# Clinical and cost-effectiveness of an intervention for reducing cholesterol and cardiovascular risk for people with severe mental illness in English primary care: a cluster randomised controlled trial

*David Osborn, Alexandra Burton, Rachael Hunter, Louise Marston, Lou Atkins, Thomas Barnes, Ruth Blackburn, Thomas Craig, Hazel Gilbert, Samira Heinkel, Richard Holt, Michael King, Susan Michie, Richard Morris, Steve Morris, Irwin Nazareth, Rumana Omar, Irene Petersen, Robert Peveler, Vanessa Pinfold, Kate Walters*

## Summary

**Background** People with severe mental illnesses, including psychosis, have an increased risk of cardiovascular disease. We aimed to evaluate the effects of a primary care intervention on decreasing total cholesterol concentrations and cardiovascular disease risk in people with severe mental illnesses.

**Methods** We did this cluster randomised trial in general practices across England, with general practices as the cluster unit. We randomly assigned general practices (1:1) with 40 or more patients with severe mental illnesses using a computer-generated random sequence with a block size of four. Researchers were masked to allocation, but patients and general practice staff were not. We included participants aged 30–75 years with severe mental illnesses (schizophrenia, bipolar disorder, or psychosis), who had raised cholesterol concentrations (5·0 mmol/L) or a total:HDL cholesterol ratio of 4·0 mmol/L or more and one or more modifiable cardiovascular disease risk factors. Eligible participants were recruited within each practice before randomisation. The Primrose intervention consisted of appointments (≤12) with a trained primary care professional involving manualised interventions for cardiovascular disease prevention (ie, adhering to statins, improving diet or physical activity levels, reducing alcohol, or quitting smoking). Treatment as usual involved feedback of screening results only. The primary outcome was total cholesterol at 12 months and the primary economic analysis outcome was health-care costs. We used intention-to-treat analysis. The trial is registered with Current Controlled Trials, number ISRCTN13762819.

**Findings** Between Dec 10, 2013, and Sept 30, 2015, we recruited general practices and between May 9, 2014, and Feb 10, 2016, we recruited participants and randomly assigned 76 general practices with 327 participants to the Primrose intervention (n=38 with 155 patients) or treatment as usual (n=38 with 172 patients). Total cholesterol concentration data were available at 12 months for 137 (88%) participants in the Primrose intervention group and 152 (88%) participants in the treatment-as-usual group. The mean total cholesterol concentration did not differ at 12 months between the two groups (5·4 mmol/L [SD 1·1] for Primrose *vs* 5·5 mmol/L [1·1] for treatment as usual; mean difference estimate 0·03, 95% CI –0·22 to 0·29; p=0·788). This result was unchanged by pre-agreed supportive analyses. Mean cholesterol decreased over 12 months (–0·22 mmol/L [1·1] for Primrose *vs* –0·36 mmol/L [1·1] for treatment as usual). Total health-care costs (£1286 [SE 178] in the Primrose intervention group *vs* £2182 [328] in the treatment-as-usual group; mean difference –£895, 95% CI –1631 to –160; p=0·012) and psychiatric inpatient costs (£157 [135] *vs* £956 [313]; –£799, –1480 to –117; p=0·018) were lower in the Primrose intervention group than the treatment-as-usual group. Six serious adverse events of hospital admission and one death occurred in the Primrose group (n=7) and 23, including three deaths, occurred in the treatment-as-usual group (n=18).

**Interpretation** Total cholesterol concentration at 12 months did not differ between the Primrose and treatment-as-usual groups, possibly because of the cluster design, good care in the treatment-as-usual group, short duration of the intervention, or suboptimal focus on statin prescribing. The association between the Primrose intervention and fewer psychiatric admissions, with potential cost-effectiveness, might be important.

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**Division of Psychiatry, Faculty of Brain Sciences** (Prof D Osborn PhD, A Burton MSc, R Blackburn PhD, S Heinkel MSc, Prof M King PhD), **Department of Primary Care and Population Health** (R Hunter MSc, L Marston PhD, H Gilbert PhD, Prof I Nazareth PhD, Prof I Petersen PhD, K Walters PhD), **Centre for Behaviour Change, Department of Clinical, Educational, and Health Psychology, Division of Psychology and Language Sciences, Faculty of Brain Sciences** (L Atkins PhD, Prof S Michie PhD), **Department of Allied Health Research** (Prof S Morris PhD), **and Department of Statistical Science** (Prof R Omar PhD), **University College London, London, UK; Camden and Islington National Health Service Foundation Trust, St Pancras Hospital, London, UK** (Prof D Osborn, Prof M King, Prof S Michie); **Department of Medicine, Faculty of Medicine, Imperial College London, London, UK** (Prof T Barnes PhD); **Institute of Psychiatry, Psychology & Neuroscience, Kings College London, London, UK** (Prof T Craig PhD); **Human Development and Health Academic Unit, Faculty of Medicine, University of Southampton, Southampton, UK** (Prof R Holt PhD, Prof R Peveler PhD); **Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK** (Prof R Morris PhD); **and The McPin Foundation, London, UK** (V Pinfold PhD)

## Introduction

An increased risk of cardiovascular disease morbidity and mortality in people with severe mental illnesses is well established, including schizophrenia, psychoses, and bipolar affective disorder.[1] This health inequality has been recognised for many years but the latest evidence suggests that the mortality gap continues to widen, partly because gains from primary prevention in the general

Correspondence to:
Prof David Osborn, Division of Psychiatry, Faculty of Brain Sciences, University College London, London W1T 7NF, UK
**d.osborn@ucl.ac.uk**

## Research in context

### Evidence before this study

People with severe mental illnesses have an increased risk of morbidity and mortality from cardiovascular disease compared with the general population. We searched for randomised controlled trials of interventions to reduce cardiovascular disease risk in people with severe mental illnesses published in English. On May 19, 2014, we searched the Cochrane Library for existing systematic reviews and the Cochrane Depression, Anxiety and Neurosis, and Cochrane Schizophrenia Group Trial Registers for additional randomised controlled trials from January, 1966, using the search terms: (schizophrenia OR severe mental illness OR bipolar OR mania OR manic OR hypomani OR psychos OR psychotic OR postpsychotic OR post psychotic OR rapid cycling OR schizoaffective) AND (physical OR cardio OR metabolic OR weight OR tobacc OR smok OR medical OR alcohol OR nutrition OR diet OR health OR diabete OR blood pressure OR hypertension OR cholesterol OR statin). 11 026 papers were identified, of which 15 systematic reviews and 28 randomised controlled trials were relevant. Although some evidence existed for effectiveness for pharmacological and behavioural interventions targeting weight (metformin, topirimate, diet, and exercise) and smoking (bupropion, nicotine replacement therapy, and standardised stop smoking services), we found no evidence for interventions targeting cholesterol, hypertension, diabetes, or multiple cardiovascular disease risk factors. Most trials had small sample sizes, short length of follow-up, and were done in secondary care, which limited their generalisability to other settings.

### Added value of this study

To our knowledge, this is the first pragmatic cluster randomised controlled trial of a behavioural change intervention targeting multiple cardiovascular disease risk factors in people with severe mental illnesses compared with treatment as usual in primary care in England. The primary outcome of total cholesterol at the 12-month follow-up did not differ between the intervention (Primrose) and treatment-as-usual groups; however, psychiatric inpatient and total health-care costs were lower in the Primrose group and total cholesterol concentrations decreased in both groups at 12 months.

### Implications of all the available evidence

The decrease in admissions and costs with the Primrose intervention might be important. General practices should continue to optimise evidence-based treatments for cardiovascular disease prevention in people with severe mental illnesses with the same interventions used in the general population.

population have not been observed to the same degree in people with severe mental illnesses.[2,3] Less evidence exists regarding which interventions effectively decrease the cardiovascular risk in people with severe mental illnesses, and few studies have taken a pragmatic or multi-risk factor approach to decreasing the cardiovascular disease risk in real-life settings. Interventions focused on single risk factors have shown some promise, including smoking cessation[4] and weight reduction,[4,5] and statins have been shown to decrease cholesterol concentrations effectively in large studies[6] of people with severe mental illnesses. Based on economic modelling, screening for cardiovascular disease risk in people with severe mental illnesses (with risk algorithms) and prescribing statins for those individuals with a 10-year risk of more than 10%, might be cost-effective in UK primary care.[7]

We developed a pragmatic intervention aimed at reducing cardiovascular disease risk factors among people with severe mental illnesses in primary care in England, using published evidence and evidence from focus groups,[8] and incorporating scientific behaviour change theory.[9] Nurses and health-care assistants were trained to deliver the intervention and to target relevant cardiovascular disease risk factors in a collaborative way, with recommended risk reduction strategies for the participant risk profile. We selected the cluster trial design to minimise the risk of contamination of the intervention between the trial groups. Our aims were to compare the clinical effectiveness and cost-effectiveness of the intervention versus treatment as usual for people with severe mental illnesses.

## Methods

### Study design and participants

We did this cluster randomised trial with general practices from across England as the unit of cluster. We included people aged 30–75 years on the Quality and Outcomes Framework register for severe mental illnesses, including schizophrenia, bipolar affective disorder, or other non-organic psychosis, with a mean total cholesterol concentration of 5·0 mmol/L or a total:HDL cholesterol ratio of 4·0 mmol/L or more and one or more additional cardiovascular disease risk factors, including hypertension, diabetes, raised glycated haemoglobin ($HbA_{1c}$; 42–47 mmol/mol), raised body-mass index (BMI; >30 kg/m²), or current smoker.[10] We excluded people currently under the care of acute psychiatric services, with organic psychoses or personality disorder diagnoses, with less than 6 months life expectancy, pre-existing cardiovascular disease, or who were pregnant. General practices in England were eligible to participate in the study if they had an available nurse or health-care assistant who could deliver the intervention and at least 40 patients on their practice register with severe mental illness. Data from screening, baseline assessments, and follow-up were collected in the general practices from patient questionnaires and medical records by research nurses.

The trial was delivered according to the published protocol.[10] Ethics approval was obtained from the