Examining Funding Patterns in European Diabetes Research from 2002 to 2013

1 A. K. Patel, E. J. Martin, 2 C. R. Fabbri, 3 L. M. Bianchi, 4 P. E. Vickers, 4 M. C. Di Stefano, 2 G. P. Mazzocchi

1Department of Epidemiology, University of California, Los Angeles, Los Angeles, USA,
2National Institute for Health Research, University College London, London, UK,
3Department of Health Sciences, University of Milan, Milan, Italy,
4Centre for Health Economics, University of York, York, UK

Abstract

AimThis study examined the outputs of research papers in diabetes from 31 European countries between 2002 and 2013, and their funding.Methods Diabetes research papers in the Web of Science were identified by means of a filter based on journals and title words. For 2009–2013 papers, the funders were coded to show their sector and nationality.Results Europe published 40 547 diabetes papers in the 12 years between 2002 and 2013. Denmark, Sweden and Finland published the most relative to their wealth, but the UK published the most absolutely despite an apparently low burden (as measured by disability-adjusted life years). The largest source of funding was government (30%), followed by the non-profit sector (18%) and industry (13%). The European Commission supported 2.7% of papers, but more in Latvia (33%) and Estonia (16%). Based on an estimated cost per paper of €260 000, the annual research expenditure in Europe was approximately €986 million in 2013.ConclusionsThe European diabetes burden in disability-adjusted life years increased by one third between 2002 and 2012, but its output of research papers has decreased from 44% to 36% of the world total. This decrease needs to be reviewed in the context of European non-communicable disease research policy.

Introduction

Diabetes represents a major global health problem and, together with other non-communicable diseases, has led to a major policy document on its prevention and control from the World Health Organization (WHO) [1]. Worldwide, 1.5 million deaths were directly associated with diabetes in 2012, and 2.2 million more were related to high blood glucose [2]. In the European region in 2015, almost 60 million people had diabetes. Based on data from the WHO website on the disease burden for the 31 European countries (EUR31; the 28 European Union Member States, plus Iceland, Norway and Switzerland) between 2002 and 2012, the average percentage of disability-adjusted life years (DALYs) from diabetes increased from 2.0% to 2.6% [3]. In 2012, the figure ranged from 1.3% in the UK to 4.9% in Cyprus. Countries in the Mediterranean and Southern Europe (Portugal 4.3%, Spain 3.7%, and Italy 3.5%) had the highest levels, except for Greece (2.2%). Besides the UK, the lowest percentages occurred in Romania, Lithuania and Finland (1.8%) and Iceland (2.0%).

This paper presents the results of a bibliometric study of outputs (i.e. scientific papers) and funding for diabetes research from 2002 to 2013. The study, of the EUR31 countries, was performed as part of the Mapping NonCommunicable Diseases (NCD) project, funded by the European Commission under the 7th Framework Programme. The aim was to map research activity and assist research funding organizations such as the Commission to identify gaps and overlaps in the current state of diabetes research, and point out areas on which to focus future strategies. Previous studies that have applied a bibliometric approach to the outputs of diabetes research have mainly focused on a specific type of diabetes [4] or on another geographical area [5–7]. The DIAMAP website gives details of funders and researchers in Europe, but does not list individual papers [8].

Methods

Articles and reviews on diabetes were extracted from the Web of Science (© Clarivate Analytics) from 2002 to 2013.

What's new?

- European diabetes research has declined from 44% of world output in 2002 to 33% in 2015 while the burden has increased from 2.0% to 2.6% of disability-adjusted life years in 10 years.
- Outputs mostly correlate with gross domestic product – Scandinavia performs well except for Norway; France, Lithuania and Romania also do less well.
- Funding between subject areas varies with high levels on latent autoimmune disease of adults and maturityonset diabetes of the young; there is very little on foot problems.
- Main funding sources are government (30%), private– non-profit organizations (18%, especially in the UK) and industry (13%, notably from Novo Nordisk).

They were selected by means of a filter that included specialist diabetes journals and title words (developed by GL, Moira Murphy and Jayne East of the British Diabetic Association, now Diabetes UK, and by OC). The filter was calibrated [9], and its precision (p, specificity) was 0.90 and its recall (r, sensitivity) was 0.98. So, the

true number of diabetes papers would have been 0.90/0.98 = 0.92 times the apparent number.

The extracted papers, 40 547 in total, were categorized by the fractional presence of each of the EUR31 countries. For example, a paper with two French and three German addresses would be counted as 0.4 for France and 0.6 for Germany. Papers were compared with the countries' national wealth in 2011, as measured by gross domestic product (GDP) [10]. They were then classified by their subject (e.g. Type 1 or Type 2, or various sequelae); these were defined by means of sub-filters based on title words, and for some topics, journal name strings that were determined by Richard Elliott and Anna Morris of Diabetes UK. Over two thirds of the diabetes papers were in one or more of these subject areas. (However, we did not analyse research domains such as genetics or methods of treatment.) Each country's research papers in each subject were compared with the number expected on the assumption that its portfolio paralleled that of the EUR31, to show which countries were relatively more, or less, active than the European average.

Results

Outputs of diabetes research papers in Europe

In 2002–2013, European output represented 39% of the world total of 104 416 papers, and 1.5% of its biomedical research papers. The European presence in diabetes research has gone down from 44% in 2002 to 36% in 2013 (and only 33% in 2015). The proportion of European biomedical research on diabetes has risen between 2002 and 2013 from 1.4% to 1.6%. However, this is lower than the disease burden from diabetes, which was 2.6% of all DALYs in 2012 (vide supra) and has been increasing at a faster rate.

The numbers of papers from the EUR31 countries are plotted against their GDP in Fig. 1, with a least-squares regression line, and two lines representing amounts twice and half the expected outputs. Relative to its wealth, Denmark carried out the most research, followed by Finland and Sweden, and then Croatia. However, France, Norway and Romania did much less than might be expected: Norway, with a GDP only slightly lower than that of Sweden, did less than a quarter as much research. (All these differences between expected and observed numbers of papers are highly statistically significant on the Poisson distribution with one degree of freedom.) The UK led the EUR31 countries in output, publishing 30% more than Germany, the secondranked country.

Almost one third of the papers were on Type 2 diabetes (33%), followed by cardiovascular complications (14%) and Type 1 diabetes (14%). Each of the other sub-fields comprised less than 10% of diabetes papers: nephropathy (7%), retinopathy complications (4%), liver complications (3%), and feet, gestational diabetes, psychosocial complications and hypoglycaemia (all < 2%). Very few papers were on maturity-onset diabetes of the young, neonatal diabetes or latent autoimmune diabetes of adults (all < 1%).

The ratios between the observed and expected numbers of papers in the different subjects for those EUR31 countries with a fractional count of > 100 papers are shown in Table 1. Individual cells in the table are shaded to emphasize values that are higher or lower than unity by factors of two and its square root. Different typefaces are used to show whether the values differ significantly from unity.

There are some interesting differences: Finland is very active in Type 1 diabetes research (although it was also the first European country to demonstrate the possibility of Type 2 diabetes being prevented [14]). Of the countries shown, the Netherlands and Greece concentrated the most on Type 2 diabetes, together with Slovenia. Among the sequelae, Poland concentrated on the kidney, Slovenia, Croatia and Norway on the retina, Portugal, Hungary, Slovakia and the Czech Republic on neuropathy, Italy on the liver, and Greece, the UK and Germany on feet. These relative strengths might guide efforts to boost a country's expertise, where it was lacking, through collaboration with a more experienced country.

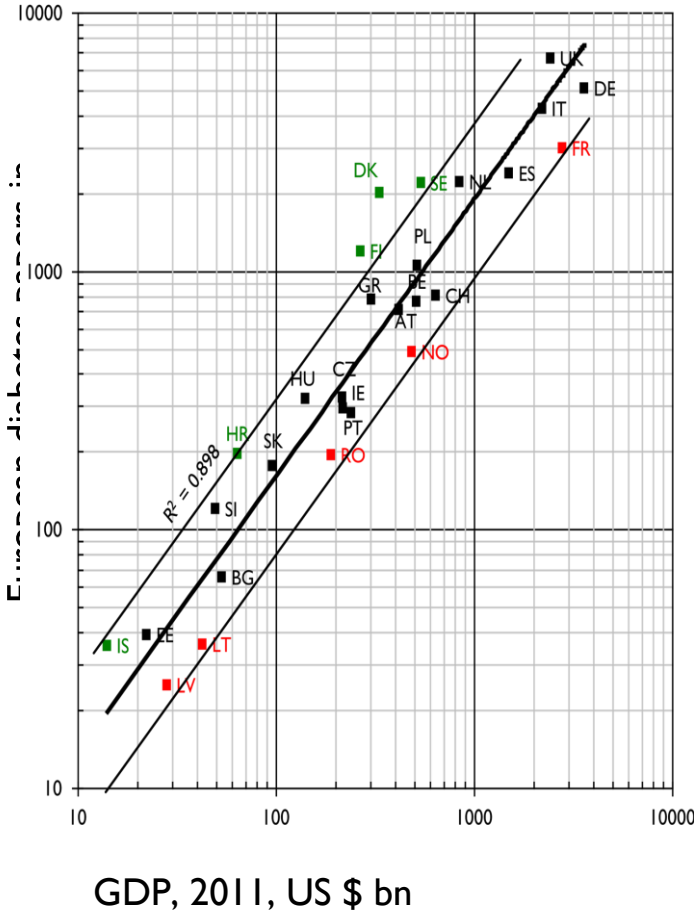

FIGURE 1 Comparison of outputs of diabetes research papers, 2002-13, from 28 European countr
Cyprus, Luxembourg and Malta omitted. AT, Austria; BE, Belgium; BG, Bulgaria; CH, Swit
Estonia; ES, Spain; FI, Finland; FR, France; GR, Greece; HR, Croatia; HU, Hungary; IE, Ir
Netherlands; NO, Norway; PL, Poland; PT, Portugal; RO, Romania; SE, Sweden; SI, Slovenia;

Table 1 Ratio of observed to expected outputs of papers from 23 European countries with at least 100 papers in nine leading subject areas of diabetes research, 2002–2013, and overall totals for each country and subject

Ratio	Total	Type 2 diabetes	Cardiovascular effects	Type 1 diabetes	Effects on kidney	Effects on retina	Neuropathy	Effects on liver	Effects on feet	Gestational diabetes
EUR 31	35 807	13 310	5720	5539	2740	1645	1573	1017	918	828
UK	6656	**0.79**	**0.74**	**0.84**	**0.65**	1.19	0.87	**0.49**	1.26	**0.62**
Germany	5119	**0.76**	**0.82**	**0.74**	0.84	**0.77**	0.97	**0.70**	1.21	**0.59**
Italy	4262	*0.99*	**1.27**	0.90	*1.03*	**0.69**	*0.92*	**1.68**	0.74	*0.86*
France	2999	**0.82**	**0.77**	**0.73**	**0.70**	0.75	**0.61**	*1.18*	*0.94*	*0.96*
Spain	2379	*1.01*	*1.00*	**0.67**	1.20	1.22	**0.66**	1.39	0.70	1.21
The Netherlands	2229	**1.12**	1.10	**0.78**	0.76	**0.48**	*1.07*	0.76	*1.13*	**0.47**
Sweden	2196	**0.88**	0.79	**1.17**	**0.72**	0.42	0.80	**0.42**	0.66	0.95
Denmark	2017	*1.02*	**0.69**	*1.07*	1.23	*1.07*	**0.46**	**0.49**	**0.35**	*0.73*
Finland	1198	*0.99*	*1.04*	**1.90**	*0.92*	*0.68*	**0.47**	*1.08*	**0.21**	1.43
Poland	1049	**0.74**	*0.88*	*1.14*	1.29	*1.03*	*1.06*	*0.67*	*0.72*	**2.42**
Switzerland	803	**0.81**	**0.70**	**0.62**	0.60	0.58	*0.69*	*1.21*	*0.66*	0.36
Greece	779	*1.09*	1.18	**0.67**	*0.88*	*0.76*	1.50	*0.95*	*1.28*	1.65
Belgium	760	**0.70**	**0.66**	1.28	0.62	0.46	0.88	0.89	*1.03*	*0.59*
Austria	708	0.87	*0.95*	*0.83*	*1.08*	1.37	*0.71*	*1.08*	*0.91*	**3.19**
Norway	490	0.81	*1.05*	1.26	*0.85*	**2.19**	*0.72*	*0.69*	*0.66*	*1.01*
Czech Republic	326	*0.93*	*0.84*	**1.49**	*1.15*	*0.82*	**1.95**	0.35	*0.68*	*0.36*
Hungary	322	**0.74**	*1.01*	*1.06*	*0.83*	*0.90*	**2.09**	*0.64*	0.12	2.07
Ireland	295	0.84	0.70	*0.80*	*1.11*	*0.86*	*0.47*	*0.47*	*0.70*	**2.93**
Portugal	282	0.75	*0.89*	**0.44**	*0.67*	1.82	**2.49**	*1.62*	*0.88*	*1.16*
Croatia	197	*0.82*	0.62	**1.61**	*0.82*	**2.71**	1.84	*0.83*	*0.94*	*0.60*
Romania	195	*0.95*	0.45	*1.00*	*1.26*	*0.37*	*0.97*	*1.44*	*0.60*	*0.11*
Slovakia	178	**0.52**	1.43	*0.76*	*0.90*	*0.84*	2.14	*0.75*	*0.88*	*0.10*
Slovenia	120	1.30	*0.92*	*0.84*	*0.93*	**4.31**	*1.18*	*0.10*	*0.50*	*0.54*

Ratios: bright green, > 2.0; pale green, > 1.41; pale yellow, < 0.71; pink, < 0.5.
Significance: P-values < 0.001 are in bold, with < 0.05 in normal type and if not significant, and > 0.05, in italics. Countries and subfields are ordered by numbers of papers, fractional counts.

funding for all diabetes research in Europe amounted to €986 million in 2013, based on 3794 papers at an average cost of €260 000 [13].

The amount of funding that different subject areas attracted is shown in Fig. 2. Research on latent autoimmune diabetes of adults and maturity-onset diabetes of the young attracted the most support, although they are relatively small subject areas. Conversely, research on the effects of diabetes on the feet attracted hardly any support, with fewer than half the papers revealing any funding.

For those papers where no research funding organization was listed, it is likely that the research work performed was supported with core or structural funding from the authors' institutions or from the government as part of the investigators' academic or clinical contracts. The organizations to which the authors were affiliated were not included as research funding organizations in our analysis except for government labs, those supported by charities, and commercial ones [11].

Funding of diabetes research in the different countries also variedonafractionalcountbasis,asshowninFig. 3forthe16 countries with at least 200 papers in 2009–2013. The percentageof'funded'papersvariedbetween86%forSweden and 24% for Greece, although it was 91% for Luxembourg and the Czech Republic (data not shown). The sources of funding between sectors also varied. Overall, governments (including regional ones) provided the most support, 30% in total, especially in France and Spain where over half the support came from this sector. Regional government support was important in five countries: Belgium (23%), Spain (19%), Norway (17%), Sweden (15%) and Italy (10%).

The private–non-profit sector made the largest contribution in the Nordic countries (including Iceland) and the Netherlands; it was only slightly less than the government sector in Norway and the UK; in total, it supported nearly 18% of the papers. Industry provided 13% of the total, and the most support from this sector occurred in Germany (equivalent to 455 papers, 19% of the country total), the UK (383 papers, 13%) and Denmark (285 papers, 29%). The European Commission in its numerous guises provided support equivalent to 460 papers, or 2.7% of total support, but much more in some small countries: 33% of papers in Latvia, 16% in Estonia and 10% in Slovakia.

Five government bodies supported more than the equivalent of 200 papers each, with the French National Health and Medical Research Institute (INSERM) as the leading organization supporting 383 papers, followed by the UK Department of Health (369 papers), Carlos III Institute in

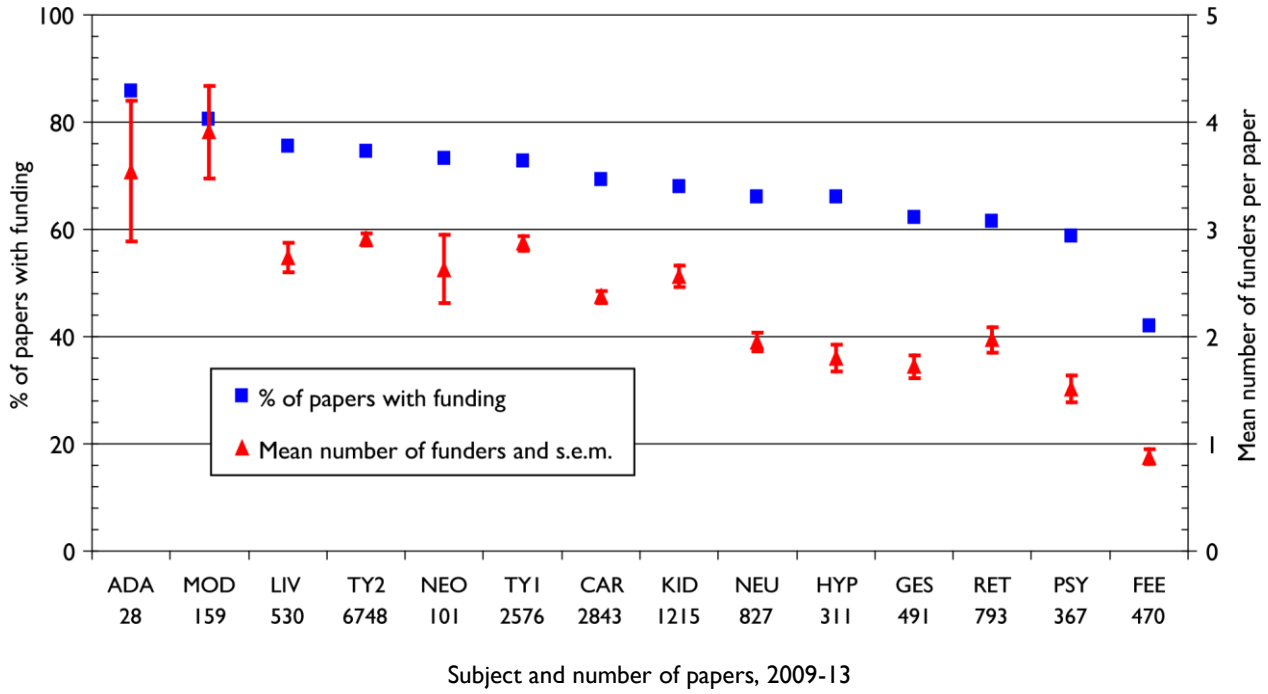

FIGURE 2 Percentage of European diabetes papers, 2009-13, with explicit or implicit funding sources (blue squares, left ordinate axis) and mean number of funders per paper (red triangles, right ordinate axis) for different disease areas. Numbers of papers given below disease area codes. ADA, latent autoimmune diabetes of adults; CAR, cardiovascular effects; FEE, effects on feet; GES, gestational diabetes; HYP, hypoglycaemia; KID, nephropathy; LIV, liver; MOD, maturity onset diabetes of the young; NEO, neonatal diabetes; NEU, neuropathy; PSY, psychosocial effects; RET, retinopathy; TY1, Type 1 diabetes; TY2, Type 2 diabetes.

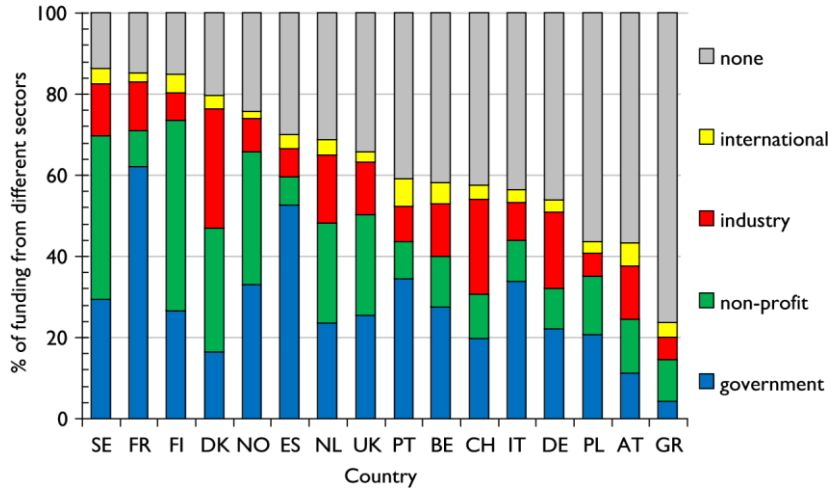

FIGURE 3 Percentages of funding for diabetes papers from four sectors, and none, for 16 European countries in 2009-13. AT, Austria; BE, Belgium; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; FR, France; GR, Greece; IT, Italy; NL, Netherlands; NO, Norway; PL, Poland; PT, Portugal; SE, Sweden; UK, United Kingdom.

Spain (326 papers), the Italian Ministry of Health (286 papers) and the German Research Association (DFG) (226 papers). The individual leading private–non-profit organizations supporting more than 100 papers each were Diabetes UK (150 papers), the UK Wellcome Trust (141 papers), the Dutch Diabetes Research Foundation (109 papers) and the British Heart Foundation (106 papers).

Nine separate industrial funders supported more than 50 papers each, with the Danish company Novo Nordisk A/S by far the leading industrial funder, contributing to the equivalent of 431 papers, followed by several pharmaceutical companies: Sanofi-Pasteur s.a. (156 papers), Eli-Lilly Co Inc. (123 papers), Novartis s.a. (90 papers), AstraZeneca plc. (87 papers), Merck and Co Inc. (83 papers), Pfizer Inc. (78 papers), Hoffman La-Roche s.a. (76 papers) and Boehringer Ingelheim AG (66 papers). There was also

a large number of smaller companies to which generic codes were given.

Discussion

The increasing burden of diabetes in the European Region [15] and the declining European presence in diabetes research (from 44% of the world total papers in 2002 to 33% in 2015), signal that a major boost in research efforts in this area appears necessary, despite the research advances that have been made.

There is considerable variation in the outputs of research papers on diabetes across Europe. This is consistent with previous studies on public health research [16]. Although GDP is a good predictor of a country's research output [17], certain countries, such as Norway and Romania, are not meeting expectations. National research outputs are also growing at different rates, with a major divide between 'western' and 'eastern' European countries: the latter countries' outputs grew more rapidly. This is also consistent with previous studies on diabetes [18].

These findings have important implications for European institutions in terms of the design of future funding streams and the promotion of exchange and international mobility for researchers between different research centres, as well as for future pan-European research funding such as from the European Research Council, Horizon 2020 and the Innovative Medicines Initiative.

Most of the papers focus on Type 2 diabetes, cardiovascular complications and Type 1 diabetes. Research on latent autoimmune diabetes of adults and maturity-onset diabetes of the young was under-represented in terms of research papers, although it appeared to attract considerable funding support. A gap in funding opportunities was shown for topics such as the effect of diabetes on the feet, which is of critical importance to patients and to clinical care, and for which few management strategies exist [19]. European funders and policy-makers should consider triangulating these findings on outputs and funding with trends in the burden of disease when planning future diabetes research portfolios.

Moreover, subject areas of preferred interest differ across Europe. Transnational research strategies should take into account such specificities and the distribution of competences across countries, given that greater openness to collaboration from scientists in smaller countries has already been pointed out in previous analyses [20,21]. It remains to be determined what the implications of current political–institutional changes at European Union level (namely, the exit of the UK from the Union) on cross-country research practices will be. The UK has led more health-related projects than any other member state [22]. Although the UK might still be able to participate in transnational projects, as do Switzerland and Norway, it is hard to predict how its role in the European landscape will change and what will be the consequent effects on research [23].

This systematic analysis of diabetes research funding in Europe reveals that the contribution of the charitable sector is large, but uneven across countries, with a large presence in the UK but a smaller one in Germany and even less in France and Italy. The three biggest private–non-profit funders in the UK made abiggercontributionthanthatoftheUKDepartmentof Health.Severalpharmaceuticalcompaniessupportedresearch but not on a big scale, and much of the industrial funding originated from Novo Nordisk A/S. Such findings show that there is an opportunity for countries, charities and pharmaceutical companies to increase their commitments to the field, particularly in regions with a high prevalence of diabetes.

Some limitations must be taken into consideration in the interpretation of the study results. First, evidence suggests that health-related articles in social sciences in languages other than English tend to be under-recorded [24]. Second, for countries where the main language of publication is other than English, clinical research articles may be underrepresented in the bibliographic databases [25]. A certain degree of publication bias related to language (language bias) should therefore be taken into account.

Third, research articles found were not individually evaluated for quality. This is a general limitation of bibliometric research [26], which assumes a correspondence between numbers of papers and contributions to the knowledge base. This may not be true, as small countries (including most of the EUR31) carry out medical research for reasons other than to make major discoveries. These reasons include the underpinning of medical education, the ability to learn about and use advances made in other countries, and the desire to recruit intellectually curious staff to deliver clinical care. For these purposes, the volume of research may indeed be a reasonable indicator of potential utility.

Fourth, it was apparent that the number of funding bodies per paper, F, increased from 2.04 in 2009 to 2.84 in 2013; this isanartefactbecausethecollectionoffundingdatainthe Web of Science was incomplete in the first few years, and did not occur at all in the Social Sciences Citation Index (SSCI) papers until 2015. The mean value of F for the whole 5-year period was 2.60, i.e. just over 9% less than the value in the last 2 years,whichislikelytobethecorrectvalue.Thismeansthat the amount of funding per paper was underestimated by 9% but as the number of papers was over-estimated by 8% (v.s.), the F values are very close to the truth. A further limitation is that funding data were not available for the 1% of papers recorded only in the SSCI. Another factor, mentioned above, is that non-contestable implicit institutional funding was not included in our analysis, although it was counted in the estimated total European research expenditure. Our estimate of total research expenditure for 2013 is based on papers published in thatyear, butbecause ofthe lagbetween research grants and publication [27] may actually relate to an earlier year, perhaps 2011.

We assumed that each funder contributed the same amount as others to a country on a paper. This probably over-estimated the support from small funders and underestimated that from larger ones. We checked this by comparing the calculated research expenditure by Diabetes UK, €7.2 million per year, with that reported by the charity in 2008–2011 in its annual reports [28], which was equivalent to €7.4 million per year. This gives some confidence that our methodology gave reasonably reliable results.

Finally, we have not here addressed the potential impact of this research. This is conventionally measured by citation counts, but we have also examined the references on
European clinical guidelines and the medical research stories in European newspapers, which will influence medical practice, and the opinions of policy-makers and the public. This will be reported in a subsequent paper.

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Competing interests None

declared.

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