

## Evidence Briefing for NHS Bradford and Airedale

### **Physical health monitoring for people with schizophrenia or other serious mental illness**

- The NICE clinical guideline on schizophrenia<sup>1</sup> recommends that GPs and other primary healthcare professionals should monitor the physical health of people with schizophrenia at least once a year. The assessment should focus on cardiovascular disease risk assessment.
- Physical health reviews for people with schizophrenia and other serious mental illness form part of the National Quality and Outcomes Framework.
- An initial audit of 12 general practices in Bradford and Airedale revealed that while all practices had a case register of people with serious mental illness, none of the patient records examined reported a formal assessment of cardiovascular risk. Only 37% of patients had a record of cholesterol within the past 15 months. If these data are representative, there is a clear need to improve physical health monitoring and risk assessment for people with serious mental illness in Bradford and Airedale.
- There is good evidence that people with mental illness are at higher risk of cardiovascular disease compared with the general population. Risk assessment allows people to be offered effective treatment on an individual basis.
- There is robust evidence that treatment with statins reduces cardiovascular events and mortality in people at high risk of cardiovascular disease but without clinical evidence of disease. NICE considers statin therapy to be cost-effective for people with a 5-year risk of cardiovascular disease of 20% or more.
- Systematic reviews provide some evidence that non-pharmacological interventions can promote weight loss in people with schizophrenia.
- There is limited evidence of the effectiveness of smoking cessation interventions for people with schizophrenia. A Cochrane review of this topic is likely to provide up-to-date evidence in the near future.
- Implementing the NICE recommendation more fully would be expected to lead to a decrease in health inequality, an issue highlighted by the Disability Rights Commission.
- Although the NICE guideline envisages physical health monitoring taking place mainly in primary care, all health professionals who work with people with severe mental illness have a responsibility for monitoring physical health as appropriate for the individual's mental health state and social circumstances.

This evidence briefing has been produced for the Leeds Partnerships NHS Foundation Trust by the Centre for Reviews and Dissemination as part of TRiP-LaB (Translating Research into Practice in Leeds and Bradford).

## **What does NICE recommend?**

The NICE guideline states that:

“GPs and other primary healthcare professionals should monitor the physical health of people with schizophrenia at least once a year. The assessment should focus on cardiovascular disease risk assessment as described in the NICE clinical guideline on ‘Lipid modification’.<sup>2</sup> A copy of the results should be sent to the care co-ordinator and/or psychiatrist, and put in the secondary care notes. Healthcare professionals in secondary care should ensure that people with schizophrenia receive physical healthcare from primary care in accordance with the recommendations.”

These recommendations assume that physical health monitoring will normally take place in primary care. However, people with schizophrenia and other serious mental illness are not a homogeneous group and vary in their degree of contact with primary care services. All health professionals who work with people with severe mental illness have a responsibility for monitoring physical health as appropriate for the individual’s mental health state and social circumstances.

## **What is the evidence base for clinical effectiveness?**

### *Evidence used by NICE*

The guideline notes that the effectiveness of physical health screening and monitoring procedures in people with schizophrenia has not been tested in randomised trials. The

recommendations are based on an updated narrative review and informal consensus among the members of the NICE Guideline Development Group.

The review presents evidence that people with schizophrenia have higher rates of morbidity and mortality compared with the general population, including increased risk of death from circulatory conditions, infections, endocrine disorders and cardiovascular disease.<sup>3</sup> People with schizophrenia have increased rates of lifestyle risk factors, including smoking, poor diet and lack of exercise. Adverse effects on physical health are also associated with long-term use of antipsychotic medication and factors such as substance abuse that are often associated with schizophrenia.

In terms of screening and monitoring the guideline states that people with schizophrenia are no less likely than others to attend for cardiovascular screening in primary care.<sup>4</sup> However, a comparison of people with schizophrenia, asthma and other attendees indicated that GPs were less likely to have recorded data on blood pressure, cholesterol and smoking status for people with schizophrenia compared with the other groups.<sup>5</sup> This evidence is relevant to those service users who are in contact with GP services and who have a relatively stable illness and lifestyle. People with more acute illness may have more contact with secondary care or community services and these services could also be involved in monitoring of physical health.

The schizophrenia guideline refers specifically to cardiovascular disease (CVD) risk assessment following the recommendations of the NICE guideline on lipid modification.<sup>2</sup> This guideline recommends the use of the Framingham 1991 10-year risk equations to assess risk of CVD, although it also notes that these equations may overestimate risk in general UK populations and may not be suitable for people with named underlying risk factors, including people treated with antipsychotic medication. If risk equations are not suitable, CVD risk estimates should be based on clinical assessment.

For people considered to be at high risk of CVD (10-year risk of 20% or more), NICE recommends statin therapy for primary prevention of cardiovascular events. However, before offering statins, other modifiable risk factors should be considered and efforts made to optimise their management. These include diet, exercise, alcohol and smoking cessation.

There is robust evidence that statins can reduce the risk of cardiovascular events in people at high risk of CVD but without clinical evidence of disease. This evidence is reviewed in the NICE technology appraisal of statins<sup>6</sup> and is likely to be applicable to people with schizophrenia or other serious mental illness who continue with treatment over the long term. The technology appraisal also examined adverse events and found that serious events affecting the muscles (rhabdomyolysis and myositis) were rare (6 and 22 cases, respectively, among over 40,000 people treated with statins).

In primary prevention trials, approximately 87% of patients were continuing with statin therapy after 3 years.<sup>6</sup> The most up-to-date systematic review of statins for primary prevention found a statistically significant 7% relative reduction in mortality in the statin group, although the true effect could be small (95% confidence interval 1% to 13%).<sup>7</sup>

There is also substantial evidence from observational and epidemiological studies that changes in lifestyle (primarily diet, physical activity and smoking cessation) can substantially modify an individual's risk of CVD. Again, this evidence is too well known to need discussion in this briefing. However, evidence that medical advice or other interventions to modify lifestyle can improve outcomes is more limited. The systematic review performed to support the NICE guideline on lipid modification<sup>2</sup> found very few randomised trials of dietary advice or physical activity interventions for people at high risk of CVD that assessed cardiovascular outcomes. The guideline did not specifically address smoking reduction, alcohol or weight management, which are dealt with in other NICE guidance and national recommendations.

Some additional evidence on lifestyle interventions for people with schizophrenia is discussed in the next section.

### *Other evidence*

Other relevant and up-to-date systematic reviews were sought by a non-systematic search of the CRD databases, including systematic reviews included in the DARE database and Cochrane reviews.

A systematic review published in 2005<sup>8</sup> assessed the efficacy of healthy living interventions (defined as individual or group interventions aimed at encouraging healthier lifestyles and/or reducing risk factors for common medical problems) for people with schizophrenia or schizo-affective disorder. The review included 16 studies but these were small (only 242 patients completed treatment across all 16 studies) and/or poor quality (only two RCTs). The strongest evidence came from studies of smoking cessation: seven studies, of which five reported cessation rates ranging from 35 to 50% at the end of treatment and 12 to 18% after 6 months. Evidence for weight reduction, exercise and nutrition interventions was even more limited. A Cochrane review of smoking cessation interventions for people with schizophrenia has been published in protocol form<sup>9</sup> and the full report is being peer-reviewed at the time of writing (October 2009) so it is likely that new evidence on this topic will be available shortly.

Two systematic reviews have assessed interventions to reduce or prevent weight gain in people with schizophrenia.<sup>10, 11</sup> A Cochrane review by Faulkner et al. looked at both pharmacological and non-pharmacological interventions (18

and five studies, respectively).<sup>11</sup> The review found statistically significant but modest beneficial effects of both drug treatment and cognitive behaviour therapy (CBT) for preventing weight gain. However, the quality of the evidence was limited by the small number of studies, small sample size, short duration of the studies and variation among the interventions. The review authors concluded that there is insufficient evidence to recommend the general use of medication for weight management in people with schizophrenia.

A systematic review focusing specifically on non-pharmacological interventions for antipsychotic-induced weight gain was published in 2008.<sup>10</sup> The review looked at prevention of weight gain and at promotion of weight loss in people who had already experienced weight gain. Ten RCTs with 482 participants were included. Interventions were classified as CBT, nutritional counselling and nutritional counselling plus exercise. Across all types of intervention, the treatment group showed a significantly greater reduction in mean body weight at the end of treatment compared with control groups receiving standard care. The difference between groups (weighted mean difference) was 2.6 kg with a 95% confidence interval of 1.9 to 3.2 kg. The probability of this being a chance effect was very low. Based on an average baseline weight of approximately 80 kg in the included studies,<sup>10</sup> this represents an approximate weight loss of 3.25% (2.4 to 4%) attributable to treatment. The clinical significance of this degree of weight loss is

uncertain. Furthermore, none of the studies reported follow-up beyond 3 months after the end of treatment, which means that the long-term effectiveness of the interventions is unknown. Based on a modified GRADE evidence profile,<sup>12</sup> the quality of the evidence for effect on weight loss is high to moderate.

### **What is the evidence base for cost-effectiveness?**

The NICE schizophrenia guideline does not contain any evidence on the cost-effectiveness of screening and monitoring of physical health of people with schizophrenia or other serious mental illness. No economic evaluations relevant to this topic were found on the NHS EED database.

An economic model developed as part of the NICE guideline on lipid modification<sup>2</sup> supported the recommendation that people requiring assessment of risk of CVD should be identified and prioritised using data from their electronic records to provide an initial estimate of risk. This strategy was considered more cost-effective than assessing people at random or on the basis of age. As noted above, people with schizophrenia and other serious mental illness are likely to be at higher risk compared with the general population and therefore should be a high priority for risk assessment. The economic model is based on using statins to reduce the risk of cardiovascular events in people considered to be at high risk.

The NICE guideline on lipid modification cites two economic evaluations of exercise

interventions. One was conducted in Canada and concluded that exercise was cost-effective in terms of life-years gained for people at risk of CVD.<sup>13</sup> The other study was conducted in the USA and reached similar conclusions but full publication details were not provided. No economic evaluations in the UK setting were found.

The NICE technology appraisal of statins<sup>6</sup> considered published economic evaluations and economic models developed by an independent academic team and by companies manufacturing statins. Statin therapy was considered to be cost-effective for people with an estimated 10-year CVD risk of 20% or more. Discussion of this evidence is outside the scope of this briefing but it is likely to be reliable and is the basis for guiding NHS practice. The guidance in this technology appraisal has been placed on the 'static list', which means that it will not be reviewed again unless new research becomes available that would materially affect the recommendations.

### **How applicable is the evidence to the NHS?**

The Framingham equations for estimating CVD risk were developed in a US population at a time when death rates from heart disease were higher than they are today. These equations may overestimate risk in general UK populations and underestimate it in high-risk populations.<sup>2</sup> The NICE Guideline Development Group for lipid modification considered them to be the best tool available but they may not be accurate for people with mental illness, who

may be at high risk because of lifestyle factors and weight gain associated with antipsychotic drugs.

Statins have been evaluated in a large number of patients with different risk factors and in different settings. There is no reason why the results of these trials should not be applicable to patients with mental illness being treated in NHS settings, although there could be issues of adherence to treatment. NICE recommends that a statin with a low acquisition cost should be used, e.g. simvastatin 40 mg. The most up-to-date systematic review of statins for primary prevention did not include any studies with simvastatin.<sup>7</sup> Only a few trials have compared different statins and there is little evidence that any one statin is more effective than the others.

The applicability of the findings of systematic reviews of non-pharmacological interventions to clinical practice is more uncertain. When these interventions are evaluated in RCTs, the intervention is often implemented by highly trained therapists and may be more intensive than interventions of the same type in clinical practice. Ideally, systematic reviews of such interventions would include pragmatic effectiveness trials in a range of clinical settings.<sup>10</sup> It is not clear whether this is the case for the systematic reviews of non-pharmacological interventions for people with schizophrenia considered in this briefing. There may also be differences between the patients who agree to take part in clinical trials and the general patient population and these could

limit the generalisability of the findings.

### **What are the potential implications of this recommendation for NHS Bradford and Airedale?**

There is evidence from an initial audit of 12 randomly selected general practices in Bradford and Airedale that many patients with serious mental illness do not have data recorded that would allow a formal assessment of their CVD risk. In particular, only 37% of patient notes examined had a record of cholesterol measurement in the previous 15 months. No patient had a record of CVD risk score based on the Framingham risk equations as recommended by NICE. Other important indicators were recorded more commonly, for example 80% for smoking status and 70% for blood pressure. These findings suggest that there is a need for GPs to improve the monitoring of physical health in people with serious mental illness whose condition is stable and who are in contact with general practices. People whose illness is more acute may be more likely to be in contact with other services, for example community and secondary care psychiatric services. Although the NICE guideline presents physical health monitoring as normally happening in primary care, all relevant health professionals could play a role in increasing the recording of important physical health information for people under their care. There may be a need for improved communication and co-ordination between primary and secondary care services for people

with serious mental illness in the Bradford and Airedale region.

Implementing physical health checks for people with serious mental illness in line with the general population would be expected to reduce inequalities in health, an issue highlighted by the Disability Rights Commission. Given that this population is at higher risk of CVD compared with the general population, an increase in prescription of statins and other cardiovascular drugs is likely. There could also be an increase in referrals for smoking cessation and other lifestyle interventions.

Statin therapy is considered effective and cost-effective by NICE and future research is unlikely to affect this conclusion. If people with schizophrenia receive and adhere to statin therapy, their risk of cardiovascular events and premature death is likely to be reduced, although the magnitude of the effect on mortality could be small. The largest primary prevention study included in the

NICE technology appraisal reported that approximately 95 people (95% confidence interval 60 to 216) would have to be treated with a statin over 3 years to avoid either a death from heart disease or a non-fatal heart attack. The availability of statins in generic form means that the acquisition cost of these drugs has been reduced.

There is some evidence to suggest that people with schizophrenia could also benefit from CBT, nutritional counselling and other non-pharmacological interventions to prevent weight gain, although the clinical significance and cost-effectiveness of such interventions is uncertain. CBT is recommended in the NICE guideline as an intervention to reduce hospitalisation<sup>1</sup> and it is possible that lifestyle issues could be incorporated into such programmes. People with schizophrenia have high rates of smoking and evidence from a Cochrane review of interventions for smoking cessation should be available in the near future.

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TRiP-LaB is a research partnership between the Leeds and Bradford NHS and the Universities of York and Leeds. TRiP-LaB is one of the five research themes of the Leeds, York and Bradford (LYBRA) Collaboration in Leadership and Applied Health Research and Care. LYBRA is one of seven partnerships between NHS organisations and leading universities being funded by the NIHR. Each partnership is undertaking high quality health research and is developing new ways of translating research findings into improved outcomes for patients.

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