# Benchmarking the burden of 100 diseases: results of a nationwide representative survey within general practices

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2011-000215 |
| Article Type: | Research |
| Date Submitted by the Author: | 13-Jun-2011 |
| Complete List of Authors: | Grimaldi-Bensouda, Lamiae; Equipe d'accueil 'Pharmacoépidémiologie et maladies infectieuses", Institut Pasteur, and LA-SER<br>Begaud, Bernard; Université de Bordeaux, U657<br>Lert, France; Centre for Epidemiology and Population Health, INSERM U1018,<br>Rouillon, Frederic; Université Paris V René Descartes, Centre Hospitalier Sainte-Anne<br>Massol, Jacques; Université de Franche Comté, UFR de Médecine,<br>Guillemot, Didier; Institut Pasteur, and Université Paris-Ile de France Ouest<br>Avouac, Bernard; LA-SER<br>Duru, Gerard; CYKLAD GROUP<br>Magnier, Anne-Marie; Université Pierre et Marie Curie, Faculté de médecine,<br>Rossignol, Michel; Department of Epidemiology, Biostatistics and Occupational Health, McGill University, and LA-SER Centre for Risk Research<br>Abenhaim, Lucien; Department of Epidemiology, London School of Hygiene & Tropical Medicine, and LA-SER |
| Primary Subject Heading: | General practice & family medicine |
| Keywords: | PRIMARY CARE, PUBLIC HEALTH, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT |
| | |

SCHOLARONE™
Manuscripts

# Benchmarking the burden of 100 diseases: results of a nationwide representative survey within general practices.

Lamiae Grimaldi-Bensouda[1], Bernard Begaud[2], France Lert[3], Frederic Rouillon[4], Jacques Massol[5], Didier Guillemot[6], Bernard Avouac[7], Gerard Duru[8], Anne-Marie Magnier[9], Michel Rossignol[10], and Lucien Abenhaim[11], for the EPI3-LA-SER group.¶

**Correspondence to:** L. Grimaldi-Bensouda LA-SER, 10 place de Catalogne, 75014 Paris, France. Email: Lamiae.Grimaldi@la-ser.com

[1]Equipe d'accueil 'Pharmacoépidémiologie et maladies infectieuses', Institut Pasteur, and LA-SER, both in Paris, France

[2] U657, Université de Bordeaux, Bordeaux, France

[3]INSERM U1018, Centre for Epidemiology and Population Health, Villejuif, France

[4]Centre Hospitalier Sainte-Anne, Université Paris V René Descartes, Paris, France

[5]UFR de Médecine, Université de Franche Comté, Besançon, France

[6]Institut Pasteur, and Université Paris-Ile de France Ouest, both in Paris, France

[7]LA-SER, Paris, France

[8]CYKLAD GROUP, Rillieux la Pape, France

[9]Faculté de médecine, Université Pierre et Marie Curie, Paris, France

[10]Department of Epidemiology, Biostatistics and Occupational Health, McGill University, and LA-SER Centre for Risk Research, both in Montreal, Canada

[11]Department of Epidemiology, London School of Hygiene & Tropical Medicine, and LA-SER, both in London, UK

For peer review only

¶**Contributing members of the EPI3-LA-SER study group are:** L. Abenhaim (UK), B. Avouac (France), B. Begaud (France), J. Bénichou (France), G. Duru (France), Pierre Engel (France), Alban Fabre (France), L. Grimaldi-Bensouda (France), F. Lert (France), A. M. Magnier (France), J. Massol (France), M. Rossignol (Canada), and F. Rouillon (France).

**Keywords**: one-day survey, cross-sectional study, morbidity, quality of life, burden of disease in general practice

**Word count** = 3335

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## Abstract

**Objective:** To assess the burden of diseases and quality of life (QOL) of patients for a large variety of diseases within general practice.

**Design:** A representative nationwide cross-sectional study. A total of 825 general practitioners (GPs) were randomly selected from across France. Independent investigators recruited 8559 patients attending the GPs' practices. Data on quality of life (12-Item Short Form questionnaire) and other individual characteristics were documented by the independent investigators for all participants at the waiting room. Medical information was recorded by GPs. Sampling was calibrated to national standards using the CALMAR weighting procedure. Associations of lower scores (i.e., below vs. above the first quartile) of physical and mental component scores (PCS and MCS, respectively) with main diseases and patients characteristics were estimated using multivariate logistic regression. Weighted morbidity rates, PCS and MCS were computed for 100 diagnoses using the international classification of diseases (ICD-9, 9$^{th}$ version).

**Results:** Overall mental impairment was observed amongst patients in primary care with an average MCS of 41.5 (SD = 8.6), ranging from 33.0 for depressive disorders to 45.3 for patients exhibiting fractures or sprains. Musculoskeletal diseases were found to have the most pronounced effect on impaired physical health [OR=2.31; 95% CI (2.08–2.57)] with the lowest PCS [45.6 (SD = 8.8)] and ranked first (29.0%) amongst main diagnoses experienced by patients followed by cardiovascular diseases (26.7%), and psychological disorders (22.0%). When combining both prevalence and quality of life, musculoskeletal diseases represented the heaviest burden in general practice.




For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Conclusions:** EPI3 is the first study to provide reference figures for burden of disease in general practice across a wide range of morbidities, particularly valuable for health economics and healthcare system evaluation.

## ARTICLE SUMMARY

### Article Focus

- The impact of the diseases on quality of life in general practice has been assessed so far amongst selected samples of patients, usually from studies including a limited number of medical practices and/or focusing mainly on chronic conditions.
- There is a clear need for more data on quality of life (QOL) of patients in primary care; the aim of the EPI3 survey was to provide reference figures for disease burden in this setting.

### Key messages

- The EPI3 study was a cross-sectional survey combining unique data from patients and general practitioners, and allowed provision of reference figures for the vast majority of diseases encountered in primary care for a large number of patients.
- The study highlighted the burden of musculoskeletal and psychological disorders, experienced by more than half the patients.

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

- Although social and medical determinants of patients' QOL were somewhat similar than those found in previous studies in primary care, the EPI3 survey showed more pronounced mental impairment in French patients.

**Strengths and limitations of this study**

**Strengths:**

- No nationwide study on burden of disease combining both prevalence measures and QOL assessment has been conducted to date, addressing such a large variety of diseases in general practice.

- On-site selection and recruitment by an independent investigator limited the possibility of selection bias amongst patients and the participation of physicians added high specificity to medical data collection.

**Limitations:**

- Study design providing high specificity in data collection led to a relatively low response rate from GPs. However, stratified recruitment phases and sample sizes from both GPs and patients highly representative of national standards ensured strong external validity of the results.

- Home consultations, which are most common amongst GPs in France, were not surveyed which could probably have led to an underestimation of burden of disease.

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# INTRODUCTION

Assessing and measuring the burden of a disease in medical practice is undoubtedly important for the evaluation of medicines and healthcare.[1] To assess such burden quantitatively, both prevalence of diseases and their impact on health status and on the quality of life (QOL) of patients need to be taken into account.[2]

In primary care, the prevalence of morbidities has been shown to be remarkably similar across different industrialised countries.[3-5] However, their effect upon QOL is only partially known.[6] The impact of the diseases on QOL in general practice has been addressed so far using selected samples of patients,[7-13] usually from studies including a limited number of medical practices,[8;10;11;13] and/or mainly focused on chronic conditions.[7;9-11] To the best of our knowledge, no nationwide study of burden of disease combining both prevalence measures and QOL assessment for a large variety of diseases is currently available. To compensate for this paucity of information, some studies evaluated the impact for diseases in primary care calling upon modelling data derived from studies in medical specialties[14-16] and/or in hospital settings,[17;18] or from general population surveys.[19-21] It is not known to what extent these extrapolations are appropriate.

The aim of the EPI3 survey was to provide reference figures for disease burden in primary care. To this purpose, a representative sample of GPs was assembled through stratified sampling and data from their patients collated during a one-day survey conducted by independent interviewers in the waiting room of the participating medical practices.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# METHODS

## Study design, settings and population

The EPI3-survey was a nationwide, observational study of a representative sample of GPs and their patients, conducted in France between March 2007 and July 2008. Its aims were to assess the burden of diseases in general practice, considering the physicians' work activity, patients' characteristics, morbidity and prescriptions.

The sample was drawn by applying a two-stage sampling process. Firstly, GPs were randomly selected from the French national directory of physicians and invited to participate, which meant also allowing a trained research assistant to conduct a one-day survey in the waiting room at the doctor's practice. GPs' sampling was stratified according to the diversity of medicine practices in the country (conventional and complementary medicine such as homeopathy).

The second stage consisted of random one-day sampling of consultations per participating physician in order to survey all patients attending the practice on a particular day. All adult and accompanied minor patients were eligible for inclusion in the EPI3-survey to the exception of those whose health status or literacy level did not allow responding to a self-administered questionnaire. The research assistant recruited on site (i.e., in the waiting room) all consecutive eligible patients, accepting to participate to the survey up to a maximum of 15 patients. Further, each physician recorded the main reason for consultation, along with the age, gender and type of national health insurance for each patient. The maximum number of patients surveyed per day was set to allow sufficient time for optimal interviews and was followed by patients' examination by the physician.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

The EPI3-survey obtained regulatory approval by the national board of physicians ("Conseil National de l'Ordre des Médecins") and ethical approval by the French data protection authority ("Commission Nationale de l'Informatique et des Libertés"). Patients were informed by the participating physician that their responses would be kept confidential and they were not remunerated for participation. Physicians received compensation fees. The study was sponsored by a pharmaceutical company, whose name was not revealed to investigators or patients. They were reassured that the sponsor's name would be disclosed to them with the results.

### Data collection

Data collected from patients included age, gender, nationality (born in France or born French versus other), educational level (secondary school and higher degrees vs. less educated), type of health insurance (regular national health insurance vs. insurance for low-income people; additional private insurance vs. none), smoking status (current, past, non-smoker), alcohol intake (never, sometimes, daily), physical activity (0-30 minutes per day, 31 minutes and over), body mass index (<25; 25-30; >30 kg/m2), employment status and occupation (employed, on unemployment benefits, homemaker, retired or unemployed, student), the number of consultations to the participating physician in the last 12 months, or, for the same period, to other GPs or medical specialists, the length or number of hospitalisations and sick leaves.

Participants were asked whether the attending physician was their regular/primary care physician. In the French health insurance system, patients have to choose a regular physician -usually a GP-, who plays a gatekeeping role for referral to specialised care. However, referral by regular GPs to other physicians is not



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

compulsory and patients are allowed to seek care from different physicians and their different reimbursement schemes.

Detailed information on physicians including age, gender, type of contract with national health insurance (regular fees, additional fees, and no contract), working days and average duration of consultation were assessed by the research assistants at the time of inclusion.

GPs completed a medical questionnaire on patients including the main reason for consultation and up to five other diagnoses present that day. GPs were requested to record their prescriptions that day for diagnostic tests, drugs and referrals. Diagnoses were coded by a trained archivist using the 9th revision of the International Classification of Diseases using 100-3 digit-categories.[22]

### Health status measurement

Amongst adult patients (18 years and over), health-related quality of life was assessed using the 12-Item Short Form questionnaire (SF-12),[23] a shortened version of the 36 short form health survey (SF-36) which has been shown to be a reliable outcome measurement tool in primary care.[24] The physical and mental component summary scores (PCS and MCS, respectively) were derived from the SF-12 questionnaire. Physical functioning (two questions), role-physical functioning (two questions), bodily pain (one question), general health (one question), vitality (one question), social functioning (one question), role-emotional functioning (two questions), and mental health (two questions), cover the same dimensions as the SF-36. The scores are standardised to population norms (based on a US norm-sample), with the mean score set at 50 (SD = 10); lower scores indicate worse-, and higher scores better



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

health. The SF-12 has been validated for use in France, the US, the UK and many other European countries.[21]

### Statistical analysis

Participating and non-participating patients were compared against the collected variables on: gender, age, length of time attending the GPs' practice, type of health insurance and main reason for consultation. A weighting procedure known in demographic studies as the CALMAR procedure was applied to calibrate the final sample according to participation so that it represents closely the patients attending the practice.[25]

Participating GPs were compared to the French "Institut de recherche et documentation en économie de la santé" sample.[26] The physicians' activity-related fractions were also calibrated to the real distribution of the participating physicians across the France. All reported results were obtained after weighting was applied to GPs' patients.

In this study, we reported weighted prevalence, PCS and MCS measures of the SF-12 computed according to the algorithm given by Ware et al for 100 different conditions, which were further grouped in 13 broad diseases categories plus one covering preventive motives of consultation and other medical acts.[23] Means and standard deviation (SD) were estimated for the whole adult sample and for each diagnosis. When a 3-digit category from ICD-9 had less than 30 patients, the category was grouped with one or several categories under the same heading. When grouping within the same heading was not relevant, categories with less than 30 patients were grouped in the category "other" within each main category.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Each disease category was calculated as a percentage reported to the whole population of participating patients over the age of 18 years, regardless of whether this diagnosis was isolated or associated with others, in order to provide a complete picture of morbidity cared for in general practice.

Amongst adults over 18 years, associations of age, gender, education, type of insurance, and 13 broad disease categories with lower MCS and PCS scores (defined as below the 1st quartile with scores of 34 and 39 for MCS and PCS, respectively) were evaluated using multivariate logistic regression. Odd Ratios (OR) and 95% confidence interval (CI) are presented for each of these factors. In addition, the same analysis was conducted for the two remaining categories: pregnancy follow-up and preventive motives, which were not considered in the multivariate analysis. The association between the number of comorbidities and the two SF-12 composite scores was tested using linear regression. We used SAS statistical software (Version 9.1) for data analysis. The present study was reported following the STROBE statement for cross-sectional studies.[27]

# RESULTS

The sequential recruitment of physicians was done by random stratified sampling from the phone directory for GPs. Amongst the 3345 GPs initially contacted, 428 (12.8%) accepted to participate to the survey. At the end of recruitment in July 2008, a final sample of 825 participating GPs recruited a total of 11 809 patients eligible for the present study. Of these, 174 were unaccompanied minors, 315 were not French speakers, 109 had severe psychiatric disorders, 2151 declined participation, 408 were beyond the maximum number possible to interview within the allocated time on site,



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

and 93 had incomplete data and were excluded, allowing a total of 8559 patients for the present analysis.

### Physicians

The median age of physicians was 52 years [Interquartile range (IQR) = 33-57] and amongst them, 24% were women; 54% worked in solo medical practice, 40% with other GPs and 6% collaborated with specialists or other healthcare professionals; 31% of the GPs practised additional medical activities within hospitals, healthcare centres, the health administration or in the pharmaceutical industry. Most of the GPs (90%) hold a regular contract with the National Health Insurance organisation, whilst 9% hold a special contract allowing extra fees; a very small proportion (0.4%) had no contract. The mean daily working time at the practice (excluding home visits) was 9 hours (IQR: 2-10.5).

### Patients

Characteristics of participating (n = 8559) and non-participating patients with complete data (n = 3157) used to calibrate the sample are presented in **Table 1**. We reported here results based on the weighted characteristics. The mean age of the 8559 participating patients was 44.9 years (SD = 21.9), and 7133 (83.3%) were adults over 18. At least 44% of patients had a secondary school degree, 16% were overweight (BMI>30 kg/m$^2$) and more than 61% exercised longer than 31 minutes per day. Nine out of ten patients were French born (90%), 9% were covered by a government-funded insurance for low-income people, and 90% had a private supplementary insurance. Amongst the 8559 patients, 8% attended the practice for the first time, 12% had attended it for one year or less, 27% between one and five years and 53% for 5 years or more. Over 84% of participants named the recruiting physician as their



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

regular treating physician. About 28% of patients were registered by the national health insurance as having multiple or severe chronic diseases owing special coverage.

**Table 1.** Characteristics of non-participating and participating patients: results of the calibrated data (the EPI3 survey 2008).

| | Non-participants* (n = 3157) | Participants (n = 8559) | **Weighted percentage** |
|---|---|---|---|
| *mean (SD)* | | | |
| **Age** (years) | **47.7 (24.0)** | **43.3 (22.8)** | 44.9 (21.9) |
| *n (%)* | | | |
| **Female gender** | **1701 (53.9)** | **5367 (62.7)** | 57.9 |
| **Length of relationship with the physician** | | | |
| first time | 265 (8.4) | 782 (9.1) | 7.7 |
| less than 1 year | 316 (10.0) | 1315 (15.4) | 11.9 |
| 1-5 years | 743 (23.5) | 2380 (27.8) | 27.4 |
| More than 5 years | 1703 (53.9) | 4015 (46.9) | 53.0 |
| **Government funded health insurance** | 308 (9.8) | 621 (7.4) | 9.4 |
| **Long-standing disease status** | | 1925 (22.5) | 27.7 |
| **Complementary health insurance** | | 7839 (91.6) | 90.3 |
| **Index physician declared as treating physician** | | 6379 (74.5) | 84.3 |
| **Body Mass Index** ($kg/m^2$) | | | |
| <25 | | 5548 (64.8) | 52.4 |
| 25-30 | | 2045 (23.9) | 31.8 |
| 30 and over | | 966 (11.3) | 15.8 |
| **Tobacco consumption** | | | |
| Non smoker | | 4303 (50.3) | 47.4 |
| Past smoker | | 1961 (22.9) | 24.4 |
| Current smoker | | 2252 (26.3) | 28.2 |
| **Alcohol Consumption** | | | |
| Never | | 2908 (34.2) | 35.2 |
| Sometimes | | 4649 (54.6) | 52.5 |
| Daily | | 957 (11,2) | 12.4 |
| **Physical exercise** | | | |
| Less than 10 minutes per day | | 2235 (26.1) | 28.3 |
| 10 minutes and over | | 6199 (72.4) | 71.7 |
| **Nationality** | | | |
| French born subjects | | 7787 (91.0) | 90.3 |
| French born abroad | | 341 (4.0) | 4.7 |
| Non-French nationality | | 357 (4.2) | 5.0 |
| **Educational attainment** | | | |
| Secondary school degree*, college, university graduation | | 4179 (48.8) | 44.0 |
| **Employment status** | | | |
| Employed | | 4544 (53.1) | 50.4 |



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | |
|---|---|---|
| On unemployment benefits | 378 (4.4) | 4.7 |
| Homemaker | 647 (7.6) | 6.6 |
| Retired and other unemployed | 2562 (29.9) | 34.3 |
| Student | 348 (4.1) | 4.1 |

*Available characteristics used for calibration

¥French baccalaureate

**Burden of one hundred diseases in primary care**

Prevalence of each of the 100 and 13 broad non-exclusive diagnosis categories are presented in **Table 2** Altogether, diseases of the musculoskeletal system were the most frequently diagnosed conditions (29%), followed by cardiovascular diseases (26.7%), and sleep, anxiety and depressive disorders (22%). Preventive care consultations, vaccinations and consultation for administrative purposes accounted for 19% of the total diagnoses. Almost half the patients (49%) exhibited two or more comorbidities.

**Table 2.** Morbidity rates and SF12 mental and physical component scores according to 100 ICD diagnoses (EPI3-LASER-2008, weighted data n = 7133)

| **Diseases** | **Morbidity* n (%)** | **PCS mean (sd)** | **MCS Mean (sd)** |
|---|---|---|---|
| **All patients** | | **45.6 (8.8)** | **41.5 (8.6)** |
| **Diseases of the musculoskeletal system** | **2069 (29.0%)** | **42.7 (8.4)** | **41.6 (8.3)** |
| Osteoarthritis | 324 (4.5%) | 41.1 (10.7) | 41.7 (11.0) |
| Unspecified joint disorders | 171 (2.4%) | 42.5 (9.9) | 42.6 (10.2) |
| Intervertebral and cervical disc disorders | 276 (3.9%) | 44.0 (11.4) | 40.6 (10.3) |
| Lumbago | 360 (5.0%) | 42.1 (10.1) | 41.6 (9.4) |
| Rotator cuff syndrome of shoulder and allied disorders | 98 (1.4%) | 42.5 (10.1) | 42.0 (9.8) |
| Other affections of shoulder region | 121 (1.7%) | 42.6 (9.7) | 42.4 (9.1) |
| Enthesopathy of elbow region | 77 (1.1%) | 41.8 (9.3) | 43.1 (10.5) |
| Unspecified enthesopathy | 257 (3.6%) | 42.3 (10.5) | 42.1 (10.0) |
| Rheumatism, excluding the back | 112 (1.6%) | 42.9 (10.1) | 42.3 (9.8) |
| Spondylosis and other inflammatory spondylopathies | 84 (1.2%) | 42.1 (9.9) | 43.1 (8.4) |
| Sciatica | 194 (2.7%) | 42.3 (10.1) | 41.7 (9.6) |
| Pain in thoracic spine | 51 (0.7%) | 42.6 (9.8) | 41.3 (9.2) |
| Osteoporosis | 162 (2.3%) | 44.0 (10.7) | 41.9 (10.8) |
| Diseases of connective tissue | 36 (0.5%) | 45.5 (9.3) | 40.5 (10.9) |
| Unspecified back disorders | 193 (2.7%) | 42.1 (10.2) | 41.3 (9.7) |



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | |
|---|---|---|---|
| Other unspecified musculoskeletal disorders | 76 (1.1%) | 40.3 (11.0) | 41.7 (11.6) |
| **Hypertension, cardiovascular and circulatory diseases** | **1904 (26.7%)** | **43.7 (9.0)** | **42.5 (8.6)** |
| Hypertension | 1111 (15.6%) | 43.9 (11.3) | 42.8 (10.7) |
| Acute myocardial infarction | 84 (1.2%) | 40.8 (11.4) | 42.0 (9.4) |
| Other symptoms involving cardiovascular system | 53 (0.7%) | 46.0 (9.5) | 43.7 (8.2) |
| Angina pectoris | 66 (0.9%) | 41.8 (11.8) | 43.7 (10.5) |
| Cardiac dysrhythmias | 139 (1.9%) | 42.9 (11.5) | 42.7 (11.1) |
| Diseases of veins and lymphatics | 92 (1.3%) | 45.3 (10.5) | 41.3 (10.8) |
| Pulmonary, artery and cerebrovascular diseases | 144 (2.0%) | 42.1 (11.7) | 42.7 (10.6) |
| Other ischaemic heart diseases | 96 (1.3%) | 41.1 (11.9) | 42.1 (11.1) |
| Other diseases of the circulatory system | 229 (3.2%) | 45.3 (10.3) | 41.8 (11.0) |
| **Anxiety, depression and sleep disorders** | **1569 (22.0%)** | **44.8 (8.9)** | **36.3 (8.5)** |
| Psychotic conditions | 68 (1.0%) | 44.2 (12.6) | 37.6 (12.3) |
| Anxiety states | 420 (5.9%) | 47.8 (10.5) | 35.5 (9.7) |
| Dysrhythmia | 182 (2.6%) | 47.2 (10.2) | 35.4 (9.2) |
| Acute and chronic stress | 85 (1.2%) | 46.9 (10.6) | 36.1 (9.5) |
| Personality disorders, disturbance of conduct, dependence syndrome | 81 (1.1%) | 46.4 (10.9) | 38.8 (11.2) |
| Eating disorders, tics, stuttering and other syndromes | 277 (3.9%) | 47.4 (10.4) | 37.1 (10.7) |
| Depressive disorders | 497 (7.0%) | 45.3 (11.4) | 33.0 (10.2) |
| Malaise and fatigue | 114 (1.6%) | 45.4 (11.1) | 38.7 (9.7) |
| Sleep disorders | 87 (1.2%) | 46.1 (10.7) | 38.5 (9.4) |
| Nervousness, cachexia and unspecified psychological distress | 30 (0.4%) | 41.9 (13.5) | 39.9 (12.8) |
| Dizziness and giddiness | 59 (0.8%) | 46.3 (9.8) | 40.2 (10.4) |
| Other general symptoms | 75 (5.8%) | 46.0 (11.1) | 39.2 (10.4) |
| **Diseases of the respiratory system** | **1419 (19.9%)** | **46.3 (8.5)** | **41.9 (8.4)** |
| Acute nasopharyngitis | 306 (4.3%) | 48.2 (9.8) | 41.6 (9.7) |
| Acute pharyngitis | 60 (0.8%) | 49.3 (10.4) | 42.5 (10.5) |
| Acute tracheitis | 120 (1.7%) | 48.4 (10.1) | 41.4 (10.4) |
| Acute bronchitis or other upper respiratory infections | 66 (0.2%) | 41.9 (12.3) | 43.0 (8.0) |
| Chronic nasopharyngitis | 52 (0.3%) | 50.0 (8.1) | 42.9 (8.7) |
| Chronic sinusitis and laryngitis | 126 (1.7%) | 48.0 (9.9) | 40.3 (8.9) |
| Allergic rhinitis | 124 (1.7%) | 47.5 (10.7) | 42.3 (9.6) |
| Pneumonia and influenza | 53 (0.6%) | 46.8 (10.2) | 41.1 (10.8) |
| Chronic obstructive pulmonary diseases (except asthma) | 160 (2.2%) | 44.8 (10.4) | 41.2 (10.0) |
| Asthma | 148 (2.1%) | 44.0 (11.5) | 41.4 (10.5) |
| Lung diseases | 64 (0.9%) | 41.0 (12.3) | 42.0 (9.5) |
| Other diseases of the respiratory system | 210 (2.9%) | 45.1 (11.6) | 42.4 (10.4) |
| **Medical exams, preventive motives** | **1101 (15.4%)** | **47.4 (9.2)** | **42.4 (10.1)** |
| Medical exam: handicap influencing health status | 41 (0.6%) | 45.9 (9.4) | 39.4 (12.6) |
| Medical exam: aftercare and specific procedures | 285 (4.0%) | 45.9 (11.6) | 41.2 (10.8) |
| Medical exam for health check-up | 286 (4.0%) | 46.9 (11.3) | 43.1 (10.8) |
| Laboratories findings | 53 (0.7%) | 48.5 (9.8) | 42.9 (10.9) |
| Vaccination | 121 (1.7%) | 50.2 (11.0) | 42.6 (10.5) |
| Pregnancy follow-up | 122 (1.7%) | 47.4 (11.8) | 41.8 (10.4) |



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | |
|---|---|---|---|
| Administrative purposes | 380 (5.3%) | 47.2 (11.7) | 42.5 (9.9) |
| **Diabetes, thyroid gland & other endocrine disorders** | **785 (11.0%)** | **43.9 (8.6)** | **41.5 (8.1)** |
| Hypothyroidism | 187 (2.6%) | 45.3 (11.0) | 39.6 (10.9) |
| Goitre | 45 (0.6%) | 46.5 (9.3) | 41.3 (9.8) |
| Diabetes mellitus | 312 (4.4%) | 42.9 (11.2) | 42.0 (10.5) |
| Diseases of other endocrine glands | 78 (1.1%) | 43.9 (11.9) | 41.0 (10.8) |
| Other thyroid disorders | 52 (0.7%) | 45.7 (10.8) | 40.0 (10.1) |
| **Obesity & dyslipidaemia** | **742 (10.4%)** | **45.2 (9.1)** | **42.0 (8.9)** |
| Hypercholesterolaemia | 266 (3.7%) | 45.1 (10.9) | 42.6 (10.2) |
| Unspecified disorder of lipoid metabolism | 135 (1.9%) | 45.5 (10.5) | 42.8 (9.2) |
| Overweight, obesity and other hyperalimentation | 169 (2.4%) | 47.6 (11.4) | 40.2 (10.4) |
| Other hyperlipidaemia | 105 (1.1%) | 45.6 (11.3) | 42.4 (10.6) |
| Other symptoms concerning nutrition, metabolism and development | 70 (1.0%) | 48.6 (10.1) | 40.3 (10.4) |
| **Diseases of the digestive system** | **742 (10.4%)** | **45.9 (8.4)** | **39.9 (8.4)** |
| Oesophageal diseases | 81 (1.1%) | 44.3 (10.3) | 41.5 (9.8) |
| Diseases of stomach | 121 (1.7%) | 45.6 (10.0) | 40.1 (9.7) |
| Diseases of intestines and peritoneum | 72 (1.0%) | 45.1 (10.1) | 40.2 (9.9) |
| Symptoms involving the abdomen | 161 (2.3%) | 46.9 (10.4) | 39.9 (11.0) |
| Non-infectious enteritis and colitis | 105 (1.5%) | 47.5 (9.5) | 41.8 (9.9) |
| Diseases of oral cavity, salivary glands and jaws | 39 (0.5%) | 49.0 (8.8) | 40.3 (10.0) |
| Appendicitis and hernia | 43 (0.6%) | 44.1 (10.6) | 40.0 (10.2) |
| Other diseases of the digestive system | 144 (2.0%) | 44.8 (10.8) | 39.7 (9.9) |
| **Diseases of the nervous system, head & neck** | **449 (6.3%)** | **43.3 (9.4)** | **39.6 (9.1)** |
| Disorders of central nervous system | 95 (1.3%) | 41.3 (13.6) | 42.2 (11.2) |
| Migraine | 114 (1.6%) | 46.6 (10.2) | 39.7 (10.1) |
| Symptoms involving head & neck | 96 (1.3%) | 46.3 (10.8) | 40.8 (10.2) |
| Diseases of the eye | 54 (0.7%) | 51.8 (9.9) | 37.4 (10.6) |
| Diseases of the ear and mastoid processes | 112 (1.6%) | 46.9 (10.8) | 41.6 (11.0) |
| Other disorders of nervous system and sense organs | 145 (2.0%) | 44.6 (10.3) | 39.9 (10.6) |
| **Diseases of the genitourinary system** | **400 (5.6%)** | **45.5 (9.6)** | **41.5 (8.9)** |
| Cystitis | 115 (1.6%) | 47.9 (11.5) | 40.3 (10.2) |
| Diseases of male genital organs | 85 (1.2%) | 46.0 (10.9) | 43.0 (11.0) |
| Diseases of female genital organs | 139 (1.9%) | 48.4 (11.3) | 39.8 (10.8) |
| Nephrosis and nephritis | 86 (1.2%) | 44.8 (11.6) | 41.7 (10.6) |
| Complications of pregnancy, congenital anomalies | 42 (0.6%) | 43.5 (12.8) | 40.4 (10.5) |
| **Injury and poisoning** | **342 (4.8%)** | **43.5 (9.2)** | **43.5 (8.3)** |
| Fractures, sprains and dislocations | 103 (1.4%) | 41.9 (10.5) | 45.3 (9.7) |
| Traumas and injuries to organs | 54 (0.8%) | 44.3 (12.9) | 44.1 (11.4) |
| Burns, amputations | 62 (0.9%) | 44.4 (11.6) | 43.1 (10.4) |
| Intoxications, allergies to toxic drugs | 108 (1.5%) | 47.3 (11.6) | 41.5 (10.7) |
| Poisoning, other allergy, side effect of surgery | 55 (0.8%) | 44.3 (11.1) | 40.3 (9.3) |
| **Cancer and infrequent diseases** | **289 (4.1%)** | **42.0 (9.3)** | **40.4 (8.5)** |
| Neoplasms | 174 (2.4%) | 41.8 (11.6) | 40.7 (10.6) |
| Benign tumours | 54 (0.8%) | 44.7 (10.9) | 40.8 (10.7) |



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | |
|---|---|---|---|
| Blood diseases | 56 (0.8%) | 45.3 (11.1) | 41.2 (9.5) |
| **Skin and subcutaneous tissue diseases** | **243 (3.4%)** | **48.8 (7.8)** | **41.7 (9.6)** |
| Infections of skin and subcutaneous tissue | 55 (0.8%) | 46.1 (11.0) | 40.4 (11.3) |
| Inflammatory conditions of skin and subcutaneous tissue | 163 (2.3%) | 47.3 (9.9) | 42.2 (10.4) |
| Other diseases of skin and subcutaneous tissue | 89 (1.2%) | 49.7 (8.5) | 40.1 (11.0) |
| **Infectious diseases** | **228 (3.2%)** | **47.1 (7.6)** | **40.7 (7.1)** |
| Parasitic diseases | 76 (1.1%) | 47.1 (11.1) | 42.1 (10.7) |
| Bacterial diseases | 82 (1.1%) | 47.0 (10.0) | 39.9 (9.8) |
| Viral diseases (including HIV) | 122 (1.7%) | 46.5 (11.6) | 40.5 (10.1) |
| Fever and other physiologic disturbances of temperature regulation | 77 (1.1%) | 46.3 (10.4) | 40.1 (8.4) |

*Each condition category is non-exclusive.

Overall mean scores for PCS and MCS were 45.6 (SD = 8.8) and 41.5 (SD = 8.6), respectively. Considering PCS, scores ranged from 40.3 (SD = 11.0) for one group of unspecified musculoskeletal conditions to 50.2 (SD =11.0) for vaccinations. On the whole, musculoskeletal disorders had the lowest scores with cancer and other severe diseases category [mean PCS = 42.7 (SD = 8.4) and 42.0 (SD = 9.3), respectively], whilst skin-related diseases, preventive care consultation and infectious diseases showed the highest PCS. With regard to MCS, scores ranged from 33.0 (SD = 10.2) for depressive disorders to 45.3 for patients with fractures, sprains or dislocation. Overall, lowest scores were found amongst patients with mood and sleep disorders [mean MCS = 36.3 (SD = 8.5)], whilst injury, preventive motives and cardiovascular diseases exhibited the highest scores. Both MCS and PCS significantly decreased with increasing number of comorbidities **(Figure 1)**. For example, MCS decreased from 43.3 for patients seeking preventive care advice to 38.5 for those with 4 diagnoses or more (p for trend <0.0001) and PCS from 49.2 to 40.4 (p for trend <0.0001).

### Determinants of health related quality of life

Associations between patient characteristics and 13 broad categories of diseases are presented in **Table 3**. Low PCS was significantly associated with older age [OR =



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

2.48; 95% CI (2.08 – 2.96) for patients over 75 years as compared to adults between 18 and 44 years]. Low PCS was negatively associated with high educational attainment [OR = 0.65; 95% CI (0.59 – 0.72) for secondary school level or higher in comparison to lower educational level]; whilst low MCS scores were associated with gender [OR = 1.62; 95% CI (1.45 – 1.81) for women as compared to men], and younger age. Government funded health insurance cover was associated with both poor PCS and MCS [OR = 1.38; 95% CI (1.15 – 1.65) and OR = 1.42; 95% CI (1.19 – 1.70), respectively].

**Table 3.** Health related quality of life. SF12. Factors and 13 broad diagnoses associated to MCS and PCS below the 25th percentile (aOR and 95%CI), EPI3-LASER-2008 (weighted data).

| | Low PCS | | low MCS | |
|---|---|---|---|---|
| | **aOR*** | **95%CI** | **aOR*** | **95%CI** |
| Age (years) | | | | |
| - 18-44 | 1 | 1 | 1 | 1 |
| - 45-64 | 1.22 | 1.08-1.39 | 0.96 | 0.85-1.08 |
| - 65-74 | 1.47 | 1.25-1.73 | 0.65 | 0.55-0.78 |
| - 75 and over | 2.48 | 2.08-2.96 | 0.70 | 0.57-0.86 |
| Gender: female vs. male | 1.03 | 0.93-1.14 | 1.62 | 1.45-1.81 |
| Education: secondary school degree vs. lower diploma | 0.65 | 0.59-0.72 | 1.00 | 0.90-1.11 |
| Government funded insurance (vs. regular health insurance) | 1.38 | 1.15-1.65 | 1.42 | 1.19-1.70 |
| Diseases of the musculoskeletal system | 2.31 | 2.08-2.57 | 0.95 | 0.85-1.06 |
| Cardiovascular diseases | 1.22 | 1.08-1.38 | 0.84 | 0.73-0.96 |
| Anxiety, depression and sleep disorders | 0.99 | 0.88-1.11 | 3.58 | 3.22-3.98 |
| Diseases of the respiratory system | 1.03 | 0.91-1.18 | 0.91 | 0.80-1.04 |
| Obesity & dyslipidaemia | 0.79 | 0.67-0.94 | 0.93 | 0.78-1.11 |
| Diabetes, thyroid gland & other endocrine disorders | 1.15 | 0.97-1.35 | 1.18 | 0.99-1.41 |
| Diseases of the digestive system | 1.01 | 0.86-1.19 | 1.15 | 0.89-1.38 |
| Diseases of the genitourinary system | 0.95 | 0.76-1.19 | 1.11 | 0.89-1.38 |
| Diseases of the nervous system, head & neck | 1.24 | 1.02-1.51 | 1.07 | 0.88-1.31 |
| Skin and subcutaneous tissue diseases | 0.68 | 0.51-0.90 | 0.92 | 0.71-1.19 |
| Bacterial, viral and parasitic systemic diseases | 1.17 | 0.89-1.54 | 1.12 | 0.86-1.48 |
| Injury and poisoning | 1.88 | 1.52-2.33 | 0.80 | 0.61-1.03 |



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | | |
|---|---|---|---|---|
| Other diseases (cancer and infrequent diseases) | 1.73 | 1.38-2.16 | 1.35 | 1.06-1.72 |

Abbreviations: PCS, Physical Component Score; MCS, Mental Component Score; aOR, Odds Ratio from multivariable logistic regression models adjusted for age, gender, education level, insurance coverage, and 13 categories of diseases.

With regard to the diseases categories, musculoskeletal diseases [OR = 2.31; 95% CI (2.08 – 2.57)], injury and poisoning [OR = 1.88; 95% CI (1.52 – 2.33)], other diseases including cancer [OR = 1.73; 95% CI (1.38 – 2.16)], diseases of the nervous system, head and neck [OR = 1.24; 95% CI (1.02 – 1.51)] and cardiovascular diseases [OR = 1.22; 95% CI (1.08 – 1.38)] were significant predictors of lower PCS score, whereas the opposite was found for skin and subcutaneous tissue diseases [OR = 0.68; 95% CI (0.51 – 0.90)] or with obesity and dyslipidaemia [OR = 0.79; 95% CI (0.67 – 0.94)]. Significantly poor MCS were observed in patients suffering from anxiety, depression and sleep disorders [OR = 3.58; 95% CI (3.22 – 3.98)], and experiencing "other diseases" including cancer [OR = 1.35; 95% CI (1.06 – 1.72)]. Conversely, OR for MCS was significantly decreased for patients with cardiovascular diseases [OR= 0.84; 95% CI (0.73 – 0.96)].

## Discussion

The EPI3 Survey is, to our knowledge, the first nationwide survey in general practice to provide 100 reference figures for burden of disease assessment, combining both on-site independent recruitment of a large number of patients and additional medical information from GPs. On-site selection and recruitment by an independent investigator limited the possibility of selection bias amongst patients and the participation of physicians added high specificity to medical data collection.

There is a clear need for more data on QOL of patients.[6] In the UK, the General Practice Research Database (GPRD) assembled a very large sample of 400 surgeries



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

and 2500 individual GPs, providing detailed information on health conditions besides prescriptions, but to our knowledge not on patients QOL.[3] The Dutch national survey of general practice carried out in 1987 and 2001 gives an assessment of quality of care but only provided by the patients themselves.[2]

The EPI3 survey found similar prevalence for both diseases[10;28] and comorbidities[7;9;10;13] as in several other studies which indicate a good representativeness of our weighted sample. Musculoskeletal and psychological disorders were experienced by more than half the patients attending physicians during the course of the study and represented significant case load at GP practices. When both physical, mental status impairment and prevalence are considered, our study further highlighted the heaviest burden of musculoskeletal disorders.

With regard to physical status, the EPI3-survey showed a similar average PCS score as other primary care[7;8;10;11] or disease specific[14;15;29] surveys using the SF-12 or SF-36 questionnaires. Mean PCS were also lower than reference values computed in the French reference sample[21] and in the 2003 Household survey (JL Lanoe, unpublished data, 2003). Within practices, older age,[30-33] low education attainment and government funded insurance,[30;32;33] were associated with lower PCS. When disease categories were considered, musculoskeletal diseases were associated with the lowest PCS,[8;34;35] with PCS of similar magnitude to other European surveys including MSD patients.[29]

Regarding mental status, although socio-demographic characteristics had similar impact on MCS, the EPI3-survey showed significantly lower MCS scores than other studies in general practice.[7;8;10;11] Additional comorbidities, which were reported for half of the EPI3-survey sample, could not explain alone this difference with other



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

studies: MCS usually scored an average three points lower than those of patients with one morbidity.[16] We believe that our findings could be explained instead by different methodology: in all other studies conducted in general practice,[7;8;10;11] mostly including a small number of medical practices,[8;10;11;13] physicians may have selected participants. Our study was exempt of this bias in view of the selection of consecutive eligible patients in the GP's waiting room. In studies in which patients were interviewed for targeted mental disorders[15] or when MCS were assessed amongst patients seeking specialty care,[36;37] MCS measures were somewhat similar to ours. In the EPI3-survey, psychological and psychiatric diseases had the greatest negative impact on mental function consistent with other surveys in primary care,[7;10] but it must be appreciated that associated MCS values were more similar to those of another study conducted on patients with specific psychiatric disorders.[15] Lower MCS may thus highlight the overall burden of psychological distress and related diseases of patients seen in primary care.

**Strengths and limitations of the study**

Amongst the main strengths of our study, the unique combined data from patients and physicians allowed provision of reference figures for the vast majority of diseases encountered in primary care for a large number of patients. Quality adjusted life years (QALYs) are usually estimated for health economics and mainly derived from QOL measures assessed from EuroQoL standardised instruments (EQ5D).[1] Interestingly, the conversion of SF-12 values to EQ5D conversion has been recently documented,[38] suggesting that our results could be extended for that purpose.

Aditionally, SF-12 questionnaires have been found to provide reliable QOL measurement across studies,[22;24] even amongst patients with acute conditions.[39]



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Although its validity in older patients is moderate,[40] our sample was representative of the general population thus minimising this possible bias on our results.

At last, lack of representativeness was an important limitation in other studies.[11;41] The weighted sample of the EPI3 survey was compared to other nationwide studies and has demonstrated its efficiency through other criteria that were not used in the calibration. For instance, patients registered by health insurance as eligible to the "long-standing disease" programme accounted for 28% in the EPI3 survey which is very close to the 27% in national statistics census amongst GPs' patients.[28] Geographic, socio-demographic and practice distributions of physicians taking part in our study were similar to those found in another national GPs' survey.[26]

Our study had also some limitations. Firstly, as outlined earlier, requirement to collect very specific data was quite intrusive leading to a relatively low response rate from the general practitioners. However, stratified recruitment phases and sample sizes from both GPs and patients highly representative of national standards ensured strong external validity of the results.

Secondly, we did not include assessment of home consultations which are most common amongst GPs in France,[27] which could probably have lead to an underestimation of burden of disease. Finally, a multiplicative effect of morbidity which has been found to be associated with QOL impairment was not assessed in our study. Some authors suggested using severity scores to complement the information on morbidity.[12;13] Although these findings were supported here, it was a deliberate choice to provide an instant overview of general practice across France and the burden of a large pattern of diseases on patients' QOL as shown in previous studies which also described an independent effect of diseases on QOL.[9-11]



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## Conclusion

The EPI3 survey is the first nationwide study to report reference values for the burden of 100 different diseases in general practice, collected from a large representative sample of patients attending primary care practices. Our findings suggest that mental impairment may be underestimated in general practice. Ongoing development of healthcare policies and clinical guidelines about treatment of diseases should rely on direct assessment of QOL and morbidities in GP medical practices.

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Acknowledgments** We thank Djamila Abed, Pierre Engel and Alban Fabre for the statistical analysis and Rémy Sitta for his advice on weighting procedures.

**Funding** Laboratoires Boiron, France, sponsored this independently run study published by the authors. The sponsor had no role in the design, management, data collection, analyses, interpretation, and writing of the manuscript or the decision to publish our findings.

**Competing interests** All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf and declare that: the institution of LGB, BA, MR and LA received support from Boiron for the submitted work; FR and DG received consulting fee or honorarium from LA-SER for the submitted work; BB, FL, JM, GD, AMM have no relationships with Boiron or any other companies that might have an interest in the submitted work in the previous 3 years; LGB, BA and MR are employees of LA-SER, the company conducting the study; LA is a stockholder in LA-SER; LGB was the recipient of a research fellowship from INSERM (French National Institute of Health and Medical Research) at the time of the study. The results reported here do not include any information on pharmaceuticals.

**Authorship** The work presented here was carried out with the involvement of every author. LGB, BB, FL, FR, JM, DG, BA, GD, AMM, MR and LA conceived both the research theme and the methods, analysed the data and interpreted the results. LGB implemented the trial in France, analysed the data, and together with FL, Pierre Engel and LA drafted and revised the paper. All members of the EPI3-LASER group designed the study. Alban Fabre and Pierre Engel analysed the data. All authors have contributed to, read and approved the final manuscript. LGB is guarantor for the study.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Lamiae Grimaldi-Bensouda, Pierre Engel, France Lert and Lucien Abenhaim had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Data sharing** No additional data available.

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# References

Reference List


(1) Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. *BMJ* 2004;329:224-7. doi: 10.1136/bmj.329.7459.224

(2) Kadam UT, Croft P, Lewis M. Use of a cross-sectional survey to estimate outcome of health care: the example of anxiety and depression. *J Clin Epidemiol* 2001;54:1112-9. doi:10.1016/S0895-4356(01)00379-1

(3) Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the General Practice Research Database: a systematic review. *Br J Gen Pract* 2010;60:e128-36. doi: 10.3399/bjgp10X483562

(4) Kerek-Bodden H, Koch H, Brenner G, et al. [Diagnostic spectrum and treatment requirements of general practice clients. Results of the ADT Panel of the Central Institute of National Health Insurance Management]. *Z Arztl Fortbild Qualitatssich* 2000;94:21-30.

(5) Westert GP, Schellevis FG, de Bakker DH, et al. Monitoring health inequalities through general practice: the Second Dutch National Survey of General Practice. *Eur J Public Health* 2005;15:59-65. doi: 10.1093/eurpub/cki116

(6) Rasanen P, Roine E, Sintonen H, et al. Use of quality-adjusted life years for the estimation of effectiveness of health care: A systematic literature review. *Int J Technol Assess Health Care* 2006;22:235-41. doi: 10.1017/S0266462306051051

(7) Rijken M, van KM, Dekker J, et al. Comorbidity of chronic diseases: effects of disease pairs on physical and mental functioning. *Qual Life Res* 2005;14:45-55. doi: 10.1007/s11136-004-0616-2

(8) Wensing M, Vingerhoets E, Grol R. Functional status, health problems, age and comorbidity in primary care patients. *Qual Life Res* 2001;10:141-8. doi: 10.1023/A:1016705615207

(9) Lam CL, Lauder IJ. The impact of chronic diseases on the health-related quality of life (HRQOL) of Chinese patients in primary care. *Fam Pract* 2000;17:159-66. doi: 10.1093/fampra/17.2.159

(10) Wang HM, Beyer M, Gensichen J, et al. Health-related quality of life among general practice patients with differing chronic diseases in Germany: cross sectional survey. *BMC Public Health* 2008;8:246. doi:10.1186/1471-2458-8-246




For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

(11) Jayasinghe UW, Proudfoot J, Barton CA, et al. Quality of life of Australian chronically-ill adults: patient and practice characteristics matter. *Health Qual Life Outcomes* 2009;7:50. doi:10.1186/1477-7525-7-50

(12) Kadam UT, Schellevis FG, van der Windt DA, et al. Morbidity severity classifying routine consultations from English and Dutch general practice indicated physical health status. *J Clin Epidemiol* 2008;61:386-93. doi:10.1016/j.jclinepi.2007.05.014

(13) Fortin M, Dubois MF, Hudon C, et al. Multimorbidity and quality of life: a closer look. *Health Qual Life Outcomes* 2007;5:52. doi:10.1186/1477-7525-5-52

(14) Johnson JA, Maddigan SL. Performance of the RAND-12 and SF-12 summary scores in type 2 diabetes. *Qual Life Res* 2004;13:449-56. doi: 10.1023/B:QURE.0000018494.72748.cf

(15) Sanderson K, Andrews G. Prevalence and severity of mental health-related disability and relationship to diagnosis. *Psychiatr Serv* 2002;53:80-6.

(16) Hopman WM, Harrison MB, Coo H, at al. Associations between chronic disease, age and physical and mental health status. *Chronic Dis Can* 2009;29:108-16.

(17) Parkerson GR Jr, Michener JL, Yarnall KS, et al. Duke Case-Mix System (DUMIX) for ambulatory health care. *J Clin Epidemiol* 1997;50:1385-94. doi:10.1016/S0895-4356(97)00217-5

(18) Harrison MB, Browne GB, Roberts J, et al. Quality of life of individuals with heart failure: a randomized trial of the effectiveness of two models of hospital-to-home transition. *Med Care* 2002;40:271-82.

(19) Kind P, Dolan P, Gudex C, at al. Variations in population health status: results from a United Kingdom national questionnaire survey. *BMJ* 1998;316:736-41.

(20) Konig HH, Heider D, Lehnert T, et al. Health status of the advanced elderly in six European countries: results from a representative survey using EQ-5D and SF-12. *Health Qual Life Outcomes* 2010;8:143. doi:10.1186/1477-7525-8-143

(21) Gandek B, Ware JE, Aaronson NK, et al. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment. *J Clin Epidemiol* 1998;51:1171-8. doi:10.1016/S0895-4356(98)00109-7

(22) Organisation mondiale de la Santé. Manuel de la classification statistique internationale des maladies, traumatismes et causes de décès, fondé sur les recommandations de la Conférence pour la 9e révision, 1975. Genève, Organisation mondiale de la Santé 1977.

(23) Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220-33.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

(24) Garratt AM, Ruta DA, Abdalla MI, et al. The SF36 health survey questionnaire: an outcome measure suitable for routine use within the NHS? *BMJ* 1993;306:1440-4.

(25) Deville JC, Särndal CE. Calibration estimators in survey sampling. *J Am Stat Assoc* 1992;87:376–82.

(26) Institut de recherche et documentation en économie de la santé (IRDES). Démographie des médecins. 2008.

(27) von Elm E, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 2007;335:806-8. doi: 10.1136/bmj.39335.541782.AD

(28) Labarthe G. Les consultations et visites des médecins généralistes. Un essai de typologie. DREES Etudes et Résultats. 2004(315):1-11.

(29) Loza E, Jover JA, Rodriguez L, et al. Multimorbidity: prevalence, effect on quality of life and daily functioning, and variation of this effect when one condition is a rheumatic disease. *Semin Arthritis Rheum* 2009;38:312-9. doi:10.1016/j.semarthrit.2008.01.004

(30) Burdine JN, Felix MR, Abel AL, at al. The SF-12 as a population health measure: an exploratory examination of potential for application. *Health Serv Res* 2000;35:885-904.

(31) Fleishman JA, Lawrence WF. Demographic variation in SF-12 scores: true differences or differential item functioning? *Med Care* 2003;41(7 Suppl):III75-86.

(32) Fone D, Dunstan F, Lloyd K, et al. Does social cohesion modify the association between area income deprivation and mental health? A multilevel analysis. *Int J Epidemiol* 2007;36:338-45. doi: 10.1093/ije/dym004

(33) Wainwright NW, Surtees PG. Places, people, and their physical and mental functional health. *J Epidemiol Community Health* 2004;58:333-9. doi:10.1136/jech.2003.012518

(34) Kadam UT, Croft PR. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. *Fam Pract* 2007;24:412-9. doi: 10.1093/fampra/cmm049

(35) Antonopoulou MD, Alegakis AK, Hadjipavlou AG, et al. Studying the association between musculoskeletal disorders, quality of life and mental health. A primary care pilot study in rural Crete, Greece. *BMC Musculoskelet Disord* 2009;10:143. doi:10.1186/1471-2474-10-143

(36) Gaynes BN, Rush AJ, Trivedi MH, et al. Major depression symptoms in primary care and psychiatric care settings: a cross-sectional analysis. *Ann Fam Med* 2007;5:126-34.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

(37) McGorm K, Burton C, Weller D, et al. Patients repeatedly referred to secondary care with symptoms unexplained by organic disease: prevalence, characteristics and referral pattern. *Fam Pract* 2010;27:479-86. doi: 10.1093/fampra/cmq053

(38) Le QA, Doctor JN. Probabilistic Mapping of Descriptive Health Status Responses Onto Health State Utilities Using Bayesian Networks: An Empirical Analysis Converting SF-12 Into EQ-5D Utility Index in a National US Sample. *Med Care* 2011;49:451-60. doi: 10.1097/MLR.0b013e318207e9a8

(39) Failde I, Medina P, Ramirez C, et al. Construct and criterion validity of the SF-12 health questionnaire in patients with acute myocardial infarction and unstable angina. *J Eval Clin Pract* 2010;16:569-73. doi: 10.1111/j.1365-2753.2009.01161.x

(40) Jakobsson U, Westergren A, Lindskov S, et al. Construct validity of the SF-12 in three different samples. *J Eval Clin Pract* 2011. doi: 10.1111/j.1365-2753.2010.01623.x. [Epub ahead of print]

(41) Sprangers MA, de Regt EB, Andries F, et al. Which chronic conditions are associated with better or poorer quality of life? *J Clin Epidemiol* 2000;53:895-907. doi:10.1016/S0895-4356(00)00204-3

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

STROBE Statement—Checklist (***cross-sectional studies***): 'Benchmarking the burden of 100 diseases: results of a nationwide representative survey within general practices' by Lamiae Grimaldi-Bensouda et al.

| | Item No | Recommendation | |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | √ |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | √ |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | √ |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | √ |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | √ |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | √ |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | √ |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | √ |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | √ |
| Bias | 9 | Describe any efforts to address potential sources of bias | √ |
| Study size | 10 | Explain how the study size was arrived at | √ |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | √ |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | √ |
| | | (*b*) Describe any methods used to examine subgroups and interactions | √ |
| | | (*c*) Explain how missing data were addressed | N/A |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | N/A |
| | | (*e*) Describe any sensitivity analyses | N/A |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | √ |
| | | (b) Give reasons for non-participation at each stage | √ |
| | | (c) Consider use of a flow diagram | N/A |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | √ |
| | | (b) Indicate number of participants with missing data for each variable of interest | N/A |
| Outcome data | 15* | Report numbers of outcome events or summary measures | √ |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which | N/A |

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | |
|---|---|---|---|
| | | confounders were adjusted for and why they were included | |
| | | (*b*) Report category boundaries when continuous variables were categorized | N/A |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | N/A |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | √ |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | √ |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | √ |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | √ |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | √ |

Symbols: √, checked; N/A, not applicable.

*Give information separately for exposed and unexposed groups.

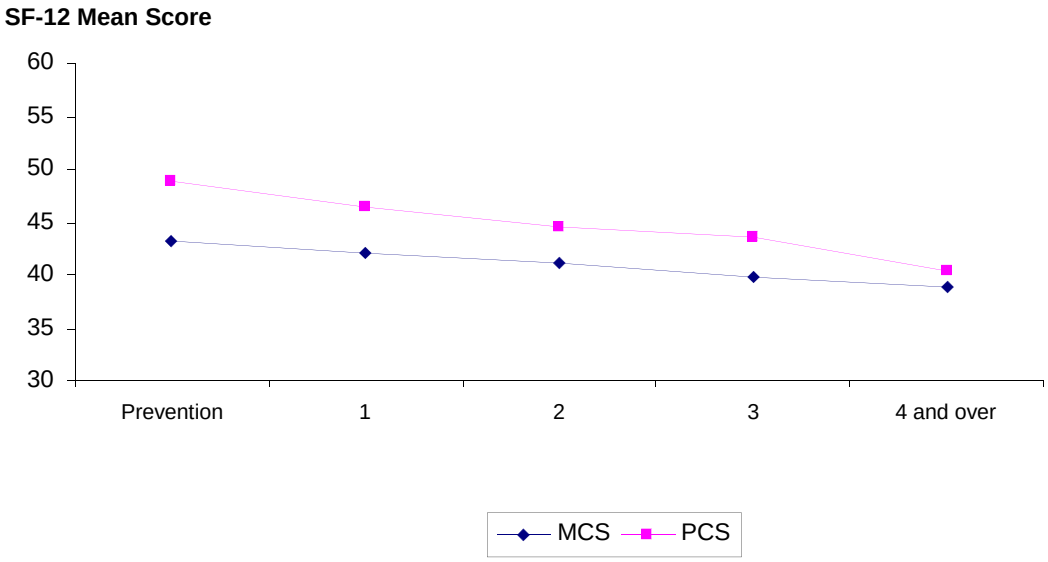
**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## SF-12 MCS and PCS according to number of comorbidities




er review only

# Benchmarking the burden of 100 diseases: results of a nationwide representative survey within general practices

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2011-000215.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 01-Sep-2011 |
| Complete List of Authors: | Grimaldi-Bensouda, Lamiae; Equipe d'accueil 'Pharmacoépidémiologie et maladies infectieuses', Institut Pasteur, and LA-SER<br>Begaud, Bernard; Université de Bordeaux, U657<br>Lert, France; Centre for Epidemiology and Population Health, INSERM U1018,<br>Rouillon, Frederic; Université Paris V René Descartes, Centre Hospitalier Sainte-Anne<br>Massol, Jacques; Université de Franche Comté, UFR de Médecine,<br>Guillemot, Didier; Institut Pasteur, and Université Paris-Ile de France Ouest<br>Avouac, Bernard; LA-SER<br>Duru, Gerard; CYKLAD GROUP<br>Magnier, Anne-Marie; Université Pierre et Marie Curie, Faculté de médecine,<br>Rossignol, Michel; Department of Epidemiology, Biostatistics and Occupational Health, McGill University, and LA-SER Centre for Risk Research<br>Abenhaim, Lucien; Department of Epidemiology, London School of Hygiene & Tropical Medicine, and LA-SER |
| Primary Subject Heading: | General practice & Family practice |
| Secondary Subject Heading: | |
| Keywords: | PRIMARY CARE, PUBLIC HEALTH, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT |
| | |

SCHOLARONE™
Manuscripts

# Benchmarking the burden of 100 diseases: results of a nationwide representative survey within general practices.

Lamiae Grimaldi-Bensouda[1], Bernard Begaud[2], France Lert[3], Frederic Rouillon[4], Jacques Massol[5], Didier Guillemot[6], Bernard Avouac[7], Gerard Duru[8], Anne-Marie Magnier[9], Michel Rossignol[10], and Lucien Abenhaim[11], for the EPI3-LA-SER group.¶

**Correspondence to:** L. Grimaldi-Bensouda LA-SER, 10 place de Catalogne, 75014 Paris, France. Email: Lamiae.Grimaldi@la-ser.com

[1]Equipe d'accueil 'Pharmacoépidémiologie et maladies infectieuses', Institut Pasteur, and LA-SER, both in Paris, France

[2] U657, Université de Bordeaux, Bordeaux, France

[3]INSERM U1018, Centre for Epidemiology and Population Health, Villejuif, France

[4]Centre Hospitalier Sainte-Anne, Université Paris V René Descartes, Paris, France

[5]UFR de Médecine, Université de Franche Comté, Besançon, France

[6]Institut Pasteur, and Université Paris-Ile de France Ouest, both in Paris, France

[7]LA-SER, Paris, France

[8]CYKLAD GROUP, Rillieux la Pape, France

[9]Faculté de médecine, Université Pierre et Marie Curie, Paris, France

[10]Department of Epidemiology, Biostatistics and Occupational Health, McGill University, and LA-SER Centre for Risk Research, both in Montreal, Canada

[11]Department of Epidemiology, London School of Hygiene & Tropical Medicine, and LA-SER, both in London, UK



For peer review only

¶**Contributing members of the EPI3-LA-SER study group are:** L. Abenhaim (UK), B. Avouac (France), B. Begaud (France), J. Bénichou (France), G. Duru (France), Pierre Engel (France), Alban Fabre (France), L. Grimaldi-Bensouda (France), F. Lert (France), A. M. Magnier (France), J. Massol (France), M. Rossignol (Canada), and F. Rouillon (France).

**Keywords**: one-day survey, cross-sectional study, morbidity, quality of life, burden of disease in general practice

**Word count =** 3677

Deleted: 3335

For peer review only

## Abstract

**Objective:** To assess the burden of diseases and quality of life (QOL) of patients for a large variety of diseases within general practice.

**Design:** A representative nationwide cross-sectional study. A total of 825 general practitioners (GPs) were randomly selected from across France. Independent investigators recruited 8559 patients attending the GPs' practices. Data on quality of life (12-Item Short Form questionnaire) and other individual characteristics were documented by the independent investigators for all participants at the waiting room. Medical information was recorded by GPs. Sampling was calibrated to national standards using the CALMAR weighting procedure. Associations of lower scores (i.e., below vs. above the first quartile) of physical and mental component scores (PCS and MCS, respectively) with main diseases and patients characteristics were estimated using multivariate logistic regression. Weighted morbidity rates, PCS and MCS were computed for 100 diagnoses using the international classification of diseases (ICD-9, 9$^{th}$ version).

**Results:** Overall mental impairment was observed amongst patients in primary care with an average MCS of 41.5 (SD = 8.6), ranging from 33.0 for depressive disorders to 45.3 for patients exhibiting fractures or sprains. Musculoskeletal diseases were found to have the most pronounced effect on impaired physical health [OR=2.31; 95% CI (2.08–2.57)] with the lowest PCS [45.6 (SD = 8.8)] and ranked first (29.0%) amongst main diagnoses experienced by patients followed by cardiovascular diseases (26.7%), and psychological disorders (22.0%). When combining both prevalence and quality of life, musculoskeletal diseases represented the heaviest burden in general practice.




For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Conclusions:** EPI3 is the first study to provide reference figures for burden of disease in general practice across a wide range of morbidities, particularly valuable for health economics and healthcare system evaluation.

## ARTICLE SUMMARY

### Article Focus

- The impact of the diseases on quality of life in general practice has been assessed so far amongst selected samples of patients, usually from studies including a limited number of medical practices and/or focusing mainly on chronic conditions.
- There is a clear need for more data on quality of life (QOL) of patients in primary care; the aim of the EPI3 survey was to provide reference figures for disease burden in this setting.

### Key messages

- The EPI3 study was a cross-sectional survey combining unique data from patients and general practitioners, and allowed provision of reference figures for the vast majority of diseases encountered in primary care for a large number of patients.
- The study highlighted the burden of musculoskeletal and psychological disorders, experienced by more than half the patients.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

- Although social and medical determinants of patients' QOL were somewhat similar than those found in previous studies in primary care, the EPI3 survey showed more pronounced mental impairment in French patients.

**Strengths and limitations of this study**

**Strengths:**

- No nationwide study on burden of disease combining both prevalence measures and QOL assessment has been conducted to date, addressing such a large variety of diseases in general practice.

- On-site selection and recruitment by an independent investigator limited the possibility of selection bias amongst patients and the participation of physicians added high specificity to medical data collection.

**Limitations:**

- Study design providing high specificity in data collection led to a relatively low response rate from GPs. However, stratified recruitment phases and sample sizes from both GPs and patients highly representative of national standards ensured strong external validity of the results.

- Home consultations, which are common amongst GPs in France, were not surveyed which could probably have led to an underestimation of burden of disease.

Deleted: most



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# INTRODUCTION

Assessing and measuring the burden of a disease in medical practice is undoubtedly important for the evaluation of medicines and healthcare.[1] To assess such burden quantitatively, both prevalence of diseases and their impact on health status and on the quality of life (QOL) of patients need to be taken into account.[2]

In primary care, the prevalence of morbidities has been shown to be remarkably similar across different industrialised countries.[3-5] However, their effect upon QOL is only partially known.[6] The impact of the diseases on QOL in general practice has been addressed so far using selected samples of patients,[7-13] usually from studies including a limited number of medical practices,[8;10;11;13] and/or mainly focused on chronic conditions.[7;9-11] To the best of our knowledge, no nationwide study of burden of disease combining both prevalence measures and QOL assessment for a large variety of diseases is currently available. To compensate for this paucity of information, some studies evaluated the impact for diseases in primary care calling upon modelling data derived from studies in medical specialties[14-16] and/or in hospital settings,[17;18] or from general population surveys.[19-21] It is not known to what extent these extrapolations are appropriate.

The aim of the EPI3 survey was to provide reference figures for disease burden in primary care. To this purpose, a representative sample of GPs was assembled through stratified sampling and data from their patients collated during a one-day survey conducted by independent interviewers in the waiting room of the participating medical practices.



For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# METHODS

## Study design, settings and population

The EPI3-survey was a nationwide, observational study of a representative sample of GPs and their patients, conducted in France between March 2007 and July 2008. Its aims were to assess the burden of diseases in general practice, considering the physicians' work activity, patients' characteristics, morbidity and prescriptions.

The sample was drawn by applying a two-stage sampling process. Firstly, GPs were randomly selected from the French national directory of physicians and invited to participate, which meant also allowing a trained research assistant to conduct a one-day survey in the waiting room at the doctor's practice. GPs' sampling was stratified according to the diversity of medicine practices in the country (conventional and complementary medicine such as homeopathy).

The second stage consisted of random one-day sampling of consultations per participating physician in order to survey all patients attending the practice on a particular day. All adult and accompanied minor patients were eligible for inclusion in the EPI3-survey to the exception of those whose health status or literacy level did not allow responding to a self-administered questionnaire. The research assistant recruited on site (i.e., in the waiting room) all consecutive eligible patients, accepting to participate to the survey up to a maximum of 15 patients. Further, each physician recorded the main reason for consultation, along with the age, gender and type of national health insurance for each patient. The maximum number of patients surveyed per day was set to allow sufficient time for optimal interviews and was followed by patients' examination by the physician.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

The EPI3-survey obtained regulatory approval by the national board of physicians ("Conseil National de l'Ordre des Médecins") and ethical approval by the French data protection authority ("Commission Nationale de l'Informatique et des Libertés"). Patients were informed by the participating physician that their responses would be kept confidential and they were not remunerated for participation. Physicians received compensation fees. The study was sponsored by a pharmaceutical company, whose name was not revealed to investigators or patients.

Deleted: They were reassured that the sponsor's name would be disclosed to them with the results.

**Data collection**

Patients were asked to self-complete a questionnaire covering demographic and social information (age, gender, educational level, employment status and occupation, smoking, alcohol intake, physical activity, height and weight for body mass index calculation), health insurance (regular national insurance, welfare health insurance for low income, with or without supplementary private insurance), the number of visits to the participating physician within the last 12 months, or, for the same period, to other GPs or medical specialists, the length and number of hospitalisations and sick leaves.

Participants were asked whether the attending physician was their regular/primary care physician. In the French health insurance system, patients have to choose a regular physician -usually a GP-, who plays a gatekeeping role for referral to specialised care. However, referral by regular GPs to other physicians is not compulsory and patients are allowed to seek care from different physicians and their different reimbursement schemes.

Deleted: Data collected from patients included age, gender, nationality (born in France or born French versus other), educational level (secondary school and higher degrees vs. less educated), type of health insurance (regular national health insurance vs. insurance for low-income people; additional private insurance vs. none), smoking status (current, past, non-smoker), alcohol intake (never, sometimes, daily), physical activity (0-30 minutes per day, 31 minutes and over), body mass index (<25; 25-30; >30 kg/m2), employment status and occupation (employed, on unemployment benefits, homemaker, retired or unemployed, student), the number of consultations to the participating physician in the last 12 months, or, for the same period, to other GPs or medical specialists, the length or number of hospitalisations and sick leaves.¶

Detailed information on physicians including age, gender, type of contract with national health insurance (regular fees, additional fees, and no contract), working days



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

and average duration of consultation were assessed by the research assistants at the time of inclusion.

GPs completed a medical questionnaire on patients including the main reason for consultation and up to five other diagnoses present that day. GPs were requested to record their prescriptions that day for diagnostic tests, drugs and referrals. Diagnoses were coded by a trained archivist using the 9th revision of the International Classification of Diseases using 100-3 digit-categories.[22]

**Health status measurement**

Amongst adult patients (18 years and over), health-related quality of life was assessed using the 12-Item Short Form questionnaire (SF-12),[23] a shortened version of the 36 short form health survey (SF-36) which has been shown to be a reliable outcome measurement tool in primary care.[24] The physical and mental component summary scores (PCS and MCS, respectively) were derived from the SF-12 questionnaire. Physical functioning (two questions), role-physical functioning (two questions), bodily pain (one question), general health (one question), vitality (one question), social functioning (one question), role-emotional functioning (two questions), and mental health (two questions), cover the same dimensions as the SF-36. The scores are standardised to population norms (based on a US norm-sample), with the mean score set at 50 (SD = 10); lower scores indicate worse-, and higher scores better health. The SF-12 has been validated for use in France, the US, the UK and many other European countries.[21]



For peer review only

### Statistical analysis

Participating and non-participating patients were compared against the collected variables on: gender, age, length of time attending the GPs' practice, type of health insurance and main reason for consultation. A weighting procedure known in demographic studies as the CALMAR procedure was applied to calibrate the final sample according to participation so that it represents closely the patients attending the practice.[25]

Participating GPs were compared to the French "Institut de recherche et documentation en économie de la santé" sample.[26] The physicians' activity-related fractions were also calibrated to the real distribution of the participating physicians across the France. All reported results were obtained after weighting was applied to GPs' patients.

In this study, we reported weighted prevalence, calculated as a percentage reported to the whole population, regardless of whether the diagnosis was isolated or associated with other diagnoses. Weighted PCS and MCS measures of the SF-12 computed according to the algorithm given by Ware et al for 100 different conditions, which were further grouped in 13 broad diseases categories plus one covering preventive motives of consultation and other medical acts.[23] Means and standard deviation (SD) were estimated for the whole adult sample and for each diagnosis. When a 3-digit category from ICD-9 had less than 30 patients, the category was grouped with one or several categories under the same heading. When grouping within the same heading was not relevant, categories with less than 30 patients were grouped in the category "other" within each main category.



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Each disease category was calculated as a percentage reported to the whole population of participating patients over the age of 18 years, regardless of whether this diagnosis was isolated or associated with others, in order to provide a complete picture of morbidity cared for in general practice.

Amongst adults over 18 years, associations of age, gender, education, type of insurance, and 13 broad disease categories with lower MCS and PCS scores (defined as below the 1st quartile with scores of 34 and 39 for MCS and PCS, respectively) were evaluated using multivariate logistic regression. Odd Ratios (OR) and 95% confidence interval (CI) are presented for each of these factors. In addition, the same analysis was conducted for the two remaining categories: pregnancy follow-up and preventive motives, which were not considered in the multivariate analysis. The association between the number of comorbidities and the two SF-12 composite scores was tested using linear regression. The possibility of a clustering effect at the practice level was tested using Generalised Estimating Equations (GEE) multivariate models. We used SAS statistical software (Version 9.1) for data analysis. The present study was reported following the STROBE statement for cross-sectional studies.[27]

## RESULTS

The sequential recruitment of physicians was done by random stratified sampling from the phone directory for GPs. Amongst the 3345 GPs initially contacted, 428 (12.8%) accepted to participate to the survey. At the end of recruitment in July 2008, an additional sample of 13 861 GPs were contacted to ensure a representative sample of GPs from all types of primary care practice in France (strictly allopaths, homeopaths, mixed practice). Despite the intrusive nature of the survey, allowing trained research assistants to collect data directly in the waiting room at the medical



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

practice on the very day of consultation, a final sample of 825 participating GPs recruited a total of 11 809 patients eligible for the present study. Of these, 174 were unaccompanied minors, 315 were not French speakers, 109 had severe psychiatric disorders, 2151 declined participation, 408 were beyond the maximum number possible to interview within the allocated time on site, and 93 had incomplete data and were excluded, allowing a total of 8559 patients for the present analysis.

### Physicians

The median age of physicians was 52 years [Interquartile range (IQR) = 33-57] and amongst them, 24% were women; 54% worked in solo medical practice, 40% with other GPs and 6% collaborated with specialists or other healthcare professionals; 31% of the GPs practised additional medical activities within hospitals, healthcare centres, the health administration or in the pharmaceutical industry. Most of the GPs (90%) hold a regular contract with the National Health Insurance organisation, whilst 9% hold a special contract allowing extra fees; a very small proportion (0.4%) had no contract. The mean daily working time at the practice (excluding home visits) was 9 hours (IQR: 2-10.5) and each of the 825 GPs participating in the study recruited on average 8.7 patients (SD = 2.2).

### Patients

Characteristics of participating (n = 8559) and non-participating patients with complete data (n = 3157) used to calibrate the sample are presented in **Table 1**. We reported here results based on the weighted characteristics. The mean age of the 8559 participating patients was 44.9 years (SD = 21.9), and 7133 (83.3%) were adults over 18. At least 44% of patients had a secondary school degree, 16% were overweight (BMI>30 kg/m$^2$) and more than 61% exercised longer than 31 minutes per day. Nine



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

out of ten patients were French born (90%), 9% were covered by a government-funded insurance for low-income people, and 90% had a private supplementary insurance. Amongst the 8559 patients, 8% attended the practice for the first time, 12% had attended it for one year or less, 27% between one and five years and 53% for 5 years or more. Over 84% of participants named the recruiting physician as their regular treating physician. About 28% of patients were registered by the national health insurance as having multiple or severe chronic diseases owing special coverage.

**Table 1.** Characteristics of non-participating and participating patients: results of the calibrated data (the EPI3 survey 2008).

| | Non-participants* (n = 3157) | Participants (n = 8559) | **Weighted percentage** |
|---|---|---|---|
| *mean (SD)* | | | |
| **Age** (years) | **47.7 (24.0)** | **43.3 (22.8)** | 44.9 (21.9) |
| *n (%)* | | | |
| **Female gender** | **1701 (53.9)** | **5367 (62.7)** | 57.9 |
| **Length of relationship with the physician** | | | |
| first time | 265 (8.4) | 782 (9.1) | 7.7 |
| less than 1 year | 316 (10.0) | 1315 (15.4) | 11.9 |
| 1-5 years | 743 (23.5) | 2380 (27.8) | 27.4 |
| More than 5 years | 1703 (53.9) | 4015 (46.9) | 53.0 |
| **Government funded health insurance** | 308 (9.8) | 621 (7.4) | 9.4 |
| **Long-standing disease status** | | 1925 (22.5) | 27.7 |
| **Complementary health insurance** | | 7839 (91.6) | 90.3 |
| **Index physician declared as treating physician** | | 6379 (74.5) | 84.3 |
| **Body Mass Index** ($kg/m^2$) | | | |
| <25 | | 5548 (64.8) | 52.4 |
| 25-30 | | 2045 (23.9) | 31.8 |
| 30 and over | | 966 (11.3) | 15.8 |
| **Tobacco consumption** | | | |
| Non smoker | | 4303 (50.3) | 47.4 |
| Past smoker | | 1961 (22.9) | 24.4 |
| Current smoker | | 2252 (26.3) | 28.2 |
| **Alcohol Consumption** | | | |
| Never | | 2908 (34.2) | 35.2 |
| Sometimes | | 4649 (54.6) | 52.5 |
| Daily | | 957 (11,2) | 12.4 |
| **Physical exercise** | | | |
| Less than 10 minutes per day | | 2235 (26.1) | 28.3 |



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | |
|---|---|---|
| 10 minutes and over | 6199 (72.4) | 71.7 |
| **Nationality** | | |
| French born subjects | 7787 (91.0) | 90.3 |
| French born abroad | 341 (4.0) | 4.7 |
| Non-French nationality | 357 (4.2) | 5.0 |
| **Educational attainment** | | |
| Secondary school degree¥*, college, university graduation | 4179 (48.8) | 44.0 |
| **Employment status** | | |
| Employed | 4544 (53.1) | 50.4 |
| On unemployment benefits | 378 (4.4) | 4.7 |
| Homemaker | 647 (7.6) | 6.6 |
| Retired and other unemployed | 2562 (29.9) | 34.3 |
| Student | 348 (4.1) | 4.1 |

*Available characteristics used for calibration
¥French baccalaureate

## Burden of one hundred diseases in primary care

Prevalence of each of the 100 and 13 broad non-exclusive diagnosis categories (a compilation of all five diagnoses recorded by the GPs) are presented in **Table 2.**

Altogether, diseases of the musculoskeletal system were the most frequently diagnosed conditions (29%), followed by cardiovascular diseases (26.7%), and sleep, anxiety and depressive disorders (22%). Preventive care consultations, vaccinations and consultation for administrative purposes accounted for 19% of the total diagnoses. Almost half the patients (49%) exhibited two or more comorbidities.

**Table 2.** Morbidity rates and SF12 mental and physical component scores according to 100 ICD diagnoses (EPI3-LASER-2008, weighted data n = 7133)

| **Diseases** | **Morbidity* n (%)** | **PCS mean (sd)** | **MCS Mean (sd)** |
|---|---|---|---|
| **All patients** | | **45.6 (8.8)** | **41.5 (8.6)** |
| **Diseases of the musculoskeletal system** | **2069 (29.0%)** | **42.7 (8.4)** | **41.6 (8.3)** |
| Osteoarthritis | 324 (4.5%) | 41.1 (10.7) | 41.7 (11.0) |
| Unspecified joint disorders | 171 (2.4%) | 42.5 (9.9) | 42.6 (10.2) |
| Intervertebral and cervical disc disorders | 276 (3.9%) | 44.0 (11.4) | 40.6 (10.3) |
| Lumbago | 360 (5.0%) | 42.1 (10.1) | 41.6 (9.4) |
| Rotator cuff syndrome of shoulder and allied disorders | 98 (1.4%) | 42.5 (10.1) | 42.0 (9.8) |
| Other affections of shoulder region | 121 (1.7%) | 42.6 (9.7) | 42.4 (9.1) |



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | |
|---|---|---|---|
| Enthesopathy of elbow region | 77 (1.1%) | 41.8 (9.3) | 43.1 (10.5) |
| Unspecified enthesopathy | 257 (3.6%) | 42.3 (10.5) | 42.1 (10.0) |
| Rheumatism, excluding the back | 112 (1.6%) | 42.9 (10.1) | 42.3 (9.8) |
| Spondylosis and other inflammatory spondylopathies | 84 (1.2%) | 42.1 (9.9) | 43.1 (8.4) |
| Sciatica | 194 (2.7%) | 42.3 (10.1) | 41.7 (9.6) |
| Pain in thoracic spine | 51 (0.7%) | 42.6 (9.8) | 41.3 (9.2) |
| Osteoporosis | 162 (2.3%) | 44.0 (10.7) | 41.9 (10.8) |
| Diseases of connective tissue | 36 (0.5%) | 45.5 (9.3) | 40.5 (10.9) |
| Unspecified back disorders | 193 (2.7%) | 42.1 (10.2) | 41.3 (9.7) |
| Other unspecified musculoskeletal disorders | 76 (1.1%) | 40.3 (11.0) | 41.7 (11.6) |
| **Hypertension, cardiovascular and circulatory diseases** | **1904 (26.7%)** | **43.7 (9.0)** | **42.5 (8.6)** |
| Hypertension | 1111 (15.6%) | 43.9 (11.3) | 42.8 (10.7) |
| Acute myocardial infarction | 84 (1.2%) | 40.8 (11.4) | 42.0 (9.4) |
| Other symptoms involving cardiovascular system | 53 (0.7%) | 46.0 (9.5) | 43.7 (8.2) |
| Angina pectoris | 66 (0.9%) | 41.8 (11.8) | 43.7 (10.5) |
| Cardiac dysrhythmias | 139 (1.9%) | 42.9 (11.5) | 42.7 (11.1) |
| Diseases of veins and lymphatics | 92 (1.3%) | 45.3 (10.5) | 41.3 (10.8) |
| Pulmonary, artery and cerebrovascular diseases | 144 (2.0%) | 42.1 (11.7) | 42.7 (10.6) |
| Other ischaemic heart diseases | 96 (1.3%) | 41.1 (11.9) | 42.1 (11.1) |
| Other diseases of the circulatory system | 229 (3.2%) | 45.3 (10.3) | 41.8 (11.0) |
| **Anxiety, depression and sleep disorders** | **1569 (22.0%)** | **44.8 (8.9)** | **36.3 (8.5)** |
| Psychotic conditions | 68 (1.0%) | 44.2 (12.6) | 37.6 (12.3) |
| Anxiety states | 420 (5.9%) | 47.8 (10.5) | 35.5 (9.7) |
| Dysrhythmia | 182 (2.6%) | 47.2 (10.2) | 35.4 (9.2) |
| Acute and chronic stress | 85 (1.2%) | 46.9 (10.6) | 36.1 (9.5) |
| Personality disorders, disturbance of conduct, dependence syndrome | 81 (1.1%) | 46.4 (10.9) | 38.8 (11.2) |
| Eating disorders, tics, stuttering and other syndromes | 277 (3.9%) | 47.4 (10.4) | 37.1 (10.7) |
| Depressive disorders | 497 (7.0%) | 45.3 (11.4) | 33.0 (10.2) |
| Malaise and fatigue | 114 (1.6%) | 45.4 (11.1) | 38.7 (9.7) |
| Sleep disorders | 87 (1.2%) | 46.1 (10.7) | 38.5 (9.4) |
| Nervousness, cachexia and unspecified psychological distress | 30 (0.4%) | 41.9 (13.5) | 39.9 (12.8) |
| Dizziness and giddiness | 59 (0.8%) | 46.3 (9.8) | 40.2 (10.4) |
| Other general symptoms | 75 (5.8%) | 46.0 (11.1) | 39.2 (10.4) |
| **Diseases of the respiratory system** | **1419 (19.9%)** | **46.3 (8.5)** | **41.9 (8.4)** |
| Acute nasopharyngitis | 306 (4.3%) | 48.2 (9.8) | 41.6 (9.7) |
| Acute pharyngitis | 60 (0.8%) | 49.3 (10.4) | 42.5 (10.5) |
| Acute tracheitis | 120 (1.7%) | 48.4 (10.1) | 41.4 (10.4) |
| Acute bronchitis or other upper respiratory infections | 66 (0.2%) | 41.9 (12.3) | 43.0 (8.0) |
| Chronic nasopharyngitis | 52 (0.3%) | 50.0 (8.1) | 42.9 (8.7) |
| Chronic sinusitis and laryngitis | 126 (1.7%) | 48.0 (9.9) | 40.3 (8.9) |
| Allergic rhinitis | 124 (1.7%) | 47.5 (10.7) | 42.3 (9.6) |
| Pneumonia and influenza | 53 (0.6%) | 46.8 (10.2) | 41.1 (10.8) |
| Chronic obstructive pulmonary diseases (except asthma) | 160 (2.2%) | 44.8 (10.4) | 41.2 (10.0) |
| Asthma | 148 (2.1%) | 44.0 (11.5) | 41.4 (10.5) |



For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | |
|---|---|---|---|
| Lung diseases | 64 (0.9%) | 41.0 (12.3) | 42.0 (9.5) |
| Other diseases of the respiratory system | 210 (2.9%) | 45.1 (11.6) | 42.4 (10.4) |
| **Medical exams, preventive motives** | **1101 (15.4%)** | **47.4 (9.2)** | **42.4 (10.1)** |
| Medical exam: handicap influencing health status | 41 (0.6%) | 45.9 (9.4) | 39.4 (12.6) |
| Medical exam: aftercare and specific procedures | 285 (4.0%) | 45.9 (11.6) | 41.2 (10.8) |
| Medical exam for health check-up | 286 (4.0%) | 46.9 (11.3) | 43.1 (10.8) |
| Laboratories findings | 53 (0.7%) | 48.5 (9.8) | 42.9 (10.9) |
| Vaccination | 121 (1.7%) | 50.2 (11.0) | 42.6 (10.5) |
| Pregnancy follow-up | 122 (1.7%) | 47.4 (11.8) | 41.8 (10.4) |
| Administrative purposes | 380 (5.3%) | 47.2 (11.7) | 42.5 (9.9) |
| **Diabetes, thyroid gland & other endocrine disorders** | **785 (11.0%)** | **43.9 (8.6)** | **41.5 (8.1)** |
| Hypothyroidism | 187 (2.6%) | 45.3 (11.0) | 39.6 (10.9) |
| Goitre | 45 (0.6%) | 46.5 (9.3) | 41.3 (9.8) |
| Diabetes mellitus | 312 (4.4%) | 42.9 (11.2) | 42.0 (10.5) |
| Diseases of other endocrine glands | 78 (1.1%) | 43.9 (11.9) | 41.0 (10.8) |
| Other thyroid disorders | 52 (0.7%) | 45.7 (10.8) | 40.0 (10.1) |
| **Obesity & dyslipidaemia** | **742 (10.4%)** | **45.2 (9.1)** | **42.0 (8.9)** |
| Hypercholesterolaemia | 266 (3.7%) | 45.1 (10.9) | 42.6 (10.2) |
| Unspecified disorder of lipoid metabolism | 135 (1.9%) | 45.5 (10.5) | 42.8 (9.2) |
| Overweight, obesity and other hyperalimentation | 169 (2.4%) | 47.6 (11.4) | 40.2 (10.4) |
| Other hyperlipidaemia | 105 (1.1%) | 45.6 (11.3) | 42.4 (10.6) |
| Other symptoms concerning nutrition, metabolism and development | 70 (1.0%) | 48.6 (10.1) | 40.3 (10.4) |
| **Diseases of the digestive system** | **742 (10.4%)** | **45.9 (8.4)** | **39.9 (8.4)** |
| Oesophageal diseases | 81 (1.1%) | 44.3 (10.3) | 41.5 (9.8) |
| Diseases of stomach | 121 (1.7%) | 45.6 (10.0) | 40.1 (9.7) |
| Diseases of intestines and peritoneum | 72 (1.0%) | 45.1 (10.1) | 40.2 (9.9) |
| Symptoms involving the abdomen | 161 (2.3%) | 46.9 (10.4) | 39.9 (11.0) |
| Non-infectious enteritis and colitis | 105 (1.5%) | 47.5 (9.5) | 41.8 (9.9) |
| Diseases of oral cavity, salivary glands and jaws | 39 (0.5%) | 49.0 (8.8) | 40.3 (10.0) |
| Appendicitis and hernia | 43 (0.6%) | 44.1 (10.6) | 40.0 (10.2) |
| Other diseases of the digestive system | 144 (2.0%) | 44.8 (10.8) | 39.7 (9.9) |
| **Diseases of the nervous system, head & neck** | **449 (6.3%)** | **43.3 (9.4)** | **39.6 (9.1)** |
| Disorders of central nervous system | 95 (1.3%) | 41.3 (13.6) | 42.2 (11.2) |
| Migraine | 114 (1.6%) | 46.6 (10.2) | 39.7 (10.1) |
| Symptoms involving head & neck | 96 (1.3%) | 46.3 (10.8) | 40.8 (10.2) |
| Diseases of the eye | 54 (0.7%) | 51.8 (9.9) | 37.4 (10.6) |
| Diseases of the ear and mastoid processes | 112 (1.6%) | 46.9 (10.8) | 41.6 (11.0) |
| Other disorders of nervous system and sense organs | 145 (2.0%) | 44.6 (10.3) | 39.9 (10.6) |
| **Diseases of the genitourinary system** | **400 (5.6%)** | **45.5 (9.6)** | **41.5 (8.9)** |
| Cystitis | 115 (1.6%) | 47.9 (11.5) | 40.3 (10.2) |
| Diseases of male genital organs | 85 (1.2%) | 46.0 (10.9) | 43.0 (11.0) |
| Diseases of female genital organs | 139 (1.9%) | 48.4 (11.3) | 39.8 (10.8) |
| Nephrosis and nephritis | 86 (1.2%) | 44.8 (11.6) | 41.7 (10.6) |
| Complications of pregnancy, congenital anomalies | 42 (0.6%) | 43.5 (12.8) | 40.4 (10.5) |



For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | |
|---|---|---|---|
| **Injury and poisoning** | **342 (4.8%)** | **43.5 (9.2)** | **43.5 (8.3)** |
| Fractures, sprains and dislocations | 103 (1.4%) | 41.9 (10.5) | 45.3 (9.7) |
| Traumas and injuries to organs | 54 (0.8%) | 44.3 (12.9) | 44.1 (11.4) |
| Burns, amputations | 62 (0.9%) | 44.4 (11.6) | 43.1 (10.4) |
| Intoxications, allergies to toxic drugs | 108 (1.5%) | 47.3 (11.6) | 41.5 (10.7) |
| Poisoning, other allergy, side effect of surgery | 55 (0.8%) | 44.3 (11.1) | 40.3 (9.3) |
| **Cancer and infrequent diseases** | **289 (4.1%)** | **42.0 (9.3)** | **40.4 (8.5)** |
| Neoplasms | 174 (2.4%) | 41.8 (11.6) | 40.7 (10.6) |
| Benign tumours | 54 (0.8%) | 44.7 (10.9) | 40.8 (10.7) |
| Blood diseases | 56 (0.8%) | 45.3 (11.1) | 41.2 (9.5) |
| **Skin and subcutaneous tissue diseases** | **243 (3.4%)** | **48.8 (7.8)** | **41.7 (9.6)** |
| Infections of skin and subcutaneous tissue | 55 (0.8%) | 46.1 (11.0) | 40.4 (11.3) |
| Inflammatory conditions of skin and subcutaneous tissue | 163 (2.3%) | 47.3 (9.9) | 42.2 (10.4) |
| Other diseases of skin and subcutaneous tissue | 89 (1.2%) | 49.7 (8.5) | 40.1 (11.0) |
| **Infectious diseases** | **228 (3.2%)** | **47.1 (7.6)** | **40.7 (7.1)** |
| Parasitic diseases | 76 (1.1%) | 47.1 (11.1) | 42.1 (10.7) |
| Bacterial diseases | 82 (1.1%) | 47.0 (10.0) | 39.9 (9.8) |
| Viral diseases (including HIV) | 122 (1.7%) | 46.5 (11.6) | 40.5 (10.1) |
| Fever and other physiologic disturbances of temperature regulation | 77 (1.1%) | 46.3 (10.4) | 40.1 (8.4) |

*Each condition category is non-exclusive.

Overall mean scores for PCS and MCS were 45.6 (SD = 8.8) and 41.5 (SD = 8.6), respectively. Considering PCS, scores ranged from 40.3 (SD = 11.0) for one group of unspecified musculoskeletal conditions to 50.2 (SD =11.0) for vaccinations. On the whole, musculoskeletal disorders had the lowest scores with cancer and other severe diseases category, whilst skin-related diseases, preventive care consultation and infectious diseases showed the highest PCS. With regard to MCS, scores ranged from 33.0 (SD = 10.2) for depressive disorders to 45.3 for patients with fractures, sprains or dislocation. Overall, lowest scores were found amongst patients with mood and sleep disorders, whilst injury, preventive motives and cardiovascular diseases exhibited the highest scores. Both MCS and PCS significantly decreased with increasing number of comorbidities (**Figure 1**). For example, MCS decreased from 43.3 for patients seeking preventive care advice to 38.5 for those with 4 diagnoses or more (p for trend <0.0001) and PCS from 49.2 to 40.4 (p for trend <0.0001).

**Deleted:** [mean PCS = 42.7 (SD = 8.4) and 42.0 (SD = 9.3), respectively]

**Deleted:** [mean MCS = 36.3 (SD = 8.5)]



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Determinants of health related quality of life**

Associations between patient characteristics and 13 broad categories of diseases are presented in **Table 3**. Low PCS was significantly associated with older age [OR = 2.48; 95% CI (2.08 – 2.96) for patients over 75 years as compared to adults between 18 and 44 years]. Low PCS was negatively associated with high educational attainment [OR = 0.65; 95% CI (0.59 – 0.72) for secondary school level or higher in comparison to lower educational level]; whilst low MCS scores were associated with gender [OR = 1.62; 95% CI (1.45 – 1.81) for women as compared to men], and younger age. Government funded health insurance cover was associated with both poor PCS and MCS [OR = 1.38; 95% CI (1.15 – 1.65) and OR = 1.42; 95% CI (1.19 – 1.70), respectively].

**Table 3.** Health related quality of life. SF12. Factors and 13 broad diagnoses associated to MCS and PCS below the 25th percentile (aOR and 95%CI), EPI3-LASER-2008 (weighted data).

| | Low PCS | | low MCS | |
|---|---|---|---|---|
| | **aOR*** | **95%CI** | **aOR*** | **95%CI** |
| Age (years) | | | | |
| - 18-44 | 1 | 1 | 1 | 1 |
| - 45-64 | 1.22 | 1.08-1.39 | 0.96 | 0.85-1.08 |
| - 65-74 | 1.47 | 1.25-1.73 | 0.65 | 0.55-0.78 |
| - 75 and over | 2.48 | 2.08-2.96 | 0.70 | 0.57-0.86 |
| Gender: female vs. male | 1.03 | 0.93-1.14 | 1.62 | 1.45-1.81 |
| Education: secondary school degree vs. lower diploma | 0.65 | 0.59-0.72 | 1.00 | 0.90-1.11 |
| Government funded insurance (vs. regular health insurance) | 1.38 | 1.15-1.65 | 1.42 | 1.19-1.70 |
| Diseases of the musculoskeletal system | 2.31 | 2.08-2.57 | 0.95 | 0.85-1.06 |
| Cardiovascular diseases | 1.22 | 1.08-1.38 | 0.84 | 0.73-0.96 |
| Anxiety, depression and sleep disorders | 0.99 | 0.88-1.11 | 3.58 | 3.22-3.98 |
| Diseases of the respiratory system | 1.03 | 0.91-1.18 | 0.91 | 0.80-1.04 |
| Obesity & dyslipidaemia | 0.79 | 0.67-0.94 | 0.93 | 0.78-1.11 |
| Diabetes, thyroid gland & other endocrine disorders | 1.15 | 0.97-1.35 | 1.18 | 0.99-1.41 |



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | | |
|---|---|---|---|---|
| Diseases of the digestive system | 1.01 | 0.86-1.19 | 1.15 | 0.89-1.38 |
| Diseases of the genitourinary system | 0.95 | 0.76-1.19 | 1.11 | 0.89-1.38 |
| Diseases of the nervous system, head & neck | 1.24 | 1.02-1.51 | 1.07 | 0.88-1.31 |
| Skin and subcutaneous tissue diseases | 0.68 | 0.51-0.90 | 0.92 | 0.71-1.19 |
| Bacterial, viral and parasitic systemic diseases | 1.17 | 0.89-1.54 | 1.12 | 0.86-1.48 |
| Injury and poisoning | 1.88 | 1.52-2.33 | 0.80 | 0.61-1.03 |
| Other diseases (cancer and infrequent diseases) | 1.73 | 1.38-2.16 | 1.35 | 1.06-1.72 |

Abbreviations: PCS, Physical Component Score; MCS, Mental Component Score; aOR, Odds Ratio from multivariable logistic regression models adjusted for age, gender, education level, insurance coverage, and 13 categories of diseases.

With regard to the diseases categories, musculoskeletal diseases [OR = 2.31; 95% CI (2.08 – 2.57)], injury and poisoning [OR = 1.88; 95% CI (1.52 – 2.33)], other diseases including cancer [OR = 1.73; 95% CI (1.38 – 2.16)], diseases of the nervous system, head and neck [OR = 1.24; 95% CI (1.02 – 1.51)] and cardiovascular diseases [OR = 1.22; 95% CI (1.08 – 1.38)] were significant predictors of lower PCS score, whereas the opposite was found for skin and subcutaneous tissue diseases [OR = 0.68; 95% CI (0.51 – 0.90)] or with obesity and dyslipidaemia [OR = 0.79; 95% CI (0.67 – 0.94)]. Significantly poor MCS were observed in patients suffering from anxiety, depression and sleep disorders [OR = 3.58; 95% CI (3.22 – 3.98)], and experiencing "other diseases" including cancer [OR = 1.35; 95% CI (1.06 – 1.72)]. Conversely, OR for MCS was significantly decreased for patients with cardiovascular diseases [OR= 0.84; 95% CI (0.73 – 0.96)]. Testing the effect of clustering at the practice level yielded similar results, but to ensure parsimony of the generated models it was decided not to report such effects.

## Discussion

The EPI3 Survey is, to our knowledge, the first nationwide survey in general practice to provide 100 reference figures for burden of disease assessment, combining both on-site independent recruitment of a large number of patients and additional medical



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

information from GPs. On-site selection and recruitment by an independent investigator limited the possibility of selection bias amongst patients and the participation of physicians added high specificity to medical data collection.

There is a clear need for more data on QOL of patients.[6] In the UK, the General Practice Research Database (GPRD) assembled a very large sample of 400 surgeries and 2500 individual GPs, providing detailed information on health conditions besides prescriptions, but to our knowledge not on patients QOL.[3] The Dutch national survey of general practice carried out in 1987 and 2001 gives an assessment of quality of care but only provided by the patients themselves.[2]

The EPI3 survey found similar prevalence for both diseases[10;28] and comorbidities[7;9;10;13] as in several other studies which indicate a good representativeness of our weighted sample. Musculoskeletal and psychological disorders were experienced by more than half the patients attending physicians during the course of the study and represented significant case load at GP practices. When both physical, mental status impairment and prevalence are considered, our study further highlighted the heaviest burden of musculoskeletal disorders.

With regard to physical status, the EPI3-survey showed a similar average PCS score as other primary care[7;8;10;11] or disease specific[14;15;29] surveys using the SF-12 or SF-36 questionnaires. Mean PCS were lower than reference values computed in the French reference sample[21] and in the 2003 Household survey (JL Lanoe, unpublished data, 2003). Within practices, older age,[30-33] low education attainment and government funded insurance,[30;32;33] were associated with lower PCS. When disease categories were considered, musculoskeletal diseases were associated with the

Deleted: also



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

lowest PCS,[8;34;35] with PCS of similar magnitude to other European surveys including MSD patients.[29]

Regarding mental status, although socio-demographic characteristics had similar impact on MCS, the EPI3-survey showed significantly lower MCS scores than other studies in general practice.[7;8;10;11] Additional comorbidities, which were reported for half of the EPI3-survey sample, could not explain alone this difference with other studies: MCS usually scored an average three points lower than those of patients with one morbidity.[16] We believe that our findings could be explained instead by different methodology: in all other studies conducted in general practice,[7;8;10;11] mostly including a small number of medical practices,[8;10;11;13] physicians may have selected participants. Our study was exempt of this bias in view of the selection of consecutive eligible patients in the GP's waiting room. In studies in which patients were interviewed for targeted mental disorders[15] or when MCS were assessed amongst patients seeking specialty care,[36;37] MCS measures were somewhat similar to ours. In the EPI3-survey, psychological and psychiatric diseases had the greatest negative impact on mental function consistent with other surveys in primary care.[7,10] It must be appreciated that associated MCS values were more similar to those of another study conducted on patients with specific psychiatric disorders.[15] Lower MCS may thus highlight the overall burden of psychological distress and related diseases of patients seen in primary care.

Deleted: ,[

Deleted: but

## Strengths and limitations of the study

Amongst the main strengths of our study, the unique combined data from patients and physicians allowed provision of reference figures for the vast majority of diseases encountered in primary care for a large number of patients. Quality adjusted life years



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

(QALYs) are usually estimated for health economics and mainly derived from QOL measures assessed from EuroQoL standardised instruments (EQ5D).[1] Interestingly, the conversion of SF-12 values into EQ5D Utility values has been recently documented,[38] suggesting that our results could be extended for that purpose as previously reported.[39]

Aditionally, SF-12 questionnaires have been found to provide reliable QOL measurement across studies,[22;24] even amongst patients with acute conditions.[40] Although its validity in older patients is moderate,[41] our sample was representative of the general population thus minimising this possible bias on our results.

At last, lack of representativeness was an important limitation in other studies.[11;42] The sample size of physicians participating in the EPI3-survey is within the range established for other French surveys (from 100 to 1006).[26] Physicians were randomly selected from the national telephone directory, which includes general practitioners currently practising in primary care. This was preferred to professional registries of physicians, which lists all registered GPs, regardless of whether they are currently practising or not.

The weighted geographical distribution of the 825 GPs participating in the survey was similar to the national distribution of GPs in private practice across the 22 French regions surveyed and the distribution of physicians' individual characteristics regarding age, gender, type of contract with national health insurance, and type of practice differed only slightly from national statistics:[26] female participation was slightly lower (23.5% compared to 26% in the IRDES sample), but the distribution between sectors was similar (8.9% vs. 8.5% in sectors 1 and 2, respectively).

Deleted: conversion

Deleted: 39

Deleted: 40

Deleted: 11;41



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

In terms of representativeness of the patients, the calibrated sample of the EPI3 survey was compared to other nationwide studies and has demonstrated its efficiency through other criteria that were not used in the calibration.[28] For instance, patients registered by health insurance as eligible to the "long-standing disease" programme accounted for 28% in the EPI3 survey, which is very close to the 27% in national census amongst GP patients.[28]Our study had also some limitations. Firstly, as outlined earlier, requirement to collect very specific data was quite intrusive leading to a relatively low response rate from the general practitioners. However, stratified recruitment phases and sample sizes from both GPs and patients highly representative of national standards ensured strong external validity of the results. Secondly, we did not include assessment of home consultations, common amongst GPs in France,[27] which could probably have lead to an underestimation of burden of disease. Finally, a multiplicative effect of morbidity which has been found to be associated with QOL impairment was not assessed in our study. Some authors suggested using severity scores to complement the information on morbidity,[12;13] and assess the impact of multimorbidity, which have already been tackled here but will be object of further development in future research within the EPI3 research project. It was a deliberate choice to provide an instant overview of general practice across France and the burden of a large pattern of diseases on patients' QOL as shown in previous studies which also described an independent effect of diseases on QOL.[9-11]

Deleted: The weighted

Deleted: statistics

Deleted: s'

Deleted: Geographic, socio-demographic and practice distributions of physicians taking part in our study were similar to those found in another national GPs' survey.[26]¶

Deleted: which are most

Deleted: .[

Deleted: Although these findings were supported here

Deleted: , i

## Conclusion

The EPI3 survey is the first nationwide study to report reference values for the burden of 100 different diseases in general practice, collected from a large representative sample of patients attending primary care practices. Our findings suggest that mental



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

impairment may be underestimated in general practice. Ongoing development of healthcare policies and clinical guidelines about treatment of diseases should rely on direct assessment of QOL and morbidities in GP medical practices.

GPs foster continuous care, sometimes requiring highly specialised therapy to deal with comorbidities and complex situations. The present study shows that the burden of diseases in primary care is not only high but can also be diverse. The EPI3 survey provides information on the overall burden of diseases in general practice along with quality of life of patients regarding comorbidities as seen in this healthcare setting. This information is of great value to public health and economic assessment of healthcare, at a time when quality of life is becoming a prevalent factor for care delivery and the development of clinical practice guidelines.

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Acknowledgments** We thank Djamila Abed, Pierre Engel and Alban Fabre for the statistical analysis and Rémy Sitta for his advice on weighting procedures.

**Funding** Laboratoires Boiron, France, sponsored this independently run study published by the authors. The sponsor had no role in the design, management, data collection, analyses, interpretation, and writing of the manuscript or the decision to publish our findings.

**Competing interests** All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf and declare that: the institution of LGB, BA, MR and LA received support from Boiron for the submitted work; FR and DG received consulting fee or honorarium from LA-SER for the submitted work; BB, FL, JM, GD, AMM have no relationships with Boiron or any other companies that might have an interest in the submitted work in the previous 3 years; LGB, BA and MR are employees of LA-SER, the company conducting the study; LA is a stockholder in LA-SER; LGB was the recipient of a research fellowship from INSERM (French National Institute of Health and Medical Research) at the time of the study. The results reported here do not include any information on pharmaceuticals.

**Authorship** The work presented here was carried out with the involvement of every author. LGB, BB, FL, FR, JM, DG, BA, GD, AMM, MR and LA conceived both the research theme and the methods, analysed the data and interpreted the results. LGB implemented the trial in France, analysed the data, and together with FL, Pierre Engel and LA drafted and revised the paper. All members of the EPI3-LASER group designed the study. Alban Fabre and Pierre Engel analysed the data. All authors have contributed to, read and approved the final manuscript. LGB is guarantor for the study.



For peer review only

Lamiae Grimaldi-Bensouda, Pierre Engel, France Lert and Lucien Abenhaim had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Data sharing** No additional data available.

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## References


1. Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. BMJ 2004;329:224-7. doi: 10.1136/bmj.329.7459.224
2. Kadam UT, Croft P, Lewis M. Use of a cross-sectional survey to estimate outcome of health care: the example of anxiety and depression. J Clin Epidemiol 2001;54:1112-9. doi:10.1016/S0895-4356(01)00379-1
3. Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the General Practice Research Database: a systematic review. Br J Gen Pract 2010;60:e128-36. doi: 10.3399/bjgp10X483562
4. Kerek-Bodden H, Koch H, Brenner G, et al. [Diagnostic spectrum and treatment requirements of general practice clients. Results of the ADT Panel of the Central Institute of National Health Insurance Management]. Z Arztl Fortbild Qualitatssich 2000;94:21-30.
5. Westert GP, Schellevis FG, de Bakker DH, et al. Monitoring health inequalities through general practice: the Second Dutch National Survey of General Practice. Eur J Public Health 2005;15:59-65. doi: 10.1093/eurpub/cki116
6. Rasanen P, Roine E, Sintonen H, et al. Use of quality-adjusted life years for the estimation of effectiveness of health care: A systematic literature review. Int J Technol Assess Health Care 2006;22:235-41. doi: 10.1017/S0266462306051051
7. Rijken M, van KM, Dekker J, et al. Comorbidity of chronic diseases: effects of disease pairs on physical and mental functioning. Qual Life Res 2005;14:45-55. doi: 10.1007/s11136-004-0616-2




For peer review only

8. Wensing M, Vingerhoets E, Grol R. Functional status, health problems, age and comorbidity in primary care patients. Qual Life Res 2001;10:141-8. doi: 10.1023/A:1016705615207
9. Lam CL, Lauder IJ. The impact of chronic diseases on the health-related quality of life (HRQOL) of Chinese patients in primary care. Fam Pract 2000;17:159-66. doi: 10.1093/fampra/17.2.159
10. Wang HM, Beyer M, Gensichen J, et al. Health-related quality of life among general practice patients with differing chronic diseases in Germany: cross sectional survey. BMC Public Health 2008;8:246. doi:10.1186/1471-2458-8-246
11. Jayasinghe UW, Proudfoot J, Barton CA, et al. Quality of life of Australian chronically-ill adults: patient and practice characteristics matter. Health Qual Life Outcomes 2009;7:50. doi:10.1186/1477-7525-7-50
12. Kadam UT, Schellevis FG, van der Windt DA, et al. Morbidity severity classifying routine consultations from English and Dutch general practice indicated physical health status. J Clin Epidemiol 2008;61:386-93. doi:10.1016/j.jclinepi.2007.05.014
13. Fortin M, Dubois MF, Hudon C, et al. Multimorbidity and quality of life: a closer look. Health Qual Life Outcomes 2007;5:52. doi:10.1186/1477-7525-5-52
14. Johnson JA, Maddigan SL. Performance of the RAND-12 and SF-12 summary scores in type 2 diabetes. Qual Life Res 2004;13:449-56. doi: 10.1023/B:QURE.0000018494.72748.cf
15. Sanderson K, Andrews G. Prevalence and severity of mental health-related disability and relationship to diagnosis. Psychiatr Serv 2002;53:80-6.



For peer review only

16. Hopman WM, Harrison MB, Coo H, et al. Associations between chronic disease, age and physical and mental health status. Chronic Dis Can 2009;29:108-16.

17. Parkerson GR Jr, Michener JL, Yarnall KS, et al. Duke Case-Mix System (DUMIX) for ambulatory health care. J Clin Epidemiol 1997;50:1385-94. doi:10.1016/S0895-4356(97)00217-5

18. Harrison MB, Browne GB, Roberts J, et al. Quality of life of individuals with heart failure: a randomized trial of the effectiveness of two models of hospital-to-home transition. Med Care 2002;40:271-82.

19. Kind P, Dolan P, Gudex C, et al. Variations in population health status: results from a United Kingdom national questionnaire survey. BMJ 1998;316:736-41.

20. Konig HH, Heider D, Lehnert T, et al. Health status of the advanced elderly in six European countries: results from a representative survey using EQ-5D and SF-12. Health Qual Life Outcomes 2010;8:143. doi:10.1186/1477-7525-8-143

21. Gandek B, Ware JE, Aaronson NK, et al. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998;51:1171-8. doi:10.1016/S0895-4356(98)00109-7

22. Organisation mondiale de la Santé. Manuel de la classification statistique internationale des maladies, traumatismes et causes de décès, fondé sur les recommandations de la Conférence pour la 9e révision, 1975. Genève, Organisation mondiale de la Santé 1977.

23. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34:220-33.



For peer review only

24. Garratt AM, Ruta DA, Abdalla MI, et al. The SF36 health survey questionnaire: an outcome measure suitable for routine use within the NHS? BMJ 1993;306:1440-4.
25. Deville JC, Särndal CE. Calibration estimators in survey sampling. J Am Stat Assoc 1992;87:376–82.
26. Institut de recherche et documentation en économie de la santé (IRDES). Démographie des médecins. 2008.
27. von Elm E, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 2007;335:806-8. doi: 10.1136/bmj.39335.541782.AD
28. Labarthe G. Les consultations et visites des médecins généralistes. Un essai de typologie. DREES Etudes et Résultats. 2004(315):1-11.
29. Loza E, Jover JA, Rodriguez L, et al. Multimorbidity: prevalence, effect on quality of life and daily functioning, and variation of this effect when one condition is a rheumatic disease. Semin Arthritis Rheum 2009;38:312-9. doi:10.1016/j.semarthrit.2008.01.004
30. Burdine JN, Felix MR, Abel AL, et al. The SF-12 as a population health measure: an exploratory examination of potential for application. Health Serv Res 2000;35:885-904.
31. Fleishman JA, Lawrence WF. Demographic variation in SF-12 scores: true differences or differential item functioning? Med Care 2003;41(7 Suppl):III75-86.



For peer review only

32. Fone D, Dunstan F, Lloyd K, et al. Does social cohesion modify the association between area income deprivation and mental health? A multilevel analysis. Int J Epidemiol 2007;36:338-45. doi: 10.1093/ije/dym004

33. Wainwright NW, Surtees PG. Places, people, and their physical and mental functional health. J Epidemiol Community Health 2004;58:333-9. doi:10.1136/jech.2003.012518

34. Kadam UT, Croft PR. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. Fam Pract 2007;24:412-9. doi: 10.1093/fampra/cmm049

35. Antonopoulou MD, Alegakis AK, Hadjipavlou AG, et al. Studying the association between musculoskeletal disorders, quality of life and mental health. A primary care pilot study in rural Crete, Greece. BMC Musculoskelet Disord 2009;10:143. doi:10.1186/1471-2474-10-143

36. Gaynes BN, Rush AJ, Trivedi MH, et al. Major depression symptoms in primary care and psychiatric care settings: a cross-sectional analysis. Ann Fam Med 2007;5:126-34.

37. McGorm K, Burton C, Weller D, et al. Patients repeatedly referred to secondary care with symptoms unexplained by organic disease: prevalence, characteristics and referral pattern. Fam Pract 2010;27:479-86. doi: 10.1093/fampra/cmq053

38. Le QA, Doctor JN. Probabilistic mapping of descriptive health status responses onto health state utilities using Bayesian networks: an empirical analysis converting SF-12 into EQ-5D utility index in a national US sample. Med Care 2011; 49:451-60. doi: 10.1097/MLR.0b013e318207e9a8



For peer review only

39. Brazier JE, Roberts J. The estimation of a preference-based measure of health from the SF-12. Med Care 2004;42:851-9.

40. Failde I, Medina P, Ramirez C, et al. Construct and criterion validity of the SF-12 health questionnaire in patients with acute myocardial infarction and unstable angina. J Eval Clin Pract 2010;16:569-73. doi: 10.1111/j.1365-2753.2009.01161.x

41. Jakobsson U, Westergren A, Lindskov S, et al. Construct validity of the SF-12 in three different samples. J Eval Clin Pract 2011. doi: 10.1111/j.1365-2753.2010.01623.x. [Epub ahead of print]

42. Sprangers MA, de Regt EB, Andries F, et al. Which chronic conditions are associated with better or poorer quality of life? J Clin Epidemiol 2000;53:895-907. doi:10.1016/S0895-4356(00)00204-3

For peer review only

STROBE Statement—Checklist (***cross-sectional studies***): 'Benchmarking the burden of 100 diseases: results of a nationwide representative survey within general practices' by Lamiae Grimaldi-Bensouda et al.

| | Item No | Recommendation | |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | √ |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | √ |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | √ |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | √ |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | √ |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | √ |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | √ |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | √ |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | √ |
| Bias | 9 | Describe any efforts to address potential sources of bias | √ |
| Study size | 10 | Explain how the study size was arrived at | √ |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | √ |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | √ |
| | | (*b*) Describe any methods used to examine subgroups and interactions | √ |
| | | (*c*) Explain how missing data were addressed | N/A |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | N/A |
| | | (*e*) Describe any sensitivity analyses | N/A |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | √ |
| | | (b) Give reasons for non-participation at each stage | √ |
| | | (c) Consider use of a flow diagram | N/A |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | √ |
| | | (b) Indicate number of participants with missing data for each variable of interest | N/A |
| Outcome data | 15* | Report numbers of outcome events or summary measures | √ |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which | N/A |

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

| | | | |
|---|---|---|---|
| | | confounders were adjusted for and why they were included | |
| | | (*b*) Report category boundaries when continuous variables were categorized | N/A |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | N/A |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | √ |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | √ |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | √ |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | √ |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | √ |

Symbols: √, checked; N/A, not applicable.

*Give information separately for exposed and unexposed groups.

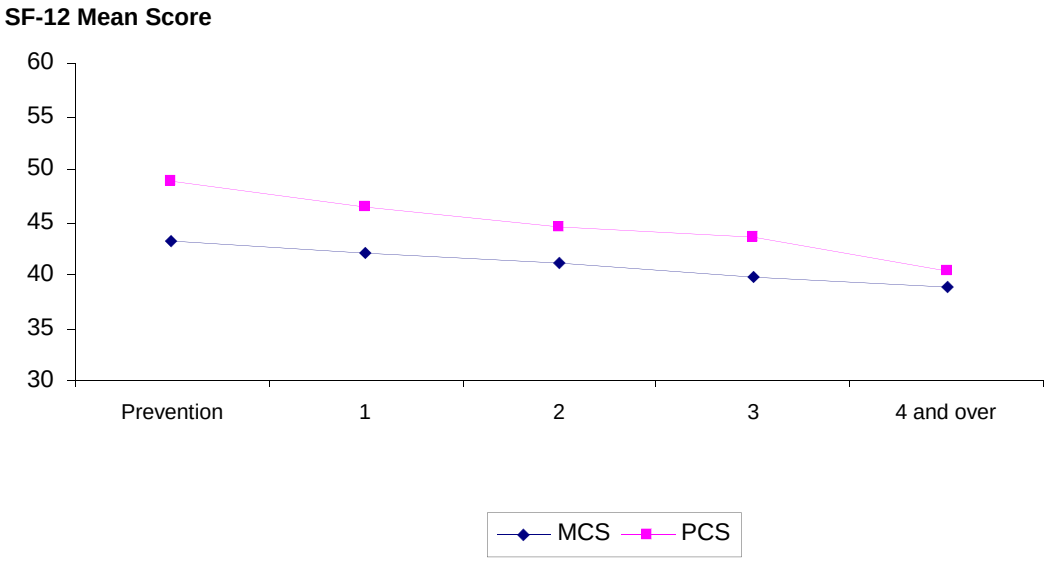
**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only



For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## SF-12 MCS and PCS according to number of comorbidities




er review only