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National Institute for Health Research

Improving diabetes outcomes for people with severe mental illness (SMI): a longitudinal observational and qualitative study of patients in England

Najma Siddiqi, Johanna Taylor, Sarah Alderson, Tim Doran, Simon Gilbody, Catherine Hewitt, Richard Holt, Rowena Jacobs, Stephanie Prady, John Radford and David Shiers

STUDY PROTOCOL

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1 Summary of research

1.1 Background

People with severe mental illness (SMI) have poorer physical health and a lower life expectancy (by around 20 years) than the general population, often dying of preventable physical illnesses (1-4). Diabetes contributes significantly to this health inequality, being two to three times more prevalent in people with SMI and leading to poorer health outcomes (5-7). This is likely to increase, as diabetes prevalence in the general population increases, and the *difference* in prevalence between people with and without SMI widens (8).

Diabetes currently costs the NHS £10 billion in direct treatment costs and £4 billion in indirect costs each year (9); and accounts for 10% of the overall health budget (10). The costs of diabetes in SMI have not been estimated, but are likely to be disproportionately high given the higher prevalence, poorer outcomes (11, 12), underlying psychological vulnerability and increased burden of care (13) in this population.

Recorded quality of care for diabetes has improved substantially in the last fifteen years following the introduction of successive national quality improvement initiatives, including diabetes National Service Frameworks and the Quality and Outcomes Framework in primary care (14). However, there remain wide variations in quality of care associated with age, gender, deprivation and co-morbidity, and there are concerns about the appropriateness and effectiveness of universal quality targets in sub-groups of diabetes patients, including those with SMI (15).

Improving diabetes care for people with SMI is a high priority area for the NHS (16). However, little is known about how SMI and other risk factors combine to generate high diabetes prevalence and poor diabetes outcomes; and how the quality and quantity of healthcare services and interventions can impact on these risk factors in people with SMI. Understanding this is a necessary first step in developing healthcare interventions to improve outcomes for people with diabetes and SMI.

1.2 Aims

The overarching goal of our research programme is to improve diabetes outcomes for people with SMI. The present proposal contributes to that goal and aims to identify the determinants of diabetes and explore variation in diabetes outcomes for people with SMI in order to develop potential healthcare interventions that can be tested further.

Our key research questions in this study are:

1) What are the socio-demographic and illness-related risk factors associated with
    a) developing diabetes in people with SMI?
    b) variation in diabetes and mental health outcomes in people with SMI and diabetes?
2) How do physical and mental health outcomes differ between people with SMI and diabetes,
    a) compared to people with SMI without diabetes?
    b) compared to people with diabetes but no SMI?
3) What factors influence access to, and receipt of, diabetes care for people with SMI, and how are diabetes healthcare interventions experienced by people with SMI?
4) How and at what cost is diabetes monitored and managed in people with SMI compared to those without SMI?
5) What healthcare interventions (e.g. medication, referrals and care pathways) are associated with better diabetes outcomes for people with SMI and diabetes?

1.3 Research plans

Under a social inequalities framework, we will use a concurrent triangulation mixed methods design comprising quantitative analyses of individual primary care patient records, and a qualitative interview study of patients with co-existing SMI and diabetes, their carers, and healthcare staff. The quantitative study will interrogate linked primary care and hospital records of a large representative sample of adults with SMI. We will quantify the role of the socio-demographic, illness- and healthcare-related factors thought to influence a) development of diabetes in people with SMI, and b) variation in health outcomes in people with comorbid SMI and diabetes. We will compare health outcomes for people with comorbid SMI and diabetes with outcomes for those without SMI, and those without diabetes. We will also explore variations in diabetes screening, monitoring and management, and estimate costs for these; and determine associations between these interventions and health outcomes in order to identify potential interventions to improve outcomes for people with SMI and diabetes. The qualitative study will explore how diabetes is managed alongside SMI and how diabetes care is experienced by patients, carers, and healthcare professionals, using thematic analysis of semi-structured interviews. The aim is to identify the healthcare needs and healthcare delivery concerns of this comorbid population. Analysis and interpretation of findings in each part (quantitative and qualitative) will be merged to inform further analyses and to develop a fuller understanding of the factors that contribute to poor outcomes and the drivers of improved health outcomes in SMI

and diabetes. Multi-stakeholder co-design workshops will be used to translate study findings into recommendations for healthcare and to design new interventions where gaps in provision exist.

The proposed study builds on and complements on-going HS&DR funded research being undertaken at the Centre for Health Economics and the Department of Health Sciences at the University of York (Study HS&DR 13/54/40). Study 13/54/40 aims to determine the effect of the quality of care for SMI in primary care on health outcomes and healthcare utilisation. Study 13/54/40 will support the current proposal in several ways:

- Technical: providing clinical (Read-code) lists for the conditions and activities of interest, and expertise in interrogating CPRD data.
- Organisational: providing i) liaison links with CPRD and expertise in obtaining data approvals and specifying datasets; ii) contacts with service users and expertise in patient and public involvement.
- Methodological: providing expertise in constructing statistical models to interrogate large, individual-level datasets to answer questions on quality and outcomes for patients with SMI.
- Evidential: identifying indicators of high quality care for patients with SMI, and providing information on the quality of primary care and its association with patient outcomes.

The proposed study will also be supported by the DIAMONDS (Diabetes and Mental Illness: Improving Outcomes and Services) research group (www.diamonds.nihr.ac.uk) and Patient and Public Involvement (PPI) Panel, who have helped to prioritise the questions for this study and improve its design, and will provide input throughout the study to ensure a focus on the needs of people with SMI and their carers.

1.4 Benefits and Potential Impact

This study will help address important gaps in evidence about which people with SMI experience poor diabetes outcomes and why; and how healthcare services can be changed to improve physical and mental health outcomes. Better prevention and management of diabetes has the potential to significantly reduce the risk of diabetes complications, deliver large cost savings for the NHS, and help reduce health inequalities (including life expectancy and morbidity), experienced by people with SMI.

2 Key terms

Severe mental illness (SMI): There is no universal definition of SMI. For this study, the term refers to illnesses where psychosis occurs, and includes schizophrenia, schizoaffective disorder, bipolar disorder and manic episodes, and non-organic psychoses (8).

Clinical Practice Research Datalink (CPRD): A computerised database of primary care medical records drawn from general practices in the UK, containing information on diagnoses, referrals, investigations and treatments. CPRD covers approximately 7% of the UK's population (17).

3 Background and rationale

Around 1% of the population in England will receive a diagnosis of SMI at some point in their lives (18). SMI interferes with mood, emotion, cognition and motivation, and affects all aspects of life including employment, relationships, housing, and personal care (19). People with SMI have poorer physical health compared to the general population, including a higher prevalence of common chronic disorders and multi-morbidity (8, 20), and a lower life expectancy by around 20 years (1-4). Diabetes contributes significantly to this health inequality: observational studies (4, 7, 8, 12, 21-25) and evidence reviews (2, 5, 6, 26-28) consistently report higher diabetes prevalence and increased diabetes complications and mortality in people with SMI compared to the general population.

The increased risk of diabetes and its associated poor outcomes is not fully understood, but likely relates to a unique set of risk factors (6, 29). These include: features of the mental illness (30); metabolic side effects of antipsychotic medication (31-33); lifestyle factors such as physical inactivity (34), poor diet and smoking (35-37); and the competing risks from other co-morbidities (38). These occur in the setting of wider socio-economic inequalities, such as higher rates of unemployment, poverty and stigma (19, 39-41).

Healthcare services may also contribute (42, 43), because of inadequate assessment and monitoring of physical health (44), 'diagnostic overshadowing', whereby physical health problems are attributed to mental illness (45), and the failure to provide healthcare proportionate to the increased needs of a disadvantaged population (46, 47). 'Silo-working', poor co-ordination between services for physical and mental health (48, 49), and ambiguity in both policy and practice about who is responsible for managing the physical health of people with SMI may also lead to fragmented care (50). Despite having more frequent contact with health services than the general population (51), people with SMI report barriers to accessing timely and appropriate services for physical health (52, 53). While there may be illness-related cognitive and motivational difficulties that contribute to under-utilisation of healthcare, there is ample evidence that the physical health needs of people with SMI are frequently overlooked by healthcare professionals (26, 28, 46, 54, 55). The more limited evidence specific to diabetes also suggests that individuals with comorbid SMI and diabetes receive fragmented and ineffective care compared to those without SMI (22, 28, 56-58). However, this evidence is conflicting with some studies suggesting people with SMI receive more diabetes

care, while others show no difference (26, 28, 59). There is no detailed published research from the UK about the diabetes care that people with SMI receive, resulting in a significant evidence gap (59).

Although a range of factors has been implicated, their relative and synergistic influence on the risk of diabetes and poor diabetes outcomes in people with SMI remains poorly understood. There is also little known about provision, uptake and costs of diabetes screening, monitoring and management for people with SMI; or the role of diabetes healthcare in influencing physical and mental health outcomes. The impact of diabetes on mental health outcomes for people with SMI is also important to understand; diabetes is linked to an increased risk of depression and distress, both of which have been found to be associated with poor diabetes control (60-64). However, there is little to no research examining the impact of diabetes on mental health outcomes in this population, despite their increased psychological and social vulnerabilities.

Understanding these inequalities and in particular how healthcare interventions may contribute to poorer outcomes is a necessary first step towards adapting and developing interventions that can help to improve health and life expectancy in people with SMI and diabetes.

4 Evidence explaining why this research is needed now

People with SMI have a two to three-fold higher prevalence of diabetes than the general population (6), and an increased risk of diabetes complications and mortality (7, 24). Estimates suggest that approximately 44,000 people in England currently live with coexisting SMI and diabetes. This is likely to increase, with recent reports showing diabetes prevalence in England increasing year-on-year for the whole population in the last 10 years, and prevalence in SMI increasing at an even higher rate (8). The direct cost of diabetes is predicted to rise by 72% by 2035 (10). Costs of diabetes care in SMI have not been estimated, but are likely to be disproportionately high given its higher prevalence (11, 12) and poorer outcomes (13).

Better diabetes care for people with SMI is clearly needed. Even modest improvements in glycaemic control, blood pressure and cholesterol can reduce the risk of complications and mortality (15) and reduce healthcare costs (10). Better diabetes care may also lead to improved mental health through better illness management, lifestyle changes and reduction of diabetes-related distress (62, 65, 66). Support for self-management has been promoted for the general population with diabetes (67) (although the evidence for self-management interventions suggests benefit primarily in terms of weight rather than glycaemic control (68, 69)). Little is known, however, about what works to improve diabetes management for people with SMI (70), who have additional social, psychological, cognitive and motivational vulnerabilities that are likely to impact on their ability to manage (and particularly to self-manage) diabetes (66). Less still is known about the patterns and costs of diabetes healthcare in this population and their influence on health outcomes (22, 23, 26, 28, 42). This has not been studied before in the UK and there are conflicting reports from international studies as to whether people with SMI and co-morbid diabetes receive better or worse care for their diabetes than those with diabetes alone (6, 59).

Ward and Druss (6) provide a narrative synthesis of studies of diabetes care in people with psychotic disorders; identifying a consistent treatment gap across countries and showing significant variation in the quality of diabetes care and health outcomes. They argue that their findings, while useful, have limited application to specific populations, and point towards important differences in the prescribing of anti-psychotic medications, monitoring of diabetes risk, and healthcare structures, resources and treatment guidelines between individual countries, which are likely to impact on health outcomes and inequalities. Findings from this review and others (26, 28, 59) demonstrate the importance of undertaking this proposed study, to address evidence gaps in the current literature. Specifically, no study has investigated the relative contribution of multiple explanatory factors using linked medical records in addition to generating knowledge about the diabetes care that people with SMI and co-morbid diabetes receive in England, and identifying potential adaptations and interventions to improve health outcomes for the socially disadvantaged SMI and diabetes population. The proposed study is also distinctive because it focuses on primary care, which has a very significant role in treating SMI in England, and in contrast to other countries, has the main responsibility for managing co-morbid illness.

Increasing access to large databases with patient-level data collected across primary and secondary care offers an opportunity to understand how multiple factors influence the risk of diabetes and diabetes outcomes, including socio-demographics and the influence of healthcare services and interventions. The applicant team has considerable experience in this area, and the proposal builds on and complements ongoing HS&DR funded research led by applicant RJ: 'Does better quality of primary care influence admissions and health outcomes for people with serious mental illness? A linked patient-level analysis of the full patient care pathway, HS&DR 13/54/40' (http://www.nets.nihr.ac.uk/projects/hsdr/135440). In this HS&DR 13/54/40 study, a systematic review and consultation process have already informed the development of indicators of primary care quality, several of which are relevant to diabetes care. We will be able to draw on these measures as indicators of diabetes management, as well as on the expertise already developed by the research team in interrogating CPRD to address healthcare questions for the SMI population.

This study also builds on and contributes to the DIAMONDS research programme (www.diamonds.nihr.ac.uk), which aims to improve outcomes and services for people with comorbid SMI and diabetes through research and translation of evidence into practice. The DIAMONDS research group has completed a systematic review to

examine effectiveness of interventions for improving diabetes outcomes in people with SMI (71). This will help inform the selection of healthcare interventions to examine in this study.

The proposed research is timely, given the increasing burden of diabetes in SMI. The UK government has pledged to improve the prevention and management of diabetes in England (72), and prioritised improving care for people with mental and physical health comorbidity to address unacceptable health inequalities, targeting in particular, patients with SMI (73-75). These priorities are reflected in NICE guidelines for managing SMI (75) and for preventing type 2 diabetes (74), and in the James Lind Alliance Schizophrenia priorities for research which include the need to understand more about interventions to monitor physical health and manage weight gain (76). Our own consultation with service users, carers, clinicians and commissioners involved in diabetes and mental healthcare has also confirmed this topic as a priority for research.

5 Aims and objectives

The overall aim of our research programme is to improve diabetes outcomes for people with SMI. The present study contributes to that goal, and specifically aims to understand the determinants of diabetes and variation in diabetes outcomes for people with SMI, in order to identify potential healthcare interventions that can be tested further.

The study has the following objectives:

1. In people with SMI, to identify which socio-demographic, illness, family history and lifestyle factors are associated with the development of diabetes.
2. In people with SMI and diabetes, to identify which socio-demographic, illness, family history and lifestyle factors are associated with variation in diabetes and mental health outcomes.
3. In people with SMI, to compare healthcare interventions, physical and mental health outcomes in those with diabetes with those without diabetes.
4. In people with diabetes, to compare healthcare interventions, physical and mental health outcomes in those with SMI and those without SMI.
5. To understand the factors that influence access to, and receipt of, diabetes care for people with SMI, and explore the experience of diabetes healthcare by people with SMI.
6. To compare diabetes care provision for people with and without SMI, and estimate costs for these.
7. To identify which healthcare interventions (e.g. medication, referrals and care pathways) may be associated with better diabetes outcomes for people with SMI and diabetes.

6 Research plan and methods

6.1 Study design

This study conceptualises as a theoretical framework, socio-economic conditions as a fundamental cause of health inequalities (77). Under this framework, the reduced access to material, financial, social or structural resources such as transport, childcare, paid leave and advocacy services that result from living in social or economic disadvantage mean individuals have less agency with which to navigate healthcare systems, less capacity to take advantage of health promotion opportunities, and more barriers to taking up interventions designed to prevent or treat illness. There is strong evidence that people with SMI are more likely to be socially disadvantaged than people without SMI (78-81), leading to a reduced ability to take advantage of resources that improve health, or prevent or treat illness, ultimately resulting in significant inequalities in health outcomes we see for this population. Further complicating, and disadvantaging factors for people with SMI are their increased risk for developing diabetes, which itself is socially patterned and more prevalent in the disadvantaged including ethnic minority groups (82). People with SMI therefore have greater healthcare needs than those without, but also have more limited resources for navigating a complex healthcare system (83). We acknowledge that as a ‘downstream’ determinant of health (84), the healthcare system cannot remediate the social causes of inequality. However, using a social inequalities lens we will seek to understand how healthcare organisation and delivery could better respond to the physical health needs of people with SMI and diabetes, and identify areas for action where healthcare appears to further generate inequalities in this vulnerable population.

We will use a concurrent triangulation mixed methods design (see study flow diagram) comprising: a) a quantitative longitudinal observational study of individual patient records of adults with diagnosed SMI and diabetes in CPRD; and b) a qualitative interview study of people with co-existing SMI and diabetes; their carers; and healthcare staff involved in diabetes and mental healthcare. The mixed methods design is underpinned by a pragmatic paradigm, which acknowledges that each data type provides a different but equally important worldview of the relationship between SMI and diabetes, and that merged together they will enable us to develop a more complete understanding of health inequalities in this population than would be possible from using either method alone (85). Findings from studies will be merged at the interpretation stage using multi-stakeholder co-design workshops to iteratively translate study findings into evidence-based recommendations for healthcare and to design tailored interventions where the study findings indicate these are needed. Following MRC guidance for the

development of complex interventions, we will also use the co-design workshops to assess the potential acceptability and feasibility of implementing these recommendations into routine healthcare.

We will conduct three concurrent work packages:

- WORK PACKAGE 1 (WP1) will co-ordinate the work, help integrate the quantitative (WP2) and qualitative (WP3) studies, and support dissemination.
- WORK PACKAGE 2 (WP2) is a longitudinal observational analysis of patients attending general practices participating in CPRD, using primary care records linked to hospital episode statistics (secondary care) data, mortality and area deprivation.
- WORK PACKAGE 3 (WP3) will involve semi-structured interviews with people who have comorbid SMI and diabetes, their carers, and healthcare staff.

6.2 Work package 1 – Study co-ordination, integration and dissemination

This will involve ongoing consultation with experts (including service users, carers, healthcare staff, the DIAMONDS Research Group and PPI panel) to refine questions and analyses in the CPRD and qualitative studies; lead the mixed methods analyses (merging of WP2 and WP3 findings); conduct co-design workshops to help transform study findings into clear practice recommendations; and help optimise dissemination of findings.

6.2.1 Evidence synthesis and expert consultation

In preparation for WP2 (quantitative) and WP3 (qualitative) studies, we will draw up lists of (i) key determinants of diabetes, (ii) determinants of poor diabetes outcomes; and (iii) diabetes care pathways and interventions (referred to collectively hereafter as 'healthcare interventions'), which may influence diabetes outcomes for people with SMI. Determinants of diabetes and poor outcomes will be identified from published systematic reviews (6). Although evidence from high quality studies is limited, nevertheless these provide a starting point for our investigation. Healthcare interventions will be identified in the following ways:

1) Constructing diabetes and SMI Quality and Outcomes Framework (QOF) indicators that can be defined as an intervention in CPRD data. The QOF is a national programme that offers financial incentives to General Practices for meeting quality of care targets across a range of conditions, including SMI (43) and diabetes (14). These indicators include, for example, annual monitoring for key biological parameters such as blood glucose and blood pressure, dietary review, foot examination, retinal screening, structured education, comprehensive care planning (86).
2) NICE recommended diabetes interventions (e.g. glucose lowering medications, referral to diabetes specialists / nutritional experts / podiatrists, blood pressure and lipid lowering medications, self-monitoring of glucose levels or blood pressure) (67).
3) Interventions identified from the systematic review and service user engagement completed in Study 13/54/40, which identified a number of diabetes-related indicators of primary care quality (e.g. diabetes screening, monitoring concomitant antipsychotic medications, BMI and weight loss, retinal and foot examination, and education about nutrition and physical activity).
4) Interventions identified from the DIAMONDS systematic review (71) and PPI consultation, and through on-going consultation with the study research team, collaborators and steering committee; and the wider DIAMONDS research group, PPI panel, and virtual stakeholder network (see Sections 9 and 11).
5) Results of our pilot interrogation of primary care data (containing records of around 1000 patients with comorbid SMI and diabetes) currently being carried out by the DIAMONDS research group to characterise the population, develop and test clinical (Read-code) lists in preparation for the proposed study (87).
6) Interventions identified from systematic reviews as being potentially effective in the UK for reducing inequalities in diabetes or SMI care and outcomes(88-93).

Below is an indicative list of the types of interventions we expect to examine:

- Diabetes 6 month/annual review
- Monitoring of HbA1c; BMI
- Referral to self-management education programme
- Antipsychotic switching
- Referrals to podiatry
- Foot checks/pulse checks
- Retinopathy screening
- Referral to secondary care
- Specialist diabetes nurse contacts

WP1 will also inform the selection of *a priori* covariates to enable us to account for important confounding effects that may impact on people with comorbid SMI and diabetes (94) (such as referral to specialist mental health or diabetes care, frequency of GP visits, order and timing of diagnoses, type and severity of illness, and multi-morbidity) in WP2 analyses.

As there are likely to be additional factors identified in WP3 that are perceived to influence response to healthcare interventions, WP2 analyses will be ordered so that identification of additional potential explanatory variables can be incorporated into the final modelling for objective 7 (see Section 6.3.8 and Section 8).

6.2.2 Mixed methods analysis

The study will use established merging techniques (e.g. data transformation and comparison matrices) to allow triangulation of study findings during the final stages of analysis (85) (see Study Flow Diagram and project timetable in Section 8). We will also use embedding techniques at earlier key points in the study so that findings from the analysis of CPRD data can inform the design of the qualitative study, and to allow for findings from the qualitative study to inform the final analysis of CPRD data. Specifically, we will do the following:

1) WP1 evidence synthesis and expert consultation will inform the selection of *a priori* variables for exploration in WP2; and inform the development of interview topic guides for WP3.
2) Sampling criteria and interview topic guides for WP3 will be informed by WP2 analysis for study objectives 1 to 3 (see Section 6.3.8), e.g. sampling for and exploring factors identified to influence variation in diabetes outcomes.
3) Emerging themes in WP3 will help to identify additional explanatory (independent and confounding) variables for final WP2 analyses of diabetes interventions (objective 7).
4) In the final stages of analysis (from month 15 onwards) we will merge findings from both quantitative and qualitative analyses (see section 6.4.6 for details). A summary of these analyses will be used to translate study findings in the co-design workshops. Specifically, we will: a) map and synthesise study findings for WP2 and WP3 by study objective into a matrix to allow for comparison (JT); b) identify and develop key themes across the study findings (ALL); c) write explanatory summaries for key themes to ensure that all findings, including any contradictory or unusual findings fit within this framework (JT / NS); c) translate study findings into draft recommendations for practice and suggest candidate interventions for testing in a future causal framework (ALL plus co-design workshops); and d) develop a logic model of how diabetes contributes to health inequalities in people with SMI and the role that healthcare plays in increasing and / or reducing these, taking into account the estimated effect of mediators and moderators on process and outcomes.

6.2.3 Co-design workshops

We will run co-design workshops in month 16 and month 20 of the study to translate study findings into recommendations for how to improve diabetes care for people with SMI. The first workshop will identify further avenues of inquiry for the final stage of analysis in WP2 and WP3, develop draft recommendations and priorities for how to improve the delivery and organisation of healthcare for this population, and identify gaps in provision where tailored interventions may be required. The second workshop will further develop the recommendations based on the final mixed methods analysis; and design tailored interventions/ care pathways where these are required, including assessing their potential acceptability and feasibility for future evaluation and implementation. We are cautious about anticipating what these recommendations and tailored interventions might encompass, but, they may, for example, include changes to the timing and venues for delivery of diabetes care or to healthcare staff training.

The co-design workshops will be attended by service users and carers (n=6-8) (recruited through the DIAMONDS PPI panel and stakeholder network as well as participants in the qualitative study); healthcare staff, including health service managers and commissioners (n=8-10); other relevant stakeholders such as third sector organisations (n=3-5) (identified through the team's extensive professional networks); and members of the research team, Study Steering Committee members and DIAMONDS Research Group (n=5-8).

Attendees will be provided with a short report of key findings prior to each workshop, and brief presentations will be delivered to summarise these. Social marketing and co-design techniques, such as concept mapping, affinity diagrams and touchpoint matrices (95), will be used to facilitate small and whole groups discussions, focused on the following:

a) Key barriers to and enablers for accessing existing diabetes care and support for people with SMI
b) Key learning for commissioners, service providers, clinicians and people with comorbid SMI and diabetes
c) How to meet additional or unmet needs for diabetes care for people with SMI, e.g. through tailored interventions.

To enable service users and carers to give their perspectives, we will ensure that we have good representation at each event; provide summary reports in accessible language and formats; and hold meetings with service users and carers at the beginning of each event to allow them to put forward their views in a smaller group, which will be presented to the full stakeholder workshop in the second part.

6.2.4 Dissemination event

We will host a one-day dissemination event in month 24 of the study to share findings. We will use a combination of printed materials, presentations, expert panels, and workshops to maximise opportunities for knowledge exchange. We will invite all study participants and other relevant stakeholders, in particular service managers, local and national commissioners, and third sector organisations involved in supporting this patient group (n=80). Detailed dissemination plans are described in Section 7.

6.3 Work package 2: Interrogation of patient health records

Using statistical analyses, we will investigate the role of known risk factors thought to influence i) development of diabetes in people with SMI (objective 1), and ii) variation in health outcomes in people with comorbid SMI and diabetes (objective 2). We will compare diabetes healthcare and outcomes for people with SMI and diabetes, with outcomes for people with either condition alone (objectives 3 and 4). We will also examine variations in diabetes screening, monitoring and management and estimate costs for these (objective 6); and explore the role of these interventions in contributing to health outcomes (objective 7).

6.3.1 Study population

The primary study population comprises adult patients living in England with a diagnosis of SMI who are registered with a general practice (GP) of up-to-standard data quality contributing data to CPRD and who have remained within CPRD for the duration of the study period.

6.3.2 Study period

The study will cover the period from 01 April 2000 to 31 March 2016.

6.3.3 Data sources

Clinical Practice Research Datalink (CPRD) data: CPRD is the world's largest computerised database of anonymised longitudinal medical records from primary care. Information includes records of clinical events (medical diagnoses), referrals to specialists and secondary care settings, prescriptions issued in primary care, records of immunisations/vaccinations, diagnostic testing, lifestyle information (e.g. smoking and alcohol status), and all other types of care administered as part of routine general practice. Currently data are collected on over 5 million active patients from over 610 general practices throughout the UK. The CPRD requires intensive data management and cleaning to produce a dataset for statistical analyses. The applicants have extensive experience of using CPRD data in quality of care related research. CPRD will be linked to the following datasets:

Hospital Episode Statistics (HES) data: Our main data source for hospital admissions will be HES, which contains a detailed record for each NHS inpatient admission to every hospital provider in England. HES contains information on patients' socio-economic characteristics, diagnoses, procedures and resource use.

HES-Office of National Statistics (ONS) mortality data: Information on patients who die in hospital can be analysed as recorded in HES, but these data alone cannot be used to identify cause of death, or to obtain information on patients who died outside of hospital. The Office of National Statistics' (ONS) mortality data are a more complete source of information on deaths based on information from medical practitioners and/or coroners. Linking ONS mortality data to HES data permits the analysis of deaths in and outside hospital for all patients with a record in HES. Again, we have expertise with the methodology for HES-ONS mortality data analysis.

Index of Multiple Deprivation (IMD) data: The IMD 2010 provides a relative measure of deprivation at small area level across England. The domains used in the IMD are: income; employment; health and disability; education; crime; barriers to housing and services; and living environment deprivation. These are combined to form a composite index.

6.3.4 Data linkages

CPRD will provide a single extract of linked HES/ONS/IMD anonymised data. Additional linkages will include distance from GP practice to the nearest mental health and acute provider, as well as socio-economic data attributed to patients on the basis of postcodes and will include measures of rurality. We will submit a single data protocol to CPRD covering CPRD-HES-ONS-IMD data, which are standard linkages. This will be adapted from a protocol approved for HS&DR Study 13/54/40, which required similar data. Data on rurality will be produced by the University of York, and linked by CPRD using postcode information. The applicants have considerable expertise in producing required data protocols and data specifications for CPRD and liaising with them about data requirements.

6.3.5 Datasets

Dataset A: Dataset A, which will be requested from CPRD, will contain the anonymised longitudinal healthcare records of a cohort of all adult patients (aged 18 and over) with a diagnosis of SMI from general practices in England. Severe mental illness will be defined within the dataset as the presence of a clinical diagnostic code for schizophrenia, affective disorder (divided into bipolar or unspecified affective disorder), and other types of psychoses. Read-codes previously tested and applied by the research team (also used in Study 13/54/40) will be used to identify the presence of SMI (8). Patients will be drawn from practices that have remained continuously

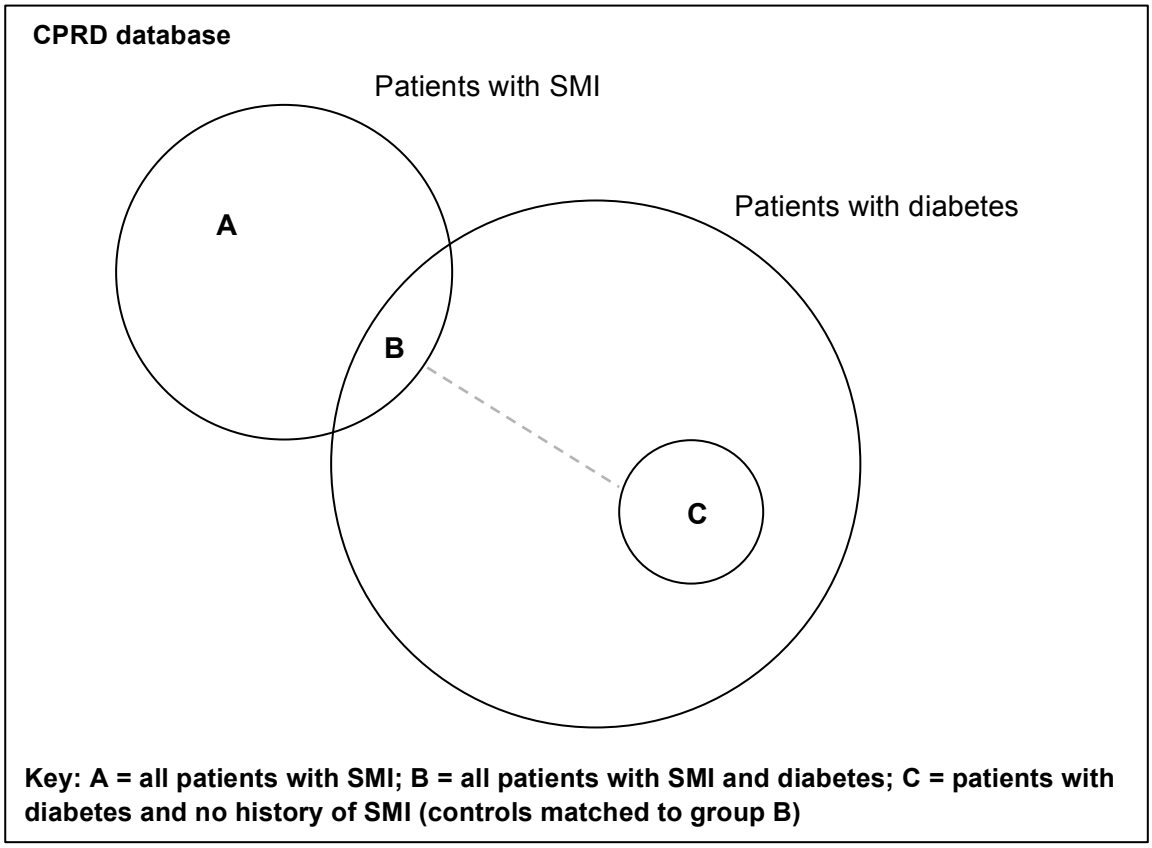
active in CPRD, and have agreed to HES/Office for National Statistics (ONS) linkages. Data will cover the period 2000/1 to 2015/16. From preliminary work, we estimate a sample size of 33,000 patients.

Dataset B: Dataset B will be constructed from Dataset A, and will comprise all adult patients with a diagnosis of SMI who also have a diagnosis of diabetes mellitus. Diabetes will be further defined as the presence of a clinical diagnostic code for Type 1 diabetes, Type 2 diabetes, drug-induced diabetes or unspecified diabetes. Individuals with a diagnostic code of gestational diabetes, cystic fibrosis and haemochromatosis will be excluded. Previously tested and validated Read-codes will be used for the purpose of identifying individuals with diabetes (15). With a predicted diabetes prevalence of 11.1% (8), we estimate approximately 3,600 patients with comorbid SMI and diabetes for whom we will have on average around 5-6 years of data for each individual.

Dataset C: Patients in Dataset B will be exact matched by CPRD to a cohort of patients who have a diagnosis of diabetes, but no recorded diagnosis of SMI ever documented in CPRD (controls). These controls will be matched to SMI patients with diabetes on a ratio of 4:1 on the basis of age, gender, practice and type of diabetes (generating approximately 14,000 patients).

Figure 1 shows how these datasets relate to each other.

Figure 1: Relationship between datasets



6.3.6 Key health and healthcare outcomes

The key outcomes we will examine in work package 2 are:

1) Diabetes status (objective 1) and onset (objective 1)
2) Diabetic and cardiovascular control (measured by recorded HbA1c, blood pressure, cholesterol levels) (objective 2)
3) Diabetic complications: acute hyperglycemic events, hypoglycemia, micro-vascular complications [retinopathy, neuropathy, nephropathy] (objectives 2 and 4); macro-vascular complications [coronary artery disease, cerebrovascular disease, peripheral arterial disease] (88) (objectives 2, 3, 4, 7)
4) Hospital admissions for the above conditions (objectives 2, 3, 4, 7);
5) Mental health outcomes (including SMI relapses and markers of depression or anxiety) (objectives 2, 3, 4, 7);
6) Mortality (3, 89) (objectives 2, 3, 4, 7);
7) Healthcare utilisation (including the number and type of primary care consultations) and costs (objective 6)
8) Healthcare interventions (e.g. medication, care pathways and referrals) (objectives 6 and 7)

We will employ validated clinical (Read-code) lists developed in Study 13/54/40 and in our previous studies to extract these data (8, 15, 43).

6.3.7 Risk factors and other explanatory variables

Known risk factors and covariates will be included in the analyses to determine their relative contribution to the development and progress of diabetes in people with SMI. Other factors will be identified in WP1 and through the integration of WP2 and WP3. Candidate risk factors include: patient demographics (sex, age, ethnic group, area deprivation, rurality), lifestyle (obesity, smoking, exercise), social vulnerability markers such as housing status, hyperlipidaemia, family history, type of SMI and diabetes (including order and timing of diagnosis), length of diagnosis, illness severity, and multi-morbidity. Treatment risk factors will include: antipsychotic medication usage, for example, olanzapine is generally associated with greater metabolic side effects and weight gain than other medications (33), and prescriptions for statins (98).

6.3.8 Statistical analysis plan

The richness of the datasets will ensure important relationships can be investigated at an appropriate level and with sufficient granularity to inform policy making. The datasets are large and complex and require an array of quantitative approaches. The team has considerable experience in the analysis of these types of data. Each dataset will consist of a panel of observations covering a number of years, with repeated observations at irregular intervals. The data are hierarchical, reflecting, for example, that activities are 'nested within' patients with SMI who in turn are nested within practices, and our analyses will take into account this hierarchical structure. We will have on average around 5-6 years of data on each individual, which will allow us to conduct more robust analyses than cross-sectional data would permit. There are two important elements to this: (i) longitudinal data afford better control for unobserved characteristics, at either the individual or practice level that plausibly impact both practice performance and patient outcomes (for example, practice style and culture) and which may otherwise confound important relationships; (ii) repeated observations at practice or patient level allow us to investigate lags in the relationship between diabetes management and outcomes as we are able to observe the timing of events. Both these factors are crucial in identifying plausible causal mechanisms linking diabetes management to outcomes.

We will address the potential for confounding by indication – and other forms of confounding – by undertaking propensity score matching, matching on index date to avoid inclusion of "ghost" patients, conducting sensitivity analyses, and evaluating the potential for unmeasured confounding and the size any observed effects. To obtain unbiased estimates of average treatment effects, we will also explore the creation of a synthetic sample using inverse probability of treatment weighting.

Analyses:

Under all objectives we will conduct analyses in line with the inequalities framework in order to quantify the absolute and relative effect of social inequalities on quality of care and outcomes. Under Objectives 1 and 3 the disparities will be modelled within the SMI population; under Objective 2 within the SMI and diabetes population, and both within and between the diabetes populations (SMI and non-SMI) under Objectives 4-7. Specifically, where sample size permits, we will stratify analyses, for example by ethnicity, and/or we will use deprivation and disadvantage markers such as IMD, housing status and rurality as independent variables to estimate gap or gradient effects.

All statistical models will include a set of relevant patient, local population and practice covariates where possible to control for confounding and interacting influences potentially masking the relationship between diabetes management and outcomes.

In sensitivity analyses, we will include non-compliance (identified by relevant Read codes, including refusal of treatment, informed dissent and non-attendance) as an independent variable in the models. We will conduct sensitivity analyses with non-compliance treated as either a time dependent ('expiring') or time independent ('non expiring') variable, and as specific to the refused treatment or as a general marker of non-compliance. We also use non-compliance to create 'offer of treatment' explanatory variables, facilitating 'intention-to-treat' type analyses.

We will carry out a variety of robustness checks to ensure our results are reliable and plausibility tests to ensure findings are meaningful in practice and can inform policy. Model assumptions will be checked for all analyses and if they are in doubt, the data will be transformed prior to analysis or alternative non-parametric analysis methods will be used.

Objective 1: Using dataset A (Figure 1) which includes those with SMI, multilevel modelling will be used to explore the impact of key explanatory variables (outlined in section 6.3.7) on both diabetes status and time to onset of diabetes. Logistic (diabetes status) and survival (time to onset of diabetes) models will be developed for each outcome. The potential clustering within practices will be accounted for by specifying practice as a random effect and the explanatory variables will be included as fixed effects. Date of diagnosis or index date will be recorded in CPRD as the earliest date of clinical diagnosis or the date of first prescription of anti-diabetic medication if this occurred before the date of diagnosis (81).

Objective 2: Using dataset B (Figure 1) which includes those with SMI and diabetes, repeated measures mixed models will be developed for each outcome. The repeated measures within practices and patients within practices will be accounted for by including patients (to allow for the clustering of data within each patient) and practices (to allow for the clustering of patients within practices) as random effects and exploring the impact of explanatory variables by specifying those as fixed effects. Different covariance patterns for the repeated measurements will be explored and the most appropriate pattern will be used for the final model. Linear, logistic, and survival models will be developed depending on the type of outcome specified (continuous, binary or time to event).

Objective 3: Using dataset A (Figure 1) which includes those with SMI, multilevel modelling will be used to explore the impact of diabetes status and other explanatory variables on physical and mental health outcomes (outlined in section 6.3.6). The status or number of outcome events per person (e.g. number of SMI relapses or episodes of depression and anxiety) will be used for each outcome measure in these analyses as appropriate. Poisson multilevel models will be developed with clustering by practice through specification as a random effect and other explanatory variables included as fixed effects. Data will be checked for over-dispersion and if required then alternative negative binomial regression models will be utilised. Similarly if the data are zero-inflated then appropriate zero-inflated Poisson or negative binomial models will be used. The models will include an exposure variable to indicate the length of follow-up. Similar to objective 1 analyses, logistic multilevel modelling will be used for binary outcomes (e.g. ever diagnosed depression or anxiety or cardiovascular disease).

Objective 4: Using dataset B (patients with SMI and diabetes) and C (a matched cohort of non-SMI patients with diabetes) (see Figure 1), multilevel modelling will be used to explore the impact of SMI status and other explanatory variables on physical and mental health outcomes (outlined in section 6.3.6 and 6.3.7). Similar multilevel models will be developed to those outlined above for objective 3. We will explore matching methods (e.g. propensity score, nearest neighbour) in addition to the exact matching by CPRD to ensure minimal bias in the estimation of treatment effects.

Objective 6: Using datasets B and C (Figure 1), disparities in diabetes care provided and received will be compared between those with and without SMI. The analysis will build on the same estimation approach as for Objective 4 (e.g. matching methods). The healthcare costs examined will include contacts with primary care (including GP and other practice staff contacts) and hospitalisations, but not medication use costs. This approach reflects learning from study HS&DR 13/54/40 and our pilot work on what is feasible with the data from CPRD and HES databases. To estimate healthcare costs, we will assign national average costs using NHS Reference Costs and PSSRU (Personal Social Services Research Unit) costs to health care contacts for diabetes related care and hospital admissions. Health care costs will be calculated by attaching unit costs to contacts recorded in the CPRD database and also hospital inpatient episodes, from the linked HES data. We will therefore cost up the care pathways for SMI patients from their date of diabetes diagnosis up to a defined censoring point (e.g. death, end of study period, end of financial year) and assess the healthcare costs of comorbid diabetes over a defined period. Our analyses will take into account the nature of the dependent variable, i.e. cost data at an individual level are non-negative, highly skewed, and leptokurtic. These are best modelled as non-linear (e.g. exponential) functions of covariates.

Objective 7: Using datasets B and C again (Figure 1), multilevel modelling will be used to explore the impact of SMI status and other explanatory variables on whether or not someone receives a diabetes intervention (e.g. monitoring blood sugar for patients with diabetes). Models will then be extended to determine associations between an intervention, SMI status and other explanatory variables and diabetes outcomes (e.g. the effect of blood sugar monitoring and SMI status on emergency diabetes admissions) including the interaction between SMI status and intervention.

6.4 Work package 3 – Interviews with service users, carers and healthcare staff

This will explore factors that influence access to, and receipt of, diabetes care for people with SMI, and how diabetes management and healthcare are experienced by people with diabetes alongside SMI.

6.4.1 Setting

Study participants will be recruited from NHS GP practices and mental health trusts, chosen to include rural and urban populations, areas of wealth and deprivation, and areas in which minority ethnic groups are well represented. Previous research indicates that around 20-30% of people with SMI are treated in primary care only and not in specialist mental health services (51); it is important, therefore, to recruit from both settings as support for diabetes may differ (99).

We have already secured support from three mental health trusts (Bradford District Care NHS Foundation Trust; Leeds and York Partnership NHS Foundation Trust; South West Yorkshire NHS Foundation Trust) in the Yorkshire and Humber region. We will engage additional mental health trust sites through our strong links with the NIHR Yorkshire and Humber's Clinical Research Network and CLAHRC (Collaboration for Leadership in Applied Health Research and Care); and collaboration with regional commissioners, who can facilitate access to national networks.

We estimate that around 10 GP practices will be required to act as PICS (Participant Information Centres) to help identify and recruit potential participants (estimating an average of 10 patients with co-existing SMI and diabetes per practice (100) and a conservative estimated response rate of around 15% (101)). Practices will also be recruited through the links described above.

6.4.2 Sample

Patients (n=30): Adult patients in participating NHS GP practices and secondary care mental health providers with recorded diagnoses of SMI and diabetes, and who meet the study eligibility criteria below:

- Aged 18 years or over
- Diagnosed with a severe mental illness (diagnosis of schizophrenia, schizoaffective disorder, bipolar disorder and manic episodes, and non-organic psychoses) (excluding those currently experiencing an acute relapse)
- Diagnosis of diabetes (excluding women with diabetes only diagnosed in pregnancy)
- Living in the community (including supported housing but not hospital settings)
- With capacity to provide informed consent to participate in the study

We will purposively sample according to the following characteristics to ensure we include patients with different backgrounds, illness profiles, and diabetes experiences.

a. Demographic (age, gender) and geographical (deprivation, region) characteristics
b. Family composition and presence of carer / supporter
c. Mental health and diabetes diagnoses
d. Diabetes medication
e. Diabetes control (determined by data obtained from health record)
f. Presence of other comorbidities
g. Provider of mental healthcare (e.g. primary or secondary mental health)
h. Provider of diabetes healthcare (e.g. primary care, secondary care, may be classified as Tiers 1 to 4 in some areas).

Our sampling strategy will also be informed by preliminary analysis of CPRD data (objective 1 and 2); for example, enabling us to include patients exposed to factors identified to influence onset of diabetes and poor diabetes outcomes in people with SMI.

We will recruit a minimum of 30 patients in the first instance to ensure we have a diverse sample according to the sampling criteria. If at this point there are new ideas still emerging, we will continue to recruit patients with a stopping criteria of 2 until we achieve data saturation, in other words when there are no new distinct ideas emerging (94).

Carers / supporters (n=15-20): We are defining 'family carers/supporters' as adults who are involved in the care of a patient taking part in the study. We expect that this will include a spouse/partner, parent or other family member, or close friend. All participating patients will be asked to identify a carer/supporter, and provide consent for the research team to approach them to take part in an interview to talk about the support they provide. As people with SMI are more likely than the general diabetes population to have inadequate social support (95) and not all carers/supporters will be willing to participate, we anticipate that the total sample will be around 15 to 20. To ensure a minimum of 15 carers we will monitor recruitment and adjust purposive sampling of patients accordingly.

Healthcare staff (n=15-20): We are defining healthcare staff as commissioners, clinicians, nurses and other healthcare staff who are involved in healthcare services for SMI and diabetes. We will use purposive sampling to ensure a mix of staff, including GPs, practice nurses, diabetes nurses, mental health nurses, case managers, psychiatrists and diabetologists. We will recruit a minimum of 15 staff, and continue to recruit participants, with a stopping criteria of 1 until we achieve data saturation or a maximum of 20 staff.

6.4.3 Recruitment

Patients: We will identify and recruit potential patient participants through two routes:

1) Community mental health teams (CMHTs) in mental health trusts – participating sites will, where possible, identify patients with a diabetes and SMI diagnosis through electronic searches; otherwise care co-ordinators in CMHTs will be asked to identify patients on their caseload who have co-existing SMI and diabetes.
2) SMI and diabetes QOF registers (100) in general practices - participating practices will identify patients who appear on both the SMI and diabetes QOF registers. This can be achieved using a simple query in the electronic patient record system.

Although we are interested in including people with SMI attending specialist diabetes services, we think that using these settings as a source for recruiting potential participants will be inefficient due to the small numbers at individual sites. However, we will seek to include people attending specialist diabetes services in our sample.

A simple checklist based on the inclusion criteria will be developed to identify potential participants; care co-ordinators and practice staff will be asked to check that those identified through electronic searches meet the eligibility criteria. Eligible participants will be provided with an information pack about the study containing information leaflet and response form. Potential participants will be asked to return a completed response form to the research team directly. A researcher will telephone interested patients to introduce the study and answer any questions they might have. Eligibility and capacity to consent will be checked over the phone, and a suitable date and time will be agreed to visit participants at home (or another suitable venue, e.g. a clinic), or to arrange a telephone interview.

Carers / Supporters: Potential carer participants identified by patients who take part in an interview will be invited to take part by post or by email. An invitation letter, information sheet and response form will be provided to participating patients to give to their named carer. Potential participants will be asked to contact the research team directly or to return a completed response form. We will not request carers' details from service users, and will not approach carers directly. This approach was used successfully in the National Audit of Schizophrenia (involving DS) and avoids additional consent issues for service user participants (104).

Healthcare staff: Eligible staff will be identified by asking participating sites to identify people involved in diabetes care for people with SMI and generating a list of those for whom contact details (email or postal address) are available. Potential participants will be provided with an invitation letter and information sheet about the study, and will be asked to contact the researcher directly to take part, either by email or telephone.

Written or audio-recorded verbal consent for all participants will be taken at the time of interview (e.g. for non-literate populations, we will read out study information and obtain verbal consent.)

6.4.4 Data Collection

Individual interviews will be carried out, with participants being offered the choice of a face-to-face or telephone interview. Face-to-face interviews are likely to take place at participants' homes (or workplaces for healthcare staff) or another suitable venue offering privacy.

A standardised semi-structured interview format will be used for all participants, tailored in length to reflect the number of topics to be covered during interviews and to minimise potential distress or inconvenience to participants. Key topics for the study include exploring factors that affect management of diabetes in people with SMI (objective 2); perceived impact of diabetes on managing SMI (objective 3); perceived impact of SMI on managing diabetes (objective 4); factors believed to influence access to and provision of diabetes care for people with SMI and experience of how diabetes interventions are delivered and received (objective 5); and perceived impact of diabetes care on SMI and diabetes management (objective 7). An overarching topic will be the extent to which the social circumstances of patients' (e.g. money for transportation, type of neighbourhood, carer role) enables or hinders their ability to receive effective healthcare and action preventative measures - both actual experiences and the perceptions (and potential misperceptions) of these factors by health care staff. Interview guides for patients, carers/supporters, and healthcare staff will be developed in partnership with study co-applicants and collaborators (WP1), including the DIAMONDS research group and PPI panel, following key principles outlined by Arthur and Nazroo (105). Interview guides will also be informed by initial analyses of data in WP2, e.g. exploring factors that are identified to influence diabetes outcomes in people with SMI. Interview guides will be employed flexibly, and where new lines of inquiry are identified in WP2 and WP3 analyses, these will be explored in later interviews.

Patient and carer interviews are expected to last approximately 45-60 minutes; staff interviews approximately 30 minutes as fewer topics will be covered. All interviews will be audio-recorded and transcribed for analysis by a sub-contractor with experience in transcribing audio for academic research (using intelligent verbatim style, i.e. removal of 'Ahs, erms' and other unnecessary noises). We will seek to include non-English speakers (our primary research sites include significant South Asian and African-Caribbean populations, who are both at greater risk of diabetes and SMI). We will use experienced interpreters known to our partner NHS organisations, who will work alongside the researchers during interviews.

6.4.5 Data Analysis

We will use the Framework method to analyse data (as described in Ritchie et al., 2003 (106)). We will use NVivo 10 software (QSR International Ply Ltd, Doncaster, Victoria, Australia) to manage and code interview transcripts. The Framework method will enable us to move iteratively through the different stages in the analytical process to develop explanatory accounts and practice recommendations, and also usefully allow for inductive analysis and analysis of a priori themes within the data, which is particularly suited to the proposed project. Analysis involves:

Step 1 ('conceptual scaffolding'): identifying and extracting recurring themes from across the data and developing a thematic coding framework, which incorporates *a priori* themes (e.g. challenges and enablers for managing diabetes and accessing healthcare) as well as those identified during analysis;

Step 2 ('indexing'): testing and modifying the framework by labelling and sorting a selection of data;

Step 3 ('coding'): coding the raw data to the framework in NVivo;

Step 4 ('descriptive analysis'): summarising and synthesising data by theme, and detecting, categorising and classifying findings into higher order themes and phenomena; and

Step 5: ('explanatory analysis'): detecting patterns and examining linkages and relationships between themes to develop an in-depth understanding about how diabetes is managed alongside SMI, and the contribution of healthcare and other factors for improving health outcomes.

As well as examining thematic patterns across the data, deviant cases will be analysed to understand the variation in managing diabetes within the sample of patients, and findings from patients, carers and healthcare staff will be triangulated to explore similarities and differences.

We will use several methods to enhance the quality of data analysis. To assure dependability (i.e. consistency or reliability), the key steps of the analysis will be carried out by at least two researchers, and we will ensure consistency in research staff; coding will be discussed regularly with JT, who will check a random sample of coded transcripts during the initial stage of coding; and summary findings discussed with the wider research team. Regular consultation with JR (service user co-investigator) and other service users involved in the study will help to assure credibility (truth value) and authenticity (that the findings represent a range of different realities) of findings. The co-design workshops will also be used to help assure authenticity of study findings.

6.4.6 Convergence of quantitative and qualitative findings

The triangulation design includes a final stage of analysis during which the qualitative findings will be merged and integrated with the results of the quantitative study (WP2). Using principles of both convergence (compare and contrast) and transformation (which allows data to interrelated and further explored) (85), we will use data transformation techniques and comparison matrices to validate, confirm, refute or corroborate study findings, and conduct further explanatory analysis (see step 5 in 6.4.5) to develop our findings further. In regular research team meetings, we will use these analyses to develop a logic model (drawing on process evaluation methodology (107)) of how diabetes contributes to health inequalities in people with SMI and the role that healthcare plays in increasing and / or reducing these, taking into account the estimated effect of mediators and moderators on process and outcomes and the influence of other factors identified in the qualitative study that could not be included in the quantitative analyses (e.g. attitudes, beliefs, social circumstances).

7 Dissemination and projected outputs

As well as hosting co-design workshops and a dissemination event, we will share study findings with the participants and likely beneficiaries of the research, with the aim of increasing understanding about factors contributing to poor diabetes outcomes in people with SMI and identifying how the organisation and delivery of diabetes care can improve health outcomes. Our PPI panel and lay members of the research team will help ensure the contents and format of dissemination activities is appropriate for patient and public audiences. Likely beneficiaries include individuals and organisations involved in health service delivery, commissioning and policy; clinicians working in primary, mental health and diabetes care; patients and carers; social care providers and managers; and other organisations in the commercial and voluntary sector who support people living with diabetes and/or mental health conditions.

We will disseminate outputs from the study using written reports, oral presentations, professional networks, websites, and social media, including:

Reports:

- A final report publicised through the HS&DR Journal
- An executive summary with clearly identified policy, managerial and practice implications, written in accessible language and made publicly available from the CLAHRC YH and DIAMONDS websites
- Scientific papers for each work package submitted to international peer reviewed journals
- Short articles in publications that practitioners and commissioners read, such as Pulse and Health Services Journal
- The DIAMONDS quarterly newsletter

Presentations:

- At national and international conferences (academic, clinical and policy) attended by mental health and/or diabetes researchers, practitioners and managers
- Public seminars hosted at the University of York, inviting patients, members of the public and charities
- Dissemination workshops, attended by identified beneficiaries

Networks:

- Including the CLAHRCs (national and local); NIHR Clinical Research Networks; Charities e.g. Diabetes UK, MIND, Rethink; and GP commissioning groups.

- The DIAMONDS stakeholder network, using the website and twitter account
- Networks identified by our PPI panel and lay members of the research team

We will reach different audiences using a format they are most likely to engage with to disseminate study findings widely. Utilising identified networks, we will bring together various stakeholders to plan how the research can be used to improve healthcare delivery and develop new interventions/pathways where these are needed. Service improvements take time to implement. However, new knowledge generated by this study about the factors (including diabetes care) that contribute to poor diabetes outcomes in people with SMI, can be readily used by commissioners, service managers and clinicians to inform current practice. The research team has established excellent links with these stakeholders, which will facilitate dissemination of findings.

8 Plan of investigation and timetable

A detailed plan of work, including key deliverables, is set out below.

Abbreviations: DPPI – DIAMONDS PPI Panel; DRG – DIAMONDS Research Group; ISAC-Independent Scientific Advisory Committee; PICs – Participant Identification Centres; SRT- Study Research Team; SSC – Study Steering Committee

Month	***Work package 1***	***Work package 2***	***Work package 3***	***Key Deliverables***
-3 to 0	• Staff recruitment and resource allocation	• Submit CPRD data protocol & agree data specification		
1 to 3	• SRT meeting	• Obtain CPRD dataset A • Test clinical code lists	• Develop study materials with DPPI	• ISAC approval for CPRD data • WP2 clinical code lists • Draft study materials for WP3
2	• SSC 1st meeting, DRG meeting, DPPI meeting			
4	• SRT meeting			
4 to 6	• Develop and agree a priori variables for WP2 analysis	• Clean dataset A & construct dataset B • Objective 1 analysis (dataset A) • Obtain dataset C	• Obtain REC and HRA approvals • Invite potential recruitment sites	• List of explanatory variables for WP2 • WP3 study approvals • Tabulated findings for WP2
6	• SRT meeting, DRG meeting, DPPI meeting			**PROGRESS REPORT 1**
7 to 9	• Study integration – WP2 to inform sampling and topics for WP3	• Objective 2 analysis (dataset B) • Objective 3 analysis (dataset A)	• Recruit PICs & set-up study • Start recruitment and data collection	• Tabulated findings for WP2
8	• SRT meeting			
10	• SRT meeting, SSC 2nd meeting, DRG meeting, DPPI meeting			
10 to 15	• Merge findings from WP2 and WP3 • Organise co-design workshop 1	• Objective 4 analysis (datasets B & C) • Objective 6 analysis (datasets B & C) • Objective 7 analysis (datasets B & C)	• Continue with data collection • Data analysis: conceptual scaffolding, indexing and coding	• Thematic framework and summary for WP3 • Tabulated findings from WP2 analyses • Short report of merged findings for co-design 1
12	• SRT meeting			**PROGRESS REPORT 2**
14	• SRT meeting			
16	• **Co-design workshop 1** • SRT meeting			
16 to 19	• Analysis of co-design data to inform final	• Objective 7 continued analysis (dataset B &	• Data analysis: coding, descriptive and	• Tabulated findings

	analyses in WP2 / WP3 • Merge and integrate findings from WP2 and WP3	C)	explanatory analyses	from WP3 analysis • Tabulated findings from WP2 analysis • Short report of merged findings for co-design 2
18	• SRT meeting, SSC 3rd meeting, DRG meeting, DPPI meeting			**PROGRESS REPORT 3**
20	• **Co-design workshop 2** • SRT meeting			
20 to 24	• Final mixed methods analysis • Prepare final report and executive summary	• Write up findings for publication • Prepare lay summary for dissemination event	• Write up findings for publication • Prepare lay summary for dissemination event	• WP2 draft paper • WP3 draft paper • Mixed methods analysis draft paper
22	• SRT meeting			
23	• SSC 4th meeting			
24	• **Dissemination event** • SRT final meeting			• Summary findings for dissemination event • **FINAL REPORT**

9 Project management

The Study Research Team (SRT) comprising all co-applicants will be responsible for day-to-day management of the project. NS will lead the project, with overall responsibility for its conduct. JT will act as project manager, co-ordinating activities in WP1 and ensuring integration of the different work packages; and preparing data requests, dealing with HRA approvals and managing funder requirements. TD and RJ will oversee WP2 and supervise a full-time research fellow on the interrogation of CPRD data. JT will oversee WP3 and supervise a research assistant allocated to this work.

WP2 and WP3 research staff will meet every fortnight with NS and JT throughout the project to maintain continued progress on key milestones. The full SRT will meet every other month, although input will also be provided as needed at other key stages of the research. Meetings will be in York and those who are not based in York will join via Skype or teleconference or in person, as appropriate. The project will be managed by ensuring work is focused on agreed key milestones and within defined Work packages (see Section 8). Financial management will be provided by a financial administrator in the Department of Health Sciences, who will handle the financial accounting and processing of all income and expenditure, and will provide the PI with quarterly financial updates.

We will establish a Study Steering Committee (SSC) with an independent chair and service user and clinical, academic and commissioning representation (to include primary care, diabetes and mental health), to ensure our study makes a difference for patients and the NHS. Dr Mark Ashworth is a GP and clinical senior lecturer at King's College London, and medical director at The Hurley Group, an NHS organisation that runs a number of practices and GP walk in centres in London. He has published widely on physical comorbidity among patients with SMI and also has expertise in research using routinely collected large health datasets. He has kindly agreed to act as the independent chair if the application is successful. In Study 13/54/40, the SSC has proven invaluable, and two PPI members from the SSC of that study have also agreed to sit on the Committee for this proposed study to ensure continuity and shared learning across the projects. The SSC will meet every 6 months (4 times over the course of the project), with the PI and two or three people from the research team also in attendance, depending on the analysis to be discussed. A dedicated administrator allocated to the project will provide administrative support to the SSC. Costs for these meetings, including PPI have all been budgeted for.

The DIAMONDS Research Group will act as an Advisory Panel for the study, bringing academic and clinical expertise on SMI and diabetes. They will not be responsible for day-to-day management of the project, but will provide input and expertise at regular intervals during the study.

10 Approval by ethics committees

Approvals will be required for WP2 and WP3 and time has been allocated appropriately to ensure successful delivery of the project, allowing for amendments where necessary, and taking into account the expertise and prior experience of the team in obtaining CPRD, and NHS ethics and governance approvals.

WP2: The use of CPRD data is subject to approval by the Independent Scientific Advisory Committee (ISAC) ethics committee run by the Medicines and Healthcare Products Regulatory Agency (MHRA). No separate ethics approval is required for CPRD as the data is anonymised and only includes patients who have not withdrawn

consent. There are formal processes in place for gaining access to CPRD and linked data which require provision of guarantees on data use and security, all of which the study co-applicants have considerable experience of undertaking. The research will comply with the University of York's data protection guidelines (www.york.ac.uk/recordsmanagement/dpa/). The linkage of CPRD will require permission from the Health Research Authority Confidentiality Advisory Group (HRA CAG), but the application for data access is made through CPRD and the linkage is undertaken by CPRD.

WP3: The qualitative study will require HRA (Health Research Authority) ethics and governance approvals, as it involves patients of the NHS as research participants and requires NHS trusts and general practices to assist with recruiting patients and healthcare staff to the study. A single application will be made through IRAS (Integrated Research Application System) outlining our arrangements for handling the following ethical issues potentially arising from this study: informed consent; confidentiality; participant burden; data protection; researcher safety.

Informed consent: We will include in the study only participants with the capacity to consent to the research. For individuals with SMI, who are potentially at risk of relapse of mental illness, this needs to be considered carefully. We will comply with the requirements of the Mental Capacity Act (108) regarding inclusion of participants who may lack or lose capacity in research. The applicant team includes clinicians with considerable experience of working with people with SMI and assessing capacity, and we have drawn on this in our research plans. We will ensure that capacity is checked at the outset during the consent process, and again before interviews are conducted by staff with training and experience of doing this. All potential participants will receive clear information about the study and be given an opportunity to ask questions. Eligibility and consent will be checked during the initial telephone call with the researcher, and written or recorded verbal consent will be taken prior to being interviewed, using standard consent forms or a pre-defined script based on the consent form. The minimum time for potential participants to consider participation will be 72 hours (i.e. the time between the initial invitation and follow-up telephone call). This ensures that potential participants are still eligible (e.g. minimises the risk of relapse) whilst allowing time for participants to process and understand the information, talk to others about the study, and to weigh up whether or not to take part. Information sheets, consent forms and interview topic guides will be developed in partnership with service users involved in the study and the DIAMONDS PPI panel prior to obtaining HRA approvals to ensure their suitability for this patient group. Outline topic guides will be submitted with the original application; these are likely to be modified prior to beginning the study, incorporating emerging findings from WP1 and WP2. Sufficient time has been allocated for the development and modification of study materials, and corresponding HRA approvals.

Participant burden: It is possible that patients and carers may feel pressurised to participate, or feel distressed by interview questions. To minimise such risks, all potential participants will receive written information about the study with only two follow-up telephone calls. They will be informed that the decision about whether to participate is voluntary and will not affect any services or benefits they receive. Consent will be checked throughout interviews, which will be timed to minimise the potential distress or inconvenience to participants. If patients or carers experience any significant distress from questions, they will be advised they can leave them out, and stop the interview at any time. Where this happens, the researcher will encourage participants, where appropriate, to contact their GP or mental health team for support, or seek permission to do so on their behalf. Out of pocket and travel expenses associated with participating in the research will be reimbursed. No incentives will be offered for participation other than to reimburse participants for their time and costs in line with INVOLVE guidance (109).

Participant confidentiality: Participants will be informed of their right to confidentiality, and what this means if they disclose information that suggests that they or others are at serious risk of harm. Participants will also be informed that they have the right to withdraw from the study at any time, and to exclude their data from the study if not already analysed as part of the research. All personal data will be stored in a password-protected file, using a participant identifier to link participants' details to their data (interview transcript). This information and all data will be stored on the University of York servers and will not be accessed by anyone outside of the research team. Quotations from participants may be used in research reports and other publications and presentations; however, care will be taken to protect the anonymity of participants so that others are not able to identify them.

Data protection: In line with the 1998 Data Protection Act and the Research Governance Framework for Health and Social Care Research, data (anonymized interview transcripts) will be securely archived by the University of York for a minimum of 5 years. Personal data of participants will be stored for up to 3 years after the study has ended for the purpose of disseminating study findings. It is unlikely that this will take longer than 12 months, however to ensure that participants receive adequate and full information about the study after it has finished, additional time has been allocated.

All information collected during the study will be kept strictly confidential. Information will be held securely on paper and electronically at the University of York. The University of York complies with all aspects of the 1998 Data Protection Act and operationally this will include obtaining consent from patients and carers to record personal details including name, postal and email address, and contact telephone numbers; and appropriate storage, restricted access and disposal arrangements for patient and carer personal details. All participants will be anonymised at the point of consent, by assignment of a study number. This will ensure that all personal data

collected for the study are anonymous. Personal data and anonymised data will be stored separately in a restricted access folder on a secure university server and access will be password protected.

Researcher safety: To ensure researcher safety, we will adhere to the University of York policy and procedure on lone working and employ a buddy system to monitor researchers' whereabouts and safety when visiting participants. The short timeframe between invitation and interview will also help to ensure that participating service users have capacity to consent and are mentally stable. We will also develop service user risk assessment and risk management protocols that are consistent with those commonly used by the Trusts and GP practices we will be working with. This approach has been used successfully by the applicants SG and RH in previous studies in this population. All research staff will be GCP (Good Clinical Practice) trained.

11 Patient and public involvement

The DIAMONDS PPI panel helped to prioritise research questions, expressing the need for a better understanding of how diabetes is prevented and managed in people with SMI. Draft research questions for this study were also reviewed by the PPI Panel in February 2015, and feedback was used to revise the research questions. The panel also expressed a need to talk to people with SMI and diabetes as well as analyse patient records, to gain a more in-depth understanding about accessing diabetes care and needs for support. This suggestion influenced us to not only include qualitative inquiry, but to make this a central and integrated element of the study, rather than adopting a sequential approach to simply follow up findings from the observational study.

PPI involvement will further benefit the research by ensuring that: (i) we continue to address questions that matter to service users; (ii) the conduct of the study minimises participant burden; (iii) approaches to recruitment are optimised; (iv) interpretation of results and findings are plausible, and (v) dissemination of findings is in an appropriate format. Two study co-applicants bring personal experience as a service user or carer and will contribute directly to project management, and interpretation and dissemination of findings; DS is a retired GP and carer of someone with comorbid SMI and diabetes, and JR is a service user with comorbid diabetes and mental illness, and a former psychiatric nurse. Three members of the SSC, which provides an overall steer for the project, also bring personal experience as a service user or carer (two of whom are also involved in study 13/54/40).

The DIAMONDS PPI panel (8 service users, 1 carer) will meet every 4 months to provide input on the study, as their perspective of how care is provided and received will be invaluable for informing our understanding of factors that contribute to diabetes outcomes, and also for developing study materials (e.g. clinical code lists, interview topic guides) and interpreting study findings. Co-applicant JR is also a member of the PPI panel and this overlap will help to ensure that the views of the DIAMONDS PPI panel are fed directly into the design and conduct of this study. The DIAMONDS panel will receive research methods training in 2016, funded by a previous research grant to support SMI and diabetes research. We will continue to recruit to the panel when needed, and training will be updated when required. All service user payments are based on INVOLVE guidance (109).

We also have a stakeholder network of organisations with an interest in DIAMONDS, which includes clinicians working in and outside the NHS, NHS service managers and commissioners, and charitable and commercial organisations involved in diabetes and mental health. Members will receive regular updates about the study in our quarterly newsletter. They and our PPI panel members will be invited to attend the co-design workshops and dissemination event, and will also help with the interpretation and dissemination of study findings.

12 Expertise and justification of support required

We have assembled a multi-disciplinary research team with extensive methodological expertise and experience to successfully deliver this project. The team includes experts in mental health (NS, SG) and diabetes (RH); primary (DS, SA) and secondary care (NS, RH, SG); clinical (TD) and social epidemiology (SP); health inequalities (SP, TD); health economics and applied econometrics (RJ); statistics (CH); expert carer/ service user (DS, JR); and mixed methods and qualitative research (NS, JT). NS has experience of leading previous grants and coordinating multi-professional teams working across traditional organisational boundaries to successfully deliver challenging research, and brings SMI clinical and research expertise. TD and RJ have considerable experience of analysis of patient-level data in SMI and obtaining linked datasets from CPRD, and will bring methods and expertise from Study 13/54/40 to the project. CH has expertise in statistical analysis of complex data; RJ, TD and SP all have expertise in coding and analysing linked medical records data. SP also brings expertise in health and social inequalities, relevant to study design, analysis and interpretation of findings.

JT (grade 6) will act as project manager to ensure successful delivery of the project and co-ordinate dissemination and PPI activities (0.3 FTE). JT has a good understanding of the relationship between SMI and diabetes, and is currently conducting other studies in this area. She also has previous experience of efficient project management and research dissemination, and is an experienced qualitative health researcher (conducting health services research outside of an academic setting for a number of years before taking up a research post in 2013). JT will be supervised by NS.

All applicants have experience of conducting high quality applied health research and will contribute to: developing new clinical code lists and interview guides; study design, integration, and interpretation of findings:

and write up and dissemination activities. 0.03 FTE has been allocated for SG and SA for this work; 0.05 FTE for RH, SP and TD (who will carry out additional tasks, e.g. SMI/diabetes expertise, supervision, CPRD data protocols); 0.10 for CH (who will provide statistical expertise and supervision for the analysis and modelling of CPRD data); 0.10 for RJ (who will draw on links with and build on Study 13/54/40 and provide supervision for the health economics analysis); and 0.20 for NS to ensure time for overall project management. One full-time research fellow (grade 6) will be allocated for WP2 for 24 months, from an expanding team of researchers with expertise in working with CPRD data at the University of York, to be supervised by TD and RJ. In Year 2, an additional 0.3 FTE has been allocated for JT to oversee the qualitative study in WP3, and to conduct analysis and write-up of this work. A research fellow (grade 6) will work full-time for 10 months on WP3 to recruit participants, conduct interviews and help with analysis and coding of data (supervised by JT). We have thought carefully about the level of expertise required and allocated grade and time to provide the best value for money.

Requested costs comprise of research staff costs (48.2%); WP2 CPRD data (6.9%); WP3 qualitative study costs (1.3%); study management including SSC costs and general travel costs (1.5%); PPI activities (0.8%); dissemination, including open access and conference fees and travel, and dissemination workshop (1%); co-design workshop costs (0.3%); and estates and indirect costs (40%). NHS support costs have been allocated for WP3 and will be requested from the Yorkshire and Humber CRN (who have agreed to support the study and have helped to calculate identified costs). This amount covers costs of identifying, recruiting and consenting eligible service users to take part; and providing backfill for participating healthcare staff. The cost to recruit staff and set-up general practices as participant identification centres (PICs) is classed as a research part-B cost, and is included in the requested costs for WP3.

During the proposed study, funding provided through the CLAHRC Yorkshire & Humber mental health and comorbidity theme will be used to support the DIAMONDS Research Group and PPI panel meetings, PPI recruitment and training, interpreter costs for interviews with participants who do not speak English, and cover the consultancy fee and travel of co-applicant DS, who is a member of the DIAMONDS Research Group. CLAHRC YH will help to promote and disseminate outputs of the work through networks, newsletters, twitter and a dedicated website. Funding for IT support to assist with maintenance and updating of the DIAMONDS website (which will be used as the project website) will be provided by CLAHRC.

13 Reference List

1. Chang CK, Hayes RD, Perera G, Broadbent MT, Fernandes AC, Lee WE, et al. Life expectancy at birth for people with serious mental illness and other major disorders from a secondary mental health care case register in London. PloS one. 2011;6(5):e19590.
2. De Hert M, Correll CU, Bobes J, Cetkovich-Bakmas M, Cohen D, Asai I, et al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. World psychiatry : official journal of the World Psychiatric Association (WPA). 2011;10(1):52-77.
3. Brown S, Kim M, Mitchell C, Inskip H. Twenty-five year mortality of a community cohort with schizophrenia. The British journal of psychiatry : the journal of mental science. 2010;196(2):116-21.
4. Woodhead C, Ashworth M, Schofield P, Henderson M. Patterns of physical co-/multi-morbidity among patients with serious mental illness: a London borough-based cross-sectional study. BMC family practice. 2014;15:117.
5. Stubbs B, Vancampfort D, De Hert M, Mitchell AJ. The prevalence and predictors of type two diabetes mellitus in people with schizophrenia: a systematic review and comparative meta-analysis. Acta psychiatrica Scandinavica. 2015;132(2):144-57.
6. Ward M, Druss B. The epidemiology of diabetes in psychotic disorders. Lancet Psychiatry. 2015;2(5):431-51.
7. Vinogradova Y, Coupland C, Hippisley-Cox J, Whyte S, Penny C. Effects of severe mental illness on survival of people with diabetes. The British journal of psychiatry : the journal of mental science. 2010;197(4):272-7.
8. Reilly S, Olier I, Planner C, Doran T, Reeves D, Ashcroft DM, et al. Inequalities in physical comorbidity: a longitudinal comparative cohort study of people with severe mental illness in the UK. BMJ open. 2015;5(12):e009010.
9. Kanavos P, van den Aardweg S, Schurer W. Diabetes expenditure, burden of disease and management in 5 EU countries. London: The London School of Economics and Political Science, 2012.
10. Hex N, Bartlett C, Wright D, Taylor M, Varley D. Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. Diabetic medicine : a journal of the British Diabetic Association. 2012;29(7):855-62.
11. De Hert M, Dekker JM, Wood D, Kahl KG, Holt RI, Moller HJ. Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA),

supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC). European psychiatry : the journal of the Association of European Psychiatrists. 2009;24(6):412-24.
12. Osborn DP, Hardoon S, Omar RZ, Holt RI, King M, Larsen J, et al. Cardiovascular risk prediction models for people with severe mental illness: results from the prediction and management of cardiovascular risk in people with severe mental illnesses (PRIMROSE) research program. JAMA psychiatry. 2015;72(2):143-51.
13. McCrone P, Dhanasiri S, Patel A, Knapp M, Lawton-Smith S. Paying the price: the cost of mental health care in England to 2026. London: King's Fund, 2008.
14. Kontopantelis E, Reeves D, Valderas JM, Campbell S, Doran T. Recorded quality of primary care for patients with diabetes in England before and after the introduction of a financial incentive scheme: a longitudinal observational study. BMJ quality & safety. 2013;22(1):53-64.
15. Kontopantelis E, Springate DA, Reeves D, Ashcroft DM, Rutter MK, Buchan I, et al. Glucose, blood pressure and cholesterol levels and their relationships to clinical outcomes in type 2 diabetes: a retrospective cohort study. Diabetologia. 2015;58(3):505-18.
16. NHS England. Action for Diabetes 2014. Available from: http://www.england.nhs.uk/wp-content/uploads/2014/01/act-for-diabetes.pdf.
17. Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, van Staa T, et al. Data Resource Profile: Clinical Practice Research Datalink (CPRD). International journal of epidemiology. 2015;44(3):827-36.
18. Hardoon S, Hayes JF, Blackburn R, Petersen I, Walters K, Nazareth I, et al. Recording of severe mental illness in United Kingdom primary care, 2000-2010. PloS one. 2013;8(12):e82365.
19. Department of Health. No health without mental health: A cross-government mental health outcomes strategy for people of all ages. Book. London: HMSO, 2011.
20. Osborn DP, Levy G, Nazareth I, Petersen I, Islam A, King MB. Relative risk of cardiovascular and cancer mortality in people with severe mental illness from the United Kingdom's General Practice Research Database. Archives of general psychiatry. 2007;64(2):242-9.
21. Carlson C, Hornbuckle K, DeLisle F, Kryzhanovskaya L, Breier A, Cavazzoni P. Diabetes mellitus and antipsychotic treatment in the United Kingdom. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology. 2006;16(5):366-75.
22. Kreyenbuhl J, Dickerson FB, Medoff DR, Brown CH, Goldberg RW, Fang L, et al. Extent and management of cardiovascular risk factors in patients with type 2 diabetes and serious mental illness. The Journal of nervous and mental disease. 2006;194(6):404-10.
23. Crawford MJ, Jayakumar S, Lemmey SJ, Zalewska K, Patel MX, Cooper SJ, et al. Assessment and treatment of physical health problems among people with schizophrenia: national cross-sectional study. The British journal of psychiatry : the journal of mental science. 2014;205(6):473-7.
24. Ribe AR, Laursen TM, Sandbaek A, Charles M, Nordentoft M, Vestergaard M. Long-term mortality of persons with severe mental illness and diabetes: a population-based cohort study in Denmark. Psychological medicine. 2014;44(14):3097-107.
25. Schoepf D, Potluri R, Uppal H, Natalwala A, Narendran P, Heun R. Type-2 diabetes mellitus in schizophrenia: increased prevalence and major risk factor of excess mortality in a naturalistic 7-year follow-up. European psychiatry : the journal of the Association of European Psychiatrists. 2012;27(1):33-42.
26. Mitchell AJ, Malone D, Doebbeling CC. Quality of medical care for people with and without comorbid mental illness and substance misuse: systematic review of comparative studies. The British journal of psychiatry : the journal of mental science. 2009;194(6):491-9.
27. Osborn DP, Wright CA, Levy G, King MB, Deo R, Nazareth I. Relative risk of diabetes, dyslipidaemia, hypertension and the metabolic syndrome in people with severe mental illnesses: systematic review and metaanalysis. BMC psychiatry. 2008;8:84.
28. Scott D, Platania-Phung C, Happell B. Quality of care for cardiovascular disease and diabetes amongst individuals with serious mental illness and those using antipsychotic medications. Journal for healthcare quality : official publication of the National Association for Healthcare Quality. 2012;34(5):15-21.
29. Foley DL, Mackinnon A, Morgan VA, Watts GF, McGrath JJ, Castle DJ, et al. Predictors of type 2 diabetes in a nationally representative sample of adults with psychosis. World psychiatry : official journal of the World Psychiatric Association (WPA). 2014;13(2):176-83.
30. Henderson DC, Vincenzi B, Andrea NV, Ulloa M, Copeland PM. Pathophysiological mechanisms of increased cardiometabolic risk in people with schizophrenia and other severe mental illnesses. The Lancet Psychiatry. 2015;2(5):452-64.

31. Stahl SM, Mignon L, Meyer JM. Which comes first: atypical antipsychotic treatment or cardiometabolic risk? Acta psychiatrica Scandinavica. 2009;119(3):171-9.
32. Llorente M, Urrutia V. Diabetes, Psychiatric Disorders, and the Metabolic Effects of Antipsychotic Medications. Clinical Diabetes. 2006;24(1):18-24.
33. Rummel-Kluge C, Komossa K, Schwarz S, Hunger H, Schmid F, Lobos CA, et al. Head-to-head comparisons of metabolic side effects of second generation antipsychotics in the treatment of schizophrenia: a systematic review and meta-analysis. Schizophrenia research. 2010;123(2-3):225-33.
34. Stubbs B, Williams J, Gaughran F, Craig T. How sedentary are people with psychosis? A systematic review and meta-analysis. Schizophrenia research. 2016;171(1-3):103-9.
35. Kilbourne AM, Rofey DL, McCarthy JF, Post EP, Welsh D, Blow FC. Nutrition and exercise behavior among patients with bipolar disorder. Bipolar disorders. 2007;9(5):443-52.
36. Holt RI. Cardiovascular disease and diabetes in people with severe mental illness : causes, consequences and pragmatic management : review. South African Journal of Diabetes and Vascular Disease. 2012;9(3):107-11.
37. Banham L, Gilbody S. Smoking cessation in severe mental illness: what works? Addiction (Abingdon, England). 2010;105(7):1176-89.
38. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet. 2012;380(9836):37-43.
39. Sacerdote C, Ricceri F, Rolandsson O, Baldi I, Chirlaque MD, Feskens E, et al. Lower educational level is a predictor of incident type 2 diabetes in European countries: the EPIC-InterAct study. International journal of epidemiology. 2012;41(4):1162-73.
40. Espelt A, Borrell C, Palencia L, Goday A, Spadea T, Gnavi R, et al. Socioeconomic inequalities in the incidence and prevalence of type 2 diabetes mellitus in Europe. Gaceta sanitaria / SESPAS. 2013;27(6):494-501.
41. Whitley R, Campbell RD. Stigma, agency and recovery amongst people with severe mental illness. Social science & medicine (1982). 2014;107:1-8.
42. De Hert M, Cohen D, Bobes J, Cetkovich-Bakmas M, Leucht S, Ndetei DM, et al. Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. World psychiatry : official journal of the World Psychiatric Association (WPA). 2011;10(2):138-51.
43. Gutacker N, Mason AR, Kendrick T, Goddard M, Gravelle H, Gilbody S, et al. Does the quality and outcomes framework reduce psychiatric admissions in people with serious mental illness? A regression analysis. BMJ open. 2015;5(4).
44. Nash M. Improving mental health service users' physical health through medication monitoring: a literature review. Journal of nursing management. 2011;19(3):360-5.
45. Blythe J, White J. Role of the mental health nurse towards physical health care in serious mental illness: an integrative review of 10 years of UK literature. International journal of mental health nursing. 2012;21(3):193-201.
46. Lawrence D, Kisely S. Inequalities in healthcare provision for people with severe mental illness. Journal of psychopharmacology (Oxford, England). 2010;24(4 Suppl):61-8.
47. Newcomer JW, Hennekens CH. Severe mental illness and risk of cardiovascular disease. Jama. 2007;298(15):1794-6.
48. Goodwin N, Lawton-Smith S. Integrating care for people with mental illness: the Care Programme Approach in England and its implications for long-term conditions management. International journal of integrated care. 2010;10:e040.
49. Reilly S, Planner C, Gask L, Hann M, Knowles S, Druss B, et al. Collaborative care approaches for people with severe mental illness. The Cochrane database of systematic reviews. 2013;11:Cd009531.
50. Bradshaw T, Pedley R. Evolving role of mental health nurses in the physical health care of people with serious mental health illness. International journal of mental health nursing. 2012;21(3):266-73.
51. Reilly S, Planner C, Hann M, Reeves D, Nazareth I, Lester H. The role of primary care in service provision for people with severe mental illness in the United Kingdom. PloS one. 2012;7(5):e36468.
52. Chadwick A, Street C, McAndrew S, Deacon M. Minding our own bodies: reviewing the literature regarding the perceptions of service users diagnosed with serious mental illness on barriers to accessing physical health care. International journal of mental health nursing. 2012;21(3):211-9.

53. Kaufman EA, McDonell MG, Cristofalo MA, Ries RK. Exploring barriers to primary care for patients with severe mental illness: frontline patient and provider accounts. Issues in mental health nursing. 2012;33(3):172-80.
54. Holt RI, Mitchell AJ. Diabetes mellitus and severe mental illness: mechanisms and clinical implications. Nature reviews Endocrinology. 2014.
55. Himelhoch S, Leith J, Goldberg R, Kreyenbuhl J, Medoff D, Dixon L. Care and management of cardiovascular risk factors among individuals with schizophrenia and type 2 diabetes who smoke. General hospital psychiatry. 2009;31(1):30-2.
56. Ascher-Svanum H, Zhu B, Ernst FR, Faries DE, Jacobson JG, Doebbeling CC. The 3-year clinical and functional course of schizophrenia among individuals with and without diabetes at study entry. Primary care companion to the Journal of clinical psychiatry. 2007;9(2):122-8.
57. Nasrallah HA, Meyer JM, Goff DC, McEvoy JP, Davis SM, Stroup TS, et al. Low rates of treatment for hypertension, dyslipidemia and diabetes in schizophrenia: data from the CATIE schizophrenia trial sample at baseline. Schizophrenia research. 2006;86(1-3):15-22.
58. Nash M. Mental health service users' experiences of diabetes care by Mental Health Nurses: an exploratory study. Journal of psychiatric and mental health nursing. 2014;21(8):715-23.
59. McGinty EE, Baller J, Azrin ST, Juliano-Bult D, Daumit GL. Quality of medical care for persons with serious mental illness: A comprehensive review. Schizophrenia research. 2015;165(2-3):227-35.
60. Nicolucci A, Kovacs Burns K, Holt RI, Comaschi M, Hermanns N, Ishii H, et al. Diabetes Attitudes, Wishes and Needs second study (DAWN2): cross-national benchmarking of diabetes-related psychosocial outcomes for people with diabetes. Diabetic medicine : a journal of the British Diabetic Association. 2013;30(7):767-77.
61. Moulton CD, Pickup JC, Ismail K. The link between depression and diabetes: the search for shared mechanisms. The Lancet Diabetes & Endocrinology. 2015;3(6):461-71.
62. Snoek FJ, Bremmer MA, Hermanns N. Constructs of depression and distress in diabetes: time for an appraisal. The lancet Diabetes & endocrinology. 2015;3(6):450-60.
63. Emsley R, Rabinowitz J, Torreman M. The factor structure for the Positive and Negative Syndrome Scale (PANSS) in recent-onset psychosis. Schizophrenia research. 2003;61(1):47-57.
64. Buckley PF, Miller BJ, Lehrer DS, Castle DJ. Psychiatric Comorbidities and Schizophrenia. Schizophrenia bulletin. 2009;35(2):383-402.
65. McGinty EE, Baller J, Azrin ST, Juliano-Bult D, Daumit GL. Interventions to Address Medical Conditions and Health-Risk Behaviors Among Persons With Serious Mental Illness: A Comprehensive Review. Schizophrenia bulletin. 2015.
66. Holt RI, Mitchell AJ. Diabetes mellitus and severe mental illness: mechanisms and clinical implications. Nature reviews Endocrinology. 2015;11(2):79-89.
67. National Institute for Health and Clinical Excellence (NICE). Type 2 diabetes in adults: management. NICE guideline [NG28] 2015. Available from: https://www.nice.org.uk/guidance/ng28.
68. Davies MJ, Heller S, Skinner TC, Campbell MJ, Carey ME, Cradock S, et al. Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. BMJ (Clinical research ed). 2008;336(7642):491-5.
69. Steinsbekk A, Rygg LO, Lisulo M, Rise MB, Fretheim A. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. BMC Health Serv Res. 2012;12:213.
70. Cimo A, Stergiopoulos E, Cheng C, Bonato S, Dewa CS. Effective lifestyle interventions to improve type II diabetes self-management for those with schizophrenia or schizoaffective disorder: a systematic review. BMC psychiatry. 2012;12:24.
71. Siddiqi N, Lewis H, Taylor J, Mahmoodi N, Wright J, McDermid K, et al. A systematic review of pharmacological and non-pharmacological interventions for improving diabetes outcomes in people with serious mental illness. PROSPERO International prospective register of systematic reviews. 2015;CRD42015015558.
72. NHS England. Building the NHS of the Five Year Forward View - NHS England Business Plan 2015-2016 2015. Available from: http://www.england.nhs.uk/wp-content/uploads/2015/03/business-plan-mar15.pdf.
73. Department of Health. Closing the Gap: Priorities for essential change in mental health 2014. Available from:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/281250/Closing_the_gap_V2_-_17_Feb_2014.pdf.
74. National Institute for Health and Clinical Excellence (NICE). Preventing type 2 diabetes: risk identification and interventions for individuals at high risk: NICE clinical guidelines PH38 2012 [30/08/16]. Available from: https://www.nice.org.uk/guidance/ph38.
75. National Institute for Health and Clinical Excellence (NICE). Psychosis and schizophrenia in adults: treatment and management. NICE clinical guideline 178 2014. Available from: http://www.nice.org.uk/guidance/cg178/chapter/key-priorities-for-implementation.
76. Lloyd K, White J, Chalmers I. Schizophrenia: Patients' research priorities get funded. Nature. 2012;487(7408):432.
77. Phelan JC, Link BG, Tehranifar P. Social conditions as fundamental causes of health inequalities: theory, evidence, and policy implications. Journal of health and social behavior. 2010;51 Suppl:S28-40.
78. Cooper B. Schizophrenia, social class and immigrant status: the epidemiological evidence. Epidemiologia e psichiatria sociale. 2005;14(3):137-44.
79. Eaton WW, Mortensen PB, Frydenberg M. Obstetric factors, urbanization and psychosis. Schizophrenia research. 2000;43(2-3):117-23.
80. Draine J, Salzer MS, Culhane DP, Hadley TR. Role of Social Disadvantage in Crime, Joblessness, and Homelessness Among Persons With Serious Mental Illness. Psychiatric Services. 2002;53(5):565-73.
81. Topor A, Andersson G, Denhov A, Holmqvist S, Mattsson M, Stefansson C-G, et al. Psychosis and poverty: Coping with poverty and severe mental illness in everyday life. Psychosis. 2014;6(2):117-27.
82. Moody A, Cowley G, Ng Fat L, Mindell JS. Social inequalities in prevalence of diagnosed and undiagnosed diabetes and impaired glucose regulation in participants in the Health Surveys for England series. BMJ open. 2016;6(2).
83. Dixon-Woods M, Cavers D, Agarwal S, Annandale E, Arthur A, Harvey J, et al. Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. BMC medical research methodology. 2006;6(1):1-13.
84. Solar O, Irwin AA. Conceptual Framework for Action on the Social Determinants of Health. . Geneva: World Health Organisation, 2010.
85. Creswell JW. Research Design: Qualitative, Quantitative, and Mixed Methods Approaches. 4th ed. Thousand Oaks, California: SAGE; 2014.
86. NHS Employers. 2016/17 General Medical Services (GMS) contract Quality and Outcomes Framework (QOF): Guidance for GMS Contract 2016/17. Leeds: NHS Employers, 2016.
87. Smith R, Han L, Ali S, Prady S, Taylor J, Hughes T, et al. Glucose, blood pressure and cholesterol levels in adults with comorbid diabetes and severe mental illness. Longitudinal observational study using the Clinical Practice Research Datalink (CPRD). Diabetic Medicine. 2017;UNDER SUBMISSION.
88. Peek ME, Ferguson M, Bergeron N, Maltby D, Chin MH. Integrated community-healthcare diabetes interventions to reduce disparities. Curr Diab Rep. 2014;14(3):467.
89. Peek ME, Cargill A, Huang ES. Diabetes health disparities: a systematic review of health care interventions. Medical care research and review : MCRR. 2007;64(5 Suppl):101s-56s.
90. Ricci-Cabello I, Ruiz-Pérez I, Nevot-Cordero A, Rodríguez-Barranco M, Sordo L, Gonçalves DC. Health Care Interventions to Improve the Quality of Diabetes Care in African Americans: A systematic review and meta-analysis. Diabetes care. 2013;36(3):760-8.
91. Ricci-Cabello I, Ruiz-Perez I, Rojas-Garcia A, Pastor G, Goncalves DC. Improving diabetes care in rural areas: a systematic review and meta-analysis of quality improvement interventions in OECD countries. PloS one. 2013;8(12):e84464.
92. Zeh P, Sandhu HK, Cannaby AM, Sturt JA. The impact of culturally competent diabetes care interventions for improving diabetes-related outcomes in ethnic minority groups: a systematic review. Diabetic medicine : a journal of the British Diabetic Association. 2012;29(10):1237-52.
93. Evans TS, Berkman N, Brown C, Gaynes B, Weber RP. AHRQ Comparative Effectiveness Technical Briefs. Disparities Within Serious Mental Illness. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016.
94. Brookhart MA, Stürmer T, Glynn RJ, Rassen J, Schneeweiss S. Confounding control in healthcare database research: challenges and potential approaches. Medical care. 2010;48(6 0):S114-S20.
95. Tassi R. Service Design Tools: Communication Methods Supporting Design Processes 2009 [25/05/2016]. Available from: http://www.servicedesigntools.org/.

96. Huang ES, Laiteerapong N, Liu JY, John PM, Moffet HH, Karter AJ. Rates of complications and mortality in older patients with diabetes mellitus: the diabetes and aging study. JAMA internal medicine. 2014;174(2):251-8.
97. Miller BJ, Paschall CB, 3rd, Svendsen DP. Mortality and medical comorbidity among patients with serious mental illness. Psychiatric services (Washington, DC). 2006;57(10):1482-7.
98. National Institute for Health and Clinical Excellence (NICE). Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline [CG181]. 2016.
99. Pendlebury J, Holt RI. Managing diabetes in people with severe mental illness. Journal of Diabetes Nursing. 2010;14(9):328-39.
100. Health and Social Care Information Centre. Quality and Outcomes Framework (QOF) - 2014-15 2015 [25 May 2016]. Available from: http://www.hscic.gov.uk/catalogue/PUB15751.
101. Gilbody S, Peckham E, Man M-S, Mitchell N, Li J, Becque T, et al. Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. The Lancet Psychiatry. 2015;2(5):395-402.
102. Francis JJ, Johnston M, Robertson C, Glidewell L, Entwistle V, Eccles MP, et al. What is an adequate sample size? Operationalising data saturation for theory-based interview studies. Psychology & health. 2010;25(10):1229-45.
103. Davis L, Brekke J. Social support and functional outcome in severe mental illness: the mediating role of proactive coping. Psychiatry research. 2014;215(1):39-45.
104. Royal College of Psychiatrists. Report of the Second Round of the National Audit of Schizophrenia (NAS) 2014. London: Healthcare Quality Improvement Partnership, 2014.
105. Arthur S, Nazroo J. Designing Fieldwork Strategies and Materials. In: Ritchie J, Lewis J, editors. Qualitative Research Practice: A Guide for Social Science Students and Researchers. London: SAGE; 2003. p. 109-37.
106. Ritchie J, Spencer L, O'Connor W. Carrying out Qualitative Analysis. In: Ritchie J, Lewis J, editors. Qualitative Research Practice: A Guide for Social Science Students and Researchers. London: SAGE; 2003. p. 199-218.
107. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ (Clinical research ed). 2015;350:h1258.
108. Department of Constitutional Affairs. Mental Capacity Act 2005 Code of Practice. 2007.
109. National Institute for Health Research. Budgeting for involvement: Practical advice on budgeting for actively involving the public in research studies. 2013. Available from: http://www.invo.org.uk/wp-content/uploads/2014/11/10002-INVOLVE-Budgeting-Tool-Publication-WEB.pdf.

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