

# Medical comorbidity in schizophrenia

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HAVING A MENTAL ILLNESS has been, and remains, a barrier to effective medical care. Schizophrenia and, indeed, most mental illnesses are associated with undue medical morbidity and mortality.<sup>1</sup>

There are two key issues relating to comorbidity: detection and prevention. In a recent article, Harris and Mercer<sup>2</sup> discussed recommendations of the Royal Australian College of General Practitioners (RACGP)<sup>3</sup> for preventive action in general practice. Based on loss of health calculated as age-standardised disability-adjusted life-years (DALYs),<sup>4</sup> targets selected by the RACGP included smoking, physical activity, high blood pressure, alcohol consumption, obesity, high blood cholesterol level, diabetes, breast cancer and bowel cancer. Although all of these conditions and behaviours are known to be particularly problematic for people with schizophrenia or various other mental illnesses,<sup>1</sup> this group, as a whole, receives less than satisfactory attention to its medical needs. The preventive role undertaken by general practitioners would be of great service to the community if it were applied more broadly to people who suffer from serious mental illness.

## Mortality

Schizophrenia has been described as a "life-shortening disease",<sup>5</sup> and there is growing evidence to support this claim.<sup>6-9</sup> Without discounting suicide, which accounts for less than a third of premature deaths, people diagnosed with schizophrenia can expect to live 9-12 years fewer, on average, than those in the general population.

Australian data support the findings of overseas studies. For example, in a study based on Victoria's Psychiatric Case Register and State coronial data, patients with schizophrenia were found to be 2.9 times more likely to die of natural causes, especially cardiovascular disease, than people in the general population.<sup>10</sup> Studies in Western Australia<sup>1</sup> and

## ABSTRACT

- Schizophrenia has been described as a "life-shortening disease", and physical comorbidity accounts for 60% of premature deaths not related to suicide.
- People with schizophrenia and other mental illnesses have a higher rate of preventable risk factors such as smoking, high alcohol consumption, poor diet, and lack of exercise.
- Recognition and management of morbidity in people with mental illness are made more difficult by barriers related to the patient, the illness, the attitudes of medical practitioners, and the structure of healthcare delivery services.
- Improved detection and treatment of medical illness in people with schizophrenia will have significant benefits for their psychosocial functioning and overall quality of life.

MJA 2003; 178: S67-S70

New South Wales<sup>7</sup> have also shown that mortality is higher in people with schizophrenia and other mental illnesses.

It is an unfortunate situation that psychotic patients present less and are hospitalised less often for a variety of medical conditions, but are at the same time over-represented in population-matched mortality figures. This suggests that morbidity in these people is less efficiently detected.

## Comorbidity

People with schizophrenia and other mental illnesses also have high rates of physical comorbidity. However, several US studies have shown that the detection rate of physical illness among people with mental illness is very poor. Koran et al<sup>11</sup> estimated that 45% of patients in California's public mental-health system had physical disease and, of these, 47% were undetected by the treating doctor. A substantial proportion of these illnesses were judged to be either causing or exacerbating the patient's mental illness. A study by Koranyi<sup>12</sup> of psychiatric clinic patients revealed remarkably similar findings: 43% of patients had physical illnesses and, of these, 46% had not been diagnosed by the referring doctor (non-psychiatrist physicians had missed 33%; psychiatrists had missed 50%). Hall et al<sup>13</sup> found that 46% of patients admitted to a research ward had an unrecognised physical illness that either caused or exacerbated their psychiatric illness; 80% had physical illnesses requiring treatment; and 4% had precancerous conditions or illnesses. Morbidity data for psychiatric populations in Australia are scant.

Illnesses that should be high in the medical practitioner's awareness are summarised in Box 1, which relates common

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## 1: Common physical conditions found in patients with mental illness, and relationship between physical illness and psychiatric condition, medication and lifestyle factors

### Diabetes<sup>14-16</sup>

- Increased risk in people with schizophrenia of developing glucose-regulation abnormalities, insulin resistance and type 2 diabetes mellitus.
- Lifestyle factors (poor diet, sedentary behaviour) exacerbate the problem.
- All antipsychotic agents (atypicals more than typicals) increase the propensity to develop diabetes.

### Hyperlipidaemia<sup>17</sup>

- Antipsychotic medications have been associated with the development of hyperlipidaemia (both related to, and independent of, weight gain).
- Some typical antipsychotics (eg, haloperidol) have no effect on lipids; phenothiazines (eg, chlorpromazine) tend to raise triglyceride levels and reduce levels of high-density lipoproteins.
- Dibenzodiazepine-derived atypical antipsychotics (eg, clozapine, olanzapine) are associated with increased levels of fasting glucose and lipids compared with risperidone.

### Cardiovascular disease (hypertension, cardiac arrhythmias)<sup>1,18-20</sup>

- People with mental illness have higher rates of cardiovascular and respiratory disorders than the general population.
- Antipsychotic agents contribute to metabolic syndrome X (hypertension, hyperlipidaemia, hyperglycaemia, insulin resistance and obesity).
- Lifestyle factors (smoking, alcoholism, poor diet, lack of exercise) contribute to increased risk of cardiac problems.
- Mortality due to ischaemic heart disease, cardiac arrhythmias and myocardial infarction is higher in people with mental illness.

### Obesity<sup>21,22</sup>

- 40%–62% of people with schizophrenia are obese or overweight.
- Both typical and atypical antipsychotics can induce weight gain.
- Dibenzodiazepine-derived atypicals (eg, clozapine, olanzapine) cause rapid weight increase in the short term. Long-term differences between agents are less clear.
- Lifestyle factors and poor ability to modify behaviour also influence obesity.

### Malignant neoplasms<sup>23,24</sup>

- People with schizophrenia are no more likely to develop cancer overall, but, in the event of cancer, have a 50% lower chance of survival.
- Differences exist for individual cancers in people with mental illness (eg, increased risk of breast cancer for women; reduced risk of lung cancer for men).

### HIV/AIDS<sup>25,26</sup>

Incidence of HIV/AIDS in people with schizophrenia (estimated to be 4%–23%) appears higher than in the general population. Associated factors include “unsafe sex”, drug injection and non-injected drug use.

### Hepatitis C<sup>25</sup>

- Increased prevalence in people with schizophrenia compared with the general population.

### Osteoporosis<sup>27</sup>

- Accelerated rates of osteoporosis in people with schizophrenia are attributed to antipsychotic-driven decreases in oestrogen and testosterone, reduced calcium due to smoking and alcoholism, and polydipsia.

### Hyperprolactinaemia<sup>28</sup>

- High doses of typical antipsychotics and the atypical antipsychotics risperidone and amisulpride raise prolactin levels, causing galactorrhoea, amenorrhoea, oligomenorrhoea, sexual dysfunction and reduced bone mineral density, and contributing to cardiovascular disease.

### Other physical illnesses<sup>29,30</sup>

- Incidence of irritable bowel syndrome in people with schizophrenia is 19% (versus 2.5% in the general population).
- Prevalence of *Helicobacter pylori* infection is significantly higher in people with schizophrenia (odds ratio, 3.0).

physical illnesses to psychiatric conditions, psychotropic medications and lifestyle factors. For any individual patient, biological proneness to mental and/or physical illness is likely to interact with the patient's treatment and lifestyle. This once again reinforces the preventive notions expounded by the RACGP.<sup>3</sup>

## The influence of lifestyle factors

High mortality and morbidity in schizophrenia may be attributed to an environment in which unhealthy and high-risk behaviours such as smoking, substance abuse, lack of exercise and poor diet are prevalent.<sup>31</sup> An Australian study examining lifestyle factors that increased cardiovascular risk found significant differences between people with mental illness and the general population: 70% v 50% were smokers or ex-smokers; 11.5% v 3.1% used harmful levels of alcohol; and 40% v 8% were obese.<sup>18</sup> The rates of obesity (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>) may in fact be even higher, approaching 51% in particular groups of mentally ill patients, with a considerable number being overweight (BMI 25–29.9 kg/m<sup>2</sup>).<sup>32</sup> Jablensky and colleagues' landmark survey of Australian low-prevalence psychotic disorders<sup>33</sup> reported that 73% of men and 56% of women with a psychotic disorder were current smokers, while 38% of all people with a psychotic illness had been drinking daily, or for several days per week, in the year preceding the study interview. These data are consistent with overseas findings.<sup>34</sup>

Smoking-related fatalities are significantly higher in people with schizophrenia than in the general population.<sup>8</sup> Smoking is a good example of how behaviour and treatment interact to increase morbidity at a number of levels. It is a risk factor for respiratory and ischaemic heart disease and stroke, and, by reducing available plasma levels of antipsychotics (notably olanzapine and clozapine), it may influence the patient's behaviour and the treatment outcome. With respect to diet, the cognitive and social deficit symptoms of schizophrenia may make patients prone to choosing easily obtainable “fast” foods (high in saturated fats and low in fibre) as their major source of nutrition. The same deficits, especially those to do with motivation, often leave the patient without any desire to keep physically active to counter the effects of their poor diet and maintain general fitness. This is further complicated by psychotropic side effects (particularly Parkinsonism, sedation and neuroleptic-induced cognitive deficits), which can compound these problems (see Lambert and Castle, *page S57*<sup>35</sup>). Substance misuse, a major contributor to both mortality and morbidity, and common in people with schizophrenia, is discussed by Lubman and

## 2: Barriers to recognition and management of medical illness in people with schizophrenia and other mental illnesses

### Doctor/healthcare system factors

- Reticence of non-psychiatrists to treat people with serious mental illness.<sup>6</sup>
- Lack of adequate follow-up of patients with mental illness, due to patients' itinerancy and lack of motivation.<sup>8</sup>
- Changes of treating doctor, with the result that many patients do not have a longitudinal history available.<sup>6,37</sup>
- Perception by specialist psychiatrists that physical health matters should be the province of referring doctors.<sup>37</sup>
- Specialists' attention focused principally on patients' psychiatric problems,<sup>38</sup> with physical examination conducted infrequently.
- Physical complaints regarded by psychiatrists as psychosomatic symptoms.<sup>38</sup>
- Time and resources for physical/medical examinations not available in current mental-health service settings.<sup>6</sup>

### Patient/illness factors

- Poor general treatment compliance.<sup>8</sup>
- Avoidance or neglect of contact with general practitioners or general healthcare services.<sup>6</sup>
- Unawareness of physical problems because of cognitive deficits associated with mental illness.<sup>6,38</sup>
- Patients' difficulty in communicating their physical needs and problems in general.
- Physical symptoms unreported/masked because of high pain tolerance in some patients, and reduction in pain sensitivity associated with use of antipsychotic drugs.<sup>37,38</sup>
- In some patients, reluctance to discuss problems or volunteer symptoms and/or general uncooperativeness.<sup>6,37</sup>
- Patients' difficulty in comprehending healthcare advice and carrying out required changes in lifestyle.

Sundram (page S71).<sup>36</sup> Together, these lifestyle factors increase the risk or severity of medical conditions, particularly the development of metabolic syndrome X (obesity, insulin resistance, dyslipidaemia, impaired glucose tolerance and hypertension).<sup>19</sup>

## Barriers to detection and treatment of medical comorbidity

Despite the high comorbidity and mortality rates in people with serious mental illness, there are significant barriers to the early detection and treatment of physical comorbidity. One patient's family described the difficulty of accessing adequate care as "falling between the cracks".

Barriers to effective physical healthcare for mentally ill patients include patient-related elements, the nature of the illness, the medical system and available resources, and the attitudes of medical practitioners themselves (Box 2). In community-based models of psychiatric care, as practised in Australia, it is reasonable to suggest that all members of multidisciplinary teams should receive support and training in the management of physical comorbidity, as they play a major role in influencing patients' day-to-day functioning and behaviour. Strategies that may help improve outcomes for mentally ill patients with physical comorbidity are outlined in Box 3.

## 3: What should be done?

- Collection of a standard checklist and core information data concerning physical health should be routine.<sup>39</sup>
- Psychiatric services should be adequately equipped to carry out basic physical medicine tasks.<sup>40</sup>
- Refresher training should be regularly provided for psychiatrists and key members of multidisciplinary community psychiatric teams. This could encompass elements of detection, management and preventive counselling.
- Specific interdisciplinary teams with broad medical and psychiatric expertise and training should be created. These could serve in enhanced models of shared care.
- Formalised programs to address training and other issues should be set up at a state or regional level. These could be modelled on, for example, the MH-OAT program in New South Wales,<sup>41</sup> or the educational tools being developed by the Alliance of NSW Divisions of General Practice in collaboration with NSW Health.

Current mental health services in many parts of Australia are under-resourced for the care of people with serious mental illness. GPs are also faced with increasing responsibilities and limited support. For those with serious mental illness, an active alliance, supported by Divisions of General Practice, State and federal health departments and government policy, is needed to ensure adequate treatment and positive outcomes.

## Acknowledgements

Thanks to Shelda Alcock and Eleanor Page for their help in preparing this manuscript.

## Competing interests

TJRL has been on advisory boards for Janssen-Cilag, Eli Lilly, Pfizer, Lundbeck, Sanofi, Novartis and Faulding; has received funding for unrestricted research from Eli Lilly, Novartis, Janssen-Cilag, Bristol-Myers Squibb, Pfizer and AstraZeneca; and has received travel assistance to attend meetings from Eli Lilly, Novartis, Janssen-Cilag and Bristol-Myers Squibb. CP has been on advisory boards for Bristol-Myers Squibb, Sanofi and Novartis; has received funding for unrestricted research from Eli Lilly, Novartis, Janssen-Cilag, Bristol-Myers Squibb and AstraZeneca; and has received travel assistance to attend meetings from Eli Lilly, Novartis, Janssen-Cilag and Bristol-Myers Squibb.

## References

1. Lawrence D, Holman C, Jablensky A. Preventable physical illness in people with mental illness. Perth: University of Western Australia, 2001. Available at: [http://www.meddent.uwa.edu.au/dph\\_new/research/docs/trctotal.pdf](http://www.meddent.uwa.edu.au/dph_new/research/docs/trctotal.pdf) (accessed Mar 2003).
2. Harris M, Mercer P. Reactive or preventive: the role of general practice in achieving a healthier Australia. *Med J Aust* 2001; 175: 92-93. <[http://www.mja.com.au/public/issues/175\\_02\\_160701/harris/harris.html](http://www.mja.com.au/public/issues/175_02_160701/harris/harris.html)>
3. Royal Australian College of General Practitioners. Guide to preventive activity in general practice. 5th ed. Melbourne: RACGP, 2001.
4. Mathers C, Vos E, Stevenson C, Begg S. The Australian Burden of Disease Study: measuring the loss of health from diseases, injuries, and risk factors. *Med J Aust* 2000; 172: 592-596. <[http://www.mja.com.au/public/issues/172\\_12\\_190600/mathers/mathers.html](http://www.mja.com.au/public/issues/172_12_190600/mathers/mathers.html)>
5. Allebeck P. Schizophrenia: a life-shortening disease. *Schizophr Bull* 1989; 15: 81-89.
6. Goldman LS. Medical illness in patients with schizophrenia. *J Clin Psychiatry* 1999; 60: 10-15.
7. Babidge N, Buhrich N, Butler T. Mortality among homeless people with schizophrenia in Sydney, Australia: a 10-year follow-up. *Acta Psychiatr Scand* 2001; 103: 105-110.
8. Brown S, Inskip H, Barraclough B. Causes of the excess mortality of schizophrenia. *Br J Psychiatry* 2000; 177: 212-217.

9. Lawrence D, Jablensky A, Holman C, Pinder T. Mortality in Western Australian psychiatric patients. *Soc Psychiatry Psychiatr Epidemiol* 2000; 35: 341-347.
10. Ruschena D, Mullen PE, Burgess P, et al. Sudden death in psychiatric patients. *Br J Psychiatry* 1998; 172: 331-336.
11. Koran LM, Sox HC Jr, Marton KI, et al. Medical evaluation of psychiatric patients. I. Results in a state mental health system. *Arch Gen Psychiatry* 1989; 46: 733-740.
12. Koranyi EK. Morbidity and rate of undiagnosed physical illnesses in a psychiatric clinic population. *Arch Gen Psychiatry* 1979; 36: 414-419.
13. Hall RC, Gardner ER, Popkin MK, et al. Unrecognized physical illness prompting psychiatric admission: a prospective study. *Am J Psychiatry* 1981; 138: 629-635.
14. Dixon L, Weiden P, Delahanty J, et al. Prevalence and correlates of diabetes in national schizophrenia samples. *Schizophr Bull* 2000; 26: 903-912.
15. Sernyak M, Leslie D, Alarcon R, et al. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. *Am J Psychiatry* 2002; 159: 561-566.
16. Felker B, Yazel JJ, Short D. Mortality and medical comorbidity among psychiatric patients: a review. *Psychiatr Serv* 1996; 47: 1356-1363.
17. Meyer JM. A retrospective comparison of weight, lipid, and glucose changes between risperidone- and olanzapine-treated inpatients: metabolic outcomes after 1 year. *J Clin Psychiatry* 2002; 63: 425-433.
18. Davidson M. Risk of cardiovascular disease and sudden death in schizophrenia. *J Clin Psychiatry* 2002; 63: 5-11. (Erratum appears in *J Clin Psychiatry* 2002; 63: 744.)
19. Ryan MC, Thakore JH. Physical consequences of schizophrenia and its treatment: the metabolic syndrome. *Life Sci* 2002; 71: 239-257.
20. Kendrick T. Cardiovascular and respiratory risk factors and symptoms among general practice patients with long-term mental illness. *Br J Psychiatry* 1996; 169: 733-739.
21. Taylor D, McAskill R. Atypical antipsychotics and weight gain — a systematic review. *Acta Psychiatr Scand* 2000; 101: 416-432.
22. Allison DB, Fontaine KR, Heo M, et al. The distribution of body mass index among individuals with and without schizophrenia. *J Clin Psychiatry* 1999; 60: 215-220.
23. Halbreich U, Shen J, Panaro V. Are chronic psychiatric patients at increased risk for developing breast cancer? *Am J Psychiatry* 1996; 153: 559-560.
24. Harris EC, Barraclough B. Excess mortality of mental disorder. *Br J Psychiatry* 1998; 173: 11-53.
25. Davidson S, Judd F, Jolley D, et al. Risk factors for HIV/AIDS and hepatitis C among the chronic mentally ill. *Aust N Z J Psychiatry* 2001; 35: 203-209.
26. Cournos F, McKinnon K. HIV seroprevalence among people with severe mental illness in the United States: a critical review. *Clin Psychol Rev* 1997; 17: 259-269.
27. Halbreich U, Palter S. Accelerated osteoporosis in psychiatric patients: possible pathophysiological processes. *Schizophr Bull* 1996; 22: 447-454.
28. Wieck A, Haddad P. Hyperprolactinaemia caused by antipsychotic drugs. *BMJ* 2002; 324: 250-252.
29. Gupta S, Masand PS, Kaplan D, et al. The relationship between schizophrenia and irritable bowel syndrome (IBS). *Schizophr Res* 1997; 23: 265-268.
30. De Hert M, Hautekeete M, De Wilde D, Peuskens J. High prevalence of *Helicobacter pylori* in institutionalized schizophrenic patients. *Schizophr Res* 1997; 26: 243-244.
31. Brown S, Birtwistle J, Roe L, Thompson C. The unhealthy lifestyle of people with schizophrenia. *Psychol Med* 1999; 29: 697-701.
32. Lambert T. Hares and tortoises: differential neuroleptic-associated weight gain in the community. In: 7th Biennial Australasian Schizophrenia Conference; 2002 October 24-26; Sydney, NSW.
33. Jablensky A, McGrath J, Herrman H, et al. People living with psychotic illness: an Australian study 1997-98. Canberra: Commonwealth Department of Health and Aged Care, 1999. Available at: <http://www.health.gov.au/hsdd/mentalhe/resources/reports/pdf/psychot.pdf> (accessed Mar 2003).
34. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA* 1990; 264: 2511-2518.
35. Lambert TJR, Castle DJ. Pharmacological approaches to the management of schizophrenia. *Med J Aust* 2003; 178 Suppl May 5: S57-S61.
36. Lubman DI, Sundram S. Substance misuse in patients with schizophrenia: a primary care guide. *Med J Aust* 2003; 178 Suppl May 5: S71-S75.
37. Anath J. Physical illness and psychiatric disorders. *Compr Psychiatry* 1984; 25: 586-593.
38. Jeste D, Gladsjo J, Lindamer L, Lacro J. Medical comorbidity in schizophrenia. *Schizophr Bull* 1996; 22: 413-430.
39. Bunce D, Jones R, Badger L, Jones S. Medical illness in psychiatric patients: barriers to diagnosis and treatment. *South Med J* 1982; 75: 941-944.
40. Karasu T, Waltzman S, Linder Mayer J, Buckley P. The medical care of patients with psychiatric illness. *Hosp Community Psychiatry* 1980; 31: 463-472.
41. Your guide to MH-OAT. Clinicians reference guide to NSW Mental Health Outcomes and Assessment Training. Sydney: New South Wales Department of Health, 2001. □