



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

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

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11 disease in general practice  
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## 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<sup>th</sup> 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.

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3 **Conclusions:** EPI3 is the first study to provide reference figures for burden of disease  
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5 in general practice across a wide range of morbidities, particularly valuable for health  
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7 economics and healthcare system evaluation.  
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## 10 11 **ARTICLE SUMMARY**

### 12 13 14 **Article Focus**

- 15  
16 • The impact of the diseases on quality of life in general practice has been  
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18 assessed so far amongst selected samples of patients, usually from studies  
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20 including a limited number of medical practices and/or focusing mainly on  
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22 chronic conditions.  
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- 25  
26 • There is a clear need for more data on quality of life (QOL) of patients in  
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28 primary care; the aim of the EPI3 survey was to provide reference figures for  
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30 disease burden in this setting.  
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### 37 38 **Key messages**

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

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12 **Strengths and limitations of this study**

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15 **Strengths:**

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- 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.

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36 **Limitations:**

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- 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.

## 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.

## 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.



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

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26 Data collected from patients included age, gender, nationality (born in France or born  
27 French versus other), educational level (secondary school and higher degrees vs. less  
28 educated), type of health insurance (regular national health insurance vs. insurance for  
29 low-income people; additional private insurance vs. none), smoking status (current,  
30 past, non-smoker), alcohol intake (never, sometimes, daily), physical activity (0-30  
31 minutes per day, 31 minutes and over), body mass index (<25; 25-30; >30 kg/m<sup>2</sup>),  
32 employment status and occupation (employed, on unemployment benefits,  
33 homemaker, retired or unemployed, student), the number of consultations to the  
34 participating physician in the last 12 months, or, for the same period, to other GPs or  
35 medical specialists, the length or number of hospitalisations and sick leaves.  
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51 Participants were asked whether the attending physician was their regular/primary  
52 care physician. In the French health insurance system, patients have to choose a  
53 regular physician -usually a GP-, who plays a gatekeeping role for referral to  
54 specialised care. However, referral by regular GPs to other physicians is not  
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3 compulsory and patients are allowed to seek care from different physicians and their  
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5 different reimbursement schemes.  
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9 Detailed information on physicians including age, gender, type of contract with  
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11 national health insurance (regular fees, additional fees, and no contract), working days  
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13 and average duration of consultation were assessed by the research assistants at the  
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15 time of inclusion.  
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19 GPs completed a medical questionnaire on patients including the main reason for  
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21 consultation and up to five other diagnoses present that day. GPs were requested to  
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23 record their prescriptions that day for diagnostic tests, drugs and referrals. Diagnoses  
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25 were coded by a trained archivist using the 9<sup>th</sup> revision of the International  
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27 Classification of Diseases using 100-3 digit-categories.[22]  
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### 30 31 32 **Health status measurement** 33

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35 Amongst adult patients (18 years and over), health-related quality of life was assessed  
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37 using the 12-Item Short Form questionnaire (SF-12),[23] a shortened version of the  
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39 36 short form health survey (SF-36) which has been shown to be a reliable outcome  
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41 measurement tool in primary care.[24] The physical and mental component summary  
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43 scores (PCS and MCS, respectively) were derived from the SF-12 questionnaire.  
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45 Physical functioning (two questions), role-physical functioning (two questions),  
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47 bodily pain (one question), general health (one question), vitality (one question),  
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49 social functioning (one question), role-emotional functioning (two questions), and  
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51 mental health (two questions), cover the same dimensions as the SF-36. The scores  
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53 are standardised to population norms (based on a US norm-sample), with the mean  
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55 score set at 50 (SD = 10); lower scores indicate worse-, and higher scores better  
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3 health. The SF-12 has been validated for use in France, the US, the UK and many  
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5 other European countries.[21]  
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### 8 9 **Statistical analysis**

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12 Participating and non-participating patients were compared against the collected  
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14 variables on: gender, age, length of time attending the GPs' practice, type of health  
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16 insurance and main reason for consultation. A weighting procedure known in  
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18 demographic studies as the CALMAR procedure was applied to calibrate the final  
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20 sample according to participation so that it represents closely the patients attending  
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22 the practice.[25]  
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28 Participating GPs were compared to the French "Institut de recherche et  
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30 documentation en économie de la santé" sample.[26] The physicians' activity-related  
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32 fractions were also calibrated to the real distribution of the participating physicians  
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34 across the France. All reported results were obtained after weighting was applied to  
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36 GPs' patients.  
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41 In this study, we reported weighted prevalence, PCS and MCS measures of the SF-12  
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43 computed according to the algorithm given by Ware et al for 100 different conditions,  
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45 which were further grouped in 13 broad diseases categories plus one covering  
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47 preventive motives of consultation and other medical acts.[23] Means and standard  
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49 deviation (SD) were estimated for the whole adult sample and for each diagnosis.  
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52 When a 3-digit category from ICD-9 had less than 30 patients, the category was  
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54 grouped with one or several categories under the same heading. When grouping  
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56 within the same heading was not relevant, categories with less than 30 patients were  
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58 grouped in the category "other" within each main category.  
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3 Each disease category was calculated as a percentage reported to the whole population  
4 of participating patients over the age of 18 years, regardless of whether this diagnosis  
5 was isolated or associated with others, in order to provide a complete picture of  
6 morbidity cared for in general practice.  
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13 Amongst adults over 18 years, associations of age, gender, education, type of  
14 insurance, and 13 broad disease categories with lower MCS and PCS scores (defined  
15 as below the 1<sup>st</sup> quartile with scores of 34 and 39 for MCS and PCS, respectively)  
16 were evaluated using multivariate logistic regression. Odd Ratios (OR) and 95%  
17 confidence interval (CI) are presented for each of these factors. In addition, the same  
18 analysis was conducted for the two remaining categories: pregnancy follow-up and  
19 preventive motives, which were not considered in the multivariate analysis. The  
20 association between the number of comorbidities and the two SF-12 composite scores  
21 was tested using linear regression. We used SAS statistical software (Version 9.1) for  
22 data analysis. The present study was reported following the STROBE statement for  
23 cross-sectional studies.[27]  
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## 40 41 **RESULTS**

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45 The sequential recruitment of physicians was done by random stratified sampling  
46 from the phone directory for GPs. Amongst the 3345 GPs initially contacted, 428  
47 (12.8%) accepted to participate to the survey. At the end of recruitment in July 2008,  
48 a final sample of 825 participating GPs recruited a total of 11 809 patients eligible for  
49 the present study. Of these, 174 were unaccompanied minors, 315 were not French  
50 speakers, 109 had severe psychiatric disorders, 2151 declined participation, 408 were  
51 beyond the maximum number possible to interview within the allocated time on site,  
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3 and 93 had incomplete data and were excluded, allowing a total of 8559 patients for  
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6 the present analysis.  
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## 8 9 **Physicians**

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12 The median age of physicians was 52 years [Interquartile range (IQR) = 33-57] and  
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14 amongst them, 24% were women; 54% worked in solo medical practice, 40% with  
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16 other GPs and 6% collaborated with specialists or other healthcare professionals; 31%  
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18 of the GPs practised additional medical activities within hospitals, healthcare centres,  
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20 the health administration or in the pharmaceutical industry. Most of the GPs (90%)  
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22 hold a regular contract with the National Health Insurance organisation, whilst 9%  
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24 hold a special contract allowing extra fees; a very small proportion (0.4%) had no  
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26 contract. The mean daily working time at the practice (excluding home visits) was 9  
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29 hours (IQR: 2-10.5).  
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## 33 34 **Patients**

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37 Characteristics of participating (n = 8559) and non-participating patients with  
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39 complete data (n = 3157) used to calibrate the sample are presented in **Table 1**. We  
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41 reported here results based on the weighted characteristics. The mean age of the 8559  
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43 participating patients was 44.9 years (SD = 21.9), and 7133 (83.3%) were adults over  
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45 18. At least 44% of patients had a secondary school degree, 16% were overweight  
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47 (BMI>30 kg/m<sup>2</sup>) and more than 61% exercised longer than 31 minutes per day. Nine  
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49 out of ten patients were French born (90%), 9% were covered by a government-  
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51 funded insurance for low-income people, and 90% had a private supplementary  
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53 insurance. Amongst the 8559 patients, 8% attended the practice for the first time, 12%  
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55 had attended it for one year or less, 27% between one and five years and 53% for 5  
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57 years or more. Over 84% of participants named the recruiting physician as their  
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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
<i>mean (SD)</i>			
<b>Age (years)</b>	<b>47.7 (24.0)</b>	<b>43.3 (22.8)</b>	44.9 (21.9)
<i>n (%)</i>			
<b>Female gender</b>	<b>1701 (53.9)</b>	<b>5367 (62.7)</b>	57.9
<b>Length of relationship with the physician</b>			
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
<b>Government funded health insurance</b>	308 (9.8)	621 (7.4)	9.4
<b>Long-standing disease status</b>		1925 (22.5)	27.7
<b>Complementary health insurance</b>		7839 (91.6)	90.3
<b>Index physician declared as treating physician</b>		6379 (74.5)	84.3
<b>Body Mass Index (kg/m<sup>2</sup>)</b>			
<25		5548 (64.8)	52.4
25-30		2045 (23.9)	31.8
30 and over		966 (11.3)	15.8
<b>Tobacco consumption</b>			
Non smoker		4303 (50.3)	47.4
Past smoker		1961 (22.9)	24.4
Current smoker		2252 (26.3)	28.2
<b>Alcohol Consumption</b>			
Never		2908 (34.2)	35.2
Sometimes		4649 (54.6)	52.5
Daily		957 (11.2)	12.4
<b>Physical exercise</b>			
Less than 10 minutes per day		2235 (26.1)	28.3
10 minutes and over		6199 (72.4)	71.7
<b>Nationality</b>			
French born subjects		7787 (91.0)	90.3
French born abroad		341 (4.0)	4.7
Non-French nationality		357 (4.2)	5.0
<b>Educational attainment</b>			
Secondary school degree*, college, university graduation		4179 (48.8)	44.0
<b>Employment status</b>			
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 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)
<b>All patients</b>		<b>45.6 (8.8)</b>	<b>41.5 (8.6)</b>
<b>Diseases of the musculoskeletal system</b>	<b>2069 (29.0%)</b>	<b>42.7 (8.4)</b>	<b>41.6 (8.3)</b>
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)

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4	Other unspecified musculoskeletal disorders	76 (1.1%)	40.3 (11.0)	41.7 (11.6)
5	<b>Hypertension, cardiovascular and circulatory diseases</b>	<b>1904 (26.7%)</b>	<b>43.7 (9.0)</b>	<b>42.5 (8.6)</b>
6	Hypertension	1111 (15.6%)	43.9 (11.3)	42.8 (10.7)
7	Acute myocardial infarction	84 (1.2%)	40.8 (11.4)	42.0 (9.4)
8	Other symptoms involving cardiovascular system	53 (0.7%)	46.0 (9.5)	43.7 (8.2)
9	Angina pectoris	66 (0.9%)	41.8 (11.8)	43.7 (10.5)
10	Cardiac dysrhythmias	139 (1.9%)	42.9 (11.5)	42.7 (11.1)
11	Diseases of veins and lymphatics	92 (1.3%)	45.3 (10.5)	41.3 (10.8)
12	Pulmonary, artery and cerebrovascular diseases	144 (2.0%)	42.1 (11.7)	42.7 (10.6)
13	Other ischaemic heart diseases	96 (1.3%)	41.1 (11.9)	42.1 (11.1)
14	Other diseases of the circulatory system	229 (3.2%)	45.3 (10.3)	41.8 (11.0)
15				
16				
17	<b>Anxiety, depression and sleep disorders</b>	<b>1569 (22.0%)</b>	<b>44.8 (8.9)</b>	<b>36.3 (8.5)</b>
18	Psychotic conditions	68 (1.0%)	44.2 (12.6)	37.6 (12.3)
19	Anxiety states	420 (5.9%)	47.8 (10.5)	35.5 (9.7)
20	Dysrhythmia	182 (2.6%)	47.2 (10.2)	35.4 (9.2)
21	Acute and chronic stress	85 (1.2%)	46.9 (10.6)	36.1 (9.5)
22	Personality disorders, disturbance of conduct, dependence syndrome	81 (1.1%)	46.4 (10.9)	38.8 (11.2)
23	Eating disorders, tics, stuttering and other syndromes	277 (3.9%)	47.4 (10.4)	37.1 (10.7)
24	Depressive disorders	497 (7.0%)	45.3 (11.4)	33.0 (10.2)
25	Malaise and fatigue	114 (1.6%)	45.4 (11.1)	38.7 (9.7)
26	Sleep disorders	87 (1.2%)	46.1 (10.7)	38.5 (9.4)
27	Nervousness, cachexia and unspecified psychological distress	30 (0.4%)	41.9 (13.5)	39.9 (12.8)
28	Dizziness and giddiness	59 (0.8%)	46.3 (9.8)	40.2 (10.4)
29	Other general symptoms	75 (5.8%)	46.0 (11.1)	39.2 (10.4)
30				
31	<b>Diseases of the respiratory system</b>	<b>1419 (19.9%)</b>	<b>46.3 (8.5)</b>	<b>41.9 (8.4)</b>
32	Acute nasopharyngitis	306 (4.3%)	48.2 (9.8)	41.6 (9.7)
33	Acute pharyngitis	60 (0.8%)	49.3 (10.4)	42.5 (10.5)
34	Acute tracheitis	120 (1.7%)	48.4 (10.1)	41.4 (10.4)
35	Acute bronchitis or other upper respiratory infections	66 (0.2%)	41.9 (12.3)	43.0 (8.0)
36	Chronic nasopharyngitis	52 (0.3%)	50.0 (8.1)	42.9 (8.7)
37	Chronic sinusitis and laryngitis	126 (1.7%)	48.0 (9.9)	40.3 (8.9)
38	Allergic rhinitis	124 (1.7%)	47.5 (10.7)	42.3 (9.6)
39	Pneumonia and influenza	53 (0.6%)	46.8 (10.2)	41.1 (10.8)
40	Chronic obstructive pulmonary diseases (except asthma)	160 (2.2%)	44.8 (10.4)	41.2 (10.0)
41	Asthma	148 (2.1%)	44.0 (11.5)	41.4 (10.5)
42	Lung diseases	64 (0.9%)	41.0 (12.3)	42.0 (9.5)
43	Other diseases of the respiratory system	210 (2.9%)	45.1 (11.6)	42.4 (10.4)
44				
45	<b>Medical exams, preventive motives</b>	<b>1101 (15.4%)</b>	<b>47.4 (9.2)</b>	<b>42.4 (10.1)</b>
46	Medical exam: handicap influencing health status	41 (0.6%)	45.9 (9.4)	39.4 (12.6)
47	Medical exam: aftercare and specific procedures	285 (4.0%)	45.9 (11.6)	41.2 (10.8)
48	Medical exam for health check-up	286 (4.0%)	46.9 (11.3)	43.1 (10.8)
49	Laboratories findings	53 (0.7%)	48.5 (9.8)	42.9 (10.9)
50	Vaccination	121 (1.7%)	50.2 (11.0)	42.6 (10.5)
51	Pregnancy follow-up	122 (1.7%)	47.4 (11.8)	41.8 (10.4)



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4	Administrative purposes	380 (5.3%)	47.2 (11.7)	42.5 (9.9)
5	<b>Diabetes, thyroid gland &amp; other endocrine disorders</b>	<b>785 (11.0%)</b>	<b>43.9 (8.6)</b>	<b>41.5 (8.1)</b>
6	Hypothyroidism	187 (2.6%)	45.3 (11.0)	39.6 (10.9)
7	Goitre	45 (0.6%)	46.5 (9.3)	41.3 (9.8)
8	Diabetes mellitus	312 (4.4%)	42.9 (11.2)	42.0 (10.5)
9	Diseases of other endocrine glands	78 (1.1%)	43.9 (11.9)	41.0 (10.8)
10	Other thyroid disorders	52 (0.7%)	45.7 (10.8)	40.0 (10.1)
11				
12				
13	<b>Obesity &amp; dyslipidaemia</b>	<b>742 (10.4%)</b>	<b>45.2 (9.1)</b>	<b>42.0 (8.9)</b>
14	Hypercholesterolaemia	266 (3.7%)	45.1 (10.9)	42.6 (10.2)
15	Unspecified disorder of lipid metabolism	135 (1.9%)	45.5 (10.5)	42.8 (9.2)
16	Overweight, obesity and other hyperalimantation	169 (2.4%)	47.6 (11.4)	40.2 (10.4)
17	Other hyperlipidaemia	105 (1.1%)	45.6 (11.3)	42.4 (10.6)
18	Other symptoms concerning nutrition, metabolism and development	70 (1.0%)	48.6 (10.1)	40.3 (10.4)
19				
20				
21	<b>Diseases of the digestive system</b>	<b>742 (10.4%)</b>	<b>45.9 (8.4)</b>	<b>39.9 (8.4)</b>
22	Oesophageal diseases	81 (1.1%)	44.3 (10.3)	41.5 (9.8)
23	Diseases of stomach	121 (1.7%)	45.6 (10.0)	40.1 (9.7)
24	Diseases of intestines and peritoneum	72 (1.0%)	45.1 (10.1)	40.2 (9.9)
25	Symptoms involving the abdomen	161 (2.3%)	46.9 (10.4)	39.9 (11.0)
26	Non-infectious enteritis and colitis	105 (1.5%)	47.5 (9.5)	41.8 (9.9)
27	Diseases of oral cavity, salivary glands and jaws	39 (0.5%)	49.0 (8.8)	40.3 (10.0)
28	Appendicitis and hernia	43 (0.6%)	44.1 (10.6)	40.0 (10.2)
29	Other diseases of the digestive system	144 (2.0%)	44.8 (10.8)	39.7 (9.9)
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32				
33	<b>Diseases of the nervous system, head &amp; neck</b>	<b>449 (6.3%)</b>	<b>43.3 (9.4)</b>	<b>39.6 (9.1)</b>
34	Disorders of central nervous system	95 (1.3%)	41.3 (13.6)	42.2 (11.2)
35	Migraine	114 (1.6%)	46.6 (10.2)	39.7 (10.1)
36	Symptoms involving head & neck	96 (1.3%)	46.3 (10.8)	40.8 (10.2)
37	Diseases of the eye	54 (0.7%)	51.8 (9.9)	37.4 (10.6)
38	Diseases of the ear and mastoid processes	112 (1.6%)	46.9 (10.8)	41.6 (11.0)
39	Other disorders of nervous system and sense organs	145 (2.0%)	44.6 (10.3)	39.9 (10.6)
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42				
43	<b>Diseases of the genitourinary system</b>	<b>400 (5.6%)</b>	<b>45.5 (9.6)</b>	<b>41.5 (8.9)</b>
44	Cystitis	115 (1.6%)	47.9 (11.5)	40.3 (10.2)
45	Diseases of male genital organs	85 (1.2%)	46.0 (10.9)	43.0 (11.0)
46	Diseases of female genital organs	139 (1.9%)	48.4 (11.3)	39.8 (10.8)
47	Nephrosis and nephritis	86 (1.2%)	44.8 (11.6)	41.7 (10.6)
48	Complications of pregnancy, congenital anomalies	42 (0.6%)	43.5 (12.8)	40.4 (10.5)
49				
50				
51	<b>Injury and poisoning</b>	<b>342 (4.8%)</b>	<b>43.5 (9.2)</b>	<b>43.5 (8.3)</b>
52	Fractures, sprains and dislocations	103 (1.4%)	41.9 (10.5)	45.3 (9.7)
53	Traumas and injuries to organs	54 (0.8%)	44.3 (12.9)	44.1 (11.4)
54	Burns, amputations	62 (0.9%)	44.4 (11.6)	43.1 (10.4)
55	Intoxications, allergies to toxic drugs	108 (1.5%)	47.3 (11.6)	41.5 (10.7)
56	Poisoning, other allergy, side effect of surgery	55 (0.8%)	44.3 (11.1)	40.3 (9.3)
57				
58				
59	<b>Cancer and infrequent diseases</b>	<b>289 (4.1%)</b>	<b>42.0 (9.3)</b>	<b>40.4 (8.5)</b>
60	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)
<b>Skin and subcutaneous tissue diseases</b>	<b>243 (3.4%)</b>	<b>48.8 (7.8)</b>	<b>41.7 (9.6)</b>
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)
<b>Infectious diseases</b>	<b>228 (3.2%)</b>	<b>47.1 (7.6)</b>	<b>40.7 (7.1)</b>
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 =

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

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

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3 and 2500 individual GPs, providing detailed information on health conditions besides  
4 prescriptions, but to our knowledge not on patients QOL.[3] The Dutch national  
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6 survey of general practice carried out in 1987 and 2001 gives an assessment of quality  
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8 of care but only provided by the patients themselves.[2]  
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13 The EPI3 survey found similar prevalence for both diseases[10;28] and  
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15 comorbidities[7;9;10;13] as in several other studies which indicate a good  
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17 representativeness of our weighted sample. Musculoskeletal and psychological  
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19 disorders were experienced by more than half the patients attending physicians during  
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21 the course of the study and represented significant case load at GP practices. When  
22  
23 both physical, mental status impairment and prevalence are considered, our study  
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25 further highlighted the heaviest burden of musculoskeletal disorders.  
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31 With regard to physical status, the EPI3-survey showed a similar average PCS score  
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33 as other primary care[7;8;10;11] or disease specific[14;15;29] surveys using the SF-  
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35 12 or SF-36 questionnaires. Mean PCS were also lower than reference values  
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37 computed in the French reference sample[21] and in the 2003 Household survey (JL  
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39 Lanoe, unpublished data, 2003). Within practices, older age,[30-33] low education  
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41 attainment and government funded insurance,[30;32;33] were associated with lower  
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43 PCS. When disease categories were considered, musculoskeletal diseases were  
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45 associated with the lowest PCS,[8;34;35] with PCS of similar magnitude to other  
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47 European surveys including MSD patients.[29]  
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53 Regarding mental status, although socio-demographic characteristics had similar  
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55 impact on MCS, the EPI3-survey showed significantly lower MCS scores than other  
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57 studies in general practice.[7;8;10;11] Additional comorbidities, which were reported  
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59 for half of the EPI3-survey sample, could not explain alone this difference with other  
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3 studies: MCS usually scored an average three points lower than those of patients with  
4 one morbidity.[16] We believe that our findings could be explained instead by  
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6 different methodology: in all other studies conducted in general practice,[7;8;10;11]  
7  
8 mostly including a small number of medical practices,[8;10;11;13] physicians may  
9  
10 have selected participants. Our study was exempt of this bias in view of the selection  
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12 of consecutive eligible patients in the GP's waiting room. In studies in which patients  
13  
14 were interviewed for targeted mental disorders[15] or when MCS were assessed  
15  
16 amongst patients seeking specialty care,[36;37] MCS measures were somewhat  
17  
18 similar to ours. In the EPI3-survey, psychological and psychiatric diseases had the  
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20 greatest negative impact on mental function consistent with other surveys in primary  
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22 care,[7;10] but it must be appreciated that associated MCS values were more similar  
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24 to those of another study conducted on patients with specific psychiatric  
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26 disorders.[15] Lower MCS may thus highlight the overall burden of psychological  
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28 distress and related diseases of patients seen in primary care.  
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### 37 **Strengths and limitations of the study**

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40 Amongst the main strengths of our study, the unique combined data from patients and  
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42 physicians allowed provision of reference figures for the vast majority of diseases  
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44 encountered in primary care for a large number of patients. Quality adjusted life years  
45  
46 (QALYs) are usually estimated for health economics and mainly derived from QOL  
47  
48 measures assessed from EuroQoL standardised instruments (EQ5D).[1] Interestingly,  
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50 the conversion of SF-12 values to EQ5D conversion has been recently  
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52 documented,[38] suggesting that our results could be extended for that purpose.  
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58 Additionally, SF-12 questionnaires have been found to provide reliable QOL  
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60 measurement across studies,[22;24] even amongst patients with acute conditions.[39]

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3 Although its validity in older patients is moderate,[40] our sample was representative  
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5 of the general population thus minimising this possible bias on our results.  
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9 At last, lack of representativeness was an important limitation in other studies.[11;41]

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11 The weighted sample of the EPI3 survey was compared to other nationwide studies  
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13 and has demonstrated its efficiency through other criteria that were not used in the  
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15 calibration. For instance, patients registered by health insurance as eligible to the  
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17 “long-standing disease” programme accounted for 28% in the EPI3 survey which is  
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19 very close to the 27% in national statistics census amongst GPs’ patients.[28]  
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23 Geographic, socio-demographic and practice distributions of physicians taking part in  
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25 our study were similar to those found in another national GPs’ survey.[26]  
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29 Our study had also some limitations. Firstly, as outlined earlier, requirement to collect  
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31 very specific data was quite intrusive leading to a relatively low response rate from  
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33 the general practitioners. However, stratified recruitment phases and sample sizes  
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35 from both GPs and patients highly representative of national standards ensured strong  
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37 external validity of the results.  
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41 Secondly, we did not include assessment of home consultations which are most  
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43 common amongst GPs in France,[27] which could probably have lead to an  
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45 underestimation of burden of disease. Finally, a multiplicative effect of morbidity  
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47 which has been found to be associated with QOL impairment was not assessed in our  
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49 study. Some authors suggested using severity scores to complement the information  
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51 on morbidity.[12;13] Although these findings were supported here, it was a deliberate  
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53 choice to provide an instant overview of general practice across France and the  
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55 burden of a large pattern of diseases on patients’ QOL as shown in previous studies  
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57 which also described an independent effect of diseases on QOL.[9-11]  
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## 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.



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21  
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37  
38 results reported here do not include any information on pharmaceuticals.  
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46  
47 author. LGB, BB, FL, FR, JM, DG, BA, GD, AMM, MR and LA conceived both the  
48  
49 research theme and the methods, analysed the data and interpreted the results. LGB  
50  
51 implemented the trial in France, analysed the data, and together with FL, Pierre Engel  
52  
53 and LA drafted and revised the paper. All members of the EPI3-LASER group  
54  
55 designed the study. Alban Fabre and Pierre Engel analysed the data. All authors have  
56  
57 contributed to, read and approved the final manuscript. LGB is guarantor for the  
58  
59 study.  
60

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2  
3 Lamiae Grimaldi-Bensouda, Pierre Engel, France Lert and Lucien Abenhaim had full  
4  
5 access to all of the data in the study and take responsibility for the integrity of the data  
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8 and the accuracy of the data analysis.  
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11 **Data sharing** No additional data available.  
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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	
<b>Title and abstract</b>	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	✓
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
<b>Methods</b>			
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
<b>Results</b>			
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

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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
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### Discussion

Key results	18	Summarise key results with reference to study objectives	✓
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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	✓
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Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
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Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
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### 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	✓
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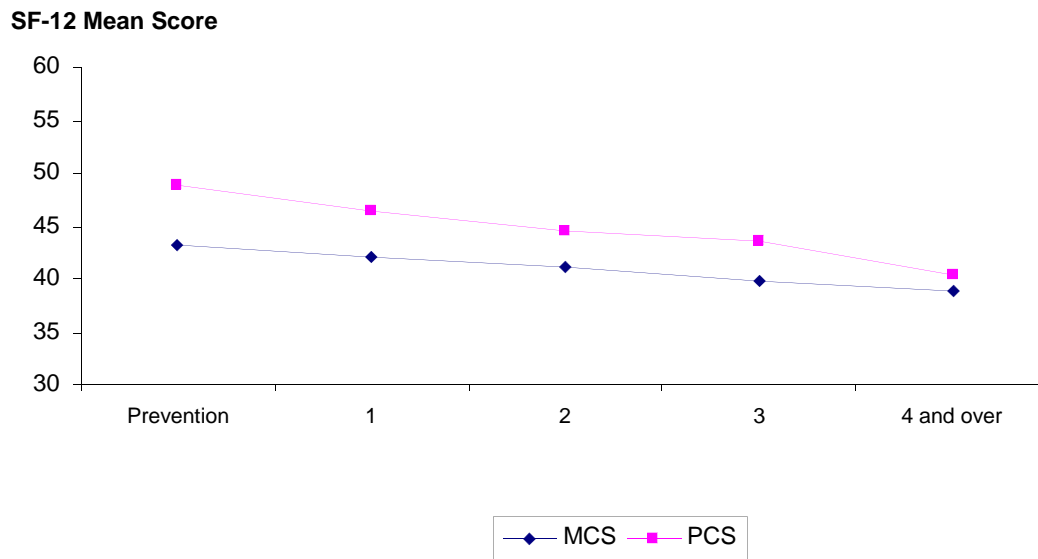
Symbols: ✓, checked; N/A, not applicable.

\*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](http://www.strobe-statement.org).



SF-12 MCS and PCS according to number of comorbidities



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

Journal:	<i>BMJ Open</i>
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Article Type:	Research
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<b>Primary Subject Heading</b>:	General practice & Family practice
Secondary Subject Heading:	
Keywords:	PRIMARY CARE, PUBLIC HEALTH, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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1 **Benchmarking the burden of 100 diseases: results of**  
2 **a nationwide representative survey within general**  
3 **practices.**

4 Lamiae Grimaldi-Bensouda<sup>1</sup>, Bernard Begaud<sup>2</sup>, France Lert<sup>3</sup>, Frederic Rouillon<sup>4</sup>,  
5 Jacques Massol<sup>5</sup>, Didier Guillemot<sup>6</sup>, Bernard Avouac<sup>7</sup>, Gerard Duru<sup>8</sup>, Anne-Marie  
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5 (France), Pierre Engel (France), Alban Fabre (France), L. Grimaldi-Bensouda  
6 (France), F. Lert (France), A. M. Magnier (France), J. Massol (France), M. Rossignol  
7 (France), F. Lert (France), A. M. Magnier (France), J. Massol (France), M. Rossignol  
8 (Canada), and F. Rouillon (France).  
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12 **Keywords:** one-day survey, cross-sectional study, morbidity, quality of life, burden of  
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15 disease in general practice

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17 **Word count =** 3677

Deleted: 3335

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2 31 **Abstract**  
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5 32 **Objective:** To assess the burden of diseases and quality of life (QOL) of patients for a  
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7 33 large variety of diseases within general practice.  
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10 34 **Design:** A representative nationwide cross-sectional study. A total of 825 general  
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12 35 practitioners (GPs) were randomly selected from across France. Independent  
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14 36 investigators recruited 8559 patients attending the GPs' practices. Data on quality of  
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16 37 life (12-Item Short Form questionnaire) and other individual characteristics were  
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18 38 documented by the independent investigators for all participants at the waiting room.  
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20 39 Medical information was recorded by GPs. Sampling was calibrated to national  
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22 40 standards using the CALMAR weighting procedure. Associations of lower scores  
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24 41 (i.e., below vs. above the first quartile) of physical and mental component scores  
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26 42 (PCS and MCS, respectively) with main diseases and patients characteristics were  
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28 43 estimated using multivariate logistic regression. Weighted morbidity rates, PCS and  
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30 44 MCS were computed for 100 diagnoses using the international classification of  
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32 45 diseases (ICD-9, 9<sup>th</sup> version).  
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35 46 **Results:** Overall mental impairment was observed amongst patients in primary care  
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37 47 with an average MCS of 41.5 (SD = 8.6), ranging from 33.0 for depressive disorders  
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39 48 to 45.3 for patients exhibiting fractures or sprains. Musculoskeletal diseases were  
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41 49 found to have the most pronounced effect on impaired physical health [OR=2.31;  
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43 50 95% CI (2.08–2.57)] with the lowest PCS [45.6 (SD = 8.8)] and ranked first (29.0%)  
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45 51 amongst main diagnoses experienced by patients followed by cardiovascular diseases  
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47 52 (26.7%), and psychological disorders (22.0%). When combining both prevalence and  
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49 53 quality of life, musculoskeletal diseases represented the heaviest burden in general  
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51 54 practice.  
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**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.

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3 74 • Although social and medical determinants of patients' QOL were somewhat  
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5 75 similar than those found in previous studies in primary care, the EPI3 survey  
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7 76 showed more pronounced mental impairment in French patients.  
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10 77 **Strengths and limitations of this study**

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12 78 **Strengths:**

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15 79 • No nationwide study on burden of disease combining both prevalence  
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17 80 measures and QOL assessment has been conducted to date, addressing such a  
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19 81 large variety of diseases in general practice.  
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22 82 • On-site selection and recruitment by an independent investigator limited the  
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24 83 possibility of selection bias amongst patients and the participation of  
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26 84 physicians added high specificity to medical data collection.  
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30 85 **Limitations:**

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33 86 • Study design providing high specificity in data collection led to a relatively  
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35 87 low response rate from GPs. However, stratified recruitment phases and  
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37 88 sample sizes from both GPs and patients highly representative of national  
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39 89 standards ensured strong external validity of the results.  
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42 90 • Home consultations, which are common amongst GPs in France, were not  
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44 91 surveyed which could probably have led to an underestimation of burden of  
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46 92 disease.  
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## 94 INTRODUCTION

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

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

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



## 116 **METHODS**

### 117 **Study design, settings and population**

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

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

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

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3 139 The EPI3-survey obtained regulatory approval by the national board of physicians  
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5 140 (“Conseil National de l'Ordre des Médecins”) and ethical approval by the French data  
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7 141 protection authority (“Commission Nationale de l’Informatique et des Libertés”).  
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9 142 Patients were informed by the participating physician that their responses would be  
10  
11 143 kept confidential and they were not remunerated for participation. Physicians received  
12  
13 144 compensation fees. The study was sponsored by a pharmaceutical company, whose  
14  
15 145 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.

#### 146 **Data collection**

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

154 Participants were asked whether the attending physician was their regular/primary  
155 care physician. In the French health insurance system, patients have to choose a  
156 regular physician -usually a GP-, who plays a gatekeeping role for referral to  
157 specialised care. However, referral by regular GPs to other physicians is not  
158 compulsory and patients are allowed to seek care from different physicians and their  
159 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/m<sup>2</sup>), 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.¶

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

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2 162 and average duration of consultation were assessed by the research assistants at the  
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4 163 time of inclusion.

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7 164 GPs completed a medical questionnaire on patients including the main reason for  
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9 165 consultation and up to five other diagnoses present that day. GPs were requested to  
10  
11 166 record their prescriptions that day for diagnostic tests, drugs and referrals. Diagnoses  
12  
13 167 were coded by a trained archivist using the 9<sup>th</sup> revision of the International  
14  
15 168 Classification of Diseases using 100-3 digit-categories.[22]

### 169 **Health status measurement**

170 Amongst adult patients (18 years and over), health-related quality of life was assessed  
171 using the 12-Item Short Form questionnaire (SF-12),[23] a shortened version of the  
172 36 short form health survey (SF-36) which has been shown to be a reliable outcome  
173 measurement tool in primary care.[24] The physical and mental component summary  
174 scores (PCS and MCS, respectively) were derived from the SF-12 questionnaire.  
175 Physical functioning (two questions), role-physical functioning (two questions),  
176 bodily pain (one question), general health (one question), vitality (one question),  
177 social functioning (one question), role-emotional functioning (two questions), and  
178 mental health (two questions), cover the same dimensions as the SF-36. The scores  
179 are standardised to population norms (based on a US norm-sample), with the mean  
180 score set at 50 (SD = 10); lower scores indicate worse-, and higher scores better  
181 health. The SF-12 has been validated for use in France, the US, the UK and many  
182 other European countries.[21]

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183 **Statistical analysis**

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

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

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

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2 206 Each disease category was calculated as a percentage reported to the whole population  
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4 207 of participating patients over the age of 18 years, regardless of whether this diagnosis  
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6 208 was isolated or associated with others, in order to provide a complete picture of  
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8 209 morbidity cared for in general practice.

10 210 Amongst adults over 18 years, associations of age, gender, education, type of  
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12 211 insurance, and 13 broad disease categories with lower MCS and PCS scores (defined  
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14 212 as below the 1<sup>st</sup> quartile with scores of 34 and 39 for MCS and PCS, respectively)  
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16 213 were evaluated using multivariate logistic regression. Odd Ratios (OR) and 95%  
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18 214 confidence interval (CI) are presented for each of these factors. In addition, the same  
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20 215 analysis was conducted for the two remaining categories: pregnancy follow-up and  
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22 216 preventive motives, which were not considered in the multivariate analysis. The  
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24 217 association between the number of comorbidities and the two SF-12 composite scores  
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26 218 was tested using linear regression. The possibility of a clustering effect at the practice  
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28 219 level was tested using Generalised Estimating Equations (GEE) multivariate models.  
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30 220 We used SAS statistical software (Version 9.1) for data analysis. The present study  
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32 221 was reported following the STROBE statement for cross-sectional studies.[27]  
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## 35 36 222 **RESULTS**

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40 223 The sequential recruitment of physicians was done by random stratified sampling  
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42 224 from the phone directory for GPs. Amongst the 3345 GPs initially contacted, 428  
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44 225 (12.8%) accepted to participate to the survey. At the end of recruitment in July 2008,  
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46 226 an additional sample of 13 861 GPs were contacted to ensure a representative sample  
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48 227 of GPs from all types of primary care practice in France (strictly allopaths,  
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50 228 homeopaths, mixed practice). Despite the intrusive nature of the survey, allowing  
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52 229 trained research assistants to collect data directly in the waiting room at the medical  
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2 230 | practice on the very day of consultation, a final sample of 825 participating GPs  
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4 231 recruited a total of 11 809 patients eligible for the present study. Of these, 174 were  
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6 232 unaccompanied minors, 315 were not French speakers, 109 had severe psychiatric  
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8 233 disorders, 2151 declined participation, 408 were beyond the maximum number  
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10 234 possible to interview within the allocated time on site, and 93 had incomplete data and  
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12 235 were excluded, allowing a total of 8559 patients for the present analysis.

### 15 236 **Physicians**

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18 237 The median age of physicians was 52 years [Interquartile range (IQR) = 33-57] and  
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20 238 amongst them, 24% were women; 54% worked in solo medical practice, 40% with  
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22 239 other GPs and 6% collaborated with specialists or other healthcare professionals; 31%  
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24 240 of the GPs practised additional medical activities within hospitals, healthcare centres,  
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26 241 the health administration or in the pharmaceutical industry. Most of the GPs (90%)  
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28 242 hold a regular contract with the National Health Insurance organisation, whilst 9%  
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30 243 hold a special contract allowing extra fees; a very small proportion (0.4%) had no  
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32 244 contract. The mean daily working time at the practice (excluding home visits) was 9  
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34 245 | hours (IQR: 2-10.5) and each of the 825 GPs participating in the study recruited on  
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36 246 | average 8.7 patients (SD = 2.2).

### 39 247 **Patients**

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42 248 Characteristics of participating (n = 8559) and non-participating patients with  
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44 249 complete data (n = 3157) used to calibrate the sample are presented in **Table 1**. We  
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46 250 reported here results based on the weighted characteristics. The mean age of the 8559  
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48 251 participating patients was 44.9 years (SD = 21.9), and 7133 (83.3%) were adults over  
49  
50 252 18. At least 44% of patients had a secondary school degree, 16% were overweight  
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52 253 (BMI>30 kg/m<sup>2</sup>) and more than 61% exercised longer than 31 minutes per day. Nine

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

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

	Non- participants* (n = 3157)	Participants (n = 8559)	Weighted percentage
<i>mean (SD)</i>			
Age (years)	47.7 (24.0)	43.3 (22.8)	44.9 (21.9)
<i>n (%)</i>			
<b>Female gender</b>	<b>1701 (53.9)</b>	<b>5367 (62.7)</b>	57.9
<b>Length of relationship with the physician</b>			
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
<b>Government funded health insurance</b>	308 (9.8)	621 (7.4)	9.4
<b>Long-standing disease status</b>		1925 (22.5)	27.7
<b>Complementary health insurance</b>		7839 (91.6)	90.3
<b>Index physician declared as treating physician</b>		6379 (74.5)	84.3
<b>Body Mass Index (kg/m<sup>2</sup>)</b>			
<25		5548 (64.8)	52.4
25-30		2045 (23.9)	31.8
30 and over		966 (11.3)	15.8
<b>Tobacco consumption</b>			
Non smoker		4303 (50.3)	47.4
Past smoker		1961 (22.9)	24.4
Current smoker		2252 (26.3)	28.2
<b>Alcohol Consumption</b>			
Never		2908 (34.2)	35.2
Sometimes		4649 (54.6)	52.5
Daily		957 (11.2)	12.4
<b>Physical exercise</b>			
Less than 10 minutes per day		2235 (26.1)	28.3

10 minutes and over	6199 (72.4)	71.7
<b>Nationality</b>		
French born subjects	7787 (91.0)	90.3
French born abroad	341 (4.0)	4.7
Non-French nationality	357 (4.2)	5.0
<b>Educational attainment</b>		
Secondary school degree <sup>‡*</sup> , college, university graduation	4179 (48.8)	44.0
<b>Employment status</b>		
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

264 \*Available characteristics used for calibration

265 <sup>‡</sup>French baccalaureate

## 266 Burden of one hundred diseases in primary care

267 Prevalence of each of the 100 and 13 broad non-exclusive diagnosis categories ([a](#)

268 [compilation of all five diagnoses recorded by the GPs](#)) are presented in **Table 2**.

269 Altogether, diseases of the musculoskeletal system were the most frequently

270 diagnosed conditions (29%), followed by cardiovascular diseases (26.7%), and sleep,

271 anxiety and depressive disorders (22%). Preventive care consultations, vaccinations

272 and consultation for administrative purposes accounted for 19% of the total diagnoses.

273 Almost half the patients (49%) exhibited two or more comorbidities.

274 **Table 2.** Morbidity rates and SF12 mental and physical component scores according

275 to 100 ICD diagnoses (EPI3-LASER-2008, weighted data n = 7133)

Diseases	Morbidity*	PCS	MCS
	n (%)	mean (sd)	Mean (sd)
<b>All patients</b>		<b>45.6 (8.8)</b>	<b>41.5 (8.6)</b>
<b>Diseases of the musculoskeletal system</b>	<b>2069 (29.0%)</b>	<b>42.7 (8.4)</b>	<b>41.6 (8.3)</b>
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)



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3	Enthesopathy of elbow region	77 (1.1%)	41.8 (9.3)	43.1 (10.5)
4	Unspecified enthesopathy	257 (3.6%)	42.3 (10.5)	42.1 (10.0)
5	Rheumatism, excluding the back	112 (1.6%)	42.9 (10.1)	42.3 (9.8)
6	Spondylosis and other inflammatory spondylopathies	84 (1.2%)	42.1 (9.9)	43.1 (8.4)
7	Sciatica	194 (2.7%)	42.3 (10.1)	41.7 (9.6)
8	Pain in thoracic spine	51 (0.7%)	42.6 (9.8)	41.3 (9.2)
9	Osteoporosis	162 (2.3%)	44.0 (10.7)	41.9 (10.8)
10	Diseases of connective tissue	36 (0.5%)	45.5 (9.3)	40.5 (10.9)
11	Unspecified back disorders	193 (2.7%)	42.1 (10.2)	41.3 (9.7)
12	Other unspecified musculoskeletal disorders	76 (1.1%)	40.3 (11.0)	41.7 (11.6)
13				
14	<b>Hypertension, cardiovascular and circulatory diseases</b>	<b>1904 (26.7%)</b>	<b>43.7 (9.0)</b>	<b>42.5 (8.6)</b>
15	Hypertension	1111 (15.6%)	43.9 (11.3)	42.8 (10.7)
16	Acute myocardial infarction	84 (1.2%)	40.8 (11.4)	42.0 (9.4)
17	Other symptoms involving cardiovascular system	53 (0.7%)	46.0 (9.5)	43.7 (8.2)
18	Angina pectoris	66 (0.9%)	41.8 (11.8)	43.7 (10.5)
19	Cardiac dysrhythmias	139 (1.9%)	42.9 (11.5)	42.7 (11.1)
20	Diseases of veins and lymphatics	92 (1.3%)	45.3 (10.5)	41.3 (10.8)
21	Pulmonary, artery and cerebrovascular diseases	144 (2.0%)	42.1 (11.7)	42.7 (10.6)
22	Other ischaemic heart diseases	96 (1.3%)	41.1 (11.9)	42.1 (11.1)
23	Other diseases of the circulatory system	229 (3.2%)	45.3 (10.3)	41.8 (11.0)
24				
25	<b>Anxiety, depression and sleep disorders</b>	<b>1569 (22.0%)</b>	<b>44.8 (8.9)</b>	<b>36.3 (8.5)</b>
26	Psychotic conditions	68 (1.0%)	44.2 (12.6)	37.6 (12.3)
27	Anxiety states	420 (5.9%)	47.8 (10.5)	35.5 (9.7)
28	Dysrhythmia	182 (2.6%)	47.2 (10.2)	35.4 (9.2)
29	Acute and chronic stress	85 (1.2%)	46.9 (10.6)	36.1 (9.5)
30	Personality disorders, disturbance of conduct, dependence syndrome	81 (1.1%)	46.4 (10.9)	38.8 (11.2)
31	Eating disorders, tics, stuttering and other syndromes	277 (3.9%)	47.4 (10.4)	37.1 (10.7)
32	Depressive disorders	497 (7.0%)	45.3 (11.4)	33.0 (10.2)
33	Malaise and fatigue	114 (1.6%)	45.4 (11.1)	38.7 (9.7)
34	Sleep disorders	87 (1.2%)	46.1 (10.7)	38.5 (9.4)
35	Nervousness, cachexia and unspecified psychological distress	30 (0.4%)	41.9 (13.5)	39.9 (12.8)
36	Dizziness and giddiness	59 (0.8%)	46.3 (9.8)	40.2 (10.4)
37	Other general symptoms	75 (5.8%)	46.0 (11.1)	39.2 (10.4)
38				
39	<b>Diseases of the respiratory system</b>	<b>1419 (19.9%)</b>	<b>46.3 (8.5)</b>	<b>41.9 (8.4)</b>
40	Acute nasopharyngitis	306 (4.3%)	48.2 (9.8)	41.6 (9.7)
41	Acute pharyngitis	60 (0.8%)	49.3 (10.4)	42.5 (10.5)
42	Acute tracheitis	120 (1.7%)	48.4 (10.1)	41.4 (10.4)
43	Acute bronchitis or other upper respiratory infections	66 (0.2%)	41.9 (12.3)	43.0 (8.0)
44	Chronic nasopharyngitis	52 (0.3%)	50.0 (8.1)	42.9 (8.7)
45	Chronic sinusitis and laryngitis	126 (1.7%)	48.0 (9.9)	40.3 (8.9)
46	Allergic rhinitis	124 (1.7%)	47.5 (10.7)	42.3 (9.6)
47	Pneumonia and influenza	53 (0.6%)	46.8 (10.2)	41.1 (10.8)
48	Chronic obstructive pulmonary diseases (except asthma)	160 (2.2%)	44.8 (10.4)	41.2 (10.0)
49	Asthma	148 (2.1%)	44.0 (11.5)	41.4 (10.5)
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3	Lung diseases	64 (0.9%)	41.0 (12.3)	42.0 (9.5)
4	Other diseases of the respiratory system	210 (2.9%)	45.1 (11.6)	42.4 (10.4)
5	<b>Medical exams, preventive motives</b>	<b>1101 (15.4%)</b>	<b>47.4 (9.2)</b>	<b>42.4 (10.1)</b>
6	Medical exam: handicap influencing health status	41 (0.6%)	45.9 (9.4)	39.4 (12.6)
7	Medical exam: aftercare and specific procedures	285 (4.0%)	45.9 (11.6)	41.2 (10.8)
8	Medical exam for health check-up	286 (4.0%)	46.9 (11.3)	43.1 (10.8)
9	Laboratories findings	53 (0.7%)	48.5 (9.8)	42.9 (10.9)
10	Vaccination	121 (1.7%)	50.2 (11.0)	42.6 (10.5)
11	Pregnancy follow-up	122 (1.7%)	47.4 (11.8)	41.8 (10.4)
12	Administrative purposes	380 (5.3%)	47.2 (11.7)	42.5 (9.9)
13				
14	<b>Diabetes, thyroid gland &amp; other endocrine disorders</b>	<b>785 (11.0%)</b>	<b>43.9 (8.6)</b>	<b>41.5 (8.1)</b>
15	Hypothyroidism	187 (2.6%)	45.3 (11.0)	39.6 (10.9)
16	Goitre	45 (0.6%)	46.5 (9.3)	41.3 (9.8)
17	Diabetes mellitus	312 (4.4%)	42.9 (11.2)	42.0 (10.5)
18	Diseases of other endocrine glands	78 (1.1%)	43.9 (11.9)	41.0 (10.8)
19	Other thyroid disorders	52 (0.7%)	45.7 (10.8)	40.0 (10.1)
20				
21	<b>Obesity &amp; dyslipidaemia</b>	<b>742 (10.4%)</b>	<b>45.2 (9.1)</b>	<b>42.0 (8.9)</b>
22	Hypercholesterolaemia	266 (3.7%)	45.1 (10.9)	42.6 (10.2)
23	Unspecified disorder of lipid metabolism	135 (1.9%)	45.5 (10.5)	42.8 (9.2)
24	Overweight, obesity and other hyperalimentionation	169 (2.4%)	47.6 (11.4)	40.2 (10.4)
25	Other hyperlipidaemia	105 (1.1%)	45.6 (11.3)	42.4 (10.6)
26	Other symptoms concerning nutrition, metabolism and development	70 (1.0%)	48.6 (10.1)	40.3 (10.4)
27				
28	<b>Diseases of the digestive system</b>	<b>742 (10.4%)</b>	<b>45.9 (8.4)</b>	<b>39.9 (8.4)</b>
29	Oesophageal diseases	81 (1.1%)	44.3 (10.3)	41.5 (9.8)
30	Diseases of stomach	121 (1.7%)	45.6 (10.0)	40.1 (9.7)
31	Diseases of intestines and peritoneum	72 (1.0%)	45.1 (10.1)	40.2 (9.9)
32	Symptoms involving the abdomen	161 (2.3%)	46.9 (10.4)	39.9 (11.0)
33	Non-infectious enteritis and colitis	105 (1.5%)	47.5 (9.5)	41.8 (9.9)
34	Diseases of oral cavity, salivary glands and jaws	39 (0.5%)	49.0 (8.8)	40.3 (10.0)
35	Appendicitis and hernia	43 (0.6%)	44.1 (10.6)	40.0 (10.2)
36	Other diseases of the digestive system	144 (2.0%)	44.8 (10.8)	39.7 (9.9)
37				
38	<b>Diseases of the nervous system, head &amp; neck</b>	<b>449 (6.3%)</b>	<b>43.3 (9.4)</b>	<b>39.6 (9.1)</b>
39	Disorders of central nervous system	95 (1.3%)	41.3 (13.6)	42.2 (11.2)
40	Migraine	114 (1.6%)	46.6 (10.2)	39.7 (10.1)
41	Symptoms involving head & neck	96 (1.3%)	46.3 (10.8)	40.8 (10.2)
42	Diseases of the eye	54 (0.7%)	51.8 (9.9)	37.4 (10.6)
43	Diseases of the ear and mastoid processes	112 (1.6%)	46.9 (10.8)	41.6 (11.0)
44	Other disorders of nervous system and sense organs	145 (2.0%)	44.6 (10.3)	39.9 (10.6)
45				
46	<b>Diseases of the genitourinary system</b>	<b>400 (5.6%)</b>	<b>45.5 (9.6)</b>	<b>41.5 (8.9)</b>
47	Cystitis	115 (1.6%)	47.9 (11.5)	40.3 (10.2)
48	Diseases of male genital organs	85 (1.2%)	46.0 (10.9)	43.0 (11.0)
49	Diseases of female genital organs	139 (1.9%)	48.4 (11.3)	39.8 (10.8)
50	Nephrosis and nephritis	86 (1.2%)	44.8 (11.6)	41.7 (10.6)
51	Complications of pregnancy, congenital anomalies	42 (0.6%)	43.5 (12.8)	40.4 (10.5)
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<b>Injury and poisoning</b>	<b>342 (4.8%)</b>	<b>43.5 (9.2)</b>	<b>43.5 (8.3)</b>
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)
<b>Cancer and infrequent diseases</b>	<b>289 (4.1%)</b>	<b>42.0 (9.3)</b>	<b>40.4 (8.5)</b>
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)
<b>Skin and subcutaneous tissue diseases</b>	<b>243 (3.4%)</b>	<b>48.8 (7.8)</b>	<b>41.7 (9.6)</b>
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)
<b>Infectious diseases</b>	<b>228 (3.2%)</b>	<b>47.1 (7.6)</b>	<b>40.7 (7.1)</b>
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)

276 \*Each condition category is non-exclusive.

277 Overall mean scores for PCS and MCS were 45.6 (SD = 8.8) and 41.5 (SD = 8.6),  
 278 respectively. Considering PCS, scores ranged from 40.3 (SD = 11.0) for one group of  
 279 unspecified musculoskeletal conditions to 50.2 (SD = 11.0) for vaccinations. On the  
 280 whole, musculoskeletal disorders had the lowest scores with cancer and other severe  
 281 diseases category, whilst skin-related diseases, preventive care consultation and  
 282 infectious diseases showed the highest PCS. With regard to MCS, scores ranged from  
 283 33.0 (SD = 10.2) for depressive disorders to 45.3 for patients with fractures, sprains or  
 284 dislocation. Overall, lowest scores were found amongst patients with mood and sleep  
 285 disorders, whilst injury, preventive motives and cardiovascular diseases exhibited the  
 286 highest scores. Both MCS and PCS significantly decreased with increasing number of  
 287 comorbidities (Figure 1). For example, MCS decreased from 43.3 for patients seeking  
 288 preventive care advice to 38.5 for those with 4 diagnoses or more (p for trend  
 289 <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)]

290 **Determinants of health related quality of life**

291 Associations between patient characteristics and 13 broad categories of diseases are  
 292 presented in **Table 3**. Low PCS was significantly associated with older age [OR =  
 293 2.48; 95% CI (2.08 – 2.96) for patients over 75 years as compared to adults between  
 294 18 and 44 years]. Low PCS was negatively associated with high educational  
 295 attainment [OR = 0.65; 95% CI (0.59 – 0.72) for secondary school level or higher in  
 296 comparison to lower educational level]; whilst low MCS scores were associated with  
 297 gender [OR = 1.62; 95% CI (1.45 – 1.81) for women as compared to men], and  
 298 younger age. Government funded health insurance cover was associated with both  
 299 poor PCS and MCS [OR = 1.38; 95% CI (1.15 – 1.65) and OR = 1.42; 95% CI (1.19 –  
 300 1.70), respectively].

301 **Table 3.** Health related quality of life. SF12. Factors and 13 broad diagnoses  
 302 associated to MCS and PCS below the 25th percentile (aOR and 95%CI), EPI3-  
 303 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
Other diseases (cancer and infrequent diseases)	1.73	1.38-2.16	1.35	1.06-1.72

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

307 With regard to the diseases categories, musculoskeletal diseases [OR = 2.31; 95% CI  
 308 (2.08 – 2.57)], injury and poisoning [OR = 1.88; 95% CI (1.52 – 2.33)], other diseases  
 309 including cancer [OR = 1.73; 95% CI (1.38 – 2.16)], diseases of the nervous system,  
 310 head and neck [OR = 1.24; 95% CI (1.02 – 1.51)] and cardiovascular diseases [OR =  
 311 1.22; 95% CI (1.08 – 1.38)] were significant predictors of lower PCS score, whereas  
 312 the opposite was found for skin and subcutaneous tissue diseases [OR = 0.68; 95% CI  
 313 (0.51 – 0.90)] or with obesity and dyslipidaemia [OR = 0.79; 95% CI (0.67 – 0.94)].  
 314 Significantly poor MCS were observed in patients suffering from anxiety, depression  
 315 and sleep disorders [OR = 3.58; 95% CI (3.22 – 3.98)], and experiencing “other  
 316 diseases” including cancer [OR = 1.35; 95% CI (1.06 – 1.72)]. Conversely, OR for  
 317 MCS was significantly decreased for patients with cardiovascular diseases [OR= 0.84;  
 318 95% CI (0.73 – 0.96)]. Testing the effect of clustering at the practice level yielded  
 319 similar results, but to ensure parsimony of the generated models it was decided not to  
 320 report such effects.

## 321 Discussion

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

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3 325 information from GPs. On-site selection and recruitment by an independent  
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5 326 investigator limited the possibility of selection bias amongst patients and the  
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7 327 participation of physicians added high specificity to medical data collection.  
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10 328 There is a clear need for more data on QOL of patients.[6] In the UK, the General  
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12 329 Practice Research Database (GPRD) assembled a very large sample of 400 surgeries  
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14 330 and 2500 individual GPs, providing detailed information on health conditions besides  
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16 331 prescriptions, but to our knowledge not on patients QOL.[3] The Dutch national  
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18 332 survey of general practice carried out in 1987 and 2001 gives an assessment of quality  
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20 333 of care but only provided by the patients themselves.[2]  
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22 334 The EPI3 survey found similar prevalence for both diseases[10;28] and  
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24 335 comorbidities[7;9;10;13] as in several other studies which indicate a good  
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26 336 representativeness of our weighted sample. Musculoskeletal and psychological  
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28 337 disorders were experienced by more than half the patients attending physicians during  
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30 338 the course of the study and represented significant case load at GP practices. When  
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32 339 both physical, mental status impairment and prevalence are considered, our study  
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34 340 further highlighted the heaviest burden of musculoskeletal disorders.  
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37 341 With regard to physical status, the EPI3-survey showed a similar average PCS score  
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39 342 as other primary care[7;8;10;11] or disease specific[14;15;29] surveys using the SF-  
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41 343 12 or SF-36 questionnaires. Mean PCS were lower than reference values computed in  
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43 344 the French reference sample[21] and in the 2003 Household survey (JL Lanoe,  
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45 345 unpublished data, 2003). Within practices, older age,[30-33] low education attainment  
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47 346 and government funded insurance,[30;32;33] were associated with lower PCS. When  
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49 347 disease categories were considered, musculoskeletal diseases were associated with the  
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2 348 lowest PCS,[8;34;35] with PCS of similar magnitude to other European surveys  
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4 349 including MSD patients.[29]  
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7 350 Regarding mental status, although socio-demographic characteristics had similar  
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9 351 impact on MCS, the EPI3-survey showed significantly lower MCS scores than other  
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11 352 studies in general practice.[7;8;10;11] Additional comorbidities, which were reported  
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13 353 for half of the EPI3-survey sample, could not explain alone this difference with other  
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15 354 studies: MCS usually scored an average three points lower than those of patients with  
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17 355 one morbidity.[16] We believe that our findings could be explained instead by  
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19 356 different methodology: in all other studies conducted in general practice,[7;8;10;11]  
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21 357 mostly including a small number of medical practices,[8;10;11;13] physicians may  
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23 358 have selected participants. Our study was exempt of this bias in view of the selection  
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25 359 of consecutive eligible patients in the GP's waiting room. In studies in which patients  
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27 360 were interviewed for targeted mental disorders[15] or when MCS were assessed  
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29 361 amongst patients seeking specialty care,[36;37] MCS measures were somewhat  
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31 362 similar to ours. In the EPI3-survey, psychological and psychiatric diseases had the  
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33 363 greatest negative impact on mental function consistent with other surveys in primary  
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35 364 care.[7,10] it must be appreciated that associated MCS values were more similar to  
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38 365 those of another study conducted on patients with specific psychiatric disorders.[15]  
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40 366 Lower MCS may thus highlight the overall burden of psychological distress and  
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42 367 related diseases of patients seen in primary care.

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#### 368 **Strengths and limitations of the study**

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47 369 Amongst the main strengths of our study, the unique combined data from patients and  
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49 370 physicians allowed provision of reference figures for the vast majority of diseases  
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51 371 encountered in primary care for a large number of patients. Quality adjusted life years

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3 372 (QALYs) are usually estimated for health economics and mainly derived from QOL  
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5 373 measures assessed from EuroQoL standardised instruments (EQ5D).[1] Interestingly,  
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7 374 the conversion of SF-12 values into EQ5D Utility values has been recently  
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9 375 documented,[38] suggesting that our results could be extended for that purpose as  
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11 376 previously reported.[39]

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13 377 Additionally, SF-12 questionnaires have been found to provide reliable QOL  
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15 378 measurement across studies,[22;24] even amongst patients with acute conditions.[40]  
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17 379 Although its validity in older patients is moderate,[41] our sample was representative  
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19 380 of the general population thus minimising this possible bias on our results.

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22 381 At last, lack of representativeness was an important limitation in other studies.[11;42]  
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24 382 The sample size of physicians participating in the EPI3-survey is within the range  
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26 383 established for other French surveys (from 100 to 1006).[26] Physicians were  
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28 384 randomly selected from the national telephone directory, which includes general  
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30 385 practitioners currently practising in primary care. This was preferred to professional  
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32 386 registries of physicians, which lists all registered GPs, regardless of whether they are  
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34 387 currently practising or not.  
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37 388 The weighted geographical distribution of the 825 GPs participating in the survey was  
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39 389 similar to the national distribution of GPs in private practice across the 22 French  
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41 390 regions surveyed and the distribution of physicians' individual characteristics  
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43 391 regarding age, gender, type of contract with national health insurance, and type of  
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45 392 practice differed only slightly from national statistics:[26] female participation was  
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47 393 slightly lower (23.5% compared to 26% in the IRDES sample), but the distribution  
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49 394 between sectors was similar (8.9% vs. 8.5% in sectors 1 and 2, respectively).  
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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]¶

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

## 415 Conclusion

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

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3 419 impairment may be underestimated in general practice. Ongoing development of  
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5 420 healthcare policies and clinical guidelines about treatment of diseases should rely on  
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7 421 direct assessment of QOL and morbidities in GP medical practices.  
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10 422 GPs foster continuous care, sometimes requiring highly specialised therapy to deal  
11 423 with comorbidities and complex situations. The present study shows that the burden  
12 424 of diseases in primary care is not only high but can also be diverse. The EPI3 survey  
13 425 provides information on the overall burden of diseases in general practice along with  
14 426 quality of life of patients regarding comorbidities as seen in this healthcare setting.  
15 427 This information is of great value to public health and economic assessment of  
16 428 healthcare, at a time when quality of life is becoming a prevalent factor for care  
17 429 delivery and the development of clinical practice guidelines.  
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11 434 collection, analyses, interpretation, and writing of the manuscript or the decision to  
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13 435 publish our findings.  
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17  
18 437 form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare that: the institution of LGB,  
19  
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21  
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23  
24 440 JM, GD, AMM have no relationships with Boiron or any other companies that might  
25  
26 441 have an interest in the submitted work in the previous 3 years; LGB, BA and MR are  
27  
28 442 employees of LA-SER, the company conducting the study; LA is a stockholder in  
29  
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32 444 National Institute of Health and Medical Research) at the time of the study. The  
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34 445 results reported here do not include any information on pharmaceuticals.  
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38  
39 447 author. LGB, BB, FL, FR, JM, DG, BA, GD, AMM, MR and LA conceived both the  
40  
41 448 research theme and the methods, analysed the data and interpreted the results. LGB  
42  
43 449 implemented the trial in France, analysed the data, and together with FL, Pierre Engel  
44  
45 450 and LA drafted and revised the paper. All members of the EPI3-LASER group  
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47 451 designed the study. Alban Fabre and Pierre Engel analysed the data. All authors have  
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49 452 contributed to, read and approved the final manuscript. LGB is guarantor for the  
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51 453 study.  
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2 454 Lamiae Grimaldi-Bensouda, Pierre Engel, France Lert and Lucien Abenheim had full  
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4 455 access to all of the data in the study and take responsibility for the integrity of the data  
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6 456 and the accuracy of the data analysis.  
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9 457 **Data sharing** No additional data available.  
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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	
<b>Title and abstract</b>	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	✓
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
<b>Methods</b>			
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
<b>Results</b>			
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

		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
<b>Discussion</b>			
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	✓
<b>Other information</b>			
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	✓

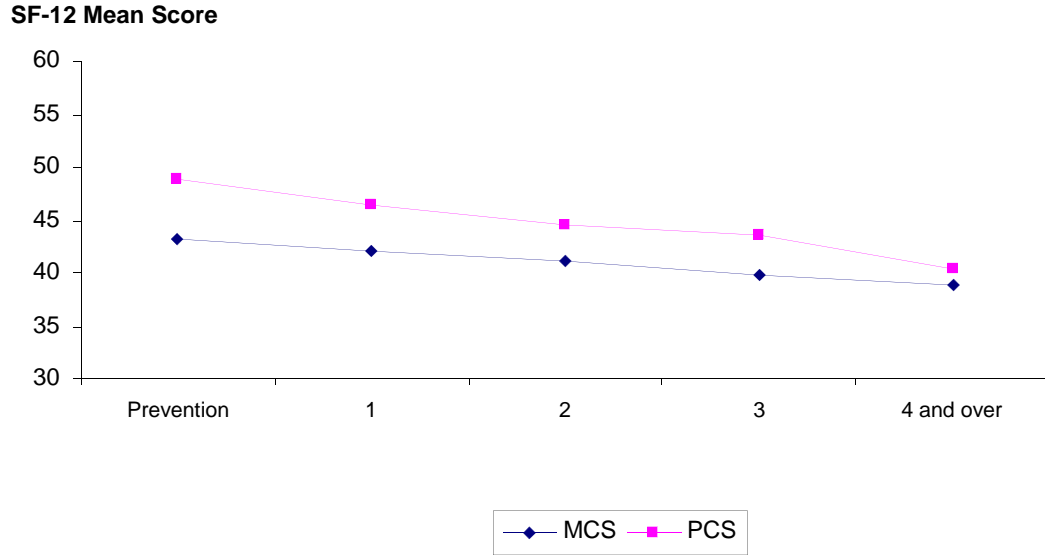
Symbols: ✓, checked; N/A, not applicable.

\*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](http://www.strobe-statement.org).

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



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