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Physical Comorbidity and Healthcare Utilization in People with Schizophrenia: a systematic review

Mercè Salvador,[1,2] Alejandro Porras-Segovia,[3,11] Olatz Lopez-Fernandez,[4-7] Enrique Baca-García,[3,7-13]

[1] Departamento de Psiquiatría, Hospital Universitario de Móstoles, Madrid, España.
[2] Departamento de Psiquiatría, Universidad Rey Juan Carlos, Madrid, España.
[3] Grupo de Investigación en Psiquiatría Traslacional, Instituto de Investigación Fundación Jiménez Díaz, Madrid, España.
[4] Departamento de Personalidad, Evaluación y Psicología Clínica, Facultad de Psicología, Universidad Complutense de Madrid, Madrid, España.
[5] Facultad de Educación y Psicología, Universidad Francisco de Vitoria, Madrid, España.
[6] Facultad de Psicología, Centro de Estudios Universitarios Cardenal Cisneros, Universidad Complutense de Madrid, Madrid, España.
[7] Departamento de Psiquiatría, Hospital Universitario Fundación Jiménez Díaz, Madrid, España.
[8] Departamento de Psiquiatría, Universidad Autónoma de Madrid, Madrid, España.
[9] Departamento de Psiquiatría, Hospital Universitario General de Villalba, Madrid, España.
[10] Departamento de Psiquiatría, Hospital Universitario Infanta Elena, Valdemoro, España.
[11] Departamento de Psiquiatría, Hospital Universitario Rey Juan Carlos, Móstoles, España.
[12] Département de psychiatrie, Centre Hospitalier Universitaire de Nîmes, France.
[13] CIBERSAM (Centro de Investigación Biomédica en Red Salud Mental), Instituto de Salud Carlos III, Madrid, España.

Correspondence:
Enrique Baca-García
Hospital Universitario Fundación Jiménez Díaz.
Avenida de los Reyes Católicos, 2, 28040, Madrid, España.
Phone: +34 (915) 550-4800
Email: EBaca@quironsalud.es

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ABSTRACT

Introduction. Schizophrenia is a mental health condition that can lead to significant disability and have a major impact on social and occupational functioning. It tends to decrease life expectancy, which could be attributed to a variety of factors, including poor health habits, barriers to healthcare access, and the stigmatization of mental illness. **Objective.** The main aim of this systematic review is to examine the physical comorbidity of these patients, and their health service utilization. **Method.** The protocol has been registered with the PROSPERO database (CRD42020139972) and follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A search of PubMed/MEDLINE, EMBASE, Scopus, Web of Science, PsycINFO, Cochrane Library, and ProQuest Health Research Premium Collection yielded 317 articles, 57 of which were selected. **Results.** The mortality rate of people with schizophrenia is often at least twice that of the general population. In addition, these individuals may be susceptible to other physical health conditions that can significantly shorten their lifespan: cardiovascular and respiratory diseases, diabetes mellitus, oncologic diseases, and chronic infections. Complications during hospitalization and prolonged length of stay due to comorbidities may impede their access to essential healthcare. **Discussion and conclusion.** Enhancing the healthcare system is crucial to providing adequate care for these patients. Adopting positive lifestyle choices, reducing substance dependence, and abstaining from unconventional antipsychotics can bolster their life expectancy. It is therefore crucial to implement intervention strategies while training professionals to detect and manage physical comorbidities associated with this disorder.

Keywords: Schizophrenia, physical comorbidity, health services, mortality, morbidity, systematic review.

RESUMEN

Introducción. La esquizofrenia puede provocar una discapacidad significativa y tener un impacto notable en el funcionamiento social y ocupacional. Este trastorno tiende a disminuir la esperanza de vida debido a una variedad de factores, incluidos malos hábitos de salud, obstáculos para acceder a la atención médica y el estigma a las enfermedades mentales. **Objetivo.** La presente revisión sistemática pretende examinar la comorbilidad física de estos pacientes y su uso de los servicios de salud. **Método.** El protocolo registrado en la base de datos PROSPERO (CRD42020139972) sigue las directrices *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA). A través de PubMed/MEDLINE, EMBASE, Scopus, Web of Science, PsycINFO, Cochrane Library y ProQuest Health Research Premium Collection se identificaron 317 artículos y se seleccionaron 57. **Resultados.** Las personas que padecen esquizofrenia se enfrentan a una tasa de mortalidad que supera al menos el doble de la población general, y son susceptibles a enfermedades cardiovasculares, respiratorias, diabetes mellitus, oncológicas e infecciones crónicas, que pueden disminuir su esperanza de vida. Las complicaciones durante la hospitalización y las estancias prolongadas dificultan su atención sanitaria. **Discusión y conclusión.** Los sistemas de salud requieren mejoras para brindar una atención adecuada a los pacientes con esquizofrenia y ayudar a incrementar su esperanza de vida. Además, estos pacientes se benefician de adoptar estilos de vida saludables, tratar la dependencia de sustancias y adaptar el tratamiento antipsicótico. Parece crucial ejecutar estrategias de intervención y capacitar a los profesionales clínicos para poder detectar y manejar las comorbilidades físicas asociadas a este trastorno mental.

Palabras clave: Esquizofrenia, comorbilidad física, servicios de salud, mortalidad, morbilidad, revisión sistemática.

INTRODUCTION

Schizophrenia is one of the most disabling medical disorder. Considered a severe mental illness (SMI), it is usually associated with impaired social and occupational functioning. Approximately seven people per 1,000 will experience it in their lifetime (McGrath et al., 2008). The economic burden of schizophrenia diagnosis and treatment was estimated at $155.7 billion USD in 2013 in the United States (US) (Cloutier et al., 2016), including health costs and those associated with productivity loss. Indeed, the mortality rate of people with schizophrenia more than doubles that of the general population, largely due to the high prevalence of comorbid physical conditions (McGrath et al., 2008), which may be associated with their limited healthcare access.

Patients with schizophrenia have a shorter life expectancy (Laursen et al., 2014) due to poor physical health, which may be associated with worse health habits (such as substance use). There may also be barriers to the adequate physical care of this population, associated with both the patient and their illness, and compounded by the attitudes of physicians and the healthcare organizational structure (McGinty et al., 2015). A fragmented healthcare system, limited healthcare access, the inability of these patients to identify their medical problems or reluctance to be treated may contribute to their poor physical healthcare (Lambert et al., 2003). The frequent stigmatization of psychiatric patients (even among physicians) may exacerbate the problem (Copeland et al., 2006; Leucht et al., 2007).

In the initial reviews of this research issue, Goldman (1999) found that 50% of patients with schizophrenia had a comorbid or undiagnosed medical pathology. These patients were often excluded from research studies (Jeste et al., 1996), making it difficult to determine the extent and consequences of this healthcare deficit. Lambert et al. (2003) noted that patients with schizophrenia had a life expectancy ten to 25 years lower than that of the general population, while other authors have observed that this difference can increase over time (Hjorthøj et al., 2017; Laursen et al., 2014; Leucht et al., 2007). Lee et al. (2018) reviewed eight longitudinal studies of mortality in schizophrenia, finding that the standardized mortality rate (SMR) of these patients compared to that of the general population increased by 37% from 2.2 in pre-1970s studies to 3.0 in post-1970s reports.

Salokangas (2007) reviewed studies of patients with schizophrenia living in community residences, observing that most had undetected physical illnesses, despite seeking medical care more frequently than the general population. The literature review by Leucht et al. (2007) found a higher prevalence of human immunodeficiency virus (HIV) infection and hepatitis, osteoporosis, altered pain sensitivity, sexual dysfunction, obstetric complications, cardiovascular diseases, overweight, diabetes, dental problems, and polydipsia than among the general population. Likewise, Oud and Meyboom-de Jong (2009) systematically reviewed the prevalence and treatment of somatic comorbidity in primary care, finding that patients with serious mental illness (SMI) were at risk of developing diabetes mellitus, metabolic syndrome, hypertension, cardiovascular or pulmonary diseases, hypothyroidism, and visual problems. A number of reviews conducted in this century have identified a group of physical health issues commonly found in individuals with SMI. These comorbidities include, but are not limited to, diabetes, and cardiovascular, infectious, metabolic, and hormonal diseases. Most of these health concerns are associated with genetic and lifestyle factors, and are compounded by the inability of these patients to identify their medical problems, reluctance to be treated or their inadequate medical assessment. Consequently, these characteristics have become a typical pattern in the lives of most individuals with schizophrenia, negatively impacting their quality of life, life expectancy, and healthcare. To the authors' knowledge, there is a dearth of systematic medical literature reviews exploring the impact of somatic comorbidity on patients with schizophrenia. In addition, according to the most recent reviews, the severity of this mental disorder is due to its increasing mortality, pointing to a possible relationship between this psychiatric diagnosis and severe physical diseases such as cancer, diabetes mellitus, and certain chronic cardiovascular diseases (Laursen et al., 2014; Nordentoft et al., 2021; Rodrigues et al., 2021). For instance, Nordentoft et al. (2021) found that patients with schizophrenia have a 50% higher risk of breast, lung, and colon cancer deaths than the general population, while Nordentoft et al. (2021) observed that those with psychotic disorders have a 69% higher risk of multimorbidity (the occurrence of multiple co-occurring, chronic conditions in which the chronic cardiovascular disease may be hypertension, coronary heart disease, myocardial infarction, ischemic stroke, or atrial fibrillation).

Kowalski and Misiak (2023) recently reviewed the multidimensional associations between schizophrenia and COVID-19 for common biological pathways, finding that environmental stress, common comorbidities of schizophrenia, and the adverse effects of antipsychotic treatment are associated with greater severity and mortality of the disease. The present systematic review aims to examine the physical comorbidity of patients diagnosed with schizophrenia, regardless of the level of severity, and the healthcare received. It also specifically seeks to determine how this relationship impacts the mortality of these SMI patients, identify the main physical conditions comorbid with a diagnosis of schizophrenia; and observe the healthcare service utilization of these patients with comorbid physical conditions to gauge the degree of access to and quality of the medical treatment they receive, and the hospital admissions rate.

METHOD

The systematic review protocol has been registered with the PROSPERO database (registration number: CRD42020139972) and adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009; Urrútia, & Bonfill, 2010; Page et al., 2021).

Inclusion and exclusion criteria

To be eligible for consideration, research studies must be original observations published in reputable, peer-reviewed journals and include cross-sectional studies of cohorts, cases and controls. Cohort studies are included in the present study because they typically involve analytical and observational research requiring at least one group of patients diagnosed with this SMI. The main methodological objective is to identify the relationship between risk factors, such as physical comorbidities, and health outcomes such as morbidity and mortality. Case-control studies are another type of observational research commonly used in healthcare settings to establish potential links between psychiatric disorders and physical comorbidities. They may also be experimental designs comparing these SMI patients with the general population, providing valuable insights. This latter type of study analyzes variations between patients with a diagnosis of schizophrenia and those without psychiatric conditions in regard to mortality, physical comorbidity, such as the occurrence of physical diseases, clinical traits of physical illnesses, prognosis, and healthcare service utilization (including length of stay, outpatient appointments, emergency room visits, and expenses).

The methodological decisions determining the selection of empirical papers sought to include the research associated with the aims of this study. Only publications in English, Spanish, and French were included, since these are the languages in which the authors are proficient.

To ensure accuracy, we excluded clinical cases, case series, and case studies with only one subject ($N = 1$). We also eliminated reviews, meta-analyses, theoretical studies, and clinical trials. No restrictions were placed on the healthcare environment or type of treatment, and the date of publication was unimportant.

Search strategy

We performed an extensive search of the literature in 2021 in scientific databases such as PubMed/MEDLINE, EMBASE, Scopus, Web of Science, PsycINFO, Cochrane Library, and ProQuest Health Research Premium Collection to collect relevant information (see Figure 1 for further details; Page et al., 2021). The search was narrowed down from 1/1/1991 to 31/12/2021.

To find the information, a search strategy was implemented involving a combination of specific terms such as "Schizophrenia" [Mesh] AND "Comorbidity" [Mesh], "Schizophrenia" [Title] AND ("medical comorbidity" OR "physical comorbidity"). We also examined the studies found in the search for any relevant references.

Selection of studies and data extraction

Two authors conducted a review of the titles and abstracts of the studies retrieved to identify potential studies that met the inclusion criteria. In addition, they manually scrutinized the reference lists of eligible publications. The two reviewers independently evaluated the full text of potentially eligible studies. They resolved discrepancies through deliberation, consulting with the last author when necessary. Thereafter, the first author meticulously analyzed each paper selected to prepare a first draft of the results summarized in the tables, which were subsequently reviewed by the third author. This involved scrutinizing the Method section to check the research design, and conduct a detailed analysis of the title, abstract, introduction (objectives), method, and results sections to extract the critical variables of the study listed in Tables 1 and 2, which include the author, design, country, year of publication, study design, sample size, age range of the sample, sex distribution, results, measures, and main conclusions.

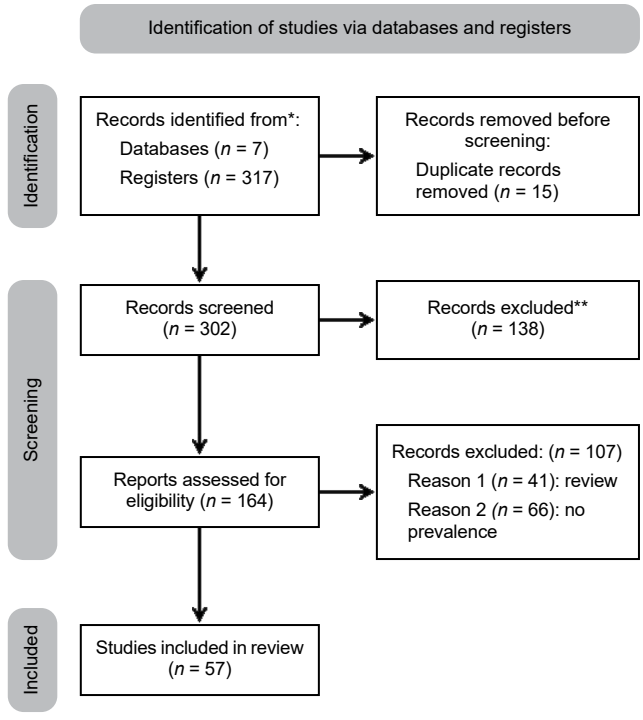

Figure 1. PRISMA 2020 Flow Diagram of the Present Systematic Review.

Table 1
Main findings of Mortality Studies Included in the Present Systematic Review

Study	*Country*	*Design*	*Population*	*Aims*	*Results*
Räsänen et al., (2003)	Finland	Cohorts	*N* = 203 patients with S ≥ 25 y/o, admitted to medium to long stay centers	To compare mortality and associated factors in patients with S *vs*. the general population.	As age increased, mortality approached that of the general population. In patients with S, the risk of death from all causes was four times that of the general population. In the 25-34 age group, the mortality risk was 12.9 times higher than that of the general population for men and 28.6 times higher for women. The diseases with the highest risk of mortality in patients with S vs. the general population were digestive (SMR = 17.5), respiratory (SMR = 9.3), and circulatory system diseases (SMR = 3.6), and neoplasms (SMR = 2.1).
D ' Avanzo et al. (2003)	Italy	Cohorts	*N* = 1,515 institutionalized patients with S, aged 20-94	To compare mortality rates in patients with S before and after deinstitutionalization.	The SMR for all causes was 2.66 before discharge from a psychiatric hospital and 2.09 after discharge. Mortality remained high after discharge from the psychiatric hospital but was not associated with an increase after discharge.
Copeland et al. (2006)	USA	Cases and controls	*N* = 27,798 veterans ≥ 18 y/o Deceased (943 with S)	To compare the number of unexpected deaths among patients with S *vs*. those without S.	There were 20% of unexpected deaths in patients with S *vs*. 7% in patients without S. S was associated with a twofold increase in the risk of unexpected death (OR = 2.4, 95% CI 1.6-3.4).
Tokuda et al. (2008)	Japan	Cases and controls	*N* = 190,157 hospitalized patients ≥ 18 y/o (1,108 with S)	To compare patients with S and without S regarding mortality rate and causes of death.	There were no significant differences in hospital mortality rates (schizophrenic patients 5.0% vs. non-schizophrenic patients 4.0%). Patients with S were more likely to be older and male, and have had longer hospital stays, and more ICU admissions. The most important risk factors for mortality among patients with S were malignancy and cardiovascular disease. The main causes of death in hospitalizations of patients with S were suicide (14.5%), malignant lymphoma or leukemia (10.9%), stroke (9.0%), and sepsis (7.3%).
Laursen et al. (2011)	Denmark	Cohort	*N* = 2,450,812 patients (16,079 with S) from 15- 52 y/o	To compare the incidence of 19 chronic physical diseases between patients with psychiatric disorders and those with no psychiatric disorders.	Patients with S had higher incidence rates of hospital contacts in almost all explored physical illnesses and a Charlson comorbidity index twice as high as people without psychiatric disorders (incidence rate = .80; 95% CI .63-1.00). Chronic physical illnesses explain half the excess mortality in patients with S. The highest mortality rates were observed in psychiatric patients who were not admitted for their physical illness (possibly due to undertreatment or underdiagnosis).
Bodén et al. (2015)	Sweden	Cohorts	*N* = 209,592 patients ≥15 years with AMI (541 with S)	To compare mortality post AMI with S, BD, and the general population.	Patients with S were younger when they had their first AMI (63 years, compared with 68 years in BD and 71 years in the general population), had higher 30-day (OR = 2.58; 95% CI 1 .88-3.54) and one year mortality (OR = 2.55, 95% CI 1.98-3.29).
Hou et al. (2015)	Taiwan	Cases and controls	*N* = 24,368 hospitalized patients ≥ 18 y/o (8,264 with S)	To estimate the incidence and risk factors of SCD in patients with S.	The standardized mortality rate for MSC was 4.5. Risk factors for SCD were physical illness (RR = 2.91, $p < .01$), aggressive behaviors (RR = 3.99, $p < .01$), electrocardiographic abnormalities (RR = 5.46, $p < .05$), and first generation antipsychotics (RR = 5.13, $p < .01$).
Sohn et al. (2015)	USA	Cross-sectional	*N* = 42,416 discharges due to AMI (16,140 patients ≥ 18 years with mental illness, 26,276 without mental illness)	To compare post-AMI hospital mortality between patients with and without mental disorders, and to analyze differences between mental disorders.	They found no differences in post-AMI hospital mortality between patients with and without mental disorders in general. Patients with S were associated with increased in-hospital mortality post AMI (OR 1.72, 95% CI 1.02-2.90).

Table 1
Main findings of Mortality Studies Included in the Present Systematic Review (continued)

Study	*Country*	*Design*	*Population*	*Aims*	*Results*
Bradford et al. (2016)	USA	Historical cohorts	*N* = 34,664 patients ≥18 y/o with lung cancer (835 with S)	To do a lung cancer survival analysis in patients with and without S.	Risk of death was significantly higher in patients with S (RR = 1.33; 95% CI 1.22-1.44). Risk factors included advanced age, being Black, smoking, substance abuse.
Bitter et al. (2017)	Hungary	Cases and controls	65,169 patients with S and 325,435 controls ≥ 18 y/o	To compare mortality in patients with S vs. the general population.	Patients with S had a higher risk of all-cause mortality (RR = 2.4; $p < .0001$), and lower life expectancy: at 20 years, 11.5 years in men and 13.7 in women; at age 45, 8.1 years in men and 9.6 in women.
Hayes et al. (2017)	United Kingdom	Cohorts	259,598 patients ≥ 18 y/o (22,497 with S, 17,714 with BD, 219,387 controls)	To compare mortality in people with S and BD and in the general population.	Patients with S had higher mortality than controls (RR = 2.08 95% CI 1.98 - 2.19). The adjusted RRs for those with S increased by .11 per year between 2004 and 2010 and by .34 per year after 2010.
Tanskanen et al. (2018)	Finland	Historical cohorts	People ≥ 16 y/o, deceased from 1975 to 2014 (79,877 with S)	To compare mortality, age and causes of death among patients with S and the general population.	In patients with S, the median age of death was seven years earlier than in the general population. It ranged from 57.6 years in 1984 to 70.1 years in 2014 (general population from 70.9 to 77.5 years). The mortality difference with the general population is stable and does not increase (SMR 2.6 in 1984 and 2.7 in 2014).
Dalton et al. (2018)	Denmark	Cohorts	*N* = 56,152 Danish women ≥ 18 y/o with breast cancer (499 with S)	To compare the survival rate of patients with breast cancer with and without S.	Breast cancer patients with S have an increased risk of dying from any cause (HR = 1.55; 95% CI 1.32-1.82), an increased risk of dying from breast cancer (HR 1, 12 (95% CI .98-1.50), and a greater likelihood of not being assigned to a prescribed treatment (OR = 1.50; 95% CI 1.15-1.94).
Kugathasan et al. (2018)	Denmark	Cohorts	*N* = 221,772 patients ≥ 18 y/o (36,962 with S)	To compare all-cause mortality and survival after AMI in patients with S and without S.	Patients with S had a higher mortality rate (HR 9.94, 95% CI 8.71 to 11.35). The SMR remained stable over the years in patients with E, and decreased in the general population.
Laursen et al. (2019)	Denmark	Cohort	6,641,608 patients 10-94 y/o (47,554 with S)	To compare years of life lost in patients with S vs. the general population.	There were improvements in years of life lost between 1995 and 2015, in both the general population and people with S. Men with S lost 13.5 more years than the general population and women 11.4 years.
Kugathasan et al. (2019)	Denmark	Historical cohorts	*N* = 5,432,821 patients 18-85 y/o (30,210 with S)	To explore the association between comorbidity and mortality rates in patients with S vs. the general population.	All somatic diseases were associated with higher mortality in S (HR = 16.3, 95% CI 15.4-17.3). Patients with S had higher mortality regardless of the number of somatic diseases diagnosed. The mortality rate was more than twice as high for all individual somatic disease categories.

Note: y/o = years old; S = Schizophrenia; COPD = Chronic Obstructive Pulmonary Disease; USA = United States of America; HR = Hazard Ratio; AMI = Acute Myocardial Infarction; HF = Heart Failure; OR = Odds Ratio; MSC = Sudden Cardiac Death; PAF = Population Attributable Fraction; SMR = Standardized Mortality Rate; SMI = Severe Mental Disorder; ICU = Intensive Care Unit; HBV = Hepatitis B Virus; HCV = Hepatitis C Virus; HIV = Human Immunodeficiency Virus.

RESULTS

A meticulous search of seven scientific databases yielded 317 entries. Removing the duplicates left 302 entries. The elimination of 138 irrelevant articles narrowed the focus to 164 relevant items. Finally, after conducting a thorough analysis of each full-text article, we identified 57 publications that met our stringent inclusion criteria (Figure 1).

Mortality

The mortality rate of patients with schizophrenia is two to four times higher than that of the general population (Bitter et al., 2017; Bouza et al., 2010b; Gur et al., 2018; Hayes et al., 2017; Kugathasan et al., 2019; Laursen et al., 2019; Räsänen et al., 2003; Schoepf et al., 2014; Tanskanen et al., 2018; Table 1). In regard to sample size, the study with the largest sample was conducted by Tanskanen et al. (2018) in Finland, with 79,877 patients with schizophrenia, detecting a mortality rate 2.7 times higher than that of the general population. The study by Kugathasan et al. (2019) in Denmark was the second largest, with a sample of 30,210 patients with schizophrenia, obtaining a similar mortality rate, twice as high as that of the general population for all somatic diseases (from 2.16 per 1,000 in endocrine diseases to 2.85 per 1,000 in skin diseases).

The studies reviewed show that although patients with schizophrenia die from the same causes as those without this diagnosis, they have a shorter life expectancy. A Finnish study by Räsänen et al. (2003) of patients ages 25 to 34 found that the risk of mortality was 12.9 times higher for men and 28.6 times higher for women compared to that of the general population. Tanskanen et al. (2018) discovered that the gap in life expectancy was more significant among younger Finnish patients. Laursen et al. (2019) observed an increase in the number of years lost between 1995 and 2015 among individuals in Denmark. Specifically, men with schizophrenia lost 13.5 more years of life than the general population.

There appear to be disparities between authors in regard to the difference in life expectancy between patients with schizophrenia and the general population. In the United Kingdom (UK), Hayes et al. (2017) showed that hazard ratios (HR) adjusted for schizophrenia gradually increased from 2004 to 2009 and rapidly thereafter. However, Tanskanen et al. (2018) did not confirm this increase, as the standardized mortality rate for 79,877 Finnish patients with schizophrenia followed between 1975 to 2014 had remained stable for the previous 30 years.

Various studies have reported the diseases with the greatest impact on mortality. Kugathasan et al. (2019) found the leading causes of death to be respiratory, digestive, and cardiovascular diseases. Conversely, Bouza et al. (2010a) reported that circulatory, respiratory, and neoplasm cases accounted for 21%, 18%, and 17% of deaths respectively. In the article by Schoepf et al. (2014), the most common comorbidity in patients with schizophrenia was Type 2 Diabetes Mellitus (DM2). It was also a predictor of hospital mortality: alcoholic hepatopathy, Parkinson's disease, Type 1 Diabetes Mellitus (DM1), kidney failure, ischemic stroke, pneumonia, ferrocene anemia, chronic obstructive pulmonary disease (COPD), and bronchitis.

In terms of morbidity, the results reveal the following physical illnesses: cardiovascular diseases, respiratory diseases, Type 2 Diabetes Mellitus (DM2), oncologic diseases, and chronic infections (Table 2).

Cardiovascular diseases

Studies on mortality from post-hospital and long-term acute myocardial infarction (AMI) in North America and Northern Europe coincide with higher post-AMI mortality rates in patients with schizophrenia (Bodén et al., 2015; Hauck, et al., 2020; Kugathasan et al., 2018; Sohn et al., 2015). In Sweden, Bodén et al. (2015) compared 541 patients with schizophrenia with AMI with those with AMI without SMI. Patients with schizophrenia were younger at the time of AMI (with a mean age of 63) and had higher mortality rates (at 30 days). Kugathasan et al. (2018) studied 36,962 Danish patients with schizophrenia and AMI from 1980 to 2015 compared with the general population. They found higher mortality rates in patients with post-AMI schizophrenia at one and five years, and the absence of a decrease in the post-AMI standardized mortality rate.

In Taiwan, studies of sudden cardiac death (SCD) showed an increase in patients with schizophrenia (Chen et al., 2021; Hou et al., 2015). The largest study, led by Chen et al. (2021), of 170,322 patients with schizophrenia, found that 1,836 died of this cause. The standardized mortality rate was always > 1.00 and highest in male patients < 35 years of age. In addition, the risk of SCD increases with age, due to hypertension, and congestive heart failure, while drug-induced mental disorders decrease.

Respiratory diseases

Schizophrenia is associated with a higher probability of diagnosis of lung disease. The most extensive study was conducted at veterans' hospitals in the United States by Copeland et al. (2007). In a sample of 28,000 patients, the 3.4% with schizophrenia had an increased likelihood of a diagnosis of lung disease during the last year of life, pneumonia and COPD, regardless of whether they smoked. The lack of outpatient medical care in the year before death was cited as an indicator of this increased risk.

Recent research conducted in Finland by Partti et al. (2015) suggested that individuals with schizophrenia may experience impaired lung function, as measured by spirometry. In Denmark, Jørgensen et al. (2018), found that patients with COPD and comorbid schizophrenia were less likely to receive long-acting muscarinic antagonists (MRI) or prolonged-acting ß2 agonists, putting them at a higher risk of mortality within 30 days. However, the study did not find any evidence of a higher risk of re-admission.

Type 2 Diabetes Mellitus

Studies agree that patients with schizophrenia have a higher prevalence of DM2. In the UK, Schoepf et al. (2012) indicated that the prevalence in patients with schizophrenia is 11.3%. In Denmark, exposure to antipsychotics was associated with ketoacidosis and DM2 in a previously non-diabetic population with schizophrenia (Polcwiartek et al., 2017). A family history of diabetes was associated with a family history of schizophrenia in an Australian study (Foley et al., 2016). In North America (Soontornniyomkij et al., 2019), patients with chronic schizophrenia had higher insulin resistance and higher body mass index (BMI). Moreover, an at-risk subpopulation was identified with a clinical profile (including negative symptoms, high BMI and being non-white) in which prevention of metabolic comorbidities was recommended. Conversely, in Canada (Kurdyak, et al., 2017), patients with diabetes and schizophrenia have lower rates of recommended tests and higher rates of diabetes-related hospital visits than patients with diabetes alone.

Table 2
Main Findings of the Morbidity Studies Included in the Present Systematic Review

Study	*Country*	*Design*	*Population*	*Aims*	*Results*
Daumit et al. (2006)	USA	Cross-sectional	*N* = 733,904 patients (1,746 with S) ≥ 18a admitted for medical-surgical pathology	To compare complications, hospital stay and healthcare costs in patients with and without S.	There was a higher risk of the following medical-surgical complications in patients with S than in those without S: infection (OR = 2.49; 95% 1.28-4.88); sepsis (OR = 2.29; 95% 1.49-3.51); respiratory failure (OR = 2.08; 95% 1.41-3.06); deep vein thrombosis (OR = 1.96; 95% 1.18-3.26). In patients with S, average length of stay was 10 days or longer, while hospital expenses averaged $20,000 more.
Carney et al. (2006)	USA	Cases and controls	*N* = 727,336 patients ≥ 18 y/o with physical disease (1,074 with S)	To compare medical comorbidity in patients with S and patients without mental illness.	People with S were significantly more likely to have ≥1 chronic medical condition than those without mental illness. More than 33% had ≥ three medical comorbidities, almost three times more than controls (33.2% *vs*. 12.1%, respectively).
Copeland et al. (2007)	USA	Cohorts	*N* = 27,735 patients ≥ 18 y/o (943 with S) who died in VA hospitals	To compare diagnosis of pneumonia or COPD in the last year of life in patients with and without S.	60% of patients without mental illness received outpatient care the year before death, compared to 40% of patients with S. Hospitalized S patients had a higher risk of pneumonia (38% vs. 31%), and COPD (46% vs. 38%), regardless of whether they smoked. S is a risk factor for lung disease in the last year of life (OR = 1.9, 95% CI 1.6-2.2), and to a lesser degree in advanced lung disease (OR = 1.5, 95% CI 1.3-1.7).
Martens et al. (2009)	Canada	Cases and controls	*N* = 338,514 women 18-69 y/o (3,220 with S)	To compare women with and without S in cervical cancer screening with Papanicolaou test.	Women with S were less likely to have Pap smears (58.8% *vs*. 67.8%, $p < .0001$) compared to other women.
Bouza et al. (2010a)	Spain	Cohorts	*N* = 16,776 patients > 15 y/o admitted with S, compared to the national health survey of the general population	To compare the medical comorbidity of patients with S and the general population.	In patients with S, physical illness appears early in life (50%, 15-31 y/o) and increases in incidence with age (in > 53 y/o, at least 84% had one physical ICD-9 code). The most prevalent medical diseases are endocrine (16%), circulatory (15%), respiratory (15%), and digestive (10%). They present higher rates than the general population in diabetes (8% in S, and 5.02% in the general population), neoplasia (4.4%, and 2.37%), AIDS (1.1%, and 1.61 per 1,000 population). No differences were found for COPD or ischemic heart disease.
Bouza et al. (2010b)	Spain	Cohorts	*N* = 20,490,332 hospital discharges in patients ≥ 15 y/o	To compare admissions due to physical illness, impact on mortality, and resource utilization in patients with S and the general population.	In patients with S, hospitalizations for medical illnesses are frequent (34% of hospital admissions). 35% 1 ICD-9-CM code, 65% ≥ 2, admission was required at younger ages (mean age 53 y/o), hospital mortality was 6.9%, and the mean age of death was 63 y/o.
Shen et al. (2011)	Taiwan	Historical cohorts	*N* = patients ≥ 18 y/o admitted to the ICU (203 with S)	To compare risks of acute organ dysfunction and death in patients with ICU with and without S.	Patients with S had a higher risk of acute organ dysfunction (OR = 1.52; 95% CI = 1.09 to 2.10), and higher hospital mortality (24.1% *vs*. 14.4%, $p < .001$; OR = 1.56, 95% CI 1.08-2.24).
Schoepf et al. (2012)	United Kingdom	Cases and controls	*N* = 89,457patients ≥ 18 y/o hospitalized (679 with S, and 88,778 controls)	To compare physical comorbidity and factors associated with in-hospital mortality between patients with S and without S.	The predictors of mortality were age (RR = 1.1), DM2 (RR = 2.2), pneumonia (RR = 2.7), heart failure (RR = 2.9), and chronic kidney failure (RR = 3,2). Patients with S had a higher prevalence of DM2 (11.3% *vs*. 6.3%).
Lin et al. (2013)	Taiwan	Cohorts	*N* = 71,317 patients > 18 y/o with S; 20,567 BD	To compare age/sex/location incidence in those with S and the general population.	Women patients with S had a higher risk of cancer (RR=1.31, 95% CI: 1.17-1.48) but not men. Cancer risk decreases with increasing duration and age of onset of S.

Table 2
Main Findings of the Morbidity Studies Included in the Present Systematic Review (continued)

Study	*Country*	*Design*	*Population*	*Aims*	*Results*
Schoepf et al. (2014)	United Kingdom	Cases and controls	*N* = 15,598 hospitalized patients (1,418 patients with S, and 14,180 controls)	To compare the prevalence of physical comorbidity, especially T2DM, and its impact on in-hospital mortality between patients with S and without S.	Schizophrenic patients had a higher proportion of admissions to the emergency room (69.8 *vs*. 43.0%), a longer average length of stay (8.1 *vs*. 3.4 days), and a greater number of hospital admissions (11.5 *vs*. 6.3) and lower survival rates (1,895 *vs*. 2,161 days).
Partti et al. (2015)	Finland	Cross-sectional	*N* = 8,028 participants ≥ 30 y/o (67 with S)	To compare lung function measured by spirometry, and the prevalence of respiratory disease among patients with S and the general population.	Patients with S had lower spirometry values after adjusting for age, sex, smoking, abdominal obesity, DM2, metabolic syndrome, and physical activity, as well as a higher probability of pneumonia (OR = 4.9), COPD (OR = 4, 2), and chronic bronchitis (OR = 3.8) than the general population.
Razzano et al. (2015)	USA	Cross-sectional	*N* = 457 people ≥ 18 y/o (179 with S)	To estimate the prevalence of more frequent medical conditions in patients with S and the general population.	The five most common medical conditions in S patients were hyperlipidemia (45%), hypertension (44%), asthma (28%), arthritis (22%), and diabetes (21%). They were less likely to report having been diagnosed with hypertension, asthma, and arthritis. The odds of being diagnosed with diabetes or dyslipidemia were similar to those of the general population.
Sørensen et al. (2015)	Denmark	Cohorts	*N* = 954,351 people aged 15-32 y/o (4,371 developed S)	To estimate the prevalence of all somatic diseases treated before the first diagnosis of S, and the association with the development of S.	Of those who developed S, 4,180 (95.6%) had previous health contact due to somatic pathology. Any previous somatic contact was associated with an increased risk of S (RR = 2.04; 95% CI 1.77-2.37).
Nielsen et al. (2016)	Denmark	Cohorts	*N* = 1,403,183 people, born between 1977 and 2002	To investigate the association between S and infections.	People with hospital contact for infection are more likely to develop S than those without it (RR = 1.53, CI 1.46-1.61). People diagnosed with S are more likely to have had a hospital contact for an infection (RR = 1.73; 95% CI 1.57-1.91). A comorbidity index between S and infection of 1.40 (95% CI 1.34-1.46) was found, indicating an overlap between S and infection.
Foley et al. (2016)	Australia	Cross-sectional	*N* = 1,624 patients 18-64 y/o with psychosis (857 with S)	To determine whether there is familial comorbidity between DM2 and psychosis.	A family history of diabetes was associated with a family history of S in patients with a psychotic disorder (OR = 1.35, *p* = .01). Adjustment for demographic factors (age, sex, diagnosis, ethnicity, education, employment, income, and marital status) slightly strengthened the association (OR = 1.74, *p* = .001).
Kisely et al. (2016)	Australia	Cohorts	*N* = 4,700,000 people ≥ 15 y/o	To compare the incidence of and mortality from cancer in psychiatric patients and the general population.	Cancer incidence was the same as for the general population for most psychiatric disorders, but rates were lower for S (RR = .84; 95% CI .72-.98). Mortality increased in psychiatric patients (OR = 2.27; 95% CI 2.15-2.39).
Schulman-Markus et al. (2016)	USA	Cohorts	*N* = 9,754,267 ≥ 18 y/o with AMI (12,590 with S)	To compare therapeutic techniques and survival after AMI in patients with and without S.	In patients with S, there were fewer reduced revascularization procedures, higher in-hospital mortality rates, a younger age at diagnosis of AMI (58 *vs*. 67 y/o), more women (44% *vs*. 38%), and a greater likelihood of having several comorbidities, and a longer length of stay.
Ishikawa et al. (2016)	Japan	Cohorts	*N* = 12,475 patients ≥ 40 y/o hospitalized for gastrointestinal cancer (2,495 with S)	To compare stages of gastrointestinal cancer, treatment, and mortality in patients with and without S.	Patients with S had a higher proportion of stage IV cancer (33.9% v. 18.1%), less probability of receiving invasive treatment (56.5% v. 70.2%, OR = .77, CI 95% .69-.85), and higher in-hospital mortality (4.2% v. 1.8%, OR = 1.35, 95% CI 1.04-1.75).

Table 2
Main Findings of the Morbidity Studies Included in the Present Systematic Review (continued)

Study	*Country*	*Design*	*Population*	*Aims*	*Results*
Brink et al. (2017)	Denmark	Cases and controls	*N* = 7754 people ≥ 70 (667 with S)	To compare medical comorbidity, medication use, and healthcare use in patients with S and the general population.	Patients with S were less likely to receive cardiovascular medication (OR = .65; 98.75% CI .00-.50), and more likely to receive analgesics (OR = 1.46, 98.75% CI 1.04-2.05), and to have fewer outpatient visits (RR = .37; 98.75% CI .24-.55).
Bauer-Staeb et al. (2017)	Sweden	Cross-sectional	*N* = 6,815,931 people ≥ 18 y/o (21,232 with S)	To compare the prevalence of HIV, HBV, and HCV in patients with S and the general population.	In patients with S, the prevalence of infections was HIV .24% with S *vs*. .09% in the general population, HBV .53% with S *vs*. 9.22 in the general population, and HCV 4.58% with S *vs*. .61 in the general population.
Attar et al. (2017)	Denmark	Cases and controls nested in a cohort	*N* = 141 patients ≥ 18 y/o with AMI (47 with S, and 94 controls)	To compare examination and treatment offers after an AMI in patients with S and patients without mental illness.	Patients with S were less likely to be offered post-AMI examinations and treatment ($p < .01$). If they were offered them, they were more likely to refuse examinations ($p = .10$) and treatment ($p = .09$).
Lu et al. (2017)	USA	Historical cohorts	*N* = 611 patients ≥ 20 y/o with HF (40 with S)	To compare readmissions at 30 days and mortality in patients with HF with and without S.	Patients with S were 4.92 times more likely to be readmitted for HF at 30 days. (RR = 4.92, $p < .001$). No associations were found for mortality.
Kurdyak et al. (2017)	Canada	Historical cohorts	*N* = 1,140,057 patients with DM2 (26,259 with S)	To compare the quality of DM2 care between patients with and without S.	S was associated with worse management of DM2 as measured by average results in HbA1c, lipid test, and eye examinations (OR = .64, 95% CI .61-.67), more emergency room visits related to DM2 (OR = 1.34, (95% CI 1.28-1.41), and more hospitalizations (OR = 1.36, (95% CI 1.28-1.43).
Gabilondo et al. (2017)	Spain	Cohorts	*N* = 2,255,406 patients ≥ 18 y/o (7,331 with S)	To compare chronic comorbidities between patients with and without S	55.6% of patients with S had one comorbidity, and 29.3% had two or more. The most prevalent comorbidity was AHT (16.8%). Patients with S had a higher risk of Parkinson's (OR = 47.89), infectious diseases (OR = 3.31) and DM2 (OR = 2.23).
Spilsbury et al. (2018)	Australia	Historical cohorts	65,508 people ≥ 20 y/o deceased between 2009-2013 (1,196 with S)	To compare the use of health services in the last year of life of people with and without S.	In patients with S, during the last year of life, there were no differences in emergency visits. They were less likely to be hospitalized (HR = .53, 95%CI .44-.65) and had less access to specialized palliative care (27.5% *vs*. 40.4% of the matched cohort, $p < .001$.
Goueslard et al. (2018)	France	Historical cohorts	*N* = 45,655 patients 15-35 y/o hospitalized for DM2 (341 with S)	To compare complications and mortality of DM2 in patients with and without S.	Patients with S had a higher risk of readmission for hypoglycemia (OR = 3.21, 95% CI 1.99-5.20, hyperglycemia (OR = 7.01, 95% CI 3.53-13.90), ketoacidosis (OR = 2.01, 95% CI 1.49-2.70) and coma (OR = 3.17, 95% CI 1.90-5.27), in addition to higher hospital mortality (OR = 2.83, 95% CI 1.50-5.36).
Bailey et al. (2018)	USA	Historical cohorts	*N* = 579,851 hospitalized patients ≥ 18 y/o (5,234 with S)	To compare surgical results in patients with and without S.	Patients with S had 70% higher odds of a more prolonged length of stay than the 75th percentile for each type of procedure and surgical approach. The odds of death were slightly lower in patients with S.
Huang et al. (2018)	Taiwan	Historical cohorts	*N* = 715,756 people ≥ 20 y/o (532 with S)	To compare in comorbidities and evolution time patients with DMT2 with and without S.	The prevalence of S is higher in patients with T2DM than in the general population, especially in those under 60 y/o. From 2000 to 2010, it increased from .64% to .85%; This increase was also observed in the general population. Patients with S and T2DM were more likely to have multiple. comorbidities.
Jørgensen et al. (2018)	Denmark	Cohorts	*N* = 72,692 patients ≥ 30a with COPD (621 with S)	To compare readmissions and mortality in patients with and without S.	Patients with S were less likely to receive treatment with long-acting muscarinic antagonists or long-acting ß2-agonists (RR = .92; 95% CI .87-.98) and to have an increased risk of mortality at 30 days (OR = 1.27, 95% CI 1.01 to 1.59).

Table 2
Main Findings of the Morbidity Studies Included in the Present Systematic Review (continued)

Study	*Country*	*Design*	*Population*	*Aims*	*Results*
Gur et al. (2018)	Israel	Cases and controls	*N* = 5,484 people ≥ 18 y/o (1,389 patients with S, and 4,095 controls)	To compare mortality, morbidity and medical resource utilization in patients with S vs. the general population.	In patients with S, the mortality rate was almost double (7% *vs*. 3.8%), and the tertiary medical resource utilization was higher (mean admissions per year .2 *vs*. .12, visits to emergency rooms .48 *vs*. .36).
Brink et al. (2019)	Denmark	Cases and controls	*N* = 27,521 people aged 18-40 (4,924 with S)	To compare medical comorbidities and mortality in people with and without S.	In patients with S, the RR of CVD and cancer was similar to that of controls. The probability of having been diagnosed with CVD, cancer, lung disease or diabetes before dying was lower.
Heiberg et al. (2019)	Norway	Cohorts	*N* = 72,451 patients ≥ 18 y/o who died from CVD (814 with S)	To compare comorbidity and use of health services in people with E or TB and people without these diagnoses.	Patients with S were 66% more likely (OR 1.66, 95% CI 1.39 to 1.98) not to be diagnosed with CVD before cardiovascular death. Almost all (98%) individuals with undiagnosed S had had somatic medical visits before they died, compared with 88% of other patients.
Soontornniyomki et al. (2019)	USA	Cross-sectional	*N* = 285 patients aged 26-65 y/o (145 with S)	To compare insulin resistance between patients with chronic S and people without mental illness.	People with S had higher insulin resistance levels and higher BMIs than those without psychiatric disorders.
Fond et al. (2019)	France	Cohorts	*N* = 224,958 patients ≥ 15 y/o who died from cancer (2,481 with S)	To compare access to palliative care and indicators of high-intensity care at the end of life among patients with S and the general population.	Patients with S were more likely to receive palliative care in the last month of life (OR = 1.61, 95% CI 1.45-1.80; *p* < 0-0001), less likely to receive palliative care for high-intensity cancer at the end of life (chemotherapy and surgery), more likely to die younger, and to have less time between cancer diagnosis and death.
Pankiewicz-Dulacz et al. (2019)	Denmark	Cohorts	*N* = 7788 born 1975-1990 diagnosed with S	To determine risk factors for infections in patients with S.	The most significant risk factors associated with the development of central infections were age < 16 y/o (HR = 1.74, 95% CI 1.16-2.60), being female (HR = 1.83, 95% CI 1.60-2.10), presenting two physical comorbidities (HR = 3.70, 95% CI 2.33-5.88), depression (HR = 1.20, 95% CI 1.04-1.39), and substance abuse (HR = 1.36, 95% CI 1.14-2.62). Antipsychotic treatment was a protective factor (HR = .75, 95% CI .65-.86).
Chen et al. (2021)	Taiwan	Cohorts	*N* = 10,422,350 people (170,322 with S)	To estimate the effect of age on SMR, the risk of physical and psychiatric comorbidity, and sudden cardiac death in patients with S.	Patients with S had a higher risk of MSD than the general population. Factors associated with increased mortality were chronic liver disease, sleep disorders, dementia, organic mental disorders, and ischemic heart disease.
Hauck et al. (2020)	Canada	Historical cohorts	*N* = 108,610 patients ≥ 20 y/o AMI (1,145 with S)	To compare mortality and cardiac interventions in patients with AMI with and without S.	Patients with S had higher mortality, with HR=1.55 (95% CI 1.37-1.77) when adjusting for age, sex, income, rurality, geographic region, location, and comorbidity. The impact of revascularization on mortality was similar between those with and without S.
Korpela et al. (2020)	Finland	Cohorts	*N* = 10,933 children followed up to age 16 (227 with S)	To compare somatic diseases in patients with and without S.	Patients with S are more likely to have the following than controls: diseases of the blood and hematopoietic organs (7.9% in S *vs*. 4.0% in non-psychotic controls; HR = 2.00; 95% CI 1.25-3.22) and endocrine, nutritional, and metabolic diseases (22.5 *vs*. 12.7%; HR = 1.81; 95% CI 1.36-2.399.

Note: y/o = years old; S = Schizophrenia; VA = veterans; COPD = Chronic Obstructive Pulmonary Disease; USA = United States; HR = Hazard Ratio; AMI = Acute Myocardial Infarction; HF = Heart Failure; OR = Odds Ratio; MSC = Sudden Cardiac Death; PAF = population attributable fraction; BD = Bipolar Disorder; SMR = Standardized Mortality Rate; SMI = Severe Mental Disorder; ICU = Intensive Care Unit; HBV = Hepatitis B Virus; HCV = Hepatitis C Virus; HIV = Human Immunodeficiency Virus.

Schizophrenia was associated with a reduced likelihood of optimal diabetes care, and an increased likelihood of emergency room visits and hospitalization.

Oncologic diseases

According to research conducted by Lin et al. (2013) in Taiwan, individuals with schizophrenia, particularly women, have a greater likelihood of developing various types of cancer. This study, which included 71,317 patients, suggested that the risk of cancer decreased with longer periods of schizophrenia and earlier diagnosis before the age of 50. The authors highlighted the incidence rates of colon, breast, cervix, and uterus cancers, which increased if schizophrenia was diagnosed after age 50. Nevertheless, Kisely et al., (2016) found lower cancer incidence rates in schizophrenia patients in Australia, although mortality increased across all psychiatric patients.

In another study with US veterans, Bradford et al. (2016) found factors associated with increased risk of death: being older, Black, smoking at the time of cancer diagnosis, and substance abuse. In regard to lung cancer, survival was significantly lower in patients with schizophrenia. Homeless shelter utilization was associated with a lower risk of death.

Concerning breast cancer, in Denmark, Dalton et al. (2018) found lower survival rates in patients with schizophrenia, since patients are less likely to be assigned to treatment.

As for cervical cancer, diagnostic procedures in Canada (Martens et al., 2009) have found that women with schizophrenia are less likely to have Pap smears to detect this type of cancer.

In regard to access to palliative care and high-intensity care at the end of life, a French national study (Fond et al., 2019) found that patients with schizophrenia were more likely to receive palliative care, less likely to receive curative care (chemotherapy and surgery), more likely to die younger, have a shorter lapse of time between cancer diagnosis and death, and more likely to develop chest cancers and comorbidities.

Chronic infections

Interestingly, in Denmark (Nielsen et al., 2016), it was found that people with hospital contact with an infection are more likely to develop schizophrenia than those without such an infection, and vice versa. Another Danish study (Pankiewicz-Dulacz et al., 2019) found that risk factors associated with severe infections in patients with schizophrenia are being young, female, having a medical comorbidity, and substance abuse. Moreover, a history of pre-diagnosis antipsychotic treatment was negatively associated with infections.

In Sweden, Bauer-Staeb et al. (2017) conducted a study to estimate the prevalence of blood-borne viruses (such as HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) in patients with SMI. Prevalence was higher in those with schizophrenia with HIV-.21%, HBV-.53%, and HCV-5.62%, with substance abuse contributing to this increased risk.

Information on the results of medical treatment and hospital access is provided in the following two sections.

Access to and Quality of Medical Treatment

Studies suggest that physical diseases in patients with schizophrenia are underdiagnosed and undertreated (Laursen et al., 2011). These patients are less likely to have required hospitalization in the year before death (Copeland et al., 2006). There were lower rates of diagnosis of cardiovascular disease, together with higher mortality rates (Brink et al., 2019; Correll et al., 2017; Heiberg et al., 2019) and utilization of tertiary medical resources. However, a study conducted in Israel by Gur et al. (2018) of 1,389 patients with schizophrenia, with follow-up for eight years, found that tertiary health care utilization was greater among patients with schizophrenia than among the general population.

A study conducted by Oud et al. (2010) in the Netherlands found that patients with psychotic disorders tended to have more frequent contact with their general practitioners (GPs), family doctors, including home visits, and telephone consultations. Additionally, they had a higher number of consultations overall. Patients aged 16 to 65 with psychosis and DM2, cardiovascular disease or COPD were assigned the same GP as other patients. Psychotic patients over the age of 65 had more frequent delirium. However, once these patients had been diagnosed, they were checked less frequently.

A study conducted in Australia (Spilsbury et al., 2018) showed there were more emergencies in a subgroup of patients with schizophrenia who died of cancer, asphyxiation, or intentional self-injury. Hospital admissions among those with schizophrenia were half those of patients without schizophrenia. However, these admissions increased by 50% when patients were treated in specialized palliative care, although patients with schizophrenia has less access to this type of care.

Hospital admissions

A study of medical-surgical discharges in the United States (Daumit et al., 2006) found that during their hospital stay, patients with schizophrenia have more complications than those admitted for the same reason without schizophrenia (such as more infections, respiratory insufficiency, deep vein thrombosis, and postoperative sepsis). These complications increase as these patients are at least twice as likely to be admitted to an intensive care unit (ICU) and to die

(Daumit et al., 2006). Similarly, hospital mortality in the ICU was 10% higher in schizophrenic patients in Taiwan, with an increased risk of acute organic dysfunction (Shen et al., 2011).

Likewise, average length of stay is higher in patients with schizophrenia. An increase of at least ten days and a minimum of $20,000 in 2001 (Daumit et al., 2006) has been estimated, together with a 70% greater likelihood of remaining above the 75 percentile (Bailey et al., 2018). Indeed, a hospital in Greece (Douzenis et al., 2012) discovered that there is a direct correlation between the length of stay of a patient and the severity of their comorbidities, the latter being the most significant factor in prolonging their stay.

DISCUSSION AND CONCLUSION

The main aim of this systematic review was to investigate the physical comorbidity of patients diagnosed with schizophrenia and the healthcare they received. The ultimate aim was to determine whether healthcare improvements in recent decades for the general population have positively impacted individuals diagnosed with schizophrenia.

The Impact of Physical Comorbidities on the Mortality of Patients with Schizophrenia

A crucial factor that could account for the increase in mortality in patients with schizophrenia is the extra medical care they receive compared to the general population (Moher et al., 2009). Patients with schizophrenia tend to receive palliative rather than curative treatment (Martens et al., 2009). Moreover, these patients are admitted for longer periods (placing them at a greater risk of infection) (Bauer-Staeb et al., 2017; Nielsen et al., 2016; Tokuda et al., 2008), yet have less access to early diagnosis (Brink et al., 2019; Heiberg et al., 2019; Laursen et al., 2014). We can therefore assume there is a lack of prevention and early intervention in these SMI patients globally that has persisted over time.

To improve the life expectancy of patients with schizophrenia, it is essential to create effective prevention plans to reduce the occurrence of physical illnesses in this vulnerable group, beginning with GPs. This task requires the involvement of both psychiatry and other medical specialties, with proper training, resources, and protocols in place, and strategies such as shared decision-making to ensure adherence to healthcare and medical protocols (Guadalajara et al., 2022).

Although the psychiatric care of patients with schizophrenia appears to have improved overall, as borne out by a 40% decrease in the number of suicides in this population (Tanskanen et al., 2018) between 1984 and 2014, the number of deaths due to physical causes such as cardiovascular disease and cancer has risen (Laursen et al., 2019; Nordentoft et al., 2021; Tanskanen et al., 2018).

Studies have shown that deinstitutionalization and liaison psychiatry have not significantly impacted mortality rates in patients with schizophrenia (D'Avanzo et al., 2003; Tokuda et al., 2008). To provide comprehensive care for these patients, it is essential to involve specialists from other areas of healthcare, particularly other physicians specializing in the comorbid illnesses detected.

Studies suggest that although the data are a matter for concern, individuals with schizophrenia are experiencing an improvement in longevity at a similar rate to the general population. However, a disparity remains as this population still has a life expectancy similar to that of the general population in 1988 (Laursen et al., 2019). One approach to reducing the metabolic impact of certain second-generation antipsychotics is to increase physical activity, which has shown promising results in various interventions (Gyllensten et al., 2020). Utilizing technology, such as mobile applications (mHealth apps), to improve lifestyle habits is an innovative, effective method worth exploring (Torous et al., 2017).

Physical Comorbidities with a Diagnosis of Schizophrenia

In regard to the principal physical comorbidities associated with this SMI diagnosis, our findings reveal a high prevalence of cardiovascular, respiratory and oncological diseases, significantly impacting the life expectancy of people with schizophrenia on every continent except Africa. The latest research indicates a rise in other illnesses (Laursen et al., 2014; Nordentoft et al., 2021).

Due to the characteristics of this psychiatric disorder, patients with schizophrenia are at a higher risk of contracting metabolic diseases, such as DM2, metabolic syndrome or cardiovascular diseases, which may be related to antipsychotic treatment, together with genetic and environmental factors (Bouza et al., 2010a; Foley et al., 2016; Korpela et al., 2020; Räsänen et al., 2003; Razzano et al., 2015; Tokuda et al., 2008). However indirectly, it has been found that these patients appear to use addictive substances associated with some of the physical comorbidities detected (such as cancer and SCD (Bradford et al., 2016; Chen et al., 2021; Kugathasan et al., 2019), the most harmful of which appears to be smoking nicotine or other substances.

A number of risk factors could therefore explain this increased risk: the tendency to lead a sedentary life (Vancampfort et al., 2017), treatment with atypical antipsychotics (Bernardo et al., 2021), the use of addictive substances (Bauer-Staeb et al., 2017; Kugathasan et al., 2019; Pankiewicz-Dulacz et al., 2019), difficulty understanding the disease itself (Oud et al., 2010), the absence of social support to access timely medical care, and the diagnosis, treatment or prevention of diseases (Laursen et al., 2011; 2014; Moher et al., 2009). Smart Screening could contribute to the early detection of physical comorbidities in patients and families if periodically provid-

ed in healthcare settings, as seen in initiatives in Mexico and Spain (Martínez-Nicolás et al., 2023a; 2023b).

The use of addictive substances (such as alcohol and tobacco), together with other unhealthy habits (such as a sedentary lifestyle and poor eating habits), could account for the increase in the incidence of these diseases (Correll, 2022). Tobacco use in patients with schizophrenia is estimated at between 49% and 80% (Hughes, 1993; Koskinen et al., 2009; Lasser et al., 2000). Conversely, alcohol abuse is estimated at around 20% (Contreras-Shannon et al., 2013), and a high BMI has been found in the profile of patients with schizophrenia and DM2. The development of atypical antipsychotics has enhanced the well-being of patients by reducing extra-pyramidal side effects. However, it has also led to an increase in metabolic-type side effects such as increased BMI and insulin resistance. Some antipsychotics have been found to elevate blood glucose levels and impair glucose tolerance, without involving intermediate mechanisms such as BMI (Stahl et al., 2009; Porras-Segovia et al., 2017). These effects could be attributed to the antagonism of MR cholinergic receptors, which could result in beta cell dysfunction (Poirier et al., 2002).

In addition, we discovered that patients with schizophrenia were receiving inadequate health care in comparison with the general population.

Healthcare utilization of Patients with Schizophrenia and Physical Comorbidities

The attitude of clinical professionals may be affected by the stigma of mental illness, such as patients' inability to use appropriate healthcare pathways, which in turn prevents them from adequately addressing their health issues (Bitter et al., 2017). Social stigma (also present in physicians), healthcare availability (community-based psychosocial interventions), and economic policies are required to ensure that patients with SMI benefit from the scientific advances and lifestyle changes that have increased the longevity of the general population (Lee et al., 2018).

Other factors related to services and providers that may hinder the treatment of medical pathology include financial barriers, and lack of time, poor integration into services, or a shortage of proper screening measures. For instance, although psychiatrists are usually the main healthcare providers for patients with schizophrenia, they are not sufficiently trained to detect or treat physical diseases (Räsänen et al., 2003). Likewise, the detection of health issues related to lifestyle factors, while easily measurable, is often overlooked in healthcare screenings. Furthermore, reference tests for critical physical parameters are not administered with the required frequency, and individuals with SMI face an array of challenges, including modifiable lifestyle factors, in addition to other medical factors (such as the side effects of psychotropic medications, and inadequate access to quality healthcare (DE Hert et al., 2011).

Limitations

This study has certain limitations, including the absence of quality verification for the research selected and the heterogeneity of the articles reviewed, although the process has been led by psychiatrists. The methodological decisions regarding the selection of papers with specific methodological designs also limited the quantitative analysis of the data provided, which is why a meta-analysis was ruled out. It is therefore not feasible to perform a quantitative synthesis of the results and generalize them. Furthermore, there were no significant findings with regard to specific variables related to genetics, moderate or severe mental health issues, or even environmental factors. This highlights the need for further analysis of comorbidities that could be limiting the healthcare access and life expectancy of this population group.

Strengths

Nonetheless, the study has covered a broad spectrum, with the methodological rigor corresponding to the most recent discoveries. Despite these limitations, we were able to achieve our main aim of exploring key research on physical comorbidities in patients diagnosed with schizophrenia to determine their morbidity, mortality, and healthcare, in addition to presenting our findings in a clear, concise manner. Future studies could replicate the strategy by incorporating quantitative and meta-analytic approaches. They could also investigate psychosocial variables together with other specific variables to determine how healthcare actions could benefit this vulnerable population group and their families.

Conclusion

Patients with schizophrenia have a higher mortality rate than the general population due to cardiovascular, oncological, respiratory, diabetes, and infectious diseases, all of which are underdiagnosed and undertreated. Uneven medical care for these patients appears to be widespread across time and space. To minimize the effects of physical illness on this group of patients, it is essential to implement effective prevention and intervention strategies and programs. It is also important to provide training for clinicians across all levels of care, from primary to tertiary. Enhancing patient survival rates and improving their quality of life requires examining the correlation between psychosocial and socio-economic factors, substance addiction, antipsychotic drug use, healthcare access, and lifestyle choices in future research.

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Conflicts of interest

None.

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