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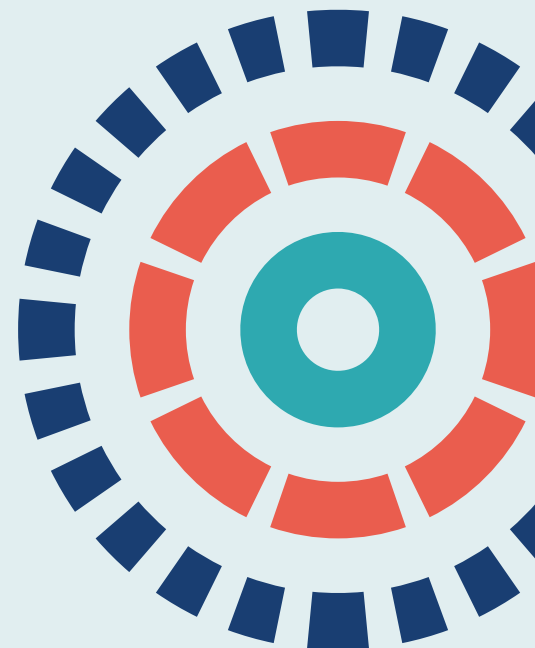
A health promotion intervention to improve lifestyle choices and health outcomes in people with psychosis: a research programme including the IMPaCT RCT

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This report

Abstract

A health promotion intervention to improve lifestyle choices and health outcomes in people with psychosis: a research programme including the IMPaCT RCT

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ABSTRACT

Background: People with psychotic disorders have reduced life expectancy largely because of physical health problems, especially cardiovascular disease, that are complicated by the use of tobacco and cannabis.

Objectives: We set out to (1) chart lifestyle and substance use choices and the emergence of cardiometabolic risk from the earliest presentation with psychosis, (2) develop a pragmatic health promotion intervention integrated within the clinical teams to improve the lifestyle choices and health outcomes of people with psychosis and (3) evaluate the clinical effectiveness and cost-effectiveness of that health promotion intervention.

Design: We performed a longitudinal cohort study of people presenting with their first episode of psychosis in three mental health trusts and followed up participants for 1 year [work package 1, physical health and substance use measures in first episode of psychosis (PUMP)]. We used an iterative Delphi methodology to develop and refine a modular health promotion intervention, improving physical health and reducing substance use in psychosis (IMPaCT) therapy, which was to be delivered by the patient's usual care co-ordinator and used motivational interviewing techniques and cognitive–behavioural therapy to improve health choices of people with psychosis (work package 2). We then conducted a multicentre, two-arm, parallel-cluster, randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of using the intervention with people with established psychosis (work package 3: IMPaCT randomised controlled trial) in five UK mental health trusts. The work took place between 2008 and 2014.

Participants: All people aged between 16 and 65 years within 6 months of their first presentation with a non-organic psychosis and who were proficient in English were eligible for inclusion in the PUMP study. Participants in the work package 2 training development were staff selected from a range of settings, working with psychosis. Participants in the phase 3 Delphi consensus and manual development comprised three expert groups of (1) therapists/researchers recruited from the local and national community, (2) clinicians and (3) service users, each of whom took part in two iterative review and feedback sessions. For work package 3, IMPaCT randomised controlled trial, care co-ordinators in participating community mental health teams who were permanently employed and had a minimum of four eligible patients (i.e. aged between 18 and 65 years with a diagnosis of a psychotic disorder) on their caseload were eligible to participate. In studies 1 and 3, patient participants were ineligible if they were pregnant or had a major illness that would have had an impact on their metabolic status or if they had a significant learning disability. All participants were included in the study only after giving written confirmed consent.

Main outcome measures: Cardiometabolic risk markers, including rates of obesity and central obesity, and levels of glycated haemoglobin (HbA_{1c}) and lipids, were the main outcomes in work package 1 (PUMP), with descriptive data presented on substance use. Our primary outcome measure for the IMPaCT randomised controlled trial was the physical or mental health component Short Form questionnaire-36 items quality-of-life scores at 12 months.

Results: Obesity rates rose from 18% at first presentation with psychosis to 24% by 1 year, but cardiometabolic risk was not associated with baseline lifestyle and substance use choices. Patterns of increase in the levels of HbA_{1c} over the year following first presentation showed variation by ethnic group. We recruited 104 care co-ordinators, of whom 52 (with 213 patients) were randomised to deliver IMPaCT therapy and 52 (with 193 patients) were randomised to deliver treatment as usual, in keeping with our power calculations. Of these 406 participants with established psychosis, 318 (78%) and 301 (74%) participants, respectively, attended the 12- and 15-month follow-ups. We found no significant effect of IMPaCT therapy compared with treatment as usual on the physical or mental health component Short Form questionnaire-36 items scores at either time point in an intention-to-treat analysis [physical health score ('d') –0.17 at 12 months and –0.09 at 15 months; mental health score ('d') 0.03 at 12 months and –0.05 at 15 months] or on costs. Nor did we find an effect on other cardiovascular risk indicators, including diabetes, except in the case of high-density lipoprotein cholesterol, which showed a trend for greater benefit with IMPaCT therapy than with treatment as usual (treatment effect 0.085, 95% confidence interval 0.007 to 0.16; $p = 0.034$).

Limitations: Follow-up in work package 1 was challenging, with 127 out of 293 participants attending; however, there was no difference in cardiometabolic measures or demographic factors at baseline between those who attended for follow-up and those who did not. In work package 3, the IMPaCT randomised controlled trial, care co-ordinators struggled to provide additional time to their patients that was devoted to the health promotion intervention on top of their usual clinical care contact with them.

Conclusions: Cardiometabolic risk is prominent even soon after first presentation with psychosis and increases over time. Lifestyle choices and substance use habits at first presentation do not predict those who will be most cardiometabolically compromised 1 year later. Training and supervising care co-ordinators to deliver a health promotion intervention to their own patients on top of routine care is not effective in the NHS for improving quality of life or reducing cardiometabolic risk.

Future work: Further work is needed to develop and evaluate effective, cost-effective and affordable ways of preventing the emergence of and reversing existing cardiometabolic risk indicators in people with psychosis.

Trial registration: Current Controlled Trials ISRCTN58667926.

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Supplementary material can be found on the NIHR Journals Library report project page (www.journalslibrary.nihr.ac.uk/programmes/pgfar/RP-PG-0606-1049/#/documentation).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

List of abbreviations

AUDIT	Alcohol Use Disorders Identification Test	IDF	International Diabetes Federation
BME	black and ethnic minority	IMPaCT	improving physical health and reducing substance use in psychosis
BMI	body mass index	MCS	mental component score
BP	blood pressure	MetS	metabolic syndrome
CBT	cognitive–behavioural therapy	MHC	mental health component
CI	confidence interval	MI	motivational interviewing
CMHT	community mental health team	MITI	Motivational Interviewing Treatment Integrity
CQUIN	Commissioning for Quality and Innovation	NICE	National Institute for Health and Care Excellence
CRP	C-reactive protein	NIHR	National Institute for Health Research
CSRI	Client Service Receipt Inventory		
CVD	cardiovascular disease	OPCRIT	operational criteria checklist for psychotic and affective illness
df	degrees of freedom		
DHSC	Department of Health and Social Care	PANSS	Positive and Negative Syndrome Scale
		PCA	prescription cost analyses
DINE	Dietary Instrument for Nutrition Education	PCS	physical component score
		PHC	physical health component
EQ-5D-3L	EuroQol-5 Dimensions, three-level version	PPHS	Psychiatric and Personal History Schedule
FEP	first episode of psychosis	PUMP	physical health and substance use in first episode of psychosis
GAF	Global Assessment of Functioning		
GP	general practitioner	QALY	quality-adjusted life-year
HbA$_{1c}$	glycated haemoglobin	QoL	quality of life
HDL	high-density lipoprotein	RCT	randomised controlled trial
HIP	Health Improvement Profile	RR	relative risk
HoNOS	Health of the Nation Outcomes Scales	SD	standard deviation
		SF-36	Short Form questionnaire-36 items
HPI	health promotion intervention	SLaM	South London and Maudsley
HPP	health promotion programme	SMI	severe mental illness
ICD-10	*International Statistical Classification of Diseases and Related Health Problems,* Tenth Revision	TAU	treatment as usual
		THC	delta-9-tetrahydrocannabinol
		WHO	World Health Organization
ICER	incremental cost-effectiveness ratio		

Plain English summary

Background

People with psychosis have poor physical health and reduced life expectancy, with cardiovascular disease causing about 60% of early deaths in this population.

Aims

We aimed to record the physical health risks and lifestyle choices of those with early psychosis, devise a way to help people make healthier choices and test whether or not this improved their quality of life.

Methods

First, we followed people for the year after they first presented with psychosis, documenting their mental and physical health and their lifestyle choices. Second, we then worked with carers and service users to develop a health promotion intervention, IMPaCT therapy, to address exercise, diet, smoking, alcohol and substance use, plus diabetes management where relevant. Finally, we ran a trial to see whether or not IMPaCT therapy helped and if it was good value. The work took place between 2008 and 2014.

Results

Patients with their first episode of psychosis had many risk factors for heart disease, such as obesity, diabetes, high levels of cholesterol, poor diet and little exercise.

In the IMPaCT therapy trial, we recruited over 100 care co-ordinators and split them into two groups randomly; half were trained in IMPaCT therapy and offered supervision of their practice, and the other half provided standard care. We reassessed the patients 1 year later to see whether or not there was any difference in quality of life and physical or mental health. We found no extra benefit for the patients allocated to IMPaCT therapy compared with those receiving standard care, although if at least 3 hours of IMPaCT therapy was received on top of standard care, waist circumference reduced. Costs of the intervention were low.

These findings signify the difficulty in reducing risk factors for physical health problems once these are established.

Scientific summary

Background

Physical health and severe mental illness

The physical health of people with severe mental illness is very poor, resulting in a markedly increased premature mortality rate. Much of the excess mortality is caused by diseases that affect the ageing population (e.g. cardiovascular and respiratory diseases and neoplasms) but affect patients with a diagnosis of severe mental illness earlier. Although intrinsic risk factors, such as age, genetics and ethnicity, may increase vulnerability to physical ill health, people with severe mental illness are more likely to have lifestyles that add to the risk of non-communicable disease, such as tobacco smoking, obesity, poor diet, lack of exercise and poor oral hygiene. Furthermore, amotivation and difficulties in executive function reduce the likelihood of people with severe mental illness engaging in the lifestyle changes needed to avoid diabetic complications, while episodes of acute illness often destabilise glucose control. The development of modifiable cardiovascular risk factors can be prevented and, as the name suggests, reversed; however, there are challenges in achieving this in practice.

Severe mental illness and substance use

Cannabis use is highly prevalent in the UK and results in a vulnerability to severe mental illness, with one-third of new cases of first episode of psychosis in south London now attributable to high-potency cannabis. Regular cannabis use increases the risk of schizophrenia two- to fourfold, and there is a dose–response relationship between the level of use and the risk of psychosis. Ongoing cannabis use by people with severe mental illness leads to increased relapse and hospitalisation, reduced adherence to treatment and longer illness. Early work suggested that cannabis users had higher blood glucose levels than non-cannabis users. A few recent studies note that cannabis use among the general population is not associated with serious physical health problems. A better understanding of the relative effect of cannabis on physical and mental health outcomes in people with severe mental illness is needed to inform the development of focused interventions.

The use of alcohol and other substances adds further complexity. A recent nationwide Danish register study has shown a clear effect on mortality; all types of substances were significantly associated with excess mortality in schizophrenia, especially alcohol and hard drugs. At a practical level, alcohol, itself a high-calorie substance, has well-described properties as an appetite stimulant, quite aside from its disinhibiting effect, which makes choosing the healthy option more difficult. However, the use of any psychoactive substance will affect one's ability to achieve consistency of physical and mental health management.

First episode of psychosis, physical health and substance use

Prior to coming into contact with mental health services, people experiencing their first episode of psychosis have physical health similar to that of the general population. A rapid emergence of cardiometabolic risk is seen on treatment initiation. It is clear that medication has a significant and rapid effect on this risk, but many other factors, including the wider determinants of health, lifestyle choices, substance use and access to preventative interventions, are also relevant. Identifying those most at risk of developing cardiometabolic risk would allow the development and, if appropriate, the targeting of prevention strategies.

Rates of tobacco smoking are very high among people with severe mental illness. This increases the risk of early death. It has long been assumed that people with severe mental illness may take up smoking because of illness-related factors, either to help with symptoms or as a result of custom and practice in inpatient units, such as smoking breaks. However, more recent analyses suggest that tobacco smoking

may predate and itself be a risk factor for schizophrenia, as pre-morbid tobacco use is associated with increased risk of psychosis and an earlier age of psychotic illness onset.

There is, overall, a pressing need to identify the factors most associated with emergent cardiometabolic risk in people with psychosis, as targeting at-risk groups and lifestyle choices may help to reduce the cardiovascular burden responsible for much early mortality.

Established psychosis, physical health and substance use

Effecting behaviour change in the general population is a challenge and likely to be even more so for people with severe mental illness. For those with enduring psychosis, no established and practical treatment programmes target both reducing substance use and improving physical health. Even interventions to improve cardiovascular risk alone encounter hurdles when applied outside selected settings. A recent meta-analysis showed that lifestyle interventions can help prevent and reduce weight gain and cardiometabolic risk in people with psychosis, but most of the interventions trialled were 'added on' to standard care or focused on an individual risk factor, such as weight or body mass index, and had few longer-term follow-ups. Recent European trials have found no effect of a multifactorial lifestyle intervention delivered in the patient's usual health-care setting on cardiovascular risk profiles. A recent trial in UK primary care also failed to show an effect. Furthermore, the patients most at risk of early death may not be those who readily sign up for extra sessions with their health teams. It is, therefore, vital to identify effective and cost-effective ways of reducing cardiovascular risk that are accessible to all people using psychosis services.

Objectives

The overall aims of the improving physical health and reducing substance use in psychosis (IMPaCT) programme were to determine the extent of physical health and lifestyle risks for people with psychosis and to develop and evaluate a culturally appropriate, innovative, practical, effective and cost-effective programme for achieving better physical and mental health in people with severe mental illness by improving lifestyle choices and decreasing substance use.

The specific objectives were to:

- Determine the prevalence of cardiovascular risk factors and substance use in people with psychosis, both at first presentation [work package 1: physical health and substance use in first episode of psychosis (PUMP)] and in those with established psychosis (work package 3: IMPaCT randomised controlled trial).
- Develop a better understanding of the roles cannabis plays in the pathophysiology and health outcomes of psychosis (see work package 1: PUMP).
- Define the development of cardiovascular risk after first presentation with psychosis (work package 1: PUMP).
- Develop guidelines for screening for the emergence of cardiometabolic risk.
- Use this information for training and screening guidelines for cardiovascular risk factors in early psychosis.
- Develop a manualised modular health promotion programme to improve health choices of people with psychosis (work package 2).
- Evaluate the effectiveness of this manualised health promotion programme on the quality of life of people with psychosis (work package 3: IMPaCT randomised controlled trial).
- Examine the costs associated with these patient groups and evaluate the cost-effectiveness of the health promotion intervention from health/social care and societal perspectives (work package 3: IMPaCT randomised controlled trial).

Methods

We divided the study into three phases, which took place between 2008 and 2014.

Work package 1: PUMP

We conducted a prospective cohort study examining physical health and substance use in people with a first episode of psychosis, aged 16–65 years. Patients were assessed at first presentation with psychosis and again 12 months later. A proportion was also assessed at 3 months. Cardiometabolic markers (including vitamin D and inflammatory markers), substance use, lifestyle choices and psychiatric symptomatology were recorded at each time point. Psychotropic medications and resource utilisation were recorded, with permission, from the electronic health records and a full economic evaluation performed.

Work package 2: development of the health promotion intervention (IMPaCT therapy)

We used the emerging knowledge base to design a manualised, modular health promotion intervention. The health promotion intervention principles and techniques were based on an adapted version of the physical health intervention used in the 'Well-being Support Programme' and a substance use intervention model, 'Managing Mental Health and Drug Use'. The intervention was integrated to cover physical health, mental health and substance use, using motivational interviewing and cognitive–behavioural therapy approaches, and aimed to be pragmatic enough to be deliverable within the NHS. We employed a Delphi technique to refine and co-produce the intervention with people with lived experience. To support the intervention, we published in book form a manual, reference guide and *Better Health Handbook* for service users.

We also developed a 4-day training programme for practitioners, encompassing skills and knowledge about physical health, substance use, cognitive–behavioural therapy and motivational interviewing.

Work package 3: IMPaCT randomised controlled trial

We undertook a Phase III randomised controlled trial comparing the clinical effectiveness and cost-effectiveness of combining treatment as usual with a 1-year IMPaCT health promotion intervention with that of treatment-as-usual alone for improving health at 1-year follow-up. The randomised controlled trial had a multicentre, two-arm, parallel-cluster design and was conducted across five mental health NHS trusts in the south of England. Eligible participants were aged 18–65 years and had a diagnosis of a psychotic disorder. The cluster was at the level of the community care co-ordinators who were randomly assigned to deliver the health promotion intervention IMPaCT therapy or treatment as usual to their own patients. The primary outcome was the physical and mental health component scores of the quality-of-life measure, the Short Form-36 questionnaire. A mixed-effects model was used to analyse the data. The trial included a comprehensive economic evaluation from two perspectives: (1) health and social care and (2) societal. Resource use data were collected by self-report using a specifically adapted interview schedule at baseline and at 12 months and 15 months; the data from 12 and 15 months were the focus for the economic evaluation. Costs estimated for each perspective were linked with outcome measures at 15 months.

Results

Work package 1: PUMP

Overall, 293 people experiencing their first episode of psychosis consented to the study [mean age 30.6 years (standard deviation 10.5 years), 65% male, 22% antipsychotic naive]. At baseline, half of the participants were overweight and 18% were obese. There were higher rates of central obesity among women (62.7%) than among men [35.3%, $\chi^2(1) = 11.34$; $p = 0.001$]. Tobacco was smoked by 76.8% of participants, and a similar proportion (77.0%) did < 150 minutes of moderate or vigorous exercise per week. One-quarter of participants had a high-fat diet and nearly half had hazardous patterns of alcohol consumption. Almost half (102/206) of the participants were current users of cannabis and

12.6% used other recreational drugs. Dietary fat scores, sedentary behaviour, alcohol use and pre-baseline olanzapine use were not significantly associated with any of the baseline cardiometabolic outcomes or change in cardiometabolic outcomes over the year, taking into account potential confounders. Patients from black and minority ethnic groups were more likely to develop glucose dysregulation over the first year, with a mean rise in HbA_{1c} levels of 3.3 mmol/mol over the year, than patients of white ethnicity, whose HbA_{1c} levels showed no change, suggesting a differential pattern of emergence of glucose dysregulation. By contrast, white men showed a marked increase in waist circumference, gaining a mean of 4.9 cm over the year, whereas men from black and minority ethnic groups gained 1.6 cm.

Obesity at baseline was associated with higher subsequent admission costs, low levels of high-density lipoprotein cholesterol at baseline were associated with lower subsequent admission costs and higher levels of high-density lipoprotein cholesterol at baseline was associated with a greater subsequent quality-of-life gain.

Together with our colleagues in the Biomedical Research Council-funded Genetics and Psychosis study, we demonstrated that one-quarter of first presentations of psychosis to the South London and Maudsley NHS Foundation Trust are attributable to the use of high-potency cannabis. This has since risen to one-third.

Substance use also had an effect on medication adherence over the first year of psychosis, thereby affecting outcomes.

Work package 2: development of the health promotion intervention (IMPaCT therapy)

Five expert therapists took part in two rounds of Delphi consultation on the therapy manual, reference book, and service user handbook, informing the redrafting after each round and providing additional qualitative feedback. Two clinicians provided quantitative feedback when they each used the therapy manual with a service user, and all four provided qualitative feedback, which informed the final version. The mean ratings for user-friendliness, spirit of motivational interviewing, integration with cognitive–behavioural therapy, usability in the NHS, length and complexity increased with development.

Work package 3: IMPaCT randomised controlled trial

We recruited 104 care co-ordinators in random order; 52 (with 213 patients overall, mean age 43.8 years, 54.9% male) were randomised to receive training and supervision in IMPaCT therapy, and the other 52 (with 193 patients, mean age 44.7 years, 60.6% male) were randomised to administer treatment as usual. Of the 406 patients randomised, 318 (78%) attended 12-month and 301 (74%) attended the 15-month follow-up assessments. There was no significant effect of IMPaCT therapy on the physical or mental health component Short Form questionnaire-36 items scores versus treatment as usual at either 12 or 15 months [physical health score ('d'): –0.17 at 12 months and – 0.09 at 15 months; mental health score ('d'): 0.03 at 12 months and –0.05 at 15 months]. No statistical difference was observed for the secondary outcomes, including cardiometabolic risk, substance use or mental health measures, compared with treatment as usual alone, except for high-density lipoprotein cholesterol, which improved more with IMPaCT therapy than with treatment as usual (treatment effect 0.085, 95% confidence interval 0.007 to –0.16; $p = 0.034$). There were challenges in delivering additional time for the intervention with just 19 (9%) out of 219 IMPaCT patients receiving six or more sessions of ≥ 30 minutes from their care co-ordinator in addition to their routine care. When participants received > 180 minutes of IMPaCT therapy in addition to usual care, they achieved a greater reduction in waist circumference than those in the treatment-as-usual group, and this was clinically significant.

The economic evaluation suggested no difference between the trial arms in costs from either perspective or for any of the four outcomes. Data suggested that the health promotion intervention was unlikely to be cost-effective from a health and social care perspective, with probabilities of cost-effectiveness ranging between 29% and 38% at willingness-to-pay thresholds of £0–50,000 per quality-of-life gain. Probabilities of cost-effectiveness were even lower from a societal perspective.

Conclusions

Work package 1: PUMP

Even within the first month of treatment, people experiencing their first episode of psychosis have high levels of cardiometabolic risk factors, which worsen over the following year, with a differential effect of ethnicity on glucose dysregulation. In addition, the use of tobacco and high-potency cannabis is common in this population, and this reduced medication adherence and the likelihood of remission in the first year.

Work package 2: development of the health promotion intervention (IMPaCT therapy)

Three books (a reference guide, a manual and a *Better Health Handbook*) to support IMPaCT therapy were written and a Delphi process was used to co-produce IMPaCT therapy with patients, staff and carers. IMPaCT therapy training significantly improved knowledge of physical health and substance use.

Work package 3: IMPaCT randomised controlled trial

Training and supervision in IMPaCT therapy was insufficient to produce significant improvements in physical or mental health quality of life or to meaningfully improve cardiovascular risk. Only a minority of patients received the intervention in six or more sessions of ≥ 30 minutes in addition to routine care. There was some dose effect, with patients who received the intervention for > 180 minutes having greater reductions in waist circumference.

Recommendations for future research

People with psychosis in the UK have extremely high levels of cardiovascular risk, which are compounded by high tobacco use; and this is evident soon after first presentation. We have demonstrated that simply enhancing care provided by the local care team is insufficient to reverse cardiovascular risks in people with established psychosis. Identifying effective, affordable interventions to improve health outcomes in psychosis remains a priority of health services internationally. Evidence-based approaches to prevent emergent cardiometabolic risk in people first presenting with psychosis are also needed.

Trial registration

The IMPaCT randomised controlled trial is registered as ISRCTN58667926.

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SYNOPSIS

Background

The physical health of people with severe mental illness (SMI) is very poor overall and the rates of premature death in this population are markedly increased, mainly attributable to natural causes,[1] similar to those in the ageing general population. Mortality rates from cardiovascular disease (CVD) in SMI are nearly threefold higher than in the general population.[2] The World Health Organization's (WHO's) definition of a 'healthy life' makes it clear that this encompasses physical, mental and social health, and, indeed, at the WHO World Mental Health Day in 2014, 'living a healthy life with schizophrenia' was highlighted (reproduced with permission from WHO[3]). Therefore, we should treat the physical health of people with psychosis alongside their mental health. The WHO's *Comprehensive Mental Health Action Plan*,[4] adopted in 2013 by the World Health Assembly,[4] advises the development of policy to improve the physical and mental health of people with SMI with a particular focus on improving access to good-quality physical health-care services.

Although intrinsic risk factors such as age, familial traits and ethnicity may increase vulnerability to physical illness, people with SMI are also more likely to have lifestyles that increase the risk of preventable physical disease, such as smoking, obesity, poor diet and lack of exercise; in addition, they are more likely to live in poverty.[5–8] Although the wider determinants of health are challenging to change in a research setting, the above knowledge brings with it the hope that lifestyle choices could be modified, leading to better outcomes.

But which outcome to choose? There is evidence that the mortality rate is highest in people with psychosis who are not on antipsychotic medication;[9,10] however, we also know that starting antipsychotic medication accelerates weight gain and diabetes risk.[11,12] Although it is important to minimise the side-effect burden of medication, to do so by inadequately treating the psychosis may well be counterproductive in terms of both short-term quality of life (QoL) and longer-term life expectancy. Taking a cardiovascular measure as one's only outcome measure runs the risk of neglecting the whole person, just as much as concentrating only on a mental health measure. It seems that QoL may be the most important measure for assessing overall health, in addition to reporting cardiovascular risk factors and measures of psychopathology and substance use. We also need to gather evidence of the costs of the cardiovascular risk states and of the cost-effectiveness of interventions to address them.

Cardiovascular risk factors include weight, blood pressure (BP) and markers of lipid and glucose metabolism, as well as smoking rates. One way of conceptualising cardiovascular risk is the metabolic syndrome (MetS). MetS is a constellation of CVD risk factors (abdominal obesity, insulin resistance/glucose intolerance, hypertension and dyslipidaemia)[13] that predict the chance of a person developing or dying from a cardiac event. Each risk factor alone almost doubles the risk of a CVD event occurring in the next decade. MetS is highly prevalent among people with psychosis,[14] at a rate of 52%;[15] in addition, the prevalence of obesity and dyslipidaemia is 50%, with diabetes at 14% and hypertension at 49.5%.[16–18] A rapid emergence of components of MetS is seen on treatment initiation.[19] Despite this, screening for cardiovascular risk factors remains poor.[20–24]

Likewise, the US CATIE[17] study found high rates of diabetes, obesity, hypertension and high cholesterol in people with SMI; this has since been confirmed in meta-analysis.[14] The emergence of cardiovascular risk and full-blown MetS can be prevented and reversed. At the time of applying for the programme, the CATIE study[17] had suggested that smoking cessation, nutrition counselling and supervised exercise programmes could help to reduce cardiovascular mortality in this population.[17] However, practice changes had yet to consolidate. Despite government initiatives to improve better physical health monitoring for UK

patients with SMI, a survey of 209 general practitioners (GPs) at that time revealed that only half provided lifestyle advice and fewer than one-third referred patients with SMI to specialist physical health support programmes.[25] Since then, Commissioning for Quality and Innovation (CQUIN) incentivisation targets have greatly improved physical health screening and intervening in mental health inpatient settings, but this has been more challenging to achieve in community settings. The recent National Audit of Schizophrenia[26] audited whether or not clinicians assess five factors [smoking, elevated body mass index (BMI), blood glucose control, blood lipids and BP] annually and found that in only 33% of people with schizophrenia were all of these factors monitored.

To add to the burden, there is a clear excess of diabetes in schizophrenia. A recent meta-analysis[27] from our wider group showed a prevalence of type 2 diabetes mellitus among 438,245 people with SMI of 11.3% [95% confidence interval (CI) 10.0% to 12.6%]. Notably, the corresponding figure in antipsychotic-naive patients was only 2.9% (95% CI 1.7% to 4.8%). We also reported[27] that people who have experienced multiple episodes of psychosis ($n = 133{,}470$) were more likely in our comparative meta-analysis to have type 2 diabetes mellitus than were matched controls [$n = 5{,}622{,}664$, relative risk (RR) 1.85, 95% CI 1.45 to 2.37; $p < 0.001$] and women were more at risk than men (RR 1.43, 95% CI 1.20 to 1.69; $p < 0.001$).

The management of diabetes and CVD risk is particularly difficult in people with SMI, and carries massive projected long- and short-term cost implications. Worryingly, patients with diabetes and SMI are treated less aggressively for CVD risk than those without mental disorders.[28] Rates of non-treatment for conditions such as diabetes, hypertension and dyslipidaemia in psychosis are high, with the discrepancy most marked in non-white women.[29] The effectiveness of cardiovascular risk management in people with SMI who have diabetes is also poor.[30] These patients are less likely to be prescribed cholesterol-lowering statin medications, angiotensin-converting enzyme inhibitors and angiotensin receptor blocking agents than diabetes patients without SMI.[28] A recent study of Danish population registers found significantly fewer prescriptions for cardiovascular medications for patients with schizophrenia or bipolar disorder than for the general population. When the authors examined the records of people without previous myocardial infarction or cerebrovascular disease, those with schizophrenia or bipolar disorder had up to 6- and 15-fold increased mortality from all causes or unnatural causes, respectively, compared with the general population; this was most pronounced among those without CVD treatment (16-fold increase). This concurs with previous work suggesting that the treatment of CVD risk factors is relatively neglected in these patients, although the excess of unnatural deaths in the untreated group also suggests that the link between CVD treatment and mortality may be confounded by illness severity.[31]

Unfortunately, evidence on optimal management of people with SMI and comorbid diabetes is lacking and there are many obstacles in practice. Poor motivation makes it difficult for people to make the lifestyle changes needed to avoid diabetic complications and episodes of acute illness can interrupt diabetic control. This cohort will put significant strain on NHS resources unless effective, evidence-based measures are developed to improve outcomes.

Those from black and ethnic minority (BME) communities face particular inequalities concerning both their physical and their mental health, and large-scale epidemiological work is under way in our wider group to specifically investigate CVD in BME groups with SMI.[32] BME groups have higher rates of not only SMI[33] but also diabetes.[34] Our study was largely based at the South London and Maudsley (SLaM) NHS Trust, where BME groups are over-represented among those attending services. The improving physical health and reducing substance use in psychosis (IMPaCT) study population contains a high proportion of BME participants to ensure that the results will be relevant to the health needs of a multiethnic society.

As well as the poor diet and sedentary lifestyles common in so much of our society, and especially in those with psychosis, health outcomes are compromised still further by concomitant substance use.

Tobacco-smoking, a major prognostic factor for health, is decreasing in the general population,[35] but remains common among people using mental health services, adding to their longer-term cardiovascular risk. Alcohol has a deleterious effect on both physical and mental health and complicates the management of psychotic conditions. Use of illicit substances also introduces complexity and unpredictability into the lives of people with psychosis.

Cannabis use

Over the last two decades, there has been a justified interest in comorbid substance use by those with a psychotic illness because of its high prevalence and significant impact on clinical and social problems, as well as the heavy burden laid on the health services. According to the Health and Social Care Information Centre's 2014 report[36] on statistics in drug misuse in England, primary diagnoses of a drug-related mental health and behavioural disorder increased by 8.5% from 2012/13 to 2013/14.[36] The size of the problem becomes even more important when those with a psychotic illness use substances significantly more than the general population.

The interaction between a psychotic illness and substance use is complex and can have major detrimental effects on the course of the illness, including a patient's risk of experiencing violence and being hospitalised, their ability to comply with treatment and even possibly the aetiology.[37,38] Such patients may also be at particular risk of deterioration in their mental health. A recent systematic meta-analysis of the outcomes associated with psychosis and comorbid substance use showed that current substance users with psychosis may have more severe positive symptoms than patients who have never used substances.[39]

Aetiological links between cannabis and psychosis

Interestingly, cannabis was used 150 years ago to treat 'insanity', while also being recognised as increasing the risk of 'madness', especially among young persons at the Maudsley Hospital.[40] Apart from some experimental studies examining the effects of cannabis during the 1960s, no interest was shown in cannabis studies. In 1987, Andréasson *et al.*[41] published a longitudinal study involving > 50,000 Swedish conscripts and reported that those who used cannabis by the age of 18 years were twice as likely to develop schizophrenia as non-users. The risk increased to sixfold in heavy cannabis users. This study was criticised and ignored until the early 2000s, when Zammit *et al.*[42] reanalysed the Swedish data, coming up with similar findings. The subject of cannabis and psychosis once more attracted empirical interest and the subsequent publications indicated a causal link.[43–45] Other studies, including systematic reviews, concluded that using cannabis increased the risk of developing a psychotic illness by two to six times, particularly in those with a predisposition to the condition and in a dose-dependent manner.[37,46,47]

Furthermore, experimental studies carried out on healthy volunteers have shown that cannabis can induce transient psychosis in some individuals, but not all.[48–50] At the same time, biochemical, imaging and genetic studies were carried out to examine the links between cannabis and psychosis, which have all added to the existing knowledge. For instance, we now know that the main psychoactive ingredient of cannabis, delta-9-tetrahydrocannabinol (THC), binds to CB1 receptors within the endocannabinoid system, and the very same brain regions are also implicated in psychoses, particularly in schizophrenia.[51–53]

Cannabis use in first episode of psychosis patients, prevalence and increased risks

Cannabis is the most frequently used illicit substance in the world, with nearly half of 15- to 34-year-olds reported to be lifetime users in the USA, Australia and Canada.[54] According to the 2015 European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) report,[55] lifetime use of cannabis among the same age group in the UK is reported to be 29.9%, whereas the last 12-month use was 11.2%. Cannabis is also the most commonly used substance after tobacco, according to epidemiological surveys of people with psychosis.[56–59] Perhaps unsurprisingly, we found that the use of substances other than cannabis

among first episode of psychosis (FEP) patients was minimal. Given the changing attitudes towards cannabis use, reflected by its ever-increasing medicinal use or decriminalisation in some countries, its more widespread use by new users is expected.[60] It is, therefore, important that the health risks of cannabis use are sufficiently researched.

At the time of the original National Institute for Health Research (NIHR) Programme Grants for Applied Research application, we wrote that a higher percentage of people with psychosis used cannabis and other drugs than the general population[61] and regular cannabis use increased the risk of schizophrenia two- to threefold.[44] We also highlighted that ongoing cannabis use in those with psychosis led to increased relapse and hospitalisation, lack of compliance with treatment and longer illness.[39]

Indeed, a considerable number of studies since have further emphasised the impact of cannabis use on people with psychosis. First, the higher prevalence of cannabis use among people with FEP has been validated in numerous studies.[62,63] A recent meta-analysis[64] on the prevalence of cannabis use in people with FEP pooled the data from 37 studies and concluded that cannabis use is highly prevalent in this group. The same study[64] also reported that the pooled estimate from 10 studies showed that regular use of cannabis begins 6.3 years before the onset of psychosis. In fact, the same research group has previously shown in another meta-analysis[65] that the age at the onset of psychosis among cannabis users was nearly 3 years earlier.

Additionally, prospective epidemiological studies and meta-analyses of such studies have concluded that using cannabis can indeed increase the risk of developing a psychotic illness and that there is a dose-related risk.[37,66–68] It should be noted that the main psychoactive compound of cannabis (i.e. THC) is nearly three times as concentrated in the cannabis used today as that used in earlier decades.

In a study in South East London, using 'skunk-like' cannabis was shown to triple the risk of psychosis and, when the results were extrapolated across the population, the use of high-potency cannabis was found to be associated with a 24% increase in new cases of psychosis.[67] It was also shown that both the frequency of use and the strength of the variety of cannabis used were associated with the increased risk. In another recent study with FEP patients carried out across Europe and Brazil in 11 sites, daily cannabis use with high-potency varieties increased the odds of psychotic disorder nearly five times in comparison with never users, and population attributable fractions calculations indicated that, if such high-THC cannabis had not been available, 12.2% of cases of FEP could have been prevented across these sites.[69]

Why do first episode of psychosis patients use cannabis?

The questions of why people with FEP use cannabis significantly more than others and why some continue to use it despite its deleterious effects remain important and have been explored using various theories. One of the first proposed theories was 'self-medication' hypothesis or 'reverse causality', suggesting that psychiatric symptoms are alleviated by cannabis or that cannabis is used to counter the side effects of psychotropic medication. However, this theory has since been disputed by several studies.[46,47,70] The recent meta-analysis[64] finding of a 6.3-year gap between the initiation of cannabis use and the onset of FEP is further evidence against this proposal.

However, some studies support the self-medication or reverse causality theory, as it is possible that some early dysphoric symptoms or anxiety make it more likely that some people will use cannabis. One such study carried out a comprehensive examination of experiences of cannabis use and reasons for using cannabis among people with psychosis and found that the primary reason given was not related to positive or negative symptoms or side effects of medication,[71] as only 10% reported using it for these reasons. Instead, the most frequently cited motivations were to reduce boredom, to improve socialisation and to alleviate some symptoms, such as agitation (47%) and difficulty sleeping (43%). Participants also reported that cannabis reduced feelings of depression.

The increased use of cannabis among people with psychosis has also been attributed to certain personality traits/disorders. There is mounting evidence that high-scoring schizotypal people who use cannabis are more likely to experience psychotic symptoms.[72–74] Another study has shown that conduct disorder symptoms are significantly associated with use of cannabis, particularly if it is used by the age of 14 years, among people with FEP; conduct disorder symptoms have been suggested to independently increase the possibility of cannabis use, which then increases the risk of psychosis.[75]

Finally, genetic studies have gained particular significance because most cannabis users do not develop psychosis; therefore, genetic factors need to be examined to find out what determines sensitivity to the psychosis-inducing effects of cannabis.[76] One of the earlier theories was genetic confounding: in other words, that cannabis use and psychosis risk shared genetic origins. However, more recently gene–environment interaction studies have gained more recognition; these refer to an environmental factor, such as the use of cannabis, being influenced by genetic factors. For instance, when there was a familial risk, taken as the measure of genetic loading, the non-psychotic siblings of people with psychosis were found to be significantly more vulnerable to mental health disturbances than the control participants.[77] Further support was provided by another study that showed increased sensitivity to the psychotogenic effects of cannabis to be associated with familial risk of psychosis.[78]

In addition to familial risk factors, there have been a number of candidate gene studies. The first of these was carried out by Caspi *et al.*,[79] who focused on a functional polymorphism of the valine allele of *catechol-O-amyltransferase* (COMT) gene in the New Zealand birth cohort study in examining the interaction between cannabis use and risk of psychosis. Later, a number of studies concentrated on this gene, leading to mixed results when further replication and validation studies were carried out.[80,81] However, one promising gene candidate is thought to be *alpha serine/threonine-protein kinase* (AKT1) as a variant of this gene displayed a twofold increased risk of a psychotic disorder after use of cannabis.[82] This finding was later independently replicated.[83] However, further studies need to be carried out because of the small evidence base.

In conclusion, the available evidence suggests that the interaction between the increased use of cannabis and the development of a psychotic illness is complex and may have both environmental and genetic causes.

What are the physical health effects of cannabis on first episode of psychosis patients?

Although the mental health risks of cannabis have been well studied, there is paucity of research on its possible health-care risks not only in psychiatric but also in general populations.

The question of why cannabis could affect physical health is linked to the knowledge that the endocannabinoid system where THC binds exists not only in the brain but also in most other organs, such as the heart, lungs, liver, kidneys, thyroid, bones and reproductive organs, as well as the immune system.[84–86]

Although knowledge about the multiple functions of this widespread neurotransmitter system is evolving, the available evidence implies that the endocannabinoid system has varied roles ranging from regulating the metabolism, circulatory system, reproduction, sleep and pain to ocular pressure.[87–90] It would therefore be possible to assume that the interference of THC, by interrupting the normal functioning of this widespread system, may lead to physical health problems. Only during the last few years has there been an interest in studying the physical health-care effects of cannabis among non-psychiatric populations.

One possible risk is to the functioning of the respiratory system as a result of the fact that cannabis is usually inhaled. The use of both cannabis and tobacco is common,[91] which also creates confounding effect problems in research. Findings so far show that there may be a dose-related risk, in that low levels of cannabis use (three to five joints per month) may increase respiratory function, whereas higher levels of use have the opposite effect.[59,92] So far, a conclusive association has not been established between cannabis use and lung cancer.[93]

The endocannabinoid system plays an important role in the regulation of food intake and reduces energy expenditure.[94,95] Based on this knowledge, some cannabis compounds are used to stimulate appetite and encourage weight gain in some patients with HIV (human immunodeficiency virus), AIDS (acquired immunodeficiency syndrome) or cancer. Interestingly, however, some recent studies have shown that in the general population cannabis use is associated with lower body mass than in non-users.[96] This paradoxical finding may be due to various factors. For instance, there may be a difference between long-term use, as found in general population studies, and short-term use, as found in appetite stimulation studies. The other explanation would be the possibility of poly-drug use or food and drugs competing for the same reward sites in the brain. It is also suggested that cannabis may act as a regulatory compound, increasing weight in those with low weight but not in those who are already overweight.[97] Interestingly, however, most recent studies carried out not only on the general population[98–100] but also on people with SMI[101] report that cannabis use is associated with lower BMI, smaller waist circumference, lower diastolic BP and more severe psychotic symptoms.

Unfortunately, no established and practical treatment programmes target both improving physical health and reducing substance use among people with psychosis, and attending parallel treatment programmes is often impractical. Treatment programmes, such as MIDAS, for people with both psychosis and substance misuse appeared promising,[102,103] but these are lengthy, complex and expensive.

The huge implications of these health gaps in terms of morbidity, mortality, QoL and projected future cost make addressing physical health in SMI a national priority. The National Service Framework and the National Institute for Health and Care Excellence (NICE) have emphasised the importance of good physical health in people with SMI and encourage primary and secondary care services to collaborate to improve physical outcomes in this population.[104,105] In 2004, the UK government emphased physical health promotion as a means of reducing CVD burden and endorsed the aims of programmes addressing physical health in people with SMI.[106] None of these programmes, however, was adequately tested in the UK to ensure that it could accurately quantify the problem in those with SMI, could identify those most at risk, could reduce physical health risk factors and was reliable and reproducible enough to be disseminated across the NHS.

This is a matter of equity. A decade ago, the UK Disability Rights Commission investigation stated overtly that people with mental health problems were more likely than others to experience major illness and develop serious health conditions earlier to and die earlier as a result.[107] Yet this group were less likely to receive some important treatments/health checks and faced real barriers to accessing services. The report called for a clear shift in approach to eliminate inequitable treatment and to target high-risk groups. The idea was that this would prevent the extra costs of serious ill health being passed on to other parts of the NHS and enable people with SMI to be healthier and participate fully in society.[107] Similar concerns were reflected in the *Choosing Health: Making Healthy Choices Easier* White Paper.[106] Since then, this topic has gathered momentum; there have been a number of high-profile policy documents, including *No Health Without Mental Health*,[108] the Department of Health and Social Care report *Closing The Gap: Priorities For Essential Change in Mental Health*,[109] *Whole-person Care: from Rhetoric to Reality*,[110] the BMA report *Recognising the Importance of Physical Health in Mental Health and Intellectual Disability*,[111] the *Annual Report of the Chief Medical Officer 2013*[112] and the London Health Commission report *Better Health for London*.[113] Indeed, the London Health Commission's ambition to reduce the gap in life expectancy between adults living with SMI and the rest of the population has led to the creation of a working group, 'Stolen Years', to work across health systems to make this a reality.

The challenge remains the evidence base. Most studies of health promotion in SMI to date have focused on selected groups of patients and achieved only modest outcomes. None has addressed comorbid substance misuse. Importantly, none has evaluated the cost-effectiveness of a combined lifestyle intervention across a service, work needed to inform health commissioning. The next logical step was to develop a more practical alternative to separate programmes, and so we set out to develop and evaluate the benefits of a well-defined, standardised, person-centred intervention, using modules,

as appropriate, to target both lifestyle and substance use to maximise physical and mental health. We also undertook an evaluation of the costs of the cardiovascular burden and the cost-effectiveness of the intervention to reduce it.

Healthy living interventions should be an integral part of the care provided to people with SMI. This must become a priority for both primary and secondary care services, although it will require a cultural shift in terms of how care is provided to those with SMI, with a greater emphasis on a holistic approach. There is an urgent need for (1) a reliable way of identifying those most at risk, (2) guidelines on how best to screen for the emergence of MetS and (3) an effective intervention to reduce modifiable cardiovascular risk factors in this group.

Aims and objectives

The aim of IMPaCT was to use the available evidence to develop culturally appropriate, innovative and cost-effective programmes to achieve better physical and mental health in people with SMI by improving lifestyle choices and decreasing illicit drug use.

Programme plan (*Figure 1*)

Work package 1: PUMP

The Physical health and substance Use Measures in first episode of Psychosis (PUMP) study was a prospective observational cohort of patients presenting with their FEP. The participants were recruited from the four boroughs of the SLaM NHS Foundation Trust, two boroughs of the Oxleas NHS Foundation Trust and two boroughs of the Sussex Partnership NHS Foundation Trust. Patients from both inpatient and outpatient services were followed up for 12 months to observe health and service utilisation markers over time and to test the association between lifestyle (diet, exercise and substance use) and antipsychotic medication factors and the emergence of components of MetS.

In the first part of the IMPaCT programme, we also wanted to examine the extent of cannabis use among our group of FEP patients, as well as finding out the mental and physical health-care effects of this use at baseline and at 12 months' follow-up, compared with non-users.
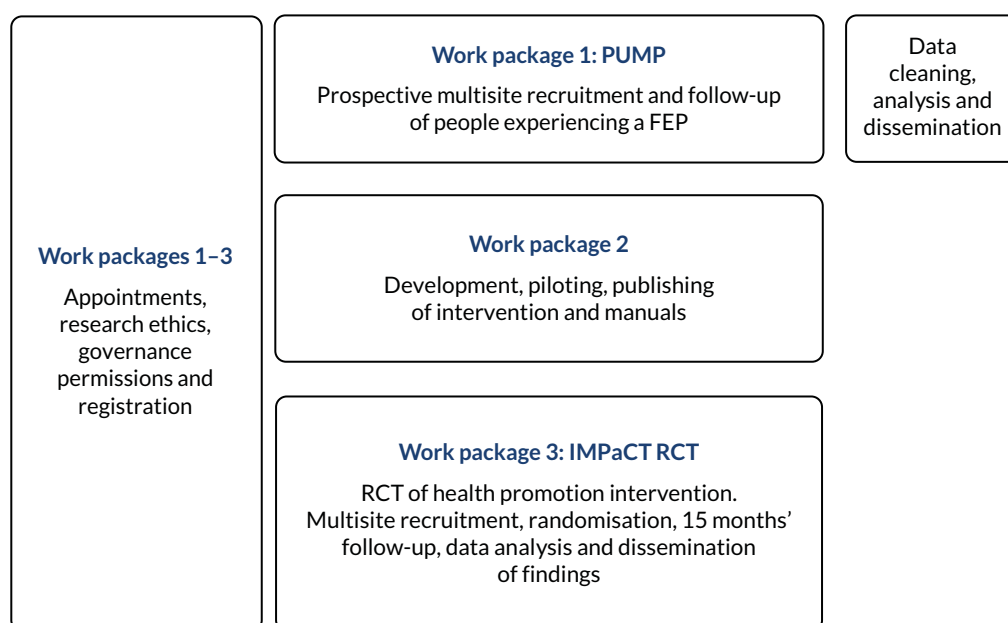
FIGURE 1 Research design pathway.

Work package 2: development of the health promotion intervention (IMPaCT therapy)

The available evidence was used to inform the development, validation and manualisation of a health promotion intervention (HPI) tailored to the needs of the individual, addressing a number of lifestyle choices, including substance use. The purpose of the development of the manual was to create a culturally appropriate, innovative and effective programme for use in routine care systems to achieve better physical and mental health in people with SMI by improving lifestyle choices and decreasing substance use. This intensive HPI (IMPaCT therapy) was designed to cover physical health, mental health and substance use using motivational interviewing (MI) and cognitive–behavioural therapy (CBT) and was designed to be sufficiently pragmatic to be deliverable within the NHS.

Work package 3: IMPaCT randomised controlled trial

A randomised controlled trial (RCT) assessing whether or not the addition of an intensive HPI (IMPaCT therapy) to usual mental health care delivered by care co-ordinators is more effective and more cost-effective than usual mental health care in improving metabolic outcomes and reducing substance use among people with SMI on completion of the intervention at 12 months and 15 months after baseline.

Work package 1: physical health and substance use in first episode of psychosis (PUMP)

Background

People with SMI experience a significant reduction in life expectancy of approximately 10 years.[1] There are a number of possible contributors to this premature death rate; for example, at the service level, risk factors such as unequal access to care followed by substandard treatment influence outcomes. At the individual level, a greater prevalence of CVD, and unhealthy lifestyle choices or substance use, may also increase risk. Some of these factors may interact; for example, lifestyle choices may have an impact on cardiometabolic status, thus reducing life expectancy. Although there is evidence surrounding the impact of unhealthy lifestyle choices, little is known about whether lifestyle choice or substance use predicts changes in cardiometabolic status. Investigating these factors among patients presenting with their FEP thus offers the opportunity to map the course and impact of lifestyle choices on cardiometabolic risk in people with psychosis. This section reports a longitudinal study that sought to observe health behaviours and the progression of cardiometabolic disease among patients with FEP and to investigate links between these factors over time.

Setting and method

A total of 293 patients with first-onset psychosis were recruited from inpatient units and community mental health teams (CMHTs) across eight boroughs in the south of England. Participants meeting the following inclusion criteria were consented to the study: (1) aged between 16 and 65 years, (2) experiencing a FEP [according to *International Statistical Classification of Diseases and Related Health Problems*, Tenth Revision (ICD-10),[114] codes F20–29 and F30–33], (3) proficient in English with no requirement for an interpreter and (4) no diagnosis of severe learning difficulties.

A total of 118 participants completed the 3-month follow-up and 127 participants completed the 12-month follow-up.

Patients who were pregnant or had an organic cause of their psychosis, those with a major medical illness or neurological disease, and those with history of previous contact with health (GP or psychiatric) services for the presence of psychosis were excluded from participating in the study.

Measures

A range of measures were collected over three time points (baseline and 3 and 12 months), including the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression Severity scale, Global Assessment of Functioning (GAF), Young Mania Rating Scale, Calgary Depression Scale and operational criteria checklist for psychotic and affective illness (OPCRIT) diagnostic scale, as well as anthropometric measures and blood sampling for cardiometabolic and inflammatory markers and measures of nicotine, alcohol and substance use, including the Nicotine Dependence questionnaire (Fagerström scale), the Alcohol Use Disorders Identification Test (AUDIT) and a modified Cannabis Experience Questionnaire (CEQ-4), along with the International Physical Activity Questionnaire (IPAQ).[72,115–121] All measures in the study were administered face to face by a trained researcher, except the OPCRIT, which was rated by a clinician based on the clinical notes.

Follow-up contacts

Clinical, sociodemographic and substance use data were also collected using the Follow-up Psychiatric and Personal History Schedule (FUPPHS). This records information about the patient's mental state, general behaviour, substance use, events and personal history over a defined period using information obtained from patients, informants, case notes and other records.[122] Researchers rating the Psychiatric and Personal History Schedule (PPHS) at follow-up achieved an intraclass correlation of 0.90 on all PPHS items when duplicate ratings were compared. Information on medication adherence and remission during the 1-year follow-up was also extracted from the PPHS, where poor adherence is defined as $1 =$ lapses of ≥ 3 days more than once, and $2 =$ not taking any prescribed medication. Remission was operationally defined as the absence of positive, negative or disorganised symptoms for at least 30 days. In our study[122] examining the effect of substance use and medication adherence on outcomes, the 1-year follow-up period was taken as the date of first contact with mental health services of the SLaM NHS Foundation Trust for psychosis to the date exactly 1 year later using the clinical records held on the SLaM electronic Patient Journey System (ePJS), with all of the PPHS measures completed by a researcher retrospectively using the electronic mental health records system (i.e. the SLaM electronic Patient Journey System).

Linear regression models were used to examine for the associations between baseline diet, alcohol use, sedentary behaviour and prescriptions of olanzapine with cardiometabolic risk both at baseline and at 12 months' follow-up. Baseline cross-sectional associations between continuous scores for lifestyle and cardiometabolic factors were investigated using unadjusted and adjusted linear regression models, as was the relationship between baseline lifestyle choices and change in cardiometabolic factors at 12 months, investigating associations between use of dibenzodiazepine medications between baseline and 12 months (yes/no) and cardiometabolic factors in the same way. We used the mi impute chained command in Stata® version 15.1 (StataCorp LP, College Station, TX, USA) with 50 imputed data sets for each MI model to account for different patterns of missingness. To account for multiple testing, a stricter alpha of 0.01 was prespecified as the significance level. The assumptions of the regression analyses of constant variance and normal distribution were assessed with a visual inspection of residual plots.

We used univariate and multivariate analyses to determine the relationship between measures of cardiometabolic risk at baseline and admission, and home treatment costs in the following year (see *Appendix 1*).

Patient and public involvement

Service user and carer experts were part of the core planning and management throughout the project (see *Programme patient and public involvement*).

Results

Metabolic characteristics and changes over 12 months

There were significant levels of cardiometabolic risk at first presentation, with rates of obesity, raised levels of glycated haemoglobin (HbA$_{1c}$), levels of C-reactive protein (CRP) and low levels of high-density lipoprotein (HDL) cholesterol increasing over the following 12 months. In the overall group, central obesity rates at baseline were higher in women (62.7%; $n = 37/59$; waist circumference ≥ 80 cm) than in men (35.3%; $n = 36/102$; waist circumference ≥ 94 cm; $\chi^2 = 11.34$; $p = 0.001$). The mean waist circumference in white men increased by 4.9 cm over the year, such that by 12 months white men had a waist measurement 7.3 cm greater than their counterparts of other ethnicities, despite having comparable measures at baseline. The average waist circumference of white women at baseline was 9.6 cm smaller than of women of other ethnicities.

The mean total cholesterol levels among those participants of white ethnicity (4.9 mmol/l) and those of other ethnicities (4.7 mmol/l) were comparable at baseline, but white patients had higher levels at 12 months (5.1 vs. 4.6 mmol/l; $p = 0.04$) (see Gaughran et al.[123]).

Baseline antipsychotic use and associated metabolic impact
The median duration of treatment with antipsychotics at baseline was 21 days (interquartile range 9–55.5 days) (mean 33.7 days, SD 50.3 days), with 95% of the sample prescribed second-generation antipsychotics. The most frequently prescribed antipsychotic was olanzapine.

Patients who had been prescribed antipsychotic medication for $\geq$ 2 weeks had an average total cholesterol higher (0.5 mmol/l, 95% CI 0.1 to 0.8 mmol/l; $p = 0.007$) than those who had been prescribed antipsychotics for less than a fortnight. Participants medicated prior to baseline had a higher baseline average waist circumference (7.7 cm, 95% CI 2.0 to 13.4 cm; $p = 0.009$) than antipsychotic-naive patients.

Lifestyle choices and baseline cardiometabolic outcomes and changes over time
There was no association between any of the baseline or 12-month cardiometabolic outcomes and Dietary Instrument for Nutrition Education (DINE) fat scores, sedentary behaviour, AUDIT scores and pre-baseline olanzapine. The lack of association remained when adjusting for potential confounders (age, gender, ethnicity or pre-baseline days on medication) and in sensitivity analyses using all non-missing data from the full data set.

Subgroup analyses were run comparing those participants who took olanzapine between baseline and 12 months and those who did not. No differences were found between the two groups in the magnitude of associations between changes in cardiometabolic outcomes at 12 months' follow-up and baseline lifestyle factors, nor were there any such associations within either of the two groups. No associations emerged from sensitivity analyses using the full data set (both unadjusted and adjusted for the same potential confounders) (see Gaughran et al.[123]).

Obesity at baseline was associated with higher subsequent admission costs, low HDL cholesterol at baseline was associated with lower subsequent admission costs and higher HDL cholesterol at baseline was associated with a greater subsequent quality-adjusted life-year (QALY) gain (see *Appendix 1*).

Cannabis use in PUMP first episode of psychosis patients
Of 206 patients with FEP, 102 used cannabis at baseline (49.5%), with 23 out of 183 (12.6%) reporting current use of other recreational drugs. Current users at baseline were more likely to be men [59.4%, degrees of freedom (df) 1; $p < 0.05$] and most were younger, belonging to the 18–33 years age group (df 1; $p < 0.05$), than the non-users. They were also more likely to be single (df 4; $p < 0.05$). In terms of ethnicity, occupation, having close confidants, ICD-10 diagnoses from OPCRIT, drug naivety and seeing GP or health specialists, there were no significant differences between cannabis users and non-users. Cannabis users also differed from non-users in terms of using cigarettes (df 1; $p < 0.0001$) and other stimulants (df 3; $p < 0.01$). At 12 months' follow-up, we had data on 105 patients and the number of current users dropped to 40 (38.1%). The corresponding figure at 12 months for those reporting use of other substances was 12 out of 102 (11.8%). From first data collection to 12 months, 12 (11.3%) participants started using cannabis, whereas 16 people (15.5%) stopped.

Effects of cannabis on outcomes in first episode of psychosis patients
In terms of physical health outcomes, non-cannabis users had higher cholesterol levels at 12 months' follow-up than non-users (df 1; $p < .045$). Female users were thinner at baseline (df 1; $p < 0.036$) but male users were heavier at 12 months (df 1; $p < 0.003$) than non-users. Female users had smaller waistlines at baseline (df 1; $p < 0.008$) than female non-users and male users had larger waistlines at 12 months (df 1; $p < 0.01$) than male non-users.

There has been much speculation about why people with a diagnosis of psychosis may use cannabis; some suggest a self-medication hypothesis, whereas other evidence suggests that it is used to alleviate dysphoria. Kolliakou et al.[124] conducted a study nested within the PUMP study, which investigated the reasons for use reported by those participants who used cannabis and how these varied over time. Participants rated their motives at baseline ($n = 69$), at 3 months ($n = 29$) and at 12 months ($n = 36$) on the Reasons for Use Scale, which has five subscales (enhancement, social motive, coping with unpleasant affect, conformity and acceptance, and relief of positive symptoms and side effects). At all of the time points, 'enhancement' received most endorsement, followed by 'coping with unpleasant affect' and 'social motive'. 'Conformity and acceptance' followed closely. The least endorsed motive was 'relief of positive symptoms and side effects'. When participants continued to use cannabis at 3 months and 12 months, they endorsed these reasons less strongly than at baseline. We found little support for the theory that people were using cannabis for self-medication or to alleviate dysphoria. Rather, in keeping with the general population, the most common reason that people with their FEP gave for their use of cannabis was 'enhancement'.

Colizzi et al.[122] demonstrated that substance use and poor medication adherence contribute to poor outcomes in the year following the FEP. Colizzi et al.'s work detailed the relative contributions of medication adherence and substance use to outcome over the year after the FEP. We had data on 205 patients on use of tobacco, alcohol, cannabis and stimulants at psychosis onset and at 1 year, along with data on medication adherence and symptom remission. Rates of overall substance use were high both before (37–65%) and after psychosis onset (45–66%). Nicotine dependence was reported in 53.2% of patients at baseline, whereas 40.5% reported premorbid problem drinking, 65.4% reported premorbid cannabis use and 36.6% reported premorbid stimulant use. A total of 44% of patients had poor medication adherence and 55% failed to reach remission from psychosis.

Both nicotine dependence and cannabis use after the onset of psychosis predicted poor medication adherence and non-remission significantly. Poor medication adherence occurred in 43.9% of patients at some point in the first year and also significantly predicted remission during the 1-year follow-up, with patients with poor medication adherence having a sixfold increased likelihood of psychosis non-remission when compared with those with good adherence. This association between medication adherence and remission was still significant when substance use in the 1-year follow-up period was added into this model. Sobel tests for mediation showed that medication adherence was a significant mediator of the relationship between nicotine dependence and remission ($z = 2.02$; $p = 0.04$) and of that between cannabis use and remission ($z = 2.12$; $p = 0.03$).[122]

Discussion

Cardiovascular disease risk emerges very soon after presentation, consistent with recent US work.[125] These findings confirm previous literature that demonstrates people with FEP lead unhealthy lifestyles marked by poor diet, lack of physical activity and high rates of nicotine, alcohol and drug use. Our sample also presented with impaired metabolic status on first contact with services as indicated by glycose dysregulation and hypertension. They also had metabolic features consistent with the emergence of type 2 diabetes mellitus. Throughout the study, there was significant weight gain in both men and women. Interestingly, despite national stop-smoking campaigns that were running alongside our study, we did not find a significant reduction in smoking rates. Indeed, a high proportion of the sample smoked at baseline (76.8%), which had changed little at 12 months.

Strengths of this study include the diverse population recruited from both inpatient and community settings in the south of England. A limitation is that there were missing data at both time points. Although booklets were produced to ensure the consistent order of the administration of questionnaires, this order was not always followed for pragmatic reasons. However, we have no reason to believe that data were not missing at random. Another limitation is the level of follow-up, with only 125 of the 293 eligible

participants completing 12 months' follow-up and 140 dropping out after baseline. The largest group of non-completers were those who declined an individual assessment point, although a smaller number withdrew from the study. The reasons for this are likely to be manifold, and the main recruitment site, south London, has a very mobile population. There was recompense for time, but no overt financial incentivisation. Where we had missing measures of key variables, these were imputed using a commonly used statistical approach and sensitivity analyses was undertaken to demonstrate the robustness of the imputation process. We have no reason to believe that attrition was not random, with no differences between demographic or baseline clinical attributes between completers and non-completers, although they may have differed on other factors.

Despite concerns regarding the use of olanzapine as a first-line antipsychotic, over half of participants had been prescribed olanzapine by the time of the baseline assessment. Not all of these participants continued to be prescribed olanzapine over the 12 months of the study, and, although we controlled for days prescribed olanzapine at baseline, we would not have been able to identify whether or not cardiometabolic risk reduced once olanzapine had been discontinued.

These high and rising levels of CVD risk are worrying outcomes and it is hugely clinically important that both nicotine dependence and cannabis use after the onset of psychosis predicted both poor medication adherence and non-remission significantly. Poor medication adherence mediated the effects of substance use on non-remission, demonstrating that medication adherence is on the causal pathway between cannabis use and nicotine dependence and a non-remission outcome.[122]

Planned future work

We plan to look further at the relationship between inflammatory markers and cardiovascular risk in this population. Preliminary work by our wider team[126] has suggested that greater increases in inflammatory markers soon after first presentation with psychosis are associated with a greater risk of short-term metabolic abnormalities, in particular dyslipidaemia, which are independent of gains in weight. We are, therefore, interested in whether or not early evidence of inflammation may predict those most likely to develop cardiometabolic disease.

Mapping health promotion programmes

As part of work package 1, we also mapped local health promotion programmes (HPPs). Below is a summary of work published in O'Brien *et al.*[127]

Background

The increased risk of physical health comorbidities combined with low socioeconomic status means that patients with SMI require higher levels of physical health care and in particular greater attention to cardiovascular risk factors. However, in practice, reports indicate that medical treatment rates for those factors are low among those with SMI and, if SMI patients receive medications, the choice of medication may be outdated.[29,31] The physical health of people with mental health problems has been set as a priority for improvement by the Department of Health and Social Care (DHSC).[128] The NHS and local authorities have been encouraged to develop HPPs, with particular emphasis on HPPs addressing modifiable health issues pertinent to SMI patients: diet, exercise and substance use. However, prior to our work, it was not clear what the distribution of such HPPs was or whether or not there were barriers to access for people with psychosis.

Aims and hypotheses

Because a systematic exploration of the provision of HPP available for SMI patients was lacking, the study objective was to assess the magnitude and type of HPPs that were available for or inclusive of people with SMI in four socially deprived boroughs in south London, UK.

Methods

The study looked at the four boroughs served by the SLaM NHS Foundation Trust: Southwark, Lewisham, Croydon and Lambeth. These boroughs (especially Lambeth, Lewisham and Southwark) have lower health-related sociodemographics than London and the national average.

The study design was a cross-sectional mapping of HPPs available to people with SMI across these four boroughs of London in 2008–9. These programmes covered a range of health promotion areas: sexual health, carer support, diabetes and nutrition, drug and alcohol use, physical activity and smoking cessation. The programmes were based in drop-in centres, outpatient services and day centres.

Mapping was stratified by local authority, the voluntary sector and the NHS. It was performed using standard scoping methodologies using internet searches of websites of the local authority, mental health charities, mental health trusts and primary care trusts. After this, confirmation was sought of the HPP identified, and further details (the costs, the access methods and the extent to which people with SMI were included in the programme) were requested from the programme convener or administrator.

Health sociodemographic details for each borough were obtained from GP registers.

The service user and carer experts in the IMPaCT Programme Management Group had input on the development of this work.

Results

The prevalence of people with SMI was 1.1% in Croydon and Southwark, 1.2% in Lewisham and 1.5% in Lambeth. A total of 145 HPPs available to people with SMI were identified: 38 in Lewisham (1 : 82 people with SMI), 50 in Southwark (1 : 60 people with SMI), 27 in Lambeth (1 : 149 people with SMI) and 30 in Croydon (1 : 121 people with SMI).

As for availability, 61 HPPs [15 in Lewisham (40%), 14 in Southwark (28%), 14 in Lambeth (52%) and 18 in Croydon (60%)] were targeted specifically at people with SMI and the rest were inclusive of people with SMI. No publicly funded local authority leisure centre across the four boroughs stated in response to direct questioning that they had the facility to perform risk assessments or had staff trained to run HPPs inclusive of this population.

A small proportion of HPPs stipulated eligibility criteria for people with SMI, which, if not satisfied, would preclude. These access to the service the programme's included the patient being required concordance with prescribed medications or to attend with their care co-ordinator.

Looking at the focus of HPPs across boroughs, physical activity was most common (51 HPPs) and sexual health was least common (10 HPPs), with only two specifically provided for or inclusive of SMI patients.

Discussion

The number of HPPs accessible to people with SMI varied across the four boroughs; for example, Lambeth had the largest number of people with SMI but provided the fewest accessible HPPs (rate of 1 : 149), in contrast to Southwark, which had fewer people with SMI but more HPPs available to them (1 : 60).

Stipulating inclusion and exclusion criteria may impede access to HPPs and cause unnecessary stress and distress, as well as adding to the stigma surrounding SMI. This is likely to act as a deterrent to this population, who are in great need of health promotion services.

The mapping was time-consuming, which may account for the difficulties that clinicians and service users themselves experience when trying to identify available HPPs. These details should ideally be readily accessible from a single source to patients and staff alike. This action would have three foreseeable benefits. First, it would facilitate the integration of physical and mental health care. Second, it would be easier for health-care professionals to recommend certain programmes to service users. Third, it would support people with SMI and their carers who may have difficulty in navigating information from multiple resources to access HPPs themselves. However, such a resource would require to be updated regularly, which has cost implications.

Conclusion

This was the first attempt to map HPPs available for patients with SMI across these South London boroughs and demonstrated that the distribution of these was inequitable. This may not reflect demand, as some HPPs set exclusion criteria and provide inadequate support to staff. Accurate and readily available information on local HPPs would benefit the population with SMI who are in dire need of such services.[127]

Work package 2: the IMPaCT therapy – development of a comprehensive, integrative manualised psychological intervention for physical health and substance use in severe mental illness

Introduction

People with psychosis experience significant and broad-ranging physical health problems, including CVD and diabetes, leading to lower QoL and a 10- to 25-year reduction in life expectancy compared with the general population.[129–131] Those with psychosis in the adult age group are 5.7 times more likely than the general population to be treated for diabetes.[132] Contributing factors include medication treatment regimes, lifestyle choices, inequities in health service access and substance use.[133–135] Despite the size of the problem, effective intervention models, tailored to the person's needs, are few and are not used in clinical settings in a standardised manner. Studies examining the topic reinforce recommendations that people with co-occurring disorders require more intensive and integrated interventions.[136]

Psychological interventions for physical health in psychosis have largely focused on a single aspect of health, such as smoking,[137] diet and weight gain,[138] exercise[139–141] and substance use.[142,143] Yet clinical presentation and research evidence suggests that these health risks often co-exist, are inter-related and contribute exponentially to morbidity and mortality. In fact, a recently published 10-year follow-up of the ÆSOP frst-episode cohort study[144] demonstrates the significant impact of substance use on both natural and unnatural causes of mortality. The authors conclude that early intervention and dual-diagnosis services may play a key role in achieving more rapid remission and carer involvement in addressing substance use problems to reduce excess mortality in psychosis. Indeed, there is a long overdue need for the development of comprehensive, person-centred intervention models tailored to individual needs to improve health and QoL and reduce the economic burden on services and society.[145]

Psychological interventions have traditionally been denied to people with psychosis not only because of a lack of resources but also because of a belief that people with psychosis cannot benefit from these because of their illness, lack of insight and cognitive deficits.

The theory behind the cognitive model of psychopathology can be defined as how thoughts and perceptions or inner interpretations of specific situations can influence one's behaviour and emotions and can even lead to physiological reactions. Cognitive–behavioural therapy is a well-researched and validated intervention model that aims to modify a person's negative thoughts and interpretations. The evidence on the effect of CBT for psychosis has accumulated over only the last 15 years.[146] Meta-analyses studying the efficacy of CBT on positive symptoms of schizophrenia,[147–149] as well as secondary outcome measures such as functioning levels, mood and social anxiety,[148,150] have revealed medium beneficial effects. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study[151] examined the decision-making capacity of patients with schizophrenia and found that negative symptoms had very little effect and positive symptoms had no effect on this. These studies have emphasised the need to develop and adapt for psychological interventions in patients with psychosis.

As a result of this renewed interest in psychological interventions in psychosis, models of psychological intervention used in non-psychotic populations, such as those with substance misuse, have been proposed for a psychosis population. One such model is MI, which is a 'directive, client-centred counselling style for eliciting behaviour change by helping people to explore and resolve ambivalence' in relation to health behaviour.[152] MI aims to build a person's motivation for change by increasing their awareness of the impact of problem behaviour, while maintaining an empathic approach to encourage responsibility as part of an open, non-judgemental therapist–client interaction and with realistic expectations about what can be achieved. There is a robust evidence base for this type of intervention in alcohol, substance use and smoking, and emerging evidence also in diet, exercise and diabetes, in non-psychotic populations.[153,154]

In a large population of university students who had been using substances, a 3-month follow-up revealed that a single session of MI had reduced their use of cigarettes, alcohol and cannabis, mainly through moderation rather than complete cessation.[155] However, it is unlikely that a single MI session would be sufficient for patients with psychosis. Indeed, a study[156] involving patients who use substances suggests that modifications be made to standard MI, particularly taking into account possible cognitive deficits by simplifying open-ended questions, refining reflective thinking skills, heightening emphasis on affirmations and integrating psychiatric issues into personalised feedback.

A number of studies have examined the effectiveness of integrative models combining different interventions, particularly comorbid psychosis and substance use studies that have used a combination of MI and cognitive approaches, as well as family therapy,[102,103,137,142] and most have found modest improvements, particularly in the medium term. This integrated approach is consistent with theoretical and aetiological models that link substance use with psychosis onset and maintenance,[157] psychosis onset with deterioration in self-beliefs, motivation and insight,[158–160] and psychosis treatments with physical health complications. However, interventions in psychosis that focus on only physical health or substance use have suffered from high attrition rates in addition to poor outcomes.[161] It is recommended that future research would need to take into account methodological standardisation, longitudinal perspectives, interventions of subgroups and stages, sequenced interventions and the changing realities of treatment systems.[162] Integrating of MI with CBT approaches provides more opportunities to address the complex mental and physical health presentations that are common in psychosis.[162]

Previous group-based interventions for substance use in psychosis and brief CBT interventions that focus on aspects of mental health such as worry, sleep and self-esteem have comprised 6–8 sessions.[142,163] Furthermore, previous 'integrated' therapies for specific behaviours, such as substance use, in the context of psychosis extended interventions to 9 months.[161] Pre-clinical modelling demonstrates that HPIs are particularly crucial for people with psychosis and should be integrated within CMHTs, ideally in a cost-effective manner.

Although there has been some interest in promoting better physical health among patients with psychosis over the last few decades, only a small number of trials have sound methodologies and a limited range of treatment models tested, as shown by a recent systematic review on the topic.[164] Different groups have tried different approaches and have concentrated on pharmacological interventions and/or behavioural interventions.[164] For instance, some studies have targeted weight gain by promoting healthy diets and physical exercises. In another systematic meta-analysis, individual or group interventions, CBT and nutritional counselling were found to be effective in reducing antipsychotic-induced weight gain.[165] More recently, however, a number of studies have taken a holistic approach by targeting patients with psychosis and their multiple health behaviours in terms of their lifestyles. For instance, Baker *et al.*[166] in their RCT compared a 90-minute face-to-face 'healthy lifestyles' intervention for smoking and cardiovascular risk behaviours with a telephone-based intervention, in addition to providing both groups with nicotine replacement therapy. Both types of interventions resulted in improvement in 12 months, with no differences between conditions.

As part of the IMPaCT programme, we thought that by integrating the two well-established intervention methods, namely CBT for psychosis and MI, we would theoretically be focusing on increasing personal awareness of the impact of one's thought processes on emotions and behaviour while applying MI principles, which would positively enhance the person's autonomy in making choices. We thought that this approach would be beneficial to patients with psychosis, as well as meeting their individual needs, whether or not the person had physical health problems and/or used substances. To validate this intervention, we had to prepare manuals that described the actual intervention, as well as providing it in a modular format, so that the therapist could use the required modules with a particular person who needed to make certain lifestyle changes towards an improved healthier life. We adapted the actual intervention, which included a combination of MI and CBT, similar to the one used by James *et al.*,[142] although applied in individual face-to-face contact.

Aims

The study was designed to develop, validate and manualise IMPaCT therapy, a HPI tailored to the needs of the individual, addressing unhealthy lifestyle factors including substance use and inter-related comorbid cognitive and mental health difficulties in psychosis. The aim of the intervention was to modify lifestyle factors that have a negative impact on health in SMI (i.e. substance use, cigarette smoking, weight gain, poor nutrition and lack of exercise). IMPaCT therapy followed a staged model of behavioural therapies development.[167–169]

Method

Design

Initially, a consultation among experts in therapeutic interventions for mental and physical health, substance use and diabetes generated the key features and focus of the intervention. After this, IMPaCT therapy was developed through three stages of design and analysis: (1) therapy and training development, and manual writing; (2) piloting, evaluation and refining the training package with clinicians; and (3) a Delphi process to reach consensus on the therapy model and manual through initial consultation followed by two rounds of follow-up questionnaire feedback. The feedback was from each of three expert groups: (1) therapists, (2) clinician providers within CMHTs and (3) psychosis service users. The emphasis was on an iterative process leading to a therapy model and manual that would be well grounded both in theory and in feedback from experts in behavioural change therapies, clinician providers within CMHTs and psychosis service users.

The intervention was based on the transtheoretical behaviour change model.[170] The training and reference guide introduced this model of behaviour change and its link with the intervention approach. The intervention manual was then framed around this model. The manual was divided into separate sections for the distinct stages of behaviour change: (1) precontemplation, (2) contemplation, (3) preparation and contingency planning, (4) action and (5) maintenance and relapse prevention. At the start of each section was an overview that defined the stage and how to identify whether or not a client was in this stage. This was followed in each section by aims, objectives and between 3 and 12 specifically behaviour change 'interventions' that were consistent with the behaviour change taxonomy[171,172] and applicable to that stage.

Participants

Participants in the phase 2 training development were eight staff selected from a range of in- and outpatient settings and backgrounds, working in the area of psychosis within the SLaM NHS Foundation Trust, but not eligible to participate in the subsequent IMPaCT RCT. Participants in the phase 3 Delphi consensus and manual development comprised three expert groups of (1) therapist/ researchers, (2) clinicians and (3) service users, each of whom took part in two iterative review and feedback sessions. Therapist/researcher experts were recruited from the local and national community

and were involved in the development, implementation or research evaluation of CBT and MI approaches in psychosis. Clinicians were staff who took part in the phase 3 training, and service users were people who were receiving a service from the relevant clinicians at the time and had provided informed consent to participate in the study.

Pilot training

All participants completed a 5-day pilot training, which comprised 10 sessions: (1) introduction to IMPaCT and the manual/basic CBT skills, (2) introduction to MI, (3) practical MI, (4) intermediate MI skills in psychosis I, (5) intermediate MI skills in psychosis II, (6) physical health awareness and monitoring, (7) physical health awareness and diabetes monitoring, (8) substance use awareness, (9) group work skills and (10) healthy living groups. The training was delivered by members of the research team (KG, SS, ZA and Manyara Mushore), as well as an expert in healthy living groups and an expert in MI for psychosis. All participants in the training self-rated of their knowledge and skills before and after the training, and their confidence in therapy delivery after training.

Delphi consultation

The Delphi process comprised three iterative stages of consultation revolving around an adapted questionnaire that incorporated feedback from each preceding stage, consistent with recommended Delphi methodology. The Delphi consultation on the model and manuals was collected in semistructured e-mail questionnaires for therapist/researchers and clinicians, and in face-to-face interviews with service users, in accordance with the algorithm presented by Jones and Hunter[173] (see *Appendix 2, Figure 2*). The Delphi process allowed us to access the acceptability and face validity of the model, manuals and training package, using expert consensus. The Delphi process was an in-depth consultation requiring the expert clinician and patient consultants to undertake a selected practice intervention session in pairs, using the intervention, reference guide, manual and handbook, and provide iterative feedback. Feedback was obtained in the form of qualitative comments and Likert scale ratings. For each feedback session, each participant read specified sections of the manuals. Therapists/researchers read all sections of all manuals (the reference guide, the manual and the *Better Health Handbook*), whereas clinicians focused preferentially on the therapy manual and handbook sections. The service users took part in two selected intervention sessions with their trained clinician and reviewed preferentially the service user resource handbook. Questions considered user-friendliness, spirit of MI, integration with CBT, usefulness in routine NHS practice, length and complexity, and whether anything was missing or should be added. Feedback was obtained from numerical ratings on a Likert scale (0–10), where 0 was least positive and 10 was most positive, as well as qualitatively. After each round of feedback, changes were made to the content and structure of the manual before the next round of feedback. In follow-up consultations, the previous individual ratings and group rating were also fed back, and participants were encouraged to revise their ratings towards or away from the group mean to determine consensus within each group. Consensus across the group as a whole was based on threshold ratings for the acceptability and user-friendliness of key elements of the manual on Likert scales of ≥ 7 in the final stage.

Alongside the Delphi process, an informal presentation and consultation were conducted with a carers group for people with SMI. The perspectives gained from this presentation were used in the development of a brief carers' section to support the therapy.

Results

Initial consultation to form key features and components of the intervention and to consider mechanisms of change

A consultation among experts in the field of MI and psychosocial interventions for physical health, substance use and diabetes and CBT for psychosis (KG, SS, ZA, KI and Gill Todd) yielded a set of broad features and foci of the intervention for consideration in subsequent stages of development. The initial therapy built on an adapted version of the physical health intervention used in the Well-Being Support Programme,[140,174]

incorporating a substance use intervention based on 'Managing Mental Health and Drug Use'.[142] Key features of the therapy were that it had to be comprehensive, integrative, flexible and pragmatic, deliverable by mental health clinicians from a range of backgrounds, and able to be readily implemented in NHS settings. The focus of the components incorporated (1) mental health and psychosis, (2) alcohol use, (3) cannabis use, (4) smoking, (5) other drug use, (6) diabetes, (7) exercise and (8) healthy eating. It was initially proposed that, based on previous research, the intervention should be delivered in a group format.

Phase 1: initial therapy training development and manual writing
Extensive review of the Well-Being Support Programme and substance use intervention, as well as of relevant literature about mental health, physical health and substance use interventions incorporating CBT and/or MI in psychosis and non-psychosis populations, led to the development of a preliminary outline of the intervention and of the training package.

Phase 2: piloting, evaluation and refining the training package
The pilot training was delivered to clinicians ($n = 8$; 50% male) from CMHTs ($n = 2$), to specialist inpatient ($n = 3$) and psychiatric intensive care units ($n = 3$), and to individuals from a range of disciplines [psychiatric nurses ($n = 5$), occupational therapists ($n = 2$) and social workers ($n = 1$)].

The knowledge/skills ratings pre and post training are presented in *Appendix 2*, *Figure 3*. The mean self-rated knowledge scores increased from pre to post training on all core areas of training (physical health, substance use, running groups and using MI).

In addition, the mean post-training confidence ratings were all high for core components (physical health 81.3%, substance use 79.4%, running groups 86.3%, MI 83.8%) and the mean ratings of the importance of these aspects of support for psychosis were also all high (physical health, 86.9%; substance use, 86.9%; running groups, 87.5%; MI, 92.5%).

Clinicians rated the core training modules on various dimensions, including training quality, resources, level, value, applicability and impact on confidence, as well as on specific skills learnt. Ratings were on a scale from 1 (poor/strongly disagree) to 5 (excellent/strongly agree). The mean ratings and ranges for physical health, substance use, healthy living groups and MI training were 4.4 (4.0–4.9), 4.7 (4.09–5.0), 4.4 (4.0–5.0) and 4.3 (4.0–4.9), respectively.

Qualitatively, clinicians recommended that the primary mode for intervention delivery be individual sessions because of the difficulty in co-ordinating and engaging service users in groups. They also requested that basic CBT be included in the training programme and the manual. They reported that the physical health training was empowering, unleashing potential, and should be more available and that the substance use training should be longer, mandatory and focused more on individual substances. The training on healthy living groups seemed to fine-tune and enhance existing skills, whereas the MI training challenged preconceived ideas and a 'nursing' model, and was well shaped for community populations. It gave a structured approach to the intervention, had good links to theory, and provided an opportunity to try things out, but it should be more focused specifically on MI in mental health as opposed to general health.

Phase 3: the Delphi consultation
A total of five expert therapist/researchers from a range of backgrounds (two psychologists, two psychiatrists and one nurse) took part in two rounds of Delphi consultation on the reference book, the therapy manual and the service user handbook. All manuals were redrafted after each round of the process, based on numerical and qualitative feedback, and re-rated such that each underwent three iterations, involving substantial modification of content, format and language. Owing to time pressures in development, no Delphi rating was obtained for the final version. One expert service user/researcher also provided qualitative feedback in both rounds. [See www.amazon.co.uk/Impact-Reference-Improving-Physical-Substance/dp/095688850X (accessed 6 December 2019) for the final versions of the reference guide, the manual and the *Better Health Handbook*.]

Among those expert therapist/researchers who completed both rounds of the Delphi process, the mean ratings of the therapy manual for user-friendliness, spirit of MI, integration with CBT, usability in the NHS, length and complexity increased over time from 7.3 to 7.6 out of 10, with a rating of 7.4 out of 10 from four participants for the second rating. Similarly, ratings for the reference book increased over time from 6.8 to 7.1 out of 10, with a rating of 7.4 from four participants for the second rating. Finally, ratings for the handbook increased over time from 7.3 to 7.7 but with a lower second rating from four participants in the second iteration of 6.4. This lower rating was as a result of a low mean score from one expert, who also provided extensive feedback that was incorporated in the final handbook.

Two clinicians (one nurse and one occupational therapist) reviewed the therapy manual quantitatively and qualitatively while using it to deliver a 'test' session each with a service user (one male and one female). These service users in turn provided qualitative feedback on their experiences of the session. For the therapist who completed both rounds of the Delphi process, the mean rating for the therapy manual increased from 7.3 to 8.2. This related to its usability for day-to-day standard NHS work, including length, complexity and confidence provided.

The expert therapists/researchers generated a large amount of qualitative feedback. The therapy manual was seen as too long, and all manuals needed more simplified language. Specific core recommendations for change included developing the therapy into modules, including practice examples and case studies, providing greater clarity on how to manage interactions with mental health and issues with medication, having built-in guidelines on training and having supervised practice to support manualised therapy delivery. In terms of therapy content and structure, recommendations were made to include a clear definition of each stage of change, what a client might say or do in this stage, and the sessions associated with this stage; that a structure should be followed for each session to include a session number and why and when to do the session, followed by clear aims and objectives and then session content; and that therapists should be advised that they can dip into the sessions and materials relevant to their client and should not be expected to cover everything. This would allow flexibility and avoid overprescription. Explicit links were recommended to be made between the sessions and linked handbook resources. Greater CBT for Psychosis coverage was requested; some concern was raised about offering too brief a CBT for Psychosis section without a preliminary formulation. Another recommendation was to include the application of CBT to enable goals to be reached at the action stage in MI. The various flow charts were often viewed as rather complex. The general point was made that outside IMPaCT therapy in the NHS there would need to be some form of physical health assessment or other means to lead to a health target.

One therapist/researcher rightly suggested that the relatives session may be too short to reduce expressed emotion at home. The relatives session did not aim to be a therapy. At the suggestion of carers who were presented with the IMPaCT study and asked for comments, the session aimed to address some of the misconceptions about and heightened expectations for change that might be held by relatives following the offer of therapy. The session therefore aimed to present only the basic tenets of behaviour change and the notion that most change occurs at a cognitive level before any behavioural change occurs. It aimed to clarify that developing intrinsic motivation will lead to more long-lasting change, as opposed to a forced change that may be short lived.

Clinicians fed back qualitatively that the theory should be clearly separated from the therapy sessions as a separate reference book. The sessions themselves needed to be simplified and clearer in their aims, and more stand-alone as individual session guides, with less 'jargon'. There was a need to ensure better cross-referencing between the therapy manual sessions and the handbook resources. The MI section was viewed very positively. Overall, echoing the view of the expert therapists/researchers, the consensus was that the initial therapy manual was too long.

The two service users provided only qualitative feedback over the two time points. They confirmed that they found the focus on health to be beneficial, leading to an increase in knowledge, motivation and ideas for improving health, and one reported a significant change in alcohol use (from heavy drinking to 2-week abstinence) following the session. Materials in the handbook were viewed positively. One expert service user/researcher provided specific and detailed feedback on the handbook. Key points included, again, using simpler language; giving greater explanation of how to use and complete the various resources, and what they are; including colour and pictures to liven up the handbook; and including positive language and hopeful messages about change. Consistent with expert therapists, a suggestion was made that terms such as 'heavy' or 'light' smoking/substance use needed to be defined; in addition, benchmarks and thresholds, for example for problematic waist circumference, should be provided for mainstream NHS use. In the research therapy, this will be provided as part of the IMPaCT assessment.

Discussion

The production of the training and manuals for the IMPaCT therapy followed multiple iterative phases of piloting, consultation and refinement. The process culminated in a 5-day training programme and a set of three manuals to support training and intervention delivery: the reference guide, the manual and the *Better Health Handbook*.

The final training retained all of the pilot training sections but extended the substance use training. The MI section was delivered with a greater focus on application for service users with comorbid physical and mental health difficulties. The training included sessions on basic skills in CBT for (1) mental health and (2) achieving goals in physical health during the action stage of behavioural change. Finally, it commenced with a specific session on how to use the reference guide, the manual and the *Better Health Handbook* as part of a therapeutic process.

The set of three manuals was designed to provide all of the basic information required to deliver IMPaCT therapy within routine NHS practice. The manuals were necessarily lengthy but significant effort was made to ensure that these were concise and used plain language.

The reference guide contained three sections:

1. An introduction to the IMPaCT study and the guiding ethos, including an overview and key information on the primary approaches of MI and CBT.
2. A section comprising the primary interventions. This encompassed an overview of the eight individual module plans for CBT in mental health, alcohol, cannabis, smoking, other drugs, diabetes, exercise and healthy eating; a chapter on working with carers in the IMPaCT approach; and a chapter on running groups. A specific emphasis here was on how to adapt the basic session and group plans for working with different target health issues, how to integrate MI and CBT for these issues, and how these issues might overlap with mental health. Outcome measurement and module-specific resources were introduced.
3. A section on setting up a service. This section contained information about how to run the training and to set up and deliver supervision as part of an IMPaCT therapy service. It also included information on how to map local community health provisions, to which service users could then be directed as part of the intervention.[127]

Finally, a set of appendices included guidance on aspects of therapy delivery, such as flow charts to determine the starting module, for transition between modules and for the evaluation of module progress. Outcome measures and psychoeducation materials were also included.

The final manual comprised introductory materials on how to use the manual and the *Better Health Handbook*, followed by information on getting started and the introductory session. In response to feedback from the Delphi process, 37 individual intervention sessions followed, grouped into:

- introductory sessions (1–3)
- supplementary session (4–7) if initial sessions did not lead to a health goal
- sessions for pre-contemplation (3, 4, 8–12)
- sessions for contemplation (13–21)
- sessions for preparation and contingency planning (22–29)
- sessions for action (30–32)
- sessions for maintenance and relapse (33–37).

This last section also included an extensive CBT session (36), which was itself broken down into eight subcomponents. Based on feedback from the Delphi process, each section commenced with a definition of the particular stage of change, what the client might say or do in this stage, and key aims and objectives for this stage, with a contents list. Then followed each individual session plan, which commenced with reasons to offer this session, when to offer this session and a guide to session content. The sessions were designed so that therapists could select the relevant sections based on the client's individual needs and stage of change. Each session included links to appendices that provided example dialogues, derived from real-case examples, to show how to implement the intervention. Each session also provided a reference to all relevant resources in the *Better Health Handbook*.

Finally, the manual also included group session plans for (1) beginner's exercise (six sessions), (2) maintaining exercise (six sessions), (3) healthy eating (nine sessions), and (4) social activities (10 sessions).

The *Better Health Handbook* comprised a set of useful resources that could be photocopied, separated according to stages of change and numbered according to the intervention session. They included diaries, worksheets, physical health summary sheets, questionnaires, and lists of coping strategies and alternative behaviours. The resources were colourful and included images, where appropriate, and could be used to develop a tailored therapy pack for each service user.

The intervention for any particular health issue was the delivery of a module of up to approximately eight sessions, lasting approximately 1 hour. Sessions were designed to be tailored to the individual's needs, to be positively framed, and to encourage opportunities to replace unhealthy with alternative health and social behaviours. Mental health support was incorporated alongside support for physical health, and modules were designed so that individuals could work flexibly alone or in groups at their own pace and level.

We designed and developed the manualised approach and training package to provide registered mental health nurses and other care co-ordinators in routine clinical care with knowledge and skills so that they would feel more confident monitoring and supporting their clients with their physical health. Resources associated with the development and implementation of the HPI will be measured to estimate its costs and inform service providers. The implementation, fidelity to protocol and efficacy of the intervention was assessed in a large-scale RCT in SMI: the IMPaCT trial (see *Work package 3: IMPaCT randomised controlled trial*).[175]

Work package 3: randomised controlled trial of the effectiveness of an integrated psychosocial health promotion intervention aimed at improving health and reducing substance use in established psychosis (IMPaCT)

This section provides a summary of work published in Gaughran *et al.*[175,176] and Heslin *et al.*[177]

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Background

Living with a diagnosis of psychosis is associated with a reduced life expectancy of 10–20 years, largely because of CVD. As detailed in work package 2, we developed a HPI to help people to make healthier choices. We aimed to determine the effect of the HPI on improving health and reducing cardiovascular risk in people with psychosis compared with treatment as usual (TAU). Additionally, given the demands on health services, we planned to examine the costs associated with these patient groups and to evaluate the economic impact of the proposed interventions (see *Work package 3: IMPaCT randomised controlled trial, Health economics*). Therefore, this trial aimed to determine the clinical effectiveness and cost-effectiveness of a modular HPI in psychosis when compared with the established normal treatment.

Aims and hypothesis

The primary objective was to test the clinical effectiveness and cost-effectiveness (see *Work package 3: IMPaCT randomised controlled trial, Health economics*) of adding IMPaCT therapy, an intensive HPI designed to improve physical health and reduce substance use, to TAU delivered by care co-ordinators to people with psychosis.

Our primary hypothesis was that the addition of IMPaCT therapy to the normal mental health care delivered by care co-ordinators over 9 months would be more effective than TAU alone in improving patients' QoL, as measured with the Short Form questionnaire-36 items (SF-36) mental health and physical health subscales[178] at 12 months from baseline, and that this advantage would be maintained at a follow-up assessment 15 months from baseline. The 12-month post-randomisation period included an initial 3 months in which the care co-ordinators were trained to provide the HPI over the subsequent 9 months.

Our secondary hypothesis was that the HPI group would see a greater improvement in metabolic outcomes and substance use than the TAU group at both time points; specifically, (1) TAU plus IMPaCT therapy would result in a greater reduction of waist circumference by at least 1 cm at 12 months than TAU alone, (2) TAU plus IMPaCT therapy would be more effective in reducing weight at 12 months compared with TAU alone, (3) TAU plus IMPaCT therapy would result in a 50% reduction in the proportion of people using cannabis compared with TAU alone and (4) TAU plus IMPaCT therapy would be more effective in reducing the symptoms of psychosis than TAU alone.

Methods

A multicentre, two-arm, parallel-cluster RCT was conducted across five mental health UK NHS trusts. Care co-ordinators were randomly assigned to either receiving training, and ongoing supervision, in delivering IMPaCT therapy or delivering TAU to their current patients with psychosis (cluster).

A more detailed explanation of all methods can be found in the published study protocol, available open access;[175] the methods are briefly described in the following sections.

Study design and setting

A pragmatic, multicentre, two-arm, parallel-cluster, RCT design was used and the HPI was integrated into routine services across five mental health trusts in South London, Kent, Sussex, Somerset and Staffordshire, including both urban and rural populations. The Consolidated Standards of Reporting Trials (CONSORT) cluster trial extension standards guided the planning and implementation of this study. Ethics approval was obtained from the joint South London and Maudsley and the Institute of Psychiatry NHS Ethics Committee (REC reference number 09/HO80/41). Colleagues with lived experience, including both service users and carers, were involved throughout the research, from contributing to funding applications, to managing steering groups, to coauthoring the papers arising from the work.

Participants

Recruitment took place between 1 March 2010 and 1 July 2014. Eligible participants were aged between 18 and 65 years and had an established diagnosis of a psychotic disorder (ICD-10[114] diagnosis F20–29, F31.2 or F31.5). Patients were excluded if they (1) had a primary diagnosis of learning disability, (2) had a pre-existing physical health problem that would independently affect the metabolic measures (as judged by medical investigators), (3) were pregnant or < 6 months post partum or (4) had a life-threatening or terminal medical condition. We did not recruit from FEP services. Recruitment started on 1 March 2010, with first randomisation on 9 August 2010.

Study procedure

There were two waves of participant recruitment. First, all permanently employed community care co-ordinators with a minimum of four psychosis patients on their caseload in participating CMHTs were approached in random order (using a random number generator) and invited to participate. Following informed consent from individual care co-ordinators, patients from their caseload who met the inclusion criteria were identified. These patients were then approached and invited to participate, also in a random order, until either four participants consented or all eligible patients had been approached. Baseline measures were then taken from the consenting patients. After baseline assessments of all consenting patients on a care co-ordinator's caseload were completed, care co-ordinators were randomised and stratified by borough using randomisation blocks of random sizes to deliver IMPaCT therapy or TAU alone to their own current patients (cluster). Both researchers and the statistician remained blind to treatment allocation for the duration of data collection.

In the treatment arm, the intervention (IMPaCT therapy) was provided by a patient's usual community care co-ordinator. In the first 3 months following a patient's randomisation, their community care co-ordinator received a 4-day IMPaCT training course. This covered physical health and substance misuse, MI, CBT techniques for running group sessions, and how to deliver IMPaCT therapy and health promotion, and it was given by trainers in MI and in CBT. An evaluation of this is reported in *Appendix 3*. Throughout the subsequent 9-month intervention, participating care co-ordinators were offered fortnightly supervision in IMPaCT therapy and all care co-ordinators were offered a 1-hour training session in best practice for physical health awareness to ensure more standardised TAU.

The intervention was rolled out into routine care by holding discussions with management, which confirmed their strong support, and then approaching local team management about the practicalities, and then informing the community teams about the RCT and offering the 1-hour education session as above. Further practicalities were addressed at the 4-day training sessions in the intervention group, including advice on planning group sessions if needed. Day-to-day practical issues that arose were dealt with in the fortnightly supervision sessions or, if these were at the team, borough or trust level, the relevant layer of management was involved.

Outcome measures
A change in outcome was defined as a difference from baseline and (1) on completion of the supervised intervention, at 12 months, and (2) 3 months after the end of treatment, at 15 months. Baseline and follow-up assessments were conducted during face-to-face interviews by researchers within established time windows (–6 weeks/+4 weeks at 12 months' follow-up and ± 4 weeks for 15 months' follow-up). Data collected outside these times were recorded but used only for sensitivity analyses and not for the main analysis.

Primary outcome
The primary outcomes were the physical and mental health component scores of the SF-36,[178] measured at 12 and 15 months. We originally proposed the SF-36 as an integrated score but revised the protocol so that each of the two components was a primary outcome.

Secondary outcomes
Secondary outcome measures were (1) physical health measures (levels of total HDL and low-density lipoprotein cholesterol, triglycerides, HbA_{1c} and CRP; anthropometric measurements, including waist circumference, BMI, BP; MetS defined according to the International Diabetes Federation criteria);[13] (2) substance use measures [alcohol use recorded using the AUDIT,[121] smoking prevalence and cigarettes per day using the Nicotine Dependence Questionnaire,[120] use of cannabis and other illegal substances (e.g. opiates, methamphetamine, cocaine) using the Time Line Follow Back];[72] (3) lifestyle measures (dietary patterns quantified using the DINE[179] and physical activity using the short-form International Physical Activity Questionnaire);[116,180] and (4) mental health status (using PANSS,[115] GAF,[117] SF-36 and Montgomery–Åsberg Depression Rating Scales).[181]

Sample size
Power analyses were performed for the two subscales measures: physical and mental health components of the SF-36 QoL scale.[178] To detect a clinically significant reduction of 5 points (using 80% power, a 5% alpha level and two-tailed assumption), and to allow for a 20% loss of care co-ordinators and an additional 30% loss of patients to follow-up, a total sample size of 70 care co-ordinators, yielding 280 participants, was needed for the physical scale ($d = 0.5$), and 98 care co-ordinators, yielding 392 participants, were needed for the mental health scale ($d = 0.42$).

Statistical analysis

Primary statistical analyses was based on the intention-to-treat principle and aimed to estimate the difference in mean outcomes between participants randomised to HPI and those randomised to TAU at 12 and 15 months using mixed-effects models. Bias as a result of missing follow-up data was assessed by comparing the baseline characteristics of those with and those without complete data. In two linear mixed-effects models, the physical and mental health component scores at 12 months and 15 months constituted the dependent variable. 'Treatment randomisation group', 'time' (with two levels, i.e. 12 and 15 months post randomisation), and the interaction between 'treatment group and time', 'centre' and the 'baseline values of physical and mental health component scores' constitute the fixed part of the model. An unstructured covariance pattern model was used to model the dependency of the repeated observations of the same subject and to account for the dependency of the subjects within a cluster, and the care co-ordinator was included as a random factor. Model assumptions were assessed by visual inspection of the residuals. Standardised effect sizes, using pre-randomisation variability for standardisation, were also reported.

Secondary outcomes were analysed using the same methods as for the primary outcome. For all models, the interaction between treatment group and time was not significant and was removed from the final analyses. Treatment effects are, therefore, estimates for both time points. Logistic mixed models were used for binary outcomes (e.g. smoking) and Poisson mixed models were used for count data (e.g. number of cigarettes per day). Because of the large number of tests, significant results need to be treated as explorative.

Sensitivity analyses

Approximately 15% of the observations were collected outside the time window, so analyses using all available data were repeated as sensitivity analyses.

Handling of missing data

Models were rerun with predictors related to outcome missingness included as further covariates in the model. For the main outcomes, a second sensitivity analysis of missing outcome data, using multiple imputations by chained regression equations, was performed using all available clinical and demographic scores. This was done separately for each treatment group. A further sensitivity analysis was carried out to explore the impact of not missing at random patterns by adding positive or negative values to the imputed data sets.

Complier average effect analyses

In addition to the standard intention-to-treat (efficiency) analysis, we estimate the measure of the treatment impact for compliers only (treatment efficacy) using an instrumental variable approach with randomisation indicator as an instrumental variable.[182] Analyses were carried out using Stata's® (StataCorp LP, College Station, TX, USA) ivregress package, with centre, treatment arm and baseline values of the outcome constituting the fixed part of the model and with cluster robust standard errors (SEs) to control for clustering effects of care co-ordinator.

Results

Key findings

A total of 104 care co-ordinators were recruited; 52 (with 213 patients) were randomised to deliver IMPaCT therapy and 52 (with 193 patients) were randomised to TAU. Of the 406 patients, 318 (78%) and 301 (74%) attended the 12- and 15-month follow-ups, respectively. The total sample size was reduced to 263 (64.8%) for 12 months (TAU, $n = 132$; HPI, $n = 131$) and to 238 (58.6%) for 15 months (TAU, $n = 114$; HPI, $n = 124$) because some of the patients who attended follow-up assessments were not seen within the required time frame. The required sample size based on the power analyses was achieved at both time points.

IMPaCT therapy showed no significant effect on the physical or mental health components of the SF-36 scores compared with TAU at 12 or 15 months.[176] Sensitivity analyses, including missing data analyses, did not alter any conclusion[176] (see *Appendix 5*). A complier average casual effect analysis did not provide evidence of the efficacy of the intervention at 12 months for the physical health component (PHC) (mean difference –2.01, 95% CI –4.18 to 0.16; $p = 0.07$) or mental health component (MHC) (mean difference 0.02, 95% CI –2.79 to 2.83; $p = 0.99$).

No effect was observed for cardiovascular risk indicators, except for HDL cholesterol, which showed greater improvement following IMPaCT therapy than following TAU (treatment effect 0.09, 95% CI 0.007 to 0.16; $p = 0.034$). The 22% of patients who received > 180 minutes of IMPaCT therapy in addition to usual care achieved a greater reduction in waist circumference (–4.2 cm, 95% CI –7.2 to –1.2 cm; $p = 0.006$) than did control patients. This reduction is clinically significant. There was no difference in the rates of serious adverse events between the groups. The fidelity assessment is detailed in *Appendix 3*.

Discussion

Strengths of the trial
The main strength of this trial is that it was a pragmatic study: the design of the HPI was centred on creating an intervention accessible to the greatest possible number of people with psychosis receiving care in CMHTs. This is a traditionally hard-to-reach group; many people are unable or unwilling to attend standard group interventions, which is particularly problematic because of the high levels of cardiometabolic risk.[183]

This study's integrated personalised approach sought to maximise representativeness of the population studied. It addressed both lifestyle choices and substance use and avoided a piecemeal approach to behavioural change. By integrating IMPaCT therapy into established mental health care and by providing the care through a patient's usual therapist, care could be adapted to the patient's individual needs. To date, few large-scale, long-term RCTs have attempted to improve health in its widest sense in people with psychosis, instead focusing on a single target and often introducing new therapists to run the trial intervention.

The study recruited to target and was sufficiently powered to detect a difference between the two groups of at least 5 points in physical and mental health component scores (Cohen's $d = 0.42$), had good follow-up rates and recruited a diverse, multiethnic sample of people with psychosis.

Limitations of the trial
Continuity of care was affected by multiple reorganisations of staff among the hospital trusts. Staff turnover sometimes delayed recruitment to the trial, as an inclusion criterion was that the staff members expected to be in post for the forthcoming year. Despite this, although not statistically different, staff turnover was slightly greater in the treatment arm than in the control group. However, when patients remained with the same trained care co-ordinator throughout the trial, there were indications that the intervention may result in significantly lower cholesterol levels and more exercise in the treatment group than in the control group. It is known that diminished continuity of care is associated with worse clinical outcomes.[184]

Care co-ordinators struggled to deliver six or more 30-minute sessions of the HPI in addition to routine care, despite the training and ongoing supervision, and had limited fidelity to the MI model. This is in keeping with the recognised challenges of delivering targeted psychosocial interventions to people with psychosis that are faced by care co-ordinators in a busy secondary care environment.[185] It is also consistent with the findings of the Health Improvement Profile (HIP) RCT, which trained community mental health nurses to administer health checks to their patients and found that the volunteer nurses

administered health checks to only a minority of participating patients.[186] However, given that the subset who received > 180 minutes of additional time devoted to IMPaCT therapy had a clinically significant reduction of –4.2 cm (95% CI –7.2 to –1.2 cm) in their waist circumference, a focus on implementation strategies in future work may be important.

A pilot trial was not conducted because the intervention was built on two pre-existing, successful, published interventions in this population, used a recognised behaviour change theory and incorporated additional recommendations for improving the preceding interventions. However, the longer combined intervention and the delivery model using non-expert care co-ordinators in a UK setting were not tested previously and raised logistical issues, which perhaps could have been identified and addressed more effectively in a large-scale pilot trial, although it is doubtful that they would have been identified in a small pilot.

The HPI was broad and participants self-selected, the target behaviours to focus on. It is conceivable that a more structured intervention targeting specific health behaviours, such as those described elsewhere,[187,188] could be more successful in demonstrating statistically significant improvements in circumscribed aspects of the physical health of this population. Nonetheless, a longer-term, sustainable and integrated approach to overall health behaviours and health outcomes is urgently needed to allow successful and accessible routine care in the NHS.

Conclusions

Training and supervising community care co-ordinators to administer IMPaCT therapy to patients with psychosis was seen to be insufficient for significantly improving physical or mental health QoL. Front-line clinical staff, although willing to take part in training and supervision, struggled to consolidate training as part of applied MI therapy. However, the data suggest that continuity of care staff and protected time to deliver HPI work may potentially enhance outcomes.

Work package 3: economic evaluation section

Introduction

To address the key question of value for money in a resource-constrained health-care system, we conducted a comprehensive within-trial economic evaluation of the IMPaCT HPI to inform future decisions about its adoption into the NHS. This section summarises the work published in Heslin *et al.*,[177] with further unpublished data presented in *Appendix 4.*

Economic evaluation methods

Data collection

An adapted version of the Client Service Receipt Inventory (CSRI)[189] was used to measure individual-level resource use. It covered the use of (all-cause) secondary and community-based health and social care services, prescription medication, time off work, and social security benefits received by participants and carers. It was administered as a retrospective, self-report, questionnaire-based interview conducted by assessors who were blind to treatment allocation. It covered the previous 6-month period at baseline and at the 12-month follow-up, and the previous 3-month period at the 15-month follow-up.

Health-related QoL was assessed with self-report questionnaires at baseline and at 12 and 15 months, and the SF-36 and EuroQol-5 Dimensions, three-level version (EQ-5D-3L),[190] were used to estimate QALY gains.

Costs

Unit costs were applied to individual-level resource use data to calculate the total costs per participant from two cost perspectives: health and social care, and societal. All-cause health and social care costs included the trial interventions (HPI for the intervention group and standard information session for the control group), specialist accommodation, inpatient services, outpatient services, community-based services, community-based professionals and prescription medications. Societal costs included the same health and social care costs plus third-sector (charity) costs, lost productivity costs due to absence from work (if in employment during the assessment period), participant out-of-pocket expenditure on community-based day services and selected social security benefits. Lost productivity costs were capped at 5 days per week (maximum of 130 days for 6-month data and 65 days for 3-month data).

Unit costs are detailed for reference in *Appendix 4, Table 9*. In brief, the unit costs for most hospital and primary care services were obtained from the NHS *Reference Costs 2010–11*[191] (inflated to 2011–12 prices using the Hospital and Community Health Services Pay and Prices Index or retail price index as appropriate) and the *Unit Costs of Health and Social Care 2012* compilation.[192] Medication unit costs, taken from the *British National Formulary*,[193] were converted into cost per milligram based on the most cost-efficient pack size, choosing maintenance doses over initial treatment doses and generic formulations over branded ones to obtain conservative estimates.

All costs are reported in Great British pounds (GBP) at 2011–12 prices. Discounting was applied to cost and outcome data related to the 12- to 15-month assessment period. Intervention costs were not discounted before being added to the 12- to 15-month costs because they were incurred in the first year. Discounting was applied at a rate of 3.5%.[194]

Cost of the health promotion intervention

We included the following resource components to estimate the costs associated with the intervention:

- the production of manuals (excluding the development work)
- the training of care co-ordinators
- the ongoing supervision of care co-ordinators
- the implementation of the intervention by care co-ordinators with trial participants.

The resources and costs associated with each of these components are available for reference in *Appendix 4, Table 9*. The costliest of the four components was the implementation with patients, at a mean cost of £92.31 per case. To estimate the total participant-level intervention costs, we first averaged out general costs using a 'top-down' approach (i.e. we summed the costs of the manual, training and supervision, and divided this by the recommended number of patients under the care of each care co-ordinator). To this average we added the individual-level implementation costs.

Health promotion intervention manual costs

Care co-ordinators randomised to the intervention arm were provided with a copy of the IMPaCT manual, the IMPaCT reference guide and the *Better Health Handbook*. The time inputs to the intellectual development of these documents were considered a sunk cost and were, therefore, excluded. However, we included the reproduction costs.

Health promotion intervention training costs

Costs related to training care co-ordinators included the following components: the cost of trainer time (contact and non-contact), the cost of care co-ordinator attendance time and the cost of materials necessary to deliver the training courses. The training programme was delivered over 4 days by members of the research team in a standardised manner, with specific staff dedicated to implementing certain parts of the programme. The total number of hours and the number of sessions for each staff type were calculated as detailed in *Appendix 4, Table 10*. Preparation time was estimated by multiplying the number of training sessions by an assumed preparation time per session of 10 minutes. Costs were calculated by multiplying the appropriate unit costs by the number of minutes for each staff type.

Each of the care co-ordinator attendees was an NHS band 6 nurse. Each training programme took 32 hours including breaks (09.00 to 17.00 for 4 days). Costs were calculated by multiplying the appropriate unit costs by this time.

Materials were broken down into one-off costs and repeat costs. One-off costs included BP machine, weighing scales, tape measure, flip-chart stand and memory stick. Repeat costs included flip-chart paper, flip-chart pens, paper and pens.

Health promotion intervention supervision costs

At the outset of the study, it was envisaged that ongoing supervision of care co-ordinators would take place in a combination of individual and group sessions, led by a band 6 nurse trainer and a band 8 nurse trainer, for 9 months after attendance at the training programme. However, because of practical limitations, group supervision was unable to be provided, so all supervision took place at the individual level in 90-minute sessions. Costs were calculated by multiplying appropriate unit costs by the number of minutes spent in supervision by both the supervisors and the supervisees.

Health promotion intervention participant implementation costs

Similarly, it was originally envisaged that the intervention would be delivered in a combination of individual and group sessions led by care co-ordinators. However, group intervention sessions were not provided, largely because of practical limitations, so all implementation occurred in individual sessions. To estimate the costs of the intervention at the level of individual patient participants, we multiplied

the cost of each individual therapy session by the care co-ordinator estimates of the proportion of time in each session spent delivering an aspect of the HPI.

Cost of the control intervention

Care co-ordinators in the control group of the trial were given a one-off information-giving session on mental and physical health issues. This involved a consultant psychiatrist delivering the session over a 1.5-hour period. The appropriate unit costs were applied and the cost per care co-ordinator was then divided by the recommended number of patients under the care of each care co-ordinator.

Outcome measures

Cost-effectiveness analyses were based on the joint primary outcome measures: the SF-36 MCS score and SF-36 PCS score. Cost–utility analyses were based on QALYs derived from the EQ-5D-3L and the SF-36 (US version 1) via the Short Form questionnaire-6 Dimensions (SF-6D). Appropriate utility weights were attached to health states for each measure at baseline and at 12 and 15 months.[178,190] QALY gains between 12 months and 15 months were then calculated using the total area under the curve approach with linear interpolation between assessment points.[195]

Analyses, missing data and sensitivity analyses

For the economic evaluation analysis, see *Appendix 4*.

Key findings

The economic evaluation showed no evidence of a clear difference in health and social care costs between the two trial groups. Societal costs may be higher in the intervention group. Alongside a lack of additional benefit, there is no evidence that the intervention is cost-effective. The integrated mental and physical health-care intervention itself involved no significant additional resource use or associated costs. However, it is unclear to what extent this finding reflects a true lack of impact on costs and outcomes, or whether or not it reflects the fact that, because very few participants in the intervention group received the intervention as planned, both groups ultimately received similar care.

Discussion

Limitations

The economic evaluation had some limitations. Data on resource use and, therefore, on costs were collected using the self-reported CSRI. This makes the data subject to participant recall bias. However, there is evidence for the reliability of self-reported resource use data in similar populations[196,197] and we considered the approach necessary given the multisite and multiperspective nature of this study; the lack of integration of all relevant health and social care sector client records necessitated such an approach to avoid restriction to a narrow definition of health and social care. Furthermore, at least some resource use would still have been needed to be collected via self-report (i.e. welfare benefits and employment losses) to enable a societal perspective to be considered, which we considered of particular relevance for a patient group whose health and care needs can have economic impacts on multiple sectors of society. Additionally, there is no reason to believe that any biases related to data collection would be unbalanced between the two trial groups, particularly because the CSRI was administered by blinded assessors.

A further limitation is that we may have double counted resource use associated with the HPI. We collected this information separately from care co-ordinators rather than from patient participants to avoid unblinding the assessors conducting the participant interviews. However, this carried the risk of participants reporting resource use related to the intervention in response to questions about their service use. Although this may skew absolute estimates of costs for the intervention arm, any bias in the calculation of treatment effects would work against the intervention group by overestimating the intervention cost.

There has been some discussion around the validity of using the SF-36 and EQ-5D-3L with study participants who have mental health problems, especially those with schizophrenia and other psychoses.[198] Brazier *et al.*[198] suggest that neither scale performs particularly well in terms of quantitative testing against psychometric criteria and that both have a limited coverage of domains identified as relevant by people with mental health problems. Thus, it is unclear whether or not the lack of QALY difference between the two trial groups reflects a lack of intervention effect or limitations associated with the measurement properties of these two health-related QoL measures. However, given the lack of effect based on the SF-36 MCS and PCS, and all other outcome measures, it is unlikely that there was a difference in QALYs that we have been unable to detect.

Finally, the time horizon of the evaluation is likely to have been insufficient to identify all relevant outcomes for this patient group, particularly given the longer-term impacts of physical health problems. However, it is unlikely that any effects of the intervention would transpire in the longer term if absent in the short term.

Conclusions

There was no evidence of a difference in costs or outcomes from a health and social care perspective. From a societal perspective, the intervention may incur higher costs for no associated benefit.

Programme discussion

People with SMI are at increased risk of poor health outcomes and have a marked premature mortality rate. The aim of the IMPaCT project was to develop culturally appropriate, innovative, practical and effective programmes to achieve better physical and mental health in patients with SMI by improving lifestyle choices and reducing illicit drug use. Three separate studies were conducted. Work package 1 ('the PUMP study') aimed to observe health behaviours, the progression of cardiometabolic disease among patients with their FEP, and the links between these factors over the course of 1 year. Consistent with previous studies, we found high rates of cardiometabolic risk at presentation, which increased over the 12-month period. No relationship was found between antipsychotic choice and emergence of cardiometabolic risk. Work package 2 saw the successful development of a HPI, IMPaCT therapy, based on MI and CBT techniques aimed at effecting behaviour change in people with established psychosis. Work package 3 was a large RCT of IMPaCT therapy among patients with established psychosis that was carried out in five NHS trusts throughout the UK. The intervention was integrated into NHS secondary care as care co-ordinators delivered it to their own patients. IMPaCT therapy was not found to affect QoL any more than did TAU, nor was it cost-effective. There was limited evidence of efficacy on secondary outcomes such as cardiovascular risk indicators, substance use or mental health measure compared with TAU alone.

Work package 1, PUMP, demonstrated that the use of substances such as tobacco and alcohol and less healthy dietary and exercise choices among people with FEP are common on presentation to clinical services and that cardiometabolic risk continues to increase over the course of the year, with rates of obesity rising from 17.8% to 23.7% in this relatively young population. These health profiles may also have an impact on service costs, with obesity at baseline showing an association with higher subsequent admission costs, low HDL cholesterol at baseline being associated with lower subsequent admission costs and higher HDL cholesterol at baseline being associated with a greater subsequent QALY gain. In the IMPaCT study group, who were older, half were obese; furthermore, 20% of our population with established psychosis had diabetes, and a further 30% had glucose dysregulation.[183] These findings both testify to the importance of preventing diabetes in the first instance and highlight the challenge in preventing diabetes among people with SMI. Management of diabetes is also difficult in this population; for example, people with diabetes and SMI have fewer routine eye checks and poorer glycaemic and lipid control,[199] and perhaps ultimately have a 50% poorer survival rate, than those with a diagnosis of diabetes alone.[200]

In both PUMP and the RCT study, we found high rates of physical inactivity alongside an unhealthy dietary intake typified by high saturated fat and low dietary fibre, which is consistent with previous literature. It is acknowledged that sedentary behaviour and unhealthy eating further increase vulnerability to ill health and early death.[201] Furthermore, we conducted a systematic review and meta-analysis of sedentary behaviour in people with psychosis, which showed that people with psychosis engage in very high levels of sedentary behaviour while awake.[202] We related sedentary behaviour in the IMPaCT population to an inflammatory marker of CVD, CRP.[203] We found that those with higher levels of sedentary behaviour have elevated CRP levels. Yet, despite the IMPaCT HPI addressing the above lifestyle behaviours, there were no significant improvements in physical activity or dietary consumption over the course of the study. The HPI exercise module aimed to increase the level of exercise and, specifically, the number of minutes patients engaged in physical activity but was unsuccessful. This is in keeping with the findings from our recent meta-analysis that people with schizophrenia engage in significantly less moderate and vigorous physical activity than do control participants.[204] The above finding suggests that although the overall aim is to make people more physically active, attention needs also to be directed at making people less sedentary. As a result of our findings, we are now running a trial of an intervention specifically to increase activity and reduce sedentary behaviour, Walk this Way.[202]

We found that 62% of our patients with established psychosis smoke tobacco, and the rates were even higher among people presenting with their FEP. Although tobacco-smoking rates are known to be high in people with psychosis, our figures are thrown into sharp relief when compared with the current 18% prevalence rate among the general UK population. We are currently investigating in our sample of people with established psychosis the effect of cigarette smoking on both depressive and psychotic symptoms over time. The very high rates of tobacco-smoking in the first episode group changed little over the following year, especially so among those from black and minority ethnic groups. A potential explanation for this may be that national smoking campaigns and incentives for health-care practitioners to address smoking behaviours are not well targeted towards this population. The potential adverse effects of nicotine dependence among our sample highlight the need for effective smoking cessation strategies in psychosis. The findings may also help both patients and clinicians to view smoking cessation more positively by understanding the detrimental effects smoking can have both on physical health and on mental health symptoms.

We failed to identify differences in cardiometabolic risk in people with established psychosis who were prescribed antipsychotic medication of different types or in emergent cardiometabolic risk in FEP patients.[176] Despite the side effects, antipsychotic medication is important in optimising one's mental health so that one is well enough to take charge of one's physical health. In a large study of 66,881 patients with schizophrenia over a 10-year period, long-term treatment with antipsychotic medication was associated with lower mortality than receiving no antipsychotic medication.[9] Additionally, the longer people were prescribed antipsychotics, the smaller the mortality gap became. Furthermore, those prescribed with clozapine, the gold-standard treatment for refractory schizophrenia that is known to have a risk of rapid weight gain and glucose dysregulation,[12] had the lowest mortality rate of all patients with schizophrenia. Therefore, antipsychotics, used thoughtfully at the lowest effective dose, should be seen as integral to mortality reduction strategies.

A relatively small proportion of our IMPaCT patients were prescribed cardiovascular medication, although further work is needed to determine the proportion of our sample for whom medications such as statins were indicated under current NICE guidelines, which are not based on blood test results alone. Nevertheless, it is an important area for attention. A Danish study[31] has shown that people with schizophrenia with concomitant CVD are prescribed most cardiovascular drug classes less often than the general population, in particular lipid-lowering and antihypertensive medication. Additionally, in that study, patients with SMI were less likely to be prescribed more potent medications (such as angiotensin-converting enzyme inhibitors or beta-blockers), suggesting inadequate treatment of CVD.

It is not immediately clear why the IMPaCT therapy intervention conferred no advantage on recipients, relative to control treatment under intention-to-treat conditions. It is possible that potential efficacy was suppressed because of factors affecting consistent implementation of the intervention in an increasingly busy NHS setting, despite ongoing supervision. A key strength of the IMPaCT RCT was its pragmatic design; the trial was integrated into the existing workforce and conducted across several NHS foundation trusts, thus widening its generalisability. Significant practical challenges were overcome during implementation; for example, as services were reconfigured or contracted, there was some emergent resistance among team leaders to allowing care co-ordinators to fully participate in the study as planned. Once care co-ordinators were randomised to the IMPaCT therapy arm of the trial, they were required to attend a mandatory 4-day training course on how to deliver IMPaCT therapy, but difficulties were experienced in encouraging care co-ordinators to attend the planned course. For example, despite initial buy-in to the IMPaCT study from team leaders, there was a degree of resistance at team level to freeing the care co-ordinator from clinical duties to attend the training. Resistance may have arisen because, within each participating centre, several care co-ordinators could be recruited from one team. Given care co-ordinators' already heavy workload, team leaders were understandably reluctant to allow to be absent from their regular duties for the full 4-day period. In anticipation of these concerns, the study team offered care co-ordinators the opportunity to attend 2-day training in any given week and to

complete the remaining 2 days at the following training session. Feedback from participating care co-ordinators indicated that the training was well received. Although a reduction in training duration appeared to have improved the acceptability of the intervention among team managers, the shortened training session may have been less immersive and, thus, less effective than the planned 4-day session, which may have had an impact on the results.

Indeed, it is questionable whether or not intensive training courses are sufficient to equip care co-ordinators with the skills needed to deliver a given psychosocial intervention. Motivational interviewing requires that therapists reframe the way in which they approach discussions with their clients. Shifting from a didactic to a more client-centred approach probably requires that care co-ordinators reconsider their ingrained practices. The care co-ordinators recruited to the study had many years' experience in their role, over which time they were likely to have formed habitual clinical practices. Indeed, no care co-ordinator ran group sessions with patients, despite receiving training in this and supervision to support group work; we noted that running groups had not been standard practice for any of the care co-ordinators before joining the study. Not only may care co-ordinators have lacked the time to organise and facilitate these sessions, but changing practice may have required them to break habits. Care co-ordinators may require support from team leaders to deliver new models of care and, although trust management and team leaders were supportive, future work may need to include an element addressing organisational barriers.

Care co-ordinators can be from a number of professions, but in the participating trusts they were predominantly from either nursing or social work backgrounds. We did not want to limit the evaluation to nurses only as the cardiometabolic risk was universal. Social workers would not have received training in physical health management as part of their professional training; additionally, in recent decades, mental health nurses will have received only limited training in physical health when completing their undergraduate course. The intervention was designed with this in mind and to address the gaps between physical and mental health care. Interventions such as the HIP RCT have also highlighted challenges in incorporating physical health management into mental health care.[186] There has also been recent consideration of other service models. The research evidence suggests that high-intensity interventions incorporating specialists in diet and exercise are most effective,[187,205] although, in the UK, service providers may be hesitant owing to the cost of such initiatives.

Additional challenges were posed by shifts in the political landscape during the study period, specifically the implementation of the Health and Social Care Act 2012,[206] accompanied by significant economic pressure and a large-scale restructuring of the NHS. The IMPaCT RCT study relied on the recruitment of CMHTs, which are embedded in mental health trusts. The main recruiting mental health trust experienced major restructuring and changes in remit during the study period, which in turn led to delays, as care co-ordinators could not commit to participation until this reorganisation was complete. The reorganisation was associated with a degree of uncertainty among staff about their job continuity, which had an impact on their ability to participate in the IMPaCT therapy training; specifically, many were unsure, because of restructuring, whether or not they would be with the team for the duration of the trial (15 months). Additionally, there may have been tensions within teams regarding care co-ordinators' involvement in the study; although training staff members is perceived as beneficial to the team, freeing staff for training purposes inevitably means distributing their workload among other staff members. However, it is important that these challenges are recognised; this intervention was designed to be easily incorporated within standard care teams and the practicalities of doing so are part of the evaluation. This context should be considered when interpreting the costs associated with IMPaCT therapy. The evaluation suggested that the intervention itself involved no significant additional resource use or associated costs, nor an impact on broader overall costs, but it is unclear to what extent this reflects a true lack of impact on costs or merely low levels of implementation and, thus, limited potential to have an impact on resource use.

Additional methodological limitations must be acknowledged. Study procedures may have been conducive to selection biases. Studies of non-participation have typically found that those who decline to participate in psychosis research studies tend to be male, have severe symptoms, substance abuse problems, low educational attainment and socioeconomic status, and be unmarried and unemployed. Additionally, patients were required to provide informed consent to participate, which presupposes sufficient cognitive ability to read, interpret and deliberate over the information presented in a patient information sheet and to make decisions regarding whether or not to consent to all aspects of the research, while acknowledging the potential risk of doing so. Obtaining informed consent risks excluding the most impaired patients from a study.

Work package 1, PUMP, was designed so that all people presenting with their FEP were potentially eligible for inclusion, whereas the RCT was carefully designed to be as representative as possible, so that all patients with a primary diagnosis of a psychotic disorder allocated to the care of a participating care co-ordinator were potentially eligible for inclusion. To further explore representativeness of psychosocial research models, we decided to test the hypothesis that, even with such an inclusive RCT design, those who consented to participate in the trial would be less ill than those who did not. We did this by comparing the Health of the Nation Outcomes Scales (HoNOS) scores at baseline among the SLaM IMPaCT RCT participants ($n = 293$) with similarly timed HoNOS scores recorded as part of clinical care in the eligible population of patients (i.e. those eligible patients of the participating care co-ordinators, $n = 774$) using an anonymised case register. The mean total HoNOS score of the eligible comparator population was indeed significantly higher than that of the IMPaCT RCT participants ($t = 3.810$; $p = 0.006$), as was the degree of overall illness severity and functional impairment, as measured with HoNOS. We concluded that the patients who participated in the RCT had better mental health at entry to the trial than the total eligible population, although we found no difference in physical health needs.[207] This is important to bear in mind when interpreting the findings of RCTs of lifestyle interventions for use in service planning. We would further speculate that the greater the effort needed to participate in an intervention and evaluation thereof, the more selective recruitment and the less generalisable the results to the overall SMI population in need.

Furthermore, in the PUMP study, the mean duration of treatment was 35 days prior to consent to the study. This time lag was the product of waiting for participants to be well enough to provide informed consent to the study. Thus, our measure of baseline symptom severity is necessarily more representative of a less ill population. This highlights the difficulties that researchers face in recruiting participants at the time of presentation to psychosis services, while also illustrating the potential for results not to generalise to people with more severe psychosis at the point of presentation. Because of these problems, it is possible that our sample under-represents the severity of illness often witnessed in people with psychosis. Indeed, the relatively low total PANSS scores in the PUMP study suggest mild to moderate symptom severity. However, it is likely that we were examining a cohort of patients representative of FEP. For example, our study[208] examining the longer-term follow-up of the same sample found that 34% of the sample were treatment resistant at 5 years, with 70% of those never achieving symptomatic remission from the time of first presentation.

Missing data also posed a challenge in the PUMP study. Partly, this may have been a result of attrition; one of the key difficulties of conducting both prospective cohort studies and RCTs is the time lag between study recruitment and follow-up, which can lead to attrition bias.[209] PUMP included a large number of assessments and so participants may have felt fatigued and unable to complete all of the tests. To minimise repetition, the PUMP study joined with the Genetics and Psychosis (GAP) study[210] that was recruiting FEP patients concurrently; although this limited the number of repeat assessments, the overall assessment battery remained intensive. Additionally, participants living in inner-city areas are highly mobile, making it harder to locate them at follow-up. This, combined with the social deprivation faced by this population, may also increase the mobility of this sample, with many participants being frequently rehoused, which may result in limited traceability.[211] However, measures were employed to limit attrition. Contact details of the participant and their relatives/friends (e.g. e-mail and postal address, mobile and home phone numbers)

were collected at the start of the study and contact was pursued using participants' preferred contact mode. We also sought to maintain interest and remind participants of the study aims by sending newsletters to participants between baseline and follow-up assessments. Additionally, a courtesy call was made midway between the assessments to remind participants of their upcoming follow-up appointments. These communications also alerted the research team to barriers to contacting the participant (e.g. newsletter returned as undelivered), and other means of contact were used to maximise the likelihood of booking follow-up assessments. Nonetheless, in the PUMP study, only 125 of 293 participants completed the 12-month face-to-face assessment measures. However, we retrieved follow-up data from a number of sources including case notes and other records, thereby, not solely relying on face-to-face measures, which resulted in high completeness rates.[122] Thus, the potential impact of attrition was mitigated.

To minimise the impact of missing data on our research findings in the PUMP study, we utilised, with consent, data from a number of sources; these included anthropometric, metabolic and biochemistry data recorded in the patients' electronic case records. However, we found low levels of documentation of physical health measures. This is in keeping with a series of national audits of schizophrenia, which have retrospectively examined the quality of physical health monitoring, including whether or not weight, BMI, BP, tobacco use, alcohol use, substance misuse, blood glucose, blood lipids and family history of CVD, diabetes, hypertension or dyslipidaemia were documented. Documented evidence in the case notes fell below agreed standards, with < 25% of patients having all nine parameters documented.[212] This highlights the need to regularly monitor and record these data systematically. However, it should be noted that this finding was before the introduction of CQUIN targets, which have since enhanced physical health data documentation substantially, particularly for those patients who have had an inpatient stay.

Finally, both studies relied heavily on self-report measures. Although these are validated for use with participants with psychosis, potential problems are associated with the accuracy of such measures, which must be acknowledged. Of note is that many participants chose not to self-administer the measures, largely because of the nature of the illness (which can result in lack of motivation, low mood, cognitive impairment), and low literacy levels. Instead, researchers were often required to read aloud each item and present the corresponding scale on which participants would indicate their response. Although researchers sought to read aloud questionnaire items in a non-biased manner, it is known that the way in which data collection is conducted, or by whom it is conducted, can have unintended potential consequences on study findings.

Recommendations for research

At the individual level, having schizophrenia makes it more difficult to engage in healthy behaviours. For example, social withdrawal reduces opportunities to participate in physical activity,[213] and negative and cognitive symptoms make it even more difficult for people with schizophrenia to organise themselves to prepare healthy meals. We have not yet had the opportunity to fully explore the effect of negative and cognitive symptoms on outcomes in our study populations, but this is work we plan to do in the future.

At a biological level, genetic factors may also influence cardiometabolic risk. An identified locus is associated with both increased CVD risk factors and schizophrenia,[214] while polymorphisms in a type 2 diabetes gene may increase susceptibility to schizophrenia.[215] We are examining the IMPaCT population to look for genetic predictors of metabolic status both in people with FEP and those with established psychosis. We have created a genetic risk score and are performing statistical analyses to establish the relationship between this score and MetS in psychosis.

Inflammatory mechanisms have been suggested as a possible driver of CVD in schizophrenia.[216] We examined the relationship between inflammation as measured by levels of CRP and metabolic risk factors in people with their FEP. We found that triglyceride dysregulation is associated with elevation of CRP levels early in the disease course of people with psychotic disorders.[126] This suggests that inflammation should be investigated as a therapeutic target in the future.

Sexual dysfunction is common in people with schizophrenia, with a reported prevalence of up to 80%.[217,218] In our service user focus group this was highlighted as a priority topic. Although sexual dysfunction is often attributed to the side effects of psychotropic medication, we have found that it exists even before the FEP in people not treated with antipsychotic medication.[219] Nevertheless, the development of sexual side effects contributes to non-adherence to psychotropic medication. This is a frequently overlooked aspect of general well-being in people with schizophrenia; it is important to QoL and should be actively enquired about by treating clinicians. Future clinical research is needed to determine how best to systematically identify and manage sexual dysfunction in people with a diagnosis of SMI, bearing in mind its multiple causes, many of which, such as medication choice, obesity, smoking and sedentary behaviour, are also relevant to cardiovascular health.

The search for effective evidence-based approaches to reduce the excess cardiometabolic risk experienced by people with SMI is proving a challenge for many research groups, following the negative results in all recent large European RCTs on the topic, namely IMPaCT, STEPWISE, PRIMROSE, HIP and CHANGE.[176,186,220–222] Although the interventions in all these studies were intuitively sensible and it was reasonable to believe that they should have been helpful, researchers are struggling to demonstrate evidence of additional effectiveness in the context of structured health-care systems. It may be that the effectiveness of more individualised long-term approaches to reverse cardiometabolic risk in this population needs to be evaluated, bearing in mind that reversing established cardiometabolic risk in the general population is also a challenge.

Conclusion

The IMPaCT programme has highlighted the high rates of cardiometabolic risk soon after first presentation with psychosis and the early emergence of additional risk. We did not find that baseline lifestyle choices and addiction behaviours identified those people most likely to increase their cardiometabolic risk in the first year, but we did note a differential pattern of emergence of cardiometabolic risk in relation to ethnicity.

We developed, in an iterative process, a modular HPI to be used in routine clinical care and implemented by the patient's usual care co-ordinator and evaluated it in what is to our knowledge the first randomised trial of such an intervention. The RCT confirmed the challenges in targeting lifestyle and substance use to modify cardiometabolic risk and highlighted the difficulties of adding specific psychosocial interventions to the workloads of increasingly stretched clinical teams.

Our work also demonstrated that, even in the early stages of psychosis, there are high rates of vitamin D deficiency, which was associated with cardiometabolic risk markers in people with established psychosis. As a result of this, we have now started a RCT of vitamin D supplementation in FEP (URL: www.clinicaltrialsregister.eu/ctr-search/trial/2014-002639-32/GB; accessed 2 December 2019).

A better understanding of the role and interplay of exercise, nutrition, substance use and medication will allow for the development, delivery and evaluation of better and more efficient interventions, for example targeting the overall individual's fitness instead of simple measure of their body shape.[223] Importantly, at a wider level, factors hindering access to care should also be addressed to improve the knowledge of service planners and to plan reasonable adjustments. The low efficacy of HPI

interventions such as IMPaCT RCT in reversing established unhealthy behaviours is consistent with other emerging work.[220] In this context, our results underlined the importance of preventing the formation of (unhealthy) habits around physical exercise, alimentation, substance use and lifestyle choices rather than modifying them later.

The IMPaCT study provides important information to health service planners, suggesting that they need to be aware that training and supervising staff to work on lifestyle choices and substance use with their patients as part of routine care is not sufficient to reduce cardiometabolic risk or improve mental and physical QoL.

Programme patient and public involvement

This whole programme was, from the outset, co-produced with experts by experience. Ms Bee Harries was a co-applicant on the original grant application. Ms Harries was involved in the planning and development of IMPaCT and facilitated our patient and public consultation, starting in the borough of Lewisham. She led the focus groups held there, which informed our study design and emphasis; for example, the inclusion of work on sexual dysfunction derived from that focus group (Reis-Marques et al.[219]). She helped generate solutions to enhance recruitment to the study and presented the work with us to collaborating services. Sadly, Ms Harries died during the course of the study. She contributed immensely to the development and accessibility of the intervention, which is dedicated to her memory.

A stakeholder engagement event was held in the Civic Suite in Lewisham on 20 March 2008 entitled 'Our Bodies are Important Too . . . as well as our mental health' (*Box 1*). The event included information, small-group work (up to six people in a group) and, at lunchtime, a well women's group, hand massage,

BOX 1 Stakeholder engagement event timetable

'Our Bodies are Important Too . . . as well as our mental health'

10.00–10.30   Sign-in and registration

Delegates can leave their addresses if they want information from the day.

11.00   Introduction of the day

 Miriam

11.15   Interview of Fiona Gaughran about the IMPaCT Project

 Bee and Kristine

11.45   Group exercise – what one thing would you say about your health to your support worker, doctor, etc.

 Collated and used in theatre after lunch

12.00   Small groups and consultation exercise around IMPaCT questions

13.00   Lunch – hot and cold food

14.00   Playback theatre around Bee's poem – I am a person 1, 2 and 3, and group exercise results

14.15   Where do we go from here – next steps

 Kristine/Miriam/Bee

Questions/areas for the group work included:
- What has worked already for you within SLaM services for your health care?
- Why did this work?
- What would you like to see more of/different?
- Talk about the health module – what is important to have on the health module (e.g. exercise, diet, etc.)?
- Any interest in getting involved in the health modules, training on the health module?
- Any interest in joining the advisory group for the IMPaCT Project?

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activity from Network Arts, information on physical activity and expert patients' group. The aim of the day was to find out from people using mental health services what is important to them in their treatment around physical health care. We wanted to find out what people would like to see more of or change and whether or not people would like to get involved in planning or advising on health promotion services. The day was co-ordinated by Ms Miriam Mica, Mental Health Promotion Co-ordinator at SLaM NHS Foundation Trust, and the sessions were led by Bee Harries. The day was co-hosted with Family Health Isis, a local African and Caribbean mental health organisation.

On the untimely death of Bee Harries, Thomas Kabir from the Mental Health Research Network helped us with the essential patient and public involvement input to the programme and then put us in touch with Maurice Arbuthnott, who also has expertise by experience. Maurice Arbuthnott has contributed hugely as an equal partner to the running of all aspects of the programme.

We set up a partnership with carers through the Mental Health Research Network body FACTOR, co-ordinated by Dr Geraldine Mason. We set up a carers' consultation group; this consisted of six to eight carers who met regularly with two IMPaCT team members to discuss the project. Two carer members of that group, Philippa Lowe and Diana Orr, started to attend the monthly IMPaCT management meetings and are important partners in the team, advising on recruitment and follow-up strategies as well as engagement and dissemination.

All our experts through lived experience have not just contributed to the development and implementation of the research, but also brought their own knowledge and expertise to enrich the quality and applicability of the work. Our carer involvement structures are described in detail in a case report by an anthropologist in Devon Partnership NHS Trust (see *Report Supplementary Material 1*; reproduced with permission from Dr Sarah Robens, Devon Partnership NHS Trust).

Expert service user input

My name is Maurice and I live in Central London. I have been using mental health services for just over 20 years. I became involved in IMPaCT through the Mental Health Research Network and I am pleased to help with representing service user interests in the IMPaCT research project. My main role is as a participant and observer at the monthly IMPaCT steering group meetings. I consider my participation at these meeting in three ways: 1. Offering advice where appropriate e.g. on how to encourage service users to get involved in the project. 2. Enquiring about the progress and methodology of the project for the sake of clarification. 3. Making constructive comments for general consideration. My perspective of the research in question comes not only as a service user experienced in psychosis and treatment but also as a lay person e.g. the proverbial man in the street so I aim to keep this perspective as wide as possible.

On occasion I have also talked to researchers about my own experiences of how my physical health needs have been met and my relationship with medical professionals, especially my community mental health team. I am very interested in being a source of reference to researchers and for them to enquire about my experiences as a service user. I also compiled a questionnaire for the service users to complete after their involvement in IMPaCT. This aimed to find out what service users found was important to them in participating in research and what they found interesting, useful or otherwise. We are soon to analyse these results.

I am particularly interested in how this project will benefit the maximum number of service users through helping them achieve the best possible physical health and I am looking forward to assisting with the dissemination of the eventual results and findings not only to the medical profession but also to my fellow service users and the lay person. I feel very positive about IMPaCT goals to empower people into better health especially as it is a well-documented observation that people with a mental illness also endure poor physical health.

Expert carer input

Written by Philippa Lowe:

There are many ways of coping as a carer for someone with mental illness and one of them is to get thoroughly involved in the subject and to take an interest in related research developments. This is the path I chose, so I was very pleased to be invited to be a carer adviser for the IMPaCT project.

The subject of the research was of particular interest to me as my son, who has had schizophrenia for nearly 20 years, is now very much better in respect of the more dramatic symptoms of the illness but has experienced considerable weight gain which puts him at risk of developing severe physical illnesses which may shorten his life. I was grateful for the opportunity to help shed light on the problem both for the sake of my own family and for others facing similar issues.

I found it a pleasure to work with a team of people from different relevant disciplines who were clearly dedicated to their subject and welcomed the various contributions with respect and interest. I found that I could make a useful input, for example, by suggesting ways of helping the research subjects cope with the various procedures which were required of them, by proposing the best ways of setting out clear information in guidance notes and newsletters and by urging the involvement of carers, where available, as the people who can offer support and encouragement for ongoing participation. Colleagues involved with the project gave a clear indication that this sort of input was of value to the project, which was very good to hear.

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Fiona Gaughran is the guarantor for the manuscript and the data contained within.

Contributions of others

Bee Harries was an expert with lived experience who was involved in the development of the study design, was a co-applicant on the grant and worked with the team to implement the research. Diana Orr (expert by lived experience) was part of the trial management team and helped in the planning of the projects. Kurtis Stewart (research worker), Simone Ciufolini (clinical research fellow), Mary Aboasu (research worker), Niamh Lyons (research worker) and all of the Institute of Psychiatry, Psychology & Neuroscience, King's College London, assisted in the preparation of the manuscript.

Publications

Please contact the first author for manuscript copies.

Lally J, Gardner-Sood P, Firdosi M, Iyegbe C, Stubbs B, Greenwood K, *et al.* Clinical correlates of vitamin D deficiency in established psychosis. *BMC Psychiatry* 2016;**16**:76.

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Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Patient data

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety, and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that it is stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation.

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Appendix 1 Work package 1: PUMP – health economics

Background

Although there is clear evidence of the increased cardiometabolic risk among people with SMI[14] and its likely consequences for long-term morbidity (diabetes, heart disease, stroke, amputation, renal failure, blindness) and care costs later in life, it is unclear whether or not there are more immediate impacts on service costs and QoL following first presentation to mental health services.

Aims and hypotheses

We aimed to investigate the relationship between metabolic factors/syndrome at first presentation to mental health services and (1) mental health hospital admission costs in the subsequent 1-year period and (2) QALYs in the subsequent 1-year period.

Method

Measures

At baseline, after giving informed, written consent, each participant was asked to complete a battery of measures. This included sociodemographics, clinical measures and health-related QoL, measured using the EQ-5D-3L.[190] Clinical measures relevant to these analyses were clinical indicators of MetS/cardiometabolic risk (obesity, triglycerides, HDL cholesterol, BP and fasting plasma glucose).[13] The EQ-5D-3L was again administered at the 12-month follow-up to enable the calculation of 1-year QALY gains.

Data on mental health care hospital admissions for the 12 months prior and 12 months following presentation for FEP were manually extracted from electronic patient record systems in each of the relevant NHS trusts using a pro forma specifically designed for the task to standardise the methodology and information that was collected. Core data included admission and discharge dates of each admission to enable the calculation of length of stay per admission, and ward type to enable more accurate estimation of costs.

Unit costs

Unit costs were applied to individual-level inpatient days according to ward type to calculate total mental health hospital admission costs per participant over 1 year. Unit costs were obtained from NHS Reference Costs for the year 2010–11 and inflated to 2011–12 prices using the Hospital and Community Health Services Pay and Prices Index.[192] We used the *Reference Costs 2010–11*[191] because they offered more detailed cost data according to the type of mental health service, which is not offered in the 2011–12 Reference Costs. Unit costs are detailed in *Table 1*. All costs are reported in GBP at 2011–12 prices. Discounting was not necessary as all costs related to a 1-year period.

Analyses

For the purpose of univariate associations with costs and QALYs, individual metabolic factors were examined in both binary (present or not) and continuous form. Furthermore, the total number of metabolic factors present was investigated.

TABLE 1 Unit costs of PUMP

Service	Unit	Unit cost (2010–11 prices)[191] (£)	Inflated unit cost (2011–12 prices)[192] (£)	Notes
Acute ward	Bed-day	319	329	MHIPA2 – adult: acute care
Assessment ward	Bed-day	319	329	MHIPA2 – adult: acute care
Accident and emergency	Bed-day	108	112	TA and EMSNA – accident and emergency services: not leading to admitted
Personality disorder	Bed-day	553	571	SCU44 – high-dependency secure provision: personality disorder
Mother and baby unit	Bed-day	651	672	MHIPMB – mother and baby units
Medium secure	Bed-day	483	499	SCU3 – medium-level secure services
Intensive assessment	Bed-day	627	647	MHIPA1 – adult: intensive care
Psychiatric intensive care	Bed-day	627	647	MHIPA1 – adult: intensive care
Low secure	Bed-day	427	441	SCU2 – low-level secure services
Adolescent inpatient	Bed-day	602	622	MHIPC1 – children
Elderly	Bed-day	329	340	MHIPE1 – elderly

To estimate QALYs, we applied general population utility weights to EQ-5D-3L health state measurements at baseline and at 12 months.[124] QALY gains between baseline and 12 months were then calculated using the total area under the curve approach with linear interpolation between assessment points.[195]

Data were analysed using Stata 11. Despite the skewed nature of the cost data, the mean and SDs for cost data are reported as recommended.[224] Associations with costs and QALYs were explored using the stepped approach.[225] Univariate associations of metabolic and sociodemographic variables with costs were examined using non-parametric bootstrap regressions (ordinary least squares); we conducted each regression both with and without a covariate for baseline costs. All independent variables that were associated ($p < 0.1$) with costs in these univariate analyses were then carried forward for inclusion in a multivariate non-parametric bootstrap regression. We examined the results of the multivariate regression to identify any variables that no longer remained significantly associated with costs ($p > 0.1$) and then reran the multivariate regression without those variables. Variables that did not appear significantly associated with costs in the univariate regressions were then added into the model and retained if they significantly improved the model or rejected if they did not. The same process was repeated for the analysis of associations with QALYs.

Results

Of 321 people initially consented, 28 were subsequently deemed ineligible, leaving 293 eligible participants recruited to the study.

Sample characteristics
Of the 293 participants, 190 (65%) were male and 136 (46.4%) were of white ethnic origin. The mean age was 30.6 years (SD 10.5 years). Seventy-six (31.8%) lived alone and 155 (66.2%) were unemployed.

Data completeness

A total of 274 out of 293 participants (93.5%) had full data on resource use/costs for both the 12 months prior to and the 12 months following presentation for FEP, which were gathered from electronic health records. However, fewer people had all relevant data on metabolic factors and QALYs. This resulted in 100 participants with all relevant data for the examination of associations with admission costs and 55 participants with all relevant data for the examination of associations with QALYs. *Table 2* shows that the two subgroups available for analyses were similar to the full sample in terms of a range of baseline characteristics. However, both subgroups had lower admission costs at baseline than the full sample. The potential implications of missing data are explored in *Discussion*.

Resource use and costs

Among the 293 participants, we were able to extract data for 278 on the number of inpatient days for the year prior to FEP. Of these, 243 participants had no inpatient days prior to FEP. Of the 35 participants who had had a mental health admission, this was mostly because of a few (1–5) days admitted for symptoms during the prodromal period before a diagnosis of psychosis was assigned. Four participants had total admission days ranging between 8 and 172 days and the most likely reason for this was an evolving clinical picture before the diagnosis of psychosis became clear. The mean cost of admissions in the year prior to FEP was £443 (SD £5814, range £0–95,957).

We were able to extract data on the number of inpatient days for the year following presentation for FEP for all 279 participants. Twenty-eight participants had no admissions. The overall mean total was 63 days [SD 69 days, range 0–367 days (exceeds 365 as a result of accounting for movement between wards)]. The associated mean cost was £25,376 (SD £34,411, range £0–236,945).

TABLE 2 Characteristics of full sample and subsamples with full data required for analyses

Variable	Full sample (N = 293)	Subsample with full data for admission cost analyses (N = 100)	Subsample with full data for utility analyses (N = 54)
Gender, *n* (%)			
Female	103 (35)	40 (40)	24 (44)
Male	190 (65)	60 (60)	31 (57)
Ethnicity, *n* (%)			
White	136 (46)	42 (42)	23 (23)
Other	157 (54)	58 (58)	32 (32)
Living alone (*n* = 239), *n* (%)			
No	217 (68)	70 (74)	40 (78)
Yes	76 (32)	25 (26)	11 (22)
Employment status (*n* = 234), *n* (%)			
Employed/student	79 (34)	29 (31)	19 (37)
Unemployed	155 (66)	64 (69)	32 (63)
Age (years), mean (SD)	30.6 (10.5)	29.8 (9.8)	30.0 (10.1)
Baseline utility score (*n* = 178), mean (SD)	0.79 (0.26)	0.82 (0.25)	0.83 (0.18)
Baseline admission costs (£) (*n* = 274), mean (SD)	443 (5814)	77 (276)	83 (320)

The proportion of participants who had at least one admission and the mean number of inpatient days for the year prior to FEP were similar in the full sample and in the subsample who had all required data for the analysis of admission costs (i.e. they also had full metabolic and sociodemographic data) (*Table 3*). This was also true for the 1 year following presentation for FEP. However, the mean cost of admissions in the year prior to FEP was lower for the subsample with full data than for the full sample [£77 (SD £276) vs. £433 (SD £5814)].

Metabolic syndrome factors and admission costs

Univariate analyses suggested that being male, obese or of non-white ethnicity was associated with higher admission costs during the 1-year follow-up ($p < 0.1$), whereas being older or having reduced HDL cholesterol (< 1.03 mmol/l for men and < 1.29 mmol/l for women) was associated with lower costs during the 1-year follow-up ($p < 0.1$) (*Table 4*). When these factors were carried through to a multivariate analysis, all except ethnicity remained significantly associated with costs (*Table 5*).

Health state utility

Of the 293 participants in the full sample, 89 had full EQ-5D-3L data at both baseline and follow-up to enable the calculation of QALY gains for the year following presentation for FEP. The mean QALY gain for these 89 participants was 0.84 (SD 0.17). The subsample was further reduced to 55 when accounting for availability of relevant metabolic and sociodemographic data; however, this subsample appeared broadly representative of the full sample of participants, who had a comparable mean QALY gain of 0.86 (SD 0.14).

Metabolic syndrome factors and quality-adjusted life-years

Both unadjusted and adjusted (for baseline utility value) univariate analyses suggested that, at baseline, having a MetS, being obese, having reduced HDL cholesterol (binary variable), having higher HDL cholesterol (continuous variable) and having more metabolic indicators were associated with lower QALY gains (*Table 6*). Having raised fasting glucose or higher triglycerides (adjusted coefficient −0.03, 95% CI −0.07 to −0.00) was associated with lower QALY gains in adjusted analyses only.

When examining these seven variables in a multivariate analysis adjusted for baseline utility, only HDL level (as a continuous variable) remained statistically associated with QALYs, with higher HDL cholesterol associated with greater QALY gains (HDL 0.09, 95% CI 0.02 to 0.17; $p = 0.013$) (*Table 7*).

TABLE 3 Admissions data for the full sample and the subsample with full data required for analyses of admission costs

	Full sample (N = 293)		Subsample with full data for admission cost analyses (N = 100)	
Baseline				
Had at least one admission (%, *n*/valid *n*)	13	35/278	12	12/100
Mean number of days (mean, SD)	1	10	< 1	1
Mean cost (£) (SD)	433	5814	77	276
Follow-up				
Had at least one admission (%, *n*/valid *n*)	90	251/279	89	89/100
Mean number of days (SD)	63	69	55	64
Mean cost (£) (SD)	25,376	34,411	20,922	25,510

TABLE 4 Univariate associations between MetS factors and 1-year mental health admission costs

Variable	Unadjusted coefficient	Unadjusted 95% CI	Adjusted coefficient[a]	Adjusted 95% CI[a]
Gender				
Female	–	–	–	–
Male	11,613	3092 to 20,133*	11,544	2861 to 20,226*
Ethnicity				
White	–	–	–	–
Other	7990	–1439 to 17,420*	8437	–1179 to 18,054*
Age				
	–606	–1078 to –134*	–631	–1119 to –143*
Binary MetS				
No	–	–	–	–
Yes	–4600	–13,945 to 4744	–4786	–14,192 to 4621
Binary obesity				
No	–	–	–	–
Yes	15,350	–408 to 311.09*	15,378	–352 to 31,108*
Binary high triglycerides				
No	–	–	–	–
Yes	–1850	–12,742 to 9041	–2150	–13,106 to 8807
Binary high BP				
No	–	–	–	–
Yes	–4224	–13,452 to 5004	–4642	–14,114 to 4830
Binary raised fasting glucose				
No	–	–	–	–
Yes	–7197	–17,472 to 3078	–7266	–17,515 to 2983
Binary reduced HDL cholesterol				
No	–	–	–	–
Yes	–9452	–17,915 to –988*	–9524	–18,069 to –979*
Triglycerides (continuous)				
	1693	–3600 to 6985	1564	–3762 to 6890
Systolic BP (continuous)				
	73	–127 to 273	69	–131 to 269
Diastolic BP (continuous)				
	–26	–486 to 434	–41	–510 to 427
Fasting glucose (continuous)				
	–6843	–16,718 to 3031	–7172	–17,302 to 2958
HDL cholesterol (continuous)				
	–2466	–12,471 to 7539	–1992	–12,467 to 8482
Number of metabolic factors (continuous)				
	–1189	–5322 to 2963	–1307	–5495 to 2880

*p < 0.1.
a Includes covariate for baseline admission costs.

TABLE 5 Multivariate associations between MetS factors and 1-year mental health admission costs

Variable	Adjusted coefficient	SE	95% CI[a]
Constant	30,496	7854	15,102 to 45,890*
Gender			
Female	–	–	–
Male	12,227*	4226	3945 to 20,509*
Age			
	–557*	224	–995 to –119*
Binary obesity			
No	–	–	–
Yes	17,691*	7173	3632 to 31,750*
Binary reduced HDL cholesterol			
No	–	–	–
Yes	–10,399*	4428	–19,077 to –1720*

*$p < 0.1$.
SE, standard error.
a Includes covariate for baseline admission costs.
Adjusted $R^2 = 0.1490$.

TABLE 6 Univariate associations between metabolic factors and EQ-5D-3L-based QALYs

Variable	Unadjusted coefficient	Unadjusted 95% CI	Adjusted coefficient[a]	Adjusted 95% CI[a]
Gender				
Female	–	–	–	–
Male	–0.01	–0.08 to 0.07	–0.03	–0.08 to 0.02
Ethnicity				
White	–	–	–	–
Other	0.00	–0.07 to 0.07	–0.02	–0.07 to 0.03
Age				
	0.00	–0.00 to 0.00	–0.00	–0.00 to 0.00
Binary MetS				
No	–	–	–	–
Yes	–0.12	–0.26 to 0.01*	–0.13	–0.25 to –0.02*
Binary obesity				
No	–	–	–	–
Yes	–0.14	–0.25 to –0.02*	–0.08	–0.17 to 0.00*
Binary high triglycerides				
No	–	–	–	–
Yes	–0.01	–0.09 to 0.06	–0.03	–0.10 to 0.03
Binary high BP				
No	–	–	–	–
Yes	0.00	–0.08 to 0.09	–0.03	–0.09 to 0.04

TABLE 6 Univariate associations between metabolic factors and EQ-5D-3L-based QALYs (*continued*)

Variable	Unadjusted coefficient	Unadjusted 95% CI	Adjusted coefficient[a]	Adjusted 95% CI[a]
Binary raised fasting glucose				
No	–	–	–	–
Yes	–0.07	–0.22 to 0.07	–0.14	–0.31 to 0.02*
Binary reduced HDL cholesterol				
No	–	–	–	–
Yes	–0.11	–0.21 to –0.02*	–0.08	–0.16 to –0.01*
Triglycerides (continuous)				
	–0.01	–0.06 to 0.04	–0.03	–0.07 to 0.00*
Systolic BP (continuous)				
	–0.00	–0.00 to 0.00	–0.00	–0.00 to 0.00
Diastolic BP (continuous)				
	–0.00	–0.01 to 0.00	–0.00	–0.01 to 0.00
Fasting glucose (continuous)				
	–0.01	–0.07 to 0.09	–0.05	–0.11 to 0.01
HDL cholesterol (continuous)				
	0.14	0.06 to 0.21*	0.09	0.02 to 0.17*
Number of metabolic factors (continuous)				
	–0.03	–0.06 to –0.00*	–0.03	–0.06 to –0.01*

*$p < 0.1$.
a Includes covariate for baseline admission costs.

TABLE 7 Multivariate associations between metabolic factors and EQ-5D-3L-based QALYs

Variable	Adjusted coefficient	SE	95% CI[a]
Constant	0.320	0.066	0.190 to 0.450*
HDL cholesterol (continuous)	0.094	0.036	0.024 to 0.166*

*$p < 0.1$.
SE, standard error.
a Includes covariate for baseline admission costs.
Adjusted $R^2 = 0.5429$.

Discussion

The results suggest that obesity at baseline is associated with higher subsequent admission costs, that low levels of HDL cholesterol at baseline is associated with lower subsequent admission costs and that higher levels of HDL cholesterol at baseline is associated with a greater subsequent QALY gain.

Strengths and limitations

To our knowledge, this is the first study to examine the association between MetS indicators and admission costs and QALYs in patients with a FEP. However, the findings should be seen as exploratory and be interpreted with caution owing to several limitations. First, missing data resulted in small sample sizes for the analyses. Although the subsamples analysed were broadly representative of the full sample in terms of mean values for costs and QALYs, they may have differed on other factors and the small sample size in general increases the risk of spurious results given the number of independent factors that we sought to examine. Second, we examined only psychiatric admission costs and the impact of MetS in this patient group is on broader health-care costs remains unclear. However, because psychiatric inpatient costs are likely to be the main driver of total care costs in this patient group,[226] the inclusion of other care costs is unlikely to substantially alter the findings.

Conclusion

Finally, this study examines cardiometabolic risk indicators that increase a person's risk of heart disease, stroke and other conditions affecting blood vessels in the long term.[192] We have focused on only short-term mental health admission costs because we were interested in any additional impacts within the mental health care sector, but longer-term and broader data would be required to better assess the full additional impact of these high levels of cardiometabolic risk.

Appendix 2 Health promotion intervention development (work package 2)
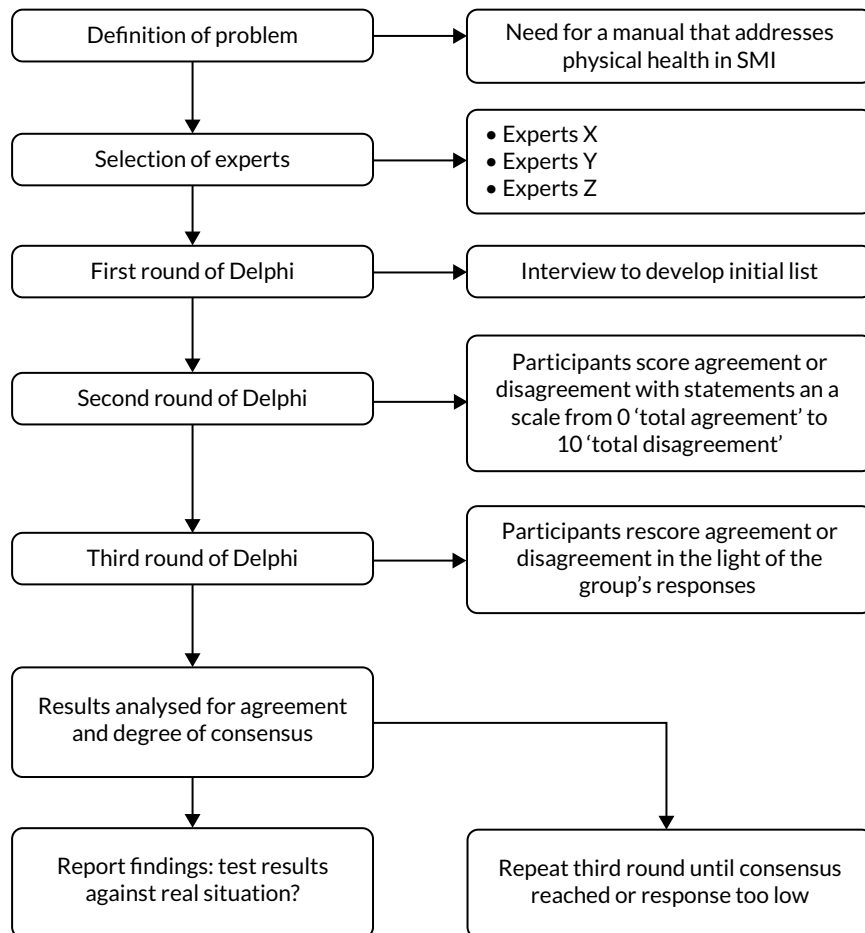
FIGURE 2 Model Delphi method adapted to our study, drawing on the method described by Jones and Hunter.[173]
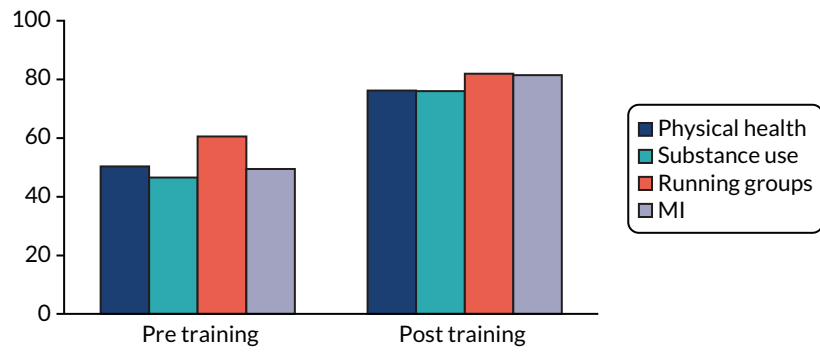
FIGURE 3 Mean self-rated knowledge and skills scores pre and post pilot training for the eight pilot-trained clinicians.

Appendix 3 Care co-ordinator fidelity to health promotion intervention (work package 3: IMPaCT randomised controlled trial)

Care co-ordinators recruited to the IMPaCT HPI trial were, importantly, randomly selected from within routine front-line NHS staff, and did not need to have prior therapy or research experience. Those randomised to deliver the intervention attended a 4-day training programme. As part of the training package, all care co-ordinators received their own copy of the IMPaCT HPI reference guide, manual and *Better Health Handbook* (described in work package 2), which outlined the guiding ethos, core therapeutic approaches and specific intervention adaptations for the different aspects of health behaviour, as well as providing all session plans, example dialogues and a full set of resources to support delivery.

A number of possible approaches were considered to determine therapeutic competence and fidelity to the HPI protocol. These included (1) the therapists' own ratings of their perceived confidence and competence in delivering the different aspects of the IMPaCT intervention immediately before compared with immediately following the training delivery, thus providing both their final perceived confidence and competence and their change during training; (2) an individual role play by each therapist of a brief section of therapy delivery with a trained actor as the patient, to be conducted during the final afternoon of training, and audio-recorded; and (3) a set of three audio-recorded sessions to be obtained during an early, middle and late phase of therapy delivery from each care co-ordinator. All audio-recordings would be transcribed, with the central 20 minutes rated by professionals trained in the use of the Motivational Interviewing Treatment Integrity (MITI) scale (see Moyers *et al.*[227]). This scale was selected as it has been well used as a research tool to determine fidelity to MI, which is the main therapeutic approach of the IMPaCT HPI. The MITI scale provides five summary scores that capture engagement with the spirit of MI, the process of MI (complex reflection, open questions, and the ratio between these) and overall MI adherence. The final approach considered was (4) in the spirit of the 'learning to learn' approach in MI, advocated by Miller and Moyers. Training alone has been shown to be insufficient to produce a change in therapeutic competence. Regular, supervised practice is also required to ensure that therapeutic competence is met and maintained (see Miller *et al.*[228]). The IMPaCT therapy was designed to be supported, for each care co-ordinator, by a 1-hour session per fortnight (see Greenwood *et al.*[229]).

On commencing the training with care co-ordinators, it was decided by consensus among the study team that for this research and therapy-naive population of clinicians, an assessment of competence through an audio-taped role play with an actor may be too threatening and may lead to therapist disengagement from the trial. As a result, this assessment was excluded from the fidelity evaluation.

Of the 52 care co-ordinators who completed the IMPaCT HPI training, 16 completed the training questionnaire both pre and post training. The questionnaire included ratings of knowledge across domains of physical health, substance use, running groups and MI therapy approaches. All ratings of knowledge and confidence post training were high (mean ratings of 73–80/100 for knowledge compared with 42–52/100 pre training and 78–81/100 for confidence). Knowledge increased significantly from pre training across all domains [physical health awareness $t = -8.4$ df(15), 95% CI -37 to -22; $p < 001$; substance use awareness $t = -8.1$ df(14) 95% CI -36 to -21; $p < 001$; running groups $t = -4.4$ df(15), 95% CI -42 to -15; $p < 001$; and MI $t = -7.1$ df(12), 95% CI -43 to -23; $p < 001$]. These outcomes are consistent with care co-ordinators having obtained stage 1 of Miller and Moyer's eight stages of learning in MI, represented by their increased understanding and confidence in the ethos of MI delivery. However, confidence does not necessarily relate to competence in clinical

practice and therapy and, as a result, additional approaches were explored to investigate the competence of the care co-ordinators to provide IMPaCT therapy.

Ten care co-ordinators each produced a single therapy audio-recording across sessions ranging from early to late therapy delivery. Each tape was transcribed and the MITI scale applied to the typed transcript by a trained professional and was independently validated by a second trained professional. The independent raters achieved 86% concordance on thresholds for proficiency and competence, and, in the case of different ratings, the higher rating was awarded. An analysis of the tapes revealed that most care co-ordinators reached beginning proficiency in at least one of the five domains scored, but only three (30%) reached this proficiency in more than two domains. These three had also obtained the higher threshold of competency in at least three domains. Of rated care co-ordinators, 50% obtained a rating that indicated adherence to a MI model. *Table 8* summarises the level of care co-ordinator proficiency and competence in therapy delivery.

The training questionnaires revealed that care co-ordinators rated themselves as having a high level of knowledge and confidence in using the information about physical health and substance use, and in offering motivational approaches and groups to address these health behaviours in their clinical practice. This was a positive endorsement of the training from the care co-ordinator perspective and reflected at least their self-reported achievement of level 1 (understanding and confidence) in the stages of learning in MI.

Owing to concerns about acceptability, an assessment of initial competence using an audio-taped role play with an actor in the final training session was dropped. This concern would appear to have been borne out in the uptake of audio-taped therapy sessions, over which care the co-ordinators had control. Despite continued encouragement to produce three audio-taped sessions of their therapy from any of their clients over the course of therapy, only 10 care co-ordinators produced any audio tape, and none produced more than one tape. The tapes that were provided are, therefore, likely to derive from the smaller proportion of more enthusiastic and committed therapists in the IMPaCT trial. It would be important to learn more about other factors that differentiate between those therapists who adhered well to a MI model and those who were less able. Support for therapy delivery within the local NHS environment, pre-existing therapist skills and commitment are just some of the candidate factors that may mediate between therapy training and successful therapy delivery (Madson *et al.*[230]). Although brief training sessions in MI have been shown to be effective in promoting MI therapy skills (Madson *et al.*[230]), routine front-line clinical staff who work with people with psychosis, even when willing to take part in a 4-day training programme and when offered fortnightly supervision, struggle to consolidate training into meaningful adherence to MI therapy.

The MITI scale assesses the spirit and process of MI, which form the first five stages of learning in MI. It does not assess the later stages of transition to behaviour change, commitment and integration with other therapies such as CBT. However, based on the fidelity outcomes of these early MI phases of therapy delivery it seems possible that therapists would also struggle with these later stages of IMPaCT therapy.

TABLE 8 Summary of MITI scores for the 10 care co-ordinators who provided an audio-taped session

MITI summary score	Care co-ordinators achieving beginning proficiency	Care co-ordinators achieving competence
Global spirit of MI	4/10	4/10
Complex reflections (%)	8/10	7/10
Open questions (%)	4/10	1/10
Reflection-to-question ratio	3/10	1/10
MI adherence (%)	5/10	5/10

Appendix 4 Economic evaluation of the IMPaCT randomised controlled trial (work package 3)

Analyses, missing data and sensitivity analyses

Data were analysed using Stata 11. Participants were analysed according to the group to which they were randomised regardless of intervention compliance.

Costs and outcomes were compared at baseline and at 12 and 15 months and are presented as mean values by arm with SDs. Mean differences and 95% CIs were obtained by non-parametric bootstrap regressions (1000 repetitions) to account for the non-normal distribution commonly found in economic data, with adjustment for clustering at the care co-ordinator level. To provide more relevant treatment-effect estimates,[189] regressions to calculate mean differences in costs included covariates for the baseline value for the same cost category, baseline SF-36 MCS, baseline SF-36 PCS, baseline SF-36 utility and baseline EQ-5D-3L utility, plus baseline demographic variables expected to be associated with costs (gender, ethnicity, borough). Similarly, comparisons of outcome data included baseline SF-36 MCS, SF-36 PCS, SF-36 utility and EQ-5D-3L utility as covariates, plus baseline demographic variables that were expected to be associated with outcome (gender, age, ethnicity, place of birth and borough).

Individual item non-response for the CSRI was minimal. When this occurred, an item cost was imputed using the mean cost for the same item for other users in the same trial arm and at the same assessment point. When this was not possible, the overall cost component was imputed using the mean cost for the same cost component in the same trial arm at the same assessment point. For medication data, a series of assumptions and imputations were necessary depending on the nature of the missing information, as follows, making use of available data components when possible. If medication name was missing, we applied an average prescription cost [from DHSC prescription cost analyses (PCA)], accounting for the reported number of days on that medication and assuming that the prescription lasted for 1 month. If number of days on medication was missing, a PCA average item cost for that medication was used, with the assumption that the patient was prescribed that medication just once in that period. If dose was missing, a PCA average item cost was used, assuming that each prescription lasted 1 month but accounting for the number of days on the medication. If the dose unit was missing, a PCA average item cost was used assuming that each prescription lasted 1 month, with an account of the number of days on medication. If dose frequency was missing, a PCA average item cost was used, assuming that each prescription lasted 1 month, again accounting for number of days. Finally, if it was unknown whether or not the medication was administered as a depot, a PCA average item cost was used assuming that each prescription lasted 1 month, accounting for the number of days on medication.

The primary analysis was undertaken using cases with available relevant cost and/or outcome data (i.e. excluding those lost to follow-up for the CSRI, EQ-5D-3L or SF-36 assessments, as relevant).

Cost-effectiveness and cost–utility analyses

Cost-effectiveness and cost–utility analyses were conducted at 15 months to focus on the more pertinent question of whether or not any effect lasted beyond the end of the intervention, but 12-month cost and outcome data are also reported for information. The economic evaluation examined eight possible cost–outcome combinations (accounting for the two cost perspectives and the four outcomes). Incremental cost-effectiveness ratios (ICERs) were calculated for any combination showing

both higher costs and better outcomes in either the intervention group or the control group (it was unnecessary to calculate ICERs for any combinations where one group showed both lower costs and better outcomes as this group was then considered to 'dominate' the other).

Uncertainty around cost-effectiveness/cost utility was explored using cost-effectiveness planes and cost-effectiveness acceptability curves based on the net-benefit approach. These curves are an alternative to CIs around ICERs and show the probability that one intervention is cost-effective compared with the other for a range of values that a decision-maker would be willing to pay for an additional unit of an outcome. Net benefits for each participant were calculated using the following formula, where λ is the willingness to pay for one additional unit of outcome: net benefit = ($\lambda \times$ outcome) – cost.

A series of net benefits were calculated for each individual for a λ range that would include any policy-making perspectives relevant at the time of analysis. After calculating net benefits for each participant for each value of λ, coefficients of differences in net benefits between the trial arms were obtained through a series of bootstrapped linear regressions (1000 repetitions) of group on net benefit that included the covariates used for the comparisons of mean costs and outcomes (i.e. baseline value of the same cost category, SF-36 MCS, SF-36 PCS, EQ-5D-3L utility score, SF-36 utility score, gender, age, ethnicity, place of birth and borough) and an adjustment for clustering by care co-ordinator. The resulting coefficients were then examined to calculate for each value of λ the proportion of times that the intervention group had a greater net benefit than the control group. These proportions were then plotted to generate cost-effectiveness acceptability curves for all eight cost–outcome combinations.

TABLE 9 Unit costs (IMPaCT) (2011/12 prices)

Item	Unit	Cost (£)	Source	Notes
Accommodation				
Supported housing	Day	100	Curtis[192]	Private-sector care home, excluding social services and benefits
Sheltered housing	Day	100	Curtis[192]	Private-sector care home, excluding social services and benefits
Hostel/shelter	Day	100	Curtis[192]	Private-sector care home, excluding social services and benefits
Inpatient services[a]				
Acute psychiatric ward	Bed-day	329	NHS[231]	TMHIP (Mental Health Inpatients) tab, MHIPA2 – adult: acute care
Psychiatric intensive care	Bed-day	647	NHS[231]	TMHIP (Mental Health Inpatients) tab, MHIPA1 – adult: intensive care
Medical ward	Bed-day	440	NHS[231]	Using activity data to calculate a cost per bed-day
Mother and baby unit	Bed-day	672	NHS[231]	TMHIPSS (Mental Health Inpatients: Specialist Services) tab, MHIPMB – mother and baby units
Accident and emergency department	Bed-day	112	NHS[231]	TA and EMSNA – Accident and Emergency Services: Not Leading to Admitted
Surgical ward	Bed-day	440	NHS[231]	Medical ward cost
Medium secure	Bed-day	499	NHS[231]	TMHSU (Mental Health Secure Units) tab, SCU3 – medium level secure services
Low secure	Bed-day	441	NHS[231]	TMHSU (Mental Health Secure Units) tab, SCU2 – low level secure services
High Down prison	Bed-day	69	Ministry of Justice[232]	Based on £26,139 per prisoner per year (deflated to 2011–12 costs)

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) (*continued*)

Item	Unit	Cost (£)	Source	Notes
Psychiatric rehabilitation	Bed-day	289	NHS[231]	TMHIP (Mental Health Inpatients) tab, MHIPA3 – adult: rehabilitation
Cardiology	Bed-day	453	NHS[231]	Using activity data to calculate a cost per bed-day for HRG chapter E items (cardiology)
Ear, nose and throat	Bed-day	440	NHS[231]	Medical ward cost
Older adults mental health	Bed-day	340	NHS[231]	TMHIP (Mental Health Inpatients: Specialist Services) tab, MHIPE1 – elderly
Stroke unit	Bed-day	325	NHS[231]	TNEI_L (Non-Elective Inpatient (Long Stay) HRG Data) tab, using activity data to calculate a cost per bed day for HRG items AA22A (Non-Transient Stroke or Cerebrovascular Accident, Nervous system infections or Encephalopathy with CC) +AA22B (Non-Transient Stroke or Cerebrovascular Accident, Nervous system infections or Encephalopathy without CC)
Acute medical ward	Bed-day	440	NHS[231]	Medical ward cost
Respiratory ward	Bed-day	326	NHS[231]	Using activity data to calculate a cost per bed-day for HRG chapter D items (respiratory system)
Emergency surgery	Bed-day	440	NHS[231]	Medical ward cost
Respite care	Bed-day	516	NHS[231]	TNEI_L (Non-Elective Inpatient (Long Stay) HRG Data) tab, PA55Z – respite care
Spinal injury unit	Bed-day	440	NHS[231]	Medical ward cost
Outpatient services[b]				
Psychiatry	Visit	171	NHS[231]	TMHCSOPFUAF tab (Mental Health Consultant Services (Outpatient Setting) – Follow-up Attendance Face to Face), MHOPFUA2 – adult other services
Non-psychiatric/general/medical	Visit	108	NHS[231]	Total – OPATT (Outpatient Attendances) tab, Total – Outpatient Attendances
Diabetes clinic	Visit	134	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 307 – diabetic medicine
Blood tests/phlebotomy	Visit	3	NHS[231]	TDAPS (Direct Access: Pathology Services) tab, DAP839 – Phlebotomy
Psychiatric day hospital	Visit	103	NHS[231]	TMHDCFRAD tab (Mental Health Day Care Facilities: Regular Attendances), DCF41 – Mental Health Patients Adult
Non-psychiatric/general/medical day hospital	Visit	686	NHS[231]	Index tab: TDC – Day Cases HRG Data
Day surgery centre	Visit	686	NHS[231]	Index tab: TDC – Day Cases HRG Data
Accident and emergency	Visit	117	NHS[231]	Index tab, average of all A&E tabs – TAandEMSAD (Accident and Emergency Services: Leading to Admitted), TAandEMSNA (Accident and Emergency Services: Not Leading to Admitted), TAandEMinAD (Accident and Emergency Services: Minor Injury Service: Leading to Admitted), TAandEMinNA (Accident and Emergency Services: Minor Injury Service: Not Leading to Admitted), TAandEWiCAD

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) *(continued)*

Item	Unit	Cost (£)	Source	Notes
				(Accident and Emergency Services: Walk In Centres: Leading to Admitted), TAandEWiCNA (Accident and Emergency Services: Walk In Centres: Not Leading to Admitted), TNon24HRDEPAD (Non 24 hr AandE/Casualty Department: Leading to Admitted), TNon24HRDEPNA (Non 24 hr AandE/Casualty Department: Not Leading to Admitted)
X-ray (X-ray only)	Visit	30	NHS[231]	Total – OPATT (Outpatient Attendances) Tab: DAPF – Direct Access Plain Film
Substance misuse clinic	Visit	99	NHS[231]	TMHCSOPFUAF tab (Mental Health Consultant Services (Outpatient Setting) – Follow-up Attendance Face to Face), MHOPFUA1 – adult drug and alcohol services
Dietetics	Visit	57	NHS[231]	Total – OPATT (Outpatient Attendances) Tab, Service Code 654 A – Adult dietetics
Electrocardiogram	Visit	58	NHS[231]	TDADS (Direct Access: Diagnostic Services) tab, DA09 – 24-hour ECG/BP monitoring
Ambulance	Visit	227	NHS[231]	Index tab, average of all paramedic activity – TPARA (Paramedic Services: Category A/Red), TPARB (Paramedic Services: Category B/Amber, TPARC (Paramedic Services: Category C/Green, TPARETU (Paramedic Services: Emergency Transfers/Urgents, TPARO (Paramedic Services: Other, TPARA(Act) (Paramedic Services: Category A/Red (Activity Data), TPARB(Act) (Paramedic Services: Category B/Amber (Activity Data), TPARC(Act) (Paramedic Services: Category C/Green (Activity Data), TPARETU(Act) (Paramedic Services: Emergency Transfers/Urgents (Activity Data), TPARO(Act) (Paramedic Services: Other (Activity Data)
Angiogram	Visit	125	NHS[231]	TDIAGIM_DA (Diagnostic Imaging: Direct Access) tab, average of all the fluoroscopy – RA16Z (Contrast Fluoroscopy Procedures less than 20 minutes), RA17Z (Contrast fluoroscopy Procedures 20–40 minutes), RA18Z (Contrast fluoroscopy Procedures more than 40 minutes), RA19Z (Mobile/Intraoperative Contrast Fluoroscopy Procedures less than 20 minutes), RA20Z (Mobile/Intraoperative Contrast Fluoroscopy Procedures 20–40 minutes), RA21Z (Mobile/Intraoperative Contrast Fluoroscopy Procedures more than 40 minutes)
Computerised tomography scan	Visit	93	NHS[231]	TDIAGIM_DA (Direct Access: Diagnostic Services) tab, average of all CT scans – RA08Z (Computerised Tomography Scan, one area, no contrast), RA09Z (Computerised Tomography Scan, one area with post contrast only), RA10Z (Computerised Tomography Scan, one area, pre and post contrast), RA11Z (Computerised Tomography Scan, two areas without contrast), RA12Z (Computerised

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) (*continued*)

Item	Unit	Cost (£)	Source	Notes
				Tomography Scan, two areas with contrast), RA13Z (Computerised Tomography Scan, three areas with contrast), RA14Z (Computerised Tomography Scan, more than three areas), RA50Z (Computerised Tomography Scan, three areas without contrast)
Chiropodist	Visit	44	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 653 – podiatry
Colonoscopy	Visit	360	NHS[231]	TOPROC (Outpatient Procedures) tab – mean of all colonoscopy procedures – FZ51Z (Diagnostic Colonoscopy 19 years and over), FZ52Z (Diagnostic Colonoscopy with biopsy 19 years and over), FZ53Z (Therapeutic Colonoscopy 19 years and over)
Chronic obstructive pulmonary disease clinic	Visit	153	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 340 – respiratory medicine
Computerised tomography scan	Visit	93	NHS[231]	TDIAGIM_DA (Direct Access: Diagnostic Services) tab, average of all CT scans – RA08Z (Computerised Tomography Scan, one area, no contrast), RA09Z (Computerised Tomography Scan, one area with post contrast only), RA10Z (Computerised Tomography Scan, one area, pre and post contrast), RA11Z (Computerised Tomography Scan, two areas without contrast), RA12Z (Computerised Tomography Scan, two areas with contrast), RA13Z (Computerised Tomography Scan, three areas with contrast), RA14Z (Computerised Tomography Scan, more than three areas), RA50Z (Computerised Tomography Scan, three areas without contrast)
Dental X-ray	Visit	30	NHS[231]	Total – OPATT (Outpatient Attendances) tab, DAPF – Direct Access Plain Film
Dentist	Visit	81	NHS[231]	Total – Other Currencies tab, CN20 row – community dental services
Diabetes eye test	Visit	134	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 307 – diabetic medicine
Endocrinology/urology	Visit	145	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 302 – endocrinology
Gynaecologist	Visit	122	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 502 – gynaecology
Hearing aid clinic	Visit	117	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 840 – audiology
Lung function clinic	Visit	153	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 340 – respiratory medicine
Lupus clinic	Visit	108	NHS[231]	Total – OPATT (Outpatient Attendances) tab, OPATT tab: Total – Outpatient Attendances

continued

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) (*continued*)

Item	Unit	Cost (£)	Source	Notes
Magnetic resonance imaging	Visit	180	NHS[231]	TDIAGIM_DA (Direct Access: Diagnostic Services) tab, mean of all MRI scans – RA01Z (Magnetic Resonance Imaging Scan, one area, no contrast), RA02Z (Magnetic Resonance Imaging Scan, one area, post contrast only), RA03Z (Magnetic Resonance Imaging Scan, one area, pre and post contrast), RA04Z (Magnetic Resonance Imaging Scan, two or three areas, no contrast), RA05Z (Magnetic Resonance Imaging Scan, two or three areas, with contrast), RA06Z (Magnetic Resonance Imaging Scan, more than three areas), RA07Z (Magnetic Resonance Imaging Scan, requiring extensive patient repositioning and/or more than one contrast agent)
Neurology assessment	Visit	173	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 400 – neurology
Ophthalmologist	Visit	86	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 130 – Ophthalmology
Physiotherapy	Visit	39	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 650 A – Physiotherapy Total Attendances – Adult (19 and Over)
Psychologist	Visit	136	Curtis[192]	£136 per hour of client contact – assumes 1-hour appointment, excludes qualification costs
Sexual health clinic	Visit	67	NHS[231]	Total – OPATT (Outpatient Attendances) tab, FPC – Sexual and Reproductive Health Clinic (previously referred to as Family Planning Clinic)
Thyroid clinic	Visit	108	NHS[231]	Total – OPATT (Outpatient Attendances) tab, OPATT tab: Total – Outpatient Attendances
Turning Point	Visit	35	Curtis[192]	Cost as care co-ordinator/key worker – £67 per hour of face-to-face contact; assumes 30-minute appointment, excludes qualification costs
Ultrasound scan	Visit	58	NHS[231]	TDIAGIM_DA (Direct Access: Diagnostic Services) tab, average of ultrasound under and over 20 minutes – RA23Z (Ultrasound Scan less than 20 minutes), RA24Z (Ultrasound Scan more than 20 minutes)
Community-based day services				
Individual therapy CMHT, etc.	Visit	68	NHS[231]	TCSCT (community therapy services) tab, N6A1 – Community Occupational Therapy Services: Adult – One-to-One
Individual therapy at home	Visit	95	NHS[231]	TCSCT (community therapy services) tab, N6A1 – Community Occupational Therapy Services: Adult – One-to-One - plus the proportion of district nurse home visit hour/ clinic hour proportion from Curtis 2010[233]
Group therapy, all locations	Visit	73	NHS[231]	TCSCT (community therapy services) tab, N6A2 – Community Occupational Therapy Services: Adult – Group Services
Medication monitoring/ administration, all locations	Visit	34	Curtis[192]	Cost as care co-ordinator

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) (continued)

Item	Unit	Cost (£)	Source	Notes
Music therapy, all locations	Visit	40	Cancer Research UK[234]	–
Art therapy, all locations	Visit	30	Curtis[192]	Cost as occupational therapist
Community-based professionals[c]				
Care co-ordinator at surgery	Occurrence	34	Curtis[192]	£67 per hour of face-to-face contact; assumes 30-minute appointment, excludes qualification costs
Care co-ordinator at home	Occurrence	47	Curtis[192]	As above, plus proportion of district nurse home visit hour/clinic hour proportion from Curtis 2010[233] (139%)
Care co-ordinator over telephone	Occurrence	10	Curtis[192]	As above; assumes same proportion of costs as a psychiatrist face to face vs. non-face to face (30%)
Home treatment team at surgery	Occurrence	188	NHS[231]	TMHSTSAF tab (Mental Health Specialist Teams: Adult – Face to Face), MHST20 (Crisis resolution home treatment teams)
Home treatment team at home	Occurrence	188	NHS[231]	As above
Home treatment team over telephone	Occurrence	60	NHS[231]	TMHSTSANF tab (Mental Health Specialist Teams: Adult – Non-Face to Face), MHST20 (Crisis resolution home treatment teams)
Crisis resolution team at surgery	Occurrence	188	NHS[231]	TMHSTSAF tab (Mental Health Specialist Teams: Adult – Face to Face), MHST20 (Crisis resolution home treatment teams)
Crisis resolution team at home	Occurrence	188	NHS[231]	As above
Crisis resolution team over telephone	Occurrence	60	NHS[231]	TMHSTSANF tab (Mental Health Specialist Teams: Adult – Non-Face to Face), MHST20 (Crisis resolution home treatment teams)
Early intervention team at surgery	Occurrence	177	NHS[231]	TMHSTSAF tab (mental health specialist teams: adult – face to face), MHST22 (early intervention in psychosis studies)
Early intervention team at home	Occurrence	177	NHS[231]	As above
Early intervention team over telephone	Occurrence	57	NHS[231]	TMHSTSANF tab (Mental Health Specialist Teams: Adult – Non-Face to Face), MHST22 (Early intervention in psychosis studies)
Community psychiatric nurse at surgery	Occurrence	34	Curtis[192]	Care co-ordinator – above
Community psychiatric nurse at home	Occurrence	47	Curtis[192]	Care co-ordinator – above
Community psychiatric nurse over telephone	Occurrence	10	Curtis[192]	Care co-ordinator – above
Social worker at surgery	Occurrence	78	Curtis[192]	£156 per hour of face-to-face contact, assume 30-minute appointment, excludes qualifications

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) (*continued*)

Item	Unit	Cost (£)	Source	Notes
Social worker at home	Occurrence	108	Curtis[192]	As above, with proportion of district nurse home visit hour/clinic hour proportion from PSSRU 2010 (139%)
Social worker over telephone	Occurrence	23	Curtis[192]	As above, assume same proportion of costs as a psychiatrist face to face vs. non-face to face (30%)
Psychiatrist at surgery	Occurrence	171	NHS[231]	TMHCSOPFUAF tab (Mental Health Consultant Services (Outpatient Setting) – Follow-up Attendance Face to Face), MHOPFUA2 (Adult other services)
Psychiatrist at home	Occurrence	238	NHS[231]	As above, with the proportion of district nurse home visit hour/clinic hour proportion from PSSRU 2010 (139%)
Psychiatrist over telephone	Occurrence	52	NHS[231]	TMHCSOPFUANF tab (Mental Health Consultant Services (Outpatient Setting) – Follow-up Attendance Non-Face to Face), MHOPFUA2 (Adult other services)
Psychologist at surgery	Occurrence	136	Curtis[192]	£136 per hour of client contact, assume 1-hour appointment, excludes qualification costs
Psychologist at home	Occurrence	189	Curtis[192]	As above, based on psychologist visit cost above but use the proportion of district nurse home visit hour/clinic hour proportion from PSSRU 2010 (139%)
Psychologist over telephone	Occurrence	41	Curtis[192]	As above, assume same proportion of costs as a psychiatrist face to face vs. non face to face (30%)
Psychotherapist at surgery	Occurrence	136	Curtis[192]	Assume same as a psychologist
Psychotherapist at home	Occurrence	189	Curtis[192]	Assume same as a psychologist
Psychotherapist over telephone	Occurrence	41	Curtis[192]	Assume same as a psychologist
Counsellor at surgery	Occurrence	59	Curtis[192]	£59 per consultation
GP at surgery	Occurrence	36	Curtis[192]	£36 per patient contact lasting 11.7 minutes, excludes qualification costs, including direct care staff costs
GP at home	Occurrence	92	Curtis[192]	£92 per patient out of surgery visit lasting 23.4 minutes, excludes qualification costs, including direct care staff costs
GP over telephone	Occurrence	22	Curtis[192]	£22 per telephone contact lasting 7.2 minutes, excludes qualification costs, including direct care staff costs
Blood test at GP surgery	Occurrence	12	Curtis[192]	Assume practice nurse
Blood test at home	Occurrence	16	Curtis[192]	Assume practice nurse
Diabetes nurse at surgery	Occurrence	12	Curtis[192]	Assume practice nurse
Diabetes nurse at home	Occurrence	16	Curtis[192]	Assume practice nurse
Diabetes nurse over telephone	Occurrence	7	Curtis[192]	Assume practice nurse
Practice nurse at surgery	Occurrence	12	Curtis[192]	£45 per hour of face-to-face contact, excluding qualifications assuming 15.5- (specified on p180) minute appointment
Practice nurse at home	Occurrence	16	Curtis[192]	As above, with the proportion of district nurse home visit hour/clinic hour proportion from Curtis 2010[233] (139%)

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) *(continued)*

Item	Unit	Cost (£)	Source	Notes
Practice nurse over telephone	Occurrence	7	Curtis[192]	As above, with same proportion of costs as a GP telephone call (61%)
District nurse at surgery	Occurrence	11	Curtis[192]	District nurse, with the proportion of clinic hour/home visit hour proportion from Curtis 2010[233] (72%)
District nurse at home	Occurrence	16	Curtis[192]	Community nurse including district, £61 per hour of home visiting including travel, excluding qualifications; assumes 15.5-minute appointment
District nurse over telephone	Occurrence	10	Curtis[192]	Assume same proportion of costs as a GP telephone call (61%)
Occupational therapist at surgery	Occurrence	30	Curtis[192]	NHS community occupational therapist – £30 per hour, assumes 1-hour meeting and excludes qualification costs
Occupational therapist at home	Occurrence	55	Curtis[192]	As above, with proportions of client time set down in PSSRU 2009–10 (183%) excluding qualifications
Occupational therapist over telephone	Occurrence	18	Curtis[192]	As above, with proportion of costs as a GP telephone call (61%)
Dietitian at surgery	Occurrence	72	NHS[231]	TOCS (Other Community Services) tab – N800 Dietetics Services
Dietitian at home	Occurrence	129	NHS[231]	As above, with proportions of client time set down in PSSRU 2009–10 (179%), excluding qualifications
Dietitian over telephone	Occurrence	44	NHS[231]	As above, with proportion of costs as a GP telephone call (61%)
Home help/care worker at home	Occurrence	12	Curtis[192]	Home care worker per hour of face-to-face contact, weighted average accounting for different rates for day/evening/weekday/weekends
Meals on wheels at home	Occurrence	5	Curtis[192]	Average of £6 local authority meal and £4 independent sector cost per day
Pharmacist for advice at surgery	Occurrence	4	Curtis[192]	£50, assuming 5-minute consultation; excludes qualification costs
Pharmacist for advice over telephone	Occurrence	4	Curtis[192]	As above
NHS Direct over telephone	Occurrence	16	NHS Direct[235]	Inflated to 2011/12 prices
Samaritans over telephone	Occurrence	4	National Register of Personal Trainers[236]	Inflated to 2011/12 prices
Other community-based professionals				
Advocate at surgery	Occurrence	76	Curtis[192]	Cost as an independent mental capacity advocates assessment
Advocate at home	Occurrence	106	Curtis[192]	As above, with the proportion of district nurse home visit hour/clinic hour proportion from Curtis 2010[233] (139%)
Podiatrist at surgery	Occurrence	15	Curtis[192]	Community chiropodist – £30 per hour; assumes 30-minute appointment
Podiatrist at home	Occurrence	42	Curtis[192]	As above, with proportion of district nurse home visit hour/clinic hour proportion from Curtis 2010[233] (139%)

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) (*continued*)

Item	Unit	Cost (£)	Source	Notes
CMHT bloods at surgery	Occurrence	12	Curtis[192]	Cost as GP surgery blood test
Emergency service over telephone	Occurrence	16	NHS Direct[235]	Cost as NHS Direct
Depot at GP surgery	Occurrence	12	Curtis[192]	Cost as practice nurse
Depot clinic surgery	Occurrence	6	Curtis[192]	Cost as community psychiatric nurse for 5 minutes
Diabetes eye test at surgery	Occurrence	134	NHS[231]	Total – OPATT (Outpatient Attendances) tab, 307 – diabetic medicine
Employment support worker at surgery	Occurrence	30	Curtis[192]	Cost as occupational therapist
Forensic team at surgery	Occurrence	34	Curtis[192]	Cost as care co-ordinator
Forensic team at home	Occurrence	47	Curtis[192]	Cost as care co-ordinator
Gym practitioner (GP referral) at surgery	Occurrence	60	National Register of Personal Trainers[236]	Costs between £20 and £100; chose mid-point – £60
Human immunodeficiency virus clinic at surgery	Occurrence	110	NHS[231]	TCSCNSN (community and outreach nursing services: specialist nursing) tab, CN208AF – band 8 – human immunodeficiency virus/acquired immunodeficiency syndrome nursing services: adult: face to face
Welfare benefits advisor at home	Occurrence	78	Curtis[192]	Cost as social worker
Housing officer at home	Occurrence	78	Curtis[192]	Cost as social worker
Lifestyle coach at surgery	Occurrence	70	Life Coach Directory[237]	Costs ranged between £40 and £100; chose mid-point
Mental health helpline over telephone	Occurrence	4	Samaritans[238]	Cost as Samaritans
Mind Advocates over telephone	Occurrence	23	Curtis[192]	Cost as advocate, with proportion of costs as a psychiatrist face to face vs. non-face to face (30%)
Osteopath at surgery	Occurrence	43	NHS Choices[239]	Costs ranged between £35 and £50 per 30- to 40-minute contact; chose mid-point
Probation officer at surgery	Occurrence	78	Curtis[192]	Cost as social worker
Spirit Release Session at surgery	Occurrence	38	Cancer Research UK[240]	Costs ranged between £15–60 per session; chose mid-point
Support worker at surgery	Occurrence	11	Curtis[192]	Clinical support worker – assumes 30-minute appointment
Support worker at home	Occurrence	15	Curtis[192]	As above, with proportion of district nurse home visit hour/clinic hour proportion from Curtis 2010[233] (139%)
Benefits				
Patient social security benefits/tax credits	Week	53.45	Direct Gov[241]	Employment and support personal allowance – assumes single < 25 years
Patient disability living allowance				
Higher	Week	73.60	Direct Gov[241]	Assumes the care component
Middle	Week	49.30	Direct Gov[241]	–
Lower	Week	19.55	Direct Gov[241]	–

TABLE 9 Unit costs (IMPaCT) (2011/12 prices) (*continued*)

Item	Unit	Cost (£)	Source	Notes
Carer benefit				
Higher	Week	55.55	Direct Gov[241]	–
Middle	Week	55.55	Direct Gov[241]	–
Lower	Week	55.55	Direct Gov[241]	–

a All long stay, non-elective, non-excess: all costs in 2010–11 prices and inflated to 2011–12 prices using the Hospital and Community Health Services index pay and prices index from Curtis.[192]
b All costs from NHS[231] are inflated to 2011–12 prices using the Hospital and Community Health Services index pay and prices index from Curtis.[192]
c All costs from NHS,[231] NHS Direct[235] and National Register of Personal Trainers[236] are inflated to 2011–12 prices using the Hospital and Community Health Services index pay and prices index from Curtis.[192]
Sources: NHS. NHS trust reference cost schedules 2010–11.[191] Inflated up to 2011–12 prices using the retail price inflation percentage from PSSRU 2012/13. URL: www.dh.gov.uk/en/Publicationsandstatistics/Publications/Publications PolicyAndGuidance/DH_131140 (accessed 19 February 2013).

TABLE 10 Resources and costs associated with the interventions

Component	Control			HPI		
	Resources	Details	Unit cost (£)	Resources	Details	Mean cost (£)
Manual	–	–	0	Development[a] Printing[b]	£35.68 per care co-ordinator, divided by a recommended average of 20 patients per care co-ordinator	1.78
Training						
Trainer's time	Consultant psychiatrist[c] (90 minutes)	£186 divided by 25 attendees, divided by a recommended average of 20 patients per care co-ordinator	0.37	Band 6 nurse[d] Band 8a nurse[e] Psychologist band 8d[f] Consultant psychiatrist[g] (total 29 hours)	Cost of £2336 divided by an average of five care co-ordinators per training course, divided by a recommended average of 20 patients per care co-ordinator	23.36
Attendee's time	Band 6 nurse[h] (90 minutes)	£63 per care co-ordinator, divided by a recommended average of 20 patients per care co-ordinator	3.15	Band 6 nurse[i] (total 32 hours)	£1344 per care co-ordinator divided by a recommended average of 20 patients per care co-ordinator	67.20
Materials	–	None	0	One-off items: BP machine[j] Weighing scales[k] Tape measure[l] Flip-chart stand[m] Memory stick[n]	£20.97 divided by nine training courses, divided by five care co-ordinators per course, divided by a recommended average of 20 patients per care co-ordinator £6.49 per care co-ordinator, divided by a recommended	0.02 0.32

TABLE 10 Resources and costs associated with the interventions (*continued*)

Component	Control		Unit cost (£)	HPI		Mean cost (£)
	Resources	Details		Resources	Details	
				Consumables:	average of 20 patients per care co-ordinator	
				Flip-chart paper[o]		
				Flip-chart pens[p]		
				Paper[q]		
				Pens[r]		
Supervision	–	None	0	Training supervisor: band 8 nurse[s] Care co-ordinator: band 6 nurse[t] (90 minutes)	£150 per session, per care co-ordinator, divided by a recommended average of 20 patients per care co-ordinator	41.41
Implementation	–	Implemented into therapy as part of continuing care	0	Band 6 nurse[u] (individual times)	Individually calculated for each participant based on number and type of sessions attended	92.31
Mean total cost (£)	3.52 per control participant			226.40 per intervention participant		

a Sunk cost: £0.
b Based on actual printing cost: £35.68 for all three documents.
c Based on a consultant psychiatrist: £124 per contract hour, excluding qualifications, for 90 minutes of training.[192]
d Based on a community nurse: £42 per hour, excluding qualifications, for 150 minutes of training plus 10 minutes' preparation time (160 minutes total).[192]
e Based on a band 8 nurse: £58 per hour (based on the same working time assumptions as applied to a band 6 nurse), excluding qualifications, for 810 minutes of training plus 40 minutes' preparation time (850 minutes in total).[192]
f Based on band 8d psychologist: £102 per hour (based on the same working time assumptions as applied to a band 8a psychologist) excluding qualifications, for 270 minutes of training plus 20 minutes' preparation time (290 minutes in total).[192]
g Based on a consultant psychiatrist: £124 per contract hour, excluding qualifications, for 420 minutes' training plus 20 minutes' preparation time (440 minutes in total).[192]
h Based on a community nurse: £42 per hour, excluding qualification costs, for 90 minutes of training.[192]
i Based on a community nurse: £42 per hour, excluding qualification costs, for 32 hours of training (9.00–17.00 for 4 days including break times).[192]
j £6.66 per machine, based on a purchase price of £30.60 deflated to correct year and annuitised by 4% assuming 5-year life. Source: www.boots.com/en/Boots-Pharmaceuticals-Basic-Blood-Pressure-Upper-Arm-Monitor_1014526/; accessed 26 February 2014.
k £1.74 per scales, based on a purchase price of £7.99 deflated to correct year and annuitised by 4% assuming 5-year. Source: www.amazon.co.uk/Jazooli-Digital-Bathroom-Electronic-Weighing/dp/B00H29ASC2/ref=sr_1_17?s=drugstore&ie=UTF8&qid=1393413251&sr=1–17&keywords=digital+weighing+scales; accessed 26 February 2014.
l £0.22 per tape measure, based on a purchase price of £1.00 deflated to correct year and annuitised by 4% assuming 5-year life. Source: www.amazon.co.uk/150cm-Plastic-Tailor-Sewing-Measure/dp/B0081OW708/ref=sr_1_10?ie=UTF8&qid=1393413801&sr=8–10&keywords=tape+measure+body; accessed 26 February 2014.
m £11.23 per stand, based on a purchase price of £51.59 deflated to correct year and annuitised by 4% assuming 5-year life. Source: www.viking-direct.co.uk/a/pb/niceday-Classic-Easel-900H-x-600Wmm/pr=Q22&id=5341293/; accessed 26 February 2014.
n £1.12 per stick, based on a purchase price of £5.15 deflated to correct year and annuitised by 4% assuming 5-year life. Source: www.viking-direct.co.uk/a/pb/Ativa-4GB-USB-Flash-Drive/pr=Q22&id=978944/; accessed 26 February 2014.
o £0.93 per care co-ordinator, based on £23.99 per pack of five, using one pad per training course, deflated to correct year and divided by an average of five care co-ordinators per training course. Source: www.viking-direct.co.uk/a/pb/Niceday-A1-Flipchart-Pads-Pack-of-5/pr=Q22&id=2650338/; accessed 26 February 2014.
p £1.58 per care co-ordinator, based on £8.15 per pack, deflated to correct year and divided by an average of five care co-ordinators per training course. Source: www.viking-direct.co.uk/a/pb/niceday-Bullet-Tip-Assorted-1-x-Black-Blue-Red-Green-Orange-Purple-Flipchart-Markers-6pk/pr=Q22&id=1644422/; accessed 26 February 2014.

q £2.52 per care co-ordinator, based on £7.79 per pack of three (one per care co-ordinator) and deflated to correct year. Source: www.viking-direct.co.uk/a/pb/Pukka-Reporters-160-Page-White-Pad-205-x-140mm-3pk/pr=Q22&id=1087752/; accessed 26 February 2014.

r £0.35 per care co-ordinator, based on £3.59 per pack of 10 (one per care co-ordinator) and deflated to correct year. Source: www.viking-direct.co.uk/a/pb/Bic-Cristal-Medium-10mm-Ballpoint-Pen-Black-Pack-of-10/pr=Q22&id=103-BK/; accessed 26 February 2014.

s Based on a band 8 nurse: £58 per hour (based on the same working time assumptions as applied to a band 6 nurse) excluding qualifications, 90-minute supervisions multiplied by number of supervisions.[192]

t Based on £42 per hour, excluding qualifications, 90-minute supervisions multiplied by number of supervisions.[192]

u Based on a community nurse: £42 per hour (£58.38 for contacts not at the care co-ordinator's base) based on the same travel time assumptions as applied to a band 6 nurse,[233] excluding qualifications.[192]

Sensitivity analyses

We conducted four sensitivity analyses to check the robustness of the base-case analyses defined above. First, we explored the potential impact of excluding those lost to follow-up. We examined key sociodemographic and clinical characteristics for those included and those excluded from the analyses and conducted an intention-to-treat analysis, which included those lost to follow-up by imputing missing total costs and outcomes using imputation in Stata 13. Imputations of costs and outcomes were based on variables that were expected to predict costs and outcomes. For cost imputations, these variables were baseline and 12-month values for the equivalent cost category, the SF-36 MCS, SF-36 PCS, EQ-5D-3L utility score, SF-36 utility score, plus gender, ethnicity, borough, age, place of birth and care co-ordinator. Imputation of outcomes was based on baseline and 12-month values of the SF-36 MCS, SF-36 PCS, EQ-5D-3L utility score, SF-36 utility score, plus gender, age, ethnicity, place of birth and borough, and care co-ordinator.

Second, to explore the potential impact of having follow-up interviews conducted more than 30 days before or after the follow-up date, we conducted a 'correct time window' analysis including only those trial participants whose data were collected within the correct window (within 30 days either side of the planned assessment date).

Third, to explore the potential impact of insufficient implementation of the HPI, we conducted a per-protocol analysis that included only those intervention arm trial participants who received the predefined minimum of six intervention sessions of at least 30 minutes each.

Finally, to explore the potential impact of care co-ordinator dropout, we conducted analyses that included only those trial participants whose care co-ordinator remained the same throughout the study.

For each of these sensitivity analyses, we examined whether or not the conclusions concerning the mean difference in costs or outcomes between the two trial arms differed from those drawn from the base-case analyses.

Economic evaluation results

In line with the analysis of the primary outcome measure and other clinical outcomes, the economic evaluation was based on all 406 participants who were randomised. We summarise the response rates in *Tables 12–14*.

Table 15 summarises the joint availability of both cost and outcome data at 15 months (a requirement for the constructions of CEACs), by outcome measure. Equivalent data are also provided for the 12-month follow-up for information.

Tables 16 and *17* suggest that there were no notable differences in the baseline characteristics of the subsamples included in the base-case analyses of those with available data against the full sample.

TABLE 11 Staff resourcing for the HPI training programme

Trainer staff type	Number of sessions delivered	Total training time (minutes)	Total preparation time (minutes)
Nurse band 6	1	150	10
Nurse band 8a	4	810	40
Psychologist band 8d	2	270	20
Consultant psychiatrist	2	420	20

TABLE 12 Client Service Receipt Inventory response rates

	Time point, n (%)			
Trial group	Baseline	12 months	15 months	All time points, n (%)
Intervention (N = 213)	212 (100)	160 (75)	152 (71)	138 (65)
Control (N = 193)	193 (100)	159 (82)	149 (77)	143 (74)
Total (N = 406)	405 (98)	319 (79)	301 (74)	281 (69)
Percentages are rounded to nearest whole number.				

TABLE 13 The SF-36 and EQ-5D-3L response rates

		Time point, n (%)			All time points, n (%)
Outcome	Trial group	Baseline	12 months	15 months	
SF-36	Intervention (N = 213)	210 (99)	158 (74)	149 (70)	132 (62)
	Control (N = 193)	192 (100)	155 (80)	148 (77)	138 (72)
	Total (N = 406)	402 (99)	313 (77)	297 (73)	270 (67)
EQ-5D-3L	Intervention (N = 213)	211 (99)	159 (75)	152 (71)	136 (64)
	Control (N = 193)	193 (100)	156 (81)	149 (77)	140 (73)
	Total (N = 406)	404 (100)	315 (78)	301 (74)	276 (68)
Percentages are rounded to nearest whole number.					

TABLE 14 Availability of intervention data

Trial group	n (%)
Intervention (n = 213)	213 (100)
Control (n = 193)	193 (100)
Total (n = 406)	406 (100)

TABLE 15 Availability of both cost and outcome data, by outcome measure

		Time point, n (%)		
Outcome	Trial group	12 months	15 months	Both 12 and 15 months
SF-36	Intervention (n = 213)	157 (74)	149 (70)	131 (62)
	Control (n = 193)	154 (80)	147 (76)	137 (71)
	Total (n = 406)	311 (77)	296 (73)	268 (66)
EQ-5D-3L	Intervention (n = 213)	158 (74)	152 (71)	135 (63)
	Control (n = 193)	155 (80)	148 (77)	139 (72)
	Total (n = 406)	313 (77)	300 (74)	274 (68)

Percentages are rounded to nearest whole number.

TABLE 16 Baseline characteristics of full sample and subsample with cost and SF-36 data

		Subsample	
Characteristic	Full sample (N = 406)	With 12-month costs and SF-36 data (N = 311)	With 15-month costs and SF-36 data (N = 296)
Gender, n (%)			
Male	234 (58)	183 (59)	172 (58)
Female	172 (42)	128 (41)	124 (42)
Ethnicity, n (%)			
White	222 (55)	174 (56)	170 (58)
Black	137 (34)	102 (33)	97 (33)
Asian	15 (4)	11 (4)	11 (4)
Mixed or other	29 (7)	23 (7)	17 (6)
Place of birth, n (%)			
UK	318 (78)	251 (81)	237 (80)
Other	88 (22)	60 (19)	59 (20)
Borough, n (%)			
Croydon	58 (14)	51 (16)	48 (16)
Lambeth	44 (11)	31 (10)	31 (11)
Lewisham	84 (21)	62 (20)	54 (18)
Southwark	83 (20)	66 (21)	66 (22)
Greenwich	30 (7)	26 (8)	26 (9)
Bromley	34 (8)	24 (8)	25 (9)
Bexley	23 (6)	18 (6)	18 (6)
East Sussex	23 (6)	20 (6)	20 (7)
Somerset	17 (4)	5 (2)	8 (3)
South Staffordshire	10 (3)	8 (3)	0 (0)
Age (years), mean (SD)	44 (10)	45 (10)	45 (10)
SF-36 MCS, mean score (SD)	43 (13)	43 (13)	43 (13)
SF-36 PCS, mean score (SD)	48 (11)	48 (11)	48 (11)

Percentages and SDs are rounded to nearest whole number.

TABLE 17 Baseline characteristics of full sample and subsample with cost and EQ-5D-3L data

| Characteristic | Full sample (N = 406) | Subsample | |
		With 12-month costs and EQ-5D-3L data (N = 313)	With 15-month costs and EQ-5D-3L data (N = 300)
Gender, n (%)			
Male	234 (58)	183 (49)	174 (58)
Female	172 (42)	130 (42)	126 (42)
Ethnicity, n (%)			
White	222 (55)	175 (56)	172 (58)
Black	137 (34)	102 (33)	98 (33)
Asian	15 (4)	12 (4)	11 (4)
Mixed or other	29 (7)	23 (7)	18 (60
Place of birth, n (%)			
UK	318 (78)	253 (81)	241 (80)
Other	88 (22)	60 (19)	59 (20)
Borough, n (%)			
Croydon	58 (14)	51 (16)	48 (16)
Lambeth	44 (11)	31 (10)	31 (10)
Lewisham	84 (21)	63 (20)	55 (18)
Southwark	83 (20)	66 (21)	66 (22)
Greenwich	30 (7)	26 (8)	27 (9)
Bromley	34 (8)	25 (8)	25 (8)
Bexley	23 (6)	18 (6)	18 (6)
East Sussex	23 (6)	20 (3)	20 (7)
Somerset	17 (4)	5 (2)	10 (3)
South Staffordshire	10 (3)	8 (3)	0 (0)
Age (years), mean (SD)	44 (10)	45 (10)	43 (11)
SF-36 MCS, mean score (SD)	43 (13)	43 (13)	43 (13)
SF-36 PCS, mean score (SD)	48 (11)	48 (11)	48 (11)

Percentages and SDs are rounded to nearest whole number.

Resource use

Resource use pattern data suggest that both arms were broadly balanced in their use of core services both before and during the study. These data are available for reference in *Tables 18–20*. As would be expected for this group of patients, service use is very broad in both nature and sector, illustrating the complexity of their care provision. These data were not compared statistically because the economic evaluation was focused on costs and cost-effectiveness/utility, and to avoid problems associated with multiple testing.

Costs

There were 52 care co-ordinators in the intervention group and a total of 213 patient participants with whom they implemented the HPI. The mean number of trial participants per care co-ordinator was four (range 1–10 participants). The total average cost per case in the intervention arm was £226.40, compared with £3.52 in the control arm.

TABLE 18 Resource use at baseline (for the previous 6 months)

Resource	Unit	Trial group					
		Intervention (N = 212)			Control (N = 193)		
		Users (n)	Meanª	SD	Users (n)	Meanª	SD
Specialist accommodation							
Supported housing/assisted living	Bed-day	51	157	50	42	166	44
Sheltered housing	Bed-day	3	154	48	6	170	29
Hostel/shelter	Bed-day	7	120	83	6	182	0
Hospital inpatient							
Inpatient	Bed-day	60	155	54	54	168	40
Hospital outpatient							
Psychiatric outpatient	Visit	35	4	5	49	3	4
Non-psychiatric/general/medical outpatient	Visit	29	3	4	22	2	1
Diabetes clinic	Visit	15	2	2	13	2	1
Blood tests	Visit	95	5	4	84	4	3
Psychiatric day hospital	Visit	12	18	33	3	58	9
Non-psychiatric/general/medical day hospital	Visit	3	1	0	3	1	1
Day surgery centre	Visit	7	2	2	7	2	2
Accident and emergency department	Visit	32	2	2	23	1	1
X-ray	Visit	24	1	1	27	1	1
Substance misuse clinic	Visit	13	9	8	7	7	9
Dietetics	Visit	7	3	2	9	3	2
Community-based day services							
Community-based services	Visit	72	34	32	73	29	31
Community-based professionals							
Care co-ordinator	Surgery visit	129	10	8	132	9	6
Care co-ordinator	Home visit	107	10	9	83	8	7
Care co-ordinator	Telephone call	39	10	19	28	7	8
Home treatment team	Surgery visit	3	2	1	4	3	2
Home treatment team	Home visit	10	9	12	14	11	12
Home treatment team	Telephone call	1	1	–	2	3	1
Crisis resolution team	Surgery visit	0	–	–	0	–	–
Crisis resolution team	Home visit	8	7	7	3	3	1
Crisis resolution team	Telephone call	1	1	–	1	1	–
Early intervention team	Surgery visit	0	–	–	0	–	–
Early intervention team	Home visit	2	10	6	0	–	–
Early intervention team	Telephone call	0	–	–	0	–	–
Community psychiatric nurse	Surgery visit	13	7	7	6	5	4
Community psychiatric nurse	Home visit	5	5	3	1	4	–
Community psychiatric nurse	Telephone call	3	4	4	3	3	1
Social worker	Surgery visit	18	1	1	22	2	2

TABLE 18 Resource use at baseline (for the previous 6 months) (*continued*)

Resource	Unit	Intervention (N = 212)			Control (N = 193)		
		Users (*n*)	Mean[a]	SD	Users (*n*)	Mean[a]	SD
Social worker	Home visit	1	12	–	3	3	3
Social worker	Telephone call	2	4	4	1	1	–
Psychiatrist	Surgery visit	85	3	5	75	3	4
Psychiatrist	Home visit	6	5	9	9	2	1
Psychiatrist	Telephone call	0	–	–	0	–	–
Psychologist	Surgery visit	19	8	9	20	9	8
Psychologist	Home visit	3	11	2	2	12	0
Psychologist	Telephone call	0	–	–	0	–	–
Psychotherapist	Surgery visit	1	5	–	3	12	11
Psychotherapist	Home visit	1	12	–	1	6	–
Psychotherapist	Telephone call	0	–	–	0	–	–
Counsellor	Surgery visit	26	3	5	19	3	5
Counsellor	Home visit	0	–	–	1	1	–
Counsellor	Telephone call	0	–	–	0	–	–
GP	Surgery visit	119	4	7	108	3	3
GP	Home visit	3	2	1	2	2	1
GP	Telephone call	1	2	–	1	1	–
Blood test at GP	Surgery visit	47	2	2	47	2	1
Diabetes nurse	Surgery visit	11	2	1	10	1	< 1
Diabetes nurse	Home visit	0	–	–	0	–	–
Diabetes nurse	Telephone call	0	–	–	2	1	0
Practice nurse	Surgery visit	27	3	5	31	2	2
Practice nurse	Home visit	0	–	–	0	–	–
Practice nurse	Telephone call	1	1	–	0	–	–
District nurse	Surgery visit	1	120	–	1	1	–
District nurse	Home visit	0	–	–	2	2	107
District nurse	Telephone call	0	–	–	0	–	–
Occupational therapist	Surgery visit	8	7	8	8	9	10
Occupational therapist	Home visit	0	–	–	2	5	4
Occupational therapist	Telephone call	0	–	–	0	–	–
Dietitian	Surgery visit	7	2	2	12	2	2
Dietitian	Home visit	0	–	–	1	1	–
Dietitian	Telephone call	0	–	–	0	–	–
Home help	Home visit	11	57	72	6	32	37
Meals on wheels	Home visit	0	–	–	2	2	1
Pharmacist for advice	Surgery visit	21	2	2	20	2	2
Pharmacist for advice	Home visit	1	2	–	0	–	–
Pharmacist for advice	Telephone call	0	–	–	1	2	–

TABLE 18 Resource use at baseline (for the previous 6 months) (*continued*)

Resource	Unit	Trial group					
		Intervention (*N* = 212)			Control (*N* = 193)		
		Users (*n*)	Mean[a]	SD	Users (*n*)	Mean[a]	SD
NHS Direct	Telephone call	3	1	1	6	2	1
Samaritans	Telephone call	3	5	5	2	52	62
Medication		208	–	–	191	–	–

a Mean for users only.
All quantities are rounded to nearest whole number.

TABLE 19 Resource use at the 12-month follow-up (for the previous 6 months)

Resource	Unit	Trial group					
		Intervention (*N* = 160)			Control (*N* = 159)		
		Users (*n*)	Mean[a]	SD	Users (*n*)	Mean[a]	SD
Specialist accommodation							
Supported housing/assisted living	Bed-day	37	182	1	30	179	12
Sheltered housing	Bed-day	1	182	–	6	158	60
Hostel/shelter	Bed-day	4	182	0	5	152	68
Hospital inpatient							
Inpatient	Bed-day	42	182	1	41	173	34
Hospital outpatient							
Psychiatric outpatient	Visit	13	4	2	6	2	1
Non-psychiatric/general/medical outpatient	Visit	14	3	2	16	2	2
Diabetes clinic	Visit	11	3	3	9	1	1
Blood tests	Visit	79	5	4	69	4	3
Psychiatric day hospital	Visit	2	2	1	1	6	-
Non-psychiatric/general/medical day hospital	Visit	2	1	0	2	4	4
Day surgery centre	Visit	4	2	1	6	1	0
Accident and emergency department	Visit	22	2	4	19	2	1
X-ray	Visit	23	1	1	14	1	< 1
Substance misuse clinic	Visit	3	10	12	3	7	4
Dietetics	Visit	4	2	3	1	1	–
Community-based day services							
Community-based services	Visit	70	44	40	63	40	36
Community-based professionals							
Care co-ordinator	Surgery visit	95	9	7	98	7	7
Care co-ordinator	Home visit	67	9	8	64	8	8
Care co-ordinator	Telephone call	32	8	10	29	6	7
Home treatment team	Surgery visit	1	1	–	1	1	–

TABLE 19 Resource use at the 12-month follow-up (for the previous 6 months) (*continued*)

| | | Trial group | | | | | |
| | | Intervention (*N* = 160) | | | Control (*N* = 159) | | |
Resource	Unit	Users (*n*)	Mean[a]	SD	Users (*n*)	Mean[a]	SD
Home treatment team	Home visit	10	17	11	3	13	7
Home treatment team	Telephone call	1	2	–	0	–	–
Crisis resolution team	Surgery visit	1	3	–	0	–	–
Crisis resolution team	Home visit	1	2	–	0	–	–
Crisis resolution team	Telephone call	1	2	–	0	–	–
Early intervention team	Surgery visit	0	–	–	0	–	–
Early intervention team	Home visit	0	–	–	0	–	–
Early intervention team	Telephone call	0	–	–	0	–	–
Community psychiatric nurse	Surgery visit	1	6	–	2	4	4
Community psychiatric nurse	Home visit	2	5	2	3	3	3
Community psychiatric nurse	Telephone call	0	–	–	0	–	–
Social worker	Surgery visit	4	3	3	5	2	1
Social worker	Home visit	2	9	4	2	3	2
Social worker	Telephone call	0	–	–	0	–	–
Psychiatrist	Surgery visit	85	2	2	86	2	4
Psychiatrist	Home visit	7	5	9	8	6	8
Psychiatrist	Telephone call	0	–	–	0	–	–
Psychologist	Surgery visit	10	11	10	15	11	13
Psychologist	Home visit	1	14	–	1	24	–
Psychologist	Telephone call	0	–	–	1	1	–
Psychotherapist	Surgery visit	1	4	–	1	3	–
Psychotherapist	Home visit	0	–	–	0	–	–
Psychotherapist	Telephone call	0	–	–	0	–	–
Counsellor	Surgery visit	9	4	5	5	4	2
Counsellor	Home visit	0	–	–	0	–	–
Counsellor	Telephone call	0	–	–	0	–	–
GP	Surgery visit	110	3	3	104	3	4
GP	Home visit	1	3	–	2	3	2
GP	Telephone call	1	1	–	1	1	–
Blood test at GP	Surgery visit	38	2	1	44	2	2
Diabetes nurse	Surgery visit	9	2	4	6	2	1
Diabetes nurse	Home visit	0	–	–	0	–	–
Diabetes nurse	Telephone call	0	–	–	3	1	0
Practice nurse	Surgery visit	33	3	3	21	11	39
Practice nurse	Home visit	0	–	–	1	6	–
Practice nurse	Telephone call	1	2	–	0	–	–
District nurse	Surgery visit	2	6	6	0	–	–
District nurse	Home visit	0	–	–	0	–	–

TABLE 19 Resource use at the 12-month follow-up (for the previous 6 months) (continued)

Resource	Unit	Trial group					
		Intervention (N = 160)			Control (N = 159)		
		Users (n)	Meanª	SD	Users (n)	Meanª	SD
District nurse	Telephone call	0	–	–	0	–	–
Occupational therapist	Surgery visit	4	6	7	2	6	4
Occupational therapist	Home visit	4	22	34	2	3	0
Occupational therapist	Telephone call	1	2	–	1	2	–
Dietitian	Surgery visit	3	1	0	6	3	3
Dietitian	Home visit	0	–	–	0	–	–
Dietitian	Telephone call	0	–	–	0	–	–
Home help	Home visit	11	53	52	7	61	59
Meals on wheels	Home visit	2	13	16	0	–	–
Pharmacist for advice	Surgery visit	16	2	2	14	3	2
Pharmacist for advice	Home visit	0	–	–	0	–	–
Pharmacist for advice	Telephone call	2	1	0	0	–	–
NHS Direct	Telephone call	0	–	–	2	2	1
Samaritans	Telephone call	5	79	90	4	24	45
Medication		159	–	–	158	–	–

a Mean for users only.
All quantities are rounded to nearest whole number.

TABLE 20 Resource use at the 15-month follow-up (for the previous 3 months)

Resource	Unit	Trial group					
		Intervention (N = 152)			Control (N = 149)		
		Users (n)	Meanª	SD	Users (n)	Meanª	SD
Specialist accommodation							
Supported housing/assisted living	Bed-day	36	90	3	30	90	3
Sheltered housing	Bed-day	2	70	30	6	91	0
Hostel/shelter	Bed-day	1	81	–	5	91	0
Hospital inpatient							
Inpatient	Bed-day	39	90	8	41	90	2
Hospital outpatient							
Psychiatric outpatient	Visit	8	2	1	1	1	–
Non-psychiatric/general/medical outpatient	Visit	7	1	< 1	10	2	2
Diabetes clinic	Visit	4	1	0	6	1	0
Blood tests	Visit	63	2	2	56	3	1
Psychiatric day hospital	Visit	2	5	1	0	–	–
Non-psychiatric/general/medical day hospital	Visit	1	2	–	3	1	0

TABLE 20 Resource use at the 15-month follow-up (for the previous 3 months) (*continued*)

| Resource | Unit | Trial group | | | | | |
| | | Intervention (N = 152) | | | Control (N = 149) | | |
		Users (*n*)	Mean[a]	SD	Users (*n*)	Mean[a]	SD
Day surgery centre	Visit	3	1	0	2	1	0
Accident and emergency department	Visit	15	1	1	15	1	1
X-ray	Visit	10	1	0	12	1	1
Substance misuse clinic	Visit	2	24	17	1	1	–
Dietetics	Visit	2	1	0	2	1	0
Community-based day services							
Community-based services	Visit	57	20	19	50	26	25
Community-based professionals							
Care co-ordinator	Surgery visit	78	5	6	70	4	4
Care co-ordinator	Home visit	59	5	3	52	4	3
Care co-ordinator	Telephone call	28	5	6	26	5	5
Home treatment team	Surgery visit	2	2	1	1	8	–
Home treatment team	Home visit	7	9	8	4	12	13
Home treatment team	Telephone call	0	–	–	0	–	–
Crisis resolution team	Surgery visit	1	1	–	0	–	–
Crisis resolution team	Home visit	1	1	–	1	1	–
Crisis resolution team	Telephone call	0	–	–	0	–	–
Early intervention team	Surgery visit	1	36	–	0	–	–
Early intervention team	Home visit	0	–	–	0	–	–
Early intervention team	Telephone call	0	–	–	0	–	–
Community psychiatric nurse	Surgery visit	6	6	4	13	4	2
Community psychiatric nurse	Home visit	2	4	1	3	1	1
Community psychiatric nurse	Telephone call	3	8	10	4	5	5
Social worker	Surgery visit	2	8	6	4	5	5
Social worker	Home visit	0	–	–	2	7	7
Social worker	Telephone call	0	–	–	1	5	–
Psychiatrist	Surgery visit	65	1	1	60	1	1
Psychiatrist	Home visit	3	5	6	5	4	5
Psychiatrist	Telephone call	0	–	–	0	–	–
Psychologist	Surgery visit	14	6	5	8	5	5
Psychologist	Home visit	1	10	–	0	–	–
Psychologist	Telephone call	0	–	–	0	–	–
Psychotherapist	Surgery visit	2	10	3	0	–	–
Psychotherapist	Home visit	0	–	–	1	1	–
Psychotherapist	Telephone call	0	–	–	0	–	–
Counsellor	Surgery visit	3	2	2	1	2	–
Counsellor	Home visit	0	–	–	0	–	–
Counsellor	Telephone call	0	–	–	0	–	–

TABLE 20 Resource use at the 15-month follow-up (for the previous 3 months) (continued)

Resource	Unit	Trial group					
		Intervention (N = 152)			Control (N = 149)		
		Users (n)	Meanᵃ	SD	Users (n)	Meanᵃ	SD
GP	Surgery visit	81	3	2	83	2	1
GP	Home visit	1	1	–	0	–	–
GP	Telephone call	1	2	–	1	4	–
Blood test at GP	Surgery visit	26	2	5	27	1	1
Diabetes nurse	Surgery visit	4	2	2	3	1	1
Diabetes nurse	Home visit	1	1	–	0	–	–
Diabetes nurse	Telephone call	0	–	–	0	–	–
Practice nurse	Surgery visit	16	2	2	21	2	1
Practice nurse	Home visit	0	–	–	0	–	–
Practice nurse	Telephone call	1	1	–	0	–	–
District nurse	Surgery visit	3	21	34	2	46	62
District nurse	Home visit	1	24	–	0	–	–
District nurse	Telephone call	0	–	–	0	–	–
Occupational therapist	Surgery visit	4	12	9	5	5	4
Occupational therapist	Home visit	2	13	16	3	12	0
Occupational therapist	Telephone call	1	3	–	0	–	–
Dietitian	Surgery visit	1	1	–	6	2	1
Dietitian	Home visit	0	–	–	1	12	–
Dietitian	Telephone call	0	–	–	0	–	–
Home help	Home visit	12	38	52	4	39	37
Meals on wheels	Home visit	4	47	33	1	15	–
Pharmacist for advice	Surgery visit	6	3	2	8	3	4
Pharmacist for advice	Home visit	0	–	–	0	–	–
Pharmacist for advice	Telephone call	2	2	1	1	1	–
NHS Direct	Telephone call	2	7	8	5	3	5
Samaritans	Telephone call	4	36	39	4	15	21
Medication		149			145		

a Mean for users only.
All quantities are rounded to nearest whole number.

Health and social care and lost productivity formed the largest components of total societal costs. Costs at baseline, 12 months and 15 months are summarised for reference in *Table 21*. The mean costs of all summary components were similar between trial arms at all assessment points, except the cost of the intervention, which was naturally higher in the intervention group given the additional inputs required compared with the control group (adjusted mean difference £311, 95% CI £267 to £355), and costs borne by charities, which were higher in the intervention group at 12 months (adjusted mean difference £80, 95% CI £9 to £151).

TABLE 21 Costs at baseline and at 12 and 15 months (2011/12 prices; all 15-month costs, except the intervention costs, are discounted)

Costs	Valid (n)	Intervention costs (£) (N = 213) Mean	SD	Valid (n)	Control costs (£) (N = 193) Mean	SD	Unadjusted mean Difference[a]	95% CI[a]	Adjusted mean Difference[b]	95% CI[b]
Costs at baseline										
Health and social care excluding intervention[c]	212	10,242	13,374	193	9714	13,767	528	−2953 to 4010	967	−2442 to 4435
Charity[c]	212	83	611	193	80	435	3	−109 to 115	−22	−137 to 94
Lost productivity[c]	212	8755	5964	193	7472	6311	1283	−354 to 2920	456	−894 to 1806
Patient[c]	212	72	433	193	188	188	35	−31 to 102	33	−37 to 104
Benefits[c]	212	2211	1006	193	2009	940	202[d]	13 to 391[d]	127	−70 to 324
Costs at 12 months										
Health and social care excluding intervention[c]	160	10,220	12,341	159	10,196	16,987	24	−4219 to 4267	−1596	−5145 to 1954
Charity[c]	160	120	369	159	61	256	60	−6 to 125	80[d]	9 to 151[d]
Lost productivity[c]	160	8882	5998	159	7707	6333	1174	−317 to 2665	1038	−367 to 2443
Patient[c]	160	84	369	159	53	300	31	−38 to 100	25	−46 to 96
Benefit[c]	160	2328	931	159	2129	957	200	−14 to 413	87	−105 to 279
Costs at 15 months										
Health and social care excluding intervention[e]	152	4874	6317	149	4708	6383	166	−1577 to 1910	−231	−1734 to 1272
Charity[e]	152	63	215	149	49	230	14	−39 to 67	24	−37 to 84
Lost productivity[e]	152	4731	2674	149	3880	3027	850[d]	127 to 1573[d]	608	−25 to 1240
Patient[e]	152	24	141	149	30	162	−6	−38 to 27	−6	−37 to 25
Benefits[e]	152	1089	439	149	1049	441	40	−70 to 150	−24	−125 to 76
Intervention	213	316	173	193	4	0	312[d]	267 to 357[d]	3142[d]	268 to 359[d]

a Controlling for clustering of care co-ordinator only.
b Includes covariates for baseline: equivalent cost, SF-36 MCS, SF-36 PCS, EQ-5D-3L utility, SF-36 utility, gender, ethnicity and borough, plus clustering for care co-ordinator.
c Costs for a 6-month retrospective period.
d CI excludes zero.
e Costs for a 3-month retrospective period.
All figures are rounded to the nearest whole number.

Comparisons of the total costs from both health and social care and societal perspectives at 15 months suggested no difference between the trial arms, although the 95% CIs suggested a tendency for societal costs to be higher in the intervention arm (*Table 22*). Imputing the missing total costs at 15 months for the sensitivity analyses confirmed this (*Table 23*).

Outcomes

There were no differences in any outcome at any time point (*Table 24*). As with cost data, imputing missing outcome data for those lost to follow-up (*Table 25*) did not alter the conclusions drawn from the base-case analyses of only those with available data.

Cost-effectiveness and cost–utility analyses

The two trial arms showed the same costs and same outcomes for all prespecified 15-month cost–outcome combinations using the base-case approach (*Table 26*); therefore, it was not necessary to compute any ICERs. Furthermore, none of the four sensitivity analyses altered the conclusions about between-group differences in total costs or outcomes.

The cost-effectiveness planes from health/social care and societal perspectives for all four outcomes are in *Figures 4–11*, showing no difference between the groups in costs or outcomes. Although cost-effectiveness planes for EQ-5D-3L-based QALYs from the health and social perspective indicate a tendency for estimates to predominate in the north-east or south-east quadrants (indicating higher or lower costs and better outcomes), those for the SF-36 MCS and SF-36 PCS show more estimates falling into the north-west or south-west quadrants (indicating higher or lower costs and worse outcomes). Cost-effectiveness planes from the societal perspective (see *Figures 8–11*) all suggest that mean costs in the intervention arm are likely to be higher than in the control arm, as was suggested by the 95% CIs for estimates of mean cost differences (see *Tables 22* and *23*).

From a health and social care perspective, the probability that the HPI is cost-effective does not exceed 0.4 for any of the examined willingness-to-pay thresholds for QALY gains (based on either the SF-36 or the EQ-5D-3L). When considering willingness to pay for point improvements in the PCS and MCS of the SF-36, the probability of the intervention being cost-effective starts at 0.34 at a willingness to pay of £0 but reduces to around 0.2 for willingness-to-pay values between £5000 and £50,000 (*Figures 12–15*).

Conclusions are similar from a societal perspective: the probability that the HPI is cost-effective does not exceed 0.12 for any of the willingness-to-pay thresholds examined for QALY gains (calculated from either the SF-36 or the EQ-5D-3L), or 0.21 for the thresholds examined for the point improvements in the two SF-36 component scores.

TABLE 22 Total costs at 15 months

Costs	Valid (*n*)	Intervention costs (£) (N = 213)		Valid (*n*)	Control costs (£) (N = 193)		Unadjusted mean difference[a]	95% CI[a]	Adjusted mean difference[b]	95% CI[b]
		Mean	SD		Mean	SD				
Health and social care including intervention[c]	152	5209	6326	149	4711	6383	498	–1248 to 2244	95	–1410 to 1599
Societal perspective including intervention[c]	152	11,116	7271	149	9720	7707	1396	–684 to 3476	675	–1039 to 2388

a Controlling for clustering of care co-ordinator only.
b Includes covariates for baseline: equivalent cost, SF-36 MCS, SF-36 PCS, EQ-5D-3L utility, SF-36 utility, gender, ethnicity and borough, plus clustering for care co-ordinator.
c Fifteen-month costs discounted.
All figures are rounded to the nearest whole number.

TABLE 23 Total costs at 15 months based on imputed missing data

Costs	Valid (*n*)	Intervention costs (£) (N = 213)		Valid (*n*)	Control costs (£) (N = 193)		Unadjusted mean difference[a]	95% CI[a]	Adjusted mean difference[b]	95% CI[b]
		Mean	SD		Mean	SD				
Health and social care including intervention[c]	213	5077	5652	193	4705	5848	372	–1047 to 1791	51	–1091 to 1192
Societal perspective including intervention[c]	213	10,830	6595	193	9683	7129	1147	–551 to 2845	537	–776 to 1850

a Controlling for clustering of care co-ordinator only.
b Includes covariates for baseline: equivalent cost, SF-36 MCS, SF-36 PCS, EQ-5D-3L utility, SF-36 utility, gender, ethnicity and borough, plus clustering for care co-ordinator.
c Fifteen-month costs discounted. Missing data at 15 months imputed from baseline and 12 months: equivalent cost, SF-36 MCS, SF-36 PCS, EQ-5D-3L utility, SF-36 utility, plus baseline gender, ethnicity, age, place of birth, borough and care co-ordinator.
All figures are rounded to the nearest whole number.

TABLE 24 Outcomes at baseline and at 12 and 15 months (with all 15-month outcomes discounted)

Time point	Intervention (N = 213)			Control (N = 193)			Unadjusted mean difference[a]	95% CI[a]	Adjusted mean difference[b]	95% CI[b]
	Valid (n)	Mean	SD	Valid (n)	Mean	SD				
Baseline										
SF-36 MCS	213	41.37	13.26	193	42.25	11.81	–0.88	–3.44 to 1.68	–0.26	–1.55 to 1.02
SF-36 PCS	213	45.83	10.94	193	47.04	9.26	–1.20	–3.31 to 0.91	–0.60	–1.72 to 0.52
SF-36 utility	210	0.69	0.16	192	0.71	0.14	–0.02	–0.05 to 0.02	0.00	–0.01 to 0.01
EQ-5D-3L utility	211	0.76	0.31	193	0.79	0.28	–0.02	–0.08 to 0.04	0.01	–0.04 to 0.06
12 months										
SF-36 MCS	160	43.18	13.31	158	44.09	13.47	–0.91	–3.94 to 2.11	–0.05	–2.64 to 2.55
SF-36 PCS	160	46.76	11.23	158	49.02	10.55	–2.27	–4.74 to 0.21	–1.45	–3.56 to 0.66
SF-36 utility	158	0.70	0.16	155	0.71	0.15	–0.02	–0.05 to 0.02	–0.00	–0.03 to 0.02
EQ-5D-3L utility	159	0.80	0.25	156	0.80	0.28	0.00	–0.06 to 0.06	0.03	–0.03 to 0.08
15 months										
SF-36 MCS	152	42.47	13.58	149	45.01	13.65	–2.54	–6.00 to 0.92	–0.80	–3.66 to 2.06
SF-36 PCS	152	47.25	11.62	149	48.54	9.88	–1.29	–4.02 to 1.44	–0.68	–3.01 to 1.65
SF-36 utility	149	0.66	0.14	148	0.70	0.15	–0.03[c]	–0.07 to –0.00[c]	–0.02	–0.05 to 0.01
SF-36-based QALY gain	134	0.17	0.03	139	0.17	0.09	–0.01	–0.01 to 0.00	–0.00	–0.01 to 0.00
EQ-5D-3L utility	152	0.77	0.24	149	0.80	0.25	–0.02	–0.09 to 0.04	0.00	–0.06 to 0.06
EQ-5D-3L-based QALY gain	137	0.19	0.05	140	0.20	0.06	–0.00	–0.02 to 0.01	0.00	–0.01 to 0.02

a Controlling for clustering of care co-ordinator.
b Includes covariates for baseline: SF-36 MCS, SF-36 PCS, EQ-5D-3L utility, SF-36 utility, gender, age, ethnicity, place of birth and borough, plus clustering for care co-ordinator.
c CI excludes zero.

TABLE 25 Outcomes at 15 months based on imputed missing data (with all 15-month outcomes discounted)

Outcome	Intervention (N = 213)			Control (N = 193)			Unadjusted mean difference[a]	95% CI	Adjusted mean difference[b]	95% CI[a]
	Valid (n)	Mean	SD	Valid (n)	Mean	SD				
SF-36 MCS	213	42.95	12.59	193	44.84	12.52	−1.88	−4.75 to 0.98	−0.64	−2.77 to 1.49
SF-36 PCS	213	47.72	10.58	193	48.97	9.18	−1.25	−3.23 to 0.73	−0.47	−2.09 to 1.14
SF-36-based QALY	213	0.17	0.03	193	0.17	0.03	−0.01	−0.01 to 0.00	−0.00	−0.00 to 0.00
EQ-5D-3L-based QALY	213	0.19	0.05	193	0.20	0.05	−0.00	−0.01 to 0.01	0.00	−0.01 to 0.01

a Controlling for clustering of care co-ordinator.
b Includes covariates for baseline: SF-36 MCS, SF-36 PCS, EQ-5D-3L utility, SF-36 utility, gender, age, ethnicity, place of birth and borough, plus clustering for care co-ordinator.
Missing data at 15 months imputed from baseline and 12 months: equivalent cost, SF-36 MCS, SF-36 PCS, EQ-5D-3L utility, SF-36 utility, plus baseline gender, ethnicity, age, place of birth, borough and care co-ordinator.
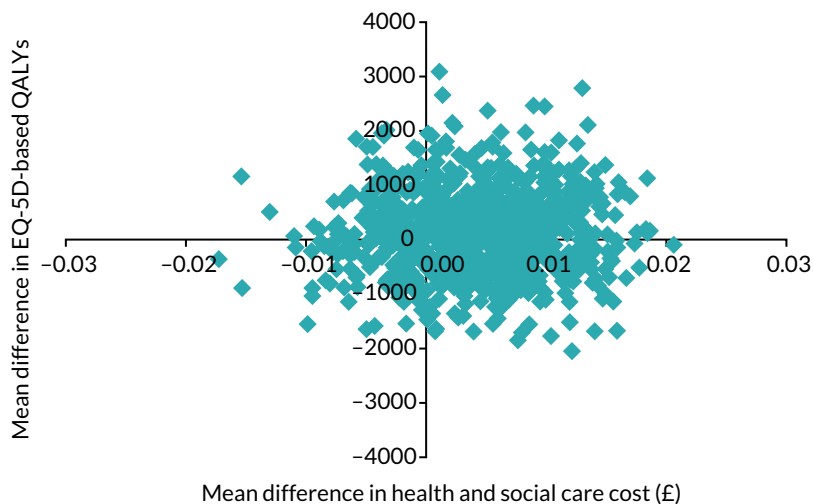
FIGURE 4 Cost-effectiveness plane of mean differences in EQ-5D-3L-based QALYs and health and social care costs.
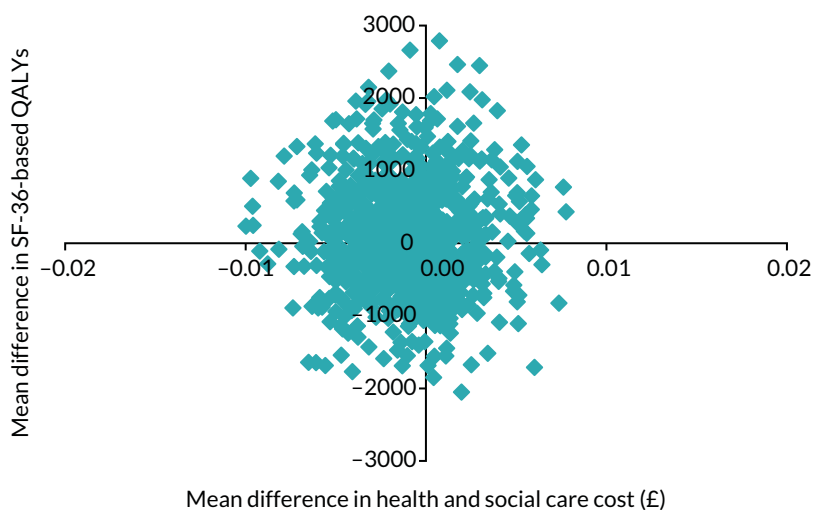
FIGURE 5 Cost-effectiveness plane of mean differences in SF-36-based QALYs and health and social care costs.
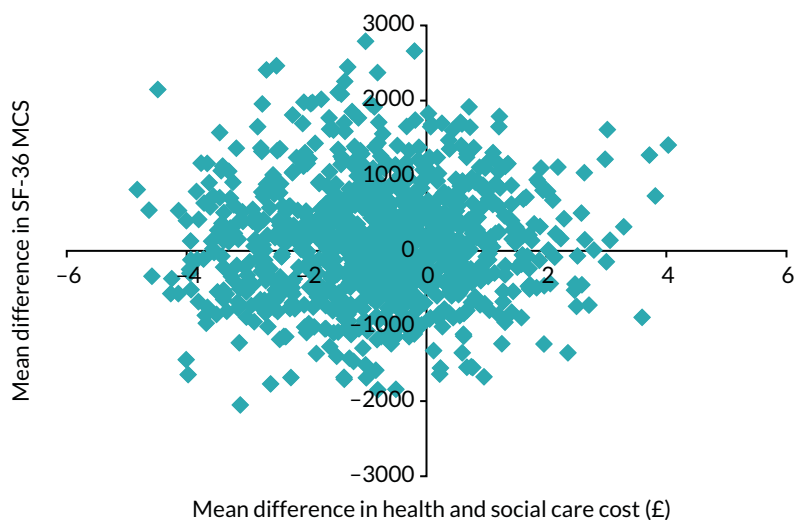
FIGURE 6 Cost-effectiveness plane of mean differences in SF-36 MCS and health and social care costs.
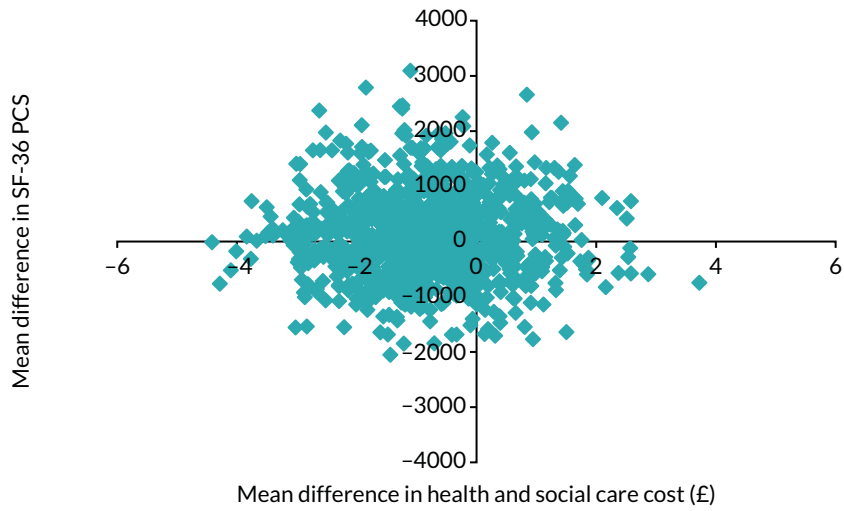
FIGURE 7 Cost-effectiveness plane of mean differences in SF-36 PCS and health and social care costs.
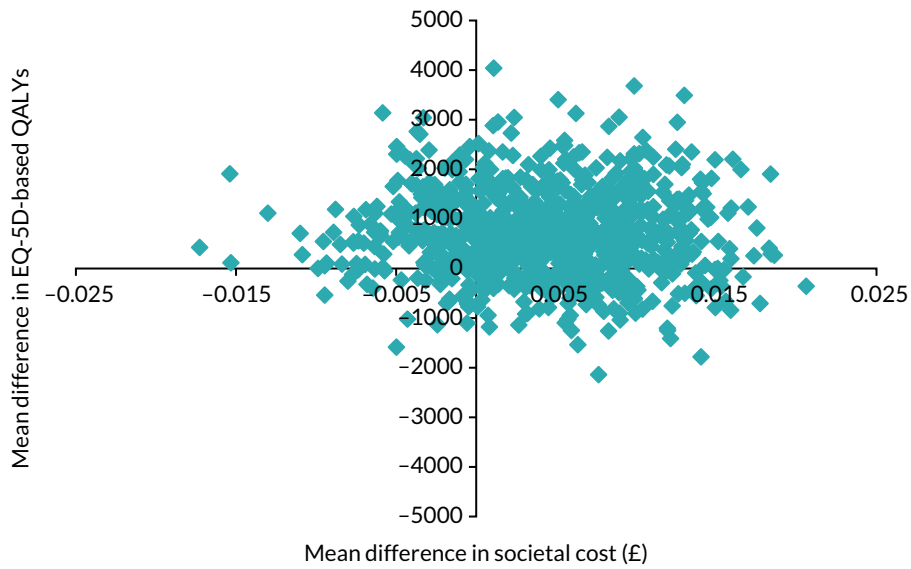
FIGURE 8 Cost-effectiveness plane of mean differences in EQ-5D-3L-based QALYs and societal costs.
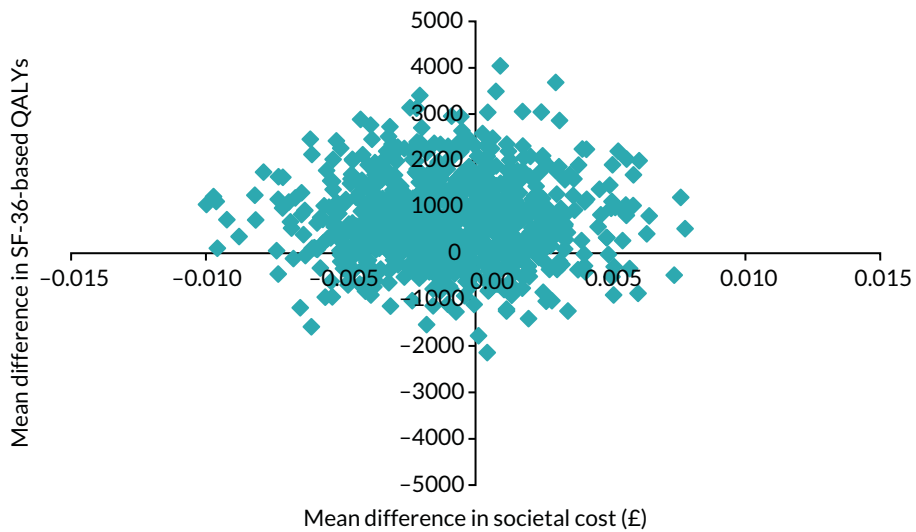
FIGURE 9 Cost-effectiveness plane of mean differences in SF-36-based QALYs and societal costs.
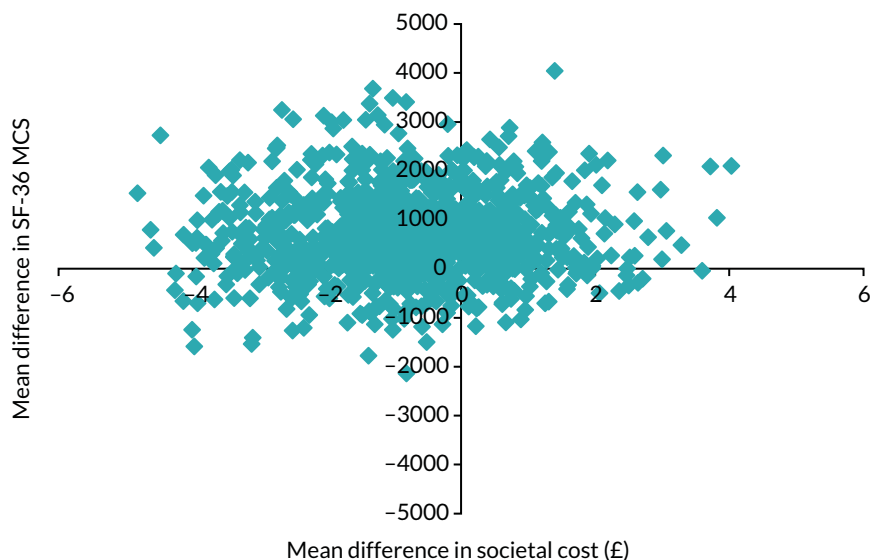
FIGURE 10 Cost-effectiveness plane of mean differences in SF-36 MCS and societal costs.
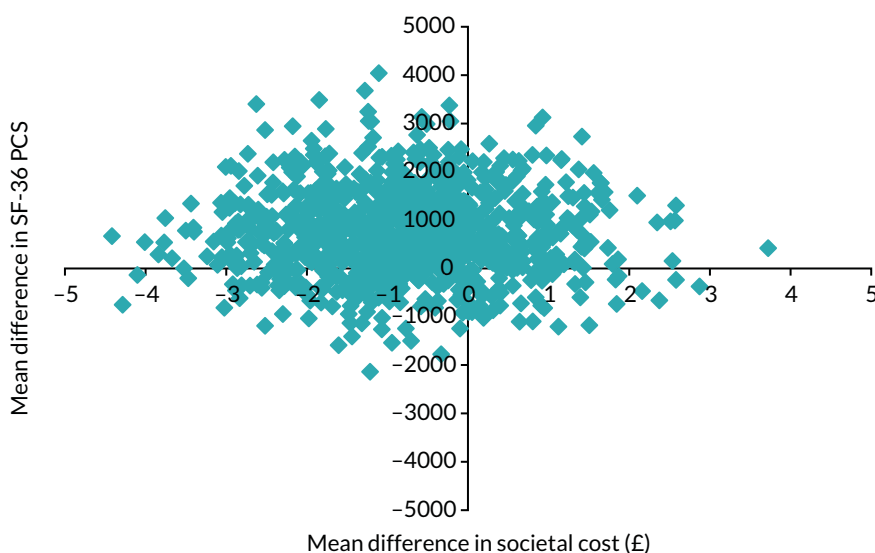
FIGURE 11 Cost-effectiveness plane of mean differences in SF-36 PCS and societal costs.
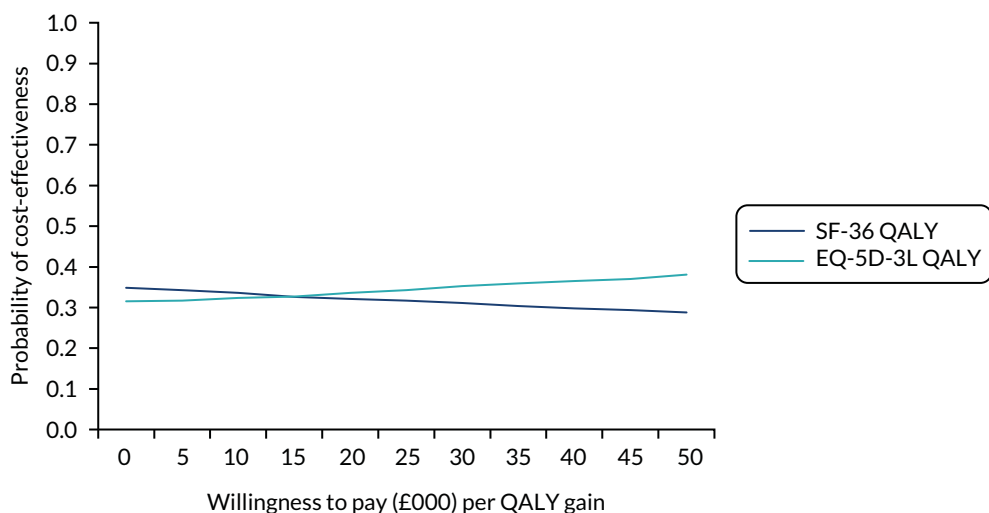
FIGURE 12 Cost-effectiveness acceptability curves for SF-36- and EQ-5D-3L-based QALYs from a health and social care perspective.
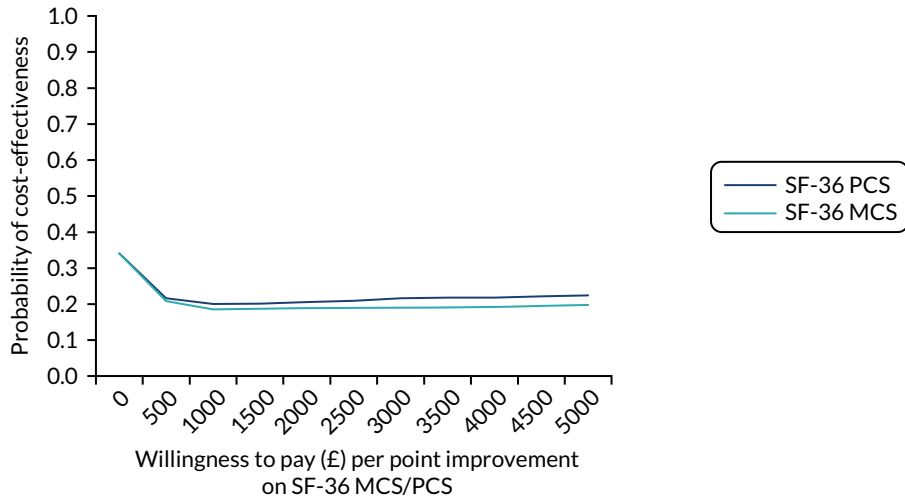
FIGURE 13 Cost-effectiveness acceptability curves for the PCS and MCS of the SF-36 from a health and social care perspective.
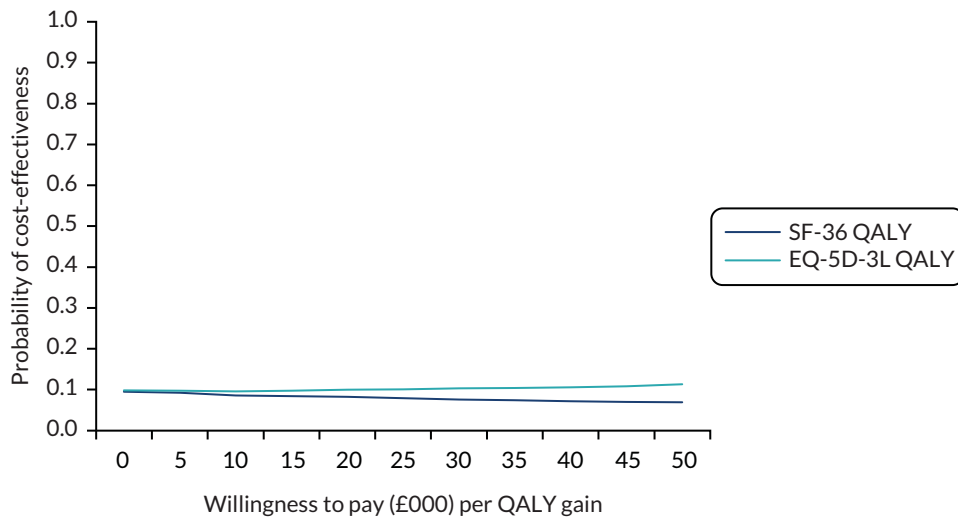
FIGURE 14 Cost-effectiveness acceptability curves for SF-36- and EQ-5D-3L-based QALYs from a societal perspective.
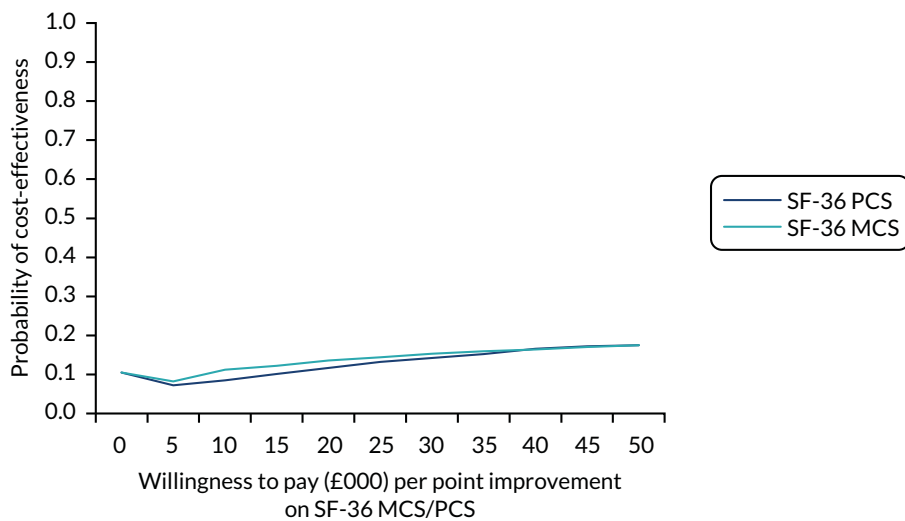
FIGURE 15 Cost-effectiveness acceptability curves for the PCS and MCS of the SF-36 from a societal perspective.

TABLE 26 Cost-effectiveness and cost–utility summary at 15 months

Costs	Cost per additional point improvement on the SF-36 PCS Control vs. intervention	Cost per additional point improvement on the SF-36 MCS Control vs. intervention	Cost per additional QALY (SF-36 based) Control vs. intervention	Cost per additional QALY (EQ-5D-3L based) Control vs. intervention
Health and social costs including intervention costs	Same cost, same outcome	Same cost, same outcome	Same cost, same outcome	Same cost, same outcome
Societal perspective costs including intervention costs	Same cost, same outcome	Same cost, same outcome	Same cost, same outcome	Same cost, same outcome

Incremental cost-effectiveness ratios are unnecessary because costs and outcomes are equivalent in both trial arms.

Appendix 5 Primary outcome analyses

*A*ppendix 4 shows that sensitivity analyses did not alter the conclusion that there was no treatment effect at any time point for the two main outcomes, PHC and MHC score. Furthermore, no changes over time could be detected. *Tables 27* and *28* show the results of the main analyses presented in Gaughran *et al.*[176]

TABLE 27 All data: PHC

Variable	Coefficient	SE	z	*p*-value	95% CI
Arm (HPI = 1)	−1.7	0.98	−1.73	0.083	−3.63 to 0.23
Time (15 months = 1)	−0.23	0.72	−0.32	0.746	−1.64 to 1.17
Arm × time	1.1	1.02	1.08	0.282	−0.9 to 3.1
Borough	$\chi^2(9) = 3.71$; $p = 0.93$				
Croydon	0				
Lambeth	1.72	1.66	1.04	0.3	−1.53 to 4.97
Lewisham	0.93	1.39	0.67	0.503	−1.8 to 3.66
Southwark	2.02	1.36	1.49	0.136	−0.64 to 4.68
Greenwich	2.09	1.74	1.2	0.229	−1.32 to 5.51
Bromley	1.75	1.77	0.99	0.323	−1.72 to 5.23
Bexley	1.24	2	0.62	0.536	−2.68 to 5.15
East Sussex	1.69	1.9	0.89	0.375	−2.04 to 5.41
Somerset	2.8	2.56	1.09	0.274	−2.22 to 7.82
South Staffordshire	3.23	3.26	0.99	0.322	−3.16 to 9.61
PHC baseline	0.61	0.04	15.77	0	0.53 to 0.69
Constant	18	2.22	8.12	0	13.66 to 22.35
Pairwise comparison	**Coefficient**	**SE**	**z**	***p*-value**	**95% CI**
12 months: TAU vs. HPI	−1.7	0.98	−1.73	0.083	−3.63 to 0.23
15 months: TAU vs. HPI	−0.6	0.99	−0.61	0.541	−2.54 to 1.33
Group HPI: 15 months vs. 12 months	−0.23	0.72	−0.32	0.746	−1.64 to 1.17
Group TAU: 15 months vs. 12 months	0.87	0.72	1.19	0.232	−0.55 to 2.29
Random-effects parameters	**Estimate**	**SE**	**95% CI**		
Care co-ordinator (SD)	0	0			
Residual					
SD (12 months)	8.58	0.34	7.94 to 9.27		
SD (15 months)	8.54	0.35	7.89 to 9.25		
Correlation (12 months, 15 months)	0.48	0.04	0.39 to 0.56		

SE, standard error.

TABLE 28 All data: MHC

Variable	Coefficient	SE	z	p-value	95% CI
Arm (HPI = 1)	−0.41	1.29	−0.32	0.751	−2.95 to 2.13
Time (15 months = 1)	1	0.87	1.16	0.248	−0.7 to 2.71
Arm × time	−0.71	1.36	−0.53	0.598	−3.37 to 1.94
Borough	$\chi^2(9) = 14.69$; $p = 0.10$				
Croydon	0				
Lambeth	−1.91	2.17	−0.88	0.378	−6.16 to 2.34
Lewisham	−1.97	1.85	−1.06	0.288	−5.6 to 1.66
Southwark	−5.33	1.8	−2.96	0.003	−8.85 to −1.8
Greenwich	−5.23	2.35	−2.23	0.026	−9.83 to −0.63
Bromley	−3.7	2.34	−1.58	0.113	−8.28 to 0.88
Bexley	−0.99	2.65	−0.37	0.709	−6.18 to 4.2
East Sussex	−4.95	2.5	−1.98	0.047	−9.84 to −0.06
Somerset	−6.91	3.37	−2.05	0.04	−13.53 to −0.3
South Staffordshire	−2.09	4.44	−0.47	0.637	−10.79 to 6.6
PHC baseline	0.58	0.04	14.23	0	0.5 to 0.67
Constant	21.25	2.32	9.15	0	16.7 to 25.79

Pairwise comparison	Coefficient	SE	z	p-value	95% CI
12 months: B vs. A	−0.41	1.29	−0.32	0.751	−2.95 to 2.13
15 months: B vs. A	−1.13	1.31	−0.86	0.389	−3.69 to 1.44
Group TAU: 15 months vs. 12 months	1	0.87	1.16	0.248	−0.7 to 2.71
Group HPI: 15 months vs. 12 months	0.29	1.04	0.28	0.78	−1.75 to 2.33

Random-effects parameters	Estimate	SE	95% CI		
Care co-ordinator (SD)	1.68	1.3	0.37 to 7.65		
Residual *Group TAU*					
SD (12 months, 15 months)	10.42	0.51	9.46 to 11.47		
Correlation (12 months, 15 months)	0.49	0.07	0.34 to 0.61		
Group HPI					
SD (12 months, 15 months)	11.22	0.52	10.24 to 12.3		
Correlation (12 months, 15 months)	0.37	0.08	0.21 to 0.51		

SE, standard error.

TABLE 29 Within time window with age as a predictor of missingness: PHC

Variable	Coefficient	SE	z	p-value	95% CI
Arm (HPI = 1)	−1.86	1.07	−1.74	0.082	−3.95 to 0.24
Time (15 months = 1)	−0.09	0.81	−0.12	0.907	−1.68 to 1.49
Arm × time	0.69	1.15	0.6	0.551	−1.57 to 2.95
Borough	$\chi^2(9) = 8.46$; $p = 0.49$				
Croydon					
Lambeth	1.3	1.76	0.74	0.461	−2.15 to 4.74
Lewisham	1.48	1.5	0.99	0.324	−1.46 to 4.41
Southwark	2.27	1.46	1.56	0.119	−0.59 to 5.12
Greenwich	4.77	1.92	2.48	0.013	1.01 to 8.53
Bromley	1.2	1.96	0.61	0.539	−2.63 to 5.04
Bexley	2.35	2.21	1.06	0.288	−1.99 to 6.69
East Sussex	2.17	2.01	1.08	0.279	−1.76 to 6.11
Somerset	3.58	2.77	1.29	0.197	−1.85 to 9.01
South Staffordshire	5.49	3.7	1.48	0.138	−1.76 to 12.75
PHC baseline	0.59	0.04	13.91	0	0.5 to 0.67
Age at baseline	−0.11	0.05	−2.4	0.016	−0.2 to −0.02
Constant	23.85	3.51	6.8	0	16.97 to 30.72
Pairwise comparison	**Coefficient**	**SE**	**z**	***p*-value**	**95% CI**
12 months: TAU vs. HPI	−1.86	1.07	−1.74	0.082	−3.95 to 0.24
15 months: TAU vs. HPI	−1.17	1.08	−1.08	0.28	−3.29 to 0.95
Group HPI: 15 months vs. 12 months	−0.09	0.81	−0.12	0.907	−1.68 to 1.49
Group TAU: 15 months vs. 12 months	0.59	0.83	0.72	0.474	−1.03 to 2.21
Random-effects parameters	**Estimate**	**SE**	**95% CI**		
Care co-ordinator (SD)	0.9	1.65	0.02 to 33.04		
Residual					
SD (12 months)	8.32	0.39	7.58 to 9.13		
SD (15 months)	8.13	0.43	7.34 to 9.01		
Correlation (12 months, 15 months)	0.48	0.06	0.36 to 0.59		

SE, standard error.

TABLE 30 Within time window with age as a predictor of missingness: MHC

Variable	Coefficient	SE	z	p-value	95% CI
Arm (HPI = 1)	0.38	1.42	0.27	0.789	−2.4 to 3.15
Time (15 months = 1)	0.19	1	0.19	0.851	−1.78 to 2.16
Arm × time	−1	1.58	−0.63	0.526	−4.09 to 2.09
Borough	$\chi^2(9) = 8.79$; $p = 0.46$				
Croydon	0				
Lambeth	−1.68	2.32	−0.73	0.468	−6.23 to 2.86
Lewisham	−2.17	2.03	−1.07	0.286	−6.15 to 1.81
Southwark	−4.3	1.96	−2.2	0.028	−8.13 to −0.46
Greenwich	−3.63	2.6	−1.4	0.163	−8.73 to 1.47
Bromley	−4.22	2.62	−1.61	0.107	−9.35 to 0.91
Bexley	−0.68	2.95	−0.23	0.819	−6.45 to 5.1
East Sussex	−4.9	2.67	−1.83	0.067	−10.13 to 0.34
Somerset	−6.15	3.69	−1.67	0.095	−13.38 to 1.08
South Staffordshire	−3.34	5.01	−0.67	0.505	−13.16 to 6.47
PHC baseline	0.58	0.04	12.96	0	0.49 to 0.67
Age at baseline	0.06	0.06	1	0.316	−0.05 to 0.17
Constant	18.59	3.54	5.26	0	11.66 to 25.52
Pairwise comparison	**Coefficient**	**SE**	**z**	**p-value**	**95% CI**
12 months: B vs. A	0.38	1.42	0.27	0.789	−2.4 to 3.15
15 months: B vs. A	−0.62	1.47	−0.42	0.671	−3.49 to 2.25
Group TAU: 15 months vs. 12 months	0.19	1	0.19	0.851	−1.78 to 2.16
Group HPI: 15 months vs. 12 months	−0.81	1.22	−0.67	0.506	−3.2 to 1.58
Random-effects parameters	**Estimate**	**SE**	**95% CI**		
Care co-ordinator (SD)	2.14	1.24	0.69 to 6.65		
Residual *Group TAU*					
SD (12 months, 15 months)	10.23	0.56	9.19 to 11.38		
Correlation (12 months, 15 months)	0.49	0.09	0.3 to 0.64		
Group HPI					
SD (12 months, 15 months)	10.79	0.58	9.72 to 11.98		
Correlation (12 months, 15 months)	0.32	0.1	0.12 to 0.5		

SE, standard error.

TABLE 31 All data with age as a predictor for missingness: PHC

Variable	Coefficient	SE	z	*p*-value	95% CI
Arm (HPI = 1)	−1.81	0.98	−1.85	0.065	−3.73 to 0.11
Time (15 months = 1)	−0.22	0.72	−0.31	0.756	−1.63 to 1.18
Arm × time	1.07	1.02	1.05	0.294	−0.93 to 3.07
Borough	$\chi^2(9) = 4.04$; $p = 0.91$				
Croydon	0				
Lambeth	0.76	1.68	0.45	0.652	−2.53 to 4.05
Lewisham	0.59	1.39	0.43	0.668	−2.12 to 3.31
Southwark	1.89	1.34	1.4	0.161	−0.75 to 4.52
Greenwich	2.07	1.72	1.2	0.229	−1.31 to 5.45
Bromley	1.96	1.76	1.11	0.266	−1.49 to 5.4
Bexley	1.33	1.98	0.67	0.503	−2.55 to 5.2
East Sussex	1.31	1.89	0.7	0.486	−2.38 to 5.01
Somerset	2.06	2.55	0.81	0.42	−2.95 to 7.06
South Staffordshire	3.81	3.25	1.17	0.241	−2.56 to 10.17
PHC baseline	0.59	0.04	14.94	0	0.51 to 0.66
Age at baseline	−0.12	0.04	−2.64	0.008	−0.2 to −0.03
Constant	24.57	3.32	7.41	0	18.07 to 31.07
Pairwise comparison	**Coefficient**	**SE**	**z**	***p*-value**	**95% CI**
12 months: TAU vs. HPI	−1.81	0.98	−1.85	0.065	−3.73 to 0.11
15 months: TAU vs. HPI	−0.74	0.98	−0.76	0.45	−2.66 to 1.18
Group HPI: 15 months vs. 12 months	−0.22	0.72	−0.31	0.756	−1.63 to 1.18
Group TAU: 15 months vs. 12 months	0.85	0.72	1.17	0.242	−0.57 to 2.27
Random-effects parameters	**Estimate**	**SE**	**95% CI**		
Care co-ordinator (SD)	0	0			
Residual					
SD (12 months)	8.54	0.34	7.9 to 9.23		
SD (15 months)	8.45	0.34	7.8 to 9.15		
Correlation (12 months, 15 months)	0.47	0.04	0.38 to 0.56		

SE, standard error.

TABLE 32 All data with age as a predictor for missingness: MHC

Variable	Coefficient	SE	z	p-value	95% CI
Arm (HPI = 1)	−0.38	1.29	−0.3	0.766	−2.92 to 2.15
Time (15 months = 1)	1	0.87	1.15	0.251	−0.7 to 2.7
Arm × time	−0.7	1.36	−0.52	0.603	−3.36 to 1.95
Borough	$\chi^2(9) = 14.65$; $p = 0.10$				
Croydon	0				
Lambeth	−1.5	2.21	−0.68	0.498	−5.82 to 2.83
Lewisham	−1.8	1.86	−0.97	0.334	−5.44 to 1.85
Southwark	−5.25	1.8	−2.92	0.003	−8.77 to −1.73
Greenwich	−5.19	2.34	−2.22	0.027	−9.79 to −0.6
Bromley	−3.83	2.34	−1.64	0.101	−8.41 to 0.75
Bexley	−1.06	2.64	−0.4	0.689	−6.24 to 4.12
East Sussex	−4.83	2.5	−1.93	0.053	−9.72 to 0.06
Somerset	−6.54	3.39	−1.93	0.054	−13.18 to 0.1
South Staffordshire	−2.36	4.44	−0.53	0.596	−11.05 to 6.34
PHC baseline	0.58	0.04	14.09	0	0.5 to 0.66
Age at baseline	0.05	0.05	0.98	0.329	−0.05 to 0.16
Constant	18.91	3.33	5.68	0	12.39 to 25.44
Pairwise comparison	**Coefficient**	**SE**	**z**	**p-value**	**95% CI**
12 months: B vs. A	−0.38	1.29	−0.3	0.766	−2.92 to 2.15
15 months: B vs. A	−1.09	1.31	−0.83	0.404	−3.65 to 1.47
Group TAU: 15 months vs. 12 months	1	0.87	1.15	0.251	−0.7 to 2.7
Group HPI: 15 months vs. 12 months	0.29	1.04	0.28	0.778	−1.75 to 2.33
Random-effects parameters	**Estimate**	**SE**	**95% CI**		
Care co-ordinator (SD)	1.68	1.3	0.37 to 7.67		
Residual *Group TAU*					
SD (12 months, 15 months)	10.42	0.51	9.46 to 11.48		
Correlation (12 months, 15 months)	0.49	0.07	0.34 to 0.61		
Group HPI					
SD (12 months, 15 months)	11.2	0.52	10.22 to 12.28		
Correlation (12 months, 15 months)	0.37	0.08	0.21 to 0.51		

Multiple imputation

The following variables were used for the imputation model: relationship with two levels (yes or no, categorical), education as an ordinal variable, age at baseline, waist, BMI, systolic and diastolic BP, levels of HbA_{1c}, GAF score, number of children, fasting glucose, PANNS total score, Montgomery–Åsberg Depression Rating Scales (MADRS), gender (categorical variable), attended 12 months within/outside follow-up (nominal variable), attended the 15-month follow-up within/outside time limits (nominal variable), MHC at baseline and at 12 and 24 months' follow-up (log-transformed), PHC at baseline and at 12 and 24 months' follow-up (log-transformed). Estimation was performed for each treatment arm (= interaction between group TAU and all variables). Fifty data sets were imputed. MHC and PHC were log-transformed to be more nearly normal during the imputation process to avoid prediction outside the possible range.

After imputation, the variables were back-transformed to the original scale. This procedure generally reduces bias and improves statistical properties.[242] The data were then analysed using the same model as in the main analyses.

TABLE 33 Multiple imputation: PHC

Variable	Coefficient	SE	z	*p*-value	95% CI
Arm (HPI = 1)	−0.98	1.73	−0.56	0.58	−4.41 to 2.46
Time (15 months = 1)	0.36	1.47	0.24	0.81	−2.55 to 3.26
Arm × time	0.45	2.01	0.23	0.82	−3.52 to 4.42
Borough					
Croydon	0.00				
Lambeth	1.08	2.26	0.48	0.63	−3.37 to 5.52
Lewisham	0.72	1.91	0.38	0.71	−3.04 to 4.48
Southwark	1.56	1.86	0.84	0.40	−2.10 to 5.21
Greenwich	2.11	2.43	0.87	0.39	−2.66 to 6.87
Bromley	0.20	2.55	0.08	0.94	−4.81 to 5.20
Bexley	1.50	2.74	0.55	0.59	−3.89 to 6.89
East Sussex	2.08	2.60	0.80	0.43	−3.02 to 7.17
Somerset	0.32	3.75	0.08	0.93	−7.09 to 7.72
South Staffordshire	2.12	4.24	0.50	0.62	−6.24 to 10.48
PHC baseline	0.61	0.06	10.34	0.00	0.49 to 0.72
Constant	17.44	3.36	5.20	0.00	10.83 to 24.06
Random-effects parameters	**Estimate**	**SE**	**95% CI**		
Care co-ordinator (SD)	−5.70	333.69	−659.73 to 648.33		
Residual					
SD (12 months)	2.32	0.09	2.14 to 2.50		
SD (15 months)	0.34	0.11	0.12 to 0.56		
Correlation (12 months, 15 months)	0.19	0.18	−0.17 to 0.55		

SE, standard error.

TABLE 34 Multiple imputation: MHC

Variable	Coefficient	SE	z	*p*-value	95% CI
Arm (HPI = 1)	0.57	2.10	0.27	0.79	−3.55 to 4.69
Time (15 months = 1)	−0.96	2.28	−0.42	0.67	−5.48 to 3.55
Arm × time	−0.60	3.70	−0.16	0.87	−7.94 to 6.74
Borough					
Croydon	0.00				
Lambeth	−1.71	3.23	−0.53	0.60	−8.06 to 4.64
Lewisham	−3.06	2.73	−1.12	0.26	−8.44 to 2.32
Southwark	−3.20	2.77	−1.16	0.25	−8.66 to 2.25
Greenwich	−2.63	3.28	−0.80	0.42	−9.06 to 3.80
Bromley	−3.06	3.52	−0.87	0.38	−9.99 to 3.86

TABLE 34 Multiple imputation: MHC (*continued*)

Variable	Coefficient	SE	z	*p*-value	95% CI
Bexley	–1.41	3.87	–0.36	0.72	–9.02 to 6.21
East Sussex	–3.82	4.01	–0.95	0.34	–11.70 to 4.07
Somerset	–6.72	4.99	–1.35	0.18	–16.58 to 3.13
South Staffordshire	–0.19	6.44	–0.03	0.98	–12.89 to 12.52
PHC baseline	0.65	0.07	9.25	0.00	0.51 to 0.78
Constant	17.19	3.79	4.54	0.00	9.73 to 24.65

Random-effects parameters	Estimate	SE	95% CI		
Care co-ordinator (SD)					
Residual	–5.10	195.33	–387.94 to 377.75		
Group TAU					
ln [SD (12 months, 15 months)]	2.76	0.17	2.43 to 3.09		
Correlation (12 months, 15 months)	0.33	0.17	0.00 to 0.67		
Group HPI					
ln [SD (12 months, 15 months)]	–0.01	0.25	–0.52 to 0.50		
Correlation (12 months, 15 months)	0.18	0.12	–0.05 to 0.42		

SE, standard error.

Multiple imputation 2: sensitivity analysis for not missing at random pattern

Some large positive and large negative values were added to the multiple imputed missing values (values correspond to approximately ± 2 SDs and ± 1 SD of baseline measure of physical and mental health scores, respectively).

(Fifty imputed data sets; same imputation data sets used in multiple imputation analyses above were used.)

Only parameter estimates for arm (HPI = 1), time (15 months = 1) and arm × time interaction are shown.

TABLE 35 Not missing at random: PHC – values added to imputed missing value were –20, –10, 0, 10 and 20, respectively (correspond to approximately ± 2 SDs, ± 1 SD and 0 SDs of baseline measure)

Value added to imputed missing values	Variable	Coefficient	SE	z	*p*-value	95% CI
–20 for missing						
	Arm (HPI = 1)	–2.48	2.03	–1.22	0.22	–6.49 to 1.53
	Time (15 months = 1)	–1.51	1.68	–0.90	0.37	–4.82 to 1.80
	Arm × time	1.38	2.31	0.60	0.55	–3.16 to 5.92
–10 for missing						
	Arm (HPI = 1)	–1.74	1.83	–0.95	0.34	–5.36 to 1.87
	Time (15 months = 1)	–0.58	1.53	–0.38	0.71	–3.59 to 2.44
	Arm × time	0.92	2.09	0.44	0.66	–3.21 to 5.04
0 for missing						
	Arm (HPI = 1)	–0.98	1.73	–0.56	0.58	–4.41 to 2.46
	Time (15 months = 1)	0.36	1.47	0.24	0.81	–2.55 to 3.26
	Arm × time	0.45	2.01	0.23	0.82	–3.52 to 4.42

TABLE 35 Not missing at random: PHC – values added to imputed missing value were –20, –10, 0, 10 and 20, respectively (correspond to approximately ± 2 SDs, ± 1 SD and 0 SDs of baseline measure) (continued)

Value added to imputed missing values	Variable	Coefficient	SE	z	p-value	95% CI
+10 for missing						
	Arm (HPI = 1)	–0.19	1.77	–0.11	0.92	–3.69 to 3.31
	Time (15 months = 1)	1.29	1.52	0.85	0.40	–1.71 to 4.29
	Arm × time	–0.01	2.08	–0.01	1.00	–4.12 to 4.10
+20 for missing						
	Arm (HPI = 1)	0.59	1.93	0.30	0.76	–3.23 to 4.40
	Time (15 months = 1)	2.22	1.67	1.33	0.19	–1.07 to 5.52
	Arm × time	–0.47	2.29	–0.21	0.84	–4.99 to 4.04

SE, standard error.

Conclusion: adding extreme values did not change major conclusions.

TABLE 36 Not missing at random: MHC – values added to imputed missing value were –25, –12, 0, 12 and 25, respectively (correspond to approximately ± 2 SDs, ± 1 SD and 0 SDs of baseline measure)

Value added to imputed missing values	Variable	Coefficient	SE	z	p-value	95% CI
–20 for missing						
	Arm (HPI = 1)	–1.28	2.38	–0.54	0.59	–5.96 to 3.40
	Time (15 months = 1)	–3.30	2.53	–1.30	0.20	–8.29 to 1.70
	Arm × time	0.56	3.95	0.14	0.89	–7.27 to 8.39
–10 for missing						
	Arm (HPI = 1)	–0.34	2.09	–0.16	0.87	–4.45 to 3.77
	Time (15 months = 1)	–2.08	2.37	–0.88	0.38	–6.77 to 2.61
	Arm × time	–0.04	3.76	–0.01	0.99	–7.50 to 7.42
0 for missing						
	Arm (HPI = 1)	0.57	2.10	0.27	0.79	–3.55 to 4.69
	Time (15 months = 1)	–0.96	2.28	–0.42	0.67	–5.48 to 3.55
	Arm × time	–0.60	3.70	–0.16	0.87	–7.94 to 6.74
+10 for missing						
	Arm (HPI = 1)	1.44	2.00	0.72	0.47	–2.51 to 5.39
	Time (15 months = 1)	0.15	2.37	0.07	0.95	–4.54 to 4.85
	Arm × time	–1.15	3.76	–0.31	0.76	–8.62 to 6.31
+20 for missing						
	Arm (HPI = 1)	2.38	2.23	1.07	0.29	–1.99 to 6.76
	Time (15 months = 1)	1.37	2.53	0.54	0.59	–3.63 to 6.37
	Arm × time	–1.76	3.95	–0.44	0.66	–9.59 to 6.08

SE, standard error.

Conclusion: adding extreme values did not change major conclusions.