Years of potential life lost and life expectancy in schizophrenia: a systematic review and meta-analysis

Carsten Hjorthøj, Anne Emilie Stürup, John J McGrath, Merete Nordentoft

Summary

Background Several studies and meta-analyses have shown that mortality in people with schizophrenia is higher than that in the general population but have used relative measures, such as standardised mortality ratios. We did a systematic review and meta-analysis to estimate years of potential life lost and life expectancy in schizophrenia, which are more direct, absolute measures of increased mortality.

Methods We searched MEDLINE, PsycINFO, Embase, Cinahl, and Web of Science for published studies on years of potential life lost and life expectancy in schizophrenia. Data from individual studies were combined in meta-analyses as weighted averages. We did subgroup analyses for sex, geographical region, timing of publication, and risk of bias (estimated with the Newcastle-Ottawa Scale).

Findings We identified 11 studies in 13 publications covering all inhabited continents except South America (Africa n=1, Asia n=1, Australia n=1, Europe n=7, and North America n=3) that involved up to 247 603 patients. Schizophrenia was associated with a weighted average of 14·5 years of potential life lost (95% CI 11·2–17·8), and was higher for men than women (15·9, 13·8–18·0 *vs* 13·6, 11·4–15·8). Loss was least in the Asian study and greatest in Africa. The overall weighted average life expectancy was 64·7 years (95% CI 61·1–71·3), and was lower for men than women (59·9 years, 95% CI 55·5–64·3 *vs* 67·6 years, 63·1–72·1). Life expectancy was lowest in Asia and Africa. Timing of publication and risk of bias had little effect on results.

Interpretation The effects of schizophrenia on years potential life lost and life expectancy seem to be substantial and not to have lessened over time. Development and implementation of interventions and initiatives to reduce this mortality gap are urgently needed.

Funding None.

Copenhagen University Hospital, Mental Health Centre Copenhagen, Hellerup, Denmark (C Hjorthøj PhD, A E Stürup MD, Prof M Nordentoft DMSc); **Lundbeck Foundation Initiative for Integrative Psychiatric Research, iPSYCH, Copenhagen and Aarhus, Denmark** (C Hjorthøj, Prof M Nordentoft); **Queensland Centre for Mental Health Research, Park Centre for Mental Health, Wacol, QLD, Australia** (Prof J J McGrath PhD); **Queensland Brain Institute, University of Queensland, St Lucia, QLD, Australia** (Prof J J McGrath); **and National Centre for Register-Based Research, Aarhus University, Aarhus, Denmark** (Prof J J McGrath)

Correspondence to:
Dr Carsten Hjorthøj, Copenhagen University Hospital, Mental Health Centre Copenhagen, Kildegårdsvej 28, opg 15, DK-2900 Hellerup, Denmark
carsten.hjorthoej@regionh.dk

Introduction

Several systematic reviews and meta-analyses have been done to investigate mortality in schizophrenia, occasionally based on more than 100 studies.[1–5] These analyses have typically focused on establishing the pooled standardised mortality ratio, which measures mortality relative to that in the background population. Other approaches have been to focus on predictors of increased mortality within populations with schizophrenia,[6,7] or on relative risks of or risk factors for cause-specific mortality (eg, suicide and cardiovascular mortality[8–10]).

Relative measures of mortality are useful, but can be difficult to interpret. Small variations in rates of rare outcomes result in high relative risks because estimates are dependent on the baseline risks. Furthermore, mortality is difficult to understand without knowing the length of follow-up. At the population level, life expectancy is often used as a measure of mortality and health status. Life expectancy at birth for a given year is defined as the mean length of time a person born in that year would live if he or she were exposed to the age-specific mortality for that year. Life expectancy may also be calculated at any given age, and is defined as the mean remaining number of years a person would expect to live given that he or she has already survived to that age. Thus, life expectancy can be calculated for a population before

anyone has died, whereas average age of death may be derived only from observed deaths. Use of life expectancy allows comparisons of subpopulations. For instance, the magnitude of difference between life expectancy of people with schizophrenia and the background population would be termed years of potential life lost due to schizophrenia.

We are unaware of any studies that have systematically reviewed the literature specifically for life expectancy or years of potential life lost in patients with schizophrenia. Similarly, whether or how these factors vary over time or geographical location have not been established. We did a systematic review and meta-analysis in which we aimed to identify studies and synthesise their findings on life expectancy and years of potential life lost in people with schizophrenia. If applicable, we aimed to stratify the findings by sex, geographical location, comorbid disorders, other risk factors, timing of publication, and risk of bias in included studies.

Methods

Search strategy

Before we started literature searches, we registered the protocol for this systematic review at PROSPERO, number CRD42016043673. On July 29, 2016, we searched MEDLINE (through PubMed), PsycINFO, Embase, Cinahl, and Web of Science, without restrictions on year

of publication, geographical location, or language of publication. In PubMed, we used the search term ("Schizophrenia"[Mesh] OR "Mental Disorders"[Majr]) AND ("Mortality"[Mesh] OR "Life Expectancy"[Mesh] OR "Survival rate"[Mesh] OR "Mortality, Premature"[Mesh]). In Embase, we used the search term (exp schizophrenia/ OR *mental disease/) AND (exp mortality/ OR exp life expectancy/ OR exp survival rate/ OR exp premature mortality/). In PsycINFO, we used the search term (exp schizophrenia/ OR *Mental Disorders) AND (exp "Death and Dying"/ OR exp life expectancy/ OR exp Mortality Rate/). In Cinahl, we used the search term ((MH "Schizophrenia+") OR (MM "Mental Disorders")) AND ((MH "Mortality+") OR (MM "Life Expectancy") OR (MM "Survival")). In Web of Science, we used the search term (TOPIC: (schizophrenia) OR Title: ("mental dis*")) AND (TOPIC: ("MORTALITY") OR TOPIC: ("LIFE EXPECTANCY") OR TOPIC: ("SURVIVAL RATE") OR TOPIC: "(PREMATURE MORTALITY")).

Inclusion criteria
We included studies that reported data on years of potential life lost or life expectancy in patients diagnosed as having schizophrenia according to ICD (any version), DSM (any version), or the Research Diagnostic Criteria. If schizophrenia was reported as part of a larger group of disorders (eg, psychotic or mental disorders), we contacted the authors to obtain schizophrenia-specific estimates. We included only original data. We did not apply any language restrictions or other exclusion criteria to the studies.

Study selection
One author (CH) initially screened the titles of retrieved papers to exclude those that were obviously irrelevant. Two authors (CH and AES) screened the abstracts and full texts of the remaining papers to determine which should be included. Discrepancies were registered and discussed by these two authors to try to reach a decision. If no consensus could be reached, the two remaining authors (JJM and MN) could act as arbiters.

Data extraction
The following data were extracted from the included studies: diagnostic system, total number, age, and sex of patients, study country or region, study period, source of data, and years of potential life lost and life expectancy (overall and within subgroups). We contacted authors to request data if background variables, years of potential life lost, or life expectancy were missing from the publication. Risk of bias was established with the Newcastle-Ottawa Scale.[11]

Synthesis of data
Distributions of life expectancy and years of potential life lost are presented graphically. Most studies did not report measures of uncertainty (eg, SEs or CIs) around their estimates of life expectancy or years of potential life lost. We could not, therefore, use the usual variance-based approaches to calculate study weights. Instead, we calculated averaged values weighted by size of the individual study populations. From the studies without SEs or CIs, we extrapolated the pooled SE from a fixed effects meta-analysis, which we used to generate CIs around the estimated weighted averages. For studies that reported CIs, we converted these to SEs before inclusion in the fixed effects meta-analysis. Weighted averages were estimated and forest plots were drawn with Stata version 13.1. The random-effects models used to estimate CIs were generated with Comprehensive Meta-Analysis version 3.3.070. We did subanalyses for sex, geographical region, timing of publication, and low versus high risk of bias. In the main synthesis of data on life expectancy, we pooled estimates regardless of the age at which they were calculated. In studies that reported remaining life expectancy at a given age, we added this age to the estimate to obtain an expected age at death.

Results
We identified 11830 unique entries in bibliographical databases, from which 762 entries remained after removal of obviously irrelevant papers (figure 1). All but