



National Institute for Health Research

Effectiveness of multiple risk behaviour interventions in people with severe mental illness

1. Summary of Research

People with severe mental illness (SMI) die 10-20 years earlier than the general population and are 2-3 times more likely to experience long term conditions. According to NHS England this is one of the greatest health inequalities in the UK.

Health risk behaviours (smoking, physical inactivity, unhealthy diet, alcohol misuse, drug misuse) are associated with increased risk for developing long term conditions (such as cancer, respiratory, cardiovascular, and liver disease). In addition, these behaviours are strongly associated with premature mortality. For example, smoking is the leading preventable cause of death in the UK. The magnitude of risk to morbidity and mortality grows as the number of risk behaviours engaged in increases.

People with SMI engage in multiple risk behaviours more frequently than the general population. For example, smoking prevalence is up to three times higher in people with SMI than in the general population, and 42% of all cigarettes in the UK are now consumed by smokers with a mental health problem. Alcohol misuse and illicit drug use are four times more likely in people with SMI. Poor diet and physical inactivity are also more likely. For example people with first episode psychosis on average increase their bodyweight by 7% in the first year after diagnosis. There are a number of additional barriers that perpetuate people with SMI engaging in risk behaviours. This greater risk is likely driven and sustained by complex interactions between social inequalities, psychosocial impairment and symptoms associated with SMI, side effects of medication and a lack of access to physical and mental health interventions.

Nevertheless a number of risk behaviour interventions for people with SMI are recommended by NICE and their implementation in the NHS are prioritised both in NICE quality standards and recent NHS England reports. Translating these approaches into clinical practice raises important implementation challenges not currently addressed by current evidence. For example, reviews to date have generally focused on interventions aiming to change a single behaviour (e.g. smoking, diet), with evidence of small benefits, but most people with SMI engage in more than one risk behaviour. This raises important questions regarding whether to target the reduction of multiple risk behaviours in parallel (i.e. target two or more behaviours simultaneously), to target one behaviour at a time, or to target multiple risk behaviours in series. Targeting multiple behaviours may result in synergistic benefits to physical health or alternatively may impair efforts to effect change. Lack of evidence to inform this decision leads to uncertainty and variation in practice in two main ways. Firstly, we do not know if it is effective to target multiple risk behaviours for people with SMI. Secondly, it is important to identify potential strategies to overcome implementation barriers identified in uptake and engagement of risk behaviour interventions. A WHO working group on risk behaviour interventions for people with SMI identified a need for further evidence to investigate optimal implementation of these interventions in terms of content, duration, and delivery. Low uptake of risk behaviour interventions in the NHS by people with SMI potentially contributes to the perpetuation of health inequalities and poor outcomes among this population.

The aim of this review is to therefore examine the effectiveness of multiple risk behaviour compared with single risk behaviour interventions, to identify active ingredients of these interventions, and to identify factors that might impede implementation, including acceptability and feasibility of risk behaviour interventions in people with SMI. In order to meet this aim we propose the following objectives:

- a) to estimate comparative effectiveness of multiple and single risk behaviour interventions using network meta-analyses compared with controls
- b) to identify which behaviour change techniques are associated with greater effectiveness in risk behaviour interventions
- c) to synthesise qualitative and quantitative data about the acceptability and feasibility of implementing risk behaviour interventions in order to increase uptake and implementation.

2. Background and Rationale

2.1 Epidemiology

2.1.1 General health risks associated with multiple risk behaviours

Health risk behaviours (smoking, physical inactivity, unhealthy diet, alcohol misuse, and illicit drug use) are common in the UK and internationally. Smoking is the single largest directly avoidable cause of death in the UK and a major cause of respiratory disease, cancer, and cardiovascular disease.¹ Physical inactivity and unhealthy diet are strongly associated with weight gain, obesity, cancer, cardiovascular disease, and type 2 diabetes.² Alcohol misuse is also associated with greater risk for cancer, liver disease, and cardiovascular disease.³ Drug misuse is associated with greater risk of developing HIV, hepatitis C, and tuberculosis.⁴

There is good evidence both in the UK and internationally that health risk behaviours cluster.^{5 6} The majority of adults report engaging in two or more risk behaviours, and approximately a quarter engage in three or more risk behaviours internationally.^{7 8} A recent Norwegian population based cohort study⁹ of over 30,000 participants found a dose response relationship between number of risk behaviours and all-cause mortality (increase in risk of all-cause mortality of 1.55 fold for 2 behaviours, 2.26 fold for 3 behaviours, 3.16 fold for 4 behaviours). There was a similar dose response effect for risk of stroke in a large UK study of over 20,000 participants: relative risks for people who engaged in four risk behaviours were 2.31 compared with none, 2.18 compared with one behaviour, 1.58 compared for two behaviours and 1.15 compared with three risk behaviours.¹⁰ There is strong evidence of social and health inequalities associated with engaging in multiple risk behaviours. People who do not complete high school or have an unskilled occupation are 3-5 times more likely to engage in multiple risk behaviours.⁵ Multiple risk behaviour interventions in general populations are associated with small reductions in smoking, unhealthy diet and physical inactivity but there is currently insufficient evidence for reductions in alcohol and drug misuse.¹¹ In addition, small benefits were found for reductions in weight, blood pressure and total cholesterol. Multiple risk behaviour interventions are more effective in populations with physical comorbidities.¹²

2.1.2 Health risk and inequalities in SMI populations

Preventing long term conditions has been a key policy priority for some time, and people with SMI constitute a particularly vulnerable subgroup of the population. People with SMI were found to engage on average in five risk behaviours.¹³ Risk of cardiovascular mortality is 2-3 times higher in people with SMI¹⁴ and life expectancy is 10-20 years lower than that of the general population.¹⁵ This great risk is likely driven and sustained by complex interactions between social inequalities^{5 16}, psychosocial

impairment and symptoms associated with SMI¹⁷, side effects of medication^{18 19} and a lack of access to physical and mental health interventions.^{16 20}

In addition, while reducing morbidity and mortality in this population is a key public health priority, as pointed out by service users and carers who reviewed our proposal, motivations for behaviour change vary among people with SMI (for example, among different age groups). A recent qualitative study found weight gain was a key factor contributing to impairments in well-being and poor self-image for young people in a mental health inpatient setting.²¹ Therefore behaviour change might be also motivated by improvements to self-esteem.

Smoking is the largest cause of premature mortality in the UK. Therefore it is particularly concerning that smoking is up to three times as prevalent in SMI populations than the general population and even higher in certain subgroups (such as mental health inpatients).²² While the prevalence of smoking in the general population has reduced by a quarter in the past 25 years, the change in prevalence for smoking in people with a mental health disorder in the same period is negligible.¹ This means that 42% of all cigarettes in the UK are now smoked by someone with a mental health disorder¹, who have been shown to lose on average 17 years of life due to tobacco smoking.²³

Similarly, people with schizophrenia are more likely to engage in an unhealthy diet including lower fibre and fruit intake and higher saturated fat and calorie intake than in the general population.²⁴ A study of people with SMI in psychiatric rehabilitation programs found only 4% met physical activity guidelines.²⁵ Inadequate fruit and vegetable intake is associated with less physical activity, greater substance use and more sedentary behaviour in people with psychosis.²⁶ People with schizophrenia engaging in multiple risk behaviours are more likely to be overweight, have high LDL cholesterol, low HDL cholesterol, and increased fasting glucose.^{24 25} Antipsychotic treatment is associated with increased weight gain particularly within the first years of psychosis. For example, a systematic review estimated an average 12Kg weight increase in the first 24 months.²⁷ People with first episode psychosis increased their body weight by 7% during first year of treatment.²⁸

People with SMI are also substantially more likely to engage in substance use. A large US study of over 20,000 participants found that people with psychosis were four times more likely to engage in heavy alcohol use, cannabis use and other recreational drugs.²⁹ A UK study of people with first episode psychosis found 30% engaged in illicit drug use, 25% in both alcohol misuse and illicit drug use and 10% alcohol misuse.³⁰

Given that people with SMI have a much higher prevalence of engaging in risk behaviours, and face a variety of complex interacting factors that make behaviour change substantially more difficult, findings on the effectiveness of risk behaviour interventions in the general population cannot be assumed to be similar in this population.

2.2 Current NHS policy and practice

Reducing the mortality gap experienced by people with SMI is a key NHS priority. This includes providing regular physical health checks and promoting engagement in programmes designed to reduce risk behaviours such as smoking, physical inactivity, and unhealthy diet.

NHS England's *Five Year Forward View for Mental Health*³¹ considers the increased prevalence of long term conditions and reduced life expectancy in people with SMI as one of the greatest health inequalities in England. Therefore, the NHS outcomes framework 2016-2017 identifies the reduction of the under 75 mortality rate in adults with SMI as a key area for improvement. The NICE quality outcomes framework (QOF) indicators for people with psychosis, bipolar affective disorder or other psychoses include: record of total cholesterol:HDL ratio in preceding 12 months, record of blood glucose or HBA1c in preceding 12 months, CVD risk assessment for those aged 25-84 years, record of alcohol consumption in preceding 15 months, record of BMI in preceding 15 months.³²

An important part of the strategy to reduce health inequalities in people with SMI is to increase uptake and engagement with interventions aiming to reduce health risk behaviours. For example, the NICE guideline on smoking (PH48)³³ recommends all people in mental health services are asked if they smoke or have recently stopped smoking at first face-to-face contact. In addition, the guideline recommends prompt provision of comprehensive evidence-based smoking cessation support for all patients accessing mental health services, in-house or via Stop Smoking Services.³³ NICE guidelines (CG178 and CG185) recommend that people with psychosis³⁴ or bipolar disorder³⁵ are offered a healthy eating and physical activity programme and help to stop smoking. The NICE quality standards on psychosis identify promoting healthy eating, physical activity and smoking cessation as one of the priority areas for quality improvement.³⁶

Integration of physical and mental health care, including offering interventions for reducing risk behaviours and preventing chronic disease in people with severe mental illness, is one of the key priority actions for the NHS by 2020/2021.³¹ Similarly, reports by the Royal College of Psychiatrists³⁷ and the King's Fund³⁸ highlighted prevention of long term conditions (e.g. support for smoking cessation, reducing unhealthy diet and physical inactivity) as a key area for service improvement in the integration of physical and mental health care. The need to tackle health risk behaviours in people with severe mental illness is also stated as key priorities in reports by the BMA³⁹ and a joint report by the Department of Health and Public Health England.⁴⁰ The recently published Tobacco Control Plan for England (July 2017)⁴¹ highlights the importance of identifying interventions that work for reducing smoking in people with mental health conditions and acknowledges past prevention strategies have failed to reduce inequalities in this group.

While the importance of promoting health behaviours and preventing long term conditions in people with SMI is widely recognised, key questions regarding the implementation of risk behaviour interventions remain unanswered. For example, although most policy documents recommend that people with SMI should be offered help to reduce risk behaviours, this recommendation is based on evidence of the effectiveness of interventions targeting single risk behaviours. However, because people with SMI typically engage in several risk behaviours evidence is needed to support decision making about the benefits of single versus multiple risk behaviour interventions. Similarly, NHS England³¹ highlight the lack of uptake of risk behaviour interventions by people with SMI. But evidence on how to reduce psychosocial (such as social inequalities and symptoms of SMI) and contextual (e.g. integration of physical and mental services) barriers to access and uptake of risk behaviour interventions in people with SMI is limited.

3. Evidence explaining why this research is needed now

3.1 Brief review of the literature

For the purposes of this proposal we have conducted a broad scoping search of MEDLINE (that identified 5,166 hits) to assess the need for this research. We identified a relatively large and developing evidence base in this important research area comprising 40 RCTs focusing on multiple risk behaviour interventions among people with SMI, 25 RCTs focusing on single risk behaviour interventions among people with SMI, and 21 qualitative studies that were potentially relevant. The multiple risk behaviour interventions were predominantly nonpharmacological in nature.

Reducing risk behaviours in people with SMI is a clear priority for the NHS in terms of improving the integration of physical and mental health care and reducing morbidity and premature mortality in people with SMI. However, there are key evidence gaps that are important in informing how services implement these interventions:

- Most people with SMI engage in multiple risk behaviours, a key question is whether interventions should target multiple risk behaviours in parallel or target single behaviours

- A WHO working group has also highlighted uncertainty regarding the effective implementation of risk behaviour interventions for people with SMI including intervention content, duration, intensity etc.
- NHS England have highlighted the importance of addressing this population's risk behaviours however there are currently no evidence syntheses to help inform an optimum approach.

3.1.1 *Multiple risk behaviour vs single risk behaviour interventions*

NICE guidance and NHS England highlight reducing risk behaviours in people with SMI as a key priority. There are several systematic reviews that have focussed on the effectiveness of behavioural interventions in people with SMI for particular behaviours: smoking,⁴⁹ unhealthy diet and/or physical activity,⁴²⁻⁴⁶ alcohol and/or drug misuse.⁴⁷ Interventions to improve diet appear to be effective in promoting weight loss, BMI, and blood glucose levels. Smoking cessation interventions are associated with a similar magnitude of benefit in people with SMI as in the general population.^{1 48 49} However, interventions to improve physical activity alone have been investigated less frequently and systematic reviews conclude there is insufficient evidence of their effectiveness. Systematic reviews of behavioural interventions to reduce substance misuse were also inconclusive.⁴⁷

Despite a relatively developed literature of primary studies in this area, there are currently no systematic reviews specifically focused on multiple risk behaviour interventions in people with SMI.⁵⁰ It is not possible from current systematic reviews to delineate the benefits of focusing on a particular risk behaviour compared with targeting multiple behaviours concurrently. Risk behaviours cluster therefore it is important to question whether services should seek to reduce risk behaviours in parallel or to target risk behaviours one at a time, as interventions to promote change in a health risk behaviour have important implications for engaging in other behaviours. For example, our systematic review of multiple risk behaviour interventions in general populations¹¹ found changes in diet were positively associated with changes in physical activity and that both in turn were associated with increased weight loss. This is consistent with evidence from qualitative studies, for example people with diabetes reported that improvements in physical activity acted as a 'gateway' to changes in diet.⁵¹ Conversely, changing some risk behaviours may have negative consequences for engaging in others. For example, we found smoking cessation was negatively associated with change in diet and physical activity.¹¹ Therefore there are important questions regarding whether smoking should be targeted as part of a multiple risk behaviour intervention.

We have identified no trials that have directly compared interventions targeting multiple risk behaviours with those targeting single risk behaviours in people with SMI. The CHANGE trial,⁵² which aimed to reduce a number of risk behaviours (such as smoking, diet and physical activity) in people with schizophrenia spectrum disorders, did not find any benefits in either behaviour change or cardiovascular risk. This trial led the authors to raise important questions regarding whether it is more beneficial to focus on multiple or single risk behaviour change. Lack of evidence to inform the effectiveness of targeting multiple risk behaviours compared with single risk behaviours potentially creates uncertainty and variation in practice across the NHS. We are currently conducting a network meta-analysis comparing multiple and single risk behaviour interventions in the general population (commissioned by the Department of Health). However, no such analyses have been conducted in people with SMI.

3.1.2 *Identifying active ingredients of risk behaviour interventions*

NHS England report implementation challenges on uptake and engagement with risk behaviour interventions in people with SMI. Similarly, a WHO working group highlighted identifying the key components (such as intervention content, duration, intensity) of effective risk behaviour interventions as a priority area for further research.⁵³ Therefore, reducing uncertainty regarding the effective components of risk behaviour interventions in people with SMI has the potential to reduce the current implementation challenges for these interventions in people with SMI in the NHS.

Behaviour change interventions are typically complex with multiple interacting components. Therefore behaviour change technique (BCT) taxonomies have been developed to help identify the effective components within these interventions to help inform future research and implementation in services.⁵⁴ While validated taxonomies have been widely used to identify effective intervention content, for example in evaluating multiple risk behaviour interventions in general populations,¹¹ no systematic reviews have investigated the impact of intervention content using these methods in SMI populations. Given the different challenges of behaviour change in people with SMI, it cannot be assumed that the effective components of risk behaviour interventions in general populations can be extrapolated to this population. The uncertainty regarding what are the most effective components of risk behaviour interventions in people with SMI inevitably leads to uncertainty and variation across the NHS regarding implementation of these interventions.

In addition, the Oxford Implementation Index⁵⁵ also identify a number of other implementation factors that impact on the effectiveness of interventions: intensity (e.g. number of sessions), delivery method, staff characteristics, non-specific intervention components, steps to promote staff and participant compliance, setting, participant characteristics, characteristics of delivering organisation, significant external events.

We will use these tools to explore, using meta-regression, factors impacting on the effectiveness of risk behaviour interventions for people with SMI.

3.1.3 Qualitative studies on acceptability, uptake, and challenges for implementing risk behaviour interventions

The lack of access and uptake of risk behaviour interventions in people with SMI is a key challenge identified by NHS England. In addition to the meta-regression analyses discussed above, there is also an important need to synthesise qualitative data on the experiences of staff and people with SMI to inform what factors impact on the acceptability and uptake of risk behaviour interventions. For example, a study in people with type 2 diabetes reported benefits for most participants targeting diet and physical activity concurrently (e.g. doing more physical activity the day after eating at a restaurant) although other participants found changing both diet and physical activity at the same time difficult to maintain long term.⁵¹ Understanding the benefits and difficulties associated with these interventions are important in helping people with SMI to reduce their risk behaviours.

Our scoping search found a developing literature of qualitative studies on the acceptability of multiple risk behaviour interventions in people with SMI. However, there are no systematic reviews that have synthesised this literature. In contrast, for single risk behaviour interventions, there are a growing number of systematic reviews. For example, reviews of qualitative and/or quantitative studies on acceptability of smoking cessation in both staff and people with mental health problems⁵⁶⁻⁵⁸ found some staff had misconceptions that may undermine implementation of these interventions (e.g. they thought most service users were not interested in quitting smoking or would not be able to cope with trying to quit). A systematic review of quantitative studies on motivating factors and barriers to physical activity in SMI populations found depression, fatigue and stress were important barriers to engagement in behaviour change.¹⁷

3.2 Summary and Implications

NICE guidance and NHS England policy documents highlight the importance of risk behaviour interventions to address the mortality gap between people with SMI and the general population. However, there are a number of questions regarding how these interventions should be implemented in the NHS including: whether to target multiple risk behaviours concurrently or instead to focus on single risk behaviours, the effective components of risk behaviour interventions, and how to improve uptake and acceptability of these interventions for people with SMI. There are no systematic reviews that have examined these implementation issues comprehensively in people with SMI.

These are important gaps in the literature with substantial implications for helping to inform future guidance on critical questions about effectiveness of interventions for reducing health inequalities in SMI populations – a key NHS priority.

4. Research objectives

We will use rigorous methods of evidence synthesis to provide a comprehensive and objective summary of available primary research about the effectiveness of behaviour change interventions that target multiple risk behaviours in people with SMI. These objectives were also informed by service user and carer feedback which highlighted that motivations and challenges of implementing behaviour change interventions may differ according to factors such as age.

More specifically, the objectives of the project are to:

1. Provide a descriptive overview of all the evidence for multiple risk behavior interventions for improving a broad range of behavioural and physical health-related outcomes in people with SMI.
2. Examine the effectiveness of multiple risk behaviour interventions compared with single risk behaviour interventions in terms of their impact on a range of outcomes
3. Examine the effect of study level moderators using meta-regression, to identify active ingredients of interventions (mapped against existing behaviour change taxonomies) and other factors (such as time from initiation of antipsychotic treatment, age).
4. Examine the acceptability of implementing risk behaviour change interventions in terms of uptake, adherence and service user satisfaction. Of particular importance, we will assess data on those who did not take part in the intervention or dropped out and also to examine whether these data differed according to the intervention format (i.e. intervention, group, digital).
5. Explore, qualitatively, key factors influencing the acceptability and feasibility (including factors such as age and motivations for behaviour change) of implementing risk behaviour change interventions for SMI in the context of the NHS.
6. Identify, from the perspective of the UK NHS and personal social services, research priorities and the potential value of future research into multiple risk behaviour interventions for improved physical health in people with SMI.

5. Research Plan / Methods

5.1 Inclusion and exclusion criteria

Population

Adults (aged 16 years or over) diagnosed with severe mental illness (SMI) defined as schizophrenia, bipolar disorders, or other psychoses. Interventions aimed at people without existing conditions or risk factors will be included. Interventions aimed at people who are overweight or obese, have long term conditions, or risk factors for long term conditions (e.g. high blood pressure, high cholesterol) will also be included.

Intervention

Behavioural interventions will be included with no restrictions regarding whether the focus of intervention content is psychological, educational, environmental etc. Nor will any restrictions be applied based on setting. We expect that interventions may be delivered in a variety of potential settings such as inpatient services, outpatient programs, and community or volunteer services.

For some risk behaviours (such as smoking, alcohol, opioid use) pharmacological treatment may be a component of standard care, where this is the case behavioural interventions in combination with standard pharmacological interventions will be included. However, if the primary aim of a study is to evaluate the effectiveness of pharmacological interventions this will be excluded.

Single risk behaviour interventions will be included if they aim to change one of the following risk behaviours: physical inactivity, unhealthy diet, smoking, alcohol misuse or drug misuse. Multiple risk behaviour interventions will be included if they aim to change two or more of these behaviours.

Comparator

- a) No intervention
- b) Waitlist
- c) Treatment as usual
- d) Active control
- e) Behavioural intervention targeting a single risk behaviour.

Outcome

- a) Changes in risk behaviours (physical activity, diet, smoking, alcohol use, illicit drug use)
- b) Anthropometric measures (weight (Kg), BMI, waist circumference)
- c) Metabolic outcomes (systolic blood pressure, diastolic blood pressure, HDL-cholesterol, LDL-cholesterol, total cholesterol)
- d) Glycaemic control (e.g. blood glucose, HbA1c)
- e) Quality of life
- f) Intermediate outcomes (e.g. knowledge, skills, self-efficacy, beliefs) classified according to the theoretical domains framework.
- g) Number of total drop outs for any reason

Study Design

For the clinical effectiveness analyses we will include randomised control trials (RCTs).

For the implementation effectiveness analyses we will include data from randomised controlled trials that address objectives 3 and 4 above (including process evaluations linked to these trials). In addition, we will conduct a separate search for qualitative studies assessing the feasibility and acceptability of risk behaviour change in people with SMI.

5.2 Search strategy

One large search will be conducted for interventions targeting unhealthy diet, physical inactivity, smoking, alcohol misuse and drug misuse in people with SMI using MEDLINE, EMBASE, PsycINFO, Science Citation Index, Cochrane Central Register for Controlled Trials, Applied Social Sciences and Index and Abstracts. We will conduct searches of these electronic databases from 1990 to the present, based on the findings of a scoping review of research on multiple risk behaviours, which found no relevant studies prior to this date.⁵⁹

Reference lists of all included studies will be manually searched by one reviewer to locate further relevant studies; those assessed as being eligible for inclusion will be checked by a second reviewer. In addition, we will check the included studies of relevant systematic reviews to identify further potentially relevant studies. Any additional online data will also be obtained.

5.3 Data extraction

The data extraction form will be pilot tested on a selection of studies by two reviewers to ensure consistency. Data will be extracted by one reviewer and checked by a second reviewer. Discrepancies will be resolved by discussion, with involvement of a third reviewer where necessary. Attempts will be made to contact authors for any missing data. Data from multiple publications of the same study (or dataset) will be extracted and reported as a single study. Where there are data from multiple time points, we will group these data in a clinically meaningful manner in consultation with the advisory group, content experts and service users. Intermediate outcomes such as knowledge, skills, self-efficacy and beliefs will be classified using the theoretical domains framework.⁶⁰

Two reviewers will independently extract information about the content of each intervention and control including adaptation in interventions for people with SMI (e.g. additional sessions related to mental health problems such as depression and anxiety; session on stress or self-esteem management; deliverers of intervention include mental health professionals). Where relevant, studies will be coded according to a published framework for characterising behaviour change techniques (for example⁶¹).

We will also extract data from any linked process evaluations. Where possible, we will identify and extract relevant contextual information. Extraction of implementation data will be based on a template adapted from the Oxford Implementation Index.⁵⁵ This is a tool designed to aid reviewers in the extraction and comparison of implementation data across primary studies.

5.4 Critical appraisal

Effectiveness analyses

The quality of the individual studies will be assessed by two reviewers using the Cochrane risk of bias tool for RCTs,⁶² disagreements will be resolved by discussion and if necessary a third reviewer will be consulted.

Qualitative analyses

Critical appraisal of qualitative research is recognised as a controversial issue.⁶³ Following the lead established by the GRADE Working Group (www.gradeworkinggroup.org) and the Cochrane Qualitative and Implementation Methods Group (cqim.cochrane.org) we will adopt the CerQual (certainty of the qualitative evidence) approach to assess both the methodological limitations of individual studies and the coherence of our review findings. CerQual is similar to GRADE⁶⁴ in that both approaches aim to assess the certainty of (or confidence in) the evidence, and both also rate this certainty for each finding across studies rather than for each individual study. Unlike GRADE, which is only relevant to evaluations of effectiveness, CerQual offers a framework to evaluate the certainty of evidence that address questions beyond effectiveness of interventions, such as acceptability. As per the approach taken by Glenton et al⁶⁵ methodological limitations will be assessed with the CASP checklist.⁶⁶ Coherence of the review will be assessed by identifying patterns across the data contributed by each of the individual included studies, for example, where findings are consistent across multiple settings or different sub-groups of people with SMI. Certainty of evidence in each individual study will be rated as high, moderate or low, ranked according to the methodological limitations and coherence of each finding of our review.

5.5 Data synthesis

Effectiveness analyses

Based on our experience of conducting meta-analyses and network meta-analyses of multiple risk behaviour and other complex interventions we expect the data synthesis to be challenging. Therefore we have assembled a multidisciplinary team with expertise in evidence synthesis (including pair-wise meta-analyses and network meta-analyses of complex interventions), behaviour change interventions and physical and mental health interventions for people with SMI in order to make informed judgements on the most appropriate methods of synthesis.

There is a great deal of variability in conceptualising and measuring many of the included outcomes (particularly risk behaviours) in our review. For example, physical activity can be measured in a variety of ways such as leisure time, commuting, sedentary time, sleep; moderate/vigorous physical activity; metabolic equivalent times etc. In addition, these physical activity outcomes can be obtained in a variety of different ways (e.g. a number of different self-report methods or based on various types of wearable technology). Similar challenges are faced for diet and other risk behaviour outcomes. For

each outcome we will assess the measures that have been used, evaluate whether they are sufficiently comparable, and then select the most appropriate method of synthesising these data. Here content expertise in outcomes (Churchill) and behaviour change interventions (Armitage) will be critical to making appropriate adjudications about the merit of meta-analysis.

Below we summarise the key aspects of the data synthesis:

- a) Standard (pair-wise) meta-analyses: we will conduct meta-analyses where the interventions, populations, comparators, outcomes and contexts are sufficiently similar. We will explore heterogeneity through inspection of forest plots and use of statistics like I^2 .
- b) Network meta-analyses: as above we will conduct network meta-analyses to analyse all available comparisons where the interventions, population, comparators, outcomes and contexts are sufficiently similar. Direct comparisons will include multiple risk behaviour interventions vs control, single risk behaviour interventions vs control (such as diet alone, physical activity alone, smoking alone) and if available multiple risk behaviour vs single risk behaviour interventions, combinations of multiple risk behaviour interventions versus other combinations of multiple risk behaviour (e.g. diet and physical activity vs diet, physical activity and smoking).

Estimates of treatment effects will be calculated using a Bayesian approach (using freely available software e.g. WinBUGS/OpenBUGS), taking into account the correlation between multi-arm trials where appropriate. Direct and indirect treatment effects will be estimated, along with credible intervals and prediction intervals. Such network analysis can only be applied to connected networks of trials. Network meta-analysis enables the comparison of indirect comparisons not addressed within the primary trials.^{67 68} We will evaluate model diagnostics and assumptions of similarity and consistency in the evidence network.^{69 70} We will also make use of current developments to illustrate graphically the findings of the network meta-analyses so that they are more easily interpretable to wider audiences.⁷¹

Moderators of clinical-effectiveness

We will provide a descriptive summary of the studies including contextual factors such as participant characteristics, settings, ethical considerations, external events happening at the time of the intervention and how interventions were delivered based on the Oxford Implementation Index.⁵⁵ We will also summarise the types and number of behaviour change techniques used in these studies based on published frameworks.⁵⁴

To complement the narrative synthesis we will explore moderators of effectiveness using meta-regression for all outcomes with more than 10 included studies, if judged to be appropriate. Differential effects between studies will be explored using the framework proposed by the Oxford Implementation Index. This will include factors found in previous reviews identified as moderators of effectiveness (such as presence of risk factors/comorbidities, time after initiation of antipsychotic medication) as well as other participant characteristics (e.g. gender, socio-economic status, ethnicity), setting, location; and intervention delivery (such as number of sessions, delivery method, staff characteristics etc). The relative effectiveness of different combinations of behaviour change techniques and the number of techniques (e.g. 2 vs 3 vs 4 etc) will be explored based on published frameworks.⁵⁴

In addition, we expect that inclusion criteria for defining people with SMI may differ across studies. In discussion with our content experts we judged limiting our review to studies that only included DSM or ICD diagnoses may miss important trials. The impact of removing studies that did not report using DSM or ICD diagnostic criteria on heterogeneity of findings will be assessed using sensitivity analyses.

Qualitative syntheses

The synthesis will follow published methods,⁷² as adapted for health science research.⁷³ Papers will be read by two researchers in detail to identify core themes for comparison across studies based on quotes from participants reported in the studies and interpretations of the authors (these two sources of data will be clearly differentiated).

Drawing on guidance for qualitative syntheses to inform policy making and research prioritisation we will use a narrative synthesis approach.⁷⁴ This offers an efficient and practical means to include a qualitative description and map of findings of included studies (presented in matrices across studies), interpretation and synthesis, and the identification of common and emergent themes. Narrative synthesis draws on the techniques of thematic analysis that we have used before to categorise emergent and recurring themes within and between transcripts.⁷⁵

Consistent with previous syntheses we have conducted,^{76 77} we will place greater emphasis on studies employing rigorous data collection/analysis techniques and providing in-depth examinations of user experience. Studies that lack this detail will be used to augment and contextualise the findings. As outlined above the relative contribution of individual studies, the impact of methodological limitations and certainty on the findings will be summarised narratively in line with the CerQual approach.

Once we have extracted and synthesised all available quantitative and qualitative data, we will seek, whenever possible, to integrate our findings. This will be achieved by exploring the extent to which our identified qualitative themes map onto the quantitative acceptability ratings reported by in the included studies.

6. Dissemination and projected outputs

Projected outputs

The proposed work will result in a number of valuable outputs:

- i. Evidence of the comparative effectiveness of multiple risk behaviour compared with single risk behaviour interventions, and acceptability of these interventions for people with SMI will be synthesised and presented in a variety of formats tailored for service users, health professionals, commissioners of services, policy makers and research funders.
- ii. An increased understanding of the relevance and applicability of international evidence to the NHS.
- iii. Identification of future research priorities and research value as judged from the perspective of the UK NHS and Personal Social Services and service users.

Dissemination strategy

Our dissemination strategy will involve communicating our research through:

- Peer-reviewed journal articles: the review will be reported according to PRISMA guidelines and submitted in a final report to the HS&DR programme, for publication as a monograph in the NIHR Journals series. A series of publications describing different aspects of the project (e.g. clinical effectiveness, acceptability) will be written and submitted to high impact academic and practice journals.

- Evidence summaries targeted at different audiences including service users, policy makers and guideline developers utilising CRD's many years of experience of knowledge mobilisation.
- Conference Presentations: we will submit an abstract to a relevant major national or international conference such as the RCPsych International Congress.
- Social media: we will use social media communications (e.g. setting up a Twitter account for the project), to promote the programme among professional and public audiences, report on progress and highlight key achievements, and cite more broadly research and patient initiatives and trends in reducing health inequalities in people with SMI.
- Animated video: increasingly information is disseminated visually and therefore we have budgeted for a professionally developed animation used to communicate research in past NIHR projects including by applicant Armitage.
- Stakeholder event: We will utilise links between applicants and members of the advisory group with health and social care professionals, policy networks, third sector organisations, and NHS England to invite a range of stakeholders. We will identify key topics for discussion based on findings of our review and present these at the meeting; we will then use consensus methods to generate recommendations on the key finding of the review; potential implications for policy, practice and commissioning; and priorities for future research. These priorities will then help to further refine the dissemination strategy.

Key stakeholders include:

- Policy and practice networks: in addition to peer-reviewed publications and conference presentations we will also pursue opportunities to disseminate our findings through applied research and practice networks relevant to promoting physical health and wellbeing in people with SMI. For example, applicant Shiers has links to several national policy networks on physical and mental health comorbidities which provide important dissemination opportunities. In addition, applicant Gilbody directs a mental health and comorbidity theme for the Yorkshire and Humber NIHR CLAHRC. We will also aim to benefit from the links of advisory group members Wright (Deputy Medical Director, Selby and York) and French (Mental Health Clinical Lead for Greater Manchester and East Cheshire Strategic Clinical Network) who have senior NHS leadership roles with input into local, regional and national policy and practice.
- Service user organisations and networks: it is important that the findings are not only communicated to professional and policy audiences but also to organisations representing service users. We will draw on existing links with local and national organisations representing service user groups for whom the research is relevant (e.g Mind, Action for Smoking and Health (ASH)) and also work with service users and a carer on the advisory group to ensure the findings are disseminated widely. For example, advisory group member Sophie Corlett is Director of External Relations at Mind and applicant Elena Ratschen is a member of the National Partnership on Smoking and Mental Health led by ASH that provides a clear avenue for disseminating the findings of the project.

- NICE mental health guideline producers: several applicants (Shiers, Gilbody, Dias, Churchill and Meader) have long standing links with producers of NICE mental health guidelines having contributed to guideline development groups for a range of mental health disorders (such as psychosis, bipolar disorder, depression, drug misuse). We will continue to build links with NICE guideline developers (such as Prof Steve Pilling) and communicate the potential impact of our findings on future updates of NICE guidance and quality standards (for example on guidelines for Psychosis and Bipolar Disorder).
- NHS England: given the prominence of reducing premature mortality in the Five Year Forward View for Mental Health and other policy documents NHS England is a key stakeholder for this project. Advisory group member French provides links through his role as North Clinical Lead for Early Intervention in Psychosis for the North West to ensure the relevance of the project to NHS England and provide dissemination opportunities.

7. Plan of investigation and timetable

The project will take 22 months:

Month 1: Protocol refinement, PROSPERO registration, and first meeting of advisory group and PPI group.

Months 2-6: Refine and test searches (effectiveness & acceptability), conduct searches, create and test data extraction templates. Study selection and retrieval, and begin data extraction process. Data synthesis and analysis (effectiveness, acceptability).

Months 7-14: Second meeting of advisory group and PPI group, continuing data extraction, complete syntheses, update searches.

Months 14-16: Writing draft report.

Months 17-19: Third meeting of advisory group and PPI group, completion of final analyses.

Months 20-22: Stakeholder meeting; development and refinement of wider dissemination/knowledge mobilisation strategy; prepare evidence summaries to be disseminated to service user, practitioner, and policy audiences; develop video with service users and content experts, and animation to be uploaded to YouTube.

8. Project management

8.1 Research team

Each applicant will be involved in the project and will contribute significant methodological (applicants Meader, Coventry, Churchill, Dias) and/or content expertise (applicants Shiers, Gilbody, Ratschen, Armitage, Churchill).

Applicant Meader will be responsible for overall project management and line management of two Research Associates (both working half time on the project) one with expertise in the synthesis of quantitative studies and the other with expertise in synthesis of qualitative studies. Applicant Coventry has been providing mentoring to Applicant Meader during the preparation of this submission as part of his role as a senior staff member at CRD and will continue to act as a mentor during the course of the project if the proposal is successful. In addition, the considerable experience of applicants Churchill and Dias (also senior staff members at CRD) will provide a further source of mentoring and support. There will be monthly team meetings during the course of the project attended by the CI, Grade 6 research fellows, and including senior input from Dr Coventry, Prof Churchill, or Prof Dias depending on the stage of the project and expertise required. This will ensure that the CI receives regular support and advice throughout the project. At key milestones during the project the CI will further

consult with Dr Coventry, Prof Churchill, and Prof Dias for their input on important decisions. In addition, to the regular and ongoing support from Dr Coventry, Prof Churchill and Prof Dias the CI will benefit from an experienced team of co-applicants with the diverse range of skills and expertise required for the project.

The Research Associates will be drawn from a pool of experienced systematic reviewers working at the Centre for Reviews and Dissemination (CRD) which specialises in evidence synthesis. Their experience at CRD and with evidence syntheses of quantitative and qualitative research will enable them to settle quickly into the project. In addition, the access to a large pool of experienced systematic reviewers allows us to ensure they will have the appropriate skill sets for the project and to develop an appropriate mentoring plan early on taking into account their strengths and weaknesses.

Applicant Meader will oversee a mentoring plan for both Research Associates ensuring they are provided with necessary support and supervision for all tasks. They will conduct the screening and data extraction in collaboration with one another and under the supervision of applicant Meader. They will assist with the synthesis of quantitative and qualitative data under the supervision of applicants Meader (clinical effectiveness) and Coventry (qualitative syntheses). Applicant Churchill will provide further supervision on the knowledge mobilisation strategy. Applicant Dias will provide further supervision on the statistical analyses. Applicant Armitage will provide further supervision on the analysis of the theoretical and technical content of the behaviour change interventions.

8.2 Advisory group

To ensure applicability and relevance of the questions addressed, and to maximise uptake of the findings, we plan to involve a range of stakeholders to guide the review process. These meetings will include two service users, a carer (applicant Shiers), Sophie Corlett (Director of External Relations, Mind), Dr Steve Wright (an early intervention psychiatrist and deputy Medical Director for York and Selby), Prof Paul French (Mental Health Clinical Lead for Greater Manchester and East Cheshire Strategic Clinical Network and NHSE North Clinical Lead for Early Intervention in Psychosis for the North West) as well as methodological and content experts (applicants Meader, Coventry, Churchill, Gilbody, Shiers, Ratschen, Armitage).

We will meet with an advisory group three times over the duration of the project. The proposed aims of each meeting are listed below:

Meeting 1: at the outset of the review to refine the protocol and set the direction of the project.

Meeting 2: after data extraction and synthesis has been completed to provide guidance on interpretation of the data and implications for research and practice.

Meeting 3: Once the report has been completed we will use this meeting to plan knowledge mobilisation and dissemination strategies to communicate the findings of the research and to identify potential barriers and facilitators to implementing the findings.

9. Patient and Public Involvement

Our proposal has been informed by the feedback from a group of service users formed as part of an existing study on diabetes in people with SMI (the DIAMONDS study⁷⁸) conducted by the Mental Health and Addictions Group at University of York. In addition, one of our co-applicants (David Shiers) provides a carer perspective through his 20 years' experience as a father of a daughter with schizophrenia.

Members of the group commented (either by phone or email depending on what was more convenient) on the topic of the proposal and confirmed that they thought this was an important issue

for people with SMI and that the plain English summary was clear and understandable to a service user audience. However, they requested further clarification on the research plan and suggested the need to clarify how the data was to be synthesised which originally wasn't emphasised enough in the plain English summary. Further, the potential impact of age on effects of intervention was highlighted by two group members. For example, some older service users may be more motivated to change their behaviour in order to prevent long term conditions or dying early whereas younger service users may be more motivated by the benefits to self-esteem from living a healthier lifestyle than to the longer term reductions in physical health risks.

This initial engagement with the group of service users will provide a platform to recruit PPI volunteers for the advisory group, stakeholder consultation, and to the dissemination of findings. This feedback from service users and a carer has validated and refined aims, objectives and plans for dissemination.

We recognise that PPI must be flexible to meet the needs of those who participate, and will therefore offer a range of PPI opportunities within the project.⁷⁹ The main contribution of service users will therefore be:

- i. Two members to sit on the Advisory Group during the project, to help oversee the overall aims and design of the research and bring the perspective of "critical friends" to the process
- ii. We also plan to have three separate PPI group meetings at similar times to the advisory group meetings attended by a larger group of service users ensuring broader input into the project and also providing support to the two members of the advisory group. These meetings will be chaired by David Shiers who is a carer and also experienced in supporting the involvement of service users in research.
- iii. The two service user members of the advisory group will contribute to dissemination activities by writing lay summaries for the funder and other organisations as well as providing links to the service user networks.
- iv. We will also liaise with service user organisations we have collaborated with in similar previous projects (such as Mind and ASH) to provide feedback on our report and lay summaries and help guide our dissemination strategy.

We will ensure that PPI activities are conducted in line with current guidance,^{80 81} including clear discussion about roles, valuing different perspectives, clear budgeting for PPI, training for both researchers and PPI representatives, and reporting of the PPI contribution.

We will provide support to our PPI representatives to contribute to the research process and to contribute to specific research activities. We will facilitate a half-day training event at York for our PPI representatives. The training will provide context for understanding the research content and the research process, and also contribute to capacity building amongst PPI partners. We will assess impact using the GRIPP checklist to ensure transparency and consistency of reporting.⁸²

10. Expertise and justification of support required

10.1 Expertise of review team

The bid team have an international track record in the delivery of evidence syntheses in mental health and behaviour change. The applicants have significant skills and experience in numerous forms of evidence syntheses. They are skilled in information retrieval and data extraction, coding, risk of bias assessments and quantitative synthesis of complex, heterogeneous data sets, including meta-analysis, meta-regression, multilevel modelling and network meta-analyses (Meader, Dias, Coventry, Churchill, Armitage). We also have experience in the delivery of qualitative syntheses to complement and cross tabulate with conventional reviews (Coventry, Meader).

Our team includes experts in smoking cessation and other behaviour change interventions in people with or without mental health problems (Ratschen, Armitage, Gilbody), psychological medicine and severe mental illness (Gilbody), physical health treatment of people with SMI (Shiers), mental and physical multimorbidity (Shiers, Coventry), health psychology (Armitage) and knowledge mobilisation (Churchill) who bring national and international expertise in understanding about multiple risk behaviour interventions in people with SMI.

Specifically, the expertise of the review team includes:

Dr Nick Meader: is a research fellow in evidence synthesis with a track record of over 13 years in leading systematic reviews of intervention effectiveness in mental health populations as well as the effectiveness of single and multiple risk behaviour interventions. He has methodological expertise in meta-regression, network meta-analyses, multivariate meta-analyses and also synthesis of qualitative studies. He has been a member of guideline development groups for eight NICE mental health guidelines (including the first NICE guideline that aimed to address physical and mental health comorbidities).

Dr Peter Coventry is a senior lecturer in health services research and holds a joint appointment with the Mental Health & Addiction Research Group and the Centre for Reviews and Dissemination at the University of York. He was a MRC Special Training Post-doctoral fellow between 2005-09 during which time he trained in systematic reviews at SchARR, University of Sheffield. He is expert in leading quantitative systematic reviews of effectiveness of psychosocial interventions for common mental health problems in adults with long term conditions, moderator analyses of treatment effects using meta-regression and individual participant data meta-analysis, and has completed qualitative meta-syntheses of complex interventions in mental and physical multimorbidity.

Dr Elena Ratschen is a senior lecturer in health services research who specialises in applied health research in the area of smoking and mental health. She has conducted various mixed-methods studies concerned with smokefree policy implementation in mental health settings, majorly contributed to the production of the 2013 joint RCP/RCPsych report on smoking and mental health¹, and involved in the development of NICE guidance PH48.

Dr David Shiers is an honorary Reader in early psychosis at Manchester University. He brings a 20 year carer perspective as father to a daughter with schizophrenia, plus experience as a retired GP, researcher and participant in NICE reviews of psychosis & schizophrenia (CG178, CG155, QS80 and QS102). He also has extensive links to research programmes and national policy networks relevant to mental and physical multimorbidity (e.g. National Audit of Schizophrenia) which would be key for promoting dissemination of the projects findings.

Prof Sofia Dias is currently Director of the NICE Guidelines Technical Support Unit and first author of the influential Evidence Synthesis NICE TSD series on pair-wise and network meta-analyses and recent book on Network Meta-analysis for Decision Making. She is experienced in conducting and advising on complex network meta-analyses and in methods for checking evidence consistency. She has been actively involved in the production of several NICE mental health guidelines including bipolar disorder, depression, and social anxiety disorder. Before the start of the project she will be relocating to the Centre for Reviews and Dissemination at the University of York.

Prof Simon Gilbody is a leading health services researcher and psychiatrist/cognitive behaviour therapist by clinical background. He directs the Mental Health & Addictions Research Group (MHARG) at the University of York, and has a strong track record of delivering health technology assessments and systematic reviews on time and in budget. Gilbody trained in systematic reviews under the auspices of an MRC Fellowship (1996-2000) held at CRD. He is a long-time contributor to the Cochrane Collaboration (contributing editor to CCMD). His systematic reviews have influenced NHS policy and practice in the management of perinatal mental health, primary care mental health and screening polices for depression. Gilbody was an inaugural NIHR Senior Investigator and he has

successfully used systematic reviews to prioritise and inform the design of some of the largest mental health trials ever funded by NIHR (CASPER, CASPER+, REEACT1 REEACT2), including smoking cessation in people with severe mental illness (SCIMITAR).

Prof Chris Armitage is a Health Psychologist registered with the UK Health and Care Professions Council who uses mixed methods (e.g., evidence synthesis) to develop tools for effective behaviour change (e.g., physical activity, diet, smoking, alcohol consumption, drug use) among diverse populations (e.g., patients, health professionals). He has published more than 120 peer-reviewed articles on these topics and has received funding to support this research from numerous sources, including the NIHR and MRC.

Prof Rachel Churchill is a Chair in Evidence Synthesis and Coordinating Editor of the Cochrane Common Mental Disorders group. She is a psychiatric epidemiologist with a long track record in undertaking and managing complex programmes of mental health systematic reviews and evidence syntheses, as well as in rapid reviews and network meta-analyses. Her work involves a variety of knowledge mobilisation and exchange activities and has been influential in both policy and practice.

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