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- Recognize physical diseases in patients with schizophrenia so that they can be diagnosed and treated

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# Cause and Rate of Death in People With Schizophrenia Across the Lifespan: A Population-Based Study in Manitoba, Canada

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### ABSTRACT

**Objective:** To compare the causes and rates of death for people with and without schizophrenia in Manitoba, Canada.

**Method:** Using de-identified administrative databases at the Manitoba Centre for Health Policy, a population-based analysis was performed to compare age- and sex-adjusted 10-year (1999–2008) mortality rates, overall and by specific cause, of decedents aged 10 years or older who had 1 diagnosis of schizophrenia (*ICD-9-CM* code 295, *ICD-10-CA* codes F20, F21, F23.2, F25) over a 12-year period (N=9,038) to the rest of the population (N=969,090).

**Results:** The mortality rate for those with schizophrenia was double that of the rest of the population (20.00% vs 9.37%). The all-cause mortality rate was higher for people with schizophrenia compared to all others (168.9 vs 99.1 per thousand; relative risk [RR]=1.70,  $P<.0001$ ); rates of death due to suicide (RR=8.67,  $P<.0001$ ), injury (RR=2.35,  $P<.0001$ ), respiratory illness (RR=2.00,  $P<.0001$ ), and circulatory illness (RR=1.64,  $P<.0001$ ) were also significantly higher in people with schizophrenia. Overall cancer deaths were similar (28.6 vs 27.3 per thousand,  $P=.42$ , NS) except in the middle-aged group (40–59), in which cancer death rates were significantly higher for those with schizophrenia (28.7 vs 11.6 per thousand; RR=2.48,  $P<.01$ ). Mortality rates due to lung cancer were significantly higher in people with schizophrenia (9.4 vs 6.4 per thousand, RR=1.45,  $P<.001$ ).

**Conclusions:** People with schizophrenia are at increased risk of death compared to the general population, and the majority of these deaths are occurring in older age from physical disease processes. Risk of cancer mortality is significantly higher in middle-aged but not younger or older patients with schizophrenia. Understanding these patients' vulnerabilities to physical illness has important public health implications for prevention, screening, and treatment as the population ages.

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Schizophrenia is a serious and chronic disorder, with prevalence between 0.5% and 2% of the general population.<sup>1–3</sup> For individuals with schizophrenia, the literature indicates a pattern of excess mortality and comorbidity compared to the general population, a gap that appears to be widening.<sup>4</sup> Those with schizophrenia are more likely to die prematurely<sup>5</sup>; however, evidence for the causes and mechanisms for this increased mortality has been mixed. Schizophrenia patients

- Patients with schizophrenia have increased risk of mortality from physical illness compared to the general population.
- Cancer mortality risk in middle age for those with schizophrenia is higher than that of the general population.
- Due to high illness and mortality rates, patients with schizophrenia require continuity of care to enhance preventative, curative, and palliative treatment efforts.

have increased risk for unnatural deaths from suicide and accidents, but ~60%–70% of excess mortality is due to other disease processes,<sup>2,6</sup> with increased risk for cardiovascular disease, respiratory disorders, diabetes, tuberculosis, and other infectious diseases.<sup>1,7</sup>

From a socio-environmental perspective, elevated comorbidity rates may be attributable to marginalization of individuals with schizophrenia within the health care system. Patients with schizophrenia are more likely to die in nursing homes<sup>8</sup> and are less likely to receive preventative screening for physical illnesses such as breast and cervical cancer.<sup>9,10</sup> They are more likely to be socially isolated,<sup>11–13</sup> experience disproportionate rates of poverty and homelessness,<sup>14,15</sup> and can feel disenfranchised and vulnerable in the health care system.<sup>16</sup> These risk factors are associated with a host of behavioral risk factors including an approximately 4 times higher rate of cigarette smoking,<sup>17,18</sup> use of licit and illicit drugs,<sup>19</sup> poor diet, and lack of exercise.<sup>17</sup> Environmental and behavioral risk factors are further complicated by the side effects of psychotropic medications, including obesity, metabolic syndrome, and cardiovascular risk.<sup>5,20,21</sup>

Despite the compelling evidence for increased mortality in schizophrenia related to many physical illnesses, there have been conflicting findings in regard to cancer deaths. Some research indicates schizophrenia is associated with reduced cancer risk, suggesting possible genetic factors that suppress tumors, and protective factors of psychotropic medications.<sup>4,22,23</sup> Some evidence suggests that men with schizophrenia are at reduced risk while women are at increased risk for developing cancer<sup>24</sup>; however, others have found increased cancer mortality for both sexes with schizophrenia, particularly, increased mortality from breast cancer for women and lung cancer for men.<sup>3</sup> In a matched-cohort study<sup>7</sup> of decedents with and without schizophrenia, the percentage of deaths due to all cancers in the schizophrenia cohort was half that of the matched cohort, but the percentage of attributable lung cancer deaths was significantly higher in those with schizophrenia compared to the matched cohort. Race may also play a role, with reported incidence ratios of cancer risk higher in Asian cohorts of patients with schizophrenia compared to their European counterparts, although this difference may be attributable to lower baseline cancer rates in Asia.<sup>25,26</sup> In terms of age effects, the all-cause rate of death in schizophrenia is 3 times higher than that of the general population, and mortality from neoplasms is twice as high.<sup>27</sup> Thus, research into cancer and schizophrenia

is well served by taking into account “age-specific risk” rather than examining lifetime incidence of cancer.<sup>25</sup>

The disparate findings regarding cancer in schizophrenia highlight the importance of considering the underlying population-based rates of cause of death. Mortality rates in schizophrenia are reported at 2 to 3 times higher than in the general population.<sup>7,27</sup> However, cohort designs, including our previous work examining the percentage of attributable deaths in patients with schizophrenia,<sup>7</sup> cannot account for the underlying population rates of death. In addressing this issue, the present study applied a decade-chronological perspective across the life trajectory of Manitoba residents. Manitoba is a prairie province located in the geographical center of Canada, with a population of 1.235 million. The objectives of this study were to compare the mortality rate and cause of death for people with and without schizophrenia. This population-based study included all people residing in Manitoba in 1998, comparing death rates over the 10-year period of 1999–2008, overall and by cause, of people with and without a diagnosis of schizophrenia.

## METHOD

This study used de-identified administrative claims data from the Population Health Research Data Repository (herein referred to as the Repository) housed at the Manitoba Centre for Health Policy (MCHP), University of Manitoba, in Winnipeg, Canada. The Repository data files include de-identified records of all hospital claims, medical claims for ambulatory physician visits, registry files (records of the person’s demographic information—age, sex, 6-digit postal code of residence, birth and death dates), and vital statistics (cause of death) for those registered under the universal health care system for the province of Manitoba. Ethnographic information is not available through the repository. Although the data are de-identified, they are linkable at the person level through an encrypted personal health number once ethics and health information privacy approvals are obtained. People 10 years and older diagnosed with schizophrenia were defined as those having at least 1 diagnosis code for schizophrenia (*ICD-9-CM* code 295, *ICD-10-CA* [Canadian Enhancement of *ICD-10*]<sup>28</sup> codes F20, F21, F23.2, F25) over a 12-year period, defined for the population-based analysis as the years 1987–1998. Crude and directly standardized 10-year mortality rates (calendar years 1999–2008) overall and by specific cause for people 10 years and older with schizophrenia ( $N = 9,038$ ) were compared to rates for the rest of Manitobans ( $N = 969,090$ ). Age was recorded as of December 1998; cause of death was coded using *ICD-9* and *ICD-10* (as of January 1, 2000), and rates were directly standardized to the 2006 provincial population. All rates based on 1 to 5 events are suppressed for confidentiality.

A generalized linear model with a negative binomial distribution tested the relationship of mortality rates by age, sex, diagnosis of schizophrenia, Socioeconomic Factor Index—Version 2 (SEFI-2) score,<sup>29</sup> and geographical area of residence. SEFI-2 reflects underlying social determinants of

**Table 1. Demographics for December 1998 Manitoba Population Aged  $\geq 10$  Years (people diagnosed with schizophrenia vs all others)**

|                            | Diagnosed With Schizophrenia (N=9,038) | All Others (N=969,090) | Group Difference  | P Value   |
|----------------------------|--|------------------------|-------------------|-----------|
| Deaths, 1999–2008, n (%)   | 1,808 (20.00)                          | 90,790 (9.37)          |                   |           |
| Age, y                     |  |                        | $t = 40.09$       | $< .0001$ |
| Mean (SD)                  | 48.70 (17.38)                          | 41.32 (20.22)          |                   |           |
| Median                     | 46                                     | 39                     |                   |           |
| Minimum                    | 10                                     | 10                     |                   |           |
| Maximum                    | 100                                    | 115                    |                   |           |
| Sex, n (%)                 |  |                        | $\chi^2 = 0.51$   | .47       |
| Males                      | 4,458 (49.33)                          | 474,335 (48.95)        |                   |           |
| Females                    | 4,580 (50.67)                          | 494,755 (51.05)        |                   |           |
| Region of residence, n (%) |  |                        | $\chi^2 = 771.35$ | $< .0001$ |
| Rural South                | 963 (10.66)                            | 186,999 (19.30)        |                   |           |
| Mid                        | 898 (9.94)                             | 134,678 (13.90)        |                   |           |
| North                      | 383 (4.24)                             | 54,955 (5.67)          |                   |           |
| Brandon                    | 434 (4.80)                             | 39,880 (4.12)          |                   |           |
| Winnipeg                   | 6,360 (70.37)                          | 552,578 (57.02)        |                   |           |
| SEFI-2 score <sup>a</sup>  |  |                        | $t = 29.96$       | $< .0001$ |
| Mean (SD)                  | 0.29 (0.95)                            | -0.01 (0.97)           |                   |           |
| Median                     | 0.20                                   | -0.02                  |                   |           |
| Minimum                    | -4.89                                  | -4.89                  |                   |           |
| Maximum                    | 3.55                                   | 5.37                   |                   |           |

<sup>a</sup>SEFI-2 scores less than zero indicate more favorable socioeconomic conditions, while scores greater than zero indicate less ideal socioeconomic conditions. Abbreviation: SEFI-2 = Socioeconomic Factor Index—Version 2.

health and includes the following Census-derived variables: average household income, percentage of single-parent households, unemployment rate, and high school graduation rate.<sup>29</sup> Geographical area of residence was divided into 5 regions of the province—the 2 urban areas of Winnipeg and Brandon, and the Rural South, Mid, and North areas of the province. In 2010, over half (N=683,100) of Manitoba residents lived in the capital city of Winnipeg, and 52,550 lived in the next largest urban center of Brandon.<sup>30,31</sup>

## RESULTS

### Rates of Death Overall and by Cause, Using a Population-Based Cohort From 1998 Followed Over 10 Years (1999–2008)

Table 1 shows the demographics of our population-based cohort as of December 1998, comparing number and percentage of deaths, age, sex, region of residence, and SEFI-2 scores for those with and without schizophrenia. In the 10-year period of 1999–2008, the mortality rate of people with schizophrenia was just over double that of the general population; 20.00% compared to 9.37%, respectively. The schizophrenia sample was older, was more likely to live in urban as compared to rural areas, and had less favorable socioeconomic conditions. The prevalence of schizophrenia in our sample is 0.92%, consistent with Canadian population norms.<sup>32</sup>

Figure 1 compares the crude rates of death of all Manitobans aged 10 and older with schizophrenia (N=9,038) to those without schizophrenia (N=969,090) over the 10-year time period 1999–2008, by various age groupings as of December 1998. At every age group except the oldest category (90+), there is a significant elevated mortality rate for people with schizophrenia.

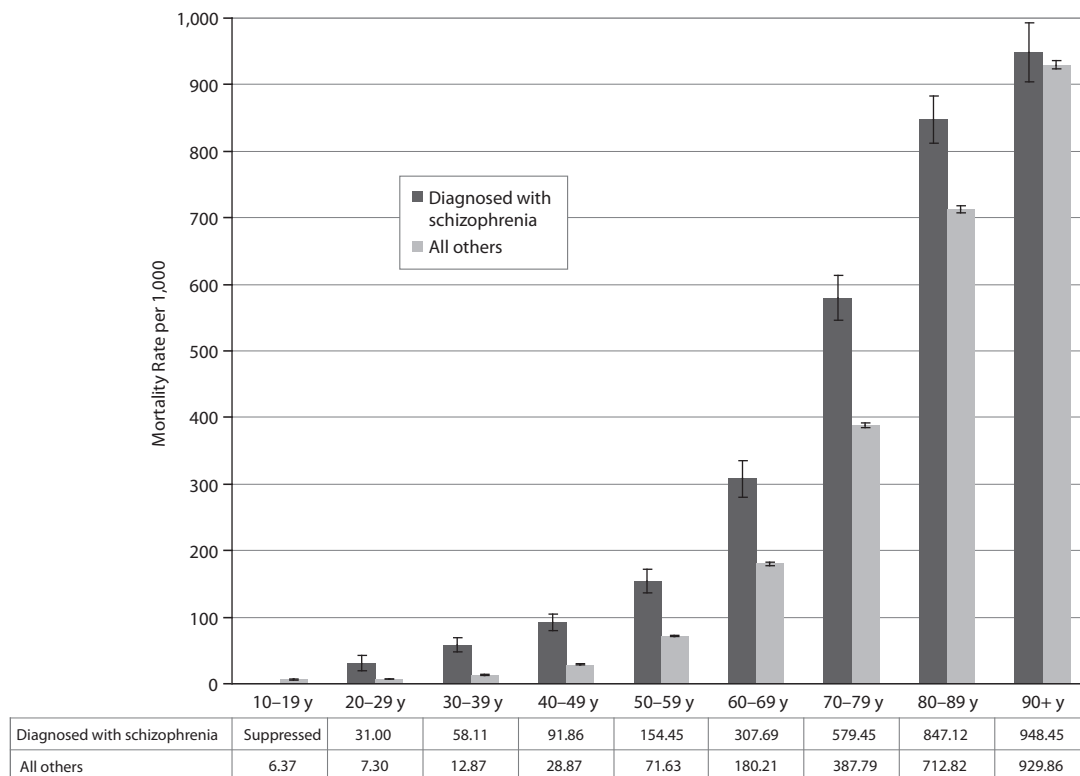
Table 2 shows the age- and sex-adjusted mortality rates, with the all-cause mortality rate substantially higher for people with schizophrenia compared to all others (168.9 vs 99.1 per thousand, relative risk [RR] = 1.70,  $P < .0001$ ); rates of death due to suicide (RR = 8.67,  $P < .0001$ ), injury (RR = 2.35,  $P < .0001$ ), respiratory illness (RR = 2.00,  $P < .0001$ ), circulatory illness (RR = 1.64,  $P < .0001$ ), and lung cancer (RR = 1.45,  $P < .001$ ) were also significantly higher in the former versus latter. While overall cancer deaths were similar (28.6 vs 27.3 per thousand, RR = 1.05, NS), mortality rates due to lung cancer were significantly higher in people with schizophrenia (9.4 vs 6.4 per thousand, RR = 1.45,  $P < .001$ ). Table 2 also shows higher all-cause mortality rates for schizophrenia across all age groups (ages 10–39, RR = 4.14,  $P < .001$ ; ages 40–59, RR = 2.50,  $P < .001$ ; age 60+, RR = 1.42,  $P < .001$ ), with similar by-cause findings.

However, combined cancer death rates were not significantly different between the groups aged 10–39 and 60+, but were almost 2.5 times higher for people aged 40–59 years with schizophrenia (28.7 vs 11.6 per thousand; RR = 2.48,  $P < .01$ ). For lung cancer specifically, death rates for both the 40–59 and 60+ age groups were significantly higher for people with schizophrenia compared to all others (ages 40–59, 8.9 vs 5.4 per thousand, RR = 1.65,  $P < .01$ ; age 60+, 29.6 vs 22.0 per thousand, RR = 1.34,  $P < .05$ ) (lung cancer rates for ages 10–39 in the schizophrenia cohort were suppressed due to small numbers).

To summarize, by age group, people with schizophrenia aged 10–39 had an over 5 times greater risk of death from circulatory causes, an over 8 times greater risk of death from respiratory causes, and an almost 12 times greater risk of death from suicide compared to all others (see Table 2). Relative risk of death from these causes remains significantly higher than that of the general population at ages 40–59, albeit lower compared to the schizophrenia patients aged 10–39 (ie, those aged 40–59 had 3 times greater risk of death from circulatory causes, just over 5 times greater risk of death from respiratory causes, and almost 6 times greater risk of death from suicide compared to all others).

In the oldest age group of 60+ years, relative risk of dying from every cause other than suicide and cancer continues to be higher for those with schizophrenia. However, we see the gap in risk decline, with a 1.41 times greater risk of dying from circulatory causes and 1.66 times greater risk of dying from respiratory causes. There was a 1.49 times greater risk of death by injury for those with schizophrenia compared to the general population, but the number of suicides in the schizophrenia group was too low to conduct comparative analysis of risk with the general population. Overall, adults with schizophrenia 60 years or older have a relative risk of death from all causes that is 1.42 times higher than that of the non-schizophrenia group.

**Figure 1. Crude Mortality Rates (by age decile) for People With Schizophrenia (diagnosed in 1989–1998) and All Others Who Died in 1999–2008 for December 1998 Manitoba Population Aged ≥ 10 Years, per 1,000<sup>a</sup>**



<sup>a</sup>Group differences for age groups from 20–29 through 80–89 are statistically significant ( $P < .05$ ), but group difference at age 90+ is not statistically significant. Point estimates of crude mortality rates per 1,000 are given below the age deciles.

Regression modeling including age, sex, geographical region, and SEFI-2 score (Table 3) resulted in the following adjusted relative risks (aRRs) of mortality, comparing those with schizophrenia to the rest of the population by age (see Table 4): overall aRR (all ages) = 2.17 (95% CI, 1.93–2.43;  $P < .0001$ ), ages 10–39, aRR = 3.82 (95% CI, 2.77–5.27;  $P < .0001$ ); ages 40–59, aRR = 2.43 (95% CI, 2.21–2.68;  $P < .0001$ ); age 60+, aRR = 1.34 (95% CI, 1.25–1.43;  $P < .0001$ ). These further adjustments show only slightly truncated values compared to the age- and sex-adjusted rates only.

## DISCUSSION

Across all age groups, all-cause mortality was significantly higher in individuals with schizophrenia, with the relative risk of death higher from suicide, injury, respiratory and circulatory illness, and lung cancer, but not all cancers combined. Increased all-cause and by-cause mortality for those with schizophrenia across age groups is consistent with previous research, showing elevated mortality in schizophrenia from both natural and unnatural causes.<sup>4</sup>

The age decile analysis was illuminating in the complicated picture of cancer mortality in schizophrenia. Compared to all others, individuals aged 40–59 with schizophrenia were at 1.65 times greater risk of death from lung cancer; in the 60+ age group, those with schizophrenia were at 1.34 times greater risk of death from lung cancer. Increased lung cancer mortality in schizophrenia has been ascribed to high rates

of smoking in this population<sup>3,26,32,33</sup> and is consistent with reported higher incidence of and death by lung cancer for both male and female patients with schizophrenia.<sup>26,33</sup>

When all age groups were collapsed, the relative risk of cancer mortality was not significantly different between those with and without schizophrenia, in line with previous research reporting no difference in standardized incidence ratios (SIRs) for all cancers in those with schizophrenia compared to those without.<sup>26</sup> Standardized mortality ratios (SMRs) for a variety of causes of mortality in people with schizophrenia show that the median SMR for neoplasms indicated 37% more cases of death from neoplasms in those with schizophrenia than would be expected in the general population.<sup>4</sup> However, this median SMR was quite low compared to mortality from other causes such as suicide, respiratory diseases, and infectious diseases. Whether schizophrenia is a risk or protective factor for the development of cancer has been extensively researched, but there continue to be inconsistent findings.<sup>25</sup> Ji and colleagues<sup>24</sup> examined cancer risk both before and after schizophrenia diagnosis, showing that before diagnosis, those with schizophrenia have lower SIRs for cancer risk compared to the general population, but after diagnosis, the SIR was equal to that of the general population, and increased when looking at women specifically. Such findings highlight the importance of examining cancer risk and mortality in schizophrenia across the illness course and the lifespan.<sup>25</sup>

**Table 2. Directly Standardized Mortality Rates, Overall and by Cause, for People With Schizophrenia (diagnosed in 1987–1998) and All Others Who Died in 1999–2008, December 1998 Manitoba Population Aged ≥ 10 Years, Standardized to 2006 Manitoba Population, per 1,000**

| Cause of Death | Directly Standardized Rate (95% CI) |                        | Relative Risk | P Value |
|----------------|-------------------------------------|------------------------|---------------|---------|
|                | Diagnosed With Schizophrenia        | All Others             |               |         |
| All ages       | N = 9,038                           | N = 969,090            |               |         |
| All causes     | 168.94 (161.15–176.72)              | 99.10 (98.45–99.74)    | 1.70          | <.0001  |
| Cancer         | 28.61 (25.43–31.78)                 | 27.33 (27.00–27.67)    | 1.05          | .4247   |
| Lung cancer    | 9.35 (7.52–11.18)                   | 6.44 (6.28–6.61)       | 1.45          | .0002   |
| Circulatory    | 54.55 (50.16–58.94)                 | 33.36 (32.98–33.73)    | 1.64          | <.0001  |
| Respiratory    | 16.43 (14.04–18.81)                 | 8.23 (8.04–8.42)       | 2.00          | <.0001  |
| Injury         | 10.54 (8.60–12.49)                  | 4.48 (4.35–4.62)       | 2.35          | <.0001  |
| Suicide        | 9.94 (7.68–12.21)                   | 1.15 (1.08–1.21)       | 8.67          | <.0001  |
| Age 10–39 y    | n = 3,023                           | n = 488,662            |               |         |
| All causes     | 36.18 (30.23–42.13)                 | 8.74 (8.48–9.00)       | 4.14          | <.0001  |
| Cancer         | 1.78 (0.68–2.89)                    | 0.89 (0.81–0.97)       | 2.00          | .4461   |
| Lung cancer    | Suppressed due to small numbers     | 0.15 (0.12–0.19)       |               |         |
| Circulatory    | 4.68 (2.84–6.51)                    | 0.89 (0.81–0.97)       | 5.24          | <.0001  |
| Respiratory    | 1.44 (0.29–2.58)                    | 0.17 (0.13–0.20)       | 8.54          | <.0001  |
| Injury         | 6.01 (3.78–8.23)                    | 2.80 (2.65–2.95)       | 2.15          | .0001   |
| Suicide        | 15.24 (10.63–19.85)                 | 1.28 (1.18–1.38)       | 11.95         | <.0001  |
| Age 40–59 y    | n = 3,642                           | n = 284,341            |               |         |
| All causes     | 121.61 (110.13–133.09)              | 48.65 (47.82–49.48)    | 2.50          | <.0001  |
| Cancer         | 28.72 (23.12–34.33)                 | 11.59 (11.19–12.00)    | 2.48          | .0011   |
| Lung cancer    | 8.94 (5.79–12.08)                   | 5.42 (5.14–5.70)       | 1.65          | .0058   |
| Circulatory    | 34.80 (28.60–41.00)                 | 11.59 (11.19–12.00)    | 3.00          | <.0001  |
| Respiratory    | 10.04 (6.76–13.32)                  | 1.91 (1.74–2.07)       | 5.27          | <.0001  |
| Injury         | 13.15 (9.47–16.83)                  | 2.65 (2.46–2.84)       | 4.95          | <.0001  |
| Suicide        | 7.41 (4.62–10.21)                   | 1.24 (1.11–1.37)       | 5.96          | <.0001  |
| Age 60+ y      | n = 2,373                           | n = 196,087            |               |         |
| All causes     | 537.07 (507.11–567.02)              | 378.11 (375.37–380.85) | 1.42          | <.0001  |
| Cancer         | 87.88 (75.73–100.03)                | 139.28 (137.61–140.95) | 0.63          | .2627   |
| Lung cancer    | 29.57 (22.44–36.71)                 | 21.99 (21.34–22.65)    | 1.34          | .0170   |
| Circulatory    | 195.90 (177.74–214.06)              | 139.28 (137.61–140.95) | 1.41          | <.0001  |
| Respiratory    | 59.63 (49.75–69.51)                 | 35.97 (35.12–36.82)    | 1.66          | <.0001  |
| Injury         | 16.53 (11.13–21.93)                 | 11.08 (10.60–11.55)    | 1.49          | .0173   |
| Suicide        | Suppressed due to small numbers     | 0.72 (0.60–0.83)       |               |         |

Considering age in cancer mortality in schizophrenia is essential in furthering our understanding of risk and underlying rates of death.<sup>7,33</sup> In our sample, those with schizophrenia were significantly older than the non-schizophrenia group, which may be due to the relatively few very young people (eg, under age 15) diagnosed with schizophrenia. In conducting further analysis by age group comparing those with schizophrenia to all others, we found that cancer mortality was 2.5 times higher in people 40–59 years of age with schizophrenia, with no significant difference in cancer mortality in the younger (10–39) and older (60+) age groups. This may be because cancer is a relatively rare event in younger people and is most often diagnosed in adults over the age of 60.<sup>33</sup> While 85% of people with schizophrenia experience illness onset before age 45, the prevalence of schizophrenia in adults over the age of 55 is expected to double in the next 2 decades as the general population ages.<sup>34</sup> Taken with our finding of elevated risk for cancer mortality in 40- to 59-year-olds with schizophrenia, health care systems and providers will need to adapt, increasing screening and treatment for this group, who face many barriers to receiving adequate health care at all stages of illness.<sup>6–9,13,14,35–37</sup> The reality of increased rates of death from natural causes in middle and old age has important implications for the care of persons with serious mental illness.

The strength of this study is its population-based analysis, accounting for the underlying general mortality rates and prevalence of diagnoses across a large number of residents spanning various age groups. The ability to control for underlying population-based rates for cause of death adds important context to deaths reported in matched-cohort studies, which do not take into account the underlying rate of death and thus cannot demonstrate relative risks of death by diagnosis.<sup>8</sup> Examining cancer risk in schizophrenia by age has recently been suggested as a way to better understand the complicated cancer-schizophrenia relationship,<sup>25</sup> and the present study provides new and important information regarding cancer mortality using population-based analyses across age groups. There are benefits and limitations to using administrative claims data in the Repository at MCHP. The coding of schizophrenia in the Repository is highly reliable and valid, particularly in comparison to the diagnoses of other mental illness, and is supported by previous research.<sup>8–10,38</sup> However, “cause of death” coding through the Manitoba government’s Department of Vital Statistics is a limitation, insofar as in Manitoba we are limited to 1 (primary) cause of death. If the primary cause of death (as coded by the attending physician or provincial coroner) is general or misleading (eg, “death by mental illness”), having additional coded causes of death would be useful.<sup>8</sup> The Repository

**Table 3. Negative Binomial Regression of Mortality for People With Schizophrenia (diagnosed in 1987–1998) Versus All Others Who Died in 1999–2008, December 1998 Manitoba Population Aged ≥ 10 Years**

| Variable  | aRR   | 95% CI      | P Value |
|---|-------|-------------|---------|
| Schizophrenia cohort (yes vs no)                                    | 1.064 | 0.86–1.13   | .5659   |
| Males (vs females)  | 1.379 | 1.36–1.40   | <.0001  |
| Age group (ref=90+ y)   |       |             |         |
| 10–19 y   | 0.006 | 0.006–0.007 | <.0001  |
| 20–29 y   | 0.007 | 0.007–0.008 | <.0001  |
| 30–39 y   | 0.013 | 0.012–0.014 | <.0001  |
| 40–49 y   | 0.030 | 0.029–0.031 | <.0001  |
| 50–59 y   | 0.075 | 0.07–0.08   | <.0001  |
| 60–69 y   | 0.186 | 0.18–0.19   | <.0001  |
| 70–79 y   | 0.405 | 0.39–0.42   | <.0001  |
| 80–89 y   | 0.750 | 0.73–0.77   | <.0001  |
| Interaction of schizophrenia cohort × age group (ref=no, age 90+ y) |       |             |         |
| Yes, age 10–19 y  | 3.341 | 1.35–8.25   | .0089   |
| Yes, age 20–29 y  | 3.597 | 2.38–4.45   | <.0001  |
| Yes, age 30–39 y  | 3.866 | 2.90–5.15   | <.0001  |
| Yes, age 40–49 y  | 2.731 | 2.12–3.53   | <.0001  |
| Yes, age 50–59 y  | 1.911 | 1.49–2.45   | <.0001  |
| Yes, age 60–69 y  | 1.579 | 1.24–2.00   | .0002   |
| Yes, age 70–79 y  | 1.376 | 1.09–1.73   | .0064   |
| Yes, age 80–89 y  | 1.151 | 0.91–1.46   | .2459   |
| Region of residence (ref=Rural South)                               |       |             |         |
| Brandon   | 1.067 | 1.03–1.10   | .0003   |
| Winnipeg  | 1.072 | 1.05–1.09   | <.0001  |
| Rural Mid   | 1.038 | 1.02–1.06   | .0009   |
| North   | 1.224 | 1.18–1.27   | <.0001  |
| SEFI-2  | 1.196 | 1.19–1.21   | <.0001  |

Abbreviations: aRR = adjusted relative risk, SEFI-2 = Socioeconomic Factor Index—Version 2.

also contains data from Manitobans only, which may limit generalizability of our findings. However, we expect that this would be mitigated due to universal health care coverage across the other 9 provinces in Canada. Use of the Repository also limited our ability to assess the various determinants of the causes of mortality often implicated in schizophrenia, such as smoking behavior, weight, and comorbid illness symptoms (eg, blood-sugar levels). Recent research in the US Veteran population has shown that schizophrenia is associated with increased mortality risk even when adjusted for comorbidity, obesity, smoking, and exercise.<sup>2</sup> Controlling for these additional markers in future research would provide helpful information for understanding physical illness and mortality in schizophrenia.

## CONCLUSION

Contrary to the idea that those with serious mental illness die young from traumatic events, our study highlights that individuals with schizophrenia are getting old and getting sick, with rates of mortality significantly higher in every age group from 20 to 89. This echoes previous research by our group indicating a median age of death of 77 years in a population-based cohort of Manitobans with schizophrenia.<sup>8</sup> While accidental death is a prominent cause of death in those under the age of 39 and, indeed, the highest rates of death in those with schizophrenia aged 10–39 in our sample were

**Table 4. Adjusted Relative Risks (aRRs) of Mortality for People With Schizophrenia (diagnosed in 1987–1998) Versus All Others Who Died in 1999–2008, by Age Group (controlling for sex, geographical region, and SEFI-2 score), December 1998 Manitoba Population Aged ≥ 10 Years<sup>a</sup>**

| Age Group | aRR  | 95% CI    | P Value |
|-----------|------|-----------|---------|
| All ages  | 2.17 | 1.93–2.43 | <.0001  |
| 10–39 y   | 3.82 | 2.77–5.27 | <.0001  |
| 40–59 y   | 2.43 | 2.21–2.68 | <.0001  |
| 60+ y     | 1.34 | 1.25–1.43 | <.0001  |

<sup>a</sup>An inverse linear relationship of aRR with age was found for those with schizophrenia (aRR = 24.57; 95% CI, 16.81–35.92;  $P < .0001$ ). Abbreviation: SEFI-2 = Socioeconomic Factor Index—Version 2.

the result of injury or suicide, these causes represented the lowest death rates (compared to other causes) in those with schizophrenia aged 60 or older. For middle-aged and older adults, the risk of dying from most causes is significantly higher for those with schizophrenia. In middle age, there is a significantly higher risk of dying from cancers, but this risk is not significantly different in younger and older age groups.

That a majority of individuals with schizophrenia are living into old age and, for the most part, are dying of physical illness at significantly higher rates than those without schizophrenia has public health implications. Coordination of care is poor for patients with serious mental illness.<sup>1</sup> Primary care for those with schizophrenia must include careful monitoring for respiratory and circulatory illness at all ages, and lung cancer in middle age. Conscious efforts by health care providers to reach out to marginalized patients can improve the situation. Among veterans in the United States with serious mental illness, those who dropped out of care but returned after being contacted by Veterans Affairs (VA) services for follow-up had an almost 6 times lower mortality rate than those patients who did not return.<sup>39</sup> At the end of life, individuals with schizophrenia are less likely to see specialists, less likely to have pain controlled, and more likely to die in institutional settings.<sup>8</sup> Yet, research examining end-of-life care in those with schizophrenia and cancer in highly integrated care settings, such as VA in the United States, shows comparable or better care than in those without mental illness.<sup>40</sup> Such findings speak to the importance of continuity of care in schizophrenia, involving extensive interprofessional and intraprofessional collaboration in medical, psychiatric, and social services. Sensitivity and advocacy by health care providers to the vulnerability and unique needs of this population are important first steps in ensuring quality preventative, curative, and palliative care.

**Disclosure of off-label usage:** The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.

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For the CME Posttest, see next page.

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## POSTTEST

To obtain credit, go to [PSYCHIATRIST.COM](http://PSYCHIATRIST.COM) (Keyword: February) to take this Posttest and complete the Evaluation.

1. **Among people with schizophrenia who were 10 to 39 years old, the risk of death from suicide was almost 12 times that of other people. What happened to this risk in older age groups?**
  - a. Increased
  - b. Decreased
  - c. Stayed the same
2. **Among people with schizophrenia who were 10 to 39 years old, what caused the greatest relative risk of death, after suicide?**
  - a. Cancer
  - b. Circulatory illness
  - c. Respiratory illness
  - d. Injury
3. **Some research has posited that schizophrenia is a protective factor against cancer. In this cohort, however, what age group had a risk of death from cancers, including lung cancer, that was significantly greater than that of people without schizophrenia?**
  - a. 10 to 39 years
  - b. 40 to 59 years
  - c. 60 years and older
  - d. All age groups
4. **You have several patients with schizophrenia who are in their twenties and thirties, a few who are in their forties and fifties, and a couple who are over 60 years old. Because of a significantly greater risk of death compared with people without schizophrenia, screening for circulatory and respiratory illnesses (and coordination with primary care) would be helpful in which group of your patients?**
  - a. Those in their twenties and thirties
  - b. Those in their forties and fifties
  - c. Those over 60 years old
  - d. All age groups