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Delphi consensus on the physical health of patients with schizophrenia: evaluation of the recommendations of the spanish societies of psychiatry and biological psychiatry by a panel of experts

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Introduction. Available data from scientific literature show that patients with schizophrenia have higher rates of physical comorbidity and excess mortality due to other physical pathologies. The growing interest to investigate and improve the health of these patients has led a group of Spanish experts to publish in 2008 a "Consensus on physical health of patients with schizophrenia from the Spanish Societies of Psychiatry and Biological Psychiatry" (2008 Consensus). These recommendations imply a significant change to the present model of medical attention.

Objective. To gauge the level of agreement of a group of expert psychiatrists on the clinical criteria and recommendations collected from the scientific literature and the 2008 Consensus on the physical health of patients with schizophrenia.

Method. The process involved four phases: 1) Scientific Committee established to manage the study and to define the 66-item questionnaire; 2) Panel of 15 experts in psychiatry is established; 3) Submission of questionnaire to the Expert Panel in two consecutive rounds, with an intermediate processing and sharing of results; 4) Evaluation of results, discussion and conclusions between Scientific Committee and Expert Panel.

Results. All items, as set by the Scientific Committee and aligned with the recommendations published in the 2008 Consensus, achieved consensus on agreement from the Expert Panel, except 5 items, for which most of the answers were placed in the indeterminate position rate.

Conclusions. The expert criteria shown in this study indicate a global agreement with regard to clinical criteria on the physical health of patients with schizophrenia, as well as with the present recommendations to improve the health of patients having, or at risk to have, other concomitant pathologies. The need to incorporate new intervention guidelines that facilitate a better control and improvement of the physical health of patients with schizophrenia must be disseminated in the psychiatric providers' collectives.

Key words: Schizophrenia, Physical health, Morbidity, Mortality, Psychiatry, Intervention guides

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Consenso delphi sobre la salud física del paciente con esquizofrenia: valoración por un panel de expertos de las recomendaciones de las sociedades españolas de psiquiatría y de psiquiatría biológica

Introducción. Los pacientes con esquizofrenia presentan una mayor tasa de comorbilidad física y mayor incidencia de mortalidad por trastornos físicos que la población general. Producto del creciente interés por conocer y mejorar el estado de la salud física de los pacientes con esquizofrenia se publicó, en 2008, el "Consenso sobre la salud física del paciente con esquizofrenia de las Sociedades Españolas de

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Psiquiatría y Psiquiatría Biológica". Sus recomendaciones suponen un cambio sustancial del modelo asistencial actual.

Objetivo. Constatar el grado de acuerdo de un grupo de expertos españoles sobre una serie de criterios clínicos y recomendaciones sobre la salud física de los pacientes con esquizofrenia recogidas de la literatura científica y del Consenso publicado en 2008.

Método. El proyecto se desarrolló en cuatro fases: 1) constitución de un Comité Científico, responsable de la dirección del proyecto y de la formulación de los 66 ítems de encuesta; 2) constitución de un panel de 15 psiquiatras expertos; 3) encuesta en dos rondas, con procesamiento intermedio de opiniones e informe a los panelistas; y 4) análisis de resultados y discusión de conclusiones en sesión presencial del Comité Científico y el panel de expertos.

Resultados. Todos los ítems fueron consensuados por el Comité de Expertos de acuerdo con las propuestas del Comité Científico y en línea con las recomendaciones del Consenso publicado en 2008, a excepción de cinco ítems en los que no se alcanzó un nivel de acuerdo suficiente para el consenso entre los miembros del panel, debido a que la mayoría se decantó por posiciones de indeterminación.

Conclusiones. Los expertos de este estudio alcanzan un acuerdo general sobre los criterios clínicos recogidos en la literatura sobre salud física de los pacientes con esquizofrenia, así como sobre las recomendaciones para la evaluación de la salud física de estos pacientes y para los procedimientos de diagnóstico y las intervenciones clínicas destinadas a controlar los factores de riesgo asociados, propuestos por la SEP-SEPB. Es importante mantener el proceso de concienciación del colectivo de psiquiatras clínicos acerca de la necesidad de implementar las recomendaciones incorporadas en guías como las aquí propuestas, que finalmente lleven al mejor control y el mejoramiento de la salud física del paciente con esquizofrenia.

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

INTRODUCTION

Patients with schizophrenia have a higher prevalence of physical illness and a higher mortality from natural causes than the general population.[1] More than half suffer concurrently from important physical problems,[2] amongst which cardiac risk factors play a preeminent role (dyslipidemia, hypertension, diabetes, smoking), followed by a wide range of respiratory, gastrointestinal, neurological, cardiac, infectious, neoplastic, and substance abuse problems.[3, 4] Because of these factors, the standardized death rate from natural causes in the population with schizophrenia is 2.3 times greater than in the general population, whereas death rate from causes "avoidable with appropriate treatment" is almost 5 times greater in this population.[5] On average estimations indicate that the life expectancy of these patients is reduced by 15 years compared with the general population,[6] mainly as a result somatic diseases (more than 60%), compared with suicide (less than 28%), and accidents (12%).[5]

The World Psychiatric Association has drawn attention to the fact that comorbid physical illnesses in patients with schizophrenia often pass unnoticed and is therefore undertreated.[4] In addition to a lower access to medical attention for their physical health, these patients receive substandard attention and their compliance with treatment is worse than that of the general population.[7-11] Antipsychotic treatment in itself frequently adds complications that contribute to worsening of the patients' physical condition.[11, 12, 14]

In 2007, the Spanish Societies of Psychiatry (SEP) and Biological Psychiatry (SEPB), to improve these treatment deficiencies and to guarantee the rights of patients with serious mental health problems to receive adequate health care, promoted the development of a consensus statement on the physical health of patients with schizophrenia, recommending diagnostic procedures and clinical interventions designed to control the modifiable risk factors that limit their physical health and their life expectation and quality of life.[2]

The proposals made in this document represent a substantial change in the model of attention of the patient with schizophrenia in Spain, and promote a greater participation of the psychiatrist in the management of the biological repercussions of this disease. Shortly after its publication,[15] almost half of a multicentre sample of clinical psychiatrists practicing in public health centres stated that they knew of these recommendations. Nevertheless, an audit of their clinical histories demonstrated that the improvement reported in the assessment of the physical health of patients with schizophrenia after the publication of the consensus document only occurred in a symbolic fraction of the professionals (less than 15% of the total). Changes in deeply rooted habits and the introduction of new practices [2, 16] would eliminate some obstacles to the effective implementation of the guidelines and consensus in psychiatric practice. [17, 18]

With the idea of validating the criteria used and facilitating the implementation of the proposals in the SEP-SEPB 2008 Consensus[2] by the majority of psychiatrists, this study explores, in a structured way, the professional opinion of a new expert panel composed of specialists from the public health system concerning the main recommendations of this document. The purpose is to achieve the highest

possible level of agreement, by expanding the group of experts who openly support it with additional respected members of the psychiatric profession who did not participate in its preparation.

MATERIALS AND METHODS

The modified Delphi method[19, 20] collects the written opinion (individual and anonymous) of a multicentre group of experts by means of a survey carried out via email. After analyzing the results obtained by the panel in the first round of the questionnaire and informing the experts of these results, a second round considering only those items where no agreement was achieved in the first round, allows the experts to reconsider their opinions and reach agreement over divergent opinions.

The study was carried out in 4 phases: 1) preparation of the questionnaire by the scientific committee in charge of the project; 2) formation of a panel of expert psychiatrists recognized for their involvement in schizophrenia; 3) two rounds of email survey and; 4) a joint session of the scientific committee and the panel of expert psychiatrists to analyze the results and discuss the conclusions.

To prepare the questionnaire, each member of the scientific committee (the coauthors of the study, in representation of SEP and SEPB) worked on the definition of items of certain parts of the survey using the conclusions of the "Consensus on the physical health of patients with schizophrenia SEP-SEPB 2008".[2] This information was updated with a literature search,[21] carried out in 2009 using PubMed, and by a manual search of the reference lists of the articles thus obtained. To categorize the quality of the evidence in these articles and to select other possible subjects to include in the survey, the recommendation to the committee was to use the Oxford Centre for Evidence-Based Medicine (CEBM) criteria.[22]

Each item of the questionnaire was written in the form of a statement (positive or negative) that expresses a professional criterion or a concrete clinical recommendation about the physical health of patients with schizophrenia. The initial proposals of the committee were revised by an external consultant and synthesized until a joint version, satisfactory to all, was achieved. It consists of 66 items grouped into three conceptual areas: a) impact of schizophrenia on the physical health of the affected patients (11 items); b) impact of antipsychotic treatment on the physical health of the patient with schizophrenia (15 items); and c) recommendations to the psychiatrist for the improvement of the physical health of his patients with schizophrenia (39 items). In this last group, recommendations concerning infectious diseases (5 items), neoplasia (6 items), endocrine/metabolic diseases (10 items), cardiovascular problems (6 items), neurological diseases (3 items), respiratory diseases (4 items) and other physical pathologies (5 items), were included.

To quantify each item in the survey, a simple 9 point, ordinal, Likert-type scale was used (1=completely disagree, 9=fully agree), modified by linguistic modifiers into groups of 3 points as follows: 1-3="in disagreement with the statement" (lower score means greater disagreement), 4-6="neither agree nor disagree", does not have a fixed opinion on the subject (choose 4 or 6 according to whether he/she is closer to disagreement or agreement, respectively), 7-9="in agreement with the subject (higher score means greater level of agreement). After each item, there was the possibility to add free text explaining the vote.

The panel of experts in schizophrenia was chosen by the "snowball" method proposed by Goodman and Coleman,[23] starting with the network of professionals of the scientific committee. The process was completed by actively searching out Spanish) authors of original research articles in related topics found in the literature databases PubMed (Medline), Embase (Excerpta Medica) and IME (*Índice Médico Español*). The 15 psychiatrists from the state system invited by the committee (annex 2) agreed to take part in the project and completed both consecutive rounds of distribution and collection of questionnaires, in October-November 2009.

To analyze the results of the Delphi survey, the method of the appropriate use of the RAND/UCLA[24, 25] proposes using the median of the scores and the "level of agreement" of the opinions of the panel members. There is "agreement" on an item when less than one third of the experts score outside the three point region (1-3, 4-6, 7-9) that includes the median (<5 persons in this project). "Disagreement" is determined when the scores of one third or more of the panel members is in the 1-3 region, and another third is in the 7-9 region. Those items where there is neither agreement nor disagreement are considered "undetermined".

To interpret the group consensus reached, the following criteria were used: when there is "agreement" and the median is greater than 6, we can consider that the panel as a whole expressed their agreement on that item (consider the recommendation appropriate); when there is "agreement" and the median is less that 4, we can consider that the panel as a whole expressed their disagreement on that item (consider the recommendation inappropriate); those items where the score is in the 4-6 region, and those where there is disagreement or indecision are considered "doubtful" and are sumitted to the panel for reconsideration in the second round of the survey.

Between the two rounds, the panel members are informed in detail about the distribution of the answers to the first round and the anonymous comments provided by the participants. After reviewing this information, they are asked to reevaluate those items where no consensus was

reached. After the second round, the same criteria are applied to distinguish between those items where the panel could not come to an agreement. For comparison, when the average score of an item is closer to one of the extremes (closer to 1 or 9), the level of agreement with the proposal expressed in the item is considered to be higher.

RESULTS

The 15 experts completed both rounds of the survey. In the first round, consensus was reached on 46 of the 66 items analysed, according to the preestablished evaluation criteria. After informing the participants of the results, in the second round, consensus was reached on 15 more items of the 20 that were reevaluated, reaching agreement on 92.4% of the items on the survey.

Table 1 summarizes both reached and failed consensus content, according to thematic blocs. Annex 1 includes the estimation of the critical parameters on the basis of these results. In each case the median and mean scores for each group are shown, as well as the proportion of experts surveyed who have an opinion different from that of the majority (whose scores fall outside the region of three points of the median).

In 5 items (3, 5, 7, 59, and 63 of the list in Annex 1), which represent 7.6% of the total, the panel members did not reach agreement after completing both rounds of the survey. Table 2 shows the detailed replies to these items. In each case, and according to the preestablished interpretation criteria, it can be seen that the group of experts surveyed do not have a joint and definitive consensus on these items, though there is no serious disagreement of opinions between the panelists (bipolarization of the group between agreement and disagreement).

A detailed analysis of the distribution of the answers of the panelists (Table 2) reveals some relevant differences within the group opinions of the subjects where there was no consensus. As such, while on the items 1, 7, 59 and 63 the panelists expressed their agreement with the proposed criterion or clinical recommendation even though not enough for consensus, in item 5, 50% of responders were undecided (region 4-6, "neither agreee nor disagree") whereas the remaining half were bimodally distributed between both extremes (agree or disagree).

DISCUSSION

Taken globally, external evaluation by the national experts in schizophrenia who participated in the multicentre panel of this study, confirms a high level of agreement (greater than 90%) with the clinical recommendations drawn from the "Consensus on the physical health of patients with schizophrenia SEP-SEPB 2008"[2] and the update proposed by the investigators. These results support the task of literature collection, interpretation and synthesis carried out by the writers of the consensus document in 2008, and reinforce the timeliness of their recommendations, whose implementation is a timely and fully justified care strategy. It is important to emphasize that the majority of these recommendations were agreed upon in the first Delphi round, and that the average scores of the experts, in the majority of these items, fall in the range of "full agreement" expressing a clear agreement of the experts surveyed with the contents of this document.

In fact, the level of agreement of the panellists in this study is higher than that observed in other projects using similar methodology.[26, 27, 33-35] Even though the validity of this statement is disputable, as the level of agreement is specific to each study (according to the heterogeneity of the professional panel and the degree of controversy of the topic under discussion), it should be pointed out that the results of the study have been achieved with a multicentre group, with very different professional backgrounds and responsibilities.

The only 5 recommendations that were not agreed upon in the study indicate different aspects of medical assistance in schizophrenia where, rather than differences of opinion, there seems to be indecision on the part of the specialists that participated in the study. This situation may reflect the absence of hard scientific evidence on these topics, or the existence of a controversy between different sources that needs to be resolved. This would justify, at the present time, the lack of consistent recommendations on these particular topics. If this is the case, the controversial areas (not agreed upon) would represent areas where a greater investigative effort would be justified, to develop the scientific evidence needed to propose new recommendations acceptable to all the experts.

However, the technical limitations in the formulation of at least three of these items should be pointed out, which could have been the main cause for the lack of consensus. In item 3 ("Patients with schizophrenia suffer higher incidences of cancer than those without mental illness, especially breast, lung and throat"), item 5 ("There does not seem to be a greater incidence of ictus, epilepsy and cephalea in patients with schizophrenia") and item 7 ("Patients with schizophrenia, compared with the general population, have a higher rate of cardiac insufficiency, arrhythmias and syncope") the inclusion of different comorbid conditions in the same item could have predisposed the answer in the "neither agree nor disagree" region by those experts who did not weigh equally the different risks proposed. Strictly, the professional opinions expressed in the Consensus 2008 should not be subject to professional consensus, according to the perception of each specialist, but should be supported by rigorous epidemiological studies that confirm or refute these impressions.

Table 1 Content agreed on and not agreed on by the panel of experts (Annex 1 gives the definition of each item on the survey and the statistical criteria used to interpret the degree of consensus)

Section 1: EXPERT OPINION ON THE IMPACT OF SCHIZOPHRENIA ON THE PHYSICAL HEALTH OF PATIENTS WITH SCHIZOPHRENIA

CONSENSUS

It is a fact that patients with schizophrenia suffer:
a) Greater prevalence than the general population of:
- Infections of hepatitis C and HIV, with little knowledge and concern about AIDS on the part of the patient
- Metabolic disorders (diabetes, glucose intolerance and metabolic syndrome), independently of their pharmacological treatment
- Spontaneous dyskinesia, even without antipsychotic treatment
- Respiratory disorders related to cigarette smoking (asthma, COPD and emphysema)
- Cardiovascular disorders

b) Excessive overall mortality from natural causes (respiratory, digestive, genitourinary, cardiovascular, infectious, mental and endocrine diseases)

Heavy smoking is one of the principal physical health risks (cardiovascular, respiratory, cancer, multiple substance abuse) related to the life style of the patient with schizophrenia

NO CONSENSUS

No unanimous agreement was reached as to whether patients with schizophrenia suffer from:
- A greater incidence of some neurological problems (stroke, epilepsy and cephalea) and cardiological diseases (cardiac insufficiency, arrhythmias and syncope) than in the general population (out of all diseases)
- A greater incidence of breast, lung and pharyngeal cancers (from all of them)

Section 2: EXPERT OPINION ON THE IMPACT OF TREATMENT FOR SCHIZOPHRENIA ON THE PHYSICAL HEALTH OF PATIENTS WITH SCHIZOPHRENIA

CONSENSUS

Concerning extrapyramidal symptoms induced by antipsychotics:
- More frequent in vulnerable patients (1st episode, elderly, chronic, nonresponders, female >40 years, etc.).
- Less frequent with atypical antipsychotics (but also produced at high dosage, rapid escalation or long-term treatment)

Treatment with anticholinergic agents is a risk factor for cognitive deterioration

Antipsychotic-induced hyperprolactinemia:
- Is a dose-dependent adverse effect, more difficult to recognize than most.
- Substantial risk with amisulpride and risperidone
- Produces clinical consequences in both sexes (in females: menstrual disturbances, gynaecomastia, galactorrhea, acne/hirsutism, osteoporosis, increased risk of breast and endometrial cancer; in males: fertility problems and erectile dysfunction)
- Sexual dysfunction, even though not a topic for consultation, leads to low treatment adherence

Metabolic disorders induced by antipsychotics:
- All antipsychotics (typical and atypical) increase risk of diabetes, though there are different levels of risk with different antipsychotic agents
- Weight increase is a potential adverse effect of antipsychotic treatment, but schizophrenia has its own risk of obesity (unhealthy life style, limited resources and lack of consciousness of the disease)
- Antipsychotics also increase the risk of dyslipidemia
- There are clinically relevant differences in the metabolic profiles of different antipsychotic agents, treatment should therefore be personalized for each patient, and should be revaluated in the presence of significant metabolic changes not controlled with other methods

Cardiac problems caused by antipsychotics:
- Some antipsychotics cause a lengthening of QT interval on the ECG, which is associated with minor symptoms (dizziness, palpitations and syncope), but also with severe ventricular arrhythmia and sudden death.
- The risk of altered QT interval increases with increasing dose, especially with typical antipsychotics, although it can also be produced by atypical antipsychotics (in decreasing order: sertindole, ziprasidone, risperidone and zotepine)
- Patients treated with antipsychotics have much greater risk of suffering severe myocardial infarction than the general population

3.1. RECOMMENDATIONS FOR INFECTIOUS DISEASES

CONSENSUS

- When schizophrenia is diagnosed, evaluate possible risky behaviour that increases the risk for viral infections HBV, HCV and HIV (ADVP with needle sharing and promiscuous sexual behaviour without protection), and if they are present or suspected, request serology for HBV, HCV, HIV and syphilis (VDRL).
- If the serology is negative, but risky behaviour continues, you should:
  - Repeat analyses periodically.
  - Provide preventive education to avoid risk of diseases transmitted by sexual, maternofetal and parenteral methods
  - Recommend Hepatitis B vaccination
- If any viral infection returns positive, you should:
  - Recommend the appropriate specialist
  - Recommend abstinence from alcohol.
  - Avoid the use of hepatotoxic drugs and keep in mind possible interactions with antiviral drugs

3.2. RECOMMENDATIONS FOR NEOPLASTIC DISEASES

CONSENSUS

- The psychiatrist should collaborate in the prevention and early detection of cancer in his patients with schizophrenia, by taking the following actions:
  - Include in the clinical history any family history of cancer, sexual and eating habits, sedentarism, body mass index, a general physical examination, and prolactin levels
  - Follow the recommendations of the "Código Europeo contra el Cáncer" for the general population (concerning smoking habits, obesity, physical activity, diet, alcohol, sun, carcinogens, and early detection programs as shown in Annex 1)
  - Actively evaluate smoking habits, evaluate the desire to stop smoking, and carry out a follow-up of the changes during treatment
- When using antipsychotics in patients with schizophrenia who are being treated for cancer, the psychiatrist should:
  - Take into account possible drug interactions.
  - Avoid drugs that cause weight increase in the case of colon and cervical cancer
  - Choose drugs that do not produce hyperprolactinemia, in the case of lung, breast and ovarian cancers

3.3. RECOMMENDATIONS FOR ENDOCRINE/METABOLIC DISEASES

CONSENSUS

- When schizophrenia is diagnosed, the psychiatrist should:
  - Record the anthropomorphic measurements of the patient (weight, height, BMI and waist circumference). Repeat every 6 months
  - Request a laboratory analysis (after an 8 hour fast), with: blood count, glucose, complete lipid profile–cholesterol, triglycerides, HDL and LDL cholesterol– and baseline creatinine. Repeat these analyses every 6 months, or if the patient changes medication, or has a weight increase
- The psychiatrist should educate his patients on a healthy life style (adequate diet and exercise) at each follow-up visit. If weight and/or glucose or lipid profiles cannot be controlled by nonpharmacological methods, you should:
  - Send the patient to his general care physician or a specialist
  - Evaluate the antipsychotic drug being used, avoiding where possible those that affect these conditions
- All patients taking antipsychotics should be evaluated for possible symptoms of hyperprolactinemia (menstrual disturbances, gynecomastia, galactorrhea, acne/hirsutism, osteoporosis, increased risk of breast and endometrial cancer, fertility problems and erectile dysfunction).
- Prolactinemia should be checked:
  - Yearly if the drug is a potential inducer of hyperprolactinemia (amisulpride, risperidone, etc.)
  - Always if there are signs of galactorrhea
- In the presence of symptomatic hyperprolactinemia or osteoporosis, evaluate changing to another antipsychotic agent with less risk of endocrine dysfunction

3.4. RECOMMENDATIONS FOR CARDIOVASCULAR DISEASES

CONSENSUS

- When schizophrenia is diagnosed, the psychiatrist should:
  - Record the vital signs (BP, pulse), and evaluate possible prior symptoms of ischemic cardiopathy or cardiac arrhythmia. Repeat every 6 months if there are cardiovascular risk factors, and after each change in medication or weight increase
  - Request an electrocardiogram (ECG) for all patients. Repeat annually if there are CV risk factors, and after each change in medication or weight increase

• Refer to general practitioner or specialist those patients with possible symptoms of cardiac ischemia, those who do not control hypertension with hygiene/diet recommendations, and those that have a prolonged QT interval on ECG, with or without symptoms (dizziness, palpitations, syncope, etc.). In this case, evaluate reduction of dosage or change of antipsychotic medication to one with a lower risk
3.5. RECOMMENDATIONS FOR NEUROLOGICAL DISEASES
CONSENSUS
• Evaluate possible extrapyramidal symptoms and tardive dyskinesia in all patients on antipsychotic treatment (with or without the help of psychometric instruments, such as the Simpson-Angus akathysia scale and the abnormal movements scale), every 3 months if a first generation medication is being used and every 6 months if it is second generation
• In high risk subjects (young men. first episode, elderly women, prior neurological damage etc.) choose atypical antipsychotics with a low risk of neurological side effects
• If neurological symptoms do appear, add the appropriate corrective medications (benzodiazepines for akathysia and anticholinergics for parkinsonism) and consider changing to an atypical antipsychotic with a low risk profile
3.6. RECOMMENDATIONS FOR RESPIRATORY DISEASES
CONSENSUS
• To detect respiratory problems in their patients with schizophrenia, psychiatrists should include auscultation in the physical examination and evaluate the possibility of ordering a chest X-ray, especially if the patient is hospitalized
• All patients with schizophrenia should be advised to reduce/stop smoking. In cases of COPD the influenza vaccination should be recommended
• In the case of respiratory decompensation in patients with schizophrenia, evaluate adjusting the doses of sedatives and benzodiazepines
NO CONSENSUS
• Specifically, the possible presence of sleep apnea should be investigated, obtaining a specific clinical history, and evaluating the level of daytime somnolence using questionnaires such as the Epworth Somnolence scale
3.7. RECOMMENDATIONS FOR OTHER PHYSICAL PATHOLOGIES
CONSENSUS
• To identify cataracts, the psychiatrist should question his patient with schizophrenia concerning changes in vision (blurry vision, poor distance vision), and recommend an opthalmologic examination (every 2 years until 40 years, very year thereafter)
• The psychiatrist should, at each visit, encourage good oral hygiene and recommend a yearly dental visit, and evaluate the need to change to an antipsychotic that causes less dryness in the mouth
• Patients treated with clozapine should: – follow a specific surveillance protocol for risk of agranulocytosis and observe the possible development of myocarditis (fatigue, dispnea, fever and palpitations, or anomalous ECG findings in the T interval or inversion of the T wave). – If problems are suspected, order a leucocyte count and serum levels of troponin. If the diagnosis is confirmed, clozapine administration should be suspended, and the patient referred to the primary care physician
NO CONSENSUS
• If the patient with schizophrenia develops cataracts, evaluate the possibility of changing to another antipsychotic

On the other hand, the remaining two items not agreed upon are specific recommendations made by the experts to improve some aspects of care of the physical health of patients with schizophrenia that are currently deficient, where debate and professional consensus are appropriate.

Item 59 ("Specifically, the possible presence of sleep apnoea should be investigated, carrying out a specific clinical history, and evaluating the level of daytime somnolence using questionnaires such as the Epworth Somnolence scale"), proposes the routine application in psychiatric practice of an instrument [36] that is little known outside certain specialized related fields (pneumology, ORL, endocrinology). There is also the impression that this instrument has had some difficulties in its Spanish language

Table 2 Criteria used to evaluate those recommendations where insufficient expert consensus was reached

	Descriptive statistical criteria[1]				
			Percentage of those surveyed		
Item Nº	Median	Mean	Disagree	Neither agree nor disagree	Agree
Item 3	7	6.53	6.7%	40%	53.3%
Item 5	6	5.79	21.4%	50%	28.5%
Item 7	7	6.67	6.7%	26.7%	66.7%
Item 59	7	6.87	6.7%	26.7%	66.7%
Item 63	7	6.07	7.1%	35.7%	57.1%

[1] Centralization measures calculated on a 1-9 scale as described in the methods. The % indicated in the last three column group the distribution of the panelists responses in three categories, according to their scores on each item ("disagree"=scores 1-3; "neither agree nor disagree"=score 4-6; "agree"=score 7-9)

version.[37, 38] However, this is a simple test (only 8 items), well-validated, and that can be self-administered by the patient, aspects not well known and not taken into consideration by those experts who did not support this recommendation.

Concerning item 63 ("In patients with schizophrenia who develop cataracts, you should consider the possibility of changing to another antipsychotic"), a frequent comment of those who disagreed that this recommendation be made to clinical psychiatrists was doubts concerning the physiopathological mechanisms that relate the two processes, and particularly the arguable nature of the benefit achieved by removing an effective antipsychotic medication on the appearance of opthalmologic complications (irreversible and only resolved by surgery). In this case, in spite of changing the drug, the side effects are permanent, and no benefit to the patient is obtained.

On the positive side of the study results, we must point out those recommendations that received almost total unanimity among the participants, without opposition from any of the experts. Among these is the agreement on relatively new concepts in the treatment of patients with schizophrenia, such as the frequency of respiratory diseases, metabolic changes, cardiovascular diseases and cancer as principal causes of morbimortality in the population group, and the need to introduce specific actions for their early detection, prevention and control during psychiatric consultation. This information is fully in agreement with recent epidemiological information on the most prevalent physical comorbidities in patients with schizophrenia in Spain.[15] From the results of this consensus, clinical psychiatrists should understand the recommendations, fully supported by expert opinion, for the routine practice of laboratory and electrocardiographic analyses during their consultations, and the necessity of introducing educational interventions on physical exercise and nutrition, to promote healthy lifestyles.

Also, taking into consideration specific interactions between antipsychotic medications and antiviral (item 32) or antitumoral (item 36) treatment, requires expert support, and also the need to evaluate adjustment of dosages of antipsychotic agents in those patients that present recurrent acute respiratory comorbidities (item 61). We also highlight the unanimity of the call to psychiatrists to play a proactive role in the detection and control of the risk of infection in their patients with schizophrenia, specifically the need to carry out periodic analytical controls to eliminate such risks (item 29).

In general, the Consensus SEP-SEPB 2008[2] receives a high level of agreement among Spanish experts concerning the management of important aspects of the physical health of patients with schizophrenia by the psychiatrist. The clinical recommendations expressed in this document should be considered as guidelines for clinical practice that are based on solid evidence and widely supported by expert opinion, such that the psychiatrists involved in managing the disease should accept them with confidence, as guidelines valid from the date of this publication until the appearance of new scientific evidence that would justify their modification, and therefore contribute to guaranteeing that patients with schizophrenia have a life expectancy and quality of life similar to that of the general population.[15]

Annex 1 **Professional criteria and clinical recommendations on the physical health of the patient with schizophrenia evaluated during the project. For each case, details on main descriptive statistical criteria used to determine the presence or the lack of consensus in the expert panel are given**

Section 1: PROFESSIONAL CONSIDERATIONS ON THE IMPACT OF SCHIZOPHRENIA ON THE PHYSICAL HEALTH OF AFFECTED PATIENTS

ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
1	Patients with schizophrenia present greater prevalence of infections by the hepatitis C virus and the HIV than the general population	7	7.00	20.0%
2	Knowledge about HIV infection among patients with schizophrenia is significantly inferior than among o the population without mental disorders, and their concern regarding this illness is low	7	7.20	13.3%
3	Generally, patients with schizophrenia present higher cancer incidence than the population without mental disorders (particularly breast, lung and pharynx cancer)	7	6.53	71.4%[2]
4	By nature, patients with schizophrenia show high rates of diabetes, glucose intolerance and metabolic syndrome compared to the general population, regardless of their pharmacological treatment	7	7.27	26.7%
5	On the basis of regular controls, it seems that there is no relevant prevalence of ictus, epilepsy and cephalea among patients with schizophrenia	6	5.79	50.0%[2]
6	The prevalence of spontaneous dyskinesia in patients with schizophrenia that have never received antipsychotics treatment is elevated and higher than in the healthy population	7	7.07	28.6%
7	Compared to general population, patients with schizophrenia present a higher rate of cardiac insufficiency, arrhythmias and syncope	7	6.67	33.3%[2]
8	The prevalence of respiratory pathologies (asthma, EPOC and emphysemas) is significantly higher than that in the general population and patients with other serious mental disorders	7	7.33	20.0%
9	Comorbid tabaquism is the main risk factor for respiratory pathologies in patients with schizophrenia	9	8.40	0%
10	High tobacco consumption, with intense (nicotine) dependency, is a main determinant factor in lifestyle-related morbimortality in patients with schizophrenia (involved in cardiovascular and respiratory diseases, cancer, polytoxicomania, etc.)	8	8.33	0%
11	Patients with schizophrenia present an excessive overall mortality for natural causes, resulting from an increased presence of respiratory, digestive, genitourinary, cardiovascular, infectious, mental and endocrine diseases	9	8.50	0%

Section 2: PROFESSIONAL CONSIDERATIONS ON THE IMPACT OF ANTISPYCHOTIC TREATMENT ON THE PHYSICAL HEALTH OF PATIENTS WITH SCHIZOPHRENIA

ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
12	Neurological toxicity of antipsychotics (extrapyramidal symptoms) is more frequent in vulnerable patients (first episodes, elders, chronicity or nonresponder patients, women, in particular >40 years old women, etc.)	8	8.27	0%
13	With respect to typical antipsychotics, atypical antipsychotics show a reduction in the risk of extrapyramidal effects, although they too may produce these effects, particularly when administered at elevated doses (or rapid escalation) and in long term treatment	8	8.20	6.7%
14	The use anticholinergics as a result of extrapyramidal symptoms is a risk factor for cognitive deterioration in patients with schizophrenia	7	7.40	20.0%
15	Hyperprolactinemia is a dose-dependent adverse effect of antipsychotic treatment which detection is more difficult than others (overweight, neurologic and metabolic effects, etc.)	7	7.40	13.3%

16	Hyperprolactinemia has clear clinical consequences for both sexes (menstrual alteration, gynecomastia, galactorrhea, acne /hirsutism, osteoporosis, increased risk for breast and endometrial cancer in women; alterations in men fertility, and sexual dysfunction in both men and women)	8	8.13	6.7%
17	Sexual dysfunction caused by hyperprolactinemia, though not an usual consultation issue, has a negative impact on the adherence to treatment	8	7.87	13.3%
18	Amisulpride and risperidone entail the risk for substantial raise of prolactin levels	9	8.33	0%
19	Although a causal relation has not yet been established, antipsychotic treatments (typical and atypical) are associated with an increased risk for diabetes in patients with schizophrenia	7	7.27	20.0%
20	There are differences between different types of antipsychotics with respect to the risk of producing diabetes	8	7.86	7.1%
21	Weight gain in patients with schizophrenia is a potential adverse effect of psychopharmacological treatment, but there are other important weight gain related variables among which the psychiatric disorder itself, unhealthy lifestyles, limited health resources and lack of awareness of the illness	8	7.67	13.3%
22	Prevalence of dyslipidemia also increases in patients receiving antipsychotic pharmacological treatment	8	7.53	13.3%
23	Different metabolic alteration profiles among the different types of antipsychotics are clinically relevant	8	7.93	0%
24	Antipsychotic treatment should be tailored as function of individual needs of each patient, assessing the possible substitution of the antipsychotic agent, in case of relevant metabolic alterations uncontrollable by other measures	8	8.13	0%
25	Some pharmacological antipsychotics are related to a pathological extension of the electrocardiographic QT interval that may be associated with minor symptoms (dizziness, palpitations and syncope) but also with ventricular arrhythmia and sudden death	7	7.27	13.3%
26	Risks caused by alterations of the QT interval increase according to dose with both typical (particularly) and atypical agents. Sertindole, ziprasidone, risperidone and zotepine (in decreasing order) are 2nd generation antipsychotics entailing greater risk	8	7.73	13.3%
27	Patients treated with pharmacological antipsychotics are in a much greater risk for acute myocardial infarction than control subjects	7	7.20	6.7%

Section 3: CLINICAL RECOMMENDATIONS TO THE PSYCHIATRIST TO IMPROVE THE PHYSICAL HEALTH OF HIS/HER PATIENTS WITH SCHIZOPHRENIA

3.1. RECOMMENDATIONS ON INFECTIOUS DISEASES

ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
28	Considering their elevated prevalence, possible risk behaviours for virus infections such as HBV, HCV and HIV (parenteral drug use with exchange of needles and promiscuous sexual behaviour without protection) should be assessed at the time of diagnosis of a patient with schizophrenias	8	8.00	13.3%
29	Serological tests for HBV, HCV and HIV should be carried out, along with a luetic serology (VDRL), in case of detection of, or suspected risk behaviours; these tests should be repeated periodically if the risk behaviours continue	9	8.67	0%
30	In case of negative serologic test results, patients with schizophrenia should receive a preventive educational intervention, specific on sexual transmission mechanisms and risks, both parenteral and maternal fetal	8	7.73	13.3%
31	All patients with schizophrenia presenting risk factors and negative hepatitis b (anti HBs negative) should be recommended the vaccination against the said agent	8	7.80	13.3%
32	In case of positive virus infection test, in addition to derive the patient to the specialist for treatment, prescription of hepatotoxic medications should be avoided, alcohol abstention should be recommended, and possible interaction with antiretroviral drug should be taken into account	9	8.60	0%

3.2. RECOMMENDATIONS ON NEOPLASTC DISEASES				
ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
33	To collaborate with early cancer detection, psychiatrist should include in all his/her patients with schizophrenia clinical histories the following data: family cancer antecedents, sexual and eating habits, sedentary, body mass index (BMI), prolactin levels, and general physical examination	9	8.20	6.7%
34	The psychiatrist should follow up the recommendations of the Codigo Europeo Contra el Cancer (European Code Against Cancer) for the general population (on tabaquism, obesity, physical activity, diet, alcohol, sun, cancerogenic factors, and early detection programs in Annex 1) in his/her patients with schizophrenia and insist and specifically reinforce them	8	7.80	13.3%
35	Because its special prevalence and intense nicotine dependency, the psychiatrist should adopt a proactive attitude aiming the identification of tabaquism while assessing the desire of breaking the habit and in following the phases of change during treatment	9	8.40	6.7%
36	The psychiatric therapeutic approach in patients with schizophrenia currently undergoing cancer treatment should take into account the possible pharmacological interactions	8	8.07	0%
37	In case of colon and cervix cancer, use of antipsychotic agents with weight gain effect must be avoided	7	7.40	13.3%
38	In case of lung, breast and ovarian cancer, antipsychotic agents not producing hyperprolactinemia should be employed	8	8.00	13.3%
3.3. RECOMMENDATION ON ENDOCRINOMETABOLIC DISEASES				
ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
39	At the time of diagnosis of the schizophrenic disorder, the psychiatrist should register the anthropometric measurements of the patient (weight, height, BMI and abdominal perimeter)	9	8.47	0%
40	At the time of diagnosis of the schizophrenic disorder, the psychiatrist should require 8 hour fasting laboratory routine tests: blood count, glycaemia, complete lipid profile –total cholesterol, triglycerides, HDL and LDL cholesterol- and the basal creatinine	9	8.60	0%
41	If results meet target values, complementary tests should be repeated annually, and the anthropometric measurements every six months	8	8.33	0%
42	Complementary tests should be repeated at each medication change or if the patient gain weight	8	8.00	6.7%
43	The psychiatrist should insist on and reinforce a healthy lifestyle (adequate diet composition and exercise) during each follow-up visit	9	8.50	0%
44	The psychiatrist should assess the convenience of the pharmacological antipsychotic selected according to the current endocrine & metabolic risk profile of the patient, avoiding, if necessary, agents capable of increased modifications of weight and glycemic or lipid profile, in situations non controllable using no pharmacological strategies	8	7.67	13.3%
45	If control is not achieved through prevention measures, the patient should be actively derived to the general practitioner or the corresponding specialist	8	7.73	6.7%
46	Every patient under antipsychotic treatment should be directly questioned about possible menstrual disorders, gynecomastia, galactorrhea, acne/hirsutism, infertility or sexual dysfunction	8	8.27	6.7%
47	Every patient under antipsychotic treatment, a potential inducer of hyperprolactinemia (amisulpride, risperidone, etc.) should have a prolactinemia assessment annually; in the presence of galactorrhea such assessment is always warranted	8	7.93	6.7%

48	In case of symptomatic hyperprolactinemia or osteoporosis diagnosis in a patient under antipsychotic treatment, change to an agent with lower risk for endocrine dysfunction	8	8.21	0%

3.4. RECOMMENDATIONS ON CARDIOVASCULAR DISEASES

ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
49	At the time of diagnosis of the schizophrenic disorder, the psychiatrist should systematically record of the patient's cardiovascular vital signs (arterial pressure and cardiac frequency) and assess prior presence of symptoms compatible with ischemic cardiopathy or arrhythmia	9	8.40	0%
50	At the time of diagnosis of the schizophrenic disorder, the psychiatrist should order ECGs to all patients	9	8.33	0%
51	In the presence of cardiovascular risk, ECGs shall be repeated annually, and vital signs (arterial pressure, pulse) shall be checked every six months	9	8.40	0%
52	These tests should be repeated in case of change of medication and weight gain	8	7.60	20.0%
53	If a silent or symptomatic extension of the QT interval (dizziness, palpitations, syncope, etc.) is detected, a possible dose reduction and/or change to an antipsychotic agent presenting lower risk should be considered	9	8.47	6.7%
54	Patients with symptoms compatible with coronary ischemia, patients who do not achieve an adequate control of their arterial pressure with hygiene and diet recommendations, and patients presenting ECG abnormalities, should be actively derived for study to the generalist practitioner or the corresponding specialist	9	8.47	6.7%

3.5. RECOMMENDATIONS ON NEUROLOGICAL DISEASES

ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
55	The presence of extrapyramidal symptoms and tardive dyskinesia should be clinically assessed in all patients, with or without the help of psychometric evaluation instruments (ie, Simpson Angus Scale and the Abnormal Movement Scale) every three months, if the patients is receiving a first generation antipsychotic treatment, and every six month if the patients is receiving a second generation antipsychotic treatment	8	7.86	6.7%
56	To prevent these complications in individuals in greater risk (young men, first episodes, older women, previous neurological damage, etc.), atypical pharmacological antipsychotic with a low profile with respect to those adverse effects should be the treatment choice	8	8.00	6.7%
57	In the presence of these neurological symptoms, the appropriate corrective pharmacological treatment should be added (benzodiazepines in the case of akathisie, and anticholinergics in the case of parkinsonism); a substitution of the current antipsychotic with an atypical one, with a lower profile with respect to these adverse effects	9	8.33	0%

3.6. RECOMMENDATIONS ON RESPIRATORY DISEASES

ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
58	To facilitate the detection of respiratory disorders, the psychiatrist will include auscultation during the physical examination of his/her patients with schizophrenia, and will assess any possible indication of a thorax Rx, particularly if the patients are hospitalised	7	6.87	26.7%
59	The possible presence of the sleep apnoea syndrome should be specifically explored, dressing a specific clinical history and assessing the degree of daytime somnolence by means of questionnaires (ie, the Epworth Sleepiness Scale)	7	6.87	33.3%[2]
60	All patients with schizophrenia will be recommended to reduce/quit tobacco consumption. Flu vaccine should be recommended in case of EPOC	9	8.33	6.7%

61	In the presence of respiratory decompensation in patients with schizophrenia, the psychiatrist will consider the adjustment of benzodiazepines and the sedation psychopharmacological medications	9	8.47	0%

3.7. RECOMMENDATIONS ON OTHER PHYSICAL PATHOLOGIES

ITEM No.	Clinical considerations explored	Median	Mean	% of respondents who disagree[1]
62	To collaborate n the detection of cataracts, the psychiatrist will question his/her patients with schizophrenia for vision changes, specially for blurry and distant vision, and recommend a revision by the ophthalmologist (annually in the case of patients > 40 years, and every two years in the case of patients <40 years)	7	7.33	20.0%
63	Patients with schizophrenia who develop cataracts should consider a possible change of treatment in favour another antipsychotic	7	6.07	42.9% [(2)]
64	Each visit should be used by the psychiatrist to reinforce oral hygiene habits and to recommend annual revisions by the dentist, and to assess the possible substitution of the current antipsychotic with another agent not producing (or producing less) mouth dryness	7	7.27	13.3%
65	Patients treated with clozapine should follow a specific monitoring protocol for agranulocytosis	9	8.64	7.1%
66	Patients treated with clozapine should be monitored for possible development of myocarditis (fatigue symptoms, dyspnea, fever and palpitations, and ECG findings such as LST segment anomalies and T wave inversion). If suspected, a leucocytes and troponin serum levels counts are warranted. If diagnosis is confirmed, clozapine should be suspended and the patient derived to the primary care physician	8	7.73	20.0%

[1]% of respondents whose opinions are in the 1-3 region (disagree), or 4-6 region (neither agree nor disagree) of the 9 point ordinal scale (1= completely disagree, 9=fully agree)
[2] Items without consensus of the expert panel, according with the criteria defined in the methodology

Annex 2 — Alphabetical listing of the panel members participating in the Delphi survey

- Mª Fe Bravo
- Antonio Benabarre
- Jorge Cervilla
- Emilio Fernández-Egea
- Manuel Franco
- Mª Paz García Portilla
- E. González Pablos
- Ana González Pinto
- Angel Luis Montejo
- José Manuel Montes Rodríguez
- Carmen Moreno Ruiz
- Luis San
- Tomás Sánchez-Araña Moreno
- J. Luis Santos
- Manuel Serrano Vázquez

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