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Work Group on Physical Health of the Patient with Schizophrenia*

Consensus on physical health of patients with schizophrenia from the Spanish Societies of Psychiatry and Biological Psychiatry

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Introduction. Schizophrenia has traditionally been associated with higher rates of physical comorbidity and excess mortality.

Objective. To develop a Spanish consensus document concerning the physical health of patients with schizophrenia and the interventions required to reduce the over-morbidity and over-mortality of these patients.

Method. The process consisted of: *a)* systematic review of the literature in the Medline database up to January 2006 and manual review of the bibliographical references of the papers obtained; *b)* reviews of national and international guides by the coordinating committee and medical specialist acting as expert advisors; *c)* multidisciplinary consensus meetings, and *d)* editing of the final consensus document.

Results. Compared to the general population, patients with schizophrenia present higher rates of infection (HBV, HCV, HIV), endocrine/metabolic disorders, cardiac and respiratory diseases (over-morbidity) and higher global death risk, as well as death from natural causes —basically respiratory, cardiovascular and oncological diseases (over-mortality)—. As a guide, therefore, this document proposes a series of interventions to be performed by psychiatrists to reduce the current rates.

Conclusions. Given the over-morbidity and over-mortality of patients with schizophrenia, awareness of these aspects should be increased among primary healthcare providers and specialists, including psychiatrists, and physical health problems should be incorporated into psycho-educational programs, and treatment compliance and severe mental disorder treatment units.

Key words:
Schizophrenia. Physical health. Morbidity. Mortality. Intervention guides.

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Consenso sobre la salud física del paciente con esquizofrenia de las Sociedades Españolas de Psiquiatría y de Psiquiatría Biológica

Introducción. La esquizofrenia se ha asociado tradicionalmente con mayores tasas de comorbilidad física y con un exceso de mortalidad.

Objetivo. Desarrollar un documento de consenso español sobre la salud física de los pacientes con esquizofrenia y las intervenciones necesarias para disminuir la sobremorbilidad y sobremortalidad de estos pacientes.

Método. El proceso de desarrollo ha consistido en: *a)* revisión sistemática de la literatura en la base de datos Medline hasta enero de 2006 y revisión manual de las referencias bibliográficas de los artículos obtenidos; *b)* revisiones de las guías nacionales e internacionales por el comité coordinador y por los médicos especialistas expertos asesores; *c)* reuniones de consenso multidisciplinares, y *d)* redacción del manuscrito de consenso final.

Resultados. Los pacientes con esquizofrenia comparados con la población general presentan mayores tasas de infecciones (VHB, VHC, VIH), enfermedades endocrino-metabólicas, enfermedades cardíacas y respiratorias (sobremorbilidad) y un mayor riesgo de muerte tanto global como por causas naturales —enfermedades respiratorias, cardiovasculares y oncológicas fundamentalmente (sobremortalidad)—. Por tanto, en este documento se proponen a modo de guía una serie de intervenciones para realizar desde la psiquiatría con objeto de disminuir las tasas actuales.

Conclusiones. Dada la sobremorbilidad y sobremortalidad de los pacientes con esquizofrenia es necesario sensibilizar sobre estos aspectos tanto a los médicos de atención primaria como a los especialistas, incluidos los psiquiatras, e incorporar los problemas de salud física a los programas psicoeducativos, a las unidades de adherencia al tratamiento y a las de atención a los trastornos mentales graves.

Palabras clave:
Esquizofrenia. Salud física. Morbilidad. Mortalidad. Guías de intervención.

INTRODUCTION

Schizophrenia has historically been associated with greater vulnerability and rates of physical comorbidity and with excess mortality. Specifically, it has been demonstrated that 50% of schizophrenic patients have at least one comorbid physical or psychiatric disease. Among the most frequent physical diseases are cardiovascular, metabolic, endocrine, neurological, infectious diseases as well as substance abuse disorders.

Parallelly, interest has been growing about the implications that the elevated physical comorbidity have on the patients, their treatments and global outcomes. Nasrallah[1] stresses the fact that the physical comorbidity of patients with schizophrenia is frequently overlooked and is therefore undertreated. Thus, in general, these patients are at high risk of not receiving adequate health cares. It is a reality that patients with schizophrenia have less access to medical cares, use less care resources and are worse compliers of the treatments than the general population.

The care insufficiencies can be directly deduced from the fact that while mean life expectancy of the general population in the United States is 76 years (72 years for men and 80 years for women), that of patients with schizophrenia is 61 (57 years for men and 65 years for women). This is 15 years or about 20% less than that of the general population[2]. Sixty percent of this excess mortality can be attributed to somatic diseases (cardiovascular diseases, metabolic syndrome), 20% to suicide and 12% to accidental factors[3].

This situation contrasts with the improvement in the quality of life offered by the current psychopharmacological treatment to the patient with schizophrenia. Furthermore, it has an enormous repercussion on both the individual clinical level as well as on the use of health care system and society resources as a whole. Due to all the above, a systematic and methodologically adequate approach to the problem of physical morbidity in schizophrenia is essential. On the other hand, the advances produced in the knowledge of the disease, improvements in the treatment and changes produced in the care supply systems make it necessary to perform an up-dated evaluation of morbidity-mortality in schizophrenia.

The purpose of the present clinical-teaching project is to develop a consensus document on the physical health of the patients with schizophrenia and the diagnostic, preventive and therapeutic interventions that the psychiatrists should make to control the changeable risk factors that affect the physical health and life expectancy of the patients with schizophrenia in Spain.

METHODS

This consensus document was motivated and supported by the Spanish Societies of Psychiatry and Biological Psychiatry in collaboration with the Health Care Technologies Evaluation Agency of the Instituto de Salud Carlos III (Health Institute Carlos III) and the Sociedad Española de Médicos de Atención Primaria (Spanish Society of Primary Health Care Doctors) (SEMERGEN).

Development procedure

The following steps were made to develop the consensus document:

- Systematic review of the literature made by the Health Care Technologies Evaluation Agency of the Instituto de Salud Carlos III.
- Review of the national and international guidelines and recommendations on physical health and schizophrenia by the scientific committee.
- Review of the national and international guidelines on prevention, diagnosis and treatment of the different diseases identified by the medical specialists acting as expert advisors and their adaptation to the patient with schizophrenia.
- Multidisciplinary consensus meeting.
- Writing of the final consensus document.

Systematic review of the literature by the Spanish Agency of Health Care of the Instituto de Salud Carlos III

The purpose of the systematic review of the literature was to analyze the scientific tests that support the hypotheses of greater morbidity-mortality due to physical causes and greater difficulty in accessibility to health services of patients with schizophrenia compared to the general population.

A systematic review was made of the literature in the Medline electronic database until January 2006 and a manual review of the bibliographic references of the articles obtained to locate others that could meet the inclusion criteria[4]. There were no language restrictions. The search terms were selected in such a way as to allow for the greatest sensitivity and specificity possible.

The inclusion criteria of the articles were: *a)* longitudinal follow-up design of cohorts without limitations regarding follow-up period; *b)* patients with formal diagnosis of schizophrenia; *c)* comparison with general population or with patients with other mental disorders; *d)* in regards to the results, quantitative information should appear in form of incidence and/or prevalence in the case of morbidity studies, rates or risk of mortality due to general and/or natural causes or contain the necessary data to calculate them in the case of mortality studies and in the form of objective measures of access, use or results both in general or more specific services (visits, diagnostic tests, treatments) in the

case of accessibility studies to the health services. Duplicated articles or those with redundancies were ruled out. When the same patients were included in more than one article, the one providing the most information was chosen.

Articles that did not provide the abstract in Medline and those that were specifically aimed at analyzing the effects of the antipsychotic drugs or comparing antipsychotic drugs were excluded.

The quality of the scientific tests was classified following the recommendations of the Oxford Centre for Evidence-Based Medicine (CEBM)[5] and those used by Marder et al[6]. Level 1 was considered to exist when the scientific tests came from multiple randomized clinical trials. Level 2 existed when the scientific tests came from cohort studies, investigation of results or low quality controlled clinical trials. Finally, level 3 was when the tests came from case-control studies.

Review of the national and international guidelines by the scientific committee and by the specialist doctors in role as expert advisors

Parallelly to the systematic review of the literature made by the AETS, the coordinating committee and medical specialists in their role as expert advisors reviewed the national and international guidelines on prevention, diagnosis and treatment of diseases identified in the systematic review of the literature.

The guidelines reviewed by the *Scientific Committee were the Physical Health Monitoring of Patients with Schizophrenia,* de Marder et al.[6]; the *Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes of the American Diabetes Association,* the *American Psychiatric Association,* the *American Association of Clinical Endocrinologists and the North American Association for the Study of Obesity*[7], the *Medical Morbidity and Mortality in Schizophrenia: Guidelines for Psychiatrists,* by Goff et al.[8]; the *Consensus Summary on Metabolic and Lifestyle Issues and Severe Mental Illness – New Connections to Well-Being?,* by Dinan et al.[9], and the *Belgian Consensus on Metabolic Problems Associated with Atypical Antipsychotics,* by De Nayer et al.[10]

Multidisciplinary consensus meetings

There were two consensus meetings. Both were multidisciplinary and were attended by the members of the scientific committee, representatives of the Spanish Agency of Health Care Technology, medical specialists in role of expert advisors and the group of participating psychiatrists.

In the first meeting, the members of the scientific committee made a presentation on the current status of the specific physical health problem it had reviewed. After, a work group was created for each specialty, made up of the corresponding medical specialists in their role as expert advisor and a group of participating psychiatrists. In each group, the specialist acting as expert advisor initially made a review of the evidence found in the bibliographic review and then formulated evidence based recommendations. After, a discussion was held with all the group to decide what was applicable or convenient or not to be applied to the patients with schizophrenia, considering the characteristics of the patients and availability and accessibility to the services. Finally, each group presented a document with recommendations on the diagnostic, monitoring, preventive and therapeutic interventions that the psychiatrists should perform.

In the second meeting, the documents generated by each one of the groups in the first meeting were discussed and specific recommendations that should be incorporated into the final consensus document were agreed on.

Statistical analysis

Descriptive statistics was used for morbidity, using measurements of incidence, prevalence and percentage of patients, given the limited quality of the description of the results, their multiplicity and the different duration of the follow-up periods.

In regards to mortality, an overall measurement of mortality risk of the patients with schizophrenia compared to the reference population was obtained using meta-analysis techniques by means of the software program SE Stata 9 (StataCorp LP Texas USA 1984-2005). The meta-analysis was performed using a conservative model of random effects. The studies were combined considering uniformity of the outcome measurements. Grade of inconsistency between the studies was analyzed with the I^2 statistics[11]. Furthermore, meta-regression techniques were used to examine the heterogeneity of the outcomes.

RESULTS

Systematic review of the literature

Infectious diseases (hepatitis B and C, human immunodeficiency virus)

Number of studies: six. There are nine more studies that analyze these diseases in severe mental disorders without specifying the population with schizophrenia.

Quality of evidence: level 2 and 3. Limited quality that make is necessary to be very cautious when generalizing the results.

Findings: less prevalence of unspecified hepatic disease than other mental disorders[12] and the same as that of the general population[13]. Greater prevalence of hepatitis C virus antibodies than the general population[14]. Greater prevalence of HIV infection than the general population[15,16] and similar prevalence to that of other severe mental diseases[12]. Knowledge of HIV infection in patients with schizophrenia is significantly lower than that of the population without mental disorder and their concern for this disease is scarce[15,17].

The risk factors identified were use of parenteral drugs with sharing of needles and promiscuous sexual behavior without protection.

Neoplastic diseases

Number of studies: nine.

Quality of evidence: level 2 and 3. Limited quality that made it necessary to use significant caution when generalizing the results.

Findings: The results show significant differences with incidences in some superior cases (cancer in general[18], breast[19], lung and pharyngeal[18]) and in others inferior (cancer in general[20,21], cancer in general in men[22], prostate[23], skin[24]) to that of the general population. It was also not possible to analyze the existence of possible protective factors in this population with the information available.

Endocrine-metabolic diseases

Number of studies: 23.

Quality of evidence: level 2 and 3. Limited quality that made it necessary to use significant caution when generalizing the results.

Findings: when analyzing the study results, it is necessary to state that the retrospective character and heterogeneity of their information sources significantly reduce their external validity. However, the only prospective study obtained the same findings as the remaining retrospective studies.

In the case of diabetes, the studies show elevated rates of diabetes and intolerance to glucose in these patients[25-34] and an incidence and prevalence of diabetes that is two to four times greater than that of the general population[35-39]. In addition, they ratify that which is already known. On the one hand, the association between schizophrenia per se and diabetes is verified: the untreated patients have greater visceral adiposity, alterations in glucose tolerance and greater resistance to insulin than the controls is verified. On the other hand, the existence of a relationship between the antipsychotic-typical and atypical treatments and diabetes is confirmed. Regarding the latter point, based on the studies, it cannot be concluded that the risk of diabetes is greater with atypical or second generation antipsychotics than with the typical or first generation ones[26-29,36,40]. One study[35] even demonstrates greater incidence rates with the typical ones. However, it must be pointed out that these patients also have other factors that may contribute to over-representation of diabetes, such as age, non-white race, family background of diabetes, obesity, sedentary life, smoking and lack of self-cares.

Regarding the metabolic syndrome, once again the results show greater rates than those of the general population, specifically a prevalence that is two-four times greater[41-46]. This difference is related with age, gender and race. These studies conclude that it is not possible to relate a specific type of antipyschotics (typical or atypical) with the metabolic syndrome but rather that there is an inverse relationship between the metabolic syndrome and antipsychotic dosing (equivalents of chlorpromazine) and direct relationship with the number of drugs administered.

Neurological diseases

Number of studies: 20.

Quality of evidence: level 2 and 3. Limited quality that made it necessary to use significant caution when generalizing the results.

Findings: the prevalence of stroke in the population with schizophrenia is equal to that of the general population[13], although the rate of cerebrovascular disease is significantly lower in patients admitted to hospital with schizophrenia than in the patients in the Danish National Patient Registry.

The data on epilepsy are controversial. While one study[47] finds a significantly greater prevalence in patients with schizophrenia regarding other patients without mental disease, the Gelisse et al.[48] study does not find such an association. There are no differences in regards to prevalence of epilepsy among patients with schizophrenia and patients with other mental disorders[12]. There are also no differences in regards to the prevalence of headaches (migraine, chronic tension or acute tension) in patients with schizophrenia regarding normal controls[49].

In regards to motor disorders, the rate of symptoms consistent with Parkinsonism in patients with schizophrenia is elevated[50-54] and clearly superior to those described in subjects without Parkinson[50]. The prevalence of spontaneous dyskinesia in patients with schizophrenia who have not received antipsychotic treatment is elevated and superior to that of the healthy population (many authors). Finally, prevalence of minor neurological signs (alterations in the right-left discrimination, mirror movements, poor coordination and abnormal gait) in patients with schizophrenia not treated with antipsychotics is elevated[55-58] and significantly greater than that of the normal controls[57,58].

Heart diseases

Number of studies: 10.

Quality of evidence: level 2 and 3. Limited quality that made it necessary to use significant caution when generalizing the results.

Findings: the results of the studies show that the patients with schizophrenia compared with the general population have a higher rate of heart failure[50,37], arrythmias[37] and syncope[37]. In regards to the incidence of cardiovascular morbidity, the studies show a greater incidence of ventricular arrhythmias and heart failure[37]. Patients treated with typical antipsychotics have a five times greater risk of acute myocardial infarction than control subjects after adjusting for age and gender[36]. Furthermore, an inverse association was observed between cardiovascular risk and intensity of the antipsychotic drug use.

Regarding the rates of hospital treatment, patients with schizophrenia compared with the population of the Danish National Registry of Patients had an increase in the rate of hospital admission for the treatment of arterial hypotension, asystole, cardiomyopathy and pulmonary edema and a lower rate of hospital admission for the treatment of acute myocardial infarction, heart disease due to arterial hypertension, arterial hypertension, atherosclerosis, atrial fibrillation, complete A-V block and angina[60].

In regards to the prevalence of symptoms of self-reported angina and/or acute myocardial infarction, the prevalence of angina symptoms is significantly greater in patients with schizophrenia compared with the general population after adjusting for relevant clinical factors[61]. However, another study[13] did not find that the self-reported heart problems (coronary disease, acute myocardial infarction, angina and others) are more frequent in patients with schizophrenia than in the controls adjusted for age, race and gender.

Finally, regarding the duration of the QT interval, the results of the three studies that analyze it disagree. While one study did not any find significant differences between the patients with schizophrenia under treatment with different antipsychotics and the healthy control subjects[62], two other studies demonstrated a significant increase of the QT interval in group of patients treated with 1st general antipsychotics, especially with certain drugs[63], and with antipsychotics in general[64].

Respiratory diseases

Number of studies: seven.

Quality of evidence: level 2 and 3. Limited quality that made it necessary to use significant caution when generalizing the results.

Findings: respiratory disease is frequent in patients with schizophrenia. They have a higher rate of respiratory symptoms and worse respiratory function[61]. Its prevalence is significantly greater to that of the general population (asthma, COPD and emphysema)[13] and to that of other serious mental disorders (COPD)[12]. When adjusted by treatment with antipsychotics, prevalence of the sleep apnea syndrome in patients with schizophrenia is equal to that of other severe mental disorders[65]. The hospitalization rate due to respiratory disease (except for emphysema and pulmonary neoplasm) in patients with schizophrenia is greater than that of the general population[60].

Tobacco is related in practically all the studies with the presence of respiratory disease. In the case of sleep apnea syndrome, antipsychotics and obesity are also risk factors.

Mortality

Systematic reviews /previous meta-analyses

Number of studies: three.

Findings: standardized mortality rates (SMR) due to natural causes in schizophrenia of 1.34 (95% CI: 1.31-1.37)[66], 1.37 (95% CI: 1.34-1.41)67 and 2.3 (95% CI: 1.8-2.9)[68]. Excess mortality in patients with schizophrenia due to natural causes is due to greater presence of respiratory, digestive, genitourinary, cardiovascular diseases[66,67], and to infectious, mental and endocrine ones[67].

Overall mortality (due to any cause)

Number of studies: 32. There is greater heterogeneity in the literature due to the differences in the design and characteristics of the primary studies. Most of the studies are retrospective analyses of hospital registries or of other databases of the health services from 17 countries (although more than half come from five countries) that have large differences in regards to date when the obtaining the data was begun (from 1934 to 1995), to the follow-up period (from <5 year to >30 years) and to volume of population analyzed (from 61 to 58761 subjects).

Findings: the analysis of the 27 studies[4,36,69-93] which, with 134,485 subjects, supplied data that could be combined with meta-analysis techniques, indicates that patients with schizophrenia have a risk of significantly greater risk of death than that of the general population (fig. 1).

Mortality risk compared to the general population is greater in men (SMR: 2.57; 95 % CI: 1.88, 3.51) compared to women (SMR: 2.38; 95% CI: 1.86, 3.04), in non-institutionalized patients (SMR: 2.53; 95% CI: 2.16, 2.95) compared to institutionalized ones (SMR: 2.23; 95% CI: 1.82, 2.72), in Asia (SMR: 2.52; 95% CI: 2.02, 3.13) and Europe (SMR: 2.45;

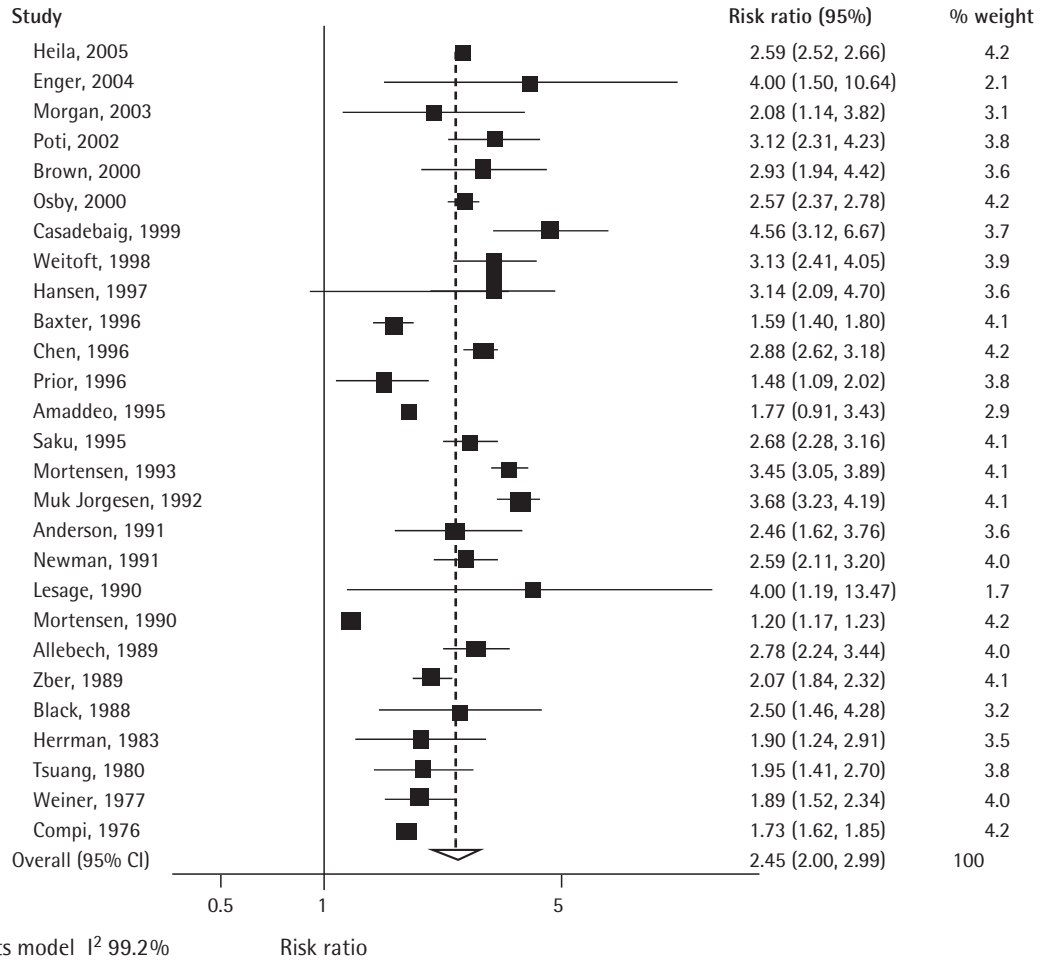

Figure 1 *Risk of death due to any cause of the patients with schizophrenia compared with the general population.*

95% CI: 1.91, 3.16) compared to North America (SMR: 1.23; 95% CI: 1.85, 2.70).

Mortality due to natural causes

Number of studies: 24 of the studies found on mortality studied it due to natural causes[4,36,71-75,77-79,81,83-90,92-96]. There is great heterogeneity in the literature due to the differences in the design and characteristics of the primary studies. Most of the studies are retrospective analyses of hospital registry or other data bases of health care services from 11 countries (although 70% come from five countries) and have large differences in regards to date of onset of obtaining the data (from 1934 to 1995), to the follow-up period (from <5 year to >30 years.)

Findings: The analysis of the 16 studies[4,36,71-73,75,77,79,81,83,85,86,88-90,93] that could be combined and analyzed with meta-analysis techniques, that grouped 109,793 patients, indicates that the patients with schizophrenia have a significantly greater risk of death from natural causes, specifically 82% greater, than the general population (fig. 2). Deaths from natural causes account for 76% of the overall deaths of the patients with schizophrenia and account for 65% of excess of mortality of these patients compared to the general population. By diseases, respiratory, cardiovascular and neoplasms are the physical diseases that contribute most significantly to the excess of mortality from natural causes in the patients with schizophrenia. Specifically, respiratory diseases are responsible for 42.4% of the excess mortality, cardiovascular 38%, neoplasms 18.5%, digestive 3.2%, urogenital 1.4% and endocrine ones 0.6% [4,36,71-75,77-79,81,83,85,86,89,90,93,97].

By gender, men had a 61% greater risk of death by natural causes than the general population while in women this risk was 86% greater than in the general population. In regard to the specific causes, men have significantly lower rates than those of the general population in regards to mortality due to cancer and significantly greater rates in regards to mortality from cardiovascular, respiratory, digestive, endocrine and urogenital diseases[4,72-73,77-79,81,83,86,90,96, 98,99].

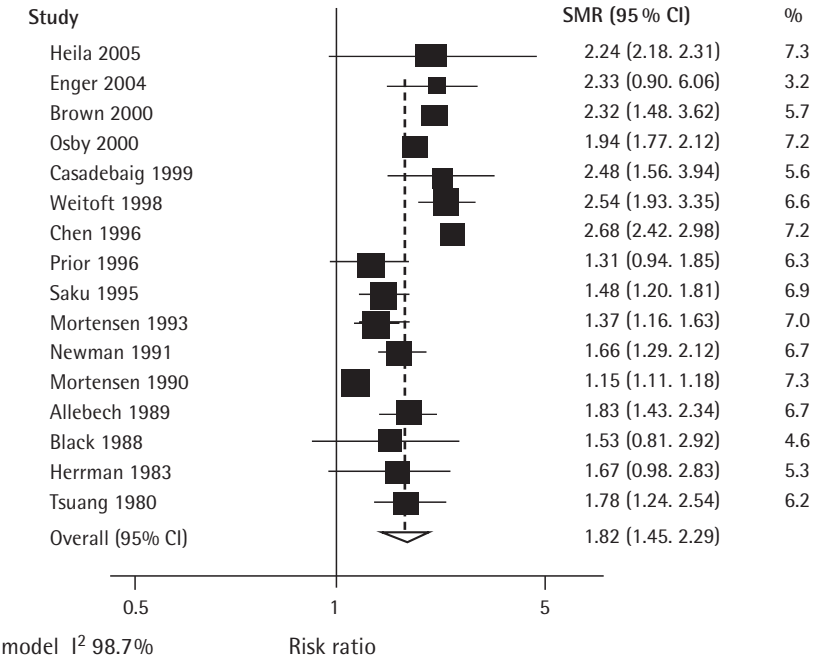

Figure 2 *Risks of death due to natural causes of patients with schizophrenia compared with the general population.*

Women had significantly higher rates in regards to mortality due to cancer, cardiovascular disease in general and coronary disease specifically, respiratory, digestive and endocrine disease[4,72,73,77-79,81,83,86,90,96,98,99] (table 1).

The excess risk of mortality due to natural causes may have increased in recent years. Studies whose inclusion date are after 1980 have a SMR of 2.56 (95% CI: 2.30, 2.83) compared to an SMR of 1.39 (95% CI 1.07, 1.81) for the studies whose inclusion date was before or equal to 19 1980.

Table 1 **Causes of natural mortality by gender. Specific diseases**

Disease	Males SMR (95% CI)	Women SMR (95% CI)
Cancer	0.88 (0.79, 0.98)	1.17 (1.05, 1.29)
Cardiovascular	1.50 (1.01, 2.21)	1.76 (1.19, 2.62)
Coronary disease	1.67 (0.73, 3.78)	3.19 (1.18, 8.66)
Respiratory	2.44 (1.94, 3.06)	2.55 (2.14, 3.04)
Digestive	2.11 (1.64, 2.70)	1.67 (1.3, 2.14)
Nervous System	2.15 (0.80, 5.7)	0.98 (0.31, 3.12)
Cerebrovascular disease	0.99 (071, 1.36)	1.19 (0.70, 2.00)
Endocrine	2.38 (1.13, 5.0)	2.16 (1.02, 4.6)
Urogenital	1.84 (1.34, 2.53)	1.36 (0.96, 1.92)

SMR: standardized mortality rate; CI: confidence interval.

Accessibility to health care services

Number of studies: 14.

Findings: the studies have important methodological differences in regards to setting and health care models, case definition, sample sizes or concept of the health care services that are analyzed in each one of them.

In general, the results have important limitations in regards to access to prevention and specialized treatment services. Specifically, it was found that there was less use of certain prevention measures and less knowledge about some diseases (worse dental hygiene and few dental monitoring visits[100,101], lower likelihood of coming to cardiovascular risk monitoring[102], higher proportion of smokers and higher levels of tobacco consumption[103], and lower education and knowledge about diabetes[103,104]), lower likelihood of early diagnostic tests (pelvic and vaginal cytology examination at 3 years and mammography at 2 years[105], bone density tests[106]), lower rates of detection of COPD, hypertension or diabetes[107], lower likelihood of certain treatments (hormone replacement therapy[105], osteoporosis treatment[106], revascularization, catheterization, beta blockers and angiotensin converting enzyme inhibitors (ACEIs) after acute myocardial infarction[108,110]), subject perception of more barriers to access health care services[100] and greater health care cost[111].

Other studies, on the contrary, report greater frequency of visits to primary health care[102] or to the general practitioner[100], greater use of certain preventive measurements

Table 2 Monitoring protocol of the physical health in the patient with schizophrenia in outpatient treatment

Parameters to monitor	Baseline	3 months	6 months	12 months	18 months	24 months	Observations
Personal and family backgrounds	X						
Physical examination	X						
Toxic habits	X						Assessment of dishabituation and follow-up of the change phases If diagnosis of abuse /dependence: urine control
Sexual function and sexual risk behaviors	X		X	X	X	X	If sexual behaviors of risk, repeat serologies
ECG	X						Follow-up if cardiovascular risk factors
Blood pressure and heart rate	X		X	X	X	X	
Weight, height (IMC = kg/m^2) and abdominal circumference	X		X	X	X	X	
Hematimetry	X						
Blood biochemistry (complete lipid profile, glycemia, creatinine, hepatic function)	X			X		X	Except for if: > 125 mg/dl glucose repeat in the next following visit Repeat at 10 weeks and 6 months after change of antipsychotic treatment Repeat if weight increase of >5 %
Serology (HBV, HCV, HIV, VDRL, papillomavirus)	X						Repeat if risk practices
Hormone profile (TSH, prolactin)	X			X		X	If symptoms of galactorrhea, repeat measurement of PRL
Assessment of extrapyramidal effects and tardive dyskinesia	X		X	X	X	X	Every 3 months if treatment is with typical antipsychotics
Review of antipsychotic treatment	X	X	X	X	X	X	

and early diagnostic measures (greater likelihood of measuring blood pressure and of flu vaccination[100]) and higher number of visits to the dentist due to dental problems[101].

Monitoring and intervention algorithms on physical health care problems of patients with schizophrenia

In the following, the recommendations made by the Medical Specialists Board in role as Expert Advisors and the final agreements reached by the participating psychiatrists on the diagnostic, preventive and therapeutic interventions that the psychiatrists should consider regarding the physical health of their patients with schizophrenia are synthesized. Table 2 shows the agreed on protocol with monitoring of physical health in the patient with schizophrenia in outpatient treatment.

Infectious diseases (hepatitis B and C, human immunodeficiency virus)

Diagnostic measures: when the schizophrenic disorder is diagnosed, serology against HBV (HbsAG and anti-HBs and anti-HBc antibodies), HC (anti-H antibodies) and against HIV (anti-HIV antibodies) should be performed in all the patients or at least in those who have risk behaviors. A syphilis test (VDRL) is also indicated in the patients who have risk behaviors. If the patient has risk behaviors, the tests should be repeated.

In the case of the hospitalized patient, urine sediment analysis should be performed on admission.

Prevention measures: if there are negative results for one or more infections:

- Education in prevention: prevention of sexual transmission (safe sex), of the parenteral (avoid sharing syringes, intervention in work accidents with vaccination in case of hepatitis B or antiretroviral drugs) and maternal-fetal.
- Follow-up of risk factors (sexual behavior: promiscuity, sexual commerce and unprotected sex; use of parenteral drugs; sharing of needles).
- If hepatitis B is negative (negative AntiHBs): recommend vaccination

Therapeutic measures: if any of the infections are positive, refer patient to the specialist. Furthermore, avoid hepatotoxic drugs, recommend abstinence from alcohol and take possible interactions with antiretroviral drugs into account.

Neoplastic diseases

Diagnostic measures: include the following data in all the clinical histories: oncological family backgrounds, sexual and eating habits, sedentary life, body mass index, prolactin levels and physical examinations.

Prevention measures: stress and reinforce follow-up of the recommendations for the general population European Code against Cancer (http://www.todocancer.com) (table 3).

Treatment measures: keep possible drug interactions in mind. In the case of lung, breast or ovarian cancer, chose antipsychotics that do not produce hyperprolactinemia. In the case of color and cervix cancer, avoid antipsychotics that lead to weight gain.

Table 3 **European Code against Cancer**

1. Do not smoke; if you smoke, quit as soon as possible. If you cannot quit, do not smoke in presence of non-smokers
2. Avoid obesity
3. Perform moderate physical activity daily
4. Increase intake of fruits and vegetables: eat at least five portions per day. Limit intake of foods with animal fats
5. Moderate alcohol intake (men a maximum of 2 standard drink measurements per day and women maximum of 1 SDM per day)
6. Avoid excessive exposure to sun, especially children and adolescents
7. Prevent exposure to substances considered cancerigens
8. Follow the public health programs to prevent or increase possibility of curing already declared cancer:
   - Women: after 25 years of age, the woman should undergo early detection tests of uterine neck cancer and after 50 years, early detection tests of breast cancer.
   - Men: early detection of prostate cancer is not currently indicated
   - Woman and men: vaccination against hepatitis B virus and after 50 years, you should under early detection test of colon cancer. currently, early detect of lung cancer or melanoma is not indicated.

Approved by the European Union (last review, June 17, 2003).

Endocrine-metabolic and cardiovascular diseases

Diagnostic measures: when the schizophrenic disorder is diagnosed, perform anthropometric and vital signs (weight, height, BMI, abdominal circumference, blood pressure and heart rate) measurements, laboratory analysis with fasting of at least 8 hours (hematimetry, complete lipid profile cholesterol, triglycerides, HDL and LDL cholesterol, baseline creatinine, glycemia) and ECG in all the patients. If they are normal, repeat yearly, except anthropometry and vital signs which should be done every 6 months.

After change of medication or weight increase repeat the measurements.

Prevention measures: stress and reinforce healthy life style (adequate dietary composition, exercise).

Treatment measures: assess the convenience of the antipsychotic drug chosen for the current somatic condition. If there is no control with the preventive measures, refer patient to the medical practitioner or corresponding specialist.

Neurological diseases (extrapyramidal symptoms and tardive dyskinesia)

Diagnostic measures: in all the patients, clinical evaluation of the extrapyramidal symptoms and tardive dyskinesia with or without help of psychometric evaluation instruments (i.e., Simpson-Angus Akathisia Scale and Abnormal Involuntary Movement Scale) every 3 months if the antipsychotic treatment is first generation and every 6 months is it is 2nd generation.

Prevention measures: in the subjects with more risk (young males, first episodes, elderly women, previous neurological lesion, etc.) choose atypical antipsychotic drugs with low profile of these adverse effects.

Treatment measures: add corrective drugs (benzodiazepines in the case of akathisia, anticholinergics in the case of Parkinsonism) and consider changing the antipsychotic to an atypical one with low profile of these adverse effects.

Respiratory diseases

Diagnostic measures: include auscultation in the physical examination and, if indicated, request chest X-ray, especially if the patient is hospitalized. When there is suspicion of sleep apnea syndrome, make a specific clinical history and evaluation of the grade of daytime sleepiness by questionnaire (i.e., The Epworth Sleepiness Scale).

Prevention measures: in all the patients, recommend decreasing/abandoning smoking. In patients with COPD, recommend flu vaccine.

Treatment measures: when there is respiratory decompensation, adjust the sedative psychodrug and benzodiazepines.

Other diseases

Cataracts: ask the patients about changes in vision, especially blurry vision and distance vision. If the patient is over 40 years, recommend yearly check-up to the ophthalmologist and if the patient is under 40 years, recommend visits every two years to the ophthalmologist. If necessary, evaluate possibility of change to another antipsychotic drug.

Bucodental: recommend yearly check-ups by the odontologist. Stress and reinforce hygienic-dental habits. Evaluate changes to an antipsychotic that does not produce or produce less mouth dryness.

Agranulocytosis: if the patient is treated with clozapine, follow specific protocol.

Myocarditis: if the patient is treated with clozapine, pay attention to the positive symptoms of myocarditis (fatigue, dyspnea, fever, palpitations) or findings in the ECG as ST abnormalities and T wave inversion. If myocarditis is suspected, ask for leukocyte count and serum levels of troponin. If myocarditis is diagnosed, suspend clozapine and referral to primary health care doctor.

Consensus decalogue

1. The Spanish Societies of Psychiatry and Biological Psychiatry consider that the physical health condition of the patients with schizophrenia may become very important due to genetic factors, factors inherent to the disease itself, to the life style of these patients and treatment with antipsychotic drugs.
2. The European Strategy of mental Health and World Health Organization encourages improving the physical health condition of the patients with mental disorders by the use of health promotion and preventive measures.
3. Patients with schizophrenia compared with the general population have greater rates of infections (HBV, HCV, HIV), endocrine-metabolic diseases, heart and respiratory diseases (over-morbidity) and greater risk of both overall death and death due to natural causes —fundamentally respiratory, cardiovascular and oncology diseases (overmortality).
4. The characteristics of the patients with schizophrenia and need for treatment with antipsychotic drugs that may negatively influence the physical health of the patients make it necessary for the psychiatrists to take these patients' physical condition into greater consideration.
5. The physical health condition of the patients with schizophrenia may and should improve from psychiatry with a greater grade of intervention on the modifiable health factors and with the continuing education of the clinical psychiatrists in this regards.
6. The international and national recommendations made must be adapted to the Spanish context of mental health care.
7. To achieve the general and specific objectives of physical health of the patients with schizophrenia, actions aimed at prevention, diagnosis and monitoring and management of the risk factors and behaviors and of the different concomitant diseases are recommended.
8. In order to improve the physical health condition of patients with schizophrenia, it is essential to have a complete clinical history with integrated therapeutic alternatives that especially incorporate attention to the physical health care aspects of the patients.
9. It is necessary to development and apply specific psychoeducational programs that incorporate the more commonly affected physical health features of these patients.
10. Finally, the Spanish Societies of Psychiatry and Biological Psychiatry consider that it is necessary to improve access of patients with schizophrenia to health care and/or health resources and to improve the grade of coordination between specialized and primary care for the treatment of the physical health problems of these patients.

CONCLUSIONS

- Compared with the general population and other mental disorders, the level of physical health of patients with schizophrenia is worse.
- Patients with schizophrenia compared with the general population have infectious, endocrine-metabolic, cardiac and respiratory over-morbidity and excess of mortality that is both overall and by natural causes (fundamentally due to respiratory, cardiovascular and oncological diseases).
- Both primary health care doctors and the specialists, including the psychiatrists, must be sensitized about these aspects.
- In order to achieve a more adequate management of the physical health care problems of these patients, physical health care problems should be incorporated into psychoeducation programs, into the treatment adherence units and into the care programs for severe mental disorders.

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