estimate time spent on the intervention and the type of psychological  
26 treatment that was delivered as part of routine care (e.g., CBT, interpersonal therapy,  
27 etc). Fidelity will also be assessed by audio recording of all treatment sessions, with a  
28 random subset of 10% of the recordings to be coded by an independent rater for  
29 adherence to the treatment manual and to discriminate between the intervention and  
30 control conditions. Fidelity will be maintained by offering quarterly online group peer  
31 supervision sessions for the clinicians in the intervention group to allow group  
32 discussion and case presentations, in addition to the face-to-face training at the  
33 commencement of the trial. Less frequent peer supervision (approximately every 6  
34 months) will be offered to the control group clinicians. Fidelity of the intervention will  
35 also be assessed using a checklist of components of the active and control conditions  
36 collected from participants at the post-intervention assessment. In addition, at the  
37 end of the intervention period, a subgroup of physical activity intervention group  
38 clinicians and young people will be invited to participate in semi-structured interviews  
39 to explore their experiences of delivering and receiving the intervention, respectively.  
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### 56 **Randomisation and allocation to treatment**

57 Clinicians will be allocated to the intervention and control groups using a minimisation  
58 procedure commencing with random assignment<sup>67</sup>. The procedure was devised by  
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3 the study statistician (AM) and will be carried out by an independent researcher,  
4 following the ICH Guideline<sup>68</sup>, to ensure allocation concealment. Minimisation factors  
5 to be incorporated are gender of clinician (2 level factor, male/female), background  
6 training of clinician (2 level factor, psychologist/non-psychologist) and *headspace*  
7 centre, to ensure equal numbers in each intervention at each site (6 centres).  
8 Participants will be stratified by age ( $\leq 17$ , 18+), gender (male/female) and QIDS-A17-  
9 C score ( $\leq 15$ , 16+). Participants will be assigned to a clinician based on a randomised  
10 list. Due to the nature of the intervention, it will not be possible to blind the clinicians  
11 and participants; however, all pre-, post-intervention and follow-up assessments will  
12 be conducted by research assistants blinded to treatment allocation. Investigators not  
13 involved in the delivery of the intervention and the trial statistician will be blind to  
14 group allocation until the analysis is completed.  
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## 27 **Statistical analysis**

### 28 Analysis plan

29 Primary quantitative analyses will be undertaken on an intent-to-treat basis, including  
30 all participants as randomised, regardless of treatment received or withdrawal from  
31 the study. Linear mixed models will be used to analyse change in the primary outcome  
32 measure (QIDS-A17-C). Models will include a random 'clinician' factor. Correlation of  
33 repeated outcome measures will be accommodated using an unstructured variance-  
34 covariance matrix. An *a priori* planned comparison of change from baseline to the  
35 post-intervention assessment will be used to test the primary hypothesis. Comparison  
36 of change from baseline to follow-up between arms will be undertaken as a secondary  
37 outcome analysis. Factors used in assignment by minimisation (clinician gender,  
38 discipline, and *headspace* centre) will be introduced in models as covariates and  
39 retained if significant. Variables associated with participant missingness or found to  
40 be substantially imbalanced between groups will be included in models on an  
41 exploratory basis<sup>69</sup>.  
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56 Mathematical transformation or categorisation of raw scores will be undertaken to  
57 meet distributional assumptions and address any violation of assumptions required in  
58 mixed models. When transformations have been undertaken to better meet  
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3 distribution assumptions, models using the transformed data will be considered the  
4 main test of the primary hypotheses. Mixed models use all available data and do not  
5 involve any substitution of missing values with supposed or estimated values. The  
6 assumptions underlying mixed modelling allow 'missingness' to be related to  
7 observed variables in the analysis but not to unobserved values (termed 'missing at  
8 random')<sup>70</sup>.  
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16 Similar analyses of scaled secondary measures will assess differential change due to  
17 intervention arm. For dichotomous outcomes such as diagnoses and ordinal or count  
18 outcomes, comparable generalised mixed modelling approach will be used. Relative  
19 and reduction in risk of depression based on SCID diagnostic status will be estimated  
20 at the trial endpoint and follow-up. Numbers needed to treat will be derived from  
21 these values. All analyses will use two-sided tests, with an alpha value set at 0.05. In  
22 the event of substantial missingness, sensitivity analyses based on identified clinically  
23 plausible mechanisms may be undertaken to determine the robustness of findings.  
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32 Qualitative analyses of the semi-structured interviews included within the process and  
33 implementation measures will be undertaken on audio recorded interviews that will  
34 be transcribed verbatim, with data analysed using thematic analysis<sup>71</sup>.  
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### 40 **Power analysis**

41 Calculations of required sample size were based on detecting a post-intervention  
42 effect size of 0.34, which is at the lower boundary of utility and also reflects the  
43 adjunctive status of the intervention. Power was set at .90, alpha = .05 (two-tailed)  
44 and correlation of .5 assumed between pre-treatment and post-treatment scores. To  
45 allow for possible clustering effects (participants with the same therapist having  
46 characteristics and outcomes more alike than between therapists) a design effect<sup>72</sup>  
47 was calculated assuming an intraclass correlation (ICC) of 0.05 and the number of  
48 clients per therapist up to 24. The estimate of the ICC is at the upper range of therapist  
49 effects and is conservative given the prescribed, manualised nature of the  
50 intervention. It is anticipated that 6-8 clinicians per *headspace* centre will be involved  
51 in the study. The resultant design effect of 2.15 reflects the possible non-  
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3 independence of cluster-sampled participants and was used to inflate the calculated  
4 sample size, which assumes independence. The estimated required sample size was  
5 784. To accommodate a potential attrition/withdrawal rate of up to 20%, the target  
6 sample size was set at 960, or 480 participants per condition.  
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### 10 11 12 **Safety Procedures and Oversight** 13

14 Each participating *headspace* centre will have a Principal Site Investigator and will also  
15 be required to nominate a lead clinician who will be responsible for the oversight of  
16 participant safety during the course of the trial. Withdrawal from the study can be at  
17 the request of the participant or if the participant meets discontinuation criteria. Once  
18 withdrawn, the young person will be reviewed using the *headspace* centre's standard  
19 clinical review procedure and either maintained in the *headspace* centre or referred  
20 to other services as necessary. Any *adverse incident*, any serious or unanticipated  
21 adverse effects of the research on study participants, and unforeseen events that  
22 might affect continued ethical acceptability of the project, will be captured and  
23 reported until resolution, stabilisation or the participant is lost to follow-up, unless the  
24 condition is unlikely to resolve as per the opinion of the medical practitioner  
25 appointed by the study sponsor to monitor adverse incidents. In the event of an  
26 adverse incident or unexpected outcome, the allied health professional or research  
27 personnel will report to the study Sponsor, Orygen. If necessary, a decision will be  
28 made as to whether to withdraw or suspend participation. The study Sponsor will  
29 conduct annual centralised monitoring visits of the study sites.  
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45 **Ethics and dissemination:** Full ethics clearances have been received for all methods  
46 described in the manuscript from the University of Melbourne's Human Research  
47 Ethics Committee HREC 1442228 (2014-2019) (Protocol Version 1, 22 May 2014).  
48 Revisions to the study protocol have been enacted following approval received from  
49 the HREC (latest version: Protocol Version 9, 1 April 2019) and these revisions have  
50 been reported in the trial registry by the study's clinical trial managers (CM, VR). Trial  
51 findings will be published in peer-reviewed journals and presented at conferences.  
52 Key messages will also be disseminated by the youth mental health services  
53 organisation (headspace National Youth Mental Health Foundation).  
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## DISCUSSION

Depressive disorders are highly prevalent and are the leading cause of disability in young people worldwide. If effective, the physical activity intervention tested in this C-RCT has the potential to improve the immediate outcomes for young people with depression by providing an additive treatment effect in conjunction with routine clinical care. Additional benefits may include improvements in social and vocational functioning, thereby reducing the likelihood of longer-term damage in these domains.

The IMPACT intervention is easily scalable. As it is set within the national network of *headspace* centres, this will increase the likelihood that any benefits are translated into routine clinical practice for the many thousands of young people who access *headspace* services per annum. There is also potential to adapt the intervention for other service delivery models (e.g. primary care, tertiary mental health services) nationally and internationally – including to regional and remote areas – which may be of interest to policy makers and those funding mental health programs or services.

### Figure 1

Flow chart of clinician and participant recruitment and study timeline

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3 **Author contributions:** AGP led the development of this manuscript. AGP, DR, AM, RP,  
4 MAJ, ARY, PM, SEH and AJ secured the funding for the project and, together with  
5 author CM, devised the research design and measures. AGP, CM, DR, RP, MAJ, ARY,  
6 PM, SEH and AJ were involved in devising the intervention content and intervention  
7 implementation strategies, which were based on those established and previously  
8 operated by AGP, RP, ARY, PM, SEH and AJ. AM was primarily responsible for the  
9 sample size and power calculations and development of proposed statistical analyses.  
10 AGP wrote the initial draft of the manuscript. All authors contributed to and approved  
11 the final version of the manuscript.  
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55 assessment of the study conducted by the study sponsor determined that a data  
56 monitoring committee was not needed due to the low-risk nature of the intervention.  
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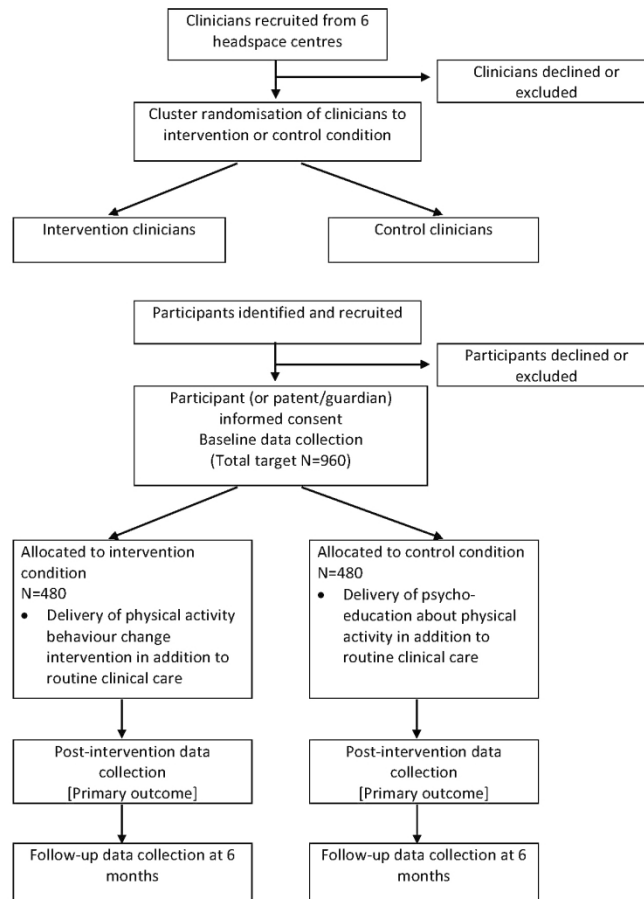
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**Competing interests:** The authors have no competing interests to declare.

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**Figure 1**  
Flow chart of clinician and participant recruitment and study timeline

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209x297mm (200 x 200 DPI)