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The cost of headache disorders in Europe: the Eurolight project

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Background and purpose: Headache disorders are very common, but their monetary costs in Europe are unknown. We performed the first comprehensive estimation of how economic resources are lost to headache in Europe.

Methods: From November 2008 to August 2009, a cross-sectional survey was conducted in eight countries representing 55% of the adult EU population. Participation rates varied between 11% and 59%. In total, 8412 questionnaires contributed to this analysis. Using bottom-up methodology, we estimated direct (medications, outpatient health care, hospitalization and investigations) and indirect (work absenteeism and reduced productivity at work) annual per-person costs. Prevalence data, simultaneously collected and, for migraine, also derived from a systematic review, were used to impute national costs.

Results: Mean per-person annual costs were €1222 for migraine (95% CI 1055–1389; indirect costs 93%), €303 for tension-type headache (TTH, 95% CI 230–376; indirect costs 92%), €3561 for medication-overuse headache (MOH, 95% CI 2487–4635; indirect costs 92%), and €253 for other headaches (95% CI 99–407; indirect costs 82%). In the EU, the total annual cost of headache amongst adults aged 18–65 years was calculated, according to our prevalence estimates, at €173 billion, apportioned to migraine (€111 billion; 64%), TTH (€21 billion; 12%), MOH (€37 billion; 21%) and other headaches (€3 billion; 2%). Using the 15% systematic review prevalence of migraine, calculated costs were somewhat lower (migraine €50 billion, all headache €112 billion annually).

Conclusions: Headache disorders are prominent health-related drivers of immense economic losses for the EU. This has immediate implications for healthcare policy. Health care for headache can be both improved and cost saving.

Introduction

Headache disorders are prevalent, and most adults have suffered from one or more types during the last year. The most common are tension-type headache (TTH), migraine and medication-overuse headache (MOH) [1].

Published evidence indicates that migraine is the most costly neurological disease for European society [2,3], although there are large variations in the cost estimates across the few countries where data are available [4]. These are probably due mainly to differences in methodology and periods of time over which estimates have been made. For example, most investigators have used a

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'top-down' approach, which carries the risk of underestimating or omitting cost items that are not fully captured in national statistics. Moreover, most studies were conducted before the impact of triptans on both direct and indirect costs [5]. The general opinion is that available estimates of the cost of migraine in Europe are underestimations [3].

Given their high prevalence, it has been suggested that non-migrainous headache disorders are at least as costly as migraine [2]. Yet, the economic impact of TTH and MOH in Europe is virtually unknown [4], and these disorders have hitherto been omitted from estimates of the cost of brain disorders in Europe [2,5]. All in all, the total costs of headache in Europe are unknown. In light of their magnitude, this constitutes a major paradox.

Using robust methodology, we provide the first comprehensive estimate of the total costs of all headache disorders to European society.

Methods

This was a cross-sectional cost-of-illness survey conducted as part of the Eurolight project (http://www.eurolight-online.eu).

Recruitment

A cross-sectional survey led by CRP-Santé, Luxembourg, was conducted in ten countries from November 2008 to August 2009. Because of inherent biases, two countries were not included in this analysis: the survey sample in Ireland was drawn from a patient organization, and the UK sample [patients visiting general practitioners (GPs) for any reason] was very small [6]. The other eight were Austria, France, Germany, Italy, Lithuania, Luxembourg, Netherlands and Spain. The national ethics committee of Luxembourg approved the general protocol of the survey and the data transfer. Where needed, local ethics committees and data inspectorates approved the protocols for individual countries. The methods of recruitment of participants differed between countries, and are fully described elsewhere [6]. In brief, adults aged 18–65 years were drawn from the general population in all countries except Austria (patients visiting GPs or neurologists for any reason), France (patients visiting GPs for any reason) and Spain (employees of the national postal services).

Diagnostic methodology

A structured questionnaire [7] was employed, self-administered except in Lithuania (medical-student interviewers). The diagnostic questions were based on the criteria of the International Classification of Headache Disorders, 2nd edition (ICHD-II) [8]. Only one headache type was diagnosed in each respondent to avoid double-counting, and respondents having more than one were instructed to consider the most bothersome. According to the algorithm used to convert responses to diagnoses, MOH over-ruled other diagnoses and TTH trumped probable migraine. In the analysis, migraine and probable migraine were merged, as were TTH and probable TTH. A small minority of headaches were unclassifiable (henceforth referred to as 'other headaches').

Prevalence-estimates in the Eurolight project (*data on file*, to be published separately) were adjusted according to national means for age and gender in Germany, Italy, Lithuania (age only), Luxembourg and the Netherlands, and also according to geographical area in Germany, Luxembourg and the Netherlands. In all countries, questionnaires were more likely to be completed and returned by those most affected by headache (interest bias). To estimate the size of this bias, studies of non-respondents were performed in Luxembourg (n = 357), Italy (n = 202), the Netherlands (n = 188) and Germany (n = 260) [6]. Non-respondents were selected randomly, called by telephone and asked about headache during the previous year. Amongst initial respondents, the 1-year prevalence of all headache was 79%, while amongst those in the non-respondent studies it was 64%. The prevalence in the source population (24% respondents, 76% non-respondents) was re-estimated at 68% (the weighted mean of these), implying that interest bias might have led to overestimation by up to 14% (11/79*100). To compensate for this, all prevalence estimates were, for this analysis, reduced by 14% (Table 1).

Compilation of data for estimation of per-person costs

The questionnaire contained 103 items and had been validated in six European countries and in seven languages for evaluating the burden of headache [7]. Questions were mostly categorical, but some were numerical or open. Enquiries at issue (questions 44, 45, 47–49, 57, 58) related to the use of healthcare resources and the impact of headache on work. Literal wordings of these questions are seen in Appendix 1 (online only).

Unit prices were obtained from official sources in each country and converted to common currency (Euro, €). Estimates of direct costs were totals of payments out-of-pocket plus whatever was paid for or reimbursed by government or insurance companies. Medication costs were estimated using wholesale acquisition prices for the cheapest packages available. For inpatient care, the *per diem* costs in a typical ward

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Table 1 The numbers of respondents, response rates, sex distribution, mean age and 1-year prevalences [adjusted downwards to compensate for interest bias (see Methods)] of most bothersome headache by country

	Participants (*n*)	Participant rate (%)	Women (%)	Mean age (years ± 1 SD)	Migraine (%)	TTH (%)	MOH (%)	Other headache (%)
Austria	646	10.8	70	49 ± 16	35.0	27.2	2.2	4.9
France	876	36.5	68	50 ± 17	33.2	25.0	4.2	4.7
Germany	338	11.3	57	45 ± 12	29.1	31.8	2.6	4.9
Italy	500	14.3	58	43 ± 13	38.2	24.9	1.6	0.9
Lithuania	616	54.2	59	41 ± 14	21.5	40.4	1.4	3.3
Luxembourg	2023	31.1	58	40 ± 13	30.4	31.2	3.0	4.1
Netherlands	2414	NA[a]	50	43 ± 13	29.2	40.6	1.4	0.2
Spain	999	58.8	59	43 ± 12	35.4	26.0	6.0	2.6

MOH, medication-overuse headache; TTH, tension-type headache.
[a]Response rate indeterminable in the Netherlands, because the survey was by Internet (denominator unknown).

(e.g., internal medicine or neurology) were used, excluding costs of investigations. Estimates of indirect costs used average gender-specific salary levels in industry and services in each country, obtained from the Eurostat database [9]. One day's wage was counted as the average gross annual earnings divided by 220 working days. The complete list of prices used is reported in Appendix 2 (online only).

Data handling and analysis

Completed questionnaires were transferred electronically to the data-management centre at CRP-Santé, Luxembourg. Double data entry and reconciliation of inconsistencies were employed as quality-control procedures. A health economist (AG) led the costing analyses.

Direct and indirect costs were estimated by applying unit-price assumptions and gender-specific wages to the patterns of resource use and reduced or lost productivity reported [10]. Direct costs were aggregated in five categories: acute medications, prophylactic medications, outpatient health care (including emergency room visits), hospitalization and diagnostic investigations. Respondents' recollections of acute medication use during the preceding month were multiplied by 12, and by the relevant tariffs for one typical dose, to arrive at gross annual costs. 'Used more than once' as a response was interpreted conservatively as twice per month. It was assumed that prophylactic medication usage reported was stable over time, and costs of recommended daily doses were multiplied by 365 days to estimate annual costs. For hospitalization, '3–7 days' was regarded as 5 days. Amongst employed respondents only, lost productivity was estimated from the number of days missed from work (absenteeism); reduced productivity was estimated from days at work when the amount done was ≥50% reduced, each such day counting as a full day lost [11] (balanced by ignoring days in which the reduction was < 50%). Each estimate was made over the previous 3 months and multiplied by four to obtain annual estimates [12].

Per-person annual costs are presented as means with 95% confidence intervals (CI) by disorder and country. Estimates are not shown for subgroups with a sample size < 10. Standard deviations are estimated with consideration to co-variance. In most countries, figures are weighted in the same manner as were the prevalence data; crude data are presented for Austria, France, and Spain, as weights adjusting to national means for age, gender or geographical area were not available.

Per-person costs for each headache type were multiplied by its prevalence to estimate total annual costs on national levels: mean per-person annual cost*1-year prevalence/100*country adult population. Mean per-person annual costs were imputed also for non-participating EU27 countries ($n = 19$), the numbers of inhabitants 18–65 years old in each country (on 1st January 2010) being retrieved from Eurostat [13]; thereby, we estimated total costs on a European level.

All analyses were carried out on Statistical Analysis System®, provided by SAS Institute Inc (Cary, NC, USA), and on Microsoft Excel®.

Role of the funding source

The EAHC were not involved in the study design, collection of data, analysis or interpretation of data, writing of the report, or in the decision to submit for publication.

Results

Participation and prevalences

In total, 8412 questionnaires were included in this analysis (Table 1). In Figs 1–4, respondents with headache in each country are distributed (*n*, crude) between the four diagnoses.

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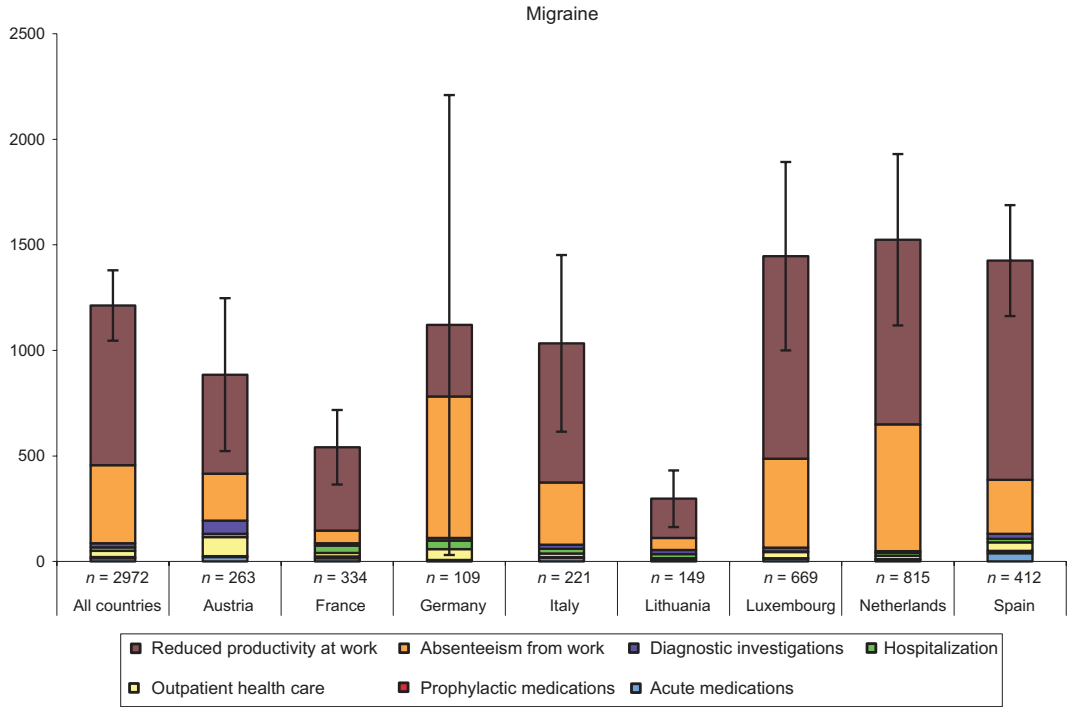

Figure 1 Indirect and direct per-person annual costs (by resource-use components) of migraine presented by disorder and country with 95% CI.

Per-person annual costs

The mean per-person annual cost of migraine in all countries was €1222 (95% CI 1055–1389) (Fig. 1). The CI in Germany was large because of the small sample. Indirect costs accounted for 93%, of which two-thirds were attributable to reduced productivity (€765) rather than absenteeism (€371). Amongst direct costs, the top contributory category was outpatient care (€30), followed by investigations (€19), acute medications (€16), hospitalization (€16) and prophylactics (€5).

The mean per-person annual cost of TTH in all countries was €303 (95% CI 230–376) (Fig. 2). Indirect costs accounted for 92%, with more attributable to reduced productivity (€173) than absenteeism (€105). Amongst direct costs, the top contributory category was outpatient care (€11), followed by investigations (€6), hospitalization (€5) and acute medications (€3). Prophylactics contributed very little. Some influential outliers appeared in Austria.

The mean per-person annual cost of MOH in all countries was €3561 (95% CI 2487–4635) (Fig. 3). Indirect costs accounted for 92%, almost equally divided between reduced productivity (€1669) and absenteeism (€1623). Amongst direct costs, the top contributory category was outpatient care (€114), followed by investigations (€57), hospitalization (€43), acute medications (€42) and prophylactics (€13).

The mean per-person annual cost of other headaches in all countries was €253 (95% CI 99–407) (Fig. 4). Indirect costs accounted for 82%, of which most was attributable to reduced productivity (€182) rather than absenteeism (€26). Amongst direct costs, the two top contributory categories were investigations (€15) and outpatient care (€15), followed by hospitalization (€11) and acute medications (€4). Prophylactics did not contribute.

National and EU annual costs

Amongst the participating countries, France, Germany, Italy and Spain had the highest total costs for headache (each in excess of €20 billion/year) (Fig. 5). In seven (88%) of the eight countries, migraine generated the highest cost. The relative cost of MOH varied, being greater than that of TTH in half of the participating countries and highest in France.

In all 27 EU countries, the total annual cost of headache amongst adults was estimated at €173 billion, apportioned as follows: migraine €111 billion (64%), TTH €21 billion (12%), MOH €37 billion (21%) and other headaches €3 billion (2%).

Discussion

This is the first comprehensive investigation of economic resources lost in Europe because of headache.

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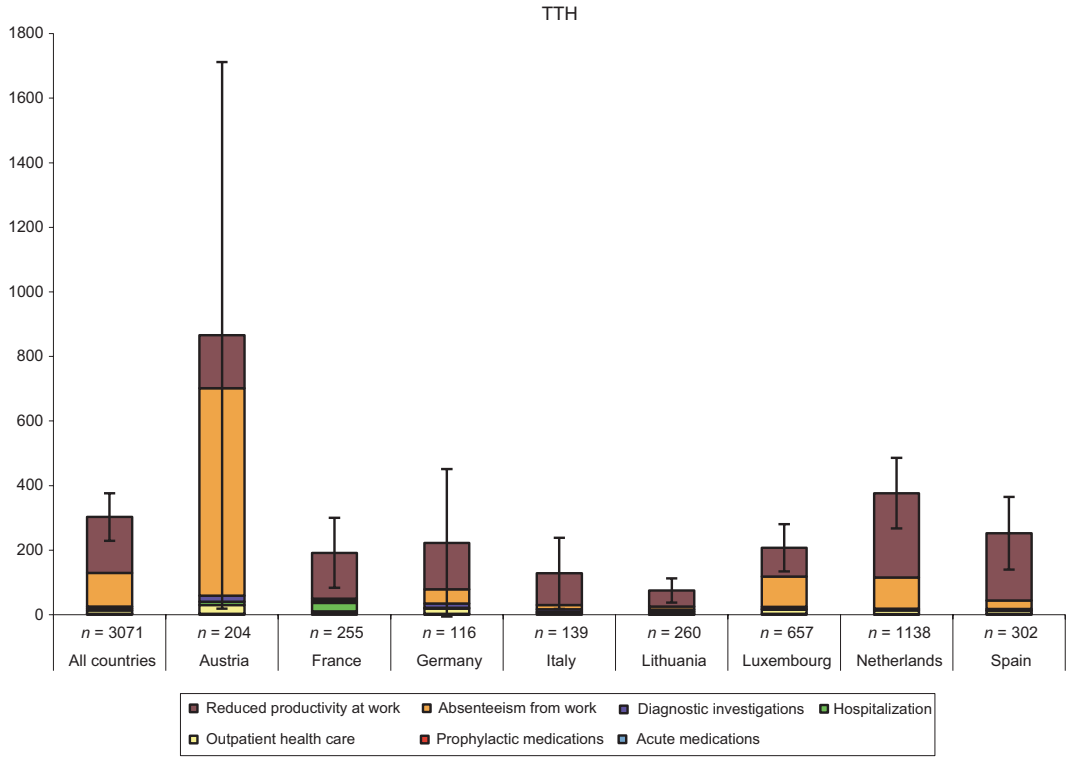

Figure 2 Indirect and direct per-person annual costs (by resource-use components) of tension-type headache presented by disorder and country with 95% CI.

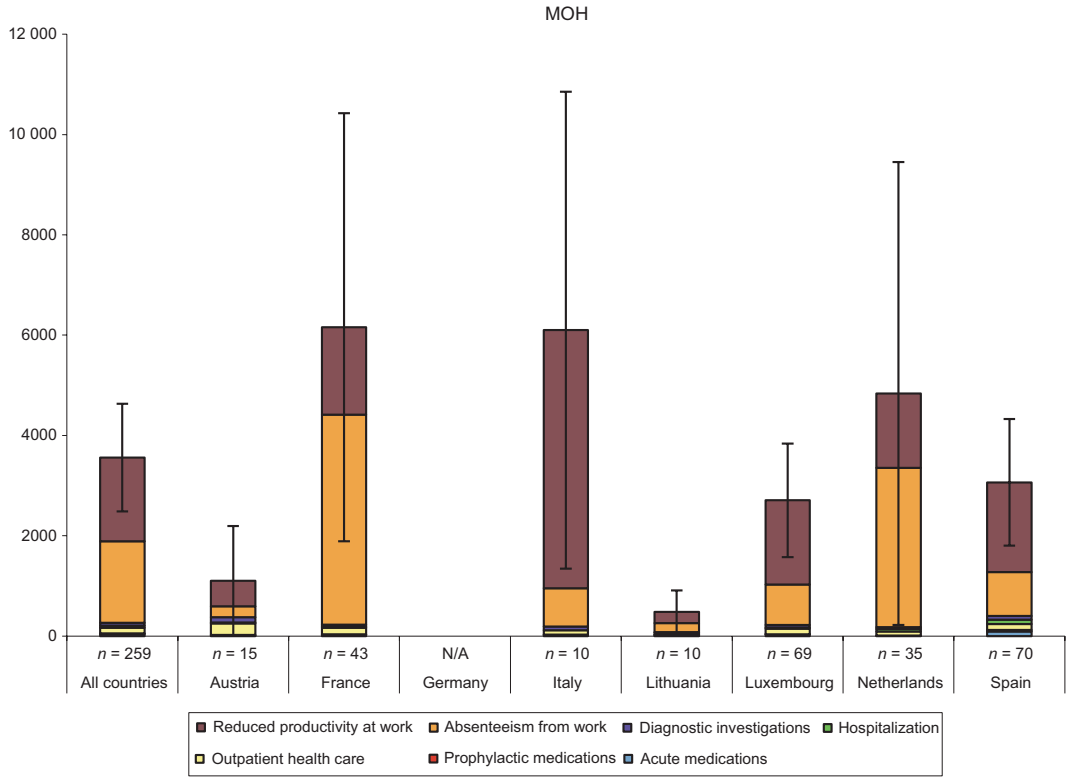

Figure 3 Indirect and direct per-person annual costs (by resource-use components) of medication-overuse headache presented by disorder and country with 95% CI. Estimates are not shown for subgroups with a sample size < 10.

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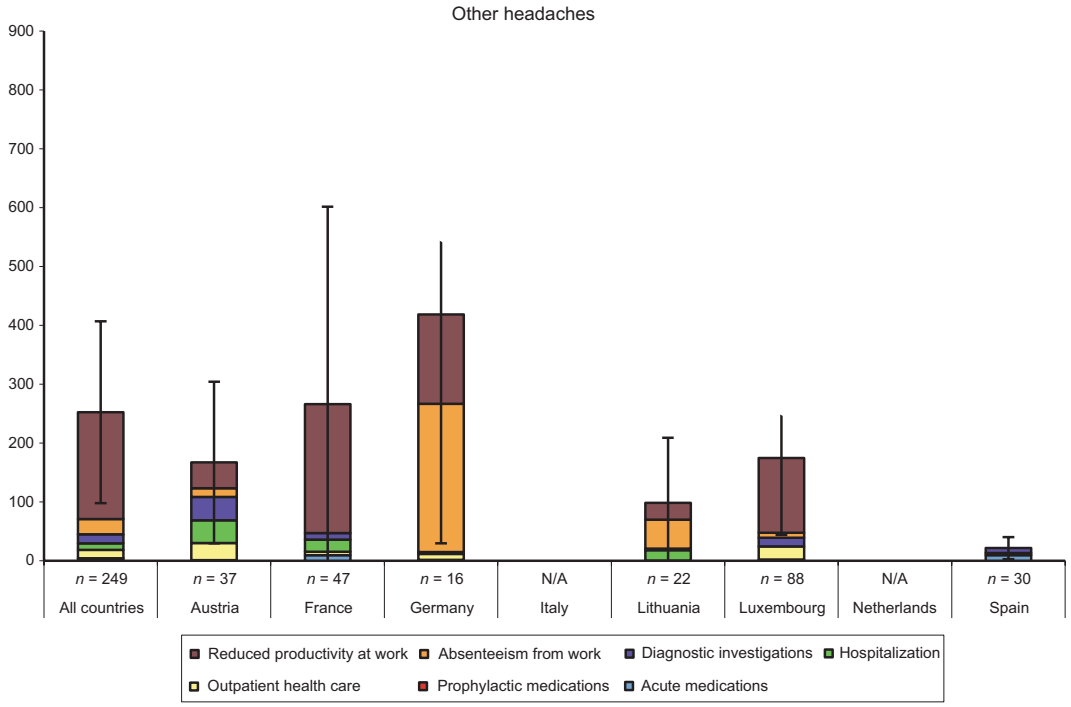

Figure 4 Indirect and direct per-person annual costs (by resource-use components) of other headaches presented by disorder and country with 95% CI. Estimates are not shown for subgroups with a sample size < 10.

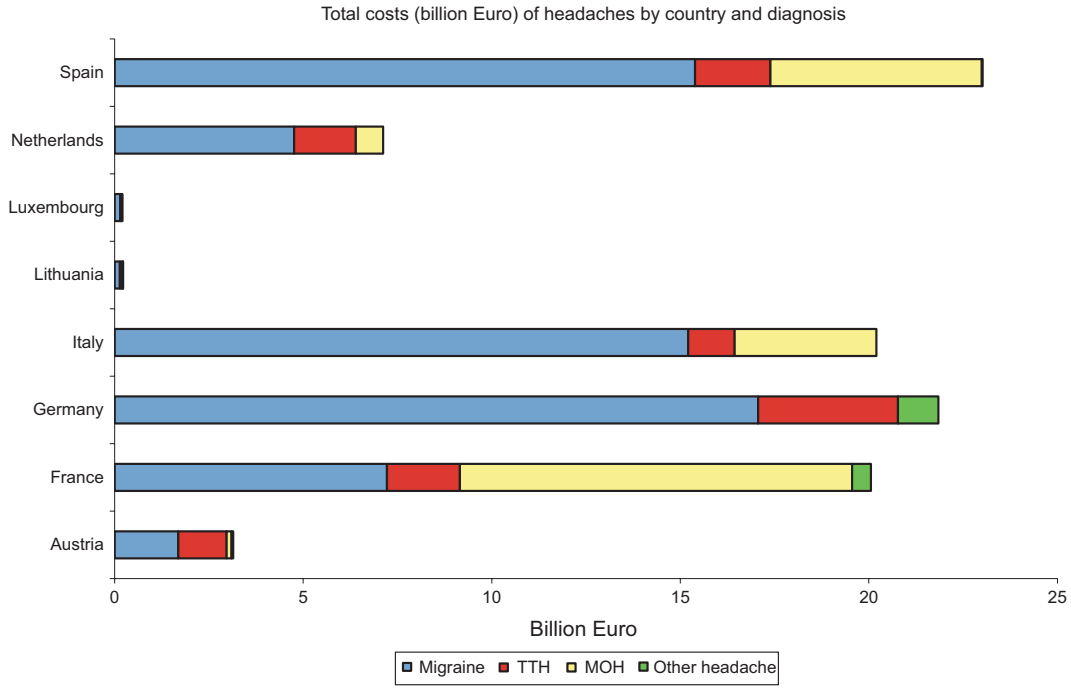

Figure 5 Total annual costs (direct and indirect) of headache presented by disorder and country.

We found that, of the diagnosed headache types, migraine was the most costly, and that, contrary to other neurological diseases [2], indirect costs dominated.

Methodological considerations

The study summarizes the monetary value of the consequences of headache disorders, which would not be

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incurred if headache did not exist. There are opportunity costs, which correspond to the best alternative use to which resources having that value might be put [14]. We applied a societal perspective, meaning that all costs, whether incurred by individuals, government or others, were taken into account. This is the most comprehensive perspective, not masking costs that might be shifted to another sector rather than saved [15].

The 'human capital' approach, which we used, is the most common method for estimating the economic value of an employee's productivity, assuming that it is equal to gross earnings in a well-functioning labour market [14]. This is especially suitable for episodic headaches where absences are mostly shorter than the time required to replace the employee ('friction period'). Our estimates did not allow for lost productivity being made good by colleagues or, later, by the employee because, when that happened, there was encroachment on other uses of colleagues' or the employee's time which, we assumed, had similar value.

Estimates were not adjusted for purchasing power parity (PPP) because our main purpose was to show actual costs. As such, they may be compared directly to national accounts such as gross domestic product in each country. However, this approach implies that part of the differences in costs between countries is caused by the differences in price and wage levels (most notable in Lithuania [Appendix 2, online only]).

The estimates of the cost per patient for the less common diagnoses (MOH and other headaches) are based on small samples for several countries. The differences across countries for these diagnoses are therefore likely to have been caused by random variation and may be misleading. This also affects the estimates of total costs of MOH and other headaches, which would probably not vary across countries to the same extent if based on larger samples of patients.

Estimates of national costs, being the product of costs per patient and prevalence, are directly proportional to both. Eurolight was not well designed to estimate prevalences in all countries surveyed, and the estimates obtained are subject particularly to the errors likely to arise from low participation rates. Better data exist in Europe for migraine, but not for TTH or MOH. The estimated costs of migraine are higher than the estimated costs of other headache disorders. Therefore, we conducted a sensitivity analysis using the prevalence of migraine in Europe (15%) established by a systematic review [1]. Recalculating on this basis reduced the cost of migraine to €50 billion annually and of all headache to €112 billion annually. In this revised estimate, migraine remains the most costly of the headache disorders Europe-wide and in every country except Austria and France.

Figure 5 shows very clearly the high relative cost of MOH in France. The explanation lies only to a limited extent in a high prevalence (4.2%, the second highest in Europe, below Spain) and much more in a very high probability of absenteeism for this disorder in France.

All findings are also sensitive to assumptions made in the costing model, and to national statistics (Appendix 2, online only). Respondents were not asked about formulations of acute drugs, and the numbers of doses were interpreted conservatively. For prophylactic drugs, it was assumed that recommended doses were used [16]. The assumption that patients on prophylactics took these every day probably led to over-estimation, because it did not take account of non-adherence. On the other hand, wastage was ignored. Direct non-medical costs were not included, as social-services support, disability adaptations and special transportation are rare within this group of brain disorders. Our approach did not capture costs related to lost career-advancement or early retirement, but employment status has not been found to be related to headache in earlier European studies [4]. The cost estimates did not include costs of disorders that may be secondary to headache, or of those sometimes consequential to its treatment (the latter including gastrointestinal, hepatic and renal damage caused by analgesic overuse, and opioid addiction). Including such costs would increase total costs of headache even further.

Whilst it is common to use retrospective questionnaires to estimate the impact of headache on work absence and productivity [3], this method does introduce a recall bias: respondents systematically under-report because of the common inclination to perceive oneself favourably [17,18]. The estimate of indirect costs is in this respect conservative. It should also be noted that our estimates did not include 'intangible costs', such as the monetary values of pain and decreased enjoyment of life, nor the indirect costs of lost time for household chores and social enjoyment, or time lost to caring for family members with migraine [19] (all of these being difficult to value objectively).

A major strength of this study is that the populations of the participating countries (180 million adults) constituted 55% of the EU27 population (325 million adults); therefore, our estimates can be used to model the economic evidence of the EU27. Extrapolation is, of course, dependent on the assumption that our mix of countries is representative of EU27. We find this reasonable because the selected countries were a diverse mix of European countries in terms of geographical location, population size, set-up of healthcare system and level of income. In most of the participating countries, there was no earlier published evidence on 1-year prevalences of TTH or MOH [1].

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A second strong point is the 'bottom-up' approach, meaning that prevalence and resource-use data were collected simultaneously in a field study, which is the preferred methodology [3]. Advantages are that individuals who had not sought medical treatment, were unemployed, not insured or not earlier diagnosed were fully captured, as were cost items in great detail. For example, drugs were counted even when not registered for the diagnosis, or when purchased over-the-counter rather than prescribed, and so were health providers whether reimbursed or paid for by patients out-of-pocket [20]. By using a direct method – questioning respondents about the use of health-care resources and lost productivity – we did not inflate the estimates of costs by counting health expenditures of comorbid disorders [21]. We used 1-year headache prevalences because they indicated the proportions of the population with active disease, which are most relevant for calculating economic consequences [5].

There were some inherent limitations of the study. Because of a limited budget, some European countries with large populations (e.g., Poland) were not included. We did not adjust for age, gender or geographical area in Austria, France and Spain, as the samples in these countries were not truly population based. Differences that might be attributable to this are not apparent. The participation rates were low in most countries. This led to participation (interest) bias, for which we made an attempt to compensate (Methods). All resources lost because of headache were counted, but their relative apportionment between diagnoses should nevertheless be interpreted with some caution. To avoid double-counting, patients were classified only on the basis of their most bothersome headache if they had headaches of more than one type, which might have led to underestimates of TTH prevalences because migraine would almost always be the more bothersome. Also, the majority of patients classified as having MOH were likely to have had histories of migraine and/or TTH.

Comparison with earlier estimates

External validity is supported by relatively strong concordance with available previous European per-person estimates, although these were logically lower because of the passing of time. More precisely, our calculations of the annual costs per case of migraine were, to varying degrees, higher than earlier estimates for Austria (now €885, earlier €768), Italy (now €1034, earlier €706) Lithuania (€297 vs. €152), Luxembourg (€1446 vs. €965), Netherlands (€1524 vs. €867) [2] and Spain (€1425 vs. €599) [22]. The mean cost was also higher than previously estimated for the US (USD 612, year 1999) [23]. These differences are in most cases emphasized by other choices of methodology. For example, the 'top-down' approach often used by others carries the risk of underestimating or omitting relevant direct cost items; or authors may have taken a work-place rather than societal perspective [24,25], imputed resource use from other countries [2], measured only direct [26] or only indirect costs [25,27], or not taken account of reduced productivity whilst present at work [27].

Regarding the origins of costs for migraine, previous estimates in Italy [28], Luxembourg [29], the Netherlands [30] and Spain [22] also concluded that indirect costs constituted the greater part (80–95%).

Conclusion

This report underlines the prominent position of headache disorders, migraine especially but far from exclusively, amongst all health disorders as drivers of immense economic losses to society. This has immediate implications for European healthcare policy because increased investments in effective health care not only have the potential to reduce these losses (whilst improving public health) but also are likely to be repaid several-fold by savings elsewhere [31].

Acknowledgements

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Disclosure of conflicts of interest

Dr. Linde has received honoraria for scientific advisory board membership concerning a new treatment for migraine at Allergan Inc. His institution has received a grant from EAHC.

Dr. Gustavsson is employed at a contract research company, providing services to the pharmaceutical industry.

Dr. Stovner has received a research grant from AstraZeneca and a travel grant to participate in a scientific meeting from Pfizer. He has received honoraria for board membership at Minster Pharmaceuticals and

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consultancy for Pfizer. His institution has received a grant from EAHC.

Dr. Steiner has received honoraria for scientific advisory board membership concerning a new treatment for migraine at Merck Inc and for consultancy related to aspirin for headache at Bayer Healthcare. His institution has received a grant and travel support from EAHC.

Ms. Barré reports no conflicts.

Dr. Katsarava has received honoraria for consultancy and lectures from Allergan, Bayer, and Biogen, and travel expenses from Allergan, Bayer, Biogen, EHF, and IHS. His institution has received a grant from The European Union.

Dr. Lainez has received honoraria for lectures from Allergan, Almirall, and Merck. He has received a travel grant from Medtronic. His institution has received fees for clinical trials from Boston Scientific, Ferrer, and Servier.

Dr. Lampl's institution has received support for travel and fees for participating in the Eurolight project from The Association for Medical Science in Neurology.

Dr. Lantéri-Minet has received compensation for board membership and lectures from Allergan and Merck. He has received compensation for consultancy from Almirall, Medtronic and Pfizer. He has received payment for manuscript preparation from Medtronic. His institution has received support for travel and fees for participating in the Eurolight project.

Dr. Rastenyte's institution has received a grant for participating in the Eurolight project.

Mrs. Ruiz de la Torre's society has received support for travel and a grant from European fundings.

Dr. Tassorelli has received support for travel through a grant from the European Commission.

Dr. Andrée has received fees as a reviewer for the European Commission. Her institution has received grants and travel support for lectures and payments for the development of educational presentations from The National Research Fund of GD Luxembourg.

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References

1. Stovner LJ, Andree C. Prevalence of headache in Europe: a review for the Eurolight project. *J Headache Pain* 2010; **11:** 289–299.
2. Andlin-Sobocki P, Jonsson B, Wittchen HU, Olesen J. Cost of disorders of the brain in Europe. *Eur J Neurol* 2005; **12**(Suppl. 1)**:** 1–27.
3. Berg J. Economic evidence in migraine and other headaches: a review. *Eur J Health Econ* 2004; **5**(Suppl. 1)**:** S43–S54.
4. Stovner LJ, Andree C. Impact of headache in Europe: a review for the Eurolight project. *J Headache Pain* 2008; **9:** 139–146.
5. Berg J, Stovner LJ. Cost of migraine and other headaches in Europe. *Eur J Neurol* 2005; **12**(Suppl. 1)**:** 59–62.
6. Andrée C, Stovner LJ, Steiner TJ, *et al*. The Eurolight project: the impact of primary headache disorders in Europe. Description of methods. *J Headache Pain* 2011; **12:** 541–549.
7. Andrée C, Vaillant M, Barre J, *et al*. Development and validation of the EUROLIGHT questionnaire to evaluate the burden of primary headache disorders in Europe. *Cephalalgia* 2010; **30:** 1082–1100.
8. Headache Classification Subcommittee of the International Headache Society. The International Classification of headache disorders. *Cephalalgia* 2004; **24**(Suppl. 1)**:** 1–160.
9. Eurostat. Average gross annual earnings in industry and services, by gender. URL: http://epp.eurostat.ec.europa. eu/tgm/table.do?tab = table&init = 1&language = en&pcode = tps00175&plugin = 1. Accessed Nov 15, 2010.
10. Luce BR, Elixhauser A. Estimating costs in the economic evaluation of medical technologies. *Int J Technol Assess Health Care* 1990; **6:** 57–75.
11. Stewart WF, Lipton RB, Kolodner KB, Sawyer J, Lee C, Liberman JN. Validity of the Migraine Disability Assessment (MIDAS) score in comparison to a diary-based measure in a population sample of migraine sufferers. *Pain* 2000; **88:** 41–52.
12. Munakata J, Hazard E, Serrano D, *et al*. Economic burden of transformed migraine: results from the American Migraine Prevalence and Prevention (AMPP) Study. *Headache* 2009; **49:** 498–508.
13. Eurostat. Yearbook 2010. URL: http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/CH_02_2010/EN/CH_02_2010-EN.PDF Accessed Jan 10, 2011.
14. Jönsson B. General principles of disease-costing. In: Olesen J, Steiner T, Lipton R, eds. *Reducing the Burden of Headache*. Oxford: Oxford University Press, 2003: 211–217.
15. Kernick D. An introduction to the basic principles of health economics for those involved in the development and delivery of headache care. *Cephalalgia* 2005; **25:** 709–714.
16. Evers S, Afra J, Frese A, *et al*. EFNS guideline on the drug treatment of migraine–revised report of an EFNS task force. *Eur J Neurol* 2009; **16:** 968–981.
17. Jones G. How often were you absent? A review of the use of self-reported absence data *J Appl Psychol* 1994; **79:** 574–591.
18. Harrisson D, Shaffer M. Comparative examinations of self-reports and perceived absenteeism norms: wading through lake Wobegon. *J Appl Psychol* 1994; **79:** 240–251.
19. Linde M, Dahlof C. Attitudes and burden of disease among self-considered migraineurs–a nation-wide population-based survey in Sweden. *Cephalalgia* 2004; **24:** 455–465.
20. Mennini FS, Gitto L, Martelletti P. Improving care through health economics analyses: cost of illness and headache. *J Headache Pain* 2008; **9:** 199–206.
21. Stovner LJ, Hagen K. Prevalence, burden, and cost of headache disorders. *Curr Opin Neurol* 2006; **19:** 281–285.
22. Láinez J. Prevalencia de la migraña en el medio laboral y su repercusiónn económica. *Rev Esp Med Trab* 1995; **4:** 3–9.
23. Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML. Burden of migraine in the United States: disability and economic costs. *Arch Intern Med* 1999; **159:** 813–818.
24. Badia X, Magaz S, Gutierrez L, Galvan J. The burden of migraine in Spain: beyond direct costs. *Pharmacoeconomics* 2004; **22:** 591–603.
25. Pop PH, Gierveld CM, Karis HA, Tiedink HG. Epidemiological aspects of headache in a workplace setting and the impact on the economic loss. *Eur J Neurol* 2002; **9:** 171–174.
26. Pradalier A, Auray JP, El Hasnaoui A, *et al*. Economic impact of migraine and other episodic headaches in France: data from the GRIM2000 study. *Pharmacoeconomics* 2004; **22:** 985–999.
27. Michel P, Dartigues JF, Duru G, Moreau J, Salamon R, Henry P. Incremental absenteeism due to headaches in migraine: results from the Mig-Access French national cohort. *Cephalalgia* 1999; **19:** 503–510.
28. Pugliatti M, Sobocki P, Beghi E, *et al*. Cost of disorders of the brain in Italy. *Neurol Sci* 2008; **29:** 99–107.
29. Bisdorff A, Sobocki P, Cloos JM, Andree C, Graziano ME. Cost of disorders of the brain in Luxembourg. *Bull Soc Sci Med Grand Duche Luxemb* 2006; **3:** 347–358.
30. van Roijen L, Essink-Bot ML, Koopmanschap MA, Michel BC, Rutten FF. Societal perspective on the burden of migraine in The Netherlands. *Pharmacoeconomics* 1995; **7:** 170–179.
31. Steiner TJ. Headache burdens and bearers. *Funct Neurol* 2000; **15**(Suppl. 3)**:** 219–223.

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Appendix 1

Wordings of the relevant questions in our questionnaire.

Question 44a: *Many different medications may be used to treat headache. This question is about any of these medications you have taken for headache in the last 30 days. Please look at these lists, and think about which of these you have used in the last 30 days. Please tick one box by each medication:*

*X-triptan**	☐ *Not used* / ☐ *Used once* / ☐ *Used more than once*
*Y-analgesic**	☐ *Not used* / ☐ *Used once* / ☐ *Used more than once*
*Z-antiemetic**	☐ *Not used* / ☐ *Used once* / ☐ *Used more than once*

[*One row for each drug in Table 1 applicable for the specific country with local trade names].

Question 44b: *Please list any other medications you have used to treat your headache in the last month. Please list medications for headache, not for any other illnesses.*

_____ ☐ *Used once* / ☐ *Used more than once*

[Repeated for up to 4 medications]

Question 45: *Medications to prevent headaches are usually taken daily. Are you taking any of these? Please enter the name(s).*

_____

[Repeated for up to 4 medications]

Question 47: *Many people with headache treat themselves, but others need professional advice. Have you had professional advice about your headaches in the last year? Who from, and how many times? (Please tick all boxes that apply, and for each ticked box, enter the number of times in the last year)*

		Number of times
Nurse	☐	_____
Physical therapist (physiotherapist, osteopath, chiropractor)	☐	_____
Primary-care doctor (GP)	☐	_____
Headache specialist	☐	_____
Hospital emergency room	☐	_____
Other (please specify)	☐	_____

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Question 48: *Most people with headache do not require any investigations, but occasionally these tests are done. Because of your headaches, have you had any of these tests in the last year? (Please tick all that apply)*

- *MRI brain scan* ☐
- *CT brain scan* ☐
- *X-rays of the neck* ☐
- *Eye tests (for glasses)* ☐
- *Blood tests* ☐
- *Other (please specify): _____* ☐
- *None* ☐

Question 49: *Have you, in the last year, been admitted to hospital because of your headaches? (Please tick the no or yes box and, if yes, also tick the box to indicate the total number of days you spent in hospital)*

- *No* ☐
- *Yes* ☐ *If yes, how many days: _____*
- *1* ☐
- *2* ☐
- *3–7* ☐
- *More than 7* ☐

Question 57: *On how many **days** in **the last 3 months** could you **not go** to work or school because of your headaches? (Please enter the number of days missed completely during the last 3 months)*

_____

Question 58: *On how many **days** in **the last 3 months** could you do **less than half** your usual amount in your job or schoolwork because of your headaches? (Please enter the number of days; do not include days you counted in question 57 where you missed work or school)*

_____

Appendix 2

Complete list of unit prices and average gender-specific salary levels by country.

Country	Austria	France	Germa	Italy	Lithua	Luxem	Netherl	Spain
Acute medication								
Almotriptan/dose (12.5 mg)	NA	4.23	7.40	5.54	NA	5.14	4.31	8.14
Eletriptan/dose (40 mg)	7.61	4.33	8.70	6.66	6.36	6.91	4.90	7.33
Frovatriptan/dose (2.5 mg)	NA	4.06	NA	5.48	NA	NA	NA	5.35
Naratriptan/dose (2.5 mg)	9.06	4.67	7.60	NA	5.38	4.92	4.50	5.31
Rizatriptan/dose (10 mg)	11.08	4.06	7.20	7.50	6.85	7.49	5.06	7.34
Sumatriptan/dose (50 mg)	2.38	3.89	2.60	3.19	1.78	5.49	1.00	4.40
Zolmitriptan/dose (2.5 mg)	6.93	4.46	9.10	6.09	9.64	5.49	4.63	6.14
Ergotamin/dose	0.32	0.15	NA	0.14	NA	NA	2.62	0.11
Domperidone/dose (10 mg)	0.16	0.08	0.30	0.13	0.16	0.23	0.36	0.10

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Appendix 2

(Continued)

Country	Austria	France	Germa	Italy	Lithua	Luxem	Netherl	Spain
Metoclopramide/dose (10 mg)	0.19	0.09	0.20	0.20	0.02	0.12	0.13	0.06
ASA/dose (500 mg)	0.17	0.20	0.40	0.14	0.03	0.27	0.05	0.07
Diclofenac/dose (50 mg)	0.16	0.12	0.15	0.14	0.01	0.12	0.09	0.05
Ibuprofene/dose (400 mg)	0.16	0.09	0.25	0.18	0.06	0.08	0.09	0.07
Ketoprofene/dose (50 mg)	0.14	0.26	0.50	0.10	0.21	NA	0.21	0.08
Naproxene/dose (500 mg)	0.35	0.22	0.50	0.21	NA	0.30	0.10	0.16
Paracetamol/dose (500 mg)	0.09	0.21	0.10	0.12	0.10	0.06	0.02	0.03
ASA + metoclopramide/ dose	NA	1.33	NA	1.85	NA	1.86	6.65	NA
Prophylactic medication								
Propranolol/day (160 mg)	0.66	0.36	0.40	0.36	0.43	0.21	0.44	0.28
Atenolol/day (100 mg)	0.40	0.25	0.30	0.21	0.19	0.33	0.28	0.12
Metoprolol/day (150 mg)	0.36	0.08	0.50	0.28	0.08	0.28	0.18	0.16
Timolol/day (20 mg)	NA	NA	NA	0.24	NA	NA	NA	NA
Pizotifen/day (1 mg)	NA	0.23	NA	0.21	NA	NA	0.38	NA
Methysergide/day (4.95 mg)	NA	0.81	NA	NA	NA	NA	0.29	0.08
Amitriptyline/day (100 mg)	0.21	0.28	0.50	0.21	0.12	0.48	0.44	0.19
Topiramate/day (100 mg)	1.85	1.09	3.40	1.85	0.94	0.89	1.20	0.96
Valproate/day (1000 mg)	0.76	0.35	0.27	0.45	0.42	NA	0.38	0.30
Gabapentine/day (1200 mg)	1.32	1.43	NA	1.67	1.28	1.32	0.76	1.11
Candesartan/day (16 mg)	1.39	2.36	NA	0.94	1.66	0.77	1.18	0.93
Flunarizine/day (10 mg)	NA	0.31	0.50	NA	NA	NA	NA	NA
Health care utilization								
Nurse/visit	25.2	NA	NA	NA	NA	NA	NA	22.4
Physiotherapist etc/visit	27.0	NA	25.0	15.0	29.0	18.0	28.5	26.5
Primary care physician/visit	60.0	22.0	47.5	18.0	2.9	35.1	18.0	37.25
Headache specialist/visit	64.8	37.0	60.0	22.5	24.0	44.3	41.6	38.71
Emergency room/visit	1140.0	47.28	80.0	216.0	19.4	78.38	84.2	64.49
Inpatient care/day	144.0	976.8	500.0	300.0	89.8	54.7	327.0	223.77
Investigations								
MRI brain/scan	261.0	69.0	70.0	249.0	103.8	136.6	148.5	150.01
CT brain/scan	150.0	25.27	70.0	83.2	55.3	84.9	82.6	109.28
X-ray neck/scan	62.64	31.92	70.0	15.2	32.4	15.5	34.5	13.92
Eye tests/time	27.0	25.0	27.0	13.6	10.1	30.6	23.4	30.45
Blood tests/time	7.12	8.33	10.0	NA	2.9	11.6	NA	10.05
EEG	45.42	NA	45.0	NA	NA	46.9	NA	NA
Indirect costs								
Income woman/day	135.66	128.71	148.18	128.69	30.65	177.77	146.82	84.91
Income man/day	194.41	155.92	193.63	128.69	36.73	216.10	200.45	105.93

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