Interventions to increase access to or uptake of physical health screening in people with severe mental illness: a realist review

Frédérique Lamontagne-Godwin,1 Caroline Burgess,2 Sarah Clement,3 Melanie Gasston-Hales,4 Carolynn Greene,4 Anne Manyande,1 Deborah Taylor,4 Paul Walters,5 Elizabeth Barley1

ABSTRACT

Objectives To identify and evaluate interventions aimed at increasing uptake of, or access to, physical health screening by adults with severe mental illness; to examine why interventions might work.

Design Realist review.

Setting Primary, secondary and tertiary care.

Results A systematic search identified 1448 studies, of which 22 met the inclusion criteria. Studies were from Australia (n=3), Canada (n=1), Hong Kong (n=1), UK (n=11) and USA (n=6). The studies focused on breast cancer screening, infection preventive services and metabolic syndrome (MS) screening by targeting MS-related risk factors. The interventions could be divided into those focusing on (1) health service delivery changes (12 studies), using quality improvement, randomised controlled trial, cluster randomised feasibility trial, retrospective audit, cross-sectional study and satisfaction survey designs and (2) tests of tools designed to facilitate screening (10 studies) using consecutive case series, quality improvement, retrospective evaluation and pre–post audit study designs. All studies reported improved uptake of screening, or that patients had received screening they would not have had without the intervention. No estimation of overall effect size was possible due to heterogeneity in study design and quality. The following factors may contribute to intervention success: staff and stakeholder involvement in screening, staff flexibility when taking physical measurements (eg, using adapted equipment), strong links with primary care and having a pharmacist on the ward.

Conclusions A range of interventions may be effective, but better quality research is needed to determine any effect size. Researchers should consider how interventions may work when designing and testing them in order to target better the specific needs of this population in the most appropriate setting. Behaviour-change interventions to reduce identified barriers of patient and health professional resistance to screening this population are required. Resource constraints, clarity over professional roles and better coordination with primary care need to be addressed.

Strengths and limitations of this study

► In line with the realist review methodology, a broad and inclusive study identification process was used, which was adapted iteratively to compensate for the inconsistency around how terms such as ‘screening’ and ‘monitoring’ are used.

► A realist review explores why interventions might work in a particular setting, however studies provide limited evidence for this, so transferability of knowledge to other settings is limited.

► A realist review is often selected to understand complex interventions, however behaviour change theory was not included in almost any intervention design, making it impossible to discern which ‘active ingredients’ are at work to produce the results.

INTRODUCTION

People with severe mental illness (SMI), such as schizophrenia or bipolar disorder, have been found to have a twofold to threefold increased risk of premature mortality.1 A reduction in life expectancy of 10–20 years has been reported.2,3 A significant cause of this disparity is attributed to preventable and treatable long-term physical health conditions, with cardiovascular disease and cancer as the first and second leading causes of death, respectively, in this group.4,5 Cancer mortality in people with SMI is more likely than in the general population,5 though the incidence of disease is similar for both groups.6 One factor which contributes to inequality in survival rates is access to cancer screening.7 The reported 30% higher case fatality rate from cancer may partly be due to those with SMI being more likely to present with metastases at diagnosis.8

Other physical health conditions found to be more prevalent in people with SMI include type 2 diabetes and metabolic...
syndrome (MS), tuberculosis, HIV, osteoporosis, poor
dentition, impaired lung function, sexual dysfunction
and obstetrical complications. MS is defined by the
WHO as glucose intolerance, diabetes mellitus and/
or insulin resistance, with two or more of the following:
central obesity (waist-to-hip ratio ≥0.90 in men and ≥0.85
in women and/or body mass index (BMI) >30 kg/m²),
raised arterial pressure (≥140/90 mm Hg), microalbumi-
muria (≥20 μg/min or albumin:creatinine ratio ≥30
μg/min) and raised plasma triglyceride (≥150 mg/dL
and/or low high-density lipoprotein cholesterol (HDL-C;
<55 mg/dL in men and <39 mg/dL in women)).

Health screening facilitates early detection and treat-
ment for many of these conditions, though rates of
screening in people with SMI may be reduced compared
with the general population. A UK survey found that
only 33% of people with schizophrenia had received
adequate cardiovascular disease screening in the previous
12 months and, internationally, uptake of breast, cervical
and bowel cancer screening has been found to be lower
among people with SMI. Effective interventions for
increasing access to, or uptake of, screening for a range of
conditions in the general population exist. In relation
to cancer screening, a Cochrane review found that no
intervention to promote uptake has been tested in people
with SMI. This is important since qualitative work
indicates there are specific barriers to cancer screening
uptake in people with SMI and that interventions effective
in the general population may not be effective in
the SMI population. Furthermore, barriers to screening
uptake or access may vary for different types of screening,
at different stages of the screening process and between
individuals.

Realist review methodology has been devised to
enable synthesis of diverse literature in order to explore
what works for whom (as in traditional systematic reviews)
and why an intervention may work.

By drawing on this methodology, our objectives were
to identify and evaluate interventions which may increase
uptake of, or access to, any kind of physical health
screening by adults with SMI, and to determine what
works for whom in what setting and why. The review is
described in accordance with the Realist And Meta-narr-
ative Evidence Syntheses: Evolving Standards (RAMESES)
reporting guidance for realist reviews.

METHODS

Study selection

Inclusion and exclusion criteria

Studies of any intervention to promote access to, or
uptake of, screening or monitoring for any physical
health condition where participants were aged 18 years
and over with a diagnosis of SMI (psychosis or bipolar
disorder however diagnosed) were eligible. Uptake of
screening was the main outcome of interest. Patient-re-
lated outcomes were not an inclusion criteria, but were
included in the online supplementary tables following
the review of the studies, to provide important additional
information and give a rounded picture of the effectiv-
ness of the interventions. The UK National Screening
Committee defines screening as a ‘public health service
in which members of a defined population…are asked
a question or offered a test, to identify those individ-
uals who are more likely to be helped than harmed by
further tests or treatment to reduce the risk of a disease
or its complications’. ‘Monitoring’ was defined in a
Cochrane review as a means ‘to obtain information
which can then be acted on to treat or prevent a physical
health problem’. We included any intervention described
as promoting either screening or monitoring; for clarity
the term ‘screening’ is used throughout. Only studies
reported in English were included.

In line with the realist approach to literature synthesis,
an inclusive approach was taken and intervention studies
of any design were eligible as long as the full text was
published in a peer-reviewed journal. We also excluded
intervention studies to improve physical health in people
with SMI which may involve screening, but where uptake
or access to screening was not a main outcome and service
evaluations or audits which considered screening, but did
not test any intervention.

Search strategy

The protocol is published on the PROSPERO (International
Prospective Register of Systematic Reviews) database.
The search strategy (online supplementary appendix 1) was informed by published, related system-
ic reviews and was checked by a specialist health
librarian at the University of West London (Marc Forster,
PhD). Searching was conducted in December 2016.

Data sources

MEDLINE, Embase, Cumulative Index to Nursing and
Allied Health Literature, PsychINFO, Cochrane Database
of Systematic Reviews, Database of Abstracts of Reviews
of Effectiveness. Reference chaining of identified studies
was also conducted. No date restrictions were applied.

Search results

The initial electronic search identified 1872 potentially
relevant publications; six others were identified through
reference chaining. Titles and abstracts were screened
independently by two team members (EB and AM). Thir-
ty-three full texts were retrieved and screened by three
team members (EB, AM, DT). Among the thirty-three
full texts was a recent systematic review of studies of
‘Strategies to implement physical health monitoring in
people affected by severe mental illness’ which included
14 studies. Though the focus of this review was slightly
different from the current, it contained one study which
we had included. It also included two studies which we
had excluded: one was not an intervention study, the
other tested the validity of a health monitoring tool.
This led to a team discussion whereby it was decided that
studies of interventions, such as health monitoring tools,
were relevant to our review question. The rationale being that, although the main aim of these interventions was to improve the quality of screening (e.g., more health indicators measured) and ongoing monitoring, this often resulted in increased uptake. We rescreened our identified studies and those included in this review. Forty-four studies were identified as potentially relevant and were screened by two reviewers. Twenty-two of these did not meet the inclusion criteria, a total of 22 studies were included. The screening and study selection processes are detailed in figure 1.

**Data extraction**

Each reviewer independently extracted information from up to five articles, with one author (EB) reviewing all studies. Data were extracted regarding study authors, geographical location and setting, year of publication, participant characteristics, features of the intervention, target of screening, outcome measures, study design and limitations.

**Approach to synthesis**

Similarities in intervention approach were identified and summarised across studies. Exploration of how and why different approaches might have worked was undertaken by searching for themes across studies, paying particular attention to disconfirming evidence. As there was considerable between-study variation in outcome measures, meta-analysis was not possible.

**RESULTS**

**Study characteristics**

Study characteristics are detailed in online supplementary tables 1 and 2. Two studies included breast cancer screening, one considered infection preventive services and 21 studies considered MS screening by targeting MS-related risk factors (cholesterol/sugar), blood pressure (BP) and BMI. Two studies involved national screening programmes and 20 studies developed ‘in-house’ screening. Study populations included...
participants with schizophrenia, bipolar disorder, schizoaffective disorder, other psychotic disorders and other mental health disorders. Some studies did not specify the SMI while other studies included patients with SMI on antipsychotics with no breakdown by condition. Some of the participants in a few of the included studies had mental health disorders other than SMI. In those studies, there was a minimum of 45% participants who had either a psychosis or bipolar disorder diagnosis.

A range of study designs was employed (pre–post audit n=9, consecutive prospective case series design n=1, repeat audit n=1, cross-sectional study n=1, QI (Quality Improvement) n=4, retrospective audit n=4, randomised controlled trial n=1, cluster randomised feasibility trial n=1). Study quality of randomised trials was assessed using the Cochrane tool for assessing risk of bias. No similar ‘gold standard’ tool exists which could be used across the other study designs, so we assessed each study informed by a simple checklist based on the STrengthening the Reporting of OBservational studies in Epidemiology statement and a recent review of tools to assess bias in observational studies. Each study was rated independently by two reviewers with discrepancies resolved by discussion. Flaws relating to the reliability of findings or the generalisability of results were highlighted in all studies (online supplementary tables 1 and 2); these data suggest that findings concerning the size of effect should be considered with caution.

Review outcomes
Interventions to increase uptake of screening are defined as interventions which support health professionals to screen for physical health conditions. Interventions to increase access to screening are defined as interventions (targeted at health professionals or health service delivery) to increase patient/client access to screening.

Intervention effects
Overall, improvements in rates of screening were reported in all studies following intervention (online supplementary tables 1-2). This appeared to be independent of screening type or study design. We identified an evidence gap as only three studies reported whether the results of screening were acted on, for instance through referral or clinical intervention.

Intervention type
Studies broadly either tested a new tool to facilitate screening for health professionals (online supplementary table 1) or made complex health services delivery changes (online supplementary table 2). One intervention primarily targeted service users, though in other studies service user-focused interventions were included, for instance targeted education, self-management support or support to attend screening. Most studies included staff education and training as part of the intervention.

The data-collection tools tested in online supplementary table 1 were designed to gather information required to improve MS screening or physical health monitoring. MS monitoring was evaluated using the following measurements: BP, smoking status, waist circumference (WC), fasting blood glucose (BG), BMI, triglycerides and HDL-C. These measures were based on the following clinical guidelines: National Institute for health and Care Excellence; Maudsley Prescribing Guidelines; US Preventive Services Task Force; National Heart, Lung and Blood Institute; American Diabetes Association; Early Psychosis Prevention and Intervention Centre; Psychotropic Therapeutic Guidelines and the American Psychiatric Association Practice. Most interventions were multifaceted, so will appear in more than one cluster. As no studies were rated of good or moderate quality, it was difficult to assess whether findings of improvements in rates of screening are valid. The size of effect was not reported for any study.

Screening template
Eight studies evaluated the effectiveness of using a screening tool to increase uptake and raise staff awareness of physical health screening. Barriers to successful intervention implementation included ‘social desirability bias’ (patients self-report their health behaviour in an overly positive picture in an effort to please their key workers); low uptake of physical measurements (eg, WC, BP, fasting BG and of data on sensitive topics); difficulty to capture monitoring results onto the tool; difficulty in obtaining equipment and accessing laboratory services; lack of integration with primary care for treatment or referral; appointment non-adherence, lack of expertise in mental health professionals to interpret physical health results, workload issues; staff reluctant to see MS screening as their responsibility. Authors across studies identified the following facilitators: investment of staff in physical health monitoring and staff flexibility by using alternative equipment and tests.

Staff education and training
Five studies included staff training as a component of the intervention. No author described the content or format of education interventions in detail. Barriers to successful intervention implementation included workload issues; lack of training to spot ‘social desirability bias’, lack of training in mean WC measurement. The following facilitators were identified: ‘booster’ education and team meetings and investment of staff in physical health monitoring.
Computer or paper prompt for staff

Four studies \(^{34}^{37}^{39}^{47}\) tested a computer-based or paper-based prompt to support clinicians to monitor and screen physical health indicators. Barriers to the successful implementation of the intervention included technical constraints in terms of collecting measurement results, \(^{39}^{47}\); low uptake of physical measurements (e.g., WC, \(^{37}\) and fasting BC, \(^{37}^{47}\); lack of expertise from mental health professionals to interpret physical health results, \(^{34}^{37}\); unclear communication channel between primary and secondary care, \(^{34}^{37}\); and limited access to equipment and resources. \(^{34}^{37}\). Having a clinical psychiatric pharmacist on the ward to remind clinicians to request investigations, such as blood tests when appropriate, and to provide the relevant guidelines and precautions when initiating hypolipidaemic medication, was a facilitator to the successful implementation of the intervention in two studies. \(^{37}^{47}\)

Online supplementary table 2 describes 12 studies which tested interventions that delivered change in a health service setting. Most interventions were multifaceted so appear in more than one cluster. All studies targeted adults, though in one study, \(^{45}\) eligible participants were 14–35 years old. Studies took place in a clozapine clinic, \(^{48}\) Early Intervention in Psychosis Services, \(^{41}^{43}\) Community Mental Health Team (CMHT), \(^{31}^{44}^{45}\) community drop-in centre, \(^{29}\) and primary care. \(^{26}^{30}\) Interventions were focused on metabolic/cardiovascular screening for all studies, except one, which was designed to increase rates of mammography uptake. One study monitored uptake of national cancer screening services and metabolic screening. The size of effect was not reported for any study. All studies reported suboptimal screening and monitoring at baseline, with improved levels postintervention. However, limited evidence of actions, such as referral or intervention, occurring as a result of these improvements was reported.

Staff education and training

Six studies \(^{40}^{42}^{43}^{45}^{46}\) provided some kind of staff (working in primary and secondary care) and patient education. All studies described increased rates of monitoring following the interventions. One study, \(^{45}\) was rated as good quality, so generalisation of results is limited. Barriers to the successful implementation of the intervention included staff time constraints, \(^{40}^{46}\); poor communication across the primary and secondary care interface, \(^{43}^{45}\) and lack of clarity over scope of practice, \(^{45}\); patient resistance to undergo physical measurements, \(^{42}^{46}\); staff resistance to change, \(^{40}^{45}^{46}\) and staff turnover, \(^{43}^{46}\). Facilitators included team ownership and team ‘champions’ to encourage screening, \(^{40}^{42}\) and high visibility/structure around monitoring and better liaison with primary care. \(^{42}^{48}\)

Invitation letter to physical health screening

Three studies \(^{26}^{40}^{42}\) used an invitation letter from primary care to encourage patients to attend screening as part of a physical health check-up. All studies described increased rates of monitoring following the interventions. Barriers to the successful implementation of the intervention included patient resistance to undergo physical measurements, \(^{42}\) and staff resistance to change. \(^{40}\). Facilitators included team ownership and team ‘champions’ to encourage screening; getting stakeholders involved \(^{40}^{42}\) and living in a suburban area, \(^{26}\) (rather than urban area).

Improving access to monitoring resources

Four studies \(^{41}^{43}^{46}^{48}\) tested interventions developed to improve the collection of physical health data to increase screening. Barriers to the successful implementation of the intervention included patient resistance and lack of motivation in the screening process, \(^{41}^{46}\); inadequate links with primary care, \(^{41}^{43}\); no clarity about who takes responsibility for screening, \(^{41}^{48}\); staff turnover, \(^{45}^{46}\); staff not perceiving physical health screening as a priority, \(^{41}^{46}\); time and resource (screening equipment) constraints, \(^{41}^{48}\); poor recording and knowledge of screening guidelines and tests. \(^{41}^{48}\) Facilitators included high visibility and structure around monitoring, \(^{35}\) and having a key worker system with key worker’s duties involving screening. \(^{41}\)

Integrating care across health settings

Seven studies, \(^{29}^{31}^{40}^{42}^{44}^{45}\) were developed to evaluate and reduce the fragmentation of care between different care providers. New clinics to improve physical health-care were set up and evaluated, \(^{29}^{31}\) two trials, \(^{44}^{45}\) evaluated nurse-led care management and two studies audited improvement in awareness, \(^{42}\) and communication, \(^{40}\) within the multidisciplinary care coordination team. All reported improvement in physical health monitoring or uptake of screening tests postintervention. Two studies, \(^{44}^{45}\) were rated as good quality. One study, \(^{44}\) reported improvement in cardiovascular disease risk among intervention subjects of an effect size comparable with that seen in underserved populations without mental illness. Barriers to the successful implementation of the intervention included lack of coordination across the primary and secondary care interface, \(^{40}^{45}\); patient reluctance to attend appointment/undergo screening, \(^{29}^{42}\); staff resistance to change, \(^{40}^{45}\) and lack of a prescribing provider. \(^{44}\) Facilitators included team investment in screening procedure and stakeholder involvement, \(^{29}^{31}^{40}^{42}\); psychosocial support and trust between patients and staff to help them obtain screening, \(^{29}^{44}\) and availability of primary and specialist care. \(^{35}^{44}\)

Staff accompaniment to appointments

Four studies, \(^{30}^{33}^{40}^{44}\) included accompaniment of service users to appointments as part of their intervention. This type of intervention addresses potential difficulties in locating and visiting unfamiliar places which has been reported as a barrier to cancer screening uptake by some service users. \(^{38}\) One study, \(^{35}\) from online supplementary table 1 was added to this cluster as it included staff accompaniment to screening. Barriers to the successful implementation of the intervention included staff workload issues, \(^{35}^{40}\); difficulty to engage staff, \(^{35}^{40}\); patient reluctance to undergo...
screening\textsuperscript{29} \textsuperscript{33} and difficulty to obtain an appointment/appointment non-adherence.\textsuperscript{29} \textsuperscript{33} Facilitators included staff feeling invested/having a sense of ownership with regard to physical health screening\textsuperscript{29} \textsuperscript{33} \textsuperscript{40}, having access to primary care/in-home phlebotomy services\textsuperscript{29} \textsuperscript{33} \textsuperscript{44} and trust between clients and staff.\textsuperscript{29} \textsuperscript{33}

**DISCUSSION**

**Statement of principal findings**

A large international body of work was identified with diversity in the number of physical health conditions and clinical settings. Challenges to increase uptake of physical health screening and monitoring in people with SMI was not unique to a particular country, setting or health service configuration. The studies illustrate that people with SMI come into contact with a number of different health services. Two tools to facilitate screening\textsuperscript{35} \textsuperscript{39} and two health service delivery change\textsuperscript{26} \textsuperscript{40} interventions were delivered in primary care. The remaining took place in inpatient and outpatient mental health services. Mental health staff performed `in-house` screening.\textsuperscript{29} \textsuperscript{31} \textsuperscript{36} \textsuperscript{37} \textsuperscript{43} \textsuperscript{46} \textsuperscript{48} ordered screening tests\textsuperscript{30} \textsuperscript{34} \textsuperscript{38} \textsuperscript{41} \textsuperscript{43} \textsuperscript{45} \textsuperscript{47} or acted as a broker between the patient and screening service.\textsuperscript{29} \textsuperscript{33} \textsuperscript{41} \textsuperscript{44} Overall, there appears to be no strong evidence as to whether an intervention to increase uptake of screening would be better suited in primary or secondary care. Performing `in-house` screening in mental health services rather than in a primary care context warrants further research, including what training and equipment this requires. In addition, mechanisms to establish and maintain strong links between primary care/screening clinics and mental health services to ensure patients attend screening appointments appear central to monitoring patients` physical health.

Identified barriers to the successful implementation of tools to facilitate screening can be clustered into resource constraints, environmental barriers, unclear boundaries around professional role and patient resistance. Authors note lack of time\textsuperscript{33} \textsuperscript{40} \textsuperscript{47} for health professionals to allocate to screening as a barrier, as well as staff turnover\textsuperscript{43} \textsuperscript{46} and other resource constraints\textsuperscript{41} \textsuperscript{44} \textsuperscript{47} such as lack of screening equipment and a prescribing provider. Environmental barriers include lack of coordination across the primary and secondary care interface\textsuperscript{30} \textsuperscript{41} \textsuperscript{45} \textsuperscript{46} and difficulty for patients and staff to obtain a screening appointment.\textsuperscript{29} \textsuperscript{33} Reluctance to engage in screening was observed from the clinician and patient perspective. In staff, limited clarity over who takes responsibility for screening\textsuperscript{41} \textsuperscript{46} was a barrier, as well as difficulty to engage staff\textsuperscript{35} \textsuperscript{40} in the project, staff resistance to change\textsuperscript{40} \textsuperscript{45} \textsuperscript{46} and staff not perceiving physical health screening as a priority.\textsuperscript{41} \textsuperscript{46} In patients, reluctance to engage with screening was identified as lack of motivation/scepticism in the screening process,\textsuperscript{41} \textsuperscript{46} appointment non-adherence\textsuperscript{29} \textsuperscript{33} \textsuperscript{42} and particular resistance to undergo physical measurements.\textsuperscript{45} \textsuperscript{46}

Facilitators to the successful implementation of health service delivery changes include having team `champions` or a key worker to encourage screening, having staff that feel invested/a sense of ownership with regard to physical health screening,\textsuperscript{29} \textsuperscript{33} \textsuperscript{40} \textsuperscript{42} \textsuperscript{47} stakeholder involvement,\textsuperscript{29} \textsuperscript{31} \textsuperscript{40} \textsuperscript{42} having strong links to primary care and specialist services\textsuperscript{39} \textsuperscript{33} \textsuperscript{42} \textsuperscript{45} \textsuperscript{48} including at-home phlebotomy services and established trust between clients and staff\textsuperscript{33} \textsuperscript{34} \textsuperscript{44} Barriers to the successful implementation of tools and health service delivery changes to facilitate screening include workload issues, resource constraints such as difficulty accessing monitoring equipment, patient resistance to screening and difficulty in arranging an appointment, fragmented links between primary and secondary care, unclear professional role boundaries for screening and staff resistance to engage in screening. Facilitators to the successful implementation of tools and health service delivery changes to facilitate screening include staff feeling invested and a sense of `ownership` to engage in physical health monitoring.
The quality of data identified was generally low, it is therefore not possible to determine the size of effect any intervention may have. Different interventions may target different aspects of screening and different barriers and facilitators may apply. However, the high level of heterogeneity and the limited quality of evidence meant that it is not possible to draw firm conclusions. Several potentially useful intervention approaches were identified however. A key aim of this review was to identify what approach worked for whom. However, this was not achieved since few studies tested this. Nevertheless, the review identified specific barriers and facilitators to screening uptake or access in people with SMI which should be considered in future studies.

Future studies should be reported using the TIDieR (Template for Intervention Description and Replication) guidelines and Medical Research Council guidance to make explicit how the components of complex interventions may work. Similarly, use of behaviour change theory was considered in one intervention design—a study acknowledged it was not considered—which provides no insight into what might have impacted on staff and service user behaviour to increase uptake. Only few interventions were designed in collaboration with service users, and their preferences were not explored.

There are no longitudinal studies; therefore, this review is unable to clarify if screening is maintained postintervention, and whether the increase in uptake is sustainable or a consequence of the Hawthorne effect whereby health professional behaviour reacts to being observed. An evidence gap was identified as only three studies were designed in collaboration with service users, and their preferences were not explored.

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Study limitations
There is inconsistency around how terms such as ‘screening’ and ‘monitoring’ are used which hampers comparative exercises. Our method of deploying them may differ to that of others who may use different terms and include different studies. To compensate for this, and in line with realist review methodology, we used a broad and inclusive study identification process which we adapted iteratively through the study selection process, as described in the Study Selection section. We identified a wide range of studies with varied participants, settings, interventions and intervention targets; a narrower review may provide answers which are more applicable to particular situations; however, the lack of good quality evidence identified suggests that this is unlikely to be the case.

CONCLUSION
Policy implications
Interventions to reduce patient and health professional resistance to screening which are informed by behaviour change theory should be developed and tested. Strategies to improve coordination between primary and secondary care are also needed, as are guidelines to clarify professional role boundaries. Resource constraints such as staff time and lack of monitoring equipment in mental health settings need to be addressed in the various clinics where screening occurs. Involving service users in intervention design is also important so that their preferences for location, frequency and type of support can be identified and targeted. Consideration of how interventions are likely to work should be made during development and testing.

Contributors EB, CB, SC and DT were involved in the study design. EB, MG-H, FRL-G and PW acquired and analysed the data. EB, SC, FRL-G and PW interpreted the data. FRL-G and AM drafted the manuscript. CB, SC, FRL-G and PW critically revised the manuscript for intellectual content. EB, CB, SC, MG-H, CG, FRL-G, AM, DT and PW contributed to writing and interpretation of the results.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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