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Counting Up the Risks – How Common are Risk Factors for Morbidity and Mortality in Young People with Psychosis?

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Abstract

Aim: This study examined the prevalence of risk factors for cardiovascular (CV) related morbidity and mortality in young people with psychosis aged 18-24 years.

Methods: The study included 132 people aged 18-24 years who participated in the 2010 second Australian national survey of people living with psychosis. The 2009 World Health Organisation (WHO) Global Health Risks report was used as a framework to determine which specific risk factors were present in each in these young people. The risk factors assessed in this study were smoking, alcohol use, hypertension, overweight/obesity, physical inactivity, high blood glucose, high cholesterol and poor diet. Each risk factor was defined according to WHO criteria. A count of the total number of risk factors present for each participant was determined. Data for male and female participants was compared.

Results: Young men had an average of 2.9 (SD 1.2) risk factors. Young women had an average of 2.4 (SD 1.2) risk factors. The most common risk factors were low fruit and vegetable intake (77.9%), cigarette smoking (67.7%), overweight/obesity (55%) and physical inactivity (39.8%). There were no significant differences between men and women in the number of risk factors present, or the prevalence of individual risk factors.

Conclusion: This study demonstrated that many of the risk factors that ultimately contribute to disability and premature death are present at an early age in people with psychosis. Preventive measures need to be an integral component of early intervention services for this client population to avert progression to serious cardiovascular morbidity and early mortality.

Key words: morbidity, mortality, risk factors, cardiovascular disease, young psychosis, world health organisation.

Introduction

There has been increasing recognition of the poor physical health and reduced life expectancy of people with chronic psychiatric disorders such as schizophrenia and bipolar disorder [1,2,3]. A 10 year follow-up study of people presenting with first episode psychosis (FEP) found a standardized mortality ratio (SMR) of 3.6[4]. Similarly, Dutta et al (2012) reported that in the UK, people with FEP have an overall mortality risk nearly double that of the general population. Most of these deaths are due to cardiovascular (CV) disease (Laursen et al., 2013), leading researchers to question why people with psychosis have a higher prevalence of CV disease, and why this CV disease progresses to death at an earlier age, compared with the general population.

The Framingham study, along with other large cohort studies, has led to the identification of CV risk factors, estimation of their relative contribution to CV disease, and the development of risk equations to predict CV mortality[6]. These risk equations can be used to identify people who should be prescribed preventive treatments such as statins. Public health campaigns have targeted modifiable risk factors such as smoking, obesity, and lack of exercise.

In Australia, consensus guidelines for the assessment of absolute CV disease risk [7] have been developed. The goal is to reduce the level of absolute risk by managing individual risk factors. The Australian CV risk charts can be used for all adults aged 45 years or over. An exception is made for Aboriginal and Torres Strait Islanders, who should be assessed if they are over 35 years of age. Despite evidence of premature CV morbidity and mortality, there is

no recommendation regarding people with chronic mental disorders. The present study was therefore undertaken to investigate CV risk factors in young people with psychosis.

The assessment of CV risk factors in young people with psychosis is complicated by evidence that they differ from the normal population even before they become unwell. Drug naive young people with psychosis are more likely to have impaired glucose tolerance [8] and are more insulin resistant [10] compared with matched controls. Further, type 2 diabetes and schizophrenia share common familial risk factors[11]. Unlike their peers without mental illness, young people with psychotic disorders take antipsychotic medications. The incidence of diabetes and cardiovascular risk (indexed by measures such as body mass index (BMI), total cholesterol, triglycerides and non-fasting glucose) increase after first exposure to any antipsychotic drug[12].

These differences are reflected in studies comparing young people with psychosis and matched general population samples. Our previous work, comparing people with psychosis aged 25-64 years with a matched general population control group, found that even at age 25 years, people with psychosis had a significantly higher mean BMI, waist circumference, triglycerides, diastolic blood pressure and significantly lower HDL-cholesterol than controls [13]. This study did not include people aged less than 25 years as population control data was not available.

In addition, young people with psychosis have much higher rates of tobacco and alcohol use than other young people[14, 15].The reasons for the higher prevalence of use of these substances is unknown; as with diabetes, it is possible that there are common familiar risk factors. These

behaviours are associated with adverse effects on physical health and have been identified as risk factors for CV disease.

This study assessed CV risk factors in young people with psychosis. Risk factor equations developed for the general population have not been adapted for young people. The Joint British Societies (JBS3) Board note that current risk estimation is very dependent on age and gender, so young people and women may not be considered for preventive measures, despite high levels of modifiable CV risk factors. There is a move to estimation of lifetime risk, and the JBS3 consensus recommendations for prevention of CV disease (2014) include a lifetime risk calculator. However, the correlational structure among risk factors may be different in people with psychosis, compared with people in the community[16].

We therefore undertook a count of CV risk factors in young men and women with psychosis. This is a simple, easily reproduced method for drawing together information about multiple risk factors in an individual person. A count of CV risk factors may provide useful information about the absolute number and relative prevalence of risk factors. This method does not allow for weighting of the various factors, but does provide a basic structure for longitudinal cohort studies that might then provide this information.

A similar method of counting risk factors was used by Lloyd-Jones et al (2006), analysing the Framingham Heart Study data. They found that the absence of established risk factors (smoking, obesity, hypertension, diabetes, and hypercholesterolemia) at the age of 50 years was associated with very low lifetime risk of CV disease and longer survival. The presence of one risk factor was associated with a reduction in median survival, and those with two risk factors had an even greater reduction in median survival.

We utilised World Health Organisation (WHO) information about the leading global risks for mortality and burden of disease (measured as Disability-Adjusted Life Years or DALYs). The eight WHO risk factors for high income countries are listed in Table 1. The population attributable fraction of disability and mortality related to each risk factor has been calculated by determining the proportional reduction in population disease or mortality that would occur if this risk factor was reduced to an ideal level. For example, if no one smoked tobacco in high income countries, the death rate would fall by 17.9% and the level of disability in these populations would be reduced by 10.7%.

There is evidence from numerous studies that each of the eight risk factors are more common in people with psychotic disorders than in the general population[18-22]. In a review of six of the WHO risk factors (hypertension, raised glucose, smoking, physical inactivity, overweight/obesity, and elevated cholesterol), Wildgust and Beary (2010) demonstrated that each of these factors are more prevalent in people with schizophrenia than in the general population.

There are some potentially important gender differences. The prevalence of FEP is higher in men, and men tend to be younger at the time of first contact with mental health services[24, 25]. Men are also more likely to smoke tobacco [26] and use alcohol [27]. For these reasons, this current study evaluated risk factors for each gender separately, as well as for the total sample.

No previous studies have applied the WHO-defined risk factor framework in young people with psychosis. The method used in this study, counting up the risk factors to provide a total number for each person, is a novel approach to quantifying CV risks. Systematically drawing together all of the risk factors using this framework provides an integrated, easily understood

picture of the total aggregate risk of death and disability, attributable to these specific well-validated factors, faced by a cohort of young people with psychosis. This method does not provide a weighting for the various factors, or tell us the long term implications of having three rather than two risk factors, but it does introduce a method that may be used in further studies to address these questions, and perhaps ultimately build an informative algorithm.

This study analysed data from young people drawn from a large, representative sample of people living with psychosis, to investigate the total number of risk factors present in each individual participant, and prevalence of each of the risk factors in these young people.

Method

This study draws on data from the 2010 second Australian national survey of people living with psychotic illness (Survey of High Impact Psychosis, SHIP). A total of 1825 people aged 18-64 years were interviewed. The survey methods have been described in detail elsewhere [28, 29]. In brief, this study was two-phase sampling design. In phase 1, people in contact with public mental health services and non-government organisations in the previous 12 months were screened for psychosis, resulting in 7955 people screening positive. Those who screened positive were randomly selected during phase 2 to take part in an interview and assessment. Of the 1825 subjects who completed the interview, 1286 provided fasting blood samples. Participants fasted overnight (minimum of 8 hours) then provided venous blood samples for measurement of plasma glucose and total cholesterol concentrations in accredited pathology laboratories. Data was collected regarding participants' gender, age, education, employment, ICD-10 diagnosis and age of onset of psychosis. Diagnoses based on the International Classification of Diseases 10th Revision (ICD-10)[30] were ascertained using the Diagnostic

Interview for Psychosis (DIP)[31]. The study was approved by institutional human research ethics committees at each of the study sites. Written informed consent was provided by all participants.

We report here on those 132 people aged 18-24 years who participated in the SHIP interview and provided fasting blood samples. Demographic data included participants' gender, age, education, employment status, and age of onset of psychosis/major affective illness.

WHO Risk Factors: The presence of each of the eight risk factors was determined by applying the WHO criteria [32] to the SHIP data. Tobacco use was defined as smoking tobacco daily in the previous 4 weeks. Blood pressure (BP) was measured by trained research staff while the participant was seated. The WHO criterion for hypertension was systolic BP e 140 mm. Participants were weighed in loose clothing, without shoes, using electronic scales measuring up to 200kg. Overweight and obesity was defined as a body mass index (BMI) e 25. Physical inactivity was assessed using the International Physical Activity Questionnaire (IPAQ) short form [33]. Achieving less than 2.5 hours per week of moderate exercise, or less than 1 hour per week of vigorous exercise, was defined as being physically inactive. The WHO (2009) definition of physical inactivity also included people who engaged in less than 600 MET (Metabolic Equivalent of Task) minutes per week of any physical exercise. MET provides a measure of the relative intensity of a physical activity.

High blood glucose was defined as a fasting blood glucose of e 5.6 mmol/l. High cholesterol was defined as a fasting total cholesterol e 6 mmol/l. Whilst the WHO (2009) defines low fruit and vegetable intake as less than 5 serves of fruit and vegetables daily, in our data low fruit and vegetable intake was defined as consuming fewer than 4 daily servings of fruit (1

serve = 1 medium piece or 2 small pieces of fruit or 1 cup of diced pieces = 150 grams) and vegetables (1 serve = 1/2 cup cooked vegetables or 1 cup of salad vegetables = 75 grams). Our data therefore tends to underestimate low fruit and vegetable intake. Alcohol abuse was defined as an average daily consumption of 4 or more standard drinks per day, four or more times per week.

Statistical analysis: Data were analysed using SPSS version 21; IMB Corp., 2012. Individual risk factor variables were coded as binary (0 = not present; 1 = present). Risk factors for each participant were summed to obtain a single variable, representing the total number of risk factors for that person. Descriptive statistics were used to summarise participant characteristics. The sample was stratified by gender, and the number of risk factors in each gender was compared. These comparisons were made using § ^{2} tests and p values < 0.05 were taken as significant.

Results

Fasting blood samples were provided by 64.7% (n= 132/204) of SHIP participants aged 18-24 years. There were no differences in age, gender or education between people who supplied a fasting blood sample and those who did not. Descriptive data for the 132 participants in this study is summarised in Table 2.

The total number of risk factors present, by gender, is shown in Table 3. There was no significant difference in the mean number of risk factors present between men and women. A small proportion of the sample had no risk factors present (3.3%). This was more common for women (7.7%) than for men (1.2%) (Table 3).The prevalence of each risk factor is shown

in Table 4. The most common risk factors were low fruit and vegetable intake, smoking, overweight/obesity and physical inactivity. Young men had an average of 2.9 (SD 1.2) risk factors and young women had an average of 2.4 (SD 1.2) risk factors; this difference was not significant. There were no significant gender differences in the prevalence of each individual risk factor.

Discussion

Ideally, young people should not have any of the WHO-defined risk factors for cardiovascular disease. Apart from rare genetic conditions (such as familial hypercholesterolemia), all of the eight risk factors investigated in this study are potentially preventable by lifestyle measures. The young people in this study already had, on average, 2-3 risk factors. Thirty men and eight women had four or more risk factors.

Obesity and smoking are responsible for 17.9% and 8.4% of mortality in high income countries respectively, and were each present in more than half of our study sample. Poor diet and lack of exercise were also common, and would be expected to contribute to a gradual increase in obesity over time. Other risk factors such as hypertension, hypercholesterolemia and diabetes can be expected to develop later, in the context of chronic obesity, poor diet and physical inactivity.

It is informative to be able to compare our results with general population data. We are not aware of any studies of Australian young people incorporating all of these WHO risk factors, but there is information about some individual measures. Over half of people in our study were overweight or obese, which is more than three times the prevalence of overweight/obesity in Australians of the same age (15.1%)[34]. In the general Australian population, 18.3% of men and 14.8% of women aged 18-24 years smoke tobacco daily. Rates of smoking amongst our study population are very high with more than two thirds (67.7%) of our sample being current smokers. Hypertension was slightly more prevalent in our psychosis

sample, with 8% of men and 6.8% of women having elevated blood pressure, compared with 6.8% of men and 5.2% of women aged 18-24 years in the general Australian population[35].

A study by Correll et al (2014) provides insight into the prevalence of cardiometabolic risks in patients with first episode-schizophrenia spectrum disorders aged 15-40 years but whose mean age (23.6 years; SD 5.0) was only slightly than the current sample. Compared to this study, our sample had higher rates of smoking (67.7% vs. 50.8%), overweight or obesity (55.0% vs. 48.3%) and higher mean systolic blood pressure (119.8 (range 104) vs. 117.1 (SD 12.4))[36]. Mean BMI in the current study was slightly higher compared with the former study while mean fasting plasma glucose in our study and in the former study were virtually identical. However, our sample had lower mean total cholesterol compared with the Correll's study[36].

Australia has a well-developed social welfare system to support people with mental illness, and the SHIP sample was drawn from people in contact with mental health services. In some catchments, early psychosis services were also available. Despite these supports, their physical health status was poor. It is therefore essential that services for young people with psychosis place a high priority on the management of their physical health. All of the WHO risk factors are potentially modifiable through low cost interventions such as diet, exercise, and cessation of smoking and alcohol abuse. Curtis et al (2015) evaluated a lifestyle and life skills intervention for young people (14-25 years) with early psychosis, who were starting treatment with antipsychotic medication. Only 13% of the intervention group experienced significant weight gain, compared to 75% of the standard care group.

The very high rates of smoking in young people with psychosis has raised the possibility that tobacco might contribute to the aetiology of psychosis[38], which would mean that it is even more imperative that young people are encouraged and assisted to stop smoking. There is little research into smoking cessation interventions for young people with psychosis, but studies in adults with chronic mental illness[39] and a systematic review of smoking cessation interventions in people with schizophrenia[40] have both shown encouraging results. Similarly, Baker et al (2015) reported some improvements with an intervention targeting both smoking and cardiovascular risk factors in people with psychotic disorders.

However, research into physical health interventions predominantly consists of trials of modest duration with small numbers of participants. Gates et al (2015) note that while weight loss and attenuation of weight gain are possible, these positive benefits might not persist beyond the end of the intervention. For example, a three month behavioural intervention combining information on nutrition and exercise in a randomized controlled trial in patients with first-episode psychosis attenuated the weight gain caused by antipsychotic medication but the differences were no longer significant at 12 month follow up[43]. Gates et al (2015) highlight the need for investigation into the aetiological factors related to poor physical health and for theory-driven interventions that target these aetiological factors. Further, larger and more sustainable results are likely to come from improved, integrated medical management of patients, with interventions like smoking cessation programs offered to appropriate individuals at times that they are most likely to benefit from them. There is a risk that short-

term programs with goals that are difficult to achieve may result in further experiences of failure and demoralisation.

This study provides information for planning intervention programs; clearly it would be sensible to target the risk factors that are most common, and associated with the most severe disability and risk of mortality. A focus on prevalence is simplistic, however, because prevalence does not equate to the impact of the risk factor or the achievable risk reduction associated with current intervention paradigms. Determining these requires longitudinal multivariate risk and outcome data in large samples of people with psychosis. Even so, as shown by Lloyd-Jones et al (2006), simply noting the presence and number of risk factors can predict median survival.

A clear methodological limitation in this study is the relatively small sample size after gender and age stratification. Furthermore, our measure underestimated low fruit and vegetable intake; even so, 77.9% of participants had inadequate intake. There is also a lack of control data for people in the general population aged 18-24 years. This study did not record family history of CVD, CKD and cancer. Comprehensive assessment of multiple risk factors and the use of the epidemiological data informing risk of disability and death is a strength of the study. Nevertheless, the findings are stark and underline the importance of physical interventions being an integral part of comprehensive care for people with an early psychosis.

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