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Original article

The societal impact of pain in the European Union: health-related quality of life and healthcare resource utilization

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Abstract

Objectives:
This paper reports on the results of a series of quantitative assessments of the association of severe and frequent pain with health-related quality of life and healthcare resource utilization in five European countries.

Methods:
The analysis contrasts the contribution of the increasing severity and frequency of pain reported against respondents reporting no pain in the previous month. The data are taken from the 2008 National Health and Wellness Survey. Single-equation generalized linear regression models are used to evaluate the association of pain with the physical and mental component scores of the SF-12 questionnaire as well as health utilities generated from the SF-6D. In addition, the role of pain is assessed in its association with healthcare provider visits, emergency room visits and hospitalizations.

Results:
The results indicate that the experience of pain, notably severe and frequent pain, is substantial and is significantly associated with the SF-12 physical component scores, health utilities and all aspects of healthcare resource utilization, which far outweighs the role of demographic and socioeconomic variables, health risk factors (in particular body mass index) and the presence of comorbidities. In the case of severe daily pain, the marginal contribution of the SF-12 physical component score is a deficit of −17.86 compared to those reporting no pain (population average score 46.49), while persons who are morbidly obese report a deficit of only −6.63 compared to those who are normal weight. The corresponding association with health utilities is equally dramatic with a severe daily pain deficit of −0.19 compared to those reporting no pain (average population utility 0.71).

Conclusions:
For the five largest EU countries, the societal burden of pain is considerable. The experience of pain far outweighs the contribution of more traditional explanations of HRQoL deficits as well as being the primary factor associated with increased provider visits, emergency room visits and hospitalizations.

Introduction

The prevalence, severity and burden of pain, in particular chronic pain, has been reported in a number of pan-European studies. Breivik *et al.* report on the results of a computer-assisted telephone survey of adults to assess pain prevalence, treatment and its impact[1]. Among respondents, they found 19% had experienced moderate or severe pain in the last month with one-third experiencing severe pain. In addition, there is a small sample study of the burden of neuropathic pain[2]. There have also been a number of country-specific or

community studies. Smith *et al.* report on the community impact of chronic pain in the Grampian region of Scotland[3]. In this study, 14.1% reported 'significant chronic pain' with 6.3% reporting 'severe chronic pain.' Other community studies have been conducted in Spain[4]. There are also studies focusing on particular subpopulations, such as primary care in Germany[5] and pain in German children and adolescents[6]. To these should be added studies that have focused on particular aspects of pain experience, notably low back pain[7].

Generic health-related quality of life (HRQoL) instruments have been used on a number of occasions to assess the prevalence of pain. Konig *et al.* report on health status in six European countries using the EQ-5D instrument and found that the most frequently reported problem was pain (28.5% of respondents)[8]. The association of neuropathic pain with quality of life has been the subject of community studies[9]. Recent reviews have found that those experiencing neuropathic pain in three UK communities recorded significant differences on all dimensions of the SF-36 compared to those reporting no pain[10,11]. Both Jensen *et al.* and Connor *et al.* reviews showed that neuropathic pain is associated with significant HRQoL deficits in multiple domains – including physical and emotional suffering. Utilizing the EQ-5D instrument as a reference[10,11], McDermott *et al.* point to substantial differences in the deficits associated with levels of pain severity[2].

While community studies and reviews have pointed to the association of pain, chronic pain and neuropathic pain with HRQoL deficits, the existing literature suffers from two main weaknesses. First, there has been a failure to compare HRQoL in pain populations as opposed to no-pain populations. Second, there has been a lack of analyses to assess the independent contribution of pain in its impact on outcomes such as HRQoL. The landmark pan-European study by Breivik *et al.*, for example, is essentially descriptive in nature[1]. While providing a useful profile of the severity and correlates of pain experience it is limited in terms of response rate. It is further limited by the absence of a 'no pain' reference group. The study also lacks modeled quantitative estimates of the independent burden of pain in the community.

The purpose of this study is to provide, for the first time, a comprehensive assessment of the independent societal burden of the severity and frequency of pain in a specific European population. This is achieved through the specification and estimation of a series of generalized linear regression models. Two outcomes are considered: (1) HRQoL and (2) healthcare resource utilization. The analysis encompasses five European Union (EU) countries – the UK, France, Spain, Germany and Italy. This analysis with a 'no pain' reference group allows a direct estimate of the overall burden of pain in the EU.

Methods

The principal research question is to assess the association between the severity and frequency of pain and self-reported HRQoL and healthcare resource utilization. The multivariate framework allows an assessment of the independent or marginal contribution of the severity and frequency of pain on outcomes. This takes account of the possible contribution of respondent socio-demographic and economic characteristics, the presence of health risk behaviors and respondent comorbidity status on these outcomes.

Two models are presented. Model 1 considers only the reported severity of pain experience on HRQoL and resource utilization; Model 2 assesses the contribution of pain severity and frequency. This approach is taken in order to see whether or not the frequency of pain experienced adds an additional dimension to our understanding of the burden of pain experience. While the presence of pain is expected to have a significant and negative effect on both HRQoL and resource utilization, it is also of interest to assess whether the HRQoL deficits and resource utilization impacts are attenuated with less severe and less frequent experience of pain.

National health and wellness survey

The National Health and Wellness Survey (NHWS) is a syndicated, annual and biannual, internet-based, cross-sectional study of the healthcare attitudes, behaviors, and characteristics of the adult population (http://www.chsinternational.com/nhws.html). It is undertaken in the US, UK, France, Spain, Germany Italy, urban China and Japan. Since its initiation in 1998, over 600,000 survey responses across approximately 140 conditions have been collected. In addition, several supplementary studies have been conducted in which NHWS respondents were re-contacted and asked further questions.

The present analysis is based on the results of the 2008 NHWS for the five major EU countries. A total of 53,524 persons 18 years of age and over were interviewed, yielding an age/gender weighted or estimated overall population of 247.3 million. After adjusting to exclude a number of minor or acute pain categories (which were assigned back to the 'no pain' category), a total of 11,891 respondents were identified as experiencing pain in the last month. This yielded an estimated population of 51.8 million experiencing pain in the last month or approximately 1 in 5 of this adult EU population. The analyses presented here are based on weighted population estimates.

Screening questions

All respondents to the 2008 NHWS were asked if they had experienced pain in the last month and the condition(s) that had caused pain. If respondents indicated that they had only experienced menstrual pain, migraine, dental pain or headache in the last month, they were excluded from the pain category. However, a significant proportion of respondents reported multiple conditions as the cause of pain in the last month. Given this, those with these as comorbid conditions are retained in the pain category.

Severity and frequency of pain

Respondents were then asked about the severity of pain reported and the frequency with which they had problems with pain. Respondents who reported severity but not the frequency of pain were excluded from the analysis. These results are summarized in Table 1. Overall, of those reporting both the severity and frequency of pain, 59.2% (29.4 million) reported moderate pain, 22.8% reported mild pain and 18.0% severe pain. A total of 43.6% reported experiencing pain in the last month on a daily basis, with 29.2% experiencing pain 2 to 6 times a week. Combining severity with frequency, the largest category is for persons reporting daily moderate pain 11.7 million (23.6%) with 8.5 million (17.1%) reporting severe, daily pain.

Table 1. Reported pain level and frequency of pain.

Pain dimension	Respondents five EU countries*	Distribution (%)
Pain level		
Mild	8,970,445	18.0
Moderate	29,439,982	59.2
Severe	11,318,103	22.8
Pain frequency		
Daily	21,703,485	43.6
2–6 times a week	14,510,928	29.2
Weekly or less	13,514,117	27.2
Pain level and frequency		
Severe and daily experience	8,506,068	17.1
Severe and 4–6 times per week	969,348	2.0
Severe and 2–3 times per week	734,408	1.5
Severe and weekly or less	1,108,279	2.2
Moderate and daily experience	11,746,535	23.6
Moderate and 4–6 times a week	4,145,306	8.3
Moderate and 2–3 times per week	6,047,471	12.2
Moderate and weekly or less	7,500,670	15.1
Mild and daily experience	1,450,882	2.9
Mild and 2–6 times per week	2,614,395	5.3
Mild and weekly or less	4,905,168	9.9

*UK, France, Spain, Germany, Italy.

Dependent variables

All respondents to the 2008 NHWS were asked to complete the SF-12 HRQoL instrument together with a series of questions to identify their use of healthcare resources in the last 6 months: traditional healthcare provider visits, emergency room visits and hospitalizations. Three dimensions of HRQoL are identified: SF-12 physical and mental summary scores and SF-6D health utilities.

SF-12 and SF-6D

The SF-12 is a multipurpose, generic HRQoL instrument comprising 12 questions[12]. The instrument is designed to report on eight health concepts. These are:

- Physical functioning
- Role physical (accomplishment)
- Bodily pain
- General health
- Vitality (energy level)
- Social functioning
- Role emotional (accomplishment)
- Mental health (feeling)

The SF-12 questions are all selected from the SF-36 health survey[13,14]. A key objective in developing the SF-12 in the early 1990s was to construct the shortest possible form that would replicate the physical and mental health summary scores generated from the SF-36 with at least 90% accuracy. A further objective was to replicate each of the eight SF-36 health concepts with at least one questionnaire item to set the stage for scoring an eight-scale profile from SF-12 responses.

It is worth noting that the SF-12 bodily pain item does not ask respondents to indicate either the severity or the frequency of the pain. Rather, the question asks respondents 'How much did pain interfere with your normal work (including both work outside the home and housework)?' with the response choice (five items) from 'not at all' to 'extremely.'

While it is possible to develop a health profile utilizing the item responses corresponding to these eight concepts, the focus here is on the two summary scores that can be generated from the respective SF-12 item responses. These are (1) the physical component summary (PCS) and (2) mental component summary (MCS). Details of how the links are established and the scoring algorithms are given in Ware *et al.*[12].

For the purpose of the present analysis, the PCS and MCS summary scores are utilized as normed scores. This is achieved by transforming the raw scores for the items to a mean of 50 and a standard deviation of 10 for the US population. Normed scores can be calculated for both the eight SF-12 scales as well as for the PCS and MCS summary scores. The appropriateness of using the US as a standard benchmark has been demonstrated for nine

Table 2. Distribution of SF-12 physical and mental component scores for persons reporting pain and no pain.

Class interval	Physical component score distribution (%)		Mental component score distribution (%)	
	No pain	Pain	No pain	Pain
90–100	0.0	0.0	0.0	0.0
80–89	0.0	0.0	0.0	0.0
70–79	0.0	0.0	0.0	0.3
60–69	5.7	2.0	8.9	7.0
50–59	50.2	25.2	35.8	27.7
40–49	25.6	29.2	30.2	29.0
30–39	12.0	23.6	18.3	23.8
20–29	5.0	15.1	5.4	9.8
10–19	1.3	4.7	1.1	2.1
Under 10	0.1	0.3	0.1	0.2
Average score	50.6	41.1	46.5	44.3

European countries (including the five countries in the NHWS)[12]. Given the cross-country nature of the present analysis, the US standard scoring algorithms are used.

The distribution of the normed SF-12 PCS and MCS scores are given for the pain and no pain populations for the five EU countries in Table 2. In the case of the PCS average score, there is a substantial difference between the score for the two populations (no pain 50.6 vs. pain 41.1). The difference for the MCS score is less marked (no pain 46.5 vs. pain 44.3). These differences are reflected in the distribution of scores by class interval. In the case of the PCS, 50.2% of respondents in the no pain category score in the range 50 to 59 compared to only 25.2% of those reporting pain.

As well as generating profile and summary PCS and MCS scores, the SF-12 can also be used to generate health state utilities. This is achieved through application of the SF-6D, which takes six items from the SF-12 (or SF-36). The SF-6D is a preference-based single index measure for health using general population values[15,16].

The SF-6D describes 18,000 health states. It comes with a set of preference weights obtained from a sample of the UK general population using the recognized standard gamble valuation technique. The SF-6D index has interval scoring properties and yields summary scores on a 0 to 1 scale (practically 0.29 to 1 with a floor effect). The preference weights have recently been revised[17].

Estimated SF-6D preference scores or health utilities for the pain and no pain populations are presented in Table 3. The average utility score for the no pain population is 0.73. This contrasts to the lower score of 0.64 for the pain population. This difference is statistically ($p<0.05$) and clinically meaningful. The distribution of scores for the no pain population is noticeably skewed to the right (higher utility scores) compared to the pain population.

Table 3. Distribution of SF-6D utility scores for persons reporting pain and no pain.

Utility score	Persons reporting no pain (%)	Persons reporting pain (%)
0.90–1.0	15.9	4.4
0.80–0.89	14.3	7.9
0.70–0.79	23.3	16.8
0.60–0.69	33.8	33.4
0.50–0.59	11.1	26.5
0.40–0.49	1.4	8.5
0.30–0.39	0.2	2.6
0.20–0.29	0.0	0.0
0.10–0.19	0.0	0.0
Under 0.10	0.0	0.0
Average	0.73	0.64

Healthcare resource utilization

The 2008 NHWS also asks respondents about their use of healthcare resources. Resource utilization is considered in terms of visits or events as they relate to:

- Number of visits in the last 6 months to traditional healthcare providers
- Emergency room visits in the last 6 months
- Number of times hospitalized in the last 6 months

The number of visits for each type of traditional healthcare provider is also identified, but this level of detail is not considered in the present analysis. Traditional healthcare providers include general practitioner/family practitioners, internists and dentists as well as more specialized physicians.

The distribution of visits reported for the no pain and pain populations are summarized in Table 4. Overall, the number of traditional provider visits reported by the pain group (8.32) was almost twice that for the no pain group (4.39) ($p<0.05$). A similar picture is presented for emergency room visits (0.34 vs. 0.18; $p<0.05$) and hospitalizations (0.29 vs. 0.14; $p<0.05$). However, in the last two healthcare resource categories, the overwhelming majority of respondents fail to report either an emergency room visit or a hospitalization.

Independent variables

Table 5 presents a summary of the non-pain independent variables applied in the various regression models. Previous research has indicated that each of the variables considered has the potential to impact significantly on both HRQoL and healthcare resource utilization. The variables are:

- Socio-demographic variables
- Country of residence
- Health risk behaviors
- Comorbidity status

Table 4. Healthcare resource utilization distribution for persons reporting pain and no pain.

Resource utilization events	Traditional healthcare provider visits (%)		Emergency room visits (%)		Hospitalizations (%)	
	No pain	Pain	No pain	Pain	No pain	Pain
0	18.1	7.4	89.7	81.9	92.7	85.0
1	14.9	7.4	7.4	11.4	5.5	10.7
2	14.6	9.4	1.7	3.8	1.0	2.5
3	11.4	9.2	0.5	1.4	0.3	0.8
4	8.7	9.2	0.2	0.4	0.1	0.3
5	6.5	7.7	0.2	0.5	0.1	0.3
6	5.6	6.6	0.1	0.2	0.05	0.1
7	3.7	5.6	0.02	0.1	0.03	0.02
8	3.2	4.8	0.03	0.1	0.03	0.05
9	2.2	4.2	0.02	0.01	0.01	0.01
10 or more	11.1	28.6	0.2	0.3	0.2	0.3
Average	4.39	8.32	0.18	0.34	0.14	0.29

Table 5. Distribution of independent variables.

Independent variable*	No pain (%)	Pain (%)
Socio-demographic variables		
Age: 18–39 years	38.0	28.9
Age: 40–59 years	35.2	41.7
Age: 60 years and older	26.8	29.4
Gender: male	50.9	39.4
Gender: female	49.1	60.7
Education: university or higher	32.1	25.1
Education: high school completed	50.7	49.2
Education: not completed high school	17.2	27.2
Income: under €20,000	25.6	33.1
Income: €20,000–39,999	35.0	34.0
Income: €40,000 and above	23.3	18.5
Income reporting declined	16.1	14.5
Country of residence		
Country: France	20.5	18.3
Country: Germany	26.0	33.8
Country: Italy	21.8	10.8
Country: Spain	14.0	11.8
Country: UK	17.7	25.3
Health risk behaviors		
BMI: underweight	2.6	2.3
BMI: normal weight	39.9	31.3
BMI: overweight	37.3	35.8
BMI: obese	16.3	24.1
BMI: morbidly obese	1.6	4.5
BMI: reporting declined	2.2	2.0
Current smoker	28.5	32.8
Alcohol user	60.4	54.8
Morbidity/comorbidity status		
Charlson Comorbidity Index = 0	80.6	65.5
Charlson Comorbidity Index = 1	13.6	20.5
Charlson Comorbidity Index = 2	3.9	8.7
Charlson Comorbidity Index > 2	1.9	5.3

*Distribution of pain variables given in Table 1.

The relationship between age and HRQoL and healthcare resource utilization is well-established. National population surveys such as the Behavioral Risk Factor Surveillance System (BRFSS) in the US have shown that on a range of measures, HRQoL declines with increasing age, while healthcare resource utilization increases. Standardizing for age, therefore, is important in any assessment of the impact of pain. As shown in Table 5, the pain population tends to be older than the no-pain population. Overall, females tend to report a higher HRQoL than males. They also report higher healthcare utilization.

The relationship between educational attainment, HRQoL and healthcare resource utilization is less well-established. Educational attainment and its association with income may be expected to result in more risk-adverse behaviors, but the accompanying increased awareness of the value of preventive measures may increase healthcare utilization. HRQoL would be expected to increase with educational attainment and income.

The potential for country-specific effects is captured by including each of the five EU countries in the model as categorical variables (with Germany the reference category). There is no expectation as to either the significance of potential country effects or the direction of change on either HRQoL or resource utilization.

Three health risk behaviors are identified: body mass index (BMI), current smoking and current alcohol consumption. The NHWS does not allow a more detailed assessment of actual alcohol consumption or number of cigarettes per day and duration of smoking behavior.

The relationship between BMI and HRQoL is well-established. A recent paper by Søltoft *et al.*, utilizing data from the 2003 Health Survey of England, found a significant association between BMI and HRQoL[18]. The study found that after controlling, among other variables, for gender, age and obesity-related comorbidities, HRQoL was at a maximum with a BMI of 26.0 in men and 24.5 in women. There was a negative association for both underweight and overweight individuals. In the present case, BMI is represented by a series of categorical variables. These capture the standard BMI categories ranging from underweight to morbidly obese. In the regression models, normal weight is the reference category. Note that the distribution of BMI scores for the pain population,

compared to the no-pain population, is skewed towards the overweight and obese BMI categories.

The relationship between smoking and HRQoL is more nuanced. Sarna *et al.*, for example, conclude that among female nurses who have recently smoked, the number of cigarettes per day and the time since quitting were associated with significantly lower PCS and MCS scores from the SF-36[19]. A more recent study based on data from the 2008 BRFSS survey[20] finds that among adults, only certain HRQoL characteristics are impacted. These were worse among smokers who unsuccessfully attempted to quit. In contrast, other characteristics were better among former smokers than among those who made no attempt to quit. At best, the expectation here is that smoking is expected to have a negative, but probably small, impact on HRQoL and a positive impact on healthcare resource utilization.

Assessing the impact of alcohol consumption on HRQoL depends on the measures of alcohol consumption used. Evidence to date would suggest a non-linear relationship[21]. Moderate drinking is associated with similar or higher HRQoL scores compared to non-drinkers. Substantial HRQoL deficits are associated with higher levels of daily alcohol consumption and binge drinking. The picture is further clouded if former drinkers are included in the assessment[22]. Given the NHWS definition of alcohol use, it is difficult to argue for an expected relationship with either HRQoL or resource utilization.

The presence of morbid/comorbid conditions is captured by the Charlson Comorbidity Index (CCI). The CCI was originally designed as a measure of the risk of 1-year mortality attributable to comorbidity in a longitudinal study of general hospitalized patients. It was then validated for the same outcome in a cohort of breast cancer patients. Its contents and weighting scheme were created on the basis of Cox proportional hazards modeling[23]. It was subsequently adapted so that *International Classification of Diseases*, Ninth Revision (ICD-9) codes could be used to calculate the Charlson Comorbidity Index with existing administrative data. The CCI contains 19 categories of comorbidity which are primarily defined using ICD-9-CM diagnoses codes (a few procedure codes are also employed). Each category has an associated weight, taken from the original Charlson paper, which is based on the adjusted risk of 1-year mortality. The overall comorbidity score reflects the cumulative increased likelihood of 1-year mortality; the higher the score, the more severe the burden of comorbidity. In the present analysis it is anticipated that the more co-morbidities reported (the higher the CCI) the greater the deficit impact on HRQoL.

Estimation

In the case of both PCS and MCS, the distribution of scores indicated that an ordinary least squares (OLS) estimator was appropriate. In the case of the SF-6D health utility scores, with the possibility of a ceiling effect, both OLS and Tobit estimators were considered. As there was no discernible difference between the two, the OLS was utilized. In the case of healthcare resource utilization, traditional provider visits, emergency room visits and hospitalizations are reported as count data. The appropriate form of generalized linear model is either a Poisson or a negative binomial. Both models were assessed. As the alpha score was substantially greater than zero, the negative binomial was selected. All models were estimated using the STATA v.11 statistical package.

Results

Health-related quality of life

The results for the three aspects of health-related quality of life (HRQoL) are presented in Table 6. Estimated regression coefficients are given for each of the two models for the SF-12 PCS and MCS scores and the SF-6D utility scores. In all cases, the respective regression coefficients are interpreted as independent or marginal impacts on the respective PCS, MCS or utility scores.

SF-12 physical component score

In Model 1 with a coefficient of −15.398, the experience of severe pain in the last month is almost twice that for moderate pain (−6.690). It is also twice that for the impact of age 60 years and over (−6.526) and morbid obesity (−0.631). All other independent variables are significant at the 5% level with all health risk behaviors (excluding alcohol use) and the CCI entering with an expected negative sign. Even so, their impact on PCS is relatively slight. Age, as expected, enters with a negative sign, with the negative association increasing with age. Income, as expected, enters with a positive sign for the higher income groups (increasing in its positive impact with higher income). Education also enters with the expected negative sign.

The results for Model 2 parallel those of Model 1. The principal difference is seen in the association of pain severity and frequency on PCS. In particular: (1) the daily experience of severe pain (−17.857); (2) the experience of severe pain 4 to 6 times a week (−12.168); and (3) the experience of moderate daily pain (−10.270) on PCS. As expected, there is a well-defined negative pain gradient associated with the PCS score, declining with persons reporting less frequent mild and moderate pain. Even so, the experience of weekly or less mild pain on PCS is still substantial (−4.107).

Table 6. Regression results: health related quality of life.

Independent variables	SF-12 physical component score		SF-12 mental component score		SF-6D health utility score	
	Model 1 Coefficient	Model 2 Coefficient	Model 1 Coefficient	Model 2 Coefficient	Model 1 Coefficient	Model 2 Coefficient
Pain level reported in last month*						
Mild	−2.180		−1.161		−0.028	
Moderate	−6.690		−2.491		−0.072	
Severe	−15.398		−5.087		−0.164	
Pain level and frequency*						
Severe pain and daily experience		−17.857		−5.496		−0.186
Severe pain and 4–6 times a week		−12.168		−5.403		−0.136
Severe pain and 2–3 times a week		−9.525		−4.779		−0.108
Severe pain and weekly or less		−4.744		−2.125		−0.066
Moderate pain and daily experience		−10.270		−2.612		−0.100
Moderate pain and 4–6 times a week		−6.718		−2.724		−0.073
Moderate pain and 2–3 times week		−5.526		−3.151		−0.067
Moderate pain and weekly or less		−2.296		−1.685		−0.037
Mild pain and daily experience		−4.107		−1.201*		−0.032
Mild pain and 2–6 times a week		−3.334		−2.482		−0.046
Mild pain and weekly or less		−0.997		−0.444*		−0.018
Socio-demographic variables						
Age: 40–59 years[1]	−2.793	−2.572	1.976	2.006	0.006	0.008
Age: 60 years and older[1]	−6.526	−6.169	6.003	6.048	0.018	0.021
Gender: male[2]	0.795	0.759	2.025	2.015	0.025	0.025
Education: university or higher[3]	1.035	1.018	0.534	0.523	0.008	0.008
Education: High school completed[3]	1.338	1.357	0.489	0.481	0.007	0.007
Income: €20,000–39,999[4]	1.111	1.041	1.304	1.296	0.019	0.018
Income: €40,000 and above[4]	1.424	1.308	2.074	2.063	0.029	0.029
Income: not stated[4]	1.246	1.174	1.555	1.544	0.025	0.024
Country: UK[5]	−0.735	−0.580	−2.007	−1.988	−0.008	−0.007
Country: France[5]	0.634	0.672	−4.143	−4.136*	−0.033	−0.033
Country: Spain[5]	−0.798	−0.723	0.210*	0.208	0.002*	0.002*
Country: Italy[5]	−0.670	−0.646	−5.812	−5.802	−0.073	−0.073
Health risk behaviors						
BMI: underweight[6]	−0.992	−1.017	−2.063	−2.049	−0.021	−0.021
BMI: overweight[6]	−0.996	−0.963	0.383	0.387	−0.001*	−0.001*
BMI: obese[6]	−3.232	−3.126	−0.303	−0.289*	−0.020	−0.019
BMI: morbidly obese[6]	−6.631	−6.307	−1.762	−1.714	−0.050	−0.048
BMI: not stated[6]	−2.335	−2.297	−0.638*	−0.627*	−0.013	−0.012
Current smoker[7]	−0.367	−0.402	−0.847	−0.848	−0.007	−0.008
Alcohol user[8]	1.021	0.971	−0.154*	−0.163*	0.002*	0.001*
Morbidity/comorbidity status						
Charlson Comorbidity Index	−1.738	−1.678	−0.987	−0.976	−0.018	−0.018
Constant	52.387	52.233	45.179	45.168	0.732	0.731
R^2	0.360	0.381	0.130	0.131	0.120	0.199

All variables significant at 5% level except (*).
Reference categories: *no pain reported in last month.
[1]Age 18–39 years; [2]females; [3]not completed high school; [4]income under €20,000; [5]country: Germany; [6]BMI normal weight; [7]non-smoker; [8]non-drinker.

Country effects are significant but small in both models, with the UK and Spain entering with negative signs and France and Italy positive signs.

The overall fit of both Models 1 and 2 are acceptable for micro-data with an R^2 of 0.3460 and 0.381, respectively. The corresponding intercept values are 52.387 and 52.233.

SF-12 mental component score

The impact of pain severity and frequency on the MCS is less than the impact on the PCS components of the SF-12.

In Model 1, the estimate for severe pain (−5.087) is less than one-third of the coefficient on the corresponding PCS. Similarly, the experience of severe daily pain in Model 2 is only −5.496 compared to the corresponding coefficient of −17.857 for the PCS. Once again, however, there is a well-defined negative gradient for pain severity and frequency on the MCS. Also, pain does not dominate the MCS models to the extent that it does in the PCS models. For those over 60 years of age, the negative association with MCS is greater than that reported for the pain variables.

Unlike the results for PCS, the country effects are more substantial. Only Spain enters with a negative sign and with the smallest country effect. The greatest country effects are found for France. These are of a similar magnitude to the mild and moderate pain variables.

The overall fit of the MCS models with an R^2 of 0.130 and 0.131 for Models 1 and 2, respectively. Corresponding intercept values are 45.179 and 45.168, respectively.

SF-6D health utilities

The results for health utilities for both Model 1 and 2 are similar to those for both PCS and MCS models. Once again, the experience of pain has a dominant negative effect on utility scores.

Compared to the no-pain reference group, the association of severe pain in Model 1 reduces health utility by −0.164 (on a scale of 0 to 1) followed by moderate pain with an impact of −0.072. Where severity and the frequency of pain are considered in Model 2, the effect of severe daily pain reduces utility scores by −0.186. The corresponding estimate for severe pain 4 to 6 times a week is −0.136. For severe pain 2 to 3 times a week, the deficit is −0.108; with a deficit for moderate daily pain of −0.100.

The relative contribution of the health risk and comorbidity variables are, as expected, consistent with the results reported for PCS and MCS. The utility deficits associated with severe and frequent pain are substantially greater than those associated with not only health risk factors, e.g. morbid obesity −0.050 and −0.048 in Models 1 and 2, respectively, but also age, gender, education and income. All coefficients are significant at the 5% level.

With the sole exception of pain, the country coefficients are significant at the 5% level, with a negative effect against the reference group. The largest deficit is for Italy (−0.073 for both models).

The overall explanatory power is similar to that reported for MCS in Model 1 with an R^2 of 0.120, but with an R^2 of 0.199 in Model 2.

Healthcare resource utilization

The results for healthcare resource utilization are presented in Table 7. As a negative binomial model has been used, the regression coefficients are interpreted as the difference in the logs of expected counts for a one unit change in the predictor variable. As this is not an intuitively obvious interpretation, the regression coefficients have been transformed to percentages.

Traditional provider visits

The contributions of pain, at all levels of severity, dominate as determinants of the number of traditional provider visits.

In Model 1, the experience of severe pain increases visits by 132.3% compared to the no-pain reference category. The combination of severe with daily pain has an even greater effect as shown in Model 2, where provider visits increase by 145.4%. The effect of moderate pain is also substantial, increasing provider visits by 63.5% in Model 1 and, combined with daily pain experience, by 84.6% in Model 2.

These percentage contributions stand in contrast to those reported for health risk behaviors where obesity and morbid obesity increase provider visits by 20–40% and where the presence of comorbidities increase the provider visits by up to 25%. With Germany as the reference category, the number of provider visits in the UK is about 30% less.

Emergency room visits

The experience of pain also has a substantial association with emergency room visits. In Model 1, severe pain is associated with a 172.7% increase in the number of emergency room visits; for moderate pain, it is 66.4%. The combination of severity and frequency in Model 2 has an even greater contribution, with severe daily pain increasing visits by 194.1%. Even moderate daily pain increases visits by 86.2%. This is a far greater contribution than that estimated for sociodemographic, health risk factors or even the CCI.

Hospitalizations

Pain also has a substantial association with hospitalizations. In Model 1, the experience of severe pain increases hospitalizations by 229.0%. This is even more striking in Model 2, where the combination of severe and daily pain increases hospitalizations by 263.1%. Again, the magnitude of these impacts stands in contrast to those associated with sociodemographic characteristics, health risk factors and the CCI. In this last case the presence of comorbidities only increases the risk of hospitalization by 60%.

It is also worth noting the country-specific impact of hospitalizations (with Germany as the reference category), with UK and Italy reporting the greatest percentage decrements.

Discussion

Despite its ubiquity, there remains much we do not know about pain. Pain is deceptively complex. Acute pain activates multiple excitatory and inhibitory systems. If acute pain transitions to chronic pain (a process not thoroughly understood), pain can change in character and take on both nociceptive and neuropathic components. Importantly, chronic and recurrent pain is now considered by many to be a disease in its own right and not merely a symptom. Pain is no longer seen as related to an evolving injury but as reflecting pathophysiological changes within

Table 7. Regression results: healthcare resource utilization.

Independent variables	Traditional provider visits		Emergency room visits		Hospitalizations	
	Model 1 Percentage change	Model 2 Percentage change	Model 1 Percentage change	Model 2 Percentage change	Model 1 Percentage change	Model 2 Percentage change
Pain level reported in last month*						
Mild	27.9		4.3*		17.0	
Moderate	63.5		66.4		44.4	
Severe	132.3		172.7		229.0	
Pain level and frequency*						
Severe pain and daily experience		145.4		194.1		263.1
Severe pain and 4–6 times a week		115.0		106.4		163.0
Severe pain and 2–3 times a week		81.3		103.6		88.9
Severe pain and weekly or less		90.6		133.2		145.1
Moderate pain and daily experience		84.6		86.2		66.5
Moderate pain and 4–6 times a week		73.6		85.4		96.1
Moderate pain and 2–3 times week		61.3		83.0		30.3*
Moderate pain and weekly or less		28.1		14.6*		−7.0*
Mild pain and daily experience		41.0		−7.6*		52.7
Mild pain and 2–6 times a week		52.2		21.7		41.5
Mild pain and weekly or less		10.9		−1.2*		−6.6*
Socio-demographic variables						
Age: 40–59 years[1]	11.4	10.4	−33.3	−33.8	−15.6	−16.8
Age: 60 years and older[1]	27.1	25.3	−32.6	−33.6	9.7*	7.8*
Gender: male[2]	−25.7	−25.5	−5.6*	−4.9*	−3.1*	−2.4*
Education: university or higher[3]	2.3*	2.3*	39.3	39.7	11.5*	12.5*
Education: high school completed[3]	4.6	4.5	37.8	37.8	11.0*	11.4*
Income: €20,000–39,999[4]	−1.4*	−1.3*	−24.1	−23.8	−20.5*	−19.8*
Income: €40,000 and above[4]	−0.9	−0.6*	−18.9	−18.5	−9.1*	−8.2*
Income: not stated[4]	−5.6	−5.3	−27.2	−26.9	−32.4	−31.6
Country: UK[5]	−30.0	−30.5	20.0	19.3	−57.9	−58.0
Country: France[5]	1.6*	1.4*	−16.9	−17.1	−27.9	−27.9
Country: Spain[5]	2.4*	2.1*	185.8	185.7	−22.7*	−22.5*
Country: Italy[5]	9.6	9.8	26.6	26.8	−53.4	−52.9
Health risk behaviors						
BMI: underweight[6]	15.4	15.2	38.8	39.1	101.3	101.0
BMI: overweight[6]	7.1	6.9	−4.7*	−5.0*	23.0	22.8
BMI: obese[6]	22.7	22.4	6.2*	5.8*	−3.8*	−4.5*
BMI: morbidly obese[6]	35.0	33.8	5.0*	3.6*	26.3*	24.2*
BMI: not stated[6]	−13.1	−13.5	27.6*	27.5*	19.0*	17.3*
Current smoker[7]	3.2	3.3	22.1	22.0	10.6	11.4
Alcohol user[8]	−6.0	−5.9	−11.4	−11.2	−20.3	−20.4
Morbidity/comorbidity status						
Charlson Comorbidity Index	24.5	24.2	48.1	47.8	61.7	61.2
Log pseudo likelihood	−159,852.2	−159,746.5	−29,036.7	−29,018.3	−23,371.4	−23,348.6
Alpha	0.011	0.011	0.326	0.326	0.789	0.792

All variables significant at 5% level except (*).
Reference categories: *no pain reported in last month.
[1]Age 18–39 years; [2]females; [3]not completed high school; [4]income under €20,000; [5]country: Germany; [6]BMI normal weight; [7]non-smoker; [8]non-drinker.

the nociceptive system with psychosocial responses that perpetuate the problem.[24]

Importantly, pharmacological treatment of pain must take into account the risk that drugs may activate inhibitory systems or block excitatory transmission. For that reason, much pain treatment today is multimodal and may involve combinations of analgesic agents. While multiple analgesics can be effective, there is a risk of drug–drug interactions which can potentially be severe. In fact, most effective analgesics carry with them the risk of adverse events. Thus, the problem of pain involves issues of diagnosis, etiology, progression, and the delicate balancing act of achieving relief with tolerable side-effects. All of these factors affect the lives of patients coping with pain, who, in turn, affect their communities, utilize local healthcare resources, and impact society in general.

This is the first analysis undertaken at the country level in the EU of the societal impact of pain utilizing multivariate modeling techniques. Perhaps the single most important finding from the present analysis is the striking role played by pain severity and pain frequency on both HRQoL and healthcare resource utilization. Compared to the other respondent characteristics, all of which have been shown to impact significantly on

HRQoL measures and the utilization of healthcare resources, pain is by far the most important determinant.

Of particular concern in view of these findings is the aging of the population in Europe and other nations. Pain is associated with advancing age, and with the 'graying' of the EU will come even more demands on healthcare resources.

Previous community assessments of pain have focused on the correlates of pain severity; but have typically failed to include a no-pain control group. The presence of a control group is critical in any assessment of the societal burden of pain – whether it is in terms of HRQoL or healthcare resource utilization. This is seen in the Smith *et al.* assessment of the community impact of pain on HRQoL[3]. Compared to the majority of respondents who have not experienced pain in the last month, those with severe and frequent pain, not only report a significantly lower HRQoL, but also more frequent utilization of healthcare resources – notably in healthcare provider visits[3]. These findings are echoed in the present analysis in the distribution of PCS, MCS and utility scores and in the patterns of resource utilization between the pain and no-pain groups. Of interest, however, is the differential impact of pain on PCS and MCS scores where pain has a substantially greater impact on the former.

What has not been noted before, however, at the community level, is the importance of separately identifying the severity and the frequency of pain. Focusing on pain severity levels is only part of the picture. The frequency with which pain is experienced can add dramatically to associated HRQoL deficits and the burden placed upon the healthcare system. A major contribution of the present analysis is to provide robust estimates of the contribution of pain frequency in a framework which not only attempts to standardize for other pain correlates but also points to the dominant impact of pain severity and frequency on these outcomes. Indeed, the analysis points unequivocally to the overriding impact of pain and its frequency on HRQoL and resource utilization compared to the no-pain population in terms of both the presence of health risk behaviors and major comorbidities.

It should also be noted that the models presented here have not attempted to isolate the factors associated with the reported pain severity and frequency. Given the fact that severe and frequent pain is characteristic of a number of disease states, including musculoskeletal conditions, the purpose here was to consider pain as it impacts both society and the utilization of resources. Pain is considered the focus of potential interventions, irrespective of its etiology. For this reason, no attempt has been made to analyze separately nociceptive as opposed to neuropathic pain or to analyze, for example, the societal impact of frequently reported low back pain or osteoarthritis pain, etc. Given the richness of the NHWS database, these more specific analyses will be the subject of future research.

Even so, there are some important implications of the present study. Severe and frequent pain is pervasive and this fact is not well appreciated even by clinicians. The clear implication of these findings is known intuitively by most practicing clinicians, namely that much pain goes untreated or is under-treated, causing considerable suffering as well as possible lost productivity. Indeed, quantifying productivity lost to pain is a seemingly impossible task but one that merits at least some speculation.

Second, the experience of pain is quantitatively different from the HRQoL deficits and patterns of healthcare resource utilization attributable to individual chronic disease states. Pain is both pervasive and pernicious in its impact, a fact that can be subsumed where the focus is on individual disease states.

Third, from the perspective of society, a focus on pain may have significant payoffs in improving both HRQoL and reducing health resource utilization. Fewer and better managed pain patients will require fewer healthcare resources. Increased understanding of the mechanisms of pain and its safe and effective treatment could lead to more cost-effective management of pain patients as well as reducing chronicity in the long-term pain experience. This study demonstrates that a better appreciation of pain and its true costs is urgently needed, particularly by the clinical community, and could have a profound impact on healthcare resources in the near-term.

Even so, there are a number of limitations to the present study that should be noted. First, as an internet-based observational study, there is the possibility of bias in the responses as only persons with internet-access will be asked to participate. While the extent of such biases are unknown, it is worth noting that internet penetration in the five EU countries covered here is overall in excess of 50% of individuals and households. Second, respondents are asked to report on their experience of pain. Apart from the potential impact of recall bias, there is no clinical confirmation of, for example, reported pain severity or frequency. Finally, this study has focused on the experience of pain. Apart from excluding more obvious acute pain types there is no attempt to try and impose an arbitrary distinction between acute and chronic pain or between, for example, primarily neuropathic and primarily nociceptive pain.

Conclusion

To date, there has been a lack of appreciation of the burden imposed by pain severity and frequency. This has been due, in large part, to the absence of well-specified and robust multivariate models directed towards the assessment of the independent contribution of pain and its frequency at the country level. This study has demonstrated

that for the five largest EU countries, the societal impact of pain is considerable. Pain outweighs by far the contribution of more traditional explanations of HRQoL deficits as well as being primarily associated with increased provider visits, emergency room visits and hospitalizations.

Transparency

Declaration of interest
This study was supported by Grünenthal GmbH, Aachen, Germany.

Declaration of financial/other relationships
P.L. has disclosed that he is a consultant to Kantar Health, a company that undertook this analysis on behalf of Grünenthal. H.L. has disclosed that she is an employee of Grünenthal GmbH. G.M.-S., A.N., J.P. and G.V. have disclosed that they are members of the Grüneththal CHANGE PAIN advisory group.

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References

1. Breivik H, Collett B, Ventafridda V, et al. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain 2006;10:287-333
2. McDermott AM, Toelle TR, Rowbotham DJ, et al. The burden of neuropathic pain: results of a cross-sectional survey. Eur J Pain 2006;10:127-135
3. Smith BH, Elliott AM, Chambers WA, et al. The impact of chronic pain in the community. Fam Pract 2001;18:292-299
4. Miro J, Paredes S, Rull M, et al. Pain in older adults: a prevalence study in the Mediterranean region of Catalonia. Eur J Pain 2007;11:83-92
5. Frießem CH, Willweber-Strumpf A, Zenz MW. Chronic pain in primary care. German figures from 1991 and 2006. BMC Public Health 2009;9:299
6. Ellert U, Neuhauser H, Roth-Isiqkeit A. Pain in children and adolescents in Germany: the prevalence and usage of medical services. Results of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS). Bundesgesundheitblatt Gesundheitforschung Gesundheitsschutz 2007;50:711-717. [in German]
7. Juniper M, Le TK, Mladsi D. The epidemiology, economic burden, and pharmacological treatment of chronic low back pain in France, Germany, Italy, Spain and the UK. Expert Opin Pharmacother 2009;10:2581-2592
8. Konig HH, Bernert S, Angermeyer MC, et al. Comparison of population health status in six European countries: results of a representative survey using the EQ-5D questionnaire. Med Care 2009;47:255-2561
9. Smith BH, Torrance N, Bennett MJ, et al. Health and quality of life associated with chronic pain of predominantly neuropathic origin in the community. Clin J Pain 2007;23:143-149
10. Jensen MP, Chodroff MJ, Dworkin RH. The impact of neuropathic pain on health-related quality of life: review and implications. Neurology 2007; 68:1178-1182
11. O'Connor AB. Neuropathic Pain. Pharmacoeconomics 2009;27:95-112
12. Ware JE, Kosinski M, Turner-Bowker DM, et al. How to Score the Version 2 of the SF-12 Health Survey (with a supplement documenting version 1). Lincoln, RI: Quality Metric, 2002
13. Ware JE, Kosinski M, Keller SD. SF-12: How to Score the SF-12 Physical and Mental Health Summary Scales, 3rd edn. Lincoln, RI: QualityMetric, 1998
14. Ware JE, Kosinski M, Keller SD. A 12-item short-form health survey (SF-12): construction of scales and preliminary tests of reliability and validity. Med Care 1996;32:220-233
15. Brazier JE, Roberts JR. The estimation of a preference-based index from the SF-12. Med Care, 2004;42:851-859
16. McCabe C, Brazier JE, Gilks P, et al. Using rank data to estimate health state utility models. J Health Econ, 2006;25:418-431
17. Kharroubi S, Brazier JE, Roberts JR, et al. Modelling SF-6D health state preference data using a nonparametric Bayesian method. J Health Econ 2007;26:597-612
18. Søltoft F, Hammer M, Kragh N. The association of body mass index and health related quality of life in the general population: data from the 2003 Health Survey of England. Qual Life Res 2009. Oct 8 (epub)
19. Sarna L, Bialous SA, Cooley ME, et al. Impact of smoking and smoking cessation on health-related quality of life in the Nurses' Health Study. Qual Life Res 2008;17:1217-1227
20. McClave AK, Dube R, Strine TW, et al. Associations between health-related quality of life and smoking status among a large sample of U.S. adults. V Med 2009;48:173-179
21. Stranges S, Notaro J, Freudenheim JL, et al. Alcohol drinking patterns and subjective health in a population-based study. Addiction 2006;101: 1265-1276
22. Van Dijk AP, Toel J, Verdumen JE. The relationship between health-related quality of life and two measures of alcohol consumption. J Stud Alcohol 2004;65:241-249
23. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-383
24. Niv D, Devor M. Chronic pain as a disease in its own right. Pain Practice 2004;4:179-181