Mortality and Its Determinants in Late-Life Schizophrenia: A 5-Year Prospective Study in a Dutch Catchment Area

Paul D. Meesters, M.D., Ph.D., Hannie C. Comijs, Ph.D., Johannes H. Smit, Ph.D., Piet Eikelenboom, M.D., Ph.D., Lieuwe de Haan, M.D., Ph.D., Aartjan T.F. Beekman, M.D., Ph.D., Max L. Stek, M.D., Ph.D.

Objective: *It is uncertain if the raised mortality in schizophrenia persists in later life. Register-based studies suggest that excess mortality continues, although at a lower level than in younger age groups. However, prospective follow-up studies of older schizophrenia samples are lacking.* **Methods:** *A cohort of 157 older patients (mean age at study entry: 68 years) diagnosed with schizophrenia or schizoaffective disorder in a psychiatric catchment area in Amsterdam, the Netherlands was studied. Standardized mortality rate (SMR) was estimated at a 5-year follow-up, in referral to the same age group in the general catchment area population. The impact on survival time of a range of independent demographic and clinical predictors was evaluated.* **Results:** *The cohort had an all-cause SMR of 1.89 (95% CI: 1.28–2.70). SMR was higher in men (2.60; 95% CI: 1.42–4.37) than in women (1.78; 95% CI: 1.02–2.90). All deaths were from natural causes. Reduced survival was associated with higher age (HR: 1.10; 95% CI: 1.05–1.16), male gender (HR: 3.94; 95% CI: 1.87–8.31), and having had one or more compulsory admissions in the past (HR: 2.61; 95% CI: 1.46–4.68). In contrast, no mortality associations were found with diagnosis (schizophrenia versus schizoaffective disorder), age at onset of the disorder, or current prescription of antipsychotics.* **Conclusion:** *The excess mortality in schizophrenia continues into late life, affecting men more often than women. Given the poor insight into the underlying mechanisms of this disquieting finding, there is a need to identify modifiable clinical and social risk factors.* (Am J Geriatr Psychiatry 2016; 24:272–277)

Key Words: schizophrenia, mortality, life expectancy, elderly, geriatric psychiatry, gender, cause of death

Received June 29, 2015; revised August 25, 2015; accepted September 15, 2015. From the GGZ inGeest (PDM, HCC, JHS, PE, ATFB, MLS); Department of Psychiatry, EMGO Institute for Health and Care Research (PDM, HCC, JHS, ATFB, MLS), VU University Medical Center, Amsterdam, The Netherlands; and Department of Psychiatry, Academic Medical Center (LdH), University of Amsterdam, Amsterdam, The Netherlands. Send correspondence and reprint requests to Dr. Paul D. Meesters, GGZ inGeest, De Nieuwe Valerius, Amstelveenseweg 589, 1081 JC Amsterdam, The Netherlands. Email: p.meesters@ggzingeest.nl

http://dx.doi.org/10.1016/j.jagp.2015.09.003

INTRODUCTION

The shortened life span of individuals with schizophrenia is a consistent finding across different populations and study methods.[1] This finding is more worrisome in that there are indications that the differential mortality gap is worsening over time,[2,3] implicating that schizophrenia patients do not benefit from healthcare improvements attainable by the general population. Overall, schizophrenia patients are estimated to have two to three times the risk of dying compared with the general population, corresponding to a 10- to 25-year reduction in life expectancy.[2,4] Excess unnatural deaths, mainly by suicide, are intrinsic to the disorder.[5] However, the larger part of the reduced life expectancy is caused by natural deaths, most likely resulting from an interplay between lifestyle and genetic and treatment factors.[6] In particular, smoking[7,8] and physical comorbidities (obesity, diabetes, hypertension, coronary heart disease)[4,6] have been implicated as likely determinants of increased mortality. In addition, inequalities in healthcare access and quality have been repeatedly documented and are likely to be another contributing cause.[9] Still, evidence on risk factors amenable to intervention is limited.[10]

Whether the increased mortality in schizophrenia persists into later life is uncertain. The relevance of this issue is becoming more urgent because the numbers of older schizophrenia patients are rapidly increasing,[11] prompting healthcare policymakers to adjust to this development. Older schizophrenia populations consist of two subgroups.[12] The largest subgroup is formed by aged early-onset schizophrenia patients. These individuals may have had a more favorable disease course or lifestyle than their peers who died at a younger age. The second subgroup comprises a sizable minority of patients with a later age at onset. Their exposure to the potentially harmful effects of the disorder by definition has been shorter.

Three register studies have reported perseverance of excess mortality of schizophrenia in later life, albeit at a lower level than in younger age groups.[13–15] However, the statistical power of studies using large health service databases may be partially offset by limitations, such as retrospective design and uncertainty regarding psychiatric diagnoses by diverse diagnosticians.[16] Therefore, prospective follow-up studies of older schizophrenia samples are needed to corroborate and extend the findings of register-based studies.

Between July 1, 2007 and June 30, 2008 we identified all schizophrenia and schizoaffective patients in contact with mental health services in a catchment area in Amsterdam, the Netherlands.[12] We now present a prospective study of the mortality rate in this cohort at 5 years follow-up. Our hypothesis was that the mortality risk would be raised in comparison with the local general population. In addition, we documented a range of demographic and clinical variables at outset and evaluated their impact on the 5-year mortality rate.

METHODS

Participants

The study was performed in the psychiatric catchment area of the southern district of Amsterdam. Psychiatric services in the area are principally delivered by the local Mental Health Organization (GGZ inGeest). The cohort for this longitudinal study included all patients with a home address in the catchment area aged 60 years and older, in contact with services on January 1, 2008, and diagnosed with schizophrenia (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* [DSM-IV-TR]: 295.10, 295.20, 295.30, 295.60, 295.90) or schizoaffective disorder (DSM-IV-TR: 295.70). The characteristics of the catchment area and the methods to identify patients, ascertain diagnosis, and determine the age at onset of the disorder were reported elsewhere in detail.[12] Age at onset was defined as the youngest age at which in retrospect DSM-IV-TR criteria for the disorder were reasonably fulfilled. At outset, the following demographic variables were registered: age, gender, presence of partner, independency of residence, and educational level (dichotomized as at best primary education versus at least secondary education). In addition, the following clinical variables were documented: duration of illness, former psychiatric admissions (including compulsory admissions), and current prescription of antipsychotics. The study was approved by the Medical Ethics Committee of the VU University Medical Center.

Follow-Up

All participants were censored as alive or dead 5 years after study entry, on January 1, 2013. Deaths were confirmed by death certificates. Information on cause of death was ascertained through the mental health organization database. In cases for which data were indeterminate, information was cross-checked with the general practitioners of the deceased patients. Causes of death were classified in accordance with the *International Classification of Diseases, Tenth Revision* (World Health Organization, 2008).[17]

Statistical Analysis

The standardized mortality ratio (SMR), determined as the observed number of deaths divided by the expected number of deaths with corresponding 95% confidence interval (CI), was estimated via indirect standardization with STATA Statistical Software (StataCorp. 2011; Release 12; College Station, TX). Data on the mortality rates of the general population in the catchment area were obtained from the Department for Research and Statistics of the municipality of Amsterdam and consisted of the same age groups (60–64, 65–69, 70–74, 75–79, 80–84, 85–89, and 90–94 years).

Cox proportional hazards regression analyses were used to examine the impact of the independent variables collected at study entry on participant survival time, in terms of model coefficients and associated hazard ratio (HR), together with 95% CIs and two-tailed probability values. Data were analyzed using the IBM SPSS 20.0 statistics package.

RESULTS

Characteristics of the Sample

At study entry, the mean age of the 157 participants (44 men, 113 women) was 68.1 years (range: 60–92 years) (Table 1). Most (68.8%) were living independently. The mean age at onset of the disorder was 35.9 years (range: 15–83 years), with 35.0% of the sample having an onset over age 40 years. The mean duration of illness was 32.1 years (range: 0–64 years), with 81.4% having had one or more psychiatric admissions. Antipsychotic medication was currently prescribed in 76.4% of participants.

TABLE 1. Characteristics of the 157 patients at entry into the prospective study (January 1, 2008)

Characteristic	Value
Mean age, y (SD)	68.1 (6.6)
Gender, male	28.0
Current partner, yes	18.5
Residence, independent	68.8
Level of education,[a] low	27.9
Diagnosis (DSM-IV-TR)	
Schizophrenia	78.3
Schizoaffective disorder	21.7
Mean age at onset, y (SD)	35.9 (14.4)
Early onset (<40 y)	65.0
Late onset (40–59 y)	28.7
Very-late onset (≥60 y)	6.4
Mean duration of illness, y (SD)	32.1 (13.8)
Psychiatric admissions,[b] one or more	81.4
Compulsory admissions,[c] one or more	37.1
Current prescription of antipsychotics, yes	76.4

Notes: Values are presented as percents, unless otherwise noted. SD: standard deviation.
[a]No data available for 17 participants.
[b]No data available for 1 participant.
[c]No data available for 6 participants.

Mortality

On the census date, 19.1% of the 157 participants (14 men, 16 women) had died. Mean age at death was 73.0 years (standard deviation: 8.8; range: 64–92 years) in men and 76.1 years (standard deviation: 9.0; range, 62–91 years) in women. The cohort had an all-cause SMR of 1.89 (95% CI: 1.28–2.70). The SMR in men was 2.60 (95% CI: 1.42–4.37) and in women 1.78 (95% CI: 1.02–2.90). All deaths were from natural causes: 11 neoplastic, 9 circulatory, 2 respiratory, 1 gastrointestinal, 1 genitourinary, and 6 unspecified natural cause.

Predictors of Reduced Survival

In univariate models including one predictor at a time (Table 2), higher age, male gender, and having had one or more compulsory admissions in the past were significant predictors of reduced survival. No association with mortality was found for diagnosis (schizophrenia versus schizoaffective disorder), age at onset of the disorder, or current prescription of antipsychotics. In a multivariate model including all variables with $p < 0.10$ in the univariate analyses, higher age (HR: 1.10; 95% CI: 1.05–1.16), male gender (HR: 3.94; 95% CI: 1.87–8.31), and having had compulsory admissions (HR: 2.61; 95% CI: 1.46–4.68), remained significant predictors.

TABLE 2. Predictors of reduced survival over 5 years by cox proportional hazards regression analysis

Variable	Wald	df	p	HR	95% CI
Age	13.6	1	<0.001	1.10	1.04–1.15
Gender (male vs. female)	6.48	1	0.01	2.54	1.24–5.21
Partner (none vs. current)	0.70	1	0.40	1.57	0.55–4.49
Residence (dependent vs. independent)	2.44	1	0.12	1.78	0.86–3.66
Level of education[a] (low vs. high)	0.55	1	0.46	1.39	0.59–3.27
Diagnosis (schizophrenia vs. schizoaffective)	0.10	1	0.76	1.15	0.47–2.82
Age at onset	0.03	1	0.88	0.998	0.97–1.02
Duration of illness	3.51	1	0.06	1.03	0.99–1.06
Psychiatric admissions[b] (one or more vs. none)	1.71	1	0.19	2.22	0.67–7.31
Compulsory admissions[c] (one or more vs. none)	12.5	1	<0.001	2.60	1.53–4.41
Prescription of antipsychotics (current vs. none)	1.98	1	0.16	2.13	0.74–6.10

Notes: [a]No data available for 17 participants.
[b]No data available for 1 participant.
[c]No data available for 6 participants.

DISCUSSION

In this study of a catchment-area based cohort of 157 older schizophrenia and schizoaffective patients, the mortality rate at 5 years follow-up (SMR: 1.89) nearly doubled the rate in the local older population. Mortality in men (SMR: 2.60) was substantially higher than in women (SMR: 1.78). All 30 deaths in the cohort were from natural causes. Male gender (HR: 3.94), having had compulsory admissions (HR: 2.61), and higher age (HR: 1.10) predicted reduced survival time. No mortality association was found with diagnosis (schizophrenia versus schizoaffective disorder), age at onset of the disorder, or current prescription of antipsychotics.

Although at the lower end, the SMR in our cohort is well within the range of elevated mortality rates reported in schizophrenia at a younger age.[2] Furthermore, our study corroborates the findings of the three reports that used large registers to document mortality in later life schizophrenia. A Canadian study found an SMR of 1.42 over a 10-year period in schizophrenia and schizoaffective patients aged 60 years or older.[13] A Finnish study reported an SMR of 2.69 (95% CI: 2.62–2.76) at 10 years follow-up in schizophrenia and schizoaffective patients aged 65 years and older.[14] Finally, in a South London–based case register study over a 3-year period, the SMR in patients aged 65 years and over was 1.63 (95% CI: 1.39–1.89) for schizophrenia,[15] 2.10 (95% CI: 1.30–3.21) for schizoaffective disorder,[15] and 1.68 (95% CI: 1.45–1.93) for the combined diagnostic groups (Chang, personal communication). In our study the subtype of diagnosis (schizophrenia versus schizoaffective disorder) was not a significant predictor of reduced survival (Table 2).

Aged patients with early-onset schizophrenia are traditionally deemed survivors. This optimistic connotation is tempered by the raised mortality rate persisting into late life. Interestingly, the age at onset of the disorder had no substantial impact on the mortality rate in our study. This finding is at variance with Talaslahti et al.,[18] who reported mortality in very-late-onset schizophrenia-like psychosis patients to be almost twice as high as in patients with an earlier onset. However, a high percentage of dementias was found in their sample. The authors suggest this may relate to incorrect diagnosis of very-late-onset schizophrenia-like psychosis at the beginning of dementia. This explanation is further supported by the high frequency of accidental falls as cause of death.[18] Next, our findings do not support the idea that the length of exposure to the disorder and to the possibly associated high-risk lifestyle has a major impact on the mortality risk. In contrast, the severity of the disorder may negatively impact on survival as is suggested by the raised mortality in participants with compulsory admissions in the past, on the premise that involuntary hospitalization can be regarded as a proxy for the severity of the disorder. To our knowledge no studies have evaluated directly whether a more severe course of schizophrenia leads to heightened mortality. However, this hypothesis finds some support in the Finnish register study cited above[14] that found a higher SMR for patients with at least one psychiatric hospitalization within 5 years before follow-up in comparison with nonrelapsed patients. Likewise, in a 10-year follow-up study (mean age at study entry: 54 years), active psychosis at outset was an independent predictor of death from natural causes.[7]

In our cohort men died at a higher rate than women, but the wide confidence intervals of the SMRs (related to the size of our cohort) should be taken into account. A gender difference in mortality to the disadvantage of males has been reported by a number of studies in schizophrenia at a younger age.[1] However, although

a systematic review found a slightly higher median SMR in males (3.02) than in females (2.37), the two distributions were not significantly different.[2] With regard to older schizophrenia populations, two of the three register studies described above provided data on gender effects. Talaslahti et al.[14] found a male SMR of 3.00 (95% CI: 2.87–3.14) and a female SMR of 2.55 (95% CI: 2.47–2.63). In the sample of Chang et al.,[15] male SMR was 2.68 (95% CI: 2.27–3.18), whereas female SMR was 1.22 (95% CI: 0.99–1.48) (Chang, both SMRs provided by personal communication). Furthermore, a large Australian register study reporting on men with a schizophrenia spectrum disorder (range: 65–85 years) found a mortality hazard of 2.3 (95% CI: 1.8–2.9) at a 14-year follow-up.[19] The excess mortality in men compared with women in schizophrenia may be related to various factors, such as smoking,[8] substance abuse,[20] and treatment noncompliance,[21] that are all more prevalent in men. A milder disease course in women may be of significance as well, although in later onset cases the reverse may be true.[22]

All deaths in our cohort were attributed to natural causes. This finding is in accordance with two register studies.[13,19] However, Talaslahti et al.[14] reported a high rate of unnatural causes of death, with falls the most prevalent cause. With respect to the excess mortality due to physical comorbidities, much attention has been drawn to the role of cardiovascular and metabolic disorders. Antipsychotic medications, especially second-generation antipsychotics, have also been implicated, although evidence for an overall negative effect remains inconsistent.[23,24] In our cohort the current prescription of antipsychotics did not predict reduced survival, but data on the lifetime use of these medications would be needed to draw further conclusions on this topic. Likewise, the possible impact on survival of hazardous lifestyle factors was outside the scope of this study. Of note, we recently reported the prevalence of metabolic syndrome in a community-living group of patients with severe mental illnesses (mean age: 69 years; 48% schizophrenia) was similar to that in age peers.[25] However, metabolic screening detected at least one new metabolic abnormality in half of the participants. This adds to the evidence that older schizophrenia patients are at risk for undetected or undertreated medical conditions.[26–28]

This study is the first prospective study of mortality in a cohort of older schizophrenia patients in contact with an essentially monopoly mental healthcare provider within a defined catchment area. The epidemiologic character of our study is further strengthened by the absence of attrition bias given the complete outcome ascertainment. This bears relevance as participants lost to follow-up may include a higher proportion of early deaths in comparison with those traced.[29] Furthermore, we had at our disposal the mortality rates in the local general population, ruling out the possible influence of geographic variation. The prospective design, the face-to-face assessments at study entry and follow-up by the same investigatory team, the completeness to follow-up, and the possibility to evaluate a range of predictors distinguish our study from register-based studies. However, a limitation that needs to be taken into account is the small size of the patient sample. Although inherent to this type of study, this decreased the precision of the SMR estimates and favored Type II errors. Next, it should be acknowledged that our recruitment procedure may have missed patients who resided in nursing homes, because these are served by private psychiatric consultations. Otherwise, private psychiatric care provided to older patients in the catchment area is limited and generally does not treat patients with severe mental illnesses. Finally, although we were able to evaluate a range of variables for their predictive value, other possible predictors of reduced survival were outside the scope of our study because of its epidemiologic design. Assessment of these variables required the consent of study participants, but 35% (N = 55) of the screened patients declined this consent. In particular, smoking[7,8] and physical comorbidities (obesity, diabetes, hypertension, coronary heart disease)[3,5] deserve evaluation as likely determinants of increased mortality. Depression,[30] alcohol use,[10] socioeconomic disadvantage,[31] and adequacy of medical care[26] are other promising candidates for future research.

In conclusion, this study confirms the persistence of increased mortality in schizophrenia into later life. The underlying mechanisms of the heightened mortality are still poorly understood, implying a clear need for studies on modifiable clinical and social risk factors for mortality. Although this research is evolving, actions to improve outcomes in this vulnerable population are urgently required. Given the existing evidence for measurable health benefits brought about by the adoption of healthy lifestyle practices even in late life,[32] promoting appropriate interventions is justified and should be prioritized in treatment programs for older people

with schizophrenia. Likewise, strategies to address the suboptimal medical care in this population[33] should be a particular area of focus.

The authors thank Birgit Witte for statistical assistance.

The authors have no conflicts of interest related to this study to report.

References

1. Brown S: Excess mortality of schizophrenia. A meta-analysis. Br J Psychiatry 1997; 171:502–508
2. Saha S, Chant D, McGrath J: A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? Arch Gen Psychiatry 2007; 64:1123–1131
3. Nielsen RE, Uggerby AS, Jensen SOW, et al: Increasing mortality gap for patients diagnosed with schizophrenia over the last three decades—a Danish nationwide study from 1980 to 2010. Schizophr Res 2013; 146:22–27
4. Laursen TM, Munk-Olsen T, Vestergaard M: Life expectancy and cardiovascular mortality in persons with schizophrenia. Curr Opin Psychiatry 2012; 25:83–88
5. Palmer BA, Pankratz VS, Bostwick JM: The lifetime risk of suicide in schizophrenia. Arch Gen Psychiatry 2005; 62:247–253
6. De Hert M, Correll CU, Bobes J, et al: Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. World Psychiatry 2011; 10:52–77
7. Brown S, Mitchell C: Predictors of death from natural causes in schizophrenia: 10-year follow-up of a community cohort. Soc Psychiatry Psychiatr Epidemiol 2012; 47:843–847
8. Kelly DL, McMahon RP, Wehring HJ, et al: Cigarette smoking and mortality risk in people with schizophrenia. Schizophr Bull 2011; 37:832–838
9. Lawrence D, Kisely S: Inequalities in healthcare provision for people with severe mental illness. J Psychopharmacol 2010; 24(4 suppl):61–68
10. Reininghaus U, Dutta R, Dazzan P, et al: Mortality in schizophrenia and other psychoses: a 10-year follow-up of the SOP first-episode cohort. Schizophr Bull 2014; 41:664–673
11. Cohen CI, Meesters PD, Zhao J: New perspectives on schizophrenia in later life: implications for treatment, policy, and research. Lancet Psychiatry 2015; 2:340–350
12. Meesters PD, de Haan L, Comijs HC, et al: Schizophrenia spectrum disorders in later life: prevalence and distribution of age at onset and sex in a Dutch catchment area. Am J Geriatr Psychiatry 2012; 20:18–28
13. Kredentser MS, Martens PJ, Chochinov HM, et al: Cause and rate of death in people with schizophrenia across the lifespan: a population-based study in Manitoba, Canada. J Clin Psychiatry 2014; 75:154–160
14. Talaslahti T, Alanen HM, Hakko H, et al: Mortality and causes of death in older patients with schizophrenia. Int J Geriatr Psychiatry 2012; 27:1131–1137
15. Chang CK, Hayes RD, Broadbent M, et al: All-cause mortality among people with serious mental illness (SMI), substance use disorders, and depressive disorders in southeast London: a cohort study. BMC Psychiatry 2010; 10:77
16. Morgan MG, Scully PJ, Youssef HA, et al: Prospective analysis of premature mortality in schizophrenia in relation to health service engagement: a 7.5-year study within an epidemiologically complete, homogeneous population in rural Ireland. Psychiatry Res 2003; 117:127–135
17. World Health Organization: The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines, Version for 2007. Geneva, Switzerland: WHO, 2008
18. Talaslahti T, Alanen HM, Hakko H, et al: Patients with very-late-onset schizophrenia-like psychosis have higher mortality rates than elderly patients with earlier onset schizophrenia. Int J Geriatr Psychiatry 2015; 30:453–459
19. Almeida OP, Hankey GJ, Yeap BB, et al: Mortality among people with severe mental disorders who reach old age: a longitudinal study of a community-representative sample of 37892 men. PLoS ONE 2014; 9:e111882
20. Leung A, Chue P: Sex differences in schizophrenia, a review of the literature. Acta Psychiatr Scand 2000; 101:3–38
21. Kreyenbuhl J, Nossel IR, Dixon LB: Disengagement from mental health treatment among individuals with schizophrenia and strategies for facilitating connections to care: a review of the literature. Schizophr Bull 2009; 35:696–703
22. Köhler S, van der Werf M, Hart B, et al: Evidence that better outcome of psychosis in women is reversed with increasing age of onset: a population-based 5-year follow-up study. Schizophr Res 2009; 113:226–232
23. Weinmann S, Read J, Aderhold V: Influence of antipsychotics on mortality in schizophrenia: systematic review. Schizophr Res 2009; 113:1–11
24. Tiihonen J, Lönnqvist J, Wahlbeck K, et al: 11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (FIN11 study). Lancet 2009; 374:620–627
25. Konz HW, Meesters PD, Paans NPG, et al: Screening for metabolic syndrome in older patients with severe mental illness. Am J Geriatr Psychiatry 2014; 22:1116–1120
26. Vahia IV, Diwan S, Bankole AO, et al: Adequacy of medical treatment among older persons with schizophrenia. Psychiatr Serv 2008; 59:853–859
27. Lahti M, Tiihonen J, Wildgust H, et al: Cardiovascular morbidity, mortality and pharmacotherapy in patients with schizophrenia. Psychol Med 2012; 42:2275–2285
28. Tsan JY, Stock EM, Gonzalez JM, et al: Mortality and guideline-concordant care for older patients with schizophrenia: a retrospective longitudinal study. BMC Med 2012; 10:147
29. Sims ACP: Importance of a high tracing-rate in long-term medical follow-up studies. Lancet 1973; 302:433–435
30. Penninx BW, Geerlings SW, Deeg DJ, et al: Minor and major depression and the risk of death in older persons. Arch Gen Psychiatry 1999; 56:889–895
31. Lantz PM, House JS, Lepkowski JM, et al: Socioeconomic factors, health behaviors, and mortality: results from a prospective study of US Adults. JAMA 1998; 279:1703–1708
32. Lee Y, Park KH: Health practices that predict recovery from functional limitations in older adults. Am J Prev Med 2006; 31:25–31
33. De Hert M, Cohen D, Bobes J, et al: Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. World Psychiatry 2011; 10:138–151