D8.1: Bibliometric mapping and analysis of papers in cardiovascular research (CARDI), diabetes (DIABE), mental disorders (MENTH), cancer (ONCOL) and respiratory diseases (RESPI), 2002-13.

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Mapping Chronic Non-Communicable Disease Research Activities and their Impact
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Abbreviations

ACI	Actual Citation Impact
CARDI	Cardiovascular
CDC	Centers for Disease Control and Prevention
CDRH	Center for Devices and Radiological Health
CE	Conformité Européene
COPD	Chronic Obstructive Pulmonary Disease
CRD	Chronic Respiratory Disease
CVD	Cardiovascular disease
DALY	Disability-adjusted life years
DIABE	Diabetes
DIAMAP	Road Map for Diabetes Research
DTI	Department for Business, Innovation and Skills
DM	Diabetes Mellitus
EASD	European Association for the Study of Diabetes
EC	European Commission
EU	European Union
EUR31	28 EU Member States, plus Iceland, Norway and Switzerland
EUDAMED	European Database on Medical Devices
GBD	Global Burden of Disease
GDP	Gross Domestic Product
HTA	Health Technology Assessment
IA	Impact Assessment
ICD	International Classification of Disease
MD	Medical device
MENTH	Mental disorders
MRG	Millennium Research Group
MS	Member State
NCD	Non-communicable disease
OECD	Organization for Economic Co-operation and Development
ONCOL	Cancer
OTC	Over-the-counter medicines
PMA	Premarket approval
PPI	Patient Public Involvement
PRO	Public Research Organizations
R&D	Research and Development
RESPI	Respiratory disease
RFO	Research Funding Organization
SCI	Science for the Science Citation Index
SSCI	Social Sciences Citation Index
UK	United Kingdom
US	United States
WHO	Word Health Organization
WoS	Web of Science

Executive Summary

1 This report describes the process for identifying and downloading papers whose details are in the Web of Science (WoS) in five non-communicable disease (NCD) areas from 31 European countries (the 28 EU Member States, plus Iceland, Norway and Switzerland) in the 12 years 2002-13.

The five NCDs were:

- Cancer research (oncology): ONCOL
- Cardiovascular research, including stroke: CARDI
- Diabetes research: DIABE
- Mental disorders research: MENTH, and
- Respiratory disease research: RESPI

The papers were identified by means of "filters" whose precision and recall were determined by means of subject experts marking sets of papers as relevant or not. Their details were written to five Excel spreadsheets for analysis. The main analyses were of country outputs, their research levels (from clinical to basic), their citation scores and percentage of reviews, and for some subject areas, the type of research or disease. Data were also obtained on the burden of disease in each of the 31 European countries and in the group as a whole.

2 The table below gives the main parameters of the five NCDs, ranked by size:

Subject	*World output*	*EUR31 output*	*% world*	*% BIOMED*
BIOMED	6075502	2442063	40	
ONCOL	748724	282055	38	11.5
CARDI	508611	211507	42	8.7
MENTH	349027	138666	40	5.7
DIABE	103792	40550	35	1.7
RESPI	33629	18822	56	0.8

3 The outputs of papers from each European country were compared with their GDP so as to reveal which countries were contributing most to each subject area, and some outliers were noted. Most of the papers were at the clinical end of the spectrum, and in most of the NCDs had become more so over the 12 years of the study. Citation scores are one measure of the impact of research, and for most NCDs, European research was better cited than the world average, although there was much variation between countries. There was generally poor correlation between the burden from particular diseases (*e.g.*, different cancer sites) and the amount of research, so some re-balancing of countries' research portfolios may be indicated.

4 Funding data were obtained, so far for DIABE and RESPI papers during the last five years, 2009-13. They showed that RESPI papers were less well funded than DIABE ones, particularly in COPD. Countries in northern and western Europe benefited from a wide variety of sources, especially from the private-non-profit sector. Some countries also saw an increasing role for local and regional authorities in funding NCD research. The European Commission was also an important source of funds, especially for the major research countries (France, Germany, Italy, Spain and the UK).

5 Impacts of the research were measured by means of citations, but also with an analysis of three new indicators:

- the research backgrounds of members of Member State health advisory committees;

- the papers references on clinical guidelines; and
- the newspaper stories about medical research and the papers that they cite.

A full analysis is presented of the first of these, based on the committee members in 21 countries, and showed that their research was well connected to that of other European countries. Data on the references on DIABE clinical guidelines showed that countries tended to over-cite their own papers (except for Portugal and Spain), and that the cited references were very clinical. Citations from lung cancer clinical guidelines showed the importance of surgery research which was the dominant type, much more important as a source of evidence than genetics. An analysis was also presented of the newspaper stories in *Le Soir*, a francophone Belgian newspaper. One finding was that Belgian research was over-cited, as expected, but we noted that there was almost no comment on the significance of the reported results from the charity sector, unlike in the UK where such commentators are frequently quoted.

1 Introduction and methodology

1.1 Partners' description of surveys of funders

1.1.1 The partners and their assignments

This project was carried out by seven European partners, each with pre-assigned tasks. It was coordinated by the London School of Economics, which was also responsible for the study on respiratory diseases (RESPI). Four other partners, in continental Europe, were each responsible for another of the five non-communicable diseases (NCDs) as follows:

- cardiovascular disease (CARDI): Technische Universität, Berlin;
- diabetes (DIABE): Università Bocconi, Milano;
- mental disorders (MENTH): URC-ECO, Paris; and
- cancer research (ONCOL): Escuela Andaluza de Salud Pública, Granada.

They undertook to identify the leading sources of funding for their NCD, both governmental (including regional authorities) and private-non-profit, and to conduct a series of personal interviews in order to explore the funding situation – how much money was being spent and by whom – and what the funders were trying to achieve. They also sought information on the difficulties faced by researchers and others.

The other two partners were the Estonian Research Council, who helped to provide information about the situation in eastern Europe among the formerly socialist "accession countries" to the European Union (EU), and King's College London, who were responsible for the bibliometric part of the project. This report is primarily concerned with bibliometrics, but each of the five disease areas is introduced by the partner responsible for its coverage with a description of the disease area(s) and a brief summary of the data that were collected. These introductions are followed by detailed descriptions of the results obtained in terms of research outputs and (for two NCDs) their funding. Separate chapters give accounts of the impacts of this research – on Member State (MS) government health policy through the research activities of members of their health advisory committees, on clinical guidelines for these five NCDs, and on newspaper stories covering NCD medical research.

1.2 Identification of research papers and country outputs

1.2.1 The countries studied and the source of bibliographic data

This project examined the research outputs of the 28 Member States (MS) of the EU as in 2014, plus Iceland, Norway and Switzerland, which participate in many European research programmes and also have strong links with the EU MS. In this report, the countries are referred to by their ISO digraph codes, listed in Table 1 below.

Table 1. List of 31 countries used to identify NCD research papers

ISO	*Country*	*ISO*	*Country*	*ISO*	*Country*	*ISO*	*Country*
AT	Austria	EE	Estonia	IS	Iceland	PL	Poland
BE	Belgium	ES	Spain	IT	Italy	PT	Portugal
BG	Bulgaria	FI	Finland	LT	Lithuania	RO	Romania
CH	Switzerland	FR	France	LU	Luxembourg	SE	Sweden
CY	Cyprus	GR	Greece	LV	Latvia	SI	Slovenia
CZ	Czech Rep.	HR	Croatia	MT	Malta	SK	Slovakia
DE	Germany	HU	Hungary	NL	Netherlands	UK	United Kingdom
DK	Denmark	IE	Ireland	NO	Norway		

The data were extracted, under a licence, from the Web of Science © Thomson Reuters (WoS) and were limited to articles and reviews from the 12 years, 2002-2013. Papers were selected (see below) from both the Science Citation Index Expanded and the Social Sciences Citation Index. There is some overlap between the two, and papers appearing only in the latter were so marked.

1.2.2 Development and calibration of the filters used to identify NCD papers

These filters consisted of two main parts: a list of specialist journals and another list of title words. The filters were first developed in consultation with representatives of leading specialist medical research charities for the Science Citation Index on CD-ROM. They have since been extensively modified to make them apply to the WoS with its different interface and software, and to take account of the additional journals covered by the WoS, and ones added recently. They have also been amended to include newly-discovered genes that predispose a person to disease, and new medicines. The list of title words also includes the names of a large number of individual diseases.

As an example, the ONCOL filter was calibrated with reference to three sets of papers taken from the WoS: ones captured by the filter (or not) and ones whose addresses included (or did not include) department names (and their contracted forms) characteristic of cancer such as CANC, ONCOL, ONKOL, TUMOR.

- Set A were papers identified by the filter AND having one or more cancer words in their address field;
- Set B were papers out with the filter but with one or more cancer words in their address field;
- Set C were papers identified by the filter but without a cancer address word.

The number of papers in each of these three sets in a given year in the WoS was then designated as N. Samples of all three sets of paper details were downloaded to a spreadsheet and presented to one of the NCD mapping partners to mark as relevant to cancer research (1) or not relevant (0). Shading of the marks with a decimal between 0 and 1 was also possible. These markings were used to determine the numbers of papers retrieved by the filter that were deemed to be relevant, and by rule-of-three, the estimated number in set D (not found by the filter and without a cancer address word). Table 1, below, shows the calculations.

Table 2. Example of calculations used to determine the precision (p) and recall (r)of the ONCOL filter.

Set	*N (WoS)*	*n (sample)*	*n* (relevant)*	*precision = p*	*N* (relevant)*
A	32670	200	190	0.950	31037
B	17316	500	22.5	0.045	779
C	42697	500	402	0.804	34328
D					862
Total					67006
Found	75367	= (32670+42697)		(31037+34328) =	65365
Precision		**p =**	**0.867**	= (65365/75367)	
Recall		**r =**	**0.976**	= (65365/67006)	

If the precision and/or recall were insufficient, then the titles of the papers causing problems were examined in detail with a view to the addition of extra title words to the filter (for papers marked “1” in set B) or their removal, or the addition of “no” words to the filter (for papers marked “0” in sets A and C). This was an iterative process, and several rounds were needed, with successive sets of papers being marked by our Spanish partners in the Escuela Andaluza de Salud Pública.

The final values of precision and recall were **p = 0.95 and r = 0.98**. A similar process took place for the other four NCD filters.

1.2.3 Downloading of the paper bibliographic details and creation of the NCD files

Papers fulfilling the time and document type bounds, and with at least one address in one of the 31 countries listed in Table 1 having been The "full record", which includes all addresses, e-mails and funding details (where given) were then downloaded to a series of 12 "year" files, 500 papers at a time. These were then processed by a special macro to produce one combined Excel spreadsheet. The 12 separate spreadsheets were then combined together to make a single sheet. This contained 282,055 papers.

Each paper in the combined sheet was given an individual index number, and the following parameters were recorded:

- Names of all authors, in the format SMITH-AB
- Paper title
- Source (journal name, year, volume, issue, pages)
- Journal name
- Document type (article or review)
- Addresses (all in upper case, separated by a forward slash). Note: in the WoS UK papers are attributed separately to ENGLAND, WALES, SCOTLAND or NORTH-IRELAND.
- Country of publication
- Year of publication
- Month of publication (for most papers where the date of the journal was given)
- Language (almost all were in English)
- E-mail address(es) of corresponding author, sometimes others
- Funders, FU (for late 2008 papers and subsequently)
- Funding acknowledgement text, FX
- Composite list of authors and their individual addresses (from 2008)
- Authors' full names (where given), in the format Wilhelm, Hans; Wanke, Isabel; Hirche, Herbert (this allows the sex of most of the authors to be determined)
- Whether in the SCI or SSCI only

Although most papers in the WoS have their chosen keywords and formal abstracts, these were not recorded in the main spreadsheet as they would have made it far too cumbersome. From the paper title, a macro was applied to determine if the paper could be classed as "clinical " or "basic" or "both", according to the presence of one or more words on two lists, see Lewison and Paraje, 2004. The research level of the journal in which the paper was published was also determined from a master list, based on the same scheme; clinical journals were classed as RL = 1 and basic ones as RL = 4, and ones in between were given an RL value as a decimal number between 1.0 and 4.0. These RL values were determined for groups of five years, 2000-04, 2005-09 and 2010-14.

1.3 Citation scores for the papers, and percentage of reviews

1.3.1 Downloading of five-year citations to the papers

As the NCD papers for each of the first eight years (2002-09) were identified, their citation scores were found on the WoS and downloaded as a series of Excel files. These were then concatenated and modified by means of another special macro so that the source was in exactly the same format as the one used for the preparation of the papers spreadsheet. The five-year citation count (designated as Actual Citation Impact, ACI) for each paper was calculated (beginning with the year of publication), and this value was then carried across to the papers spreadsheet by means of a look-up function based on paper titles. A few citation scores could not be determined either because the

paper title was too long (> 255 characters) or contained quote marks. For these papers, the source was used as the look-up field.

In order to determine the mean citation score for each country and other citation statistics, the spreadsheet was annotated with 31 additional columns each of which contained the product of the paper's citation score, ACI, with the fractional presence of each country among its addresses[1]. The sum of these products, divided by the fractional count of the country for the relevant years (in the first instance, the eight years 2002-09), then gave the country's citation score on a fractional count basis, which is more appropriate than the score based on integer counts.

These individual country scores could then be compared with the ACI values for the EUR31 countries as a group and those for the world. These were obtained for each year's NCD publications directly from the WoS, although the sets of papers needed to be divided into sub-sets, based on journal initial letters, in order that each one should have no more than 10,000 papers, as this is the limit in the WoS for citation reports.

We also determined how many of a country's papers received enough cites to put them in the top 5% of EUR31 papers in the eight-year period, for which the qualification (for the ONCOL set) was 53 cites. [There were actually 5.15% of European papers that achieved this number of citations.] This may be a better measure of how effective a country's research output is because it is normally the most influential papers that are really important to the development of a field.

1.3.2 The percentage of reviews

Another indicator of "quality", or more accurately the esteem with which a country's researchers are held, is the percentage of reviews (Lewison, 2009) which are usually invited by journal editors from senior scientists. This is easily determined as the spreadsheet shows the document type but it is only a useful indicator where a country (or other group) has published several hundred papers. The percentage of reviews has been steadily rising with time, and it is higher for biomedical research and clinical medicine than for other major fields such as physics and mathematics. It correlates fairly well with citation measures, but it actually measures something quite different. For example, Greece often shows to advantage on this indicator, whereas the Scandinavian countries do not score highly, whereas the reverse is the case for citations.

1.4 Research in different subject areas and of different types

1.4.1 Creation of sub-filters for research application, disease or disorder

We were also able to sub-classify the papers in the five NCD files by their subject area, i.e., the disease or disorder that they were addressing. This was accomplished by means of "sub-filters", developed in close consultation with one or more experts in the NCD. They normally consisted of sets of title words, and sometimes also of journal name strings, and for each NCD they were combined into a special macro (again written by Philip Roe of Evaluametrics Ltd) so that the file of papers could be analysed very quickly. Not all the papers in an NCD could be classed in this way, and some papers involved study of more than one disease or disorder. Fractional counts were not used for the classification of papers by disease area, but they were used for the analysis of individual countries' outputs, where address counts were used. [This also made the process of analysis much easier.] This was particularly useful in order to compare a country's disease burden from this disease manifestation with its research output and show if was unduly low (or high).

1.4.2 Creation of sub-filters for type of research

A similar process was used to create a classification of the papers by the type of research, although this was only completed for the MENTH and ONCOL files. The types of research included drugs

[1] A paper with two German addresses and one from France would be classified as DE 0.67, FR 0.33.

(chemotherapy), epidemiology, genetics, surgery and other treatments. Again, fractional country counts were used to show whether individual countries were specialising in, or neglecting, particular modalities.

1.5 The burden of disease

1.5.1 Source of data

The most recent source of data on disease burden is from the World Health Organization's Global Burden of Disease study (Murray *et al.*, 2012), which provides elegant graphical representations of the burden from each of more than 150 disease manifestations, as for example that reproduced in Figure 1.

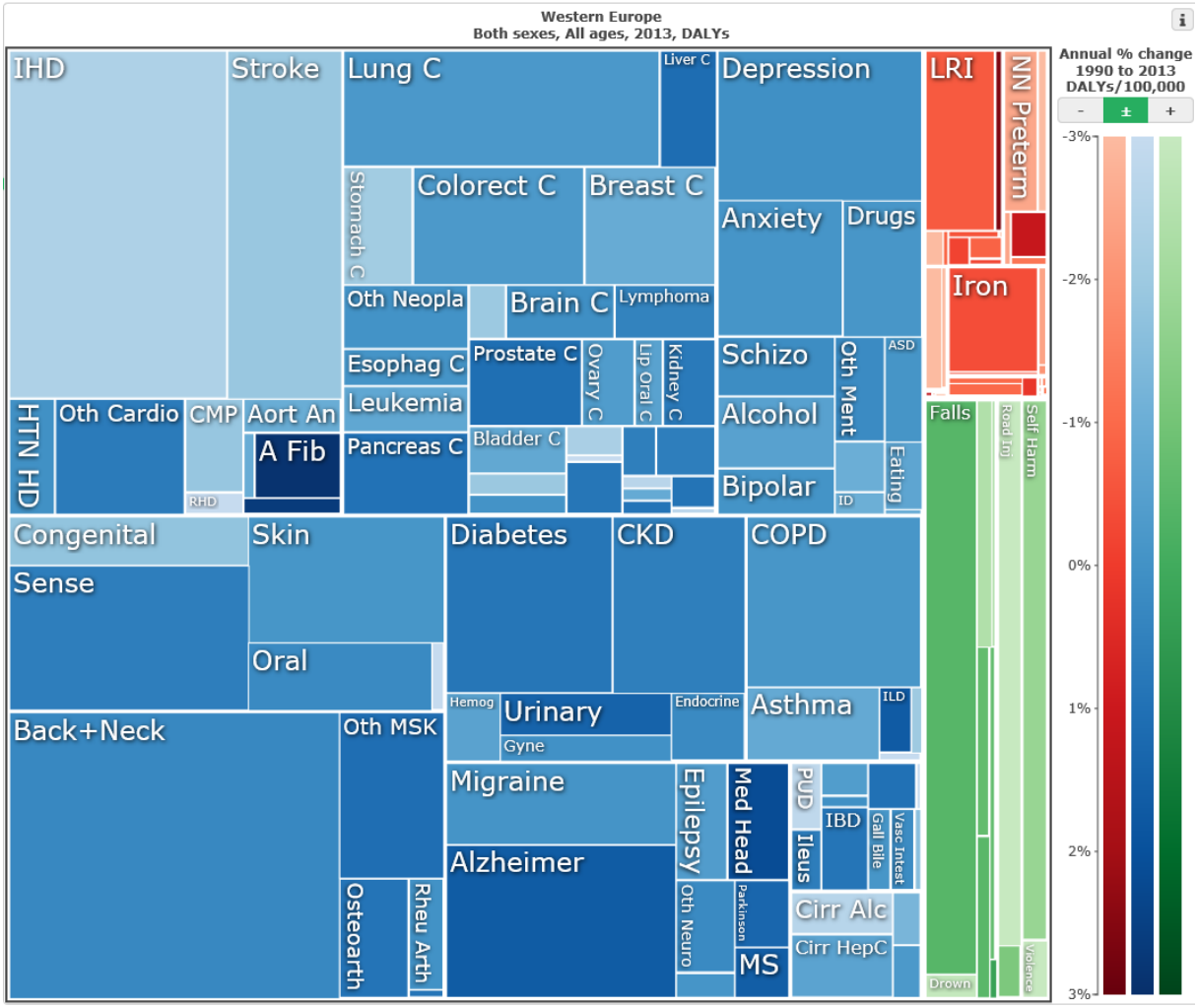

Figure 1. Global Burden of Disease map of the disease burden in Western Europe, 2013.
The intensity of the colours indicates which diseases or disorders are increasing most rapidly. Red: communicable, maternal, perinatal and nutritional diseases; blue: non-communicable diseases; green: injuries.

This figure shows that in western Europe, non-communicable diseases account for the large majority of the disease burden, some 86% of the total. This is here measured in Disability-Adjusted Life Years (DALYs), which take account both of lost years of life because of early death from the disease and of years living with a disability, which is weighted according to its impact on the patient (higher for blindness, for example, than for vitiligo).

In the EUR31 countries as a group, the percentage of the overall disease burden from the five NCDs studied here was 55%: CARDI 19.5%, ONCOL 17.2%, MENTH 11.2%, RESPI 4.7% and DIABE 2.5%. There was not much variation between countries in cancer (from 13% to 19%) but in the other four NCDs the burden varied greatly, as shown in Table 3.

Table 3. Disease burden (percent of DALYs) for 31 European countries from five NCDs, 2013

Least healthy countries from five NCDs						*Most healthy countries from five NCDs*					
	CARDI	*DIABE*	*MENTH*	*ONCOL*	*RESPI*		*CARDI*	*DIABE*	*MENTH*	*ONCOL*	*RESPI*
BG	37.0	2.8	6.8	13.0	4.5	IT	18.5	3.2	10.5	18.5	4.2
HR	25.2	2.8	11.4	17.1	3.8	MT	17.3	3.1	14.1	15.6	4.5
LV	32.1	2.2	10.2	13.0	2.1	LU	15.7	1.8	15.9	16.5	4.6
HU	26.7	2.9	7.6	17.8	4.2	AT	18.1	3.2	12.4	15.9	4.8
EE	27.9	2.4	12.7	13.3	2.0	CY	17.8	4.6	13.0	13.1	5.4
RO	31.6	1.8	7.7	13.7	3.3	NO	14.5	3.2	15.6	15.5	5.0
CZ	24.1	2.5	8.9	18.5	3.5	ES	16.2	3.6	11.7	17.5	4.8
PL	23.7	2.5	10.7	16.3	4.0	SE	18.0	2.5	12.3	15.6	5.0
GR	22.8	2.1	10.5	16.1	5.6	SI	18.2	2.6	10.8	17.9	3.9
SK	26.1	2.3	9.3	16.1	3.2	PT	17.5	3.6	10.0	16.9	5.1
DK	15.9	2.9	12.3	18.8	6.4	BE	17.2	2.4	10.2	17.7	5.6
LT	27.9	1.8	10.6	13.2	2.6	UK	16.1	1.2	11.5	16.9	7.1
DE	19.4	2.7	11.4	17.9	4.5	FI	19.3	1.7	13.2	14.2	3.5
NL	14.2	2.0	14.5	19.3	5.3	FR	13.3	2.0	13.0	19.1	4.2
CH	15.2	2.9	13.7	16.7	6.6	IE	15.1	2.1	13.1	15.5	5.8
EUR 31	**19.5**	**2.5**	**11.2**	**17.2**	**4.7**	IS	13.5	1.8	15.5	14.7	4.6

The table shows that the eight countries most affected by these five NCDs are all "accession states" in eastern Europe, but Slovenia (SI) is among those less affected. The differences are mainly occasioned by the burden from CARDI, which varies from 37% in Bulgaria to only 13% in France.

The source also goes into detail for many manifestations of cancer and mental disorders, and the main contributors to CARDI (ischaemic heart disease and stroke) and RESPI (Chronic Obstructive Pulmonary Disease and asthma), and these data are presented in the main NCD sections of this report. For diabetes there is no breakdown by type or by *sequelae.* However the table shows big differences between the most affected (Cyprus, 4.6%) and the least affected (UK, 1.2%). On the other hand, the UK suffers relatively most from RESPI (7.1%) and the three Baltic states the least (all less than 2.7%).

1.6 Research funding

1.6.1 Explicit and implicit funding sources, and exclusions

The funding of research is now recognised as an important source of information for its evaluation (Lewison & Dawson, 1998; Lewison & Devey, 1999; Lewison & van Rooyen, 1999; Lewison, Grant & Jansen, 2001; Roe *et* al., 2010; Rigby, 2013). At its simplest, the acknowledgement of a funding source on a paper indicates that an agency, usually an external one, has reviewed the research project and judged that it is worthy of support. Multiple funding sources would indicate that the project has found favour in several places.

In the past, the recording of the funding sources on a paper was a labour-intensive task as each paper needed to be inspected individually, usually in a big library. It was, however, worthwhile if the work could serve to provide many different funding bodies with a tally of papers that they had supported. This was the principle behind the creation of the Wellcome Trust's Research Outputs Database (Jeschin *et al*, 1995; Dawson *et al.,* 1998; Webster, 2005). This covered all UK biomedical

papers over the 14 years, 1988-2001, and was based on the papers in the Science Citation Index on CD-ROM, which was purchased from the Institute for Scientific Information in Philadelphia (now Thomson Reuters) and operated under licence from them. The data were made available to members of the "ROD club", who paid a graduated annual fee and in return received a list of their papers, together with access to consultancy advice.

It was immediately apparent that the authors of papers recorded their funding acknowledgements in a wide variety of ways, and that many papers had multiple funding acknowledgements[2]. It was therefore decided to use a coding system, with four parts:

- a trigraph (three character) code designating the individual funding body;
- a single letter code showing the form of support (no longer used);
- a digraph (two character) code designating the sector and sub-sector of the funder; and
- another digraph showing the country of the funder based on the ISO codes.

The trigraphs were designed to be easily memorable, *e.g.*, MRC = UK Medical Research Council; BHF = British Heart Foundation, although it turned out that there were so many different funders of UK research papers that many had to be given odd combinations of letters[3].

It also became apparent that some papers did not carry an acknowledgement because they had been supported internally – in a government lab (such as one supported by a research council or Government department), by a collecting charity, or by a commercial company. So the decision was made to include these "implicit" acknowledgements along with the "explicit" ones in the acknowledgement paragraph to form a composite acknowledgement[4].

Although in principle the research described in all published papers has to be paid for in some way, in practice there are many papers (especially ones describing clinical work) that do not contain any formal acknowledgement. Most of their authors would be academics or medical personnel working in a hospital or clinic, supported by general university funds or by salary support from the health service. But such support would not be peer-reviewed, and so such papers would perhaps be of a lower standard. In any event, it did not seem appropriate to record this nominal support, and the ROD was set up to record such papers as "unfunded", and the hospital or university or research institute address was not given a code. However, if a specific acknowledgement appeared to a university or department, or to a hospital, then it was presumed that some system of grants was in place and the contribution of the employing organisation WAS recorded with a code. This gave rise to three sub-sectors of the private-non-profit sector, namely HT = hospital trustees, MI = academic[5] and NP = other non-profit. The other two were CH = collecting charity and FO = endowed foundation.

1.6.2 The coding system, generic codes and thesaurus development

The commercial sector was similarly divided up into five sub-sectors, with companies divided into three: pharmaceutical, biotech and industrial. The first and third of these were further divided into independent and subsidiary. The original purpose was to distinguish between the research activities of UK subsidiaries of large multi-national companies which might be relatively independent of the parent, *e.g.*, the Merck Neuroscience Park in Harlow, which did its own research and also gave funding to universities. However there were many takeovers of small biotech (and not so small

[2] There are also acknowledgements to individuals who have provided help or advice. These are not considered further in this report.

[3] Initially, every UK research funder was given an individual trigraph in order to cater for the possibility that it would become a ROD member, although membership seldom rose above 30.

[4] Several of the ROD members maintained their own labs and also gave external research grants and this system allowed them to compare their respective outputs.

[5] This term was used because many universities and colleges are both endowed with capital and are still collecting money (*e.g.*, from their alumni).

pharma) companies and it seemed appropriate to regard the takeover as a way in which the new parent company would thereby gain the intellectual property of the new acquisition. This meant that many of the commercial codes became out-of-date. This had two consequences for the analysis of funding sources. First, the country of a company was effectively undefined, and second, the sub-sector could change when a biotech company had brought a new drug to market and so had become a pharma company[6].

The public sector was divided into three sub-sectors: government department (controlled by ministers), government agency (nominally independent of ministerial directives) and local authorities (including regions, counties and cities). They were given sectoral codes: GD, GA and LA, respectively. Although the latter form of support hardly exists in the UK, it is becoming increasingly common in several continental European countries (Länder in Germany, régions in France, provinces in Spain) and also in north America (provinces in Canada and states in the USA) and in Australia(states and territories). Most of these regions have been given their own trigraphs, although some smaller regions have generic codes, see below.

There is also a tendency for government departments (and sometimes agencies) to change their names to reflect incoming ministers' changed roles. This can cause confusion, particularly as there is likely to be an overlap between the old and new names, which can differ substantially, and their functions. Thus the UK Department of Trade and Industry has morphed into the Department for Business, Innovation and Skills (but retains many of its former functions of technology support, so keeps its trigraph of DTI). It has no fewer than 48 agencies and public bodies, including the seven research councils (which each have their own trigraph), the UK Atomic Energy Authority and the UK Space Agency (which are active in research) and many other bodies which are not, such as the British Hallmarking Council and the Land Registry. Some of these may do some research, and could be coded with their own trigraph, or that of their parent.

Because of international collaboration on biomedical research papers, many of the UK papers covered in the ROD also had foreign partners and acknowledgements to foreign funding sources. The thesaurus soon began to run out of trigraph codes, and we started to use "generic" codes for the smaller organisations (in terms of their biomedical research spend). These consisted of a single letter (X, Y or Z) followed by one digit (to designate the country) and another to designate the sector and sub-sector. Individual countries that supported a lot of biomedical research were given their own digraph (*e.g*, X1 = USA); others were given one that showed their continent, see Table 1. There is, of course, some redundancy as the country and sector/sub-sector are also given by the second and third digraphs, but these are needed for the main analyses. For example, X1B-BT-US indicates a US biotechnology company in two ways. Generic codes for the UK were not used initially, but have been introduced to cater for the large number of new British funding bodies, and codes UK1, UK2 etc. are employed.

[6] There is in principle a clear distinction between a company that is licensed to sell a medicinal drug, one that has no intention to do so, and one that would like to do so when it obtains approval. These are coded respectively IP, IN and BT.

Table 4. List of digraphs used for countries with generic codes, and the digit to designate their sector or sub-sector.

Digits 1 & 2	*ISO*	*Country*		*Digit 3*	*Code*	*Category*
X0	NL	Netherlands		1	CH	Charity
X1	US	USA		2	FO	Foundation
X2	DE	Germany		3	GD/GA	Government
X3	JP	Japan		4	HT	Hosp. Trustees
X4	SE	Sweden		5	IN	Industry (non-pharma)
X5	NZ	New Zealand		6	IP	Pharma industry
X6	CA	Canada		7	LA	Local/regional authority
X7	FR	France		8	MI	Mixed (*i.e.*, academic)
X8	ZA	South Africa		9	NP	Non-profit (*e.g.,* professional body)
X9	IT	Italy		B	BT	Biotech company
Y0	BR	Brazil		Z0	EU	Europe
Y1	IE	Ireland		Z1	CN	China
Y2	CH	Switzerland		Z2	HU	Hungary
Y3	DK	Denmark		Z3	AT	Austria
Y4	NO	Norway		Z4	HK	Hong Kong
Y5	ES	Spain		Z5	AU	Australia
Y6	FI	Finland		Z6	XX	not known
Y7	BE	Belgium		Z7	AF	Africa
Y8	IL	Israel		Z8	AS	Asia
Y9	IN	India		Z9	LA	Latin America

The code "Z4" for Hong Kong is still used, although the country digraph of CN for China shows that this is now part of the People's Republic.

These trigraphs, and the associated sectoral and country codes, have been assembled into a large thesaurus of funding bodies. It is structured so that the different names and formats given to a funding body (and in some cases its dependent agencies, bodies or companies) are all listed to facilitate the allocation of codes. At the time of writing, there were 17,485 entries and 10,045 (out of a possible 17,576) individual letter trigraphs. This suggests that there is still plenty of opportunity for new codes, but it is often difficult to find appropriate letter combinations for new organisations with many funded papers. These are appearing in continental European countries as work on the project develops, because the thesaurus was originally developed mainly for UK funding bodies.

1.6.3 The Web of Science and Conflict of Interest statements

When the ROD was being developed and operated, the Science Citation Index was available mainly in the form of CD-ROMs. During the mid-1990s, the Web of Science was developed by Thomson Reuters as an online resource, available to most higher education establishments and to some individuals under licence. Since its introduction, the facilities available for searching and for retrieving data have been steadily enhanced. During 2008, Thomson Reuters started to provide details of funding for individual papers – quite likely stimulated by the earlier existence of the ROD!

There are two individually searchable fields, FO = funding organization and FT = funding text[7]. The FO field lists the names of the acknowledged funders and FT gives the full text of the acknowledgement, including recognition of individuals who have helped with the research. For some funding bodies, the FO field also lists the grant numbers, although they are often absent and have not been considered in this analysis.

It became apparent that there were some papers with a very large number of acknowledgements in the FO field to pharma companies. Inspection of the corresponding FT field showed that this usually also incorporated a "conflict of interest" statement, to the effect that some authors had been paid consultants to a company, or had served on an advisory board, or had spoken on their behalf at a conference, or owned stock in the company – or had benefited in some other way, not connected to the research being reported in the paper. Very often it appeared that these company names had been carried across (wrongly) to the FO field. Careful inspection of the funding text, FT, revealed just which companies or other organizations (if any) should be credited with support of the paper, and the FU column in the spreadsheet was redacted accordingly. Fortunately conflict of interest statements only occurred on a few percent of the relevant papers, but this process needed to be undertaken first in order to save the work of unnecessary coding of irrelevant company acknowledgements. Many of the acknowledgements with conflict of interest statements were very long and the process of reading them to decipher which companies, if any, had supported the research described in the paper was quite difficult. The identification of papers with a conflict of interest statement was performed with the aid of a special macro written by Philip Roe of Evaluametrics Ltd.

Below is an example of a conflict of interest FX statement. The original FU statement listing the funders was:

B.C. Lung Association; Canadian Institutes of Health Research [MOP42539]; GlaxoSmithKline; AstraZeneca; Schering Plough; Wyeth Pharmaceuticals; Merck Frosst; NIH

but the funding text makes clear that the only sources of funding for this paper were the first two, so the redacted FU field was as follows:

B.C. Lung Association; Canadian Institutes of Health Research [MOP42539]

and the corresponding codes were
LBC-CH-CA CAM-GA-CA

Supported by the B.C. Lung Association and by grant MOP42539 from the Canadian Institutes of Health Research.J.L.W. received up to $1,000 from GlaxoSmithKline in lecture fees and more than $100,001 from AstraZeneca in industry-sponsored grants as a contract. S.Z. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. O.P. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. C.M. is an employee of AstraZeneca. D.D.S. received up to 81,000 from Schering Plough in consultancy fees, $1,001-$5,000 from AstraZeneca and $1,001-$5,000 from GlaxoSmithKline in advisory board fees, $10,001-$50,000 from GlaxoSmithKline and $10,001450,000 from AstraZeneca in lecture fees, more than $100,001 from AstraZeneca, more than $100,001 from Wyeth Pharmaceuticals, $50,001-$100,000 from Merck Frosst, and more than $100,001 from GlaxoSmithKline in industry-sponsored grants, and more than $100,001 from the NIH in research funding. IL does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. S.G. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. A.M.C. received up to $1,000 from GlaxoSmithKline

[7] When details of papers are downloaded to file, FO becomes FU and FT becomes FX.

in lecture fees and more than $100,001 from AstraZeneca in industry-sponsored grants as a collaborative research agreement.

A more detailed discussion of the incidence of conflict of interest statements and their effect on the numbers of papers supported by the individual pharma companies is given in Lewison and Sullivan, (2014). However, in order to use a consistent approach to the redaction of the list of funding bodies, we drew up some simple rules on when a funding credit should be given, and when it should not be. For a credit to be given, we looked for one or more of the following phrases or clauses:

- "this study was supported by..." or "sponsored by ..."
- A.B. "was employed by .." or "was an employee of ..." or "had a fellowship from "
- X company "provided (or donated).(a service, goods, or funded the manuscript preparation, or paid journal page charges)"
- A.B. "receives/ed an unrestricted grant from ..." or "receives/ed research support from ..."

but we did *not* give funding credit when the wording was as follows:

- "data collection/analysis was performed by ..." (a standard personal acknowledgement)
- A.B. "has received support/funding from ..." or "currently has research grants from ..."
- "the project was endorsed by..."
- A.B. "has carried out consultancy" or "has given lectures" or "is/was an advisory board member" or "receives royalties from ..."
- A.B. "reports receiving" (unless it explicitly says that it applied to the present study)
- "departmental funding was received from ...." (unless explicitly for the present study).

1.6.4 Coding of explicit funders: procedure and thesaurus

Once the conflict of interest statements have been individually read to redact the list of funding bodies in the FU column, this was processed so that the funding bodies could be coded individually. First the grant numbers (always given in square brackets) were removed, and then the individual funding body credits, which are separated by a semi-colon and one or two spaces, were listed alphabetically in a single spreadsheet column each with the number of occurrences. These were then matched to a "new thesaurus of funding bodies" which was developed from several earlier studies where funding bodies had been coded. This provided codes for many of the funding bodies; a few acknowledgements were to more than one funder so two or three codes were occasionally given. The funding bodies without codes were then investigated individually – by a search of the papers to ascertain from which country they came, also by reference to the funding text, FX, and by a search of the web. Many, but not all, funding bodies had a website that allowed us to determine their country and sub-sector. This procedure was better than reliance on the name of the funding body – some were called "foundations" but were not endowed, simply collecting charities.

The new thesaurus will increase with each set of papers examined, and will contain all the variations of name of the various funding bodies as they are encountered. Many of these are similar so that once a funding body has been coded, many other versions of its name can be coded also when they are listed alphabetically.

1.6.5 Coding of addresses: government, charities and commercial

As with the "new funding thesaurus", we developed an "institution funding thesaurus" that will grow with each set of papers processed. It consisted of two parts: one part with organisations that merited funding codes (government labs, charities and commercial companies) and another part with organisations not to be coded (universities, hospitals and health centres and research institutions). These were given the code "0" so as to distinguish them from organisations that had not been coded yet.

The allocation of codes was facilitated by searching the full address (including the institution name) for suffixes indicating a limited company (*e.g.*, Ltd in the UK, sa in France, ag or GmbH in Germany

and Austria, SpA in Italy, AB in Sweden). These were mostly small companies that were given generic codes but variants of the names of bigger companies and subsidiaries could also be recognised and coded.

1.6.6 Conversion of funders and addresses to codes

Once the funding bodies and some of the institutions had all been coded, another macro, again written by Philip Roe, was used to add three columns to the spreadsheet of papers: one for the FU codes, one for the address codes, one for the composite of these two with duplicates removed. This was used for the funding analysis. The number, F, of funding bodies credited was then determined from the length of the entry in the composite code column, 9 characters indicating one funding body, 19 two, 29 three and so on. This process also enabled us to spot any errors in the typing of funding codes[8]. For any given group of papers, we could then determine the average number of funding acknowledgments and the percentage with one or more funding codes.

1.6.7 The number of funders and its significance

The literature clearly shows that more funders are positively correlated with publication in higher impact journals, and with receipt of more citations in a given time window, even when other possible confounding factors are taken into account by means of multiple regression analysis (Roe *et al*., 2010). We have found that an important confounding factor is the research level of the paper (clinical or basic), see Lewison and Paraje (2004). Basic papers tend to receive more funding and receive more citations than clinical ones. This may put clinicians at a disadvantage when they apply for research grants.

Another important factor in the European context is that researchers in some countries may have many more potential sources of support than others. In particular, the pharma industry is more prominent in western Europe, and there are also many more charities and endowed foundations. In addition, there may be more governmental and regional sources, as we have observed in Belgium, France, Germany, Italy, Spain and Sweden. The countries of eastern Europe have been freed from the centralised system of government support for research for nearly 25 years, but we have not so far observed significant numbers of private-non-profit organisations that sponsor biomedical research in these countries. One of the topics that we should like to explore in this project is why this is so, and what changes would be needed, both fiscally and in society, in order to stimulate their creation and growth. [There is a rather similar problem in India, which we discussed earlier (Lewison & Roe, 2012); the charitable sector does exist there and is growing, but medical research is not supported in this way.]

In this project, it will be worthwhile to explore the relationship between numbers of funding bodies (and other parameters) and citation counts, even though these are only currently available for the year 2009, which is the first year for which funding information exists in the WoS, because of the sheer scale of the project – there are a total of 62,234 papers in the five NCD areas. Moreover, when the funding information on all five NCDs is available (during the summer of 2015), five-year citation data for the 2010 papers will also be available (citations from 2010 through to 2014).

We can also examine how the average number of funding bodies per paper varies with disease area and with the type of research. This will reveal if some aspects of research in an NCD are under-funded compared with others, and if these outputs appear low in relation to need, which funders may have a bigger role to play in improving the situation.

[8] A common error was to insert an extra space after the code, and this was corrected by use of the "trim" function.

1.7 Impacts: outputs of members of health advisory committees

1.7.1 Collection of data on membership

Our initial thoughts on this type of impact was that EU Member State governments would devise their health policies on the basis of research evidence, and that policy statements would have some scientific references. However, it turned out that, since these documents were intended for public consumption, instead of references they had pretty pictures showing people either in splendid health, or being treated by medical personnel in white coats and using shiny equipment. So we looked to see from whom governments might be getting advice, in the form of members of advisory committees, who could be expected to advise their governments from the standpoint of their own research experience. .

We sought the health advisory committees relevant to the five NCDs in the various European countries. This proved somewhat challenging, as the system for the provision of advice varied greatly. In order to find the details of these committees, we needed to recruit research assistants with the necessary language skills to find them and identify their remits and membership lists. Fortunately, King's College has graduate students from almost all European (and incidentally, many other) countries who are able to work part-time, and we retained eight students for this work (and the work described in sections 1.8 and 1.9). We were also assisted by our partners in Estonia, France, Germany, Italy and Spain, and by volunteers in Hungary and Sweden who searched for relevant committees in their own and neighbouring countries. We were able to obtain lists of members for committee members in 21 countries.

1.7.2 Committee members' papers

Having obtained the lists of members of these advisory committees, we searched for the papers that they had written and that were covered in the WoS for the five years, 2009-13, and were classified as articles or reviews. For some of the advisers, the city in which they worked was listed, and this reduced the risk of our finding papers by their homonyms. Nevertheless, there remained many papers by homonyms in fields remote from biomedical research, and so we used the topic search facility in the WoS to remove these. When the papers had been downloaded to files and converted to an Excel spreadsheet, we further examined the journals in which they had been published. Ones that were clearly non-medical were also removed, and ones in related fields (such as psychology or biology) were checked to see if their titles showed that they were relevant. We also removed papers in medical fields unconnected to the five NCDs, such as gynaecology and infectious diseases.

The next piece of analysis was more complex, and involved a comparison of the papers in the combined spreadsheet with the ones in five large files of research papers in NCDs that we had created for the period 2002-13. We assumed that the advisory committee papers would have had an address in Europe, even though a few committee members had addresses in another EU Member State, and performed a look-up function so as to identify which papers were in cancer, diabetes, etc. This allowed us to see the balance of the expertise available to the Member State governments. The look-up not only provided information on which papers were in each of the five NCDs, but also the sub-fields within them (see section 1.4).

However our main interest was to see whether the advisers were well-connected to research in other European countries, or whether they were relatively lacking in international contacts, or better connected to north America than to the rest of Europe. This would then show if health policy in the MS was informed by research in the European Research Area, so that lessons learned in one country could benefit others.

1.8 Impacts: references on clinical guidelines

1.8.1 Previous work on cancer clinical guidelines

This measure of impact has been used previously both to evaluate the research being cited, and to show the evidence base of recommendations for clinical practice. However, the mere presence of such guidelines is no guarantee that they will be effective at improving healthcare (Schrader *et al*., 2006). The first study, on a small scale, examined the cited papers on a sample of 15 UK clinical guidelines (Grant *et al.*, 2000). It found that they were very clinical and that UK research was over-cited by 2.5 times.

A subsequent study of 43 cancer clinical guidelines in the UK (Lewison *et al.,* 2008) reached similar conclusions, and showed that they could also be used as a means to evaluate research in other countries, for example six Swedish universities. This work was subsequently updated (Pallari and Lewison, 2014) and showed that surgery featured strongly among the cited references (over 25% of the total). It also showed a big variation in whether a country's papers were over- or under-cited relative to its presence in cancer research. Thus UK research was over-cited by almost four, Danish, Dutch and Swedish research by more than two, but that from the "accession" Member States (Poland, Czech Republic and Romania) by half or less.

In this report, the results for the five individual NCDs are given (and discussed) at the end of the relevant main section (2, 3, 4, 5 and 6).

1.8.2 Selection of European clinical guidelines

We investigated the clinical guidelines currently available in the different European Member States in order to extend the work to other countries. Although many countries had a set of national guidelines, some had regional ones as well, and there were yet others published by European societies of professionals in various branches of medicine. We even learned that in Sweden, each of the 21 counties had their own clinical guidelines. Clearly, it would have been impossible for us to collect the references on all of these, and so we decided to limit the study to national guidelines.

We found that the numbers of national clinical guidelines that were relevant to one of the five NCDs was still too great for us to be able to cover them adequately in the time available, so we decided to select those guidelines concerned with the most burdensome diseases in Europe. These were the ones causing 1% or more of the disease burden, as shown below.

Table 5. List of diseases causing 1% or more of the disease burden in EUR31 countries, based on the Global Burden of Disease for 2010.

Disease area	*%*		*Disease area*	*%*
Ischaemic heart disease	9.7		Anxiety disorders	1.7
Cerebrovascular disease	5.3		Alzheimer's dis. & other dementias	1.7
Unipolar depressive disorders	4.3		Breast cancer	1.5
Trachea, bronchus & lung cancers	3.5		Alcohol use disorders	1.3
Chronic obstructive pulmonary dis.	2.9		Drug use disorders	1.3
Diabetes mellitus	2.5		Asthma	1.1
Colon and rectum cancers	2.0			

1.8.3 Processing of the guidelines to extract references; development of the macro

In the earlier studies on UK guidelines, the identification of the references with papers processed for the Web of Science involved much labour as each one had to be sought individually. It would not have been practical in the scope of this project to continue in this way for guidelines for the other NCDs and for all the other European countries, but we were able to semi-automate the process by means of a visual basic macro, written by Dr Philip Roe of Evaluametrics Ltd. This worked as follows. First, the references sections of a guideline in PDF format were copied and pasted to an Excel spreadsheet. Second, these were slightly tidied by removal of page numbers, document running heads, etc. The macro was then operated, and it generated sets of search statements, eight at a time, ready for copying and pasting into the search panel of the WoS.

Author names (AU) up to six in number were given without initials as sometimes they were given incorrectly by the guideline although if there was only one author the first initial was given. Any diacritical marks on letters in author names had to be removed, so that á became a and ü became u. The title words (TI) were selected to be the longest three in the paper title, but they needed checking to ensure that there were no punctuation marks associated with them. The journal name (source, SO) was given by just its initial letter as the guidelines usually gave an abbreviated name and this would have needed to be substituted by its full name, which would have had to be researched and entered into the macro. Finally, the publication year (PY) was given for completeness.

This process worked well, even though the search statements needed to be inspected individually (to remove author names with non-Roman characters which are not recognized by the WoS and to delete any punctuation marks attached to title words. The macro also listed references that did not satisfy its specific requirements so that any errors could be corrected manually and the macro then run again.

1.9 Impacts: newspaper stories of medical research

1.9.1 The importance of newspaper stories for science communication

This part of the project was intended to show the effects of European NCD research on six groups of people:

- politicians and other decision-makers;
- senior officials and advisers;
- health-care administrators;
- medical personnel (doctors, other professionals);
- researchers;
- the general public.

There is regrettably abundant evidence that politicians are unduly sensitive to stories in the media. Some of these are based on individual cases, in which it is reported that named patients do not have access to particular means of therapy (expensive drugs, for example). Ministers react by making special provision for them, but this can distort the overall health-care system as with the Cancer Drugs Fund in the UK (Thornton, 2011; Knapton, 2014). Senior officials can use the stories to bring news of research to their ministers; most will not have the time to read the literature extensively and need help to learn about interesting developments.

The same is true for health-care administrators in hospitals and clinics, who may learn about new methods of health-care delivery that offer potential cost savings. Medical personnel will also benefit, though the media can also provide misinformation that can cause doctors to misdiagnose (Schmidt *et al.*, 2014). They can also influence researchers, and there is evidence that media coverage increases modestly the numbers of citations (Phillips *et al*., 1991; Lewison *et al*., 2008). The print media may even be a source in their own right (Hicks & Wang, 2013).

The biggest influence may be on ordinary people, and could assist the public to choose healthier life styles (Nishtar *et al*., 2004; Caburnay *et al*., 2008; Hellyer & Haddock-Fraser, 2011), including enrolment for vaccinations (Olufowote, 2011; Robbins, Pang & Leask, 2012), although sensational press coverage of supposed links between MMR (measles, mumps, rubella) vaccination and autism has had a negative effect (Holton *et al*., 2012).

They may also add to the political pressure for public investment in medical research, particularly if own-country papers are well-cited. In some countries, commentators on the significance of the research often come from medical research charities, which thereby gain exposure (Lewison *et al*., 2012). Print newspapers are in decline in many countries, but many have a strong web presence and are still important despite the growing influence of social websites such as Twitter and Facebook.

1.9.2 Description of the work: collection of stories

We therefore embarked on an ambitious programme of study on the coverage of research in the five NCDs during the 12-year period, 2002-13, in a large number of European newspapers. Some of these have their own searchable websites; others can be searched through full-text databases such as Factiva ©Dow Jones, to which KCL subscribes. Wherever possible, we used five composite search strategies to identify potential stories. These were as shown in Table 6, below, together with the translations of these terms into other European languages, as needed.

Table 6. Search terms used for identification of newspaper stories about research on five NCDs.

NCD	*search words*
ONCOL	cancer or leukaemi* or melanoma* or lymphoma*
CARDI	heart attack or heart failure or stroke or blood pressure or hypertension
DIABE	diabet*
MENTH	addict* OR ADHD OR alcoholi* OR Alzheimer's OR anorexia OR anxiety OR bipolar OR bulimia OR dementia OR depression OR hyperactivity OR schizophrenia OR self-harm* OR suicide*
RESPI	asthma or COPD or chronic obstructive pulmonary disease or allergic rhinitis or cystic fibrosis or emphysema
ALL	research* or study or scientists or expert*

The process of data collection is quite complex, and involves the following steps:

- select appropriate newspapers in the selected countries;
- search an electronic archive of each of the newspapers to identify potentially relevant stories. The search strategy uses a combination of simple terms for research stories on each

of the five NCDs, see Table 10 above, and details of the selected stories are entered to an of Excel spreadsheet (phase 1);

- scan the selected stories to retain those deemed relevant (because they cite NCD research) and copy and paste pertinent data to the appropriate spreadsheet(s). These include codes for the newspaper and country, date, journalist name and job title (if given), codes for the research being cited, names and affiliations of researchers (if provided) and any commentators. If available, we also note the number of Facebook "likes" and the number of "shares"; these are markers of the story's influence on its readers (phase 2);
- identify the cited papers in the Web of Science (WoS) where possible, download details and copy to the spreadsheet (phase 3);
- determine the main parameters of the cited papers, such as countries of origin, funding data and type of research, and annotate the spreadsheet (phase 4);
- analyse the data on the resulting spreadsheet (both the stories and the cited papers) to answer a number of research questions.

Because the newspapers are in many different languages, we asked our project partners to assist us by the provision of research assistants who could scan papers from their own country (and sometimes others nearby). We were also assisted by volunteers from Hungary and Sweden, who kindly contributed to the project in exchange for information on how Hungarian and Swedish NCD research was reported in newspapers in many European countries; this would assist them in the evaluation of their own country's NCD research output. However, this still left many countries with no coverage of their newspapers, so we recruited ten temporary research assistants from among the KCL graduate students who had the required language abilities (usually natives of the Member State) and trained them, and the others, in the business of newspaper scanning and recording. As a result, we aimed to cover one or more newspapers in 30 of the 31 countries (the omission is Iceland), and the table below shows the tally, with the names and origins of the RAs working on each paper.

Table 7. List of European newspapers to be covered in the EU NCD mapping project, with their countries, languages and the names and affiliations of those who will be covering them.

Country	***ISO***	***Newspaper***	***Lang.***	***Research assistant***	***Origin***
Austria	AT	*Die Presse*	DE	Natalia Kelsch/Anne Spranger/Victor Stephani/Tobias Schumacher	TU Berlin
Belgium	BE	*Het Laatste Nieuws*	NL	Ann-Sophie de Mol	KCL
Belgium	BE	*Le Soir*	FR	Gabrielle Emanuel	KCL
Bulgaria	BG	*Dnevnik*	BG	Eva Nacheva	KCL
Bulgaria	BG	*Trud*	BG	Christina Tencheva	KCL
Croatia	HR	*Morningtimes*	HR	Ria Ivandic	KCL
Cyprus	CY	*Cyprus MaiL*	EN	Cristina Pallari	Evaluametrics Ltd
Czech Rep.	CZ	*Blesk*	CZ	Kasia Zemanek	KCL
Denmark	DK	*Jyllands-Posten*	DK	Maria Dahl	KCL
Estonia	EE	*Ohtuleht*	EE	Argo Soon	EE Res Council
Estonia	EE	*Postimees*	EE	Argo Soon	EE Res Council
Finland	FI	*Helsingin Sanomat*	FI	Laura Mantovani	KCL
Finland	FI	*Hufvudstadsbladet*	SE	Argo Soon	EE Res Council
France	FR	*Le Monde*	FR	Anshoo Lumba	Urc-Eco, Paris
Germany	DE	*Süddeutsche Zeitung*	DE	Natalia Kelsch/ Anne Spranger/ Victor Stephani/ Tobias Schumacher	TU Berlin

Country	*ISO*	*Newspaper*	*Lang.*	*Research assistant*	*Origin*
Germany	DE	*Frankfurter Allgemeine Zeitung*	DE	Ann-Sophie de Mol	KCL
Greece	GR	*Ethnos/ Ta Nea*	GR	Laura Mantovani	KCL
Hungary	HU	*Magyar Nemzet*	HU	Edit Csajbok	Semmelweis Univ
Hungary	HU	*Népszabadság*	HU	Edit Csajbok	Semmelweis Univ
Iceland	IS	*Fréttablaðið*	IS	Not yet appointed	Evaluametrics Ltd
Ireland	IE	*Irish Times*	EN	Kamil Mahmood	KCL
Italy	IT	*Corriere della Sera*	IT	Ludovica Borsoi	Un. Bocconi, Milan
Italy	IT	*La Repubblica*	IT	Ludovica Borsoi	Un. Bocconi, Milan
Italy	IT	*La Stampa*	IT	Ludovica Borsoi	Un. Bocconi, Milan
Latvia	LV	*Latvijas Avīze*	LV	Argo Soon	EE Res Council
Lithuania	LT	*15min*	LT	Ingrid Jaselskyte	LT Science Council
Lithuania	LT	*Lietuvos rytas*	LT	Ingrid Jaselskyte	LT Science Council
Luxembourg	LU	*Luxemburger Wort*	DE	Ann Sophie de Mol	KCL
Malta	MT	*The Times*	EN	Elena Pallari	KCL
Netherlands	NL	*Het Algemeen Dagblad*	NL	Ann-Sophie de Mol	KCL
Netherlands	NL	*De Telegraaf*	NL	Ann-Sophie de Mol	KCL
Norway	NO	*Aftenposten*	NO	Ane Auraaen	Urc-Eco, Paris
Poland	PL	*Fakt*	PL	Kasia Zemanek	KCL
Portugal	PT	*Correio da Manhã*	PT	Elisabeth Mariailidio	Andalusia Sch Publ Hlth
Portugal	PT	*Jornal de Notícias*	PT	Elisabeth Mariailidio	Andalusia Sch Publ Hlth
Romania	RO	*Adevărul*	RO	Maria-Cristina Juverdeanu	KCL
Slovakia	SK	*SME*	SK	Argo Soon	EE Res Council
Slovenia	SI	*Delo*	SI	Ria Ivandic	KCL
Spain	ES	*ABC*	ES	Diana Gosalvez-Prados	Andalusia Sch Publ Hlth
Spain	ES	*El País*	ES	Diana Gosalvez-Prados	Andalusia Sch Publ Hlth
Spain	ES	*La Vanguardia*	ES	Diana Gosalvez-Prados	Andalusia Sch Publ Hlth
Sweden	SE	*Dagens Nyheter*	SE	Gustaf Nelhans	Sahlgrenska Göteborg
Sweden	SE	*Svenska Dagbladet*	SE	Gustaf Nelhans	Sahlgrenska Göteborg
Switzerland	CH	*Berner Zeitung*	DE	Natalia Kelsch/ Anne Spranger/ Victor Stephani/ Tobias Schumacher	TU Berlin
Switzerland	CH	*Le Matin*	FR	Ann Sophie de Mol	KCL
UK	UK	*Daily Mail*	EN	Elena Pallari	KCL
UK	UK	*The Guardian*	EN	Elizabeth Desalu/ Ade Oyegoke	KCL

This is an ambitious programme of work. We sought to cover three newspapers from each of the large EU Member States (France, Germany, Italy, Poland, Spain and the UK); two each from the medium-sized ones with a population of around 10 million (including Switzerland), and one each from the small ones (including Norway). Each research assistant would cover one newspaper at a time from their chosen country, so that a limited number of newspapers will be complete even if we are not able to cover all the ones in Table 7.

The standard format for the data taken from newspaper stories and from the cited papers is as follows. All the entries are in English and in roman script except for the original story title.

Table 8. Layout of spreadsheet containing details of newspaper stories of NCD research and the cited papers, and the columns in the Excel spreadsheet.

Phase 1: perusal of story			***Phase 2: note story details***	
A	Index number		O	Type (of research)
B	Date		P	Relevance
C	Country ISO code		Q	Scientists (named in story)
D	Source		R	Institutions
E	Headings (original)		S	Journal (given in story)
F	Headings (English)		T	Funding
G	Synopsis (original)		U	Commentators
H	Synopsis (English)		V	Organisations (of commentators)
I	Length		W	Notes
J	Journalist		X	Full title
K	Position		Y	URL
L	Job		Z	Link to study
M	Subjects		AA	Resource (for non-English
N	Application (of research)		AB	Number of views
Phase 3: cited paper details from WoS			***Phase 4: analysis of cited papers***	
AC	Authors (WoS)		AR	Modified title (with $ between words)
AD	Title of cited paper		AS	Clinical?
AE	Source of cited paper (WoS)		AT	Basic?
AF	Journal (WoS, from records sheet)		AU	Both?
AG	Doc type (WoS)		AV	RL journal
AH	Addresses (WoS)		AW	Country fractional counts
AI	Country of publication (WoS)			
AJ	Publication year (WoS)			
AK	Publication month (WoS)			
AL	LA = language of paper (WoS)			
AMM	EM = e-mail of author(s) (WoS)			
AN	FU = funding sources (WoS)			
AO	FX = acknowledgement text (WoS)			
AP	C1 = addresses linked to authors (WoS)			
AQ	AF = authors' full names (WoS)			

The two spreadsheets (phase 1 and 2; phase 3 and 4) are then merged together into a coherent working file for the particular country.

2 Cardiovascular research (CARDI)

2.1 Survey of funding organisations (Technische Universität, Berlin)

2.1.1 Definition of Cardiovascular Diseases (CVDs, CARDI)

Cardiovascular diseases include a wide range of serious disease categories, but are commonly described as disorders of the heart and blood vessels. CVDs can be categorized by aetiology (*e.g.* inborn, atherosclerosis), location (*e.g.* heart, arteries, veins) or function (*e.g.* heart failure). This report compares "diseases of the circulatory system" as classified under Chapter IX of the International Statistical Classification of Diseases and Related Health Problems after the tenth revision (ICD-10) of the World Health Organization (WHO) as CVD, to other diseases. More precisely, CVDs are categorised under the following diseases:

Table 9: Diseases of the circulatory system

ICD-10	*Diseases of the circulatory system (here CARDI)*
I00-I02	Acute rheumatic fever
I05-I09	Chronic rheumatic heart diseases (RHD)
I10-I15	Hypertensive diseases
I20-I25	Ischaemic heart diseases (here Coronary heart diseases or CHD)
I26-I28	Pulmonary heart disease and diseases of pulmonary circulation
I30-I52	Other forms of heart disease
I60-I69	Cerebrovascular diseases (or Stroke)
I70-I79	Diseases of arteries, arterioles and capillaries
I80-I89	Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere
I95-I99	Other and unspecified disorders of the circulatory system

2.1.2 Data gathering from literature and the Web

A systematic search was conducted that identified all relevant public, non-profit and commercial research funding organizations (RFOs) at the regional, national, supranational and EU levels. A baseline threshold of €0.5 million in overall investment was set in order to identify funding that could be expected to influence the content or direction of major research programs. Because of the limited number of RFOs active in CARDI, the threshold for was lowered to €0.2 million.

Subsequently, a survey tool was used to collect quantitative and qualitative data from RFOs from April 2014 to December 2014. The quantitative data included average annual research funding for CARDI. Additional website interrogations were undertaken to gather available funding data for the identified RFOs. The qualitative data encompassed the methods and processes by which RFOs made decisions regarding funding and levels of spend. The scientific and grey literature was also searched to obtain information regarding interventions, key risk factors and expert perspectives.

We identified 132 entities in 20 countries investing in cardiovascular research in Europe. Few of the RFOs surveyed were devoted exclusively to CARDI research. Most of these RFOs could only estimate the amount they had allocated to CARDI in relation to the other disease areas.

Qualitative data were obtained for 92% (n = 119) and quantitative data for 55% (n=75) of all identified RFOs. After RFOs with annual funding under €0.2 million were excluded, 63 RFOs were included in the quantitative analysis. Because the survey asked for an average funding amount within an average year for the period 2002 to 2013, it was not possible to report historic trends.

Table 10 Cardiovascular Research Funding by threshold

Threshold	*N*	*Total reported expenditures in 2013*
> € 500K	40	€ 764 million
€ 500K > & > € 200K	4	€ 1.55 million
< € 200K	11	€ 0.86 million

This table makes clear that the huge majority of expenditure on CARDI was from the major funders.

For the majority of RFOs in our sample (60%), the main funding source was governmental. The primary motivation for funding CARDI research was to support the research and policy agenda, with nearly 36% of RFOs selecting this as the main reason for funding. Publication of scientific articles was the clear leader as a metric for monitoring progress in meeting RFOs' expectations (see figure 1). This underscores the importance of bibliometric analysis in describing and measuring the impact of CVD research investment.

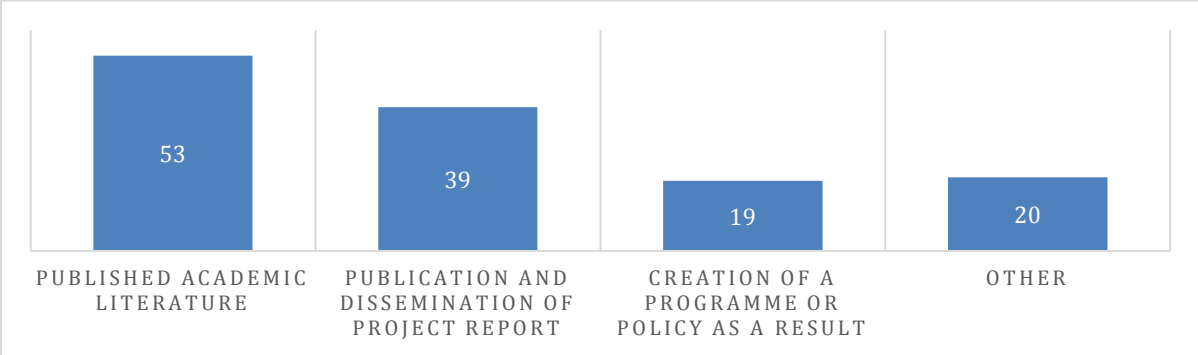

Figure 2: Measuring Impact of CVD Research Funding (n=64) *Note: RFOs could provide more than one response to this question.*

2.1.3 Interviews: people contacted and methodology

In order to contextualize the data and knowledge obtained through the project's mixed methods, we undertook semi-structured interviews with key CARDI and research experts in Germany and other countries in Europe. The aim was to solicit views and experiences of people involved in both the conduct and funding of research across the European area. In total, 10 interviews were conducted (4 face-to-face, 2 telephone and 3 Skype interviews). All were recorded and transcribed. Consent was gained from all interviewees and their anonymity has been respected.

2.1.4 Interviews: main findings

Interviews with key stakeholders in the CARDI research area have revealed valuable insights and confirmed the quantitative analysis that CARDI is underfunded in Europe. Although the disease burden is persistent in a majority of European countries, funding has falling short compared with cancer-related funding and does not reflect urgent needs as shown by the rising admission rates for heart failure to German hospitals and CARDI is the leading cause of mortality. However, European researchers have been able to carry out novel CARDI research in recent years, especially compared to US research a decade ago.

Interviews also shed light on the disincentives for researchers and other players in individual phases of CARDI innovation. Funding should therefore include a wide range starting from basic science to the support of innovations that are close to market approval. CARDI in particular can benefit from pharmaceutical innovations as well as medical devices. Interviewees wanted funding for longer periods of time, flexible in its spending formalities and that has immanent tools of networking and disseminating findings. A majority of stakeholders are involved in a mixture of funding by sub-national, national and supranational players as well as by the commercial sector. Interviewees also

pointed out that efficient project coordination is far more important than the volume of funding as a means to guarantee its effectiveness.

2.2 Downloading of papers and country outputs

2.2.1 Creation and calibration of the filter

This filter was developed in three phases: first with Dr Mary Philips at the Wellcome Trust, in London; second with Professor Gerry Bloomfield of Duke University Medical Center, Durham, NC 27705, USA; and third with the advice of Suzanne Edwards and Professor Reinhard Busse of the Technical University, Berlin.

The final version of the filter was created to reflect two rounds of marking of papers by Suzanne Edwards and was finalized on 25 April 2014; the **precision p = 0.947** and the **recall r = 0.900.** It consisted of two search statements based on specialist journals and four based on title words, but also a "no" statement of 12 title words whose presence on a paper would exclude it. Altogether there were 211,507 CARDI papers, of which only 1536 were in the SSCI and not the SCI.

2.2.2 Analysis of European and individual country outputs, and research level

Table 14 presents the overall outputs, year by year, for CARDI papers on both integer and fractional counts. The former when divided by the world total gives the European presence, which has declined slightly from 43% to 40%, somewhat less than for cancer research.

Table 11. Outputs of cardiovascular research papers (CARDI) in the Web of Science from 2002 to 2013 from EUR31 group of countries, integer and fractional counts.

Year	*CARDI*					*CARDI/BIOMED, %*	
	World	*EUR31 int*	*EUR31 frac*	*EUR %*	*Int'l, %*	*World*	*EUR31*
2002	32161	13964	12874	43.4	7.8	8.6	8.8
2003	33349	14310	13153	42.9	8.1	8.6	8.8
2004	34924	14847	13571	42.5	8.6	8.6	8.8
2005	36791	15482	14091	42.1	9.0	8.7	8.8
2006	38082	16275	14818	42.7	9.0	8.5	8.8
2007	40846	17345	15723	42.5	9.4	8.4	8.8
2008	43687	18072	16306	41.4	9.8	8.4	8.6
2009	45632	19072	17122	41.8	10.2	8.4	8.8
2010	47531	19664	17558	41.4	10.7	8.3	8.7
2011	49108	19978	17671	40.7	11.5	8.1	8.5
2012	51847	20759	18380	40.0	11.5	8.1	8.4
2013	54653	21739	19024	39.8	12.5	8.2	8.5

The difference between integer and fractional counts represents the non-European contribution, which has risen from 8% to 12% over the 12 years, similar to the figures for ONCOL. CARDI represents just over 8% of biomedical research output, both in the EUR31 countries and in the world overall; the percentage has declined slightly over the 12-year period of the study, whereas it increased for cancer research.

The next table shows the results for the individual countries.

Table 12. Outputs of 31 European countries in cardiovascular research (CARDI), 2002-13 (12 years) in both the SCI and SSCI. Integer and fractional counts, the percent foreign contribution and the annual growth rate. *The countries are ranked by their fractional count outputs. Codes are in Table 2.*

ISO	*Int cts*	*Frac cts*	*% int*	*AAPG*		*ISO*	*Int cts*	*Frac cts*	*% int*	*AAPG*
DE	43718	33708	22.9	1.4		HU	2542	1686	33.7	3.2
UK	41117	29770	27.6	1.8		IE	2320	1533	33.9	5.7
IT	30911	24289	21.4	5.3		PT	1975	1464	25.9	18.1
FR	23452	17866	23.8	1.0		HR	996	837	16.0	11.9
NL	21614	15562	28.0	5.3		SK	1124	782	30.4	6.5
ES	15382	12253	20.3	5.5		SI	964	746	22.6	4.6
SE	11294	7639	32.4	2.0		RO	909	622	31.6	27.8
CH	10454	6526	37.6	4.0		LT	558	442	20.8	15.5
PL	7854	6330	19.4	14.9		BG	414	286	30.8	5.4
GR	6519	5160	20.8	7.3		EE	303	169	44.4	0.4
BE	7803	4808	38.4	3.5		IS	318	162	49.1	7.2
DK	6355	4290	32.5	8.0		CY	195	86	55.9	20.3
AT	6175	4146	32.9	0.2		LU	163	76	53.4	19.6
FI	5322	3870	27.3	0.6		LV	132	69	48.0	4.2
NO	4603	3105	32.5	6.3		MT	34	25	27.2	9.5
CZ	2703	1983	26.6	8.7						

Several countries are expanding their CARDI output rapidly, for example Poland, Greece, Portugal and Iceland. For others the reverse is true, such as Germany, France, Austria, Ireland, Slovenia, Bulgaria and Estonia. The correlation of output with GDP is again highly positive, see Figure 7. There is relatively little scatter relative to the trend-line, but Romania publishes less than half what might be expected from its wealth. This is unfortunate, as it has a very high burden from cardiovascular disease, nearly 32% of all its DALYs, see Table 3. Greece and the Netherlands are relatively the most productive relative to their wealth.

The amount of international co-authorship varies slightly with each country's fractional count output, but the correlation is quite poor with $r^2 = 0.17$, and is really only different from zero because of the high degree of internationalism shown by Estonia and Iceland, two very small countries.

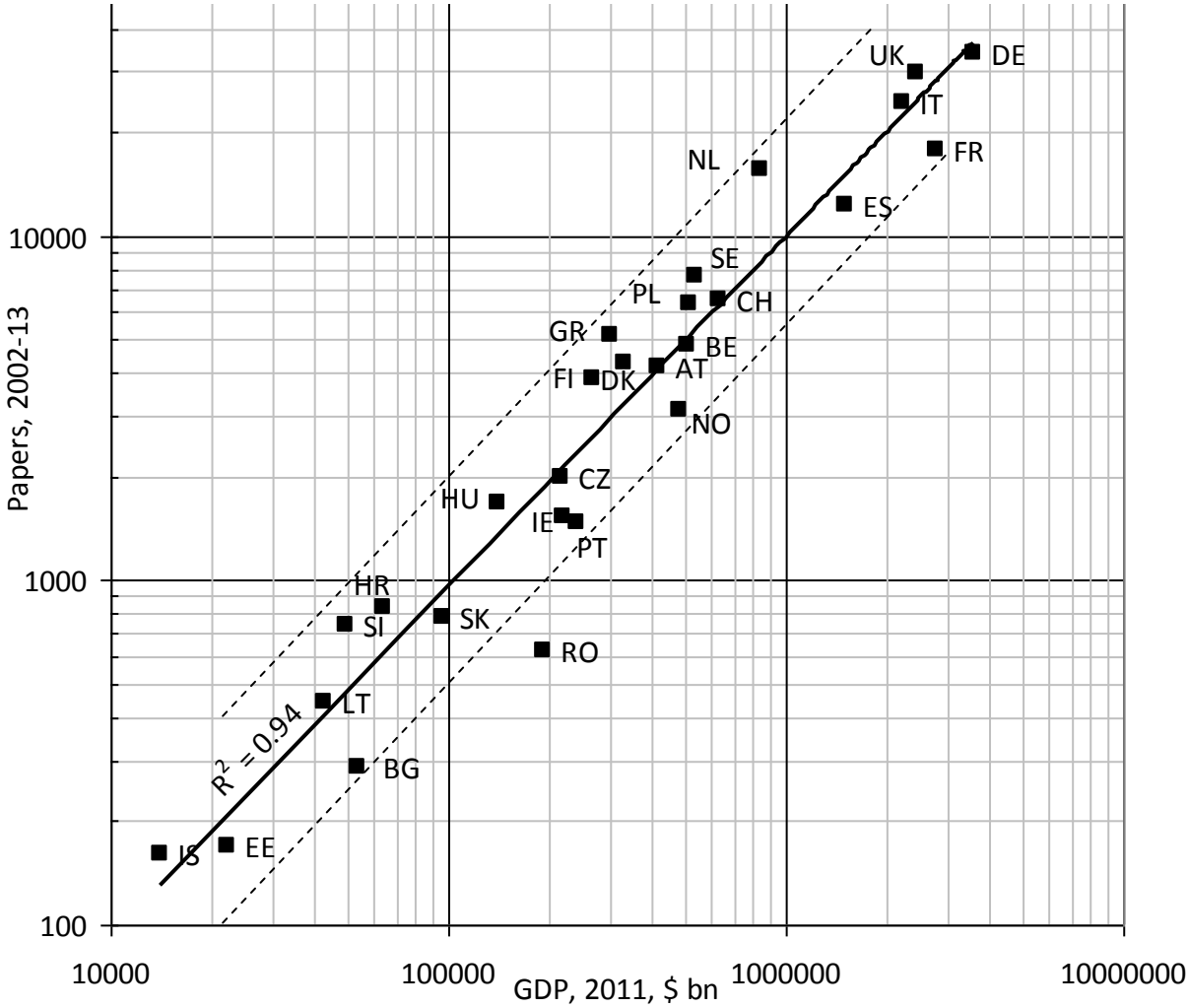

Figure 3. Plot of CARDI paper output, 2002-13, against GDP for 27 European countries. *Note: CY, LU, LV and MT omitted. Dashed lines show values x2 or x0.5 relative to power trend-line. For codes, see Table 2.*

Most countries' papers had a mean research level of close to 1.5, which is rather clinical, on a scale from clinical observation = 1.0 to basic research = 4.0. An exception was Slovakia, with mean RL of 2.46. Over the study period, the mean RL declined from 1.71 to 1.49 and so became more clinical.

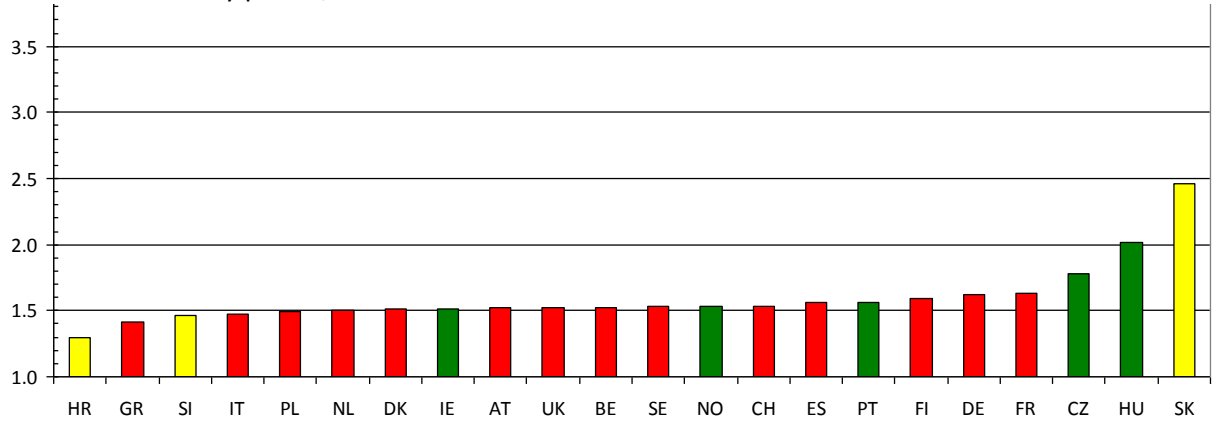

Figure 4. Chart showing the mean research level of CARDI papers from 22 European countries, 2002-13, with 100 or more classed papers. *Red bars: > 3000 classed papers (frac. cts); green bars: > 1000 papers; yellow bars: > 300 papers*

2.3 Analysis of citations and percentage of reviews

2.3.1 Citation counts and percent in top 5%

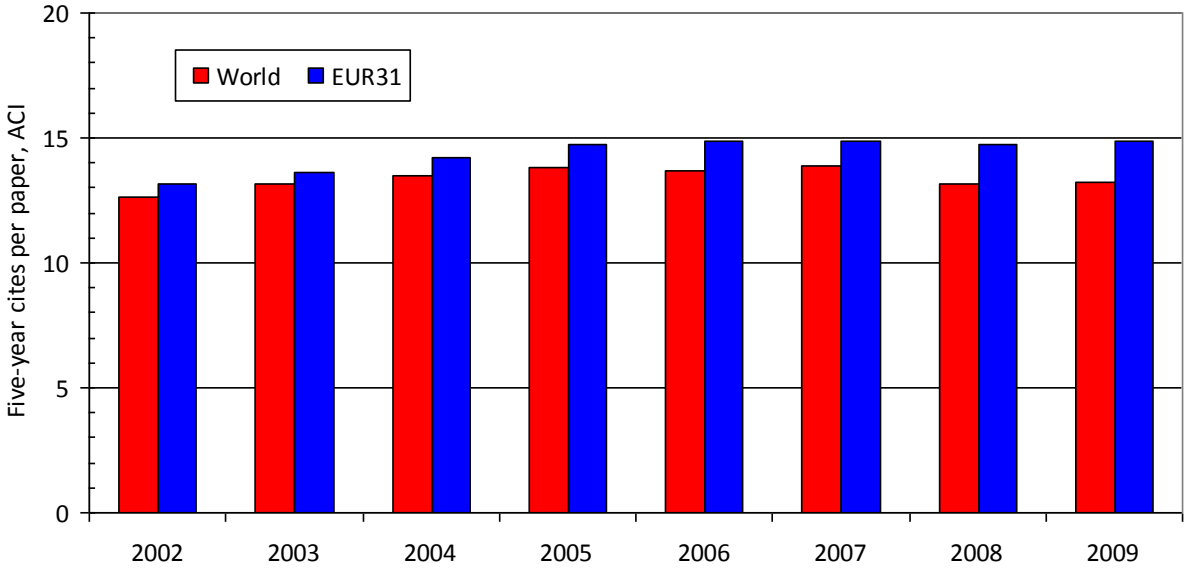

Figure 5. Chart showing the increase in mean citations per CARDI paper with publication year, 2002-09, for world and for EUR31 papers.

Figure 5 shows that European CARDI papers have always been more highly cited, on average, than the world mean, and that the difference is becoming larger. However, CARDI papers tend to receive fewer citations than ONCOL papers: in 2009 the world ACI values were 13.2 and 16.3, and the EUR31 values were 14.9 and 17.4. The next table shows the citation scores for the 26 individual countries with at least 100 citable papers and the percentage of papers with enough cites (48) to put them in the top 5% of EUR31 papers (actually, 5.12%).

Table 13. Citation performance of 26 EUR31 countries in CARDI in 2002-09 with at least 100 citable papers, ranked by the percent with 48 or more cites in the five years following publication (ACI) (Top 5%) rather than the mean value.

ISO	*ACI*	*Top 5%*	*%*		*ISO*	*ACI*	*Top 5%*	*%*		*ISO*	*ACI*	*Top 5%*	*%*
NL	16.9	581.1	6.20		FR	12.2	495.5	4.26		GR	9.3	50.2	1.61
UK	15.6	1070.4	5.60		IT	13.1	624.5	4.26		PL	6.3	42.3	1.33
DK	16.3	124.5	5.33		IE	12.9	37.3	3.98		CZ	7.7	12.6	1.14
CH	14.9	209.7	5.25		AT	12.0	99.8	3.62		SI	6.0	4.0	0.89
DE	13.5	1068.7	4.89		EE	9.4	3.1	2.91		SK	7.0	4.2	0.88
BE	13.9	140.3	4.65		ES	10.0	180.7	2.47		LT	3.7	1.2	0.48
SE	15.2	226.9	4.64		PT	9.4	10.8	2.09		BG	5.3	0.5	0.28
FI	14.6	116.8	4.43		HU	9.0	19.4	1.84		HR	3.7	1.0	0.23
NO	15.2	80.0	4.38		RO	7.5	3.8	1.77					

In comparison with ONCOL, Denmark has risen to third place and Switzerland has dropped from first to fourth place.

2.3.2 Percentage of reviews

The percentages of reviews are shown in Figure 6 for the 21 countries with at least 50 reviews during the 12 year study period. Overall, the percent of reviews for the EUR31 countries rose from 6.4% to 10.3%, with a mean value of 9.1%.

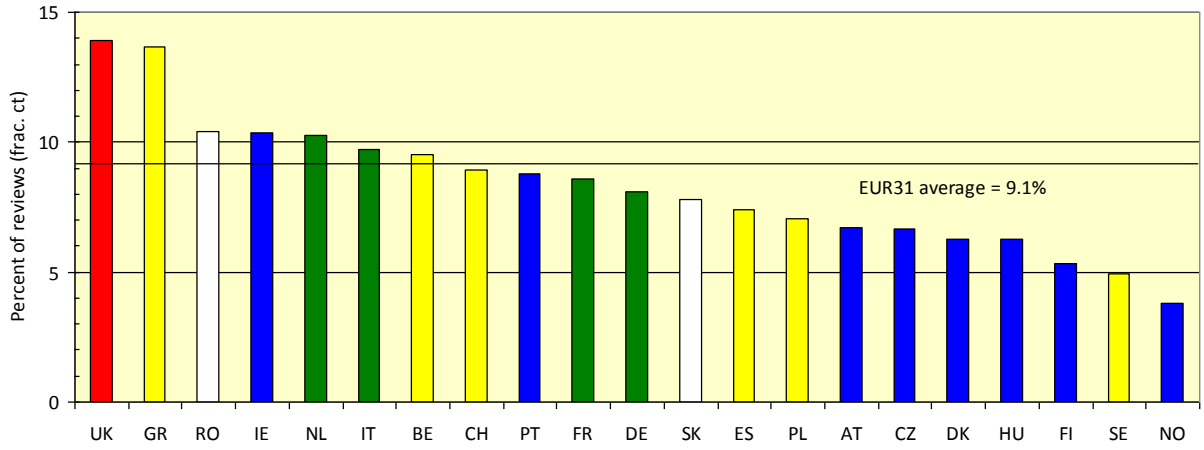

Figure 6 Chart showing the percentage of CARDI papers by 21 European countries with over 50 reviews that are classed as "reviews" in the WoS during 2002-13. *Red bars: > 3000 reviews (frac. cts); green bars: > 1000 reviews; yellow bars: > 300 reviews; blue bars: > 100 reviews; white bars: < 100 reviews.*

2.4 Analysis by disease subject area

2.4.1 Burden of disease in European countries

Whereas the European countries suffered similarly from the disease burden caused by cancer, with the highest being the Netherlands at 19% and Latvia the smallest at 13%, there is a far greater variation in the burden from cardiovascular disease. Bulgaria suffers 37% of all its DALYs from cardiovascular diseases but France only 13%. Figures 7 and 8 show the variation between countries and also the composition of the DALYs: for all countries, the biggest contributors are ischaemic heart disease (averaging 10.7%) and stroke (averaging 5.6%) in that order, except for Portugal.

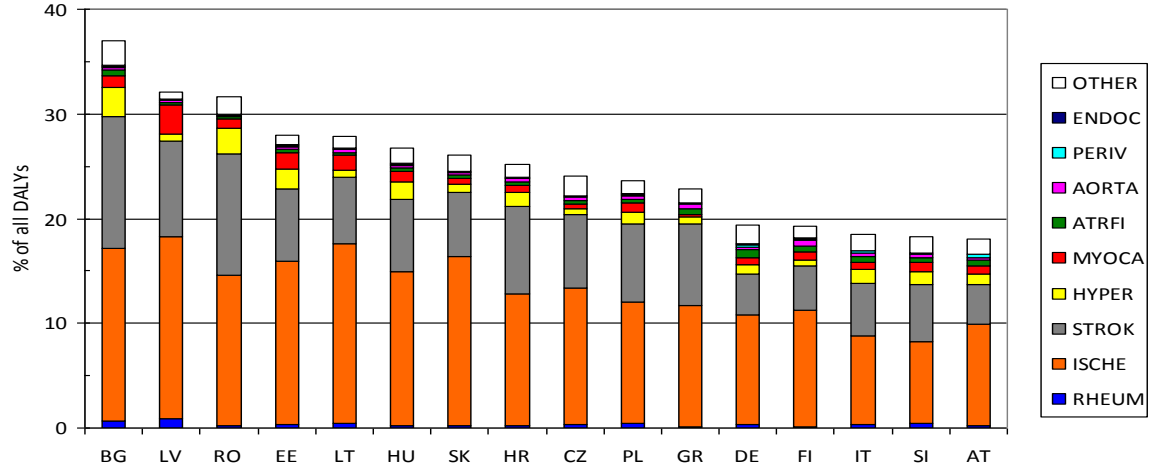

Figure 7. Composition of DALYs from cardiovascular disease for 16 European countries where it exceeds 18% of all DALYs. *RHEUM = Rheumatic heart disease; ISCHE = Ischemic heart disease; STROK = Cerebrovascular disease; HYPER = Hypertensive heart disease; MYOCA = Cardiomyopathy and myocarditis; ATRFI = Atrial fibrillation and flutter; AORTA = Aortic aneurysm; PERIV = Peripheral vascular disease; ENDOC = Endocarditis.*

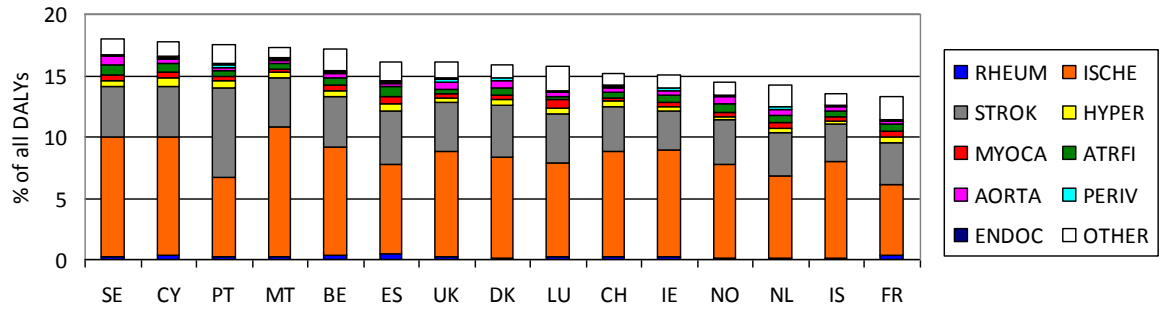

Figure 8. Composition of DALYs from cardiovascular disease for 15 European countries where it is less than 18% of all DALYs. *For key to subject codes, see caption to Figure 10, above.*

It is clear from the two figures that ischaemic heart disease and stroke are the dominant causes.

2.4.2 Research in different subject areas

We next investigated whether some European countries concentrated their CARDI research on particular subject areas. These were defined as a series of 13 sub-filters by Dr Uy Hoang and Dr Benjamin Bray of King's College London; the filters consisted of sets of title words and journal name strings. Table 17 shows the 13 subject areas selected, with their codes, the number of papers in the CARDI file, and the percentage that this represented. Some of the subject areas corresponded closely to the ones used to define the disease burden, but others did not, or covered more than one such area. However a large minority of the papers (43%) were not covered by any of the subject area definitions.

Table 14. List of 13 subject areas within CARDI research, as defined by Uy Hoang and Benjamin Bray, with the numbers and percentages of European CARDI papers in 2002-13.

Subject area	*Code*	*DALY code*	*Papers*	*%*
cerebrovascular disease (stroke)	CER	STROK	25836	12.2
arterial disease incl. atherosclerosis & aortic aneuryms	ART	AORTA	24507	11.6
hypertension	HYP	HYPER	16251	7.7
arrhythmias, incl. atrial fibrillation	ARR	ATRFI	15129	7.2
ischaemic heart disease, including acute MI	ISC	ISCHE	12963	6.1
hypercholesterolaemia	CHO		9960	4.7
heart failure	FAI		9454	4.5
heart valve disease incl. chronic rheumatic disease	VAL	ENDOC, RHEUM	8573	4.1
cardiomyopathies	CAR	MYOCA	7588	3.6
congenital defects	GEN		5693	2.7
venous thromboembolism	VTH		2573	1.2
auto-immune vascular disease, incl. vasculitis	VAS		1344	0.6
peripheral vascular disease	PVD	PERIV	1009	0.5
not classified	none		92446	43.7

There are two large subject areas, stroke and arterial disease. The former is a major cause of disease burden, but the latter is not. So it appears that ischaemic heart disease including myocardial infarction is under-researched relative to its burden within CARDI, and that arterial disease is over-researched.

We next determined the outputs of papers from each of the 31 European countries in ten of the 13 subject areas (the ones with the largest outputs), and Table 15 shows the ratio of observed output to that expected if each European country had the same proportional distribution of their CARDI research between subject areas for all of them.

Table 15. Fractional count outputs from 31 European countries in 10 leading cardiovascular subject areas, 2002-13.

Subfield:	*CER*	*ART*	*HYP*	*ARR*	*ISC*	*CHO*	*FAI*	*VAL*	*CAR*	*GEN*
Total	25835	24506	16251	15128	12963	9960	9454	8573	7588	5693
DE	4341	4107	1874	2564	1793	997	1306	1659	1636	877
UK	3971	3335	2037	1879	1389	1215	1301	1027	859	980
IT	2739	2924	2435	1776	1458	1015	1308	1135	1028	640
FR	1988	2113	1526	1197	941	741	668	973	565	406
NL	1924	1847	970	1275	1063	876	737	472	413	553
ES	1653	1154	1330	852	769	750	561	522	689	253
SE	1106	1054	481	454	707	437	424	232	152	170
CH	832	780	424	410	259	246	221	280	193	209
PL	634	715	473	592	576	350	301	312	311	184
GR	440	781	557	432	309	399	295	199	167	124
BE	464	557	328	333	216	170	185	283	178	191
DK	431	357	291	413	583	230	237	195	73.4	75.0
AT	456	616	179	251	165	209	153	133	189	108
FI	608	564	297	239	256	357	97.1	82.6	91.1	72.8
NO	355	292	205	153	330	184	205	100	65.0	102
CZ	307	205	227	172	106	160	79.6	66.0	93.4	31.8
HU	246	171	127	132	97.4	109	32.6	44.2	48.1	46.0
IE	185	199	145	59.0	54.8	59.9	54.5	37.7	29.9	56.2
PT	186	129	120	88.4	102	45.7	82.7	84.6	53.7	56.8
HR	188	56.3	73.9	44.0	59.2	47.4	8.1	31.0	15.3	18.4
SK	116	53.3	128	62.7	34.1	53.0	10.2	10.2	17.2	13.4
SI	68.8	82.8	34.1	58.5	75.4	49.5	35.8	37.0	23.0	23.7
RO	51.9	68.5	51.7	48.1	33.0	40.0	29.0	29.2	17.7	6.3
LT	45.2	23.7	16.3	29.4	74.2	4.3	15.6	16.2	7.4	10.8
BG	36.1	31.0	37.2	14.4	9.7	22.9	4.3	4.9	2.3	3.8
EE	23.6	18.2	25.9	0.4	12.2	7.0	1.9	0.0	0.7	9.0
IS	15.6	8.8	20.4	13.8	12.1	10.8	3.3	5.2	1.2	2.5
CY	22.9	7.5	2.7	1.6	4.1	4.6	3.8	2.0	2.5	3.2
LU	8.7	4.6	2.3	0.8	17.0	2.6	10.9	1.6	1.3	0.3
LV	7.8	8.3	5.2	2.3	5.3	1.7	0.8	2.5	2.0	1.5
MT	1.7	3.0	2.3	0.0	3.2	0.0	0.0	1.3	1.0	3.0

Germany had the highest overall output, but the UK had more output in hypertension (HYP), hypercholesterolaemia (CHO) and congenital defects (GEN), and Italy in the first two of these. Table 19 shows that German output in hypercholesterolaemia is in fact particularly low (relative to its

overall output in CARDI). As expected, the tinted cells are mainly in the lower half of the table, where outputs are quite small, typically less than 10 papers per year, so that a few papers can make a big difference in the ratio of observed to expected numbers. However a few results stand out – Danish papers in ischemia (ISC; 583 papers with 263 expected) and Austrian output in peripheral vascular disease (PVD; 58 papers with 20 expected).

Table 16. Ratio of observed to expected outputs of papers from 31 European countries in 10 leading subfields of CARDI research, 2002-13. *Values > 2.0 tinted bright green; values > 1.41 tinted pale green, values < 0.71 tinted pale yellow; values < 0.5 tinted pink.*

Subfield	*CER*	*ART*	*HYP*	*ARR*	*ISC*	*CHO*	*FAI*	*VAL*	*CAR*	*GEN*	*VTH*	*VAS*	*PVD*
DE	1.05	1.05	0.72	1.06	0.87	0.63	0.87	1.21	1.35	0.97	1.01	1.25	0.88
UK	1.09	0.97	0.89	0.88	0.76	0.87	0.98	0.85	0.80	1.22	0.69	0.76	1.23
IT	0.92	1.04	1.30	1.02	0.98	0.89	1.20	1.15	1.18	0.98	0.98	1.24	0.96
FR	0.91	1.02	1.11	0.94	0.86	0.88	0.84	1.34	0.88	0.84	1.40	1.58	0.86
NL	1.01	1.02	0.81	1.15	1.11	1.20	1.06	0.75	0.74	1.32	1.32	0.48	1.39
ES	1.11	0.81	1.41	0.97	1.02	1.30	1.02	1.05	1.57	0.77	1.10	0.99	1.07
SE	1.19	1.19	0.82	0.83	1.51	1.21	1.24	0.75	0.55	0.83	0.86	0.81	0.92
CH	1.04	1.03	0.85	0.88	0.65	0.80	0.76	1.06	0.83	1.19	1.65	1.21	1.40
PL	0.82	0.97	0.97	1.31	1.49	1.17	1.06	1.21	1.37	1.08	1.46	1.00	0.60
GR	0.70	1.31	1.41	1.17	0.98	1.64	1.28	0.95	0.90	0.89	0.67	1.29	1.07
BE	0.79	1.00	0.89	0.97	0.73	0.75	0.86	1.45	1.03	1.47	1.06	1.20	0.78
DK	0.82	0.72	0.88	1.34	2.22	1.14	1.24	1.12	0.48	0.65	0.94	0.34	1.21
AT	0.90	1.28	0.56	0.85	0.65	1.07	0.83	0.79	1.27	0.97	1.56	0.77	2.92
FI	1.29	1.26	1.00	0.86	1.08	1.96	0.56	0.53	0.66	0.70	0.34	0.84	0.51
NO	0.94	0.81	0.86	0.69	1.73	1.26	1.48	0.80	0.58	1.23	0.75	0.89	0.47
CZ	1.27	0.89	1.49	1.21	0.87	1.72	0.90	0.82	1.31	0.60	0.79	0.54	0.55
HU	1.19	0.87	0.98	1.10	0.94	1.38	0.43	0.65	0.79	1.01	0.28	1.06	0.33
IE	0.99	1.12	1.23	0.54	0.58	0.83	0.80	0.61	0.54	1.36	0.87	1.01	1.17
PT	1.04	0.76	1.07	0.84	1.13	0.66	1.26	1.43	1.02	1.44	1.39	1.99	0.25
HR	1.84	0.58	1.15	0.74	1.15	1.20	0.22	0.91	0.51	0.82	1.18	0.76	0.50
SK	1.22	0.59	2.13	1.12	0.71	1.44	0.29	0.32	0.61	0.63	0.34	0.52	0.00
SI	0.75	0.96	0.59	1.10	1.65	1.41	1.07	1.22	0.86	1.18	1.89	0.56	3.02
RO	0.68	0.95	1.08	1.08	0.87	1.37	1.04	1.16	0.79	0.37	1.17	0.61	1.69
LT	0.84	0.46	0.48	0.93	2.74	0.20	0.79	0.90	0.47	0.91	0.19	0.36	0.00
BG	1.03	0.93	1.69	0.70	0.55	1.70	0.33	0.42	0.22	0.49	0.57	0.29	0.00
EE	1.14	0.93	2.00	0.04	1.18	0.88	0.25	0.00	0.11	1.98	0.00	0.03	4.82
IS	0.79	0.47	1.64	1.19	1.22	1.42	0.45	0.80	0.21	0.57	1.42	0.03	0.00
CY	2.17	0.75	0.40	0.26	0.78	1.14	0.98	0.57	0.82	1.37	0.21	1.83	0.81
LU	0.94	0.52	0.39	0.15	3.66	0.73	3.22	0.51	0.47	0.15	0.00	0.50	0.46
LV	0.93	1.05	0.98	0.47	1.27	0.53	0.26	0.91	0.81	0.81	0.00	0.12	2.14
MT	0.56	1.06	1.18	0.00	2.11	0.00	0.00	1.25	1.13	4.55	0.00	0.00	0.00

3 Diabetes research (DIABE)

3.1 Survey of funding organisations (Università Bocconi, Milano)

3.1.1 Definition of Diabetes (DIABE)

The operational definition of diabetes we relied on throughout the whole Mapping NCDs project was the one published by the World Health Organization (WHO): "a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both". According to the WHO, diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin produced[9]. Insulin is a hormone that regulates blood sugar levels. As a consequence, an increased concentration of glucose in the blood is observed, also called hyperglycaemia. Prolonged raised blood sugar levels lead to serious damage to many of the body's tissues, which may result in organ and system failure. Long-term consequences of diabetes include diabetic retinopathy, diabetic neuropathy (e.g. diabetic foot), diabetic nephropathy and macrovascular disease, such as cardiomyopathy or heart failure.

For the purposes of data collection and analysis in this project, research investment in diabetes was defined as "research into causation, occurrence, prevention, diagnosis, pathophysiology and treatment of diabetes mellitus (DM) and its long-term consequences". Four main aetiological categories fall under the DM category: type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), 'other specific types' of DM and 'gestational DM' (WHO, 1999). Relevant codes for the diabetes categories under the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) are outlined under the five ICD-10 codes E10-14 (Table 177). Each of these codes has ten fourth-character subdivisions (i.e. from no complications to coma).

Table 17 Diabetes: International Disease Classifications (IDC)

ICD-10	*Disease*
E10	Type 1 diabetes mellitus
E11	Type 2 diabetes mellitus
E12	Malnutrition-related diabetes mellitus
E13	Other specified diabetes mellitus
E14	Unspecified diabetes mellitus

3.1.2 Data gathering: methods and results

Along with our partners, UB undertook a systematic search to identify the relevant public, non-profit and commercial research funding organizations (RFOs) at the regional, national, supranational and EU levels. A baseline threshold of €0.5 million to €1 million in overall investment was set in order to identify funding that could be expected to influence the content or direction of major research programs. Because of the limited number of RFOs specifically active in diabetes, the threshold for was subsequently lowered to €0.1 million.

A survey tool was used to collect quantitative and qualitative data from RFOs over a 10-month period from April 2014 to February 2015. The quantitative data included average annual research funding for diabetes. Additional website interrogations were undertaken to gather available funding data for the identified RFOs. The qualitative data encompassed the methods and processes by which RFOs made decisions regarding funding and levels of spend. The scientific and grey literature was also searched to obtain information regarding interventions, key risk factors and expert perspectives.

[9] WHO. Health Topics. Diabetes http://www.who.int/topics/diabetes_mellitus/en/

We identified 120 RFOs in 20 countries investing in diabetes research (DIABE) in Europe. The survey response rate was approximately 40% for all the RFOs surveyed. All identified RFOs, responding and non-responding, were followed up with website interrogations to gather any available data. No diabetes RFOs were identified for the following countries: Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Greece, Iceland, Lichtenstein, Malta, Romania, Sweden. Few of the RFOs surveyed were devoted exclusively to DIABE, with an overwhelming majority of 88% (n=106) investing in other NCD areas. Most of these RFOs could only estimate the amount they had allocated to diabetes in relation to the other disease areas.

From the 120 RFOs identified as investing in diabetes research in Europe, 92% (n = 111) provided a good amount of qualitative survey data and 68% (n=82) provided at least some quantitative data. Although the threshold set for the whole Mapping NCD project was higher (*i.e.* € 0.5 million), we adjusted the value for this disease in order to account for smaller research initiatives, often at the regional level, that can still play a significant role in this disease area (Table 2).

Table 18 DIABE RFOs Annual Funding Threshold reports for 2013

Threshold	N	Max	Min	Total reported
> € 500K	25	€ 25.000.000	€ 660.179	€ 154 million
> € 100K	14	€ 486.498	€ 112.000	€ 3.8 million
< € 100K	16	€ 95.500	€ 8.390	€ 0.68 million
Total with financial data reported for 2013	55*			

**Represents the number of RFOs that provided financial data for the year 2013*

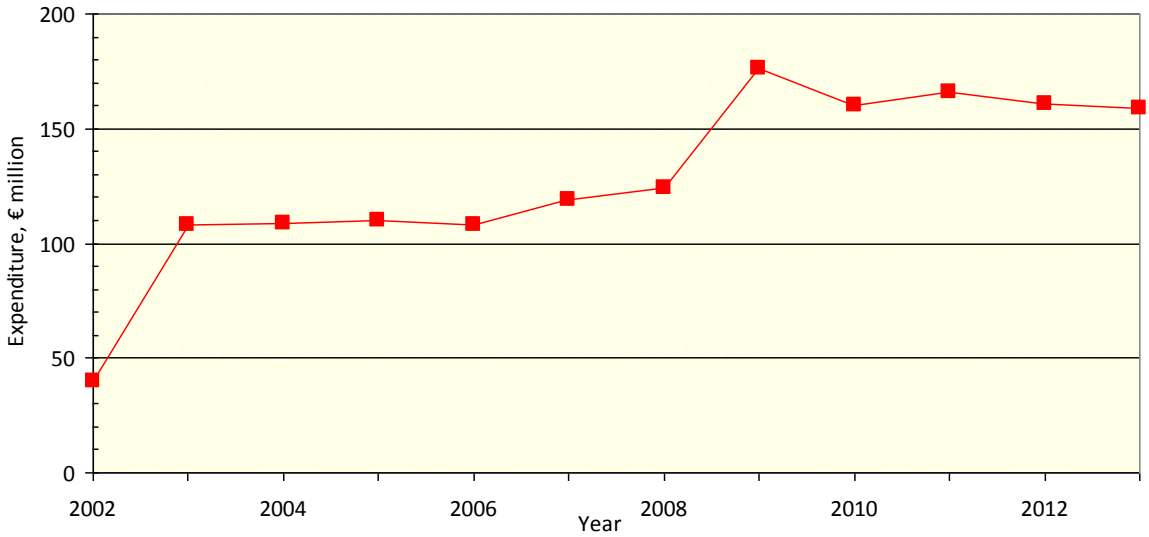

Figure 9 Historic levels of expenditure of diabetes RFOs (2002-13)

For the majority of RFOs in our sample (64%), the main funding source was governmental, and the primary funding mechanism (45% of RFOs) was calls for proposals. The primary motivation for funding diabetes research was to support the research and policy agenda, with 36% of RFOs selecting this as the main reason for funding. Publication of scientific articles was the clear leader as a metric for monitoring progress in meeting RFOs' expectations. This underscores the importance of bibliometric analysis in describing and measuring the impact of diabetes research investment.

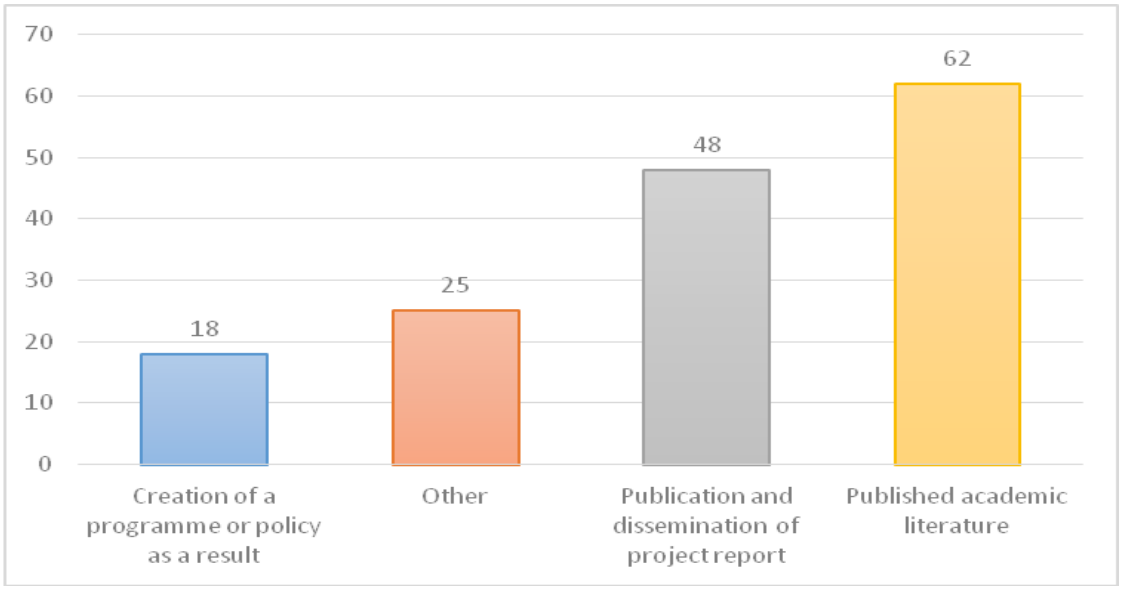

Figure 10 RFOs impact measurement (N=84)*
**The bar chart shows the type of measure that the RFOs use to capture the impact of their research. The RFOs were able answer with more than one option. The point number is 153. Results combine data from the Survey and online sources*

3.1.3 Interviews: people contacted and methodology

Accurate mapping of RFOs and their funding activities *via* surveys and bibliometrics can assist government in identifying the most fruitful approaches to investments in NCD research, however policy makers must also take account of the often strong visions and firm priorities of leaders in the field of diabetes research. In this regard, Mapping NCD involved the conduct of semi-structured interviews as a means for eliciting the preferences and opinions of key diabetes stakeholders.

As a research methodology, semi-structured interviews can answer the 'how' and 'why' of diabetes research funding, allowing interviewers to understand how funding activities are influenced by individuals and the contexts in which they are embedded (Baxter and Jack 2008, 556).

Under WP4, stakeholders were purposely selected to reflect a range of factors including: expertise in diabetes research, geographic location and expertise in awarding research funding or conducting research as a principal investigator (PI). A list of the interviewees is not provided because some of them asked for their anonymity to be preserved. The interview questions explored (1) current threads of research; (2) future research areas; (3) types of collaborations; (4) working with collaborators; (5) working with the commercial sector; (6) types of funding organizations; (7) working with funding organizations; (8) future strategies for funding NCD research, with slight differences for PIs or RFOs' representatives. All interviews were conducted *via* phone or Skype. They were recorded and typed verbatim, proof read and corrected, while notes and comments were collected and made into memos. Qualitative analysis was implemented using inductive thematic analysis (Silverman, 2004).

3.1.4 Interviews: main findings

The themes that emerged from the stakeholders' interviews were organized in six major areas: i) challenges in diabetes research, ii) duplication in diabetes research, iii) research gaps, iv) impact of research and priority-setting, v) partnerships and vi) the role of the EU. According to the informants, the challenges faced by researchers and RFOs in DIABE are financial (*i.e.* a perceived decrease in targeted funding over the last years, mainly associated with the economic crisis that hit Europe in 2008) and organizational. In particular, human resources management can be difficult in a very

competitive environment, with scarce resources available and long prospects of temporary or insecure employment for most of the workforce.

The majority of diabetes research funding was coming from commercial pharmaceutical companies according to our informants. They suggest that industry has implemented conservative management practices for the purpose of increasing the predictability of drug discovery and the sustainability of returns on capital investment in R&D. Duplication can only apparently be considered a challenge. Turning redundant funding in opportunities to tackle the most under-investigated areas or replicating results in settings where generalisability is critical were common discussion points.

In terms of research gaps or unmet need, informants pointed out the broad area of aetiology (*i.e*. pathogenesis of hypo/hyperglycaemic events, pathogenesis of chronic complications), prevention (*i.e*. genetic factors linked to T2DM) or treatment (i.e. adjunct therapies, artificial pancreas, beta-cell transplantation, cell line conversion). As regards infrastructures, bio-bank development was the most frequently recommended suggestion to speed up genetic-based studies. Social and health related quality-of-life aspects of people living with the disease were also highlighted for future investment. Finally, recommendations to the EU go from engagement in fruitful discussions with all stakeholders (*e.g*. inviting charities and private-non-profit funders to major discussion tables on research initiatives) and better scoping of experts in drafting programme calls.

3.2 Downloading of papers and country outputs

3.2.1 Creation and calibration of the filter

This filter was much smaller than the ones used so far, and consisted of a set of specialist diabetes journals and a set of title words, but with a "no" statement to exclude papers with *cancer* or *carcinoma* in their title unless they also contained *diabet**. The original filter was developed in consultation with Dr Moira Murphy and Dr Jayne East of the British Diabetic Association (now Diabetes UK). It was updated to take account of journals now covered in the WoS and to reflect the definition of the subject provided by our partner, Oriana Ciani of the Bocconi University, Milan, Italy. The filter had **precision, p = 0.900** and **recall, r = 0.976**. Papers were downloaded from both the SCI and the SSCI but there were hardly any solely in the latter database.

3.2.2 Analysis of European and individual country outputs

Table 19. Outputs of diabetes research papers (DIABE) in the Web of Science from 2002 to 2013 from EUR31 group of countries, integer and fractional counts.

Year	*DIABE*					*DIABE/BIOMED, %*	
	World	*EUR31 int*	*EUR31 frac*	*EUR %*	*Int'l, %*	*World*	*EUR31*
2002	5393	2368	2173	43.9	8.2	1.45	1.50
2003	5810	2535	2306	43.6	9.0	1.50	1.55
2004	6449	2736	2472	42.4	9.6	1.59	1.62
2005	6815	2908	2613	42.7	10.1	1.60	1.65
2006	7321	3033	2697	41.4	11.1	1.63	1.64
2007	8200	3288	2921	40.1	11.2	1.69	1.66
2008	9179	3664	3250	39.9	11.3	1.76	1.75
2009	9477	3677	3218	38.8	12.5	1.74	1.70
2010	10165	3805	3314	37.4	12.9	1.78	1.69
2011	10806	3963	3435	36.7	13.3	1.78	1.68
2012	11824	4169	3614	35.3	13.3	1.84	1.68
2013	12353	4404	3796	35.7	13.8	1.86	1.71

The world and European outputs, year by year, of diabetes research papers are given in the table above. Although diabetes is a small field, its presence within biomedical research has increased from 1.45% to 1.86%, and by slightly less in Europe. The European presence has declined from almost 44% of the world total to under 36% because of larger increases elsewhere.

The results for the individual European countries are shown in Table 20, below. The UK has much the highest output, contrasting with its position in ONCOL and CARDI. Figure 11 shows that it is publishing over 50% more than expected, but the three Scandinavian countries, Denmark, Sweden and Finland (but not Norway) are doing even better. On the other hand, Romania and Norway are publishing only half as much as their wealth would suggest.

Table 20. Outputs of 31 European countries in diabetes research (DIABE), 2002-13 (12 years) in both the SCI and SSCI. Integer and fractional counts, the percent foreign contribution and the annual growth rate. *The countries are ranked by their fractional count outputs. Codes are in Table 1.*

ISO	*Int ct*	*Frac ct*	*% int'l*	*AAPG*		*ISO*	*Int ct*	*Frac ct*	*% int'l*	*AAPG*
UK	9557	6657	30.3	2.9		HU	513	322	37.3	5.7
DE	6847	5119	25.2	4.9		IE	492	295	40.0	12.9
IT	5589	4262	23.7	4.9		PT	381	282	26.1	20.2
FR	4219	2999	28.9	1.2		HR	249	197	20.7	11.5
ES	3054	2379	22.1	8.2		RO	268	196	26.7	29.8
NL	3251	2229	31.4	6.8		SK	257	178	30.9	1.8
SE	3400	2196	35.4	1.6		SI	186	120	35.4	10.9
DK	3127	2017	35.5	3.9		BG	97	66	32.1	4.7
FI	1782	1198	32.8	1.4		EE	71	39	44.5	15.9
PL	1288	1049	18.5	15.7		LT	65	36	44.5	15.2
CH	1504	803	46.6	5.4		IS	66	36	46.2	6.1
GR	992	779	21.4	12.7		LV	56	25	55.3	11.9
BE	1251	760	39.2	4.4		MT	30	25	17.2	7.9
AT	1156	708	38.8	4.4		LU	57	12	78.7	28.2
NO	833	490	41.2	11.0		CY	22	10	56.1	11.8
CZ	485	326	32.9	3.7						

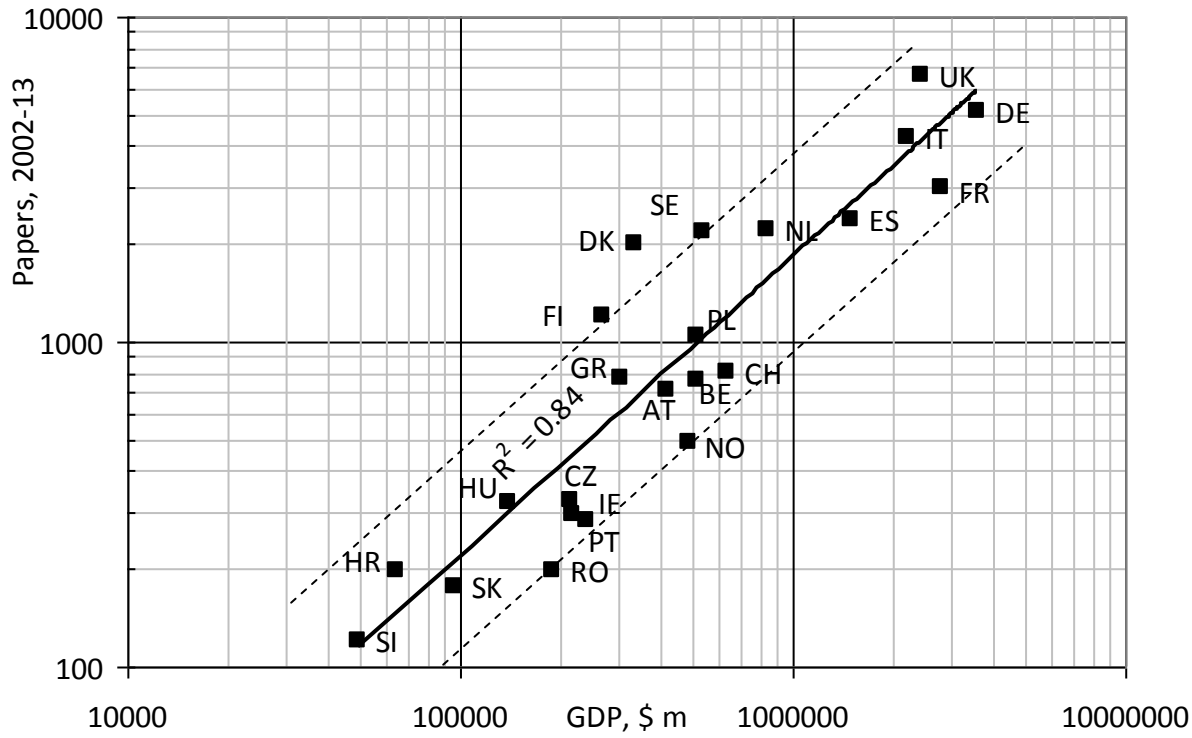

Figure 11. Plot of DIABE paper output, 2002-13, against GDP for 23 European countries. *Note: BG, CY, EE, IS, LT, LU, LV and MT omitted. Dashed lines show values x 2 or x 0.5 relative to power trend-line. For codes, see Table 1.*

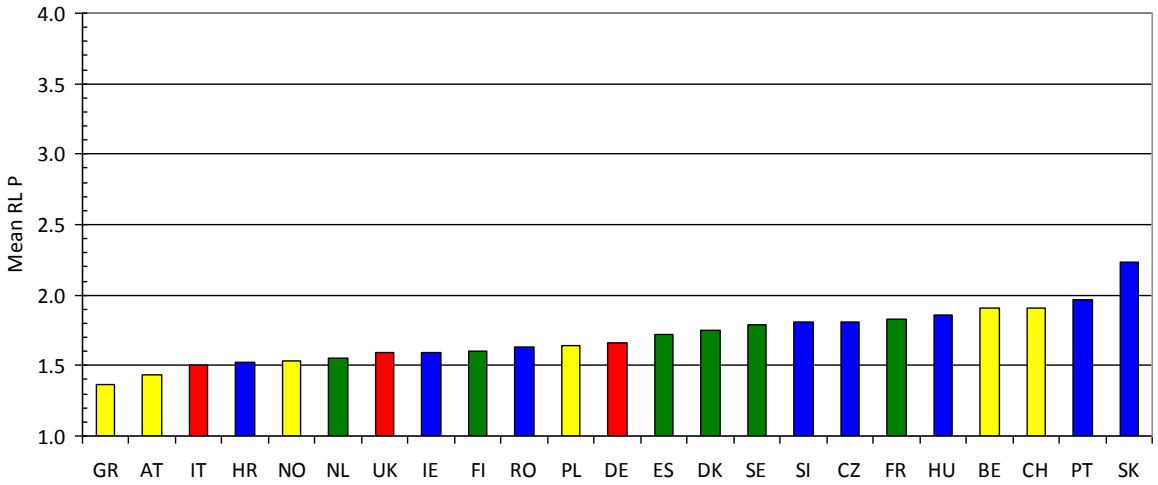

Figure 12. Chart showing the mean research level of DIABE papers from 23 European countries, 2002-13, with 100 or more classed papers. *Red bars: > 3000 classed papers (frac. cts)*; *green bars: > 1000 papers; yellow bars: > 300 papers; blue bars: > 100 papers*

The mean RL of the papers is 1.70, somewhat higher (more basic) than the result for CARDI, but more clinical than the mean for ONCOL. Once again, Slovakia's papers are the most basic. Over the 12-year study period, the average European research level declined from 1.87 to 1.55, with the work becoming more clinical.

3.3 Analysis of citations, and percentage of reviews

3.3.1 Five-year citation counts

Figure 13 shows how the European papers were behind the world average in citations in 2002, but received more cites on average than the world mean after 2005.

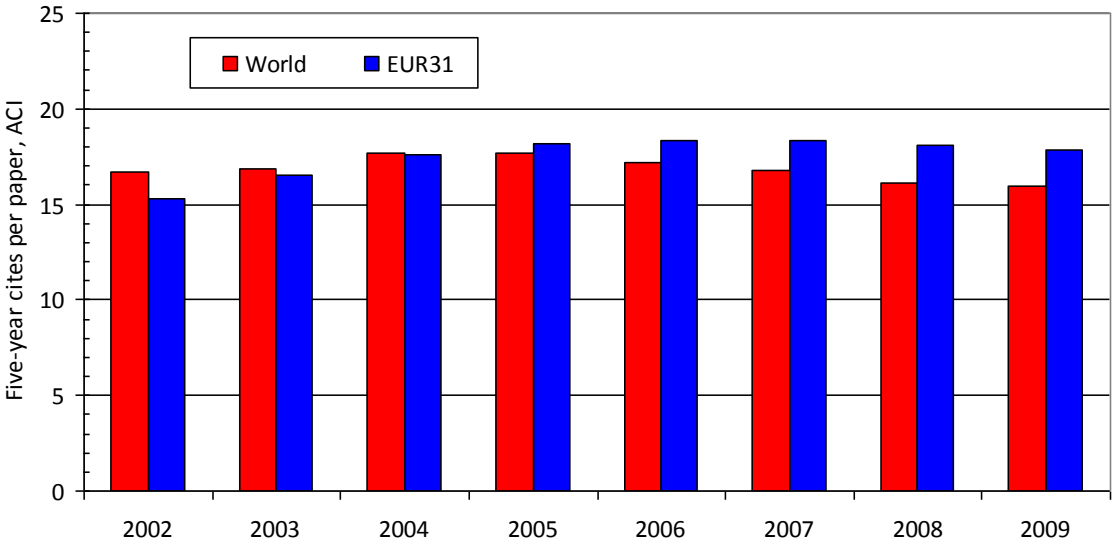

Figure 13. Chart showing the increase in mean citations per DIABE paper with publication year, 2002-09, for world and for EUR31 papers.

The citation performance of the individual countries is shown in Table 21 for countries with at least 100 citable papers. To be in the top 5% (actually 5.15%) a paper requires 58 cites – higher than for ONCOL or CARDI as the citation norms for DIABE are higher.

Table 21. Citation performance of 20 EUR31 countries in DIABE in 2002-09 with at least 100 citable papers, ranked by the percent with 58 or more cites in the five years following publication (ACI) (Top 5%) rather than the mean value.

ISO	*ACI*	*Top 5%*	*%*		*ISO*	*ACI*	*Top 5%*	*%*		*ISO*	*ACI*	*Top 5%*	*%*
FI	22.1	60.8	7.97		AT	14.5	21.5	5.00		IE	12.2	3.4	2.32
CH	19.3	32.6	6.70		IT	16.0	106.5	4.19		PT	12.1	2.3	2.13
DK	21.2	69.7	5.75		SE	17.9	58.8	4.05		HU	10.0	3.5	1.79
UK	19.6	234.5	5.56		DE	13.4	118.7	3.74		GR	10.5	3.8	0.88
BE	18.5	24.1	5.34		NO	16.2	8.5	3.19		PL	7.7	3.0	0.60
NL	18.1	66.3	5.15		ES	11.9	33.9	2.58		SK	7.0	0.5	0.41
FR	15.3	99.7	5.03		CZ	10.0	5.1	2.46					

3.3.2 The percentage of reviews

The percentages of reviews are shown below. As with CARDI, the UK and Greece perform well on this indicator of esteem, but Denmark, Sweden and Finland do less well than the EUR31 average.

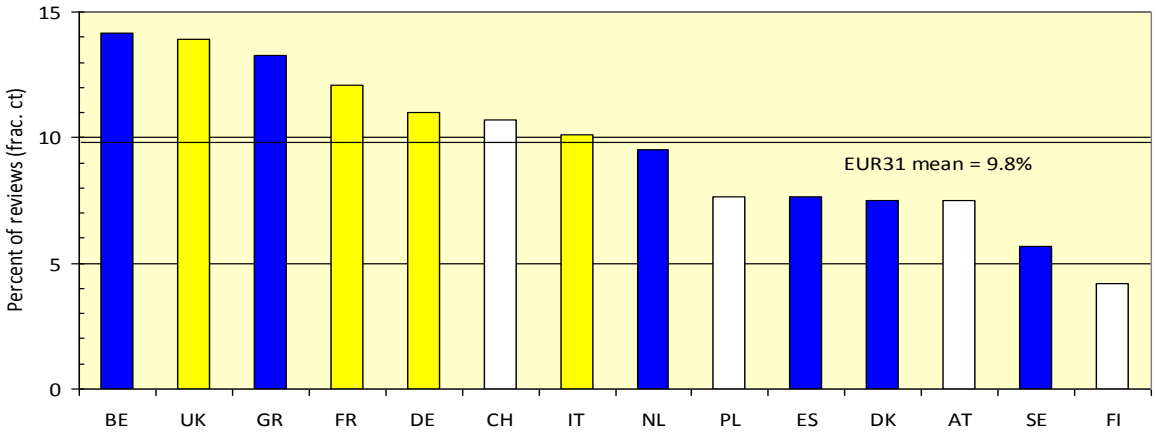

Figure 14. Chart showing the percentage of DIABE papers by 14 European countries with over 50 reviews that are classed as "reviews" in the WoS during 2002-13. *Yellow bars: > 300 reviews; blue bars: > 100 reviews; white bars: < 100 reviews.*

3.4 The burden of disease from diabetes

3.4.1 Additional data on diabetes incidence

The percentages of all DALYs for each of the 31 European countries are listed in Table 3 in section 1.5. There is a big variation, from 4.6% for Cyprus to 1.2% for the UK. It is curious that despite having the lowest percentage disease burden from diabetes, the UK nevertheless publishes substantially more than would be expected and easily the most papers of any of the EUR31 countries. The Mediterranean and southern European countries appear to suffer from this disease relatively the most, with the notable exception of Greece.

We were initially sceptical that the above-mentioned table, with the UK suffering the least relative burden from diabetes, could represent the amount of diabetes actually occurring in the populations, so we compared these data with figures on the prevalence of diabetes in countries with large populations provided by Shaw et al., 2009. The figure below shows their data (percentages of the population with the disease) as abscissa and the DALY burden (percent) as ordinate.

While the correlation between the two sets of data is positive but not very strong, it is clear that on both measures the UK is suffering less from diabetes than any of the other European countries considered in the study by Shaw, Sicree and Zimmel. However, its DALY percentage is lower than the trend-line would suggest, and this could possibly be the result of a large investment in research. This cannot be the whole story because Romania also has a lower DALY percentage than expected, but it also does less research than expected.

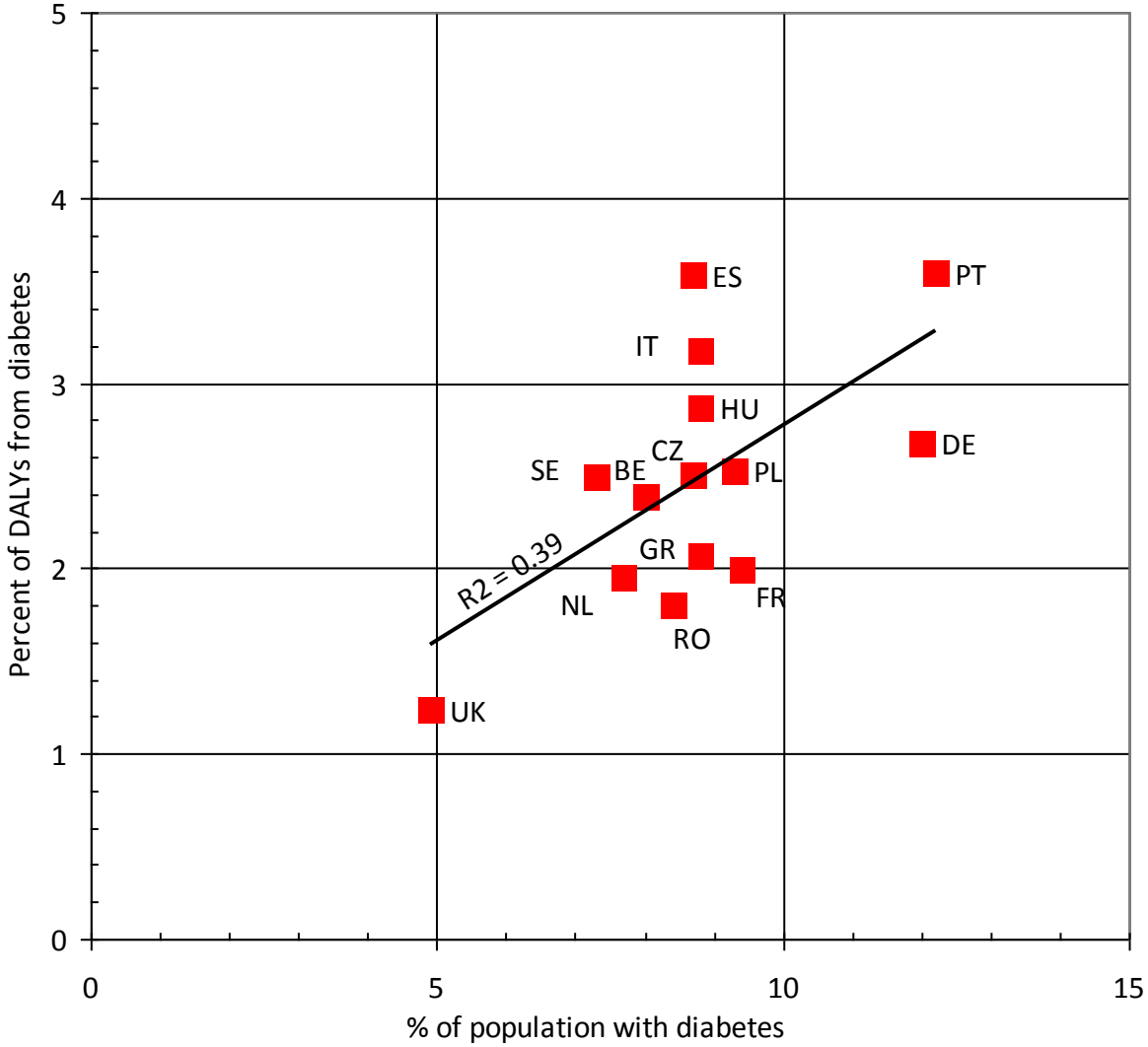

Figure 15. Scatter plot showing disease burden (DALYs) in 2010 for 14 European countries as a function of the estimated incidence of the disease in the same year (% of population affected).

3.5 Research in different subject areas of diabetes

3.5.1 Definition of 14 subject areas and overall outputs

We sought assistance from Diabetes UK, the leading specialist medical research charity in this subject area, which was kindly provided by Dr Richard Elliott, their Director of Communications, and his colleague Dr Anna Morris. They defined 14 subject areas, type 1 and type 2; four other types; and eight "complications" caused by diabetes. Each sub-filter consisted of title words (sometimes abbreviated to strings of characters) and of journal name strings, and they are listed in Table 21, with their outputs and percentages of the DIABE total. Unlike in CARDI, these subject areas sum to 87% of the total of DIABE papers, though there is considerable overlap between subject areas and 12,436 papers (31% of the total) were not in one of these 14.

Table 21. List of diabetes research subject areas, with codes used for the tables (in the first report) and figures that follow. N = number of DIABE papers in 2002-13.

Code	*Subject area*	*N*	*%*		*Code*	*Complications*	*N*	*%*
ONE	Type 1	5543	13.7		FEE	Feet	918	2.3
TWO	Type 2	13310	32.8		CAR	Cardiovascular	5720	14.1
GES	Gestational diabetes	828	2.0		NEP	Nephropathy	2740	6.8
NEO	Neonatal diabetes	206	0.5		NEU	Neuropathy	1573	3.9
MOD	Maturity Onset Diabetes of the Young	346	0.9		LIV	Liver	1017	2.5
ADA	Latent Autoimmune Diabetes of Adults	76	0.2		HYP	Hypoglycaemia	638	1.6
RET	Complications: Retinopathy	1646	4.1		PSY	Psychosocial	730	1.8

3.5.2 Outputs of EUR31 countries and relative commitments to different subjects

The different European countries varied in the amount of research effort that they put into each of these 14 areas. Table 22 shows the numbers of papers by the 31 countries in the 10 largest areas (with at least 2% of the DIABE papers based on the European fractional total of 35806 papers). In all countries except for Estonia, type I diabetes has less research than type II. However we do not have access to data on the relative burden from different forms of diabetes and its varied *sequelae*, so it is not possible to say whether this finding parallels the disease burden. The major complication from diabetes, at least so far as the need for research is concerned, is cardiovascular, and many of the words used for this sub-filter were taken from the words used to define the CARDI sub-filters. Following on are the deleterious effects on the kidneys, eyes, nerves, liver and feet.

The ratios between observed and expected numbers of paper for each European country and each diabetes subject area are calculated in Table 23. This table shows that there is a tendency for the northern European countries, especially Estonia and Finland, to devote relatively more effort to Type 1 diabetes, and for the southern European countries to do the reverse. The Scandinavian countries on the whole (Denmark being an exception) under-research the complications of diabetes. Its effects on the liver are relatively under-researched by several other countries, notably the UK and Ireland, the Czech Republic and several other east European countries except for Latvia and Romania.

Table 22. Fractional count outputs from 31 European countries in 10 leading diabetes subject areas, 2002-13. *Codes for countries in Table 1; for subject areas in Table 21.*

	TWO	*CAR*	*ONE*	*KID*	*RET*	*NEU*	*LIV*	*FEE*	*GES*	*PSY*
UK	1949	784	862	330	363	256	92.8	215	95.7	180
DE	1439	669	582	331	181	217	102	158	70.3	101
IT	1566	862	596	337	135	172	203	80.5	84.9	47.3
FR	912	367	340	160	104	80.3	101	72.4	66.5	38.2
ES	894	381	247	219	133	69.3	93.7	42.5	66.6	25.8
NL	926	392	269	130	49.2	104	48.1	64.3	24.3	91.2
SE	721	277	399	122	42.4	77.2	26.4	37.2	48.2	32.7
DK	762	224	334	190	100	41.0	27.9	17.9	33.9	13.6
FI	441	200	352	84.4	37.7	24.7	36.8	6.3	39.6	17.0
PL	289	147	185	104	49.5	48.8	20.0	19.3	58.7	15.1
CH	242	90.2	77.6	36.8	21.3	24.3	27.7	13.6	6.7	8.7
GR	315	147	80.6	52.3	27.3	51.5	20.9	25.6	29.8	12.8
BE	198	80.6	151	35.9	16.2	29.4	19.2	20.0	10.4	15.4
AT	228	107	90.8	58.7	44.6	22.2	21.7	16.5	52.2	13.8
NO	147	82.3	95.7	31.7	13.6	15.5	9.6	8.2	11.4	13.2
CZ	113	43.5	75.6	28.6	12.3	27.7	3.2	5.7	2.8	3.0
HU	88.0	52.0	52.8	20.4	13.3	29.5	5.8	1.0	15.4	2.4
IE	92.1	33.0	36.6	25.1	11.6	6.1	4.0	5.3	20.0	6.6
PT	78.2	40.2	19.3	14.4	23.6	30.9	13.0	6.4	7.6	7.1
HR	60.1	19.6	49.1	12.3	24.5	15.9	4.7	4.8	2.7	10.9
RO	68.7	13.9	30.1	18.8	3.3	8.3	8.0	3.0	0.5	3.4
SK	34.3	40.8	20.9	12.2	6.9	16.7	3.8	4.0	0.4	0.5
SI	57.8	17.6	15.5	8.5	23.8	6.2	0.3	1.5	1.5	2.0
BG	21.1	4.7	6.7	1.5	1.5	7.0	0.0	0.3	2.0	1.0
EE	8.7	5.9	18.9	0.2	0.1	1.0	0.0	0.0	0.7	1.3
LT	11.3	6.0	7.9	0.0	2.5	1.0	0.0	0.0	2.0	0.0
IS	14.6	4.2	5.6	1.2	8.7	0.3	0.0	1.0	0.0	0.0
LV	11.0	3.6	4.2	0.0	0.4	0.9	1.0	0.0	0.0	0.0
MT	6.3	3.3	4.2	3.3	3.0	1.3	0.0	0.5	4.6	0.0
LU	1.8	0.9	1.8	0.2	0.0	0.1	0.0	0.0	0.0	0.0
CY	4.0	0.6	1.6	0.0	0.0	0.2	0.0	0.0	0.0	0.0
EUR31	13310	5720	5543	2740	1646	1573	1017	918	828	730

Table 23. Ratio of observed to expected outputs of papers from 31 European countries in 10 leading subfields of DIABE research, 2002-13. *Values > 2.0 tinted bright green; values > 1.41 tinted pale green, values < 0.71 tinted pale yellow; values < 0.5 tinted pink. Codes for countries in Table 1; for subject areas in Table 21.*

	TWO	*CAR*	*ONE*	*KID*	*RET*	*NEU*	*LIV*	*FEE*	*GES*	*PSY*
UK	0.79	0.74	0.84	0.65	1.19	0.87	0.49	1.26	0.62	1.33
DE	0.76	0.82	0.74	0.84	0.77	0.97	0.70	1.21	0.59	0.97
IT	0.99	1.27	0.90	1.03	0.69	0.92	1.68	0.74	0.86	0.54
FR	0.82	0.77	0.73	0.70	0.75	0.61	1.18	0.94	0.96	0.62
ES	1.01	1.00	0.67	1.20	1.22	0.66	1.39	0.70	1.21	0.53
NL	1.12	1.10	0.78	0.76	0.48	1.07	0.76	1.13	0.47	2.01
SE	0.88	0.79	1.17	0.72	0.42	0.80	0.42	0.66	0.95	0.73
DK	1.02	0.69	1.07	1.23	1.07	0.46	0.49	0.35	0.73	0.33
FI	0.99	1.04	1.90	0.92	0.68	0.47	1.08	0.21	1.43	0.70
PL	0.74	0.88	1.14	1.29	1.03	1.06	0.67	0.72	2.42	0.70
CH	0.81	0.70	0.62	0.60	0.58	0.69	1.21	0.66	0.36	0.53
GR	1.09	1.18	0.67	0.88	0.76	1.50	0.95	1.28	1.65	0.80
BE	0.70	0.66	1.28	0.62	0.46	0.88	0.89	1.03	0.59	0.99
AT	0.87	0.95	0.83	1.08	1.37	0.71	1.08	0.91	3.19	0.95
NO	0.81	1.05	1.26	0.85	0.61	0.72	0.69	0.66	1.01	1.33
CZ	0.94	0.84	1.50	1.15	0.82	1.94	0.35	0.68	0.37	0.45
HU	0.74	1.01	1.06	0.83	0.90	2.09	0.64	0.12	2.07	0.37
IE	0.84	0.70	0.80	1.11	0.85	0.47	0.47	0.71	2.94	1.09
PT	0.75	0.89	0.44	0.67	1.82	2.50	1.62	0.88	1.16	1.24
HR	0.82	0.62	1.61	0.81	2.70	1.84	0.83	0.94	0.60	2.71
RO	0.95	0.45	0.99	1.26	0.37	0.97	1.44	0.60	0.11	0.86
SK	0.52	1.44	0.76	0.90	0.84	2.15	0.75	0.88	0.10	0.14
SI	1.30	0.92	0.83	0.93	4.30	1.17	0.10	0.50	0.54	0.82
BG	0.86	0.44	0.65	0.29	0.50	2.43	0.00	0.15	1.31	0.75
EE	0.59	0.93	3.10	0.07	0.04	0.58	0.00	0.00	0.73	1.56
LT	0.84	1.03	1.42	0.00	1.49	0.63	0.00	0.00	2.40	0.00
IS	1.11	0.74	1.02	0.43	5.33	0.16	0.00	1.10	0.00	0.05
LV	1.18	0.91	1.08	0.00	0.35	0.85	1.41	0.00	0.00	0.00
MT	0.68	0.82	1.09	1.71	2.63	1.15	0.00	0.78	7.92	0.00
LU	0.39	0.48	0.95	0.18	0.00	0.23	0.00	0.00	0.00	0.00
CY	1.11	0.39	1.07	0.00	0.00	0.47	0.00	0.00	0.00	0.00

3.6 The funding of diabetes research

3.6.1 Funding sources in a country

The main analysis is of the funding of research in each of the 31 countries in the European area, as this is the way that the questionnaires to funding bodies has been administered. It is logical, because many funding sources support research in different subject areas, and indeed their reporting systems may not provide for a breakdown by subject area in the same way as we have used in this project. We have assumed that national funding sources (both public and private-non-profit) only support researchers in their own country; that European Union and other European non-profit sources support research in the 31 European countries; and that industrial/commercial companies may support research in any country.

A macro has been developed that, for each country, counts the contributions of funding bodies acknowledged in the "composite" column in four different groups: national public sector, national private-non-profit, industrial/commercial, and the European Union. There may also be a small fifth group, obtained by difference, consisting of private-non-profit international groups, such as European or world professional associations, and international sources such as the World Health Organization (WHO). And there will also be many papers without any formal funding acknowledgement, either explicit or implicit.

This calculation will be made on a doubly fractionated count basis. This means that a funding body's contribution to a country's research in an NCD will take account first of that country's fractional presence among the addresses, and secondly of any other funding that the country may have received from national sources, the EU or from industry. An example will make this clearer. Suppose we have a paper with one Austrian, one French and one US address, and the list of funders contains one Austrian government body, one French charity, the US National Institutes of Health and a pharma company (e.g., Novartis SA). Then we assume first that each of these four funders contributed equally to the research, and second that the Austrian researchers were supported only by their government funder and by Novartis, and not by the other two funders. So the contributions of the Austrian funder and Novartis to the Austrian research tally would each be 0.33 x 0.5 = 0.17 of a paper.

The national public sector group has three sub-groups: government department (GD), government agency (GA) and local authority (LA). In some countries it will be worth-while to determine how many papers are funded regionally. The second group, with five sub-sectors or sub-groups, has five components: collecting charity (CH), endowed foundation (FO), hospital trustees (HT), mixed (*i.e.*, academic; MI) and other non-profit (NP). We know that the private-non-profit (PNP) sector expenditure on cancer research is similar to that by government (or it was in 2002-03; Eckhouse *et al*, 2005), and that in some countries charitable expenditure exceeded that by the public sector. However it is likely that for other NCDs, the proportion by PNP sources will be much lower as they do not attract donations from the public on the same scale. For each country, a breakdown of the five types of PNP funding will be useful as it will show which the dominant sources are, and information can be sought on how each of them is faring.

The third major source is commercial or industrial funding. Here we make no distinction between countries because the pharma industry has so many subsidiaries, and there is a tendency for some companies to register in a country other than their own for tax reasons. Although it is expected that the major sources of commercial support will be pharma companies, there are an increasing number of small companies that provide analytical and consulting services to the healthcare industry and many of them are contributing to the costs of research. There are also a growing number of medical device companies, some of which provide equipment for use directly with the patients (*e.g.*, stents, imaging contrast agents) and some equipment when the patient is absent (*e.g.*, for the analysis of samples).

The fourth source is international, and in Europe, the European Commission is expected to play the major role. It will be useful to see how much it contributes to research on the five NCDs in the different Member States. Other international contributors are likely to be the World Health Organization (WHO), other UN bodies, and a number of European professional associations.

3.6.2 Basic parameters

DIABE was the second of the five NCDs to be analysed in accordance with the methodology described above. The file consisted of 40,547 papers, of which 20 015 were published during the last five years, 2009-13. Of these, 1161 or 5.8% had a conflict of interest statement, and needed to be examined individually in order to check the funding bodies listed in the FU column of the spreadsheet, and redact them if necessary. Some papers originally crediting funding bodies were found not to be funded explicitly, and others had the number sharply reduced; a very few should have had additional funders credited. After the redaction, 13,718 papers had one or more funders (69%) and the remaining 31% had none. Figure 16 shows the percentages of papers with given numbers of funders or more.

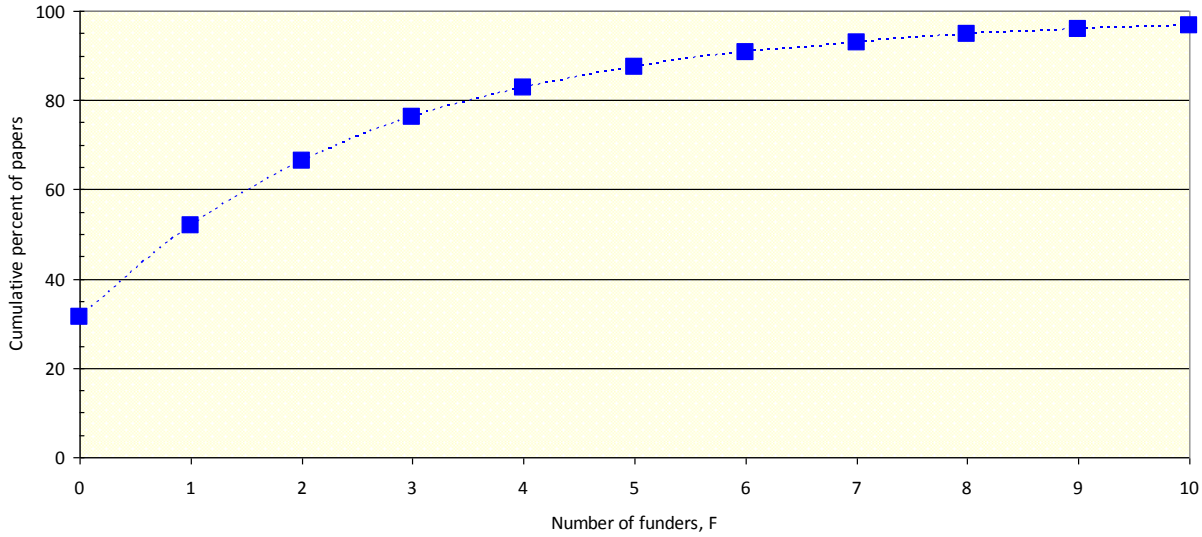

Figure 16. Cumulative percentage of numbers of DIABE papers with different numbers of funders, 2009-13.

3.6.3 Overall analysis and breakdown by country

The first analysis was in terms of the mean number of funders per country, and there was a big variation, with the Scandinavian countries having the most and (of the major countries) Poland and Greece the least, see Figure 17 overleaf.

The number of funders has been calculated on a fractional count basis. The analysis by main sector, using fractional counts of sectors for each paper and fractional country counts, is shown in Figure 18. This chart also shows that the Scandinavian countries have many private-non-profit sources, especially endowed foundations, and rather few of their DIABE papers do not have a funding acknowledgement, explicit or implicit. [Iceland is not shown as it has too few papers, but it would rank third in this chart, between Sweden and Norway.] The Czech Republic, France and Spain are notable for the high percentage of their papers explicitly funded by the public sector. This percentage is very low in Greece and Austria, where many papers are "unfunded", *i.e.* supported by higher education funds or the national health service.

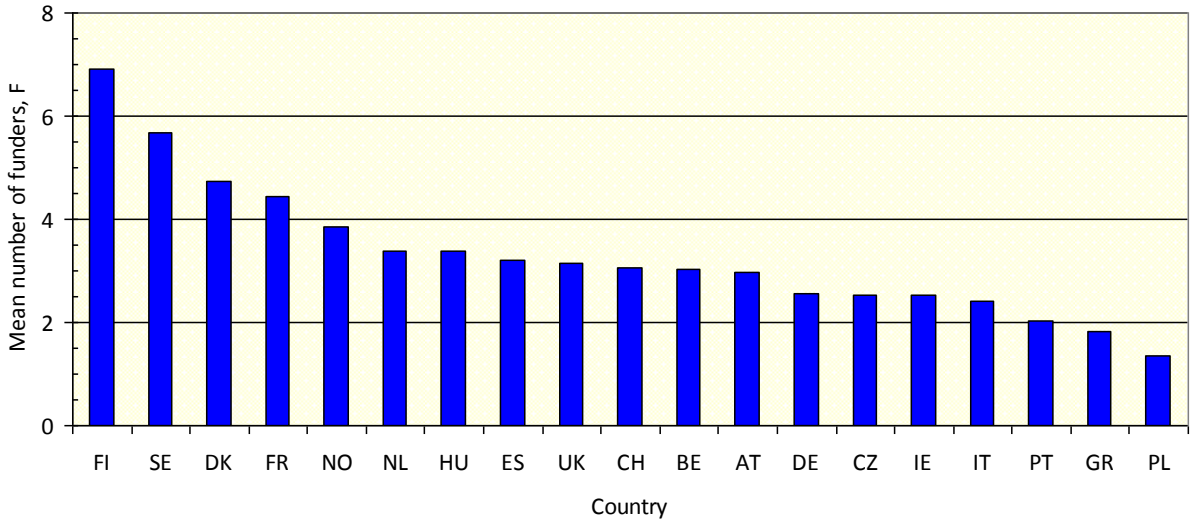

Figure 17. Mean number of funders per paper for DIABE papers, 2009-13, fractional count basis, for countries with at least 200 papers.

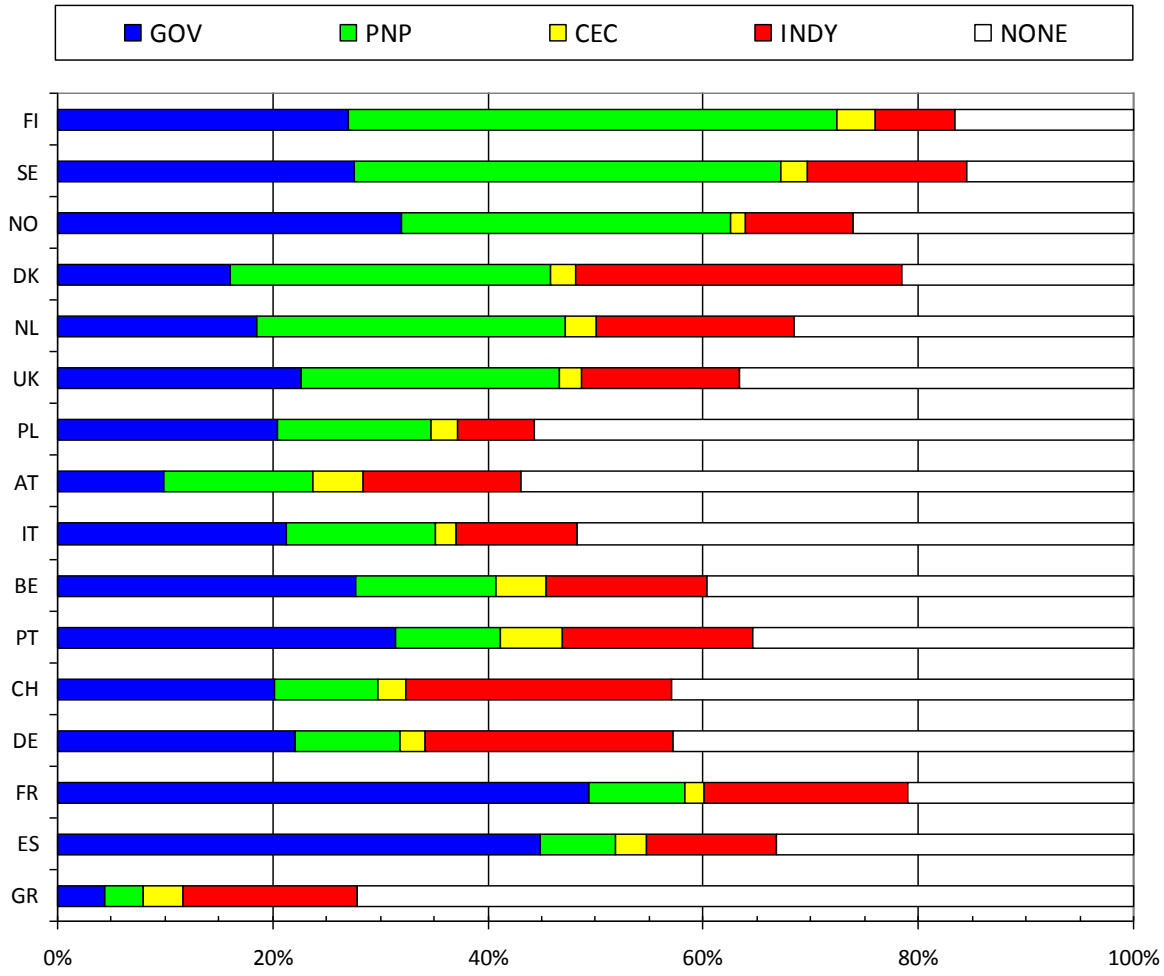

Figure 18. Funding sources for DIABE papers from 16 leading European countries with at least 200 papers, 2009-13, based on fractional country counts and also on fractional funding counts for each paper. *The countries are ranked by the percentage of private-non-profit funded papers.*

Overall, government plays a large role in the support of DIABE research, 26% of the total compared with just 18% for PNP sources. The exception was again for the five Scandinavian countries where the percentages were 24% and 36%, respectively. Industry supported 16% of the papers, with a particularly high percentage (30%) in Denmark because of the presence in that country of Novo Nordisk A/S, a leading producer of insulin.

For most countries the percentage of papers funded by the European Union is quite low, averaging 2.6% – but it is very high for two of the Baltic states, Latvia (31% on a fractional count basis) and Estonia (16%), but not for Lithuania (only 3.5%). The major countries in terms of DIABE research are also the major recipients of EU financial support: UK 59 papers on a fractional count basis with CEC funding, DE 55 papers, ES 40 papers, IT 39 papers and NL 34 papers although the percentages are below 10%.

The leading individual funders of DIABE research in Europe are listed in Table 24. The top funding source, divided among many contributors, is US biotechnology companies that do not have individual codes. Of European sources, the European Union is the major contributor with just over 2.5% of the papers being funded by it (a very similar figure to that for RESPI, see Table 5). The next highest contributor is the Danish company, Novo Nordisk A/S. There follow a number of large public-sector funders, such as the French Institut National de Santé et de la Recherche Médicale (INSERM) and Conseil National de la Recherche Scientifique (CNRS), the British Medical Research Council (MRC) and the National Institute for Health Research (NIHR), and four charities, three in the UK and one in the Netherlands. [There are also large contributions from Scandinavian foundations, totalling 232 papers, including 53 from the Novo Nordisk foundation in Denmark.] In contrast to the situation in RESPI, the big pharma companies are much less prominent. The top ten in DIABE accounted for 4.8% of the European papers, but the top ten in RESPI supported 9.0% of the EUR31 papers.

Table 24. The top funders of diabetes research in Europe, 2009-13, with fractional counts of numbers of papers and percentage of European output (17374 papers).

	Funder name	*Papers*	*% of EUR31*
X1B	US biotech companies	652.2	3.75
CEC	European Union	445.9	2.57
NOV	Novo Nordisk A/S	418.1	2.41
INS	FR INSERM	393.5	2.26
DOH	UK Department of Health	321.8	1.85
ESS	ES Instituto Carlos III	233.7	1.35
DFG	DE Deutsche Forschungsgesellschaft	215.7	1.24
MRC	UK Medical Research Council	180.3	1.04
BDA	Diabetes UK	150.6	0.87
SLU	Sanofi-Aventis s.a.	147.4	0.85
WEL	UK Wellcome Trust	147.0	0.85
BEW	DE Bundesministerium für Bildung und Forschung	144.4	0.83
CNR	IT Consiglio Nazionale delle Ricerche	134.3	0.77
MUR	IT Ministry of Universities and Research	133.7	0.77
LLL	Eli Lilly Inc.	119.7	0.69
DIB	NL Diabetes Fond	109.0	0.63
MEC	ES Ministerio de Educación y Ciencia	108.1	0.62
CRS	FR CNRS	97.2	0.56

X25	DE Industrial companies	93.5	0.54
	Funder name	*Papers*	*% of EUR31*
X98	IT universities	93.3	0.54
NVP	Novartis s.a.	89.2	0.51
ZAT	AstraZeneca plc	85.1	0.49
FNT	FI Ministry of Health	83.7	0.48
PL8	PL universities	83.7	0.48
MRK	Merck Inc.	82.7	0.48
SNS	SE Natural Science Research Council	81.0	0.47
PFZ	Pfizer Inc.	78.3	0.45
CZG	Academy of Sciences of the Czech Republic	76.6	0.44
CHN	CH Fonds National Suisse de la Recherche Scientifique	74.4	0.43
NWO	Netherlands Organisation for Scientific Research	73.8	0.43
SGO	Netherlands Health Research Council	73.2	0.42
BHF	British Heart Foundation	71.5	0.41
HLR	Hoffman LaRoche s.a.	70.9	0.41
Y32	DK endowed foundations(not Novo Nordisk)	69.4	0.40
BOI	Boehringer Ingelheim AG, Ingelheim	66.9	0.39
JNI	Instituto Portugues de Investigacao Cientifica e	61.8	0.36
POM	PL State Committee for Scientific Research	61.2	0.35

3.6.3 Analysis by research level, number of authors and subject area

Overall, papers in clinical journals tend to give fewer funding acknowledgements than ones in basic journals. This also holds true for papers with clinical title words compared with ones containing basic title words, see Table 25. A comparison of this table with table 4, for the RESPI papers, shows that diabetes is much better funded and far fewer papers have no funding acknowledgements.

Table 25. Numbers of funding bodies per paper for DIABE papers, 2009-13, in journals of different RL (RL 1 is clinical; RL4 is basic) and containing clinical and/or basic title words. *N = total number of papers in each group; F = 0 is number with no funding acknowledgements.*

RL (J)	*F*	*N*	*F = 0*	*% fund*		*Title words*	*F*	N	*F = 0*	*% fund*
1.0 to 1.5	1.91	6895	2871	58.4		Clinical not basic	2.14	12008	4374	63.6
1.5 to 2.0	1.94	3529	1317	62.7		All clinical	2.33	14507	4877	66.4
2.0 to 2.5	3.31	1760	358	79.7		Clinical and basic	3.28	2510	503	80.0
2.5 to 3.0	3.86	1780	288	83.8		All basic	3.58	4643	789	83.0
3.0 to 3 .5	3.34	1057	176	83.3		Basic not clinical	3.94	2133	286	86.6
3.5 to 4 .0	4.35	541	44	91.7						

It is not surprising that the average number of funders per paper rises with the number of authors, A, as the additional authors may be expected to be able to tap extra funding sources, and papers with many authors are likely to be international and attract funding from different countries, but nevertheless the correlation is striking, see Figure 19.

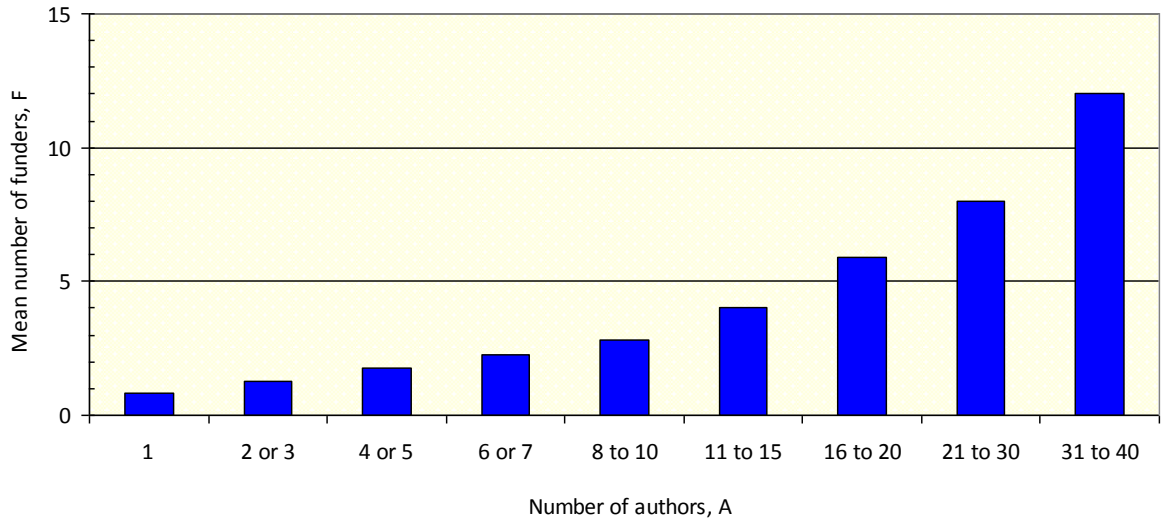

Figure 19. Mean number of funding bodies per paper for DIABE papers, 2009-13, as a function of the numbers of authors.

Table 26 shows the relative concentration on the different aspects of diabetes research, relative to the European average, of the leading funding bodies. We have also included the Juvenile Diabetes Research Foundation (JDB) as, although American in origin, it has autonomous branches in the UK and several other countries.

Table 26. Eleven leading European funders of diabetes research, 2009-13, and the ratio of numbers of supported papers observed compared with those expected on the basis of the European average in each of 14 subject areas, integer counts. *For funding body codes, see Table 7. Cells with values > 2.0 tinted green; > 1.41 tinted pale green; < 0.71 tinted yellow; < 0.5 tinted pink.*

	TWO	*CAR*	*ONE*	*NEP*	*NEU*	*RET*	*LIV*	*GES*	*FEE*	*PSY*	*HYP*	*MOD*	*NEO*	*ADA*
CEC	1.02	0.87	1.21	0.97	0.70	0.50	1.26	0.82	0.38	0.42	0.49	2.46	2.64	1.88
NOV	1.17	0.66	1.45	1.15	0.52	0.48	0.75	0.54	0.25	0.76	2.14	1.15	0.66	0.62
INS	1.06	1.04	0.89	0.79	0.73	0.51	1.74	0.52	0.59	0.51	0.42	0.67	0.85	0.00
DOH	1.01	0.92	1.44	0.62	0.56	0.98	0.46	0.60	0.98	0.91	1.40	3.40	2.69	2.01
JDB	0.36	0.36	3.55	1.07	1.02	1.32	0.51	0.28	0.23	0.26	1.40	0.85	0.81	1.01
MRC	1.25	0.93	0.80	0.39	0.57	0.39	1.13	0.96	0.47	1.44	0.82	1.98	1.57	0.00
ESS	1.27	1.08	0.68	0.83	0.78	0.98	1.96	1.02	0.23	0.77	0.69	1.12	3.56	0.00
DFG	0.88	0.89	0.91	1.14	0.73	0.70	1.98	0.99	0.32	0.72	0.73	1.42	1.87	0.00
WEL	0.91	0.65	1.54	0.57	0.47	0.58	0.65	1.02	0.41	0.55	1.12	2.66	7.67	0.00
BEW	1.15	0.96	1.24	0.80	0.71	0.55	1.38	1.39	0.10	1.64	0.95	1.23	0.49	1.82
BDA	0.82	0.68	1.52	1.35	0.62	0.64	0.77	1.25	1.31	0.86	0.50	4.50	2.04	0.00

This table confirms that the JDRF concentrates, as it states in its mission statement, on type I diabetes (although 12% of its papers were on type II), and that Novo Nordisk, along with the UK Department of Health, the Wellcome Trust and Diabetes UK, also relatively prioritise type I diabetes, though less exclusively, and actually support absolutely more type II than type I papers.

Figure 20 shows the numbers of funders and the mean research level of the papers in each area. The two are fairly well correlated, with r^2 = 0.53, meaning that subject areas that are more basic tend to receive more funding. Complications involving the feet is the most clinical subject area, and receives much less funding than any other area. Type I and type II diabetes appear to be treated almost equally in terms of funding.

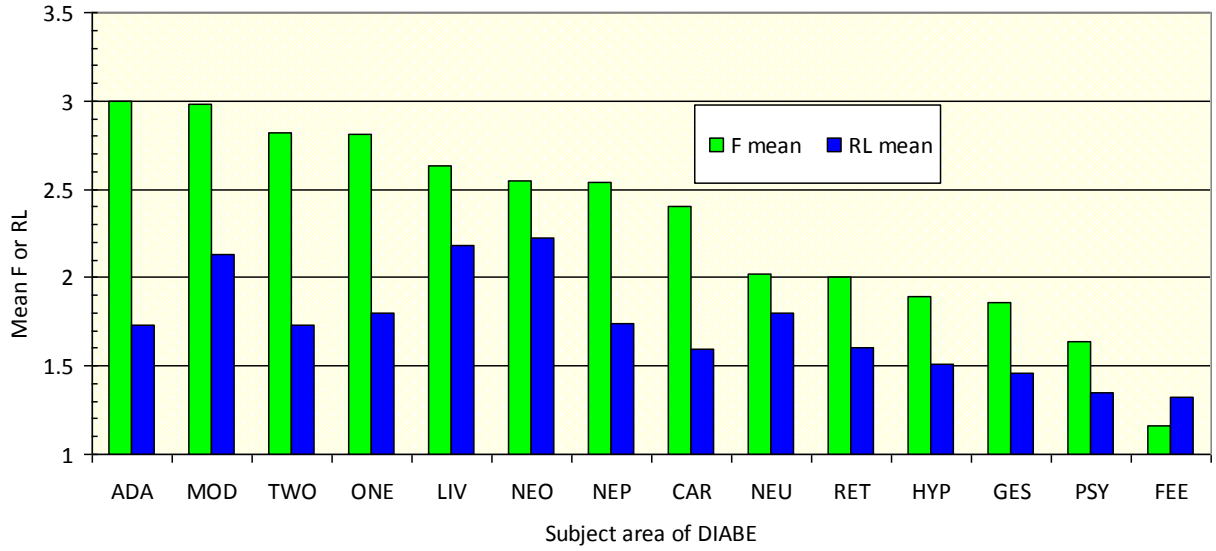

Figure 20. Mean number of funders per paper (F) and mean research level (RL) on a scale from 1 = clinical to 4 = basic research for all DIABE papers in 14 subject areas, 2009-13. *Codes in Table 21.*

3.6.4 2009 papers: correlation of funding with citation scores

We found that, for 2009 papers, the numbers of funding bodies correlated positively with the mean citation score, see Figure 12. The increase in actual citation impact (ACI) for papers with many funding acknowledgements is very clear, and the relationship will be expected to hold even when account is taken of factors such as the papers tending to be basic and having more authors (Lewison & Dawson, 1998; Roe *et al.*, 2010). The effects of other factors will be explored in detail later, when 2010 citation data are available and in other disease areas where there are many more papers.

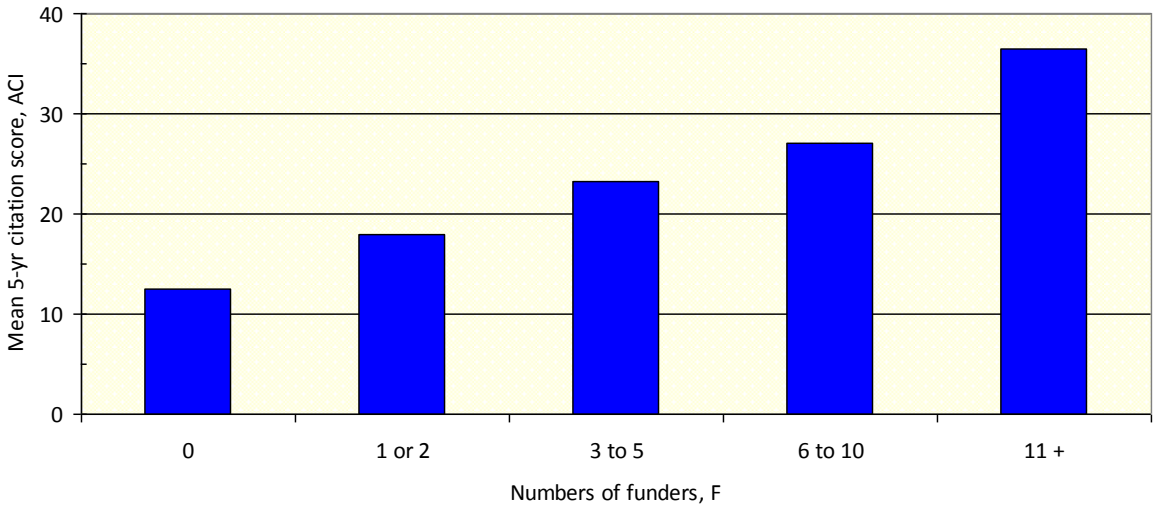

Figure 21. Mean five-year citation count (ACI) for groups of 2009 DIABE papers with different numbers of funding acknowledgements.

3.7 References on diabetes clinical guidelines

3.7.1 Collection of the guidelines and their references

Our research assistants from our partners, volunteers and King's recruits sought out national clinical guidelines for any form of diabetes. They were sent in the form of pdf files, and the references were copied and pasted to an Excel spreadsheets for analysis as described in section 1.8 above. The tally of the total numbers of guidelines found, the number processed and the numbers of cited references found in the WoS is shown in Table 27, below.

Table 27. Numbers of diabetes clinical guidelines found in 24 different European countries, the numbers that we were able to process in order to extract the references, and the numbers of cited WoS papers. *Data correct as at 29 Sept 2015; more will be added later.*

Country	*Total CGs*	*Processed*	*WoS refs*		*Country*	*Total CGs*	*Processed*	*WoS refs*
AT	3	2	412		HR	2	2	81
BE	1	1	152		HU	3	3	98
BG	1	0	0		IT	17	9	179
CH	2	2	57		LT	3	0	0
CY	1	0	0		LV	1	1	7
CZ	10	8	81		NL	8	7	654
DE	9	7	349		PL	2	0	0
DK	2	2	44		PT	27	13	262
EE	2	2	15		RO	1	1	79
ES	16	9	629		SE	2	2	347
FI	5	4	634		SK	14	11	79
FR	6	4	43		UK	11	4	377
GR	3	1	70		Total	149	92	4551

Many of the guidelines contained references that were not journal papers, and there were some that were in journals not processed for the WoS. The number of unique references was much less than 4551 as some papers were cited on many different guidelines. The most-cited paper was:

> Holman-RR Paul-SK Bethel-MA Matthews-DR Neil-HAW. (2008) 10-year follow-up of intensive glucose control in type 2 diabetes. *New England Journal of Medicine*, Vol 359, Iss 15, pp 1577-1589

and it was cited 13 times on different clinical guidelines. The numbers of papers receiving given numbers of cites on the 92 guidelines are shown in Figure 22. This suggests a log-linear relationship between counts of papers and numbers of CG cites.

3.7.2 The dates of the guidelines and their cited papers

There has been an increase in recent years in the numbers of clinical guidelines, as shown in Figure 23. After a short pause in 2007-08,.possibly connected with the financial crisis of those years, growth resumed and has continued. The cited references went back as far as 1961, but most were published in the period 1995-2010, see Figure 24. The gaps between the date of the guidelines and those of the cited papers are shown in Figure 25. The peak of the "curve" (it is really just a series of spots and the connecting line has no significance) is just over two years, but the median gap is 4.8 years and the mean gap is as much as 7.2 years.

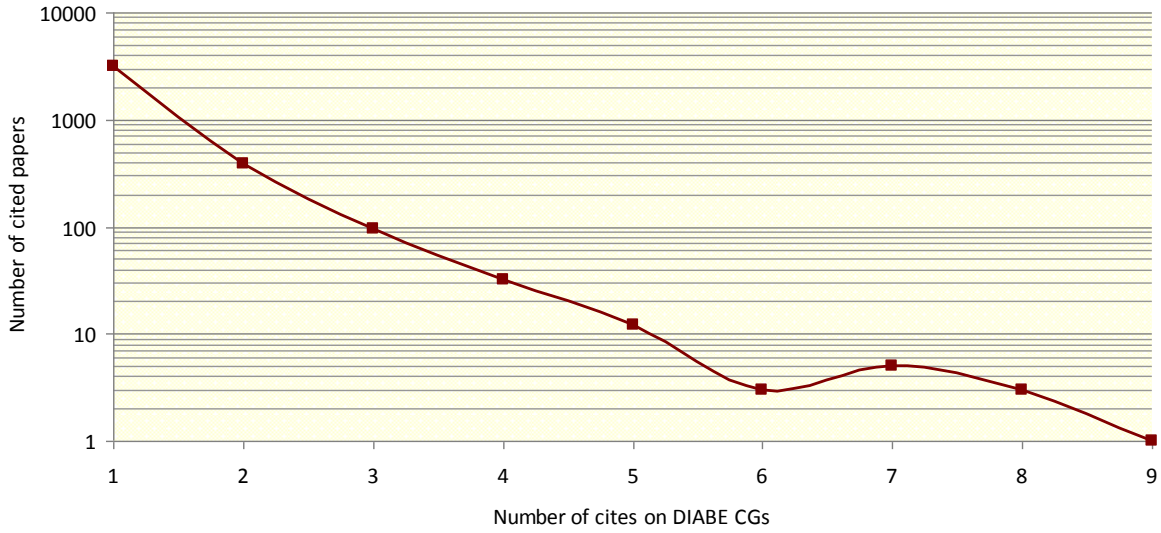

Figure 22. Numbers of papers cited on European diabetes clinical guidelines with given numbers of citations on these 92 guidelines.

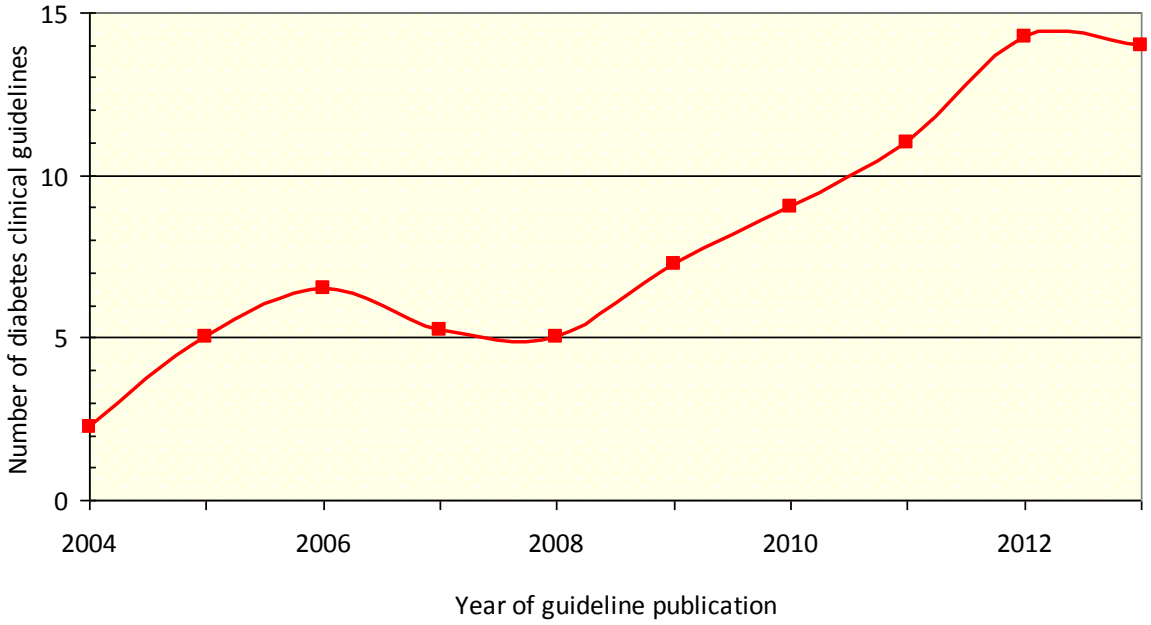

Figure 23. Publication years, 2003-14, of European diabetes clinical guidelines (N = 92) and numbers published each year (three-year running means).

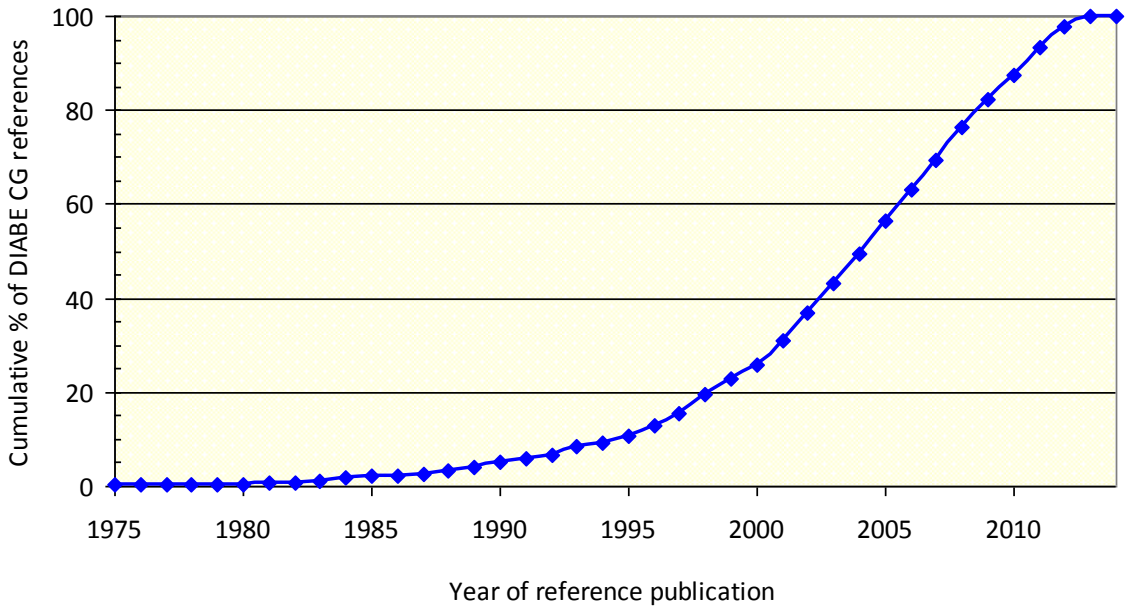

Figure 24. Cumulative percentage distribution of publication years of WoS papers cited by DIABE clinical guidelines from 19 European countries.

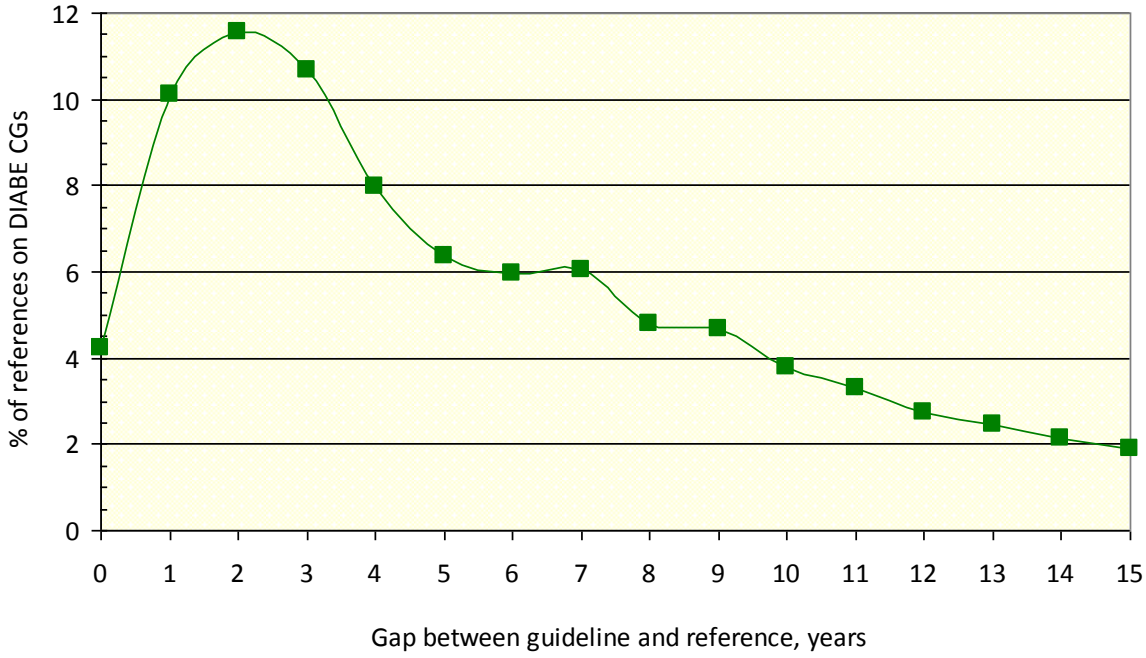

Figure 25. Gap in years between publication of DIABE clinical guidelines and those of their WoS cited references.

3.7.3 Research level of the cited references

The research level based on title words in the cited papers was 1.08 on the scale clinical observation = 1.0 and basic research = 4.0, which is very clinical. The mean RL based on the journals in which the cited references were published was 1.44, rather less clinical. So the cited references were mostly published in journals that were less clinical than their individual content.

3.7.4 Countries of the cited references

As expected, some countries' research in diabetes was more highly cited (relative to its presence in world diabetes research) than that of others. The table below shows the results for those European countries with at least one cited paper; data are given for both integer and fractional counts, and the countries are ranked by the mean value.

Table 28. Over citation ratio (OCR) for European countries' papers cited on European diabetes clinical guidelines on both integer (int) and fractional (frac) counts. *Cells with values > 2.0 tinted green; > 1.41 tinted pale green; < 0.71 tinted yellow; < 0.5 tinted pink.*

Country	*OCR int*	*OCR frac*	*Mean*		*Country*	*OCR int*	*OCR frac*	*Mean*
IS	3.86	2.52	3.19		BG	1.67	1.08	1.37
FI	2.82	2.73	2.77		IT	1.49	1.07	1.28
UK	2.33	2.28	2.31		DE	1.31	0.99	1.15
NL	2.44	1.99	2.22		IE	1.41	0.68	1.04
AT	2.24	2.09	2.17		CZ	1.48	0.33	0.91
LT	3.21	0.91	2.06		FR	1.14	0.64	0.89
EE	3.59	0.34	1.96		GR	1.19	0.49	0.84
LV	3.31	0.60	1.96		ES	1.04	0.59	0.82
DK	2.07	1.74	1.91		SI	1.12	0.35	0.74
SE	2.02	1.71	1.87		PL	0.97	0.33	0.65
NO	2.28	1.41	1.85		HR	0.93	0.33	0.63
BE	1.98	1.36	1.67		LU	0.81	0.33	0.57
CH	1.85	1.19	1.52		PT	0.55	0.38	0.46
HU	1.72	1.15	1.43		RO	0.35	0.06	0.20

An analyis of the countries of origin of the papers cited by the guidelines from those ten countries with more than 150 references (see Table 27): Austria, Belgium, Finland, Germany, Italy, Netherlands, Portugal, Spain, Sweden and the UK, shows that all except Portugal and Spain favour their own researchers much more than those of other countries, see Figure 26.

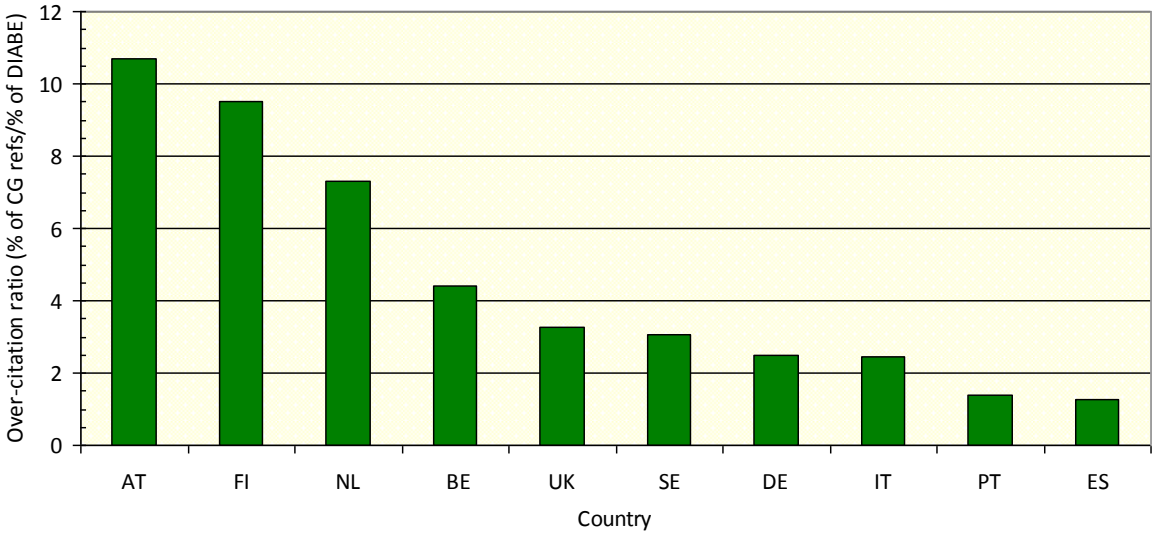

Figure 26. Over-citation ratio for 10 countries of own-country papers on DIABE clinical guidelines (fractional counts).

4 Mental disorders research (MENTH)

4.1 Survey of funding organisations (URC-ECO, Paris)

4.1.1 Definition of mental health disorders (MHDs, MENTH)

For purposes of the MAPPING_NCD project, MHD research (MENTH) was defined as 'research into the causation, occurrence, presentation, diagnosis, treatments and care of disorders affecting the mental health of their sufferers in childhood, adolescence, adulthood and older age.' The following MHD categories as defined in the ICD-10 were included in our analysIs: dementias (*e.g.*, Alzheimer's disease); psychoactive substance use disorders (*e.g.*, alcohol and drug abuse); schizophrenia; unipolar depression and bipolar disorder; neurotic and stress-related disorders (*e.g.,* obsessive compulsive disorder); behavioural syndromes (*e.g.*, eating disorders); adult personality disorders; behavioural/emotional disorders in children and adolescents (*e.g.*, ADHD); and intentional self-harm (*e.g.*, suicide) (Table 1). Mental retardation and disorders of psychological development (*e.g.*, autism) were excluded.

Table 29 Mental health disorders: International Disease Classifications, 10th revision (ICD-10)

ICD-10	*Disease category*
F00-F03	The dementias
F10-19	Disorders due to psychoactive substance use
F20-29	Schizophrenia and other psychotic disorders
F30-F39	Mood affective disorders
F40-46	Neurotic, stress-related and somatoform disorders
F50-59	Behavioural syndromes
F60-69	Adult personality and behaviour disorders
F90-98	Behavioural and emotional disorders with onset in childhood or adolescence
X60-84	Intentional self-harm

4.1.2 Data gathering: methods and results

Along with our partners, UPEC undertook a systematic search to identify the relevant public, private-non-profit and commercial research funding organizations (RFOs) at the regional, national, supranational and EU levels. A baseline threshold of €0.5 million to €1 million in overall investment was set in order to identify funding that could be expected to influence the content or direction of major research programmes. Because of the limited number of RFOs active in MHDs, the threshold for was subsequently lowered to €0.1 million.

A survey tool was used to collect quantitative and qualitative data from RFOs over a 10-month period from April 2014 to February 2015. The quantitative data included average annual research funding for MENTH. Additional website interrogations were undertaken to gather available funding data for the identified RFOs. The qualitative data encompassed the methods and processes by which RFOs made decisions regarding funding and levels of spend. The scientific and grey literature was also searched to obtain information regarding interventions, key risk factors and expert perspectives.

We identified 129 RFOs in 17 countries investing in MHDs in Europe. We followed up with all identified RFOs and found data for 32 non-responding RFOs on the Internet or in financial reports. No MHD RFOs were identified for the following countries: Sweden, Croatia, Slovenia and Greece. Few of the RFOs surveyed were devoted exclusively to MHD research, with an overwhelming

majority of 84% investing in other NCD areas. Most of these RFOs could only estimate the amount they had allocated to MHDs in relation to the other disease areas.

From the 129 RFOs identified as investing in MHD research in Europe, 72% (n = 93) provided a good amount of qualitative survey data and 60% (n=77) provided at least some quantitative data. After excluding RFOs with annual funding under €0.1 million (n=25), 52 RFOs were included in the quantitative analysis. Because the survey asked for an average funding amount within an average year for the period 2002 to 2013, it was not possible to report historic trends. Nonetheless, the funding data provided insight into the broad range of MHD research investments by RFOs, including a large number of smaller RFOs, often at the regional level (Table 2).

Table 30 MENTH RFO 2013 reported research funding by threshold

Threshold	*N*	*Max*	*Min*	*Total reported*
> 500K	29	€92,000,000	€507,956	€ 457 million
> 100K	9	€492,000	€141,000	€ 2.8 million
< 100K	19	€83,496	€5,000	€ 0.77 million
Total RFOs with 2013 funding data	57			

For the majority of RFOs in our sample (69%), the main funding source was governmental, and the primary funding mechanism (40% of RFOs) was calls for proposals. The primary motivation for funding MHD research was to support the research and policy agenda, with nearly 40% of RFOs selecting this as the main reason for funding. Publication of scientific articles was the clear leader as a metric for monitoring progress in meeting RFOs' expectations. This underscores the importance of bibliometric analysis in describing and measuring the impact of MHD research investment.

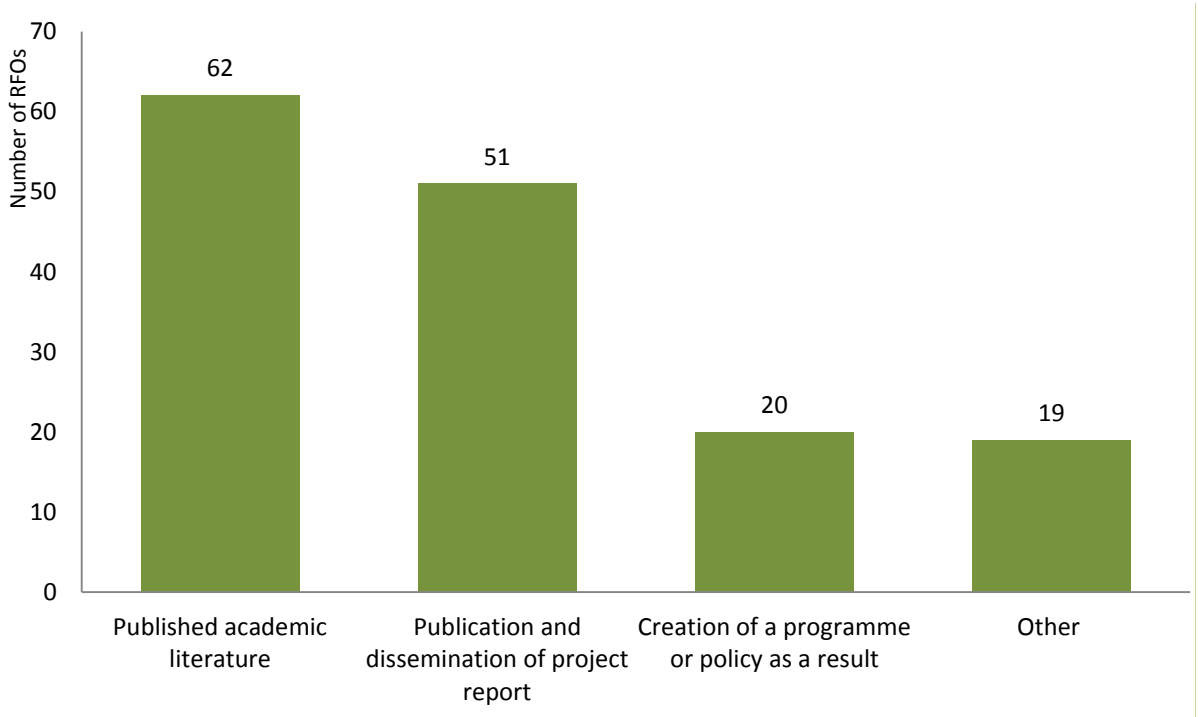

Figure 27 Measuring Impact of MENTH Research Funding (n=83) **Note: RFOs could provide more than one response to this question.*

4.1.3 Interview methodology

In order to contextualize the data and knowledge obtained through the project's mixed methods, we undertook semi-structured interviews with key MENTH experts in Europe to obtain their views on the strengths and weaknesses of the MHD research environment in Europe. We developed an

interview guide that included questions regarding priorities and funding trends in mental health research; the respective roles and priorities of the public and private entities; the issue of coordination and redundancy; and initiatives beyond funding that could improve MHD research in Europe.

Purposive sampling was used to identify potential interviewees with the goal of interviewing a range of experts with broad knowledge and perspectives on the MENTH research landscape in Europe, including RFOs, researchers and policy experts. Twenty-two experts were contacted by email and requested to participate in 20-30 minute telephone interviews. Respondents consented to the interviews, which were anonymous to elicit candid responses and were recorded and transcribed.

The Framework Method was used for the qualitative analysis of the interviews because it affords a highly systematic method for categorizing and organizing data with a matrix output from which descriptive and explanatory conclusions may be brought out by theme. The qualitative data were then charted into a framework matrix to allow thematic analysis across the interviews.

4.1.4 Interview findings

Ten semi-structured interviews were conducted between April and July 2015. Respondents included psychiatrists, researchers and policy analysts from Belgium, Finland, France, Germany, Spain and the UK, and most had engaged in research at both at the Member State (MS) and EU levels. After coding the interviews and charting them into the framework matrix, four general themes emerged: funding, the role of the commercial sector, coordination and research priorities.

All respondents expressed concern that while mental health research funding in Europe has increased in recent years it remains too low and is not consistent with the burden of disease. These experts disagreed regarding whether MENTH research funding should be prioritized based on severity or frequency of specific MHDs and also whether the orientation should favour public health initiatives or the development of individual medical treatments.

The diminished level of R&D investment in MENTH by the pharmaceutical industry was cited as a significant challenge. Public institutions will probably have to step into the gap to fund basic research aimed at identifying biological targets because current MHD drug development is based on a clinical rather than pre-clinical model.

In terms of the reasons for underfunding, several respondents mentioned the role of stigma. One way to address the effects of stigma could be through awareness campaigns by charities, which play a large role in patient advocacy for several major NCDs. However, there is a significant lack of charity engagement for MENTH in Europe, especially compared to other NCDs such as cancer.

Several respondents pointed out that EU funding strongly influences priorities but argued that a coordinating structure at the European level specifically devoted to MENTH was needed. This was also seen as a means to facilitate inclusion of all stakeholders in setting priorities for MENTH research, including patients, caregivers and community members.

4.2 Downloading of papers and country outputs

4.2.1 Creation and calibration of the filter

The filter was initially developed in consultation with Professor George Szmukler of the Institute of Psychiatry, King's College London in connection with another project. It was subsequently updated under his guidance and further updated, and calibrated, in consultation with our French partner, Professor Isabelle Durand-Zaleski of the Department of Public Health, Université Paris Est Val de Marne. The calibration gave a **precision, p = 0.729** and a **recall, r = 0.879**.

Unlike the other NCD research outputs, in MENTH a significant number of papers (29,617 out of a total of 138,666, or 21%) were covered only in the Social Sciences Citation Index (SSCI) and not the

Science Citation Index (SCI). [There were also many papers in both indexes.] These papers had different citation characteristics (fewer within five years from publication, and a peak between five and seven years after publication rather than two to three. However they were grouped together with the other papers for the main analyses.

4.2.2 Analysis of European and individual country outputs

World and European outputs, year by year, of mental disorders research papers are given below.

Table 31. Outputs of mental disorders research papers (MENTH) in the Web of Science from 2002 to 2013 from EUR31 group of countries, integer and fractional counts.

	MENTH					*MENTH/BIOMED, %*	
Year	*World*	*EUR31 int*	*EUR31 frac*	*EUR %*	*Int'l, %*	*World*	*EUR31*
2002	19830	7700	7041	35.5	8.6	5.33	4.87
2003	20786	8123	7380	35.5	9.1	5.36	4.97
2004	22142	8774	7948	35.9	9.4	5.46	5.20
2005	23779	9396	8446	35.5	10.1	5.59	5.32
2006	25896	10122	9096	35.1	10.1	5.75	5.46
2007	28503	11283	10067	35.3	10.8	5.88	5.70
2008	30189	11831	10496	34.8	11.3	5.79	5.66
2009	32162	12721	11276	35.1	11.4	5.90	5.87
2010	33300	13508	11940	35.9	11.6	5.83	5.99
2011	35252	14176	12486	35.4	11.9	5.82	6.03
2012	37532	15067	13220	35.2	12.3	5.85	6.07
2013	39656	15965	13904	35.1	12.9	5.96	6.22

Table 32. Outputs of 31 European countries in mental disorders research (MENTH), 2002-13 (12 years) in both the SCI and SSCI. Integer and fractional counts, the percent foreign contribution (For, %) and the annual growth rate. *The countries are ranked by their fractional count outputs.*

ISO	*Int ct*	*Frac ct*	*For, %*	*AAPG*		*ISO*	*Int ct*	*Frac ct*	*For, %*	*AAPG*
UK	38199	28072	26.5	4.7		PT	1412	926	34.4	19.9
DE	28903	22945	20.6	4.3		HU	1431	898	37.2	5.8
NL	13815	10241	25.9	11.7		CZ	1157	869	24.9	12.2
IT	13523	10226	24.4	8.2		HR	950	801	15.7	11.4
FR	12202	9468	22.4	6.1		RO	516	337	34.7	37.1
ES	11405	9079	20.4	9.4		SI	495	329	33.5	15.1
SE	8082	5652	30.1	4.6		EE	346	203	41.3	12.1
CH	7055	4128	41.5	4.9		IS	300	149	50.2	8.8
FI	4014	3001	25.2	3.0		SK	244	149	38.9	9.8
NO	4040	2970	26.5	8.3		LT	188	122	34.8	16.2
BE	4617	2773	39.9	7.8		BG	236	102	56.7	8.5
PL	3048	2480	18.6	12.0		LU	127	63	50.5	15.7
DK	3693	2460	33.4	8.6		CY	85	47	44.6	23.5
AT	3304	2045	38.1	1.2		LV	36	21	42.4	13.4
GR	1860	1368	26.5	8.2		MT	35	17	51.5	5.0
IE	2256	1358	39.8	11.2						

European output has remained remarkably constant at just over 35% of world output; this may be because mental disorders research is still not a major research area in east Asia. European mental disorders research is now more prominent within biomedical research (6.2% compared with 4.9% in 2002), whereas world-wide it has changed less (from 5.3% to 6.0%). The results for the individual European countries are shown in Table 32.

Again, as in DIABE, the UK has much the highest output, and the comparison of outputs with GDP in Figure 28 shows which other countries are publishing more than expected and which, less. Several countries besides the UK are publishing about twice the amount shown by the trend-line: Croatia, Iceland, Finland, Netherlands, Sweden and Estonia. But Slovakia, Romania, Bulgaria are publishing fewer than half the expected number of papers, and Lithuania and France barely half as many.

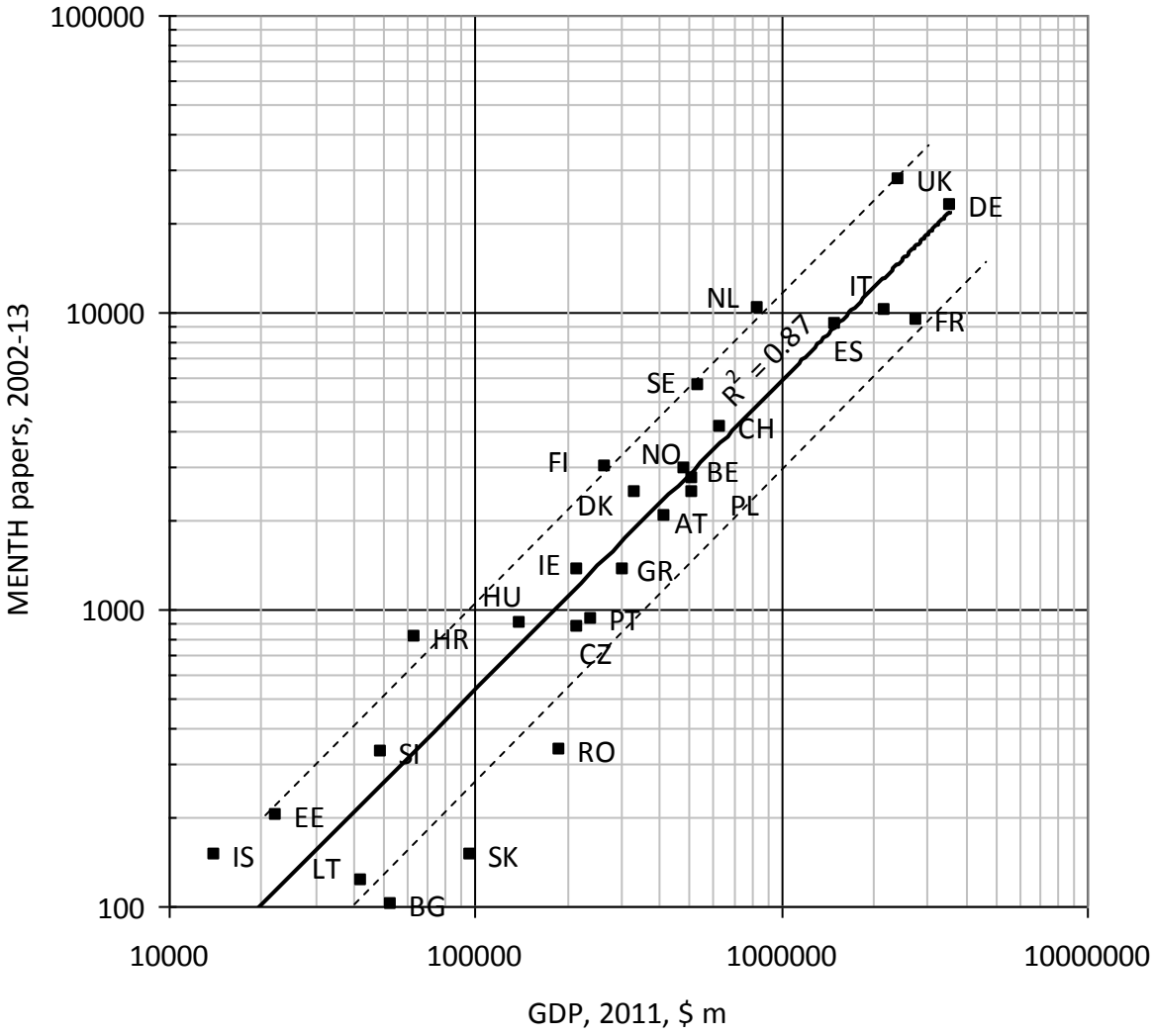

Figure 28. Plot of MENTH paper output, 2002-13, against GDP for 27 European countries. *Note: CY, LU, LV and MT omitted. Dashed lines show values x2 or x0.5 relative to power trend-line*

4.3 Analysis of research level, citations and percentage of reviews

4.3.1 The research level of MENTH papers

As expected, the papers in mental disorders tend to be very clinical, as shown by Figure 29. For most large countries, the RL is around 1.5, and only exceeds 2.0 for Estonia and Poland – the latter perhaps because its clinical mental health journals are in Polish and not covered in the WoS. Over

the years, the mean RL declined (as in the previously presented NCDs) from 1.60 to 1.47 and so the work became somewhat more clinical although the difference was less than for the other NCDs.

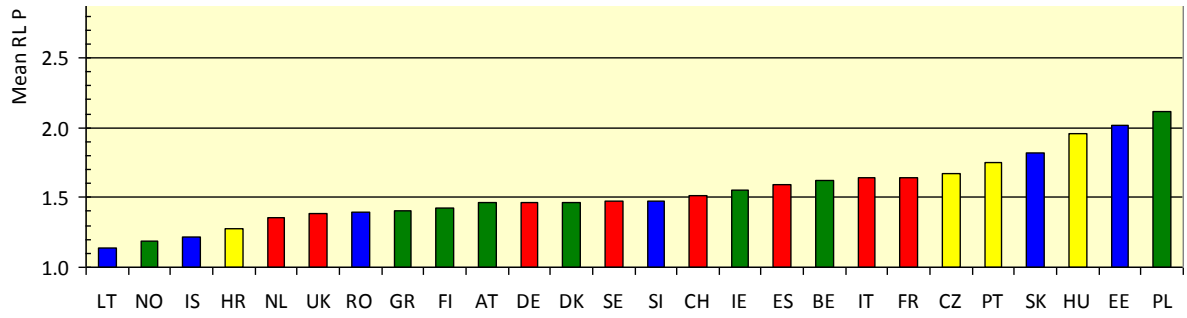

Figure 29. Chart showing the mean research level of MENTH papers from 26 European countries, 2002-13, with 100 or more classed papers. *Red bars: > 3000 classed papers (frac. cts); green bars: > 1000 papers; yellow bars: > 300 papers; blue bars: > 100 papers.*

4.3.2 Citation analysis of MENTH papers

The MENTH papers have been divided for the purposes of citation analysis into two groups: those in the SCI (some of which are also in the SSCI) and those in the SSCI but not the SCI. The citation scores (five-year cite scores, ACI) for the world and for the EUR31 countries are given in the figure below.

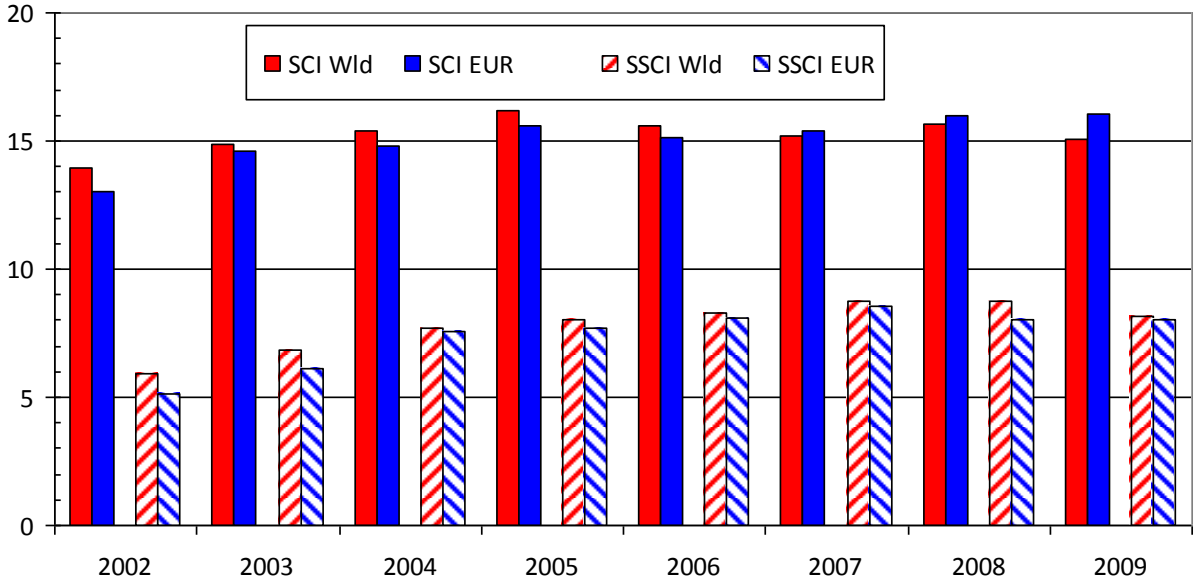

Figure 30. Chart showing the increase in mean citations per MENTH paper with publication year, 2002-09, for world (red) and for EUR31 (blue) papers. *Values for papers only in the SSCI shown striped.*

The results for the SCI papers are similar to those for ONCOL, with European papers less cited in 2002-06, but more cited in 2007-09. However, for the approximately one fifth of papers in the SSCI only, the European papers are less cited than the world mean throughout, probably because the world output is dominated by the USA and the rise of east Asian output has not yet spread into SSCI journals.

The next table shows the citation scores (ACI) for individual countries and also the numbers of papers whose citations put them in the top 5% of the cohort in terms of citations, for which the qualifying numbers were 49 cites (SCI) and 26 cites (SSCI).

Table 33. Citation scores for MENTH papers from 16 European countries in the SCI and in the SSCI only, with numbers of papers from each country with enough cites to put them in the top 5% of the EUR31 cohort (49 and 26 cites).

ISO	*SCI ACI*	*Top 5%*	*% of N*		*SSCI ACI*	*Top 5%*	*% of N*
BE	15.52	58.8	5.18		8.92	38.1	8.94
AT	14.50	54.4	5.76		11.17	18.5	7.76
IE	16.62	39.8	6.31		6.67	8.8	5.11
NL	14.01	195.3	4.47		7.86	98.2	6.36
FR	15.08	226.8	5.05		8.51	34.0	5.56
UK	15.07	575.0	5.01		7.68	255.2	5.23
IT	15.66	263.2	5.04		6.47	26.6	4.54
FI	15.51	90.3	5.90		7.14	12.9	3.58
DE	14.61	522.5	5.20		7.63	140.0	4.21
ES	14.95	201.9	4.87		5.72	44.7	4.20
SE	15.47	130.4	5.03		7.91	31.1	3.74
HR	11.68	14.7	4.71		5.80	6.3	4.03
CH	14.71	83.6	4.58		7.12	21.7	3.79
DK	15.12	57.5	4.72		6.30	4.7	1.94
NO	11.52	30.0	2.87		6.54	18.3	3.38
GR	12.94	27.7	4.27		5.61	1.3	0.88

4.3.3 Percentage of reviews of MENTH papers

The percentages of countries' papers that were classed as reviews are shown in Figure 21 for the 20 countries with at least 50 reviews during the 12-year study period. The European average was 9.6% compared with the world average of 8.6%.

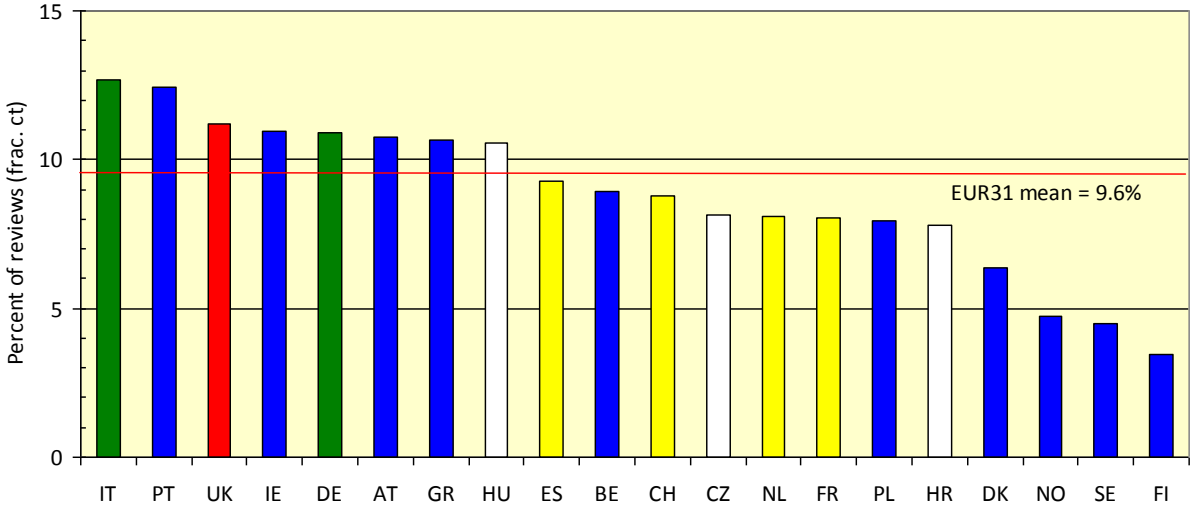

Figure 31. Chart showing the percentage of MENTH papers by 20 European countries with over 50 reviews that are classed as "reviews" in the WoS during 2002-13. *Red bars: > 3000 reviews; green bars: > 1000 reviews; yellow bars: > 300 reviews; blue bars: > 100 reviews; white bars: < 100 reviews.*

4.4 Analysis of MENTH papers by mental disorder

4.4.1 Development of filters for 16 individual mental disorders

A series of sub-filters was developed (in association with Professor George Szmukler of the Institute of Psychology, Psychiatry and Neuroscience of King's College) to identify the mental disorders papers that described research into each one of 16 different disorders. However the disease burden in DALYs associated with only 10 of them were listed in the Global Burden of Disease study. They were as shown in the table below.

Table 34. List of the 16 individual mental disorders investigated, with their codes used in the tables and figures that follow. Disorders whose disease burden were obtained shown in **bold**.

Mental disorder	*Code*		*Mental disorder*	*Code*
Drug use and other addictions	**ADD**		**Attention-deficit hyperactivity**	**HYP**
Alcohol use	**ALC**		Obsessive-compulsive disorder	OBS
Alzheimer's and other dementias	**ALZ**		Personality disorder	PER
Anxiety disorder	**ANX**		Post-traumatic stress disorder	PTS
Bipolar affective disorder	**BIP**		**Schizophrenia**	**SCH**
Chronic Fatique Syndrome	CFS		Sexual disorder	SEX
Unipolar depression	**DEP**		Sleep disorder	SLE
Eating disorder	**EAT**		**Suicide and self-harm**	**SUI**

4.4.2 Outputs of papers on individual mental disorders

The increase in mental disorders research between 2002 and 2013, which more than doubled (x 2.07), was seen in most individual disorders, in particular in hyperactivity (x 4.5), sexual disorders (x 3.7, but from a low base), post-traumatic stress (x 3.4), suicide and self-harm (x 2.7) and eating disorders (x 2.5). However research on some disorders, although increasing, fared less well, for example chronic fatigue syndrome (x 1.1), bipolar disorder (x 1 .7) and schizophrenia (x 1.8). The changes in output are shown in Figure 32.

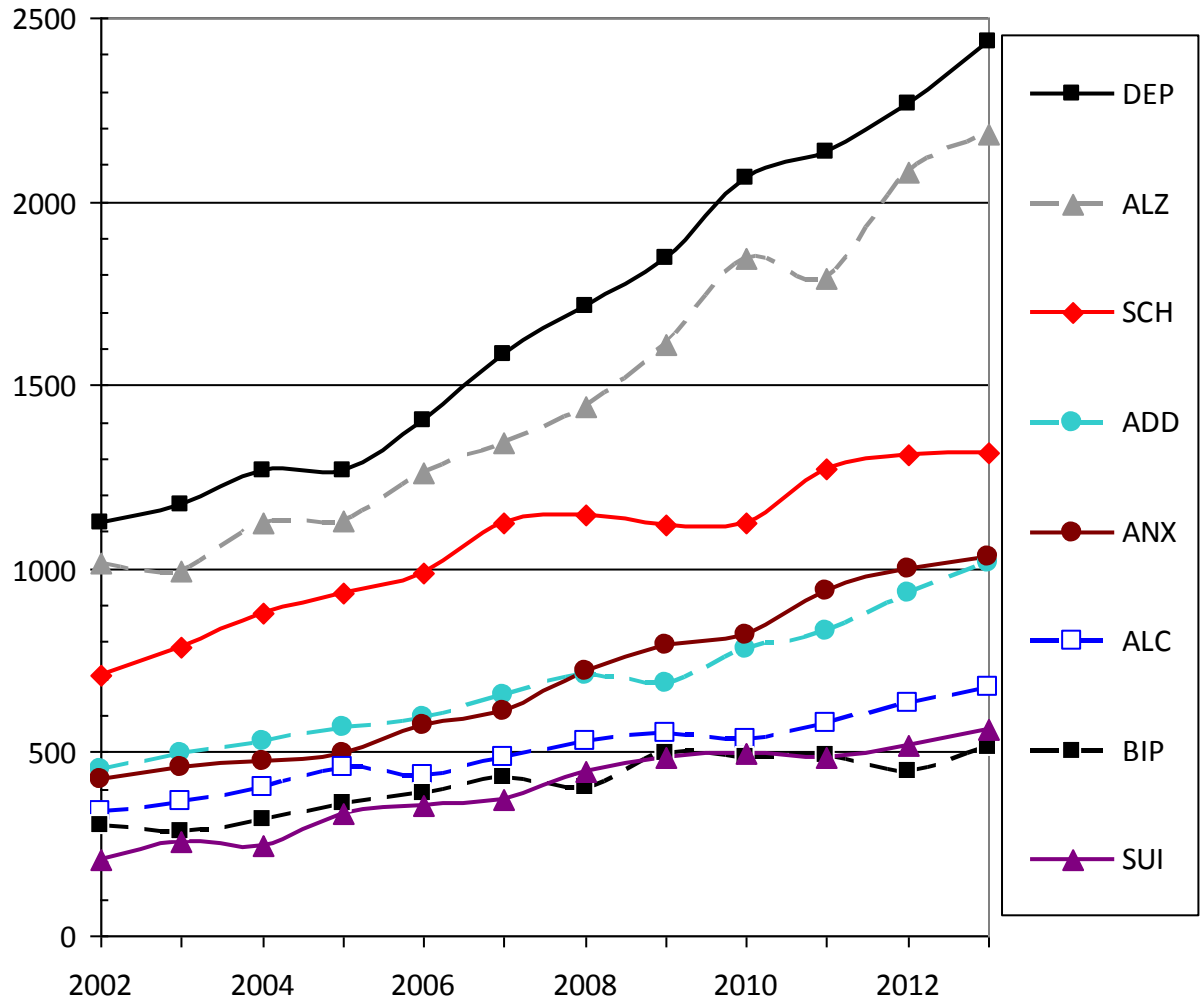

Figure 32. Growth of output of mental disorders research in eight areas, 2002-13, from the EUR31 countries. *For codes see Table 34.*

4.4.3 Outputs of the European countries in individual mental disorders

The individual countries varied in their relative commitments to research on these individual disorders, see Table 35 below.

This table gives numbers of papers, but of more interest is the ratio of each country's output to what would be expected on the assumption that its mental disorders research portfolio was similar to that of all 31 countries combined. This is shown in Table 36, with the individual cells coloured to show particularly high or low relative commitment to research on the particular disorder. Data are only shown for the top 20 countries, with at least 800 papers in total (fractional count basis).

Table 35. Outputs of EUR31 countries in each of the top 10 mental disorders, 2002-13; fractional counts.

ISO	*DEP*	*ALZ*	*SCH*	*ADD*	*ANX*	*ALC*	*BIP*	*SUI*	*PER*	*EAT*	*Total*
UK	3250	3065	2371	1493	1617	947	916	1110	944	793	28072
DE	3097	2212	2144	920	1267	915	543	572	728	550	22945
NL	1980	1103	672	518	1037	425	187	159	444	120	10241
IT	1463	2206	847	737	490	325	542	273	293	418	10226
FR	1364	1447	914	768	430	328	339	279	183	241	9468
ES	1137	1486	963	850	572	504	449	161	375	360	9079
SE	723	1071	319	273	385	430	113	318	122	133	5652
CH	497	402	418	367	190	188	122	159	102	66.9	4128
FI	594	354	261	126	127	317	67.5	149	72.3	34.1	3001
NO	453	206	202	223	257	103	102	150	132	84.7	2970
BE	450	387	201	124	165	140	63.6	90	132	87.6	2773
PL	644	276	270	153	140	140	158	50.9	29	91.8	2480
DK	556	179	329	134	110	146	115	126	61.5	42	2460
AT	283	418	203	131	118	56.2	71.4	147	45.1	44.2	2045
GR	287	161	156	80.3	112	45.1	84.5	48.5	34.3	19.3	1368
IE	200	158	173	81	62.6	46.1	54.8	79.1	21	2.26	1358
PT	140	175	55.9	67.1	59	41.2	45.7	16.9	31.2	23.8	926
HU	169	108	103	62	58	25	35.8	76.7	16.4	18.3	898
CZ	149	119	124	58.8	25.4	16.3	39.1	28	23.8	46.8	869
HR	155	75.8	117	22.6	49.7	26.2	31.7	69	14.9	11.6	801
RO	48.2	37.2	17.1	29.1	27.8	8.81	44.8	15	5.7	1.74	337
SI	60.2	26.4	35.2	24.3	21	24.2	9.57	47	7.05	4.27	329
EE	56.3	11.5	2.2	13	27.9	15.8	1.55	26	3.05	5.53	203
IS	22.4	11.4	11.4	8.42	12.8	5.97	0.77	10.8	4.34	3.74	149
SK	26.9	25.1	7.24	14.2	21.6	8.02	3.24	3.95	0	0.75	149
LT	28.3	6.7	7.87	11.2	5.81	13.6	3.67	8.88	0.63	3	122
BG	21	13.4	17.3	9.93	4.64	0.46	8.17	2.23	1.94	0.91	102
LU	2.98	4.32	1.73	6.31	6.87	2.96	3.08	2.66	3.2	3.42	63
CY	6.37	5.88	3.67	3.75	6.78	2.33	0.83	0.58	2.67	2.5	47
LV	0.83	0	0.83	1.67	0	1.13	0	0.67	0.67	0	21
MT	3.17	4.33	0.25	1.7	0.67	0	0	0.84	0	0	17
EUR31	17868	15755	10948	7312	7408	5247	4156	4181	3834	3214	123301

Table 36. Ratio of observed to expected numbers of papers relevant to 13 main mental disorders for the leading 20 European countries, 2002-13, with > 800 papers. Countries are ranked by total output, fractional counts. Mental disorders ranked from left to right by amount of research output, based on integer counts. *Values > 2 tinted bright green; values > 1.41 tinted pale green; values < 0.71 tinted gold; values < 0.5 tinted pink. For codes, see Table 34.*

ISO	*DEP*	*ALZ*	*SCH*	*ADD*	*ANX*	*ALC*	*BIP*	*SUI*	*PER*	*EAT*	*HYP*	*PTS*	*OBS*
UK	0.80	0.85	0.95	0.90	0.96	0.79	0.97	1.17	1.08	1.08	0.83	0.99	0.87
DE	0.93	0.75	1.05	0.68	0.92	0.94	0.70	0.74	1.02	0.92	1.37	1.07	1.29
NL	1.33	0.84	0.74	0.85	1.69	0.98	0.54	0.46	1.39	0.45	1.45	1.99	1.45
IT	0.99	1.69	0.93	1.22	0.80	0.75	1.57	0.79	0.92	1.57	0.60	0.46	1.49
FR	0.99	1.20	1.09	1.37	0.76	0.81	1.06	0.87	0.62	0.98	0.56	0.64	0.82
ES	0.86	1.28	1.19	1.58	1.05	1.30	1.47	0.52	1.33	1.52	1.28	0.30	1.29
SE	0.88	1.48	0.64	0.81	1.13	1.79	0.59	1.66	0.69	0.90	1.41	0.91	0.36
CH	0.83	0.76	1.14	1.50	0.77	1.07	0.88	1.14	0.79	0.62	0.77	2.02	0.78
FI	1.37	0.92	0.98	0.71	0.70	2.48	0.67	1.46	0.77	0.44	0.63	0.16	0.14
NO	1.05	0.54	0.77	1.27	1.44	0.81	1.02	1.49	1.43	1.09	1.37	1.44	0.69
BE	1.12	1.09	0.82	0.75	0.99	1.19	0.68	0.96	1.53	1.21	1.24	0.48	0.91
PL	1.79	0.87	1.23	1.04	0.94	1.33	1.89	0.61	0.38	1.42	0.32	0.51	0.36
DK	1.56	0.57	1.51	0.92	0.74	1.39	1.39	1.51	0.80	0.66	0.88	1.59	0.79
AT	0.95	1.60	1.12	1.08	0.96	0.65	1.04	2.12	0.71	0.83	0.39	0.80	0.66
GR	1.45	0.92	1.28	0.99	1.36	0.77	1.83	1.05	0.81	0.54	0.34	1.04	1.24
IE	1.02	0.91	1.43	1.01	0.77	0.80	1.20	1.72	0.50	0.06	1.71	0.15	0.23
PT	1.04	1.48	0.68	1.22	1.06	1.05	1.46	0.54	1.08	0.99	0.32	0.45	0.67
HU	1.30	0.94	1.29	1.16	1.07	0.65	1.18	2.52	0.59	0.78	0.60	0.39	0.68
CZ	1.18	1.07	1.61	1.14	0.49	0.44	1.33	0.95	0.88	2.06	1.07	0.22	0.85
HR	1.34	0.74	1.65	0.48	1.03	0.77	1.17	2.54	0.60	0.56	0.38	9.42	0.32

There are some big variations shown in this table, and most of the differences between observed and expected values are statistically significant at the 5% level, and often much less. Research on Alzheimer's disease and the other dementias, which has received a significant political push recently, is somewhat low in the UK, but much less in Norway and Denmark. However it is being pursued vigorously in Italy, Austria, Sweden and Portugal.

4.5 Burdens of individual mental disorders

4.5.1 Burdens for the EUR31 countries

The Global Burden of Disease data gives percentages of all DALYs for 10 mental disorders, and a breakdown of some of them by sub-category, such as addiction to different classes of drugs. Table 37 gives these percentages.

This table is instructive in revealing differences between countries, and also similarities: thus none of the cells are coloured in the columns for schizophrenia or bipolar disease. The bottom row shows which disorders are of most importance, and clearly depression is the dominant one, followed by dementia, and anxiety and suicide & self-harm. Alcoholism and addiction to proscribed drugs cause a similar burden overall, but addiction leads to almost 40% more research than alcoholism, see below, which appears to need more attention, particularly because of its pervasive social effects (Rajendram *et al.,* 2006).

Table 37. Percentages of DALYs attributable to mental disorders in the EUR31 countries, 2010. *Countries are listed in order of MENTH research output in 2002-13; disorders are listed in order of research output – see Tables25 and 26. Cell tinting in reverse from that of research outputs: where mental disorder DALYs > 2 x European averge, cells tinted pink; if DALYs > 1.41 x average, cells tinted gold; if DALYs < 0.71 x average, cells tinted pale green; if DALYs > 0.5 x average, cells bright green.*

ISO	*DEP*	*ALZ*	*SCH*	*ADD*	*ANX*	*ALC*	*BIP*	*SUI*	*EAT*	*HYP*	*MENTH*
UK	3.23	2.30	0.87	2.29	2.10	1.35	0.64	1.28	0.31	0.022	11.54
DE	4.57	1.91	0.81	1.12	1.79	1.50	0.61	1.63	0.29	0.015	11.36
NL	7.76	2.39	0.83	1.02	2.01	1.05	0.67	1.46	0.37	0.020	14.51
IT	4.81	2.46	0.84	1.43	1.40	0.40	0.66	0.88	0.27	0.016	10.50
FR	4.75	2.66	0.84	1.03	2.60	1.96	0.64	2.67	0.42	0.019	13.05
ES	4.82	3.19	0.98	1.88	1.21	0.80	0.76	1.05	0.52	0.019	11.72
SE	4.79	3.04	0.86	1.26	1.83	1.82	0.65	2.00	0.39	0.020	12.35
CH	6.60	2.34	0.95	1.28	1.70	1.19	0.73	2.54	0.44	0.020	13.67
FI	5.58	4.08	0.83	1.24	1.27	2.67	0.61	2.86	0.31	0.018	13.19
NO	5.72	2.52	0.85	2.12	2.83	2.16	0.65	1.77	0.45	0.021	15.55
BE	3.85	2.86	0.80	1.27	1.31	1.21	0.62	2.69	0.46	0.018	10.22
PL	3.49	0.92	0.77	0.99	1.90	2.13	0.63	2.41	0.15	0.014	10.70
DK	4.58	2.27	0.72	1.35	1.35	2.66	0.60	1.73	0.35	0.019	12.31
AT	4.94	1.68	0.84	1.68	1.43	1.60	0.66	2.16	0.55	0.018	12.41
GR	4.65	1.62	0.82	1.18	1.83	0.41	0.65	0.49	0.29	0.017	10.47
IE	4.63	1.66	0.93	2.14	1.81	1.39	0.78	2.13	0.55	0.026	13.10
PT	4.13	1.78	0.81	0.94	1.76	0.92	0.64	1.69	0.19	0.017	10.04
HU	2.58	1.22	0.68	0.62	1.59	1.00	0.53	2.45	0.13	0.011	7.65
CZ	3.15	1.04	0.83	0.72	1.94	0.74	0.67	2.02	0.22	0.013	8.92
HR	5.51	1.09	0.77	0.85	1.69	1.09	0.58	1.83	0.16	0.013	11.36
RO	3.34	0.74	0.71	0.71	0.80	0.97	0.57	1.36	0.08	0.012	7.73
SI	4.39	1.12	0.90	0.86	1.65	1.31	0.70	2.88	0.27	0.014	10.75
EE	5.18	1.09	0.69	1.64	0.91	2.91	0.59	1.94	0.15	0.012	12.66
IS	5.78	2.81	1.06	1.98	2.85	1.44	0.82	1.97	0.55	0.029	15.48
SK	3.33	0.78	0.79	0.82	1.65	1.20	0.66	1.91	0.19	0.015	9.27
LT	3.59	0.87	0.65	1.21	0.92	3.04	0.56	4.01	0.12	0.012	10.64
BG	3.21	0.73	0.64	0.57	0.81	0.49	0.50	1.20	0.09	0.010	6.79
LU	6.51	2.06	0.92	1.89	2.36	1.71	0.70	1.67	1.00	0.021	15.90
CY	6.04	1.64	0.91	1.22	2.00	0.95	0.74	0.57	0.32	0.026	13.03
LV	4.27	0.95	0.62	1.07	0.81	2.32	0.53	2.15	0.10	0.010	10.23
MT	6.64	1.82	0.91	1.53	2.37	0.89	0.70	0.69	0.27	0.022	14.10
EUR31	4.34	2.03	0.82	1.30	1.74	1.32	0.64	1.72	0.30	0.017	11.16

5 Cancer research (ONCOL)

5.1 Survey of funding organisations (Escuela Andaluza de Salud Pública, Granada)

5.1.1 Definition of cancer research (ONCOL)

"Cancer" is a generic term for a large group of diseases that can affect any organs or tissues of the body (e.g. breast, lung, skin or bone marrow). There are more than 100 types of cancer, which are usually named for the organs or tissues where the cancers form. Other terms used are malignant tumours or malignant neoplasms. They have been defined with reference to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), and are comprised within groups C00-C97, including all malignant neoplasms. *In situ* neoplasms (D00-D09), benign neoplasms (D10-D36) and neoplasms of uncertain or unknown behavior were excluded from this definition. Cancer types included under the codes C00-C67 are listed below.

Table 38: Neoplasms. International Disease Classifications, 10th revision (ICD-10)

ICD-10	*Disease category*
C00–C14	Malignant neoplasms, lip, oral cavity and pharynx
C15–C26	Malignant neoplasms, digestive organs
C30–C39	Malignant neoplasms, respiratory system and intrathoracic organs
C40–C41	Malignant neoplasms, bone and articular cartilage
C43–C44	Malignant neoplasms, skin
C45–C49	Malignant neoplasms, connective and soft tissue
C50–C58	Malignant neoplasms, breast and female genital organs
C60–C63	Malignant neoplasms of male genital organs
C64–C68	Malignant neoplasms, urinary organs
C69–C72	Malignant neoplasms, eye, brain and central nervous system
C73–C75	Malignant neoplasms, endocrine glands and related structures
C76–C80	Malignant neoplasms, secondary and ill-defined
C81–C96	Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic
C97	Malignant neoplasms of independent (primary) multiple sites

5.1.2 Data gathering: methods and results

We identified cancer research funding organizations (RFOs with overall investments in cancer research (ONCOL) above a baseline threshold of €0.5 million. These RFOs were asked about their sources of cancer research funding, annual spends in cancer and other NCDs research over the period 2002-2013, level of operation and coverage, expected impacts and impact measurements, basis of the funding decisions, future research plans, and other issues. Several reminders were sent and phone contacts were made to improve the response rate. The data gathered were cross-checked through online/web-searches, which also offered a tool to retrieve data from those RFOs that did not respond to the questionnaire.

The main results are the following:

- Across the EU, we found 169 Research Funding Organizations (RFOs) investing in cancer research. Some 78 of these RFOs (46%) are devoted exclusively to ONCOL, but the majority make research investments in other NCD disease areas.

- For the majority of RFOs in our sample (46%), the main funding source was governmental, and the primary funding mechanism (33% of RFOs) was calls for proposals. The primary motivation for funding ONCOL was what "benefits patients", with nearly 27% of RFOs selecting this as the main reason for their funding. Publication of scientific articles was the clear leader as a metric for monitoring progress in meeting RFOs' expectations. This underscores the importance of bibliometric analysis in describing and measuring the impact of investment in ONCOL.

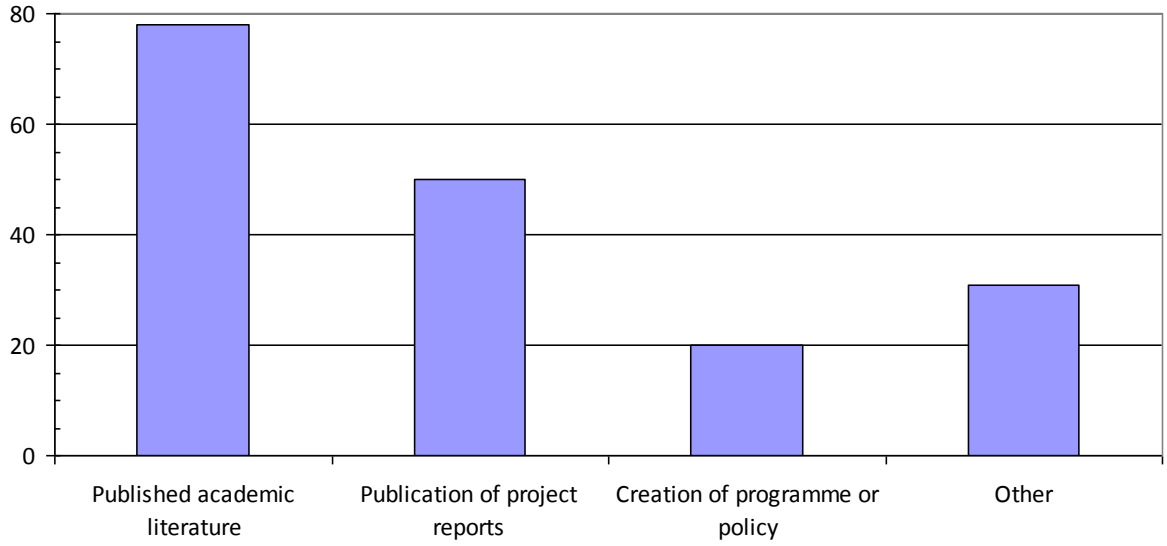

Figure 33. Measuring the impact of research funding (n=107)* *The bar chart shows the type of measure that the RFOs use to capture the impact of their research. Results combine data from the survey and online sources*

- The funding figures for Europe are substantial, with over € 1 billion *per annum* (from the year 2009 onwards, mainly). The total amount of funding over the study period (2002-2013) exceeded € 10 billion for the EU-28. For the EUR31 countries, the total expenditure on ONCOL was above € 13 billion. Figure 34 shows the expenditures for the five years, 2009-13, where data were available.

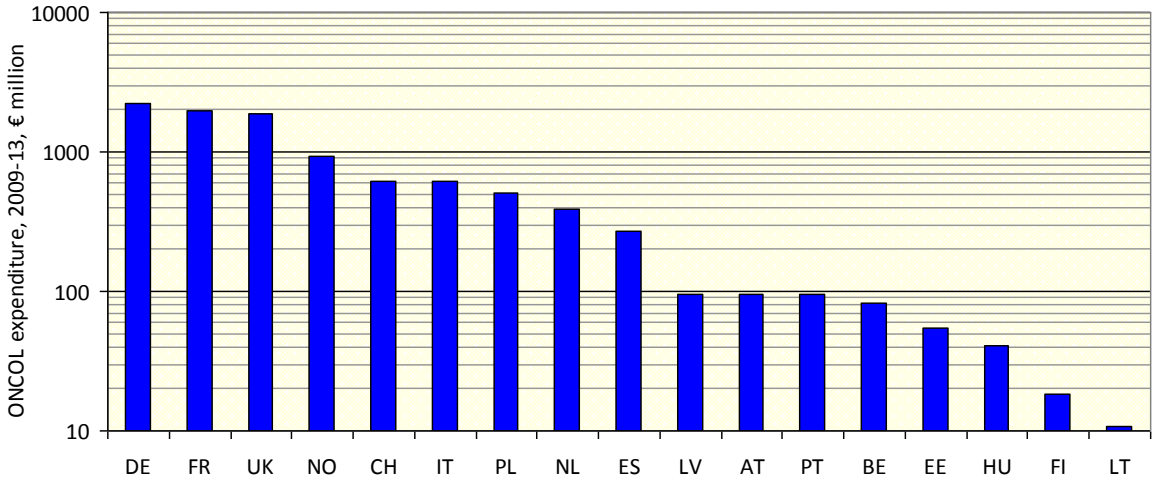

Figure 34 Reported expenditures on ONCOL in 17 EUR31 countries, 2009-13. *Note: data not available for 11 countries, including GR, SE and SI, whose spends may be > €10 M in the 5 years.*

5.1.3 Interviews: methodology

The aim of the interviews was to gather opinions and information from major policy makers, researchers, leaders of the past, present and future strategies in cancer research funding. For this purpose, a systematic process was followed for the selection of interviewees (researchers and stakeholders), the conduct of the interview, and the subsequent analysis of the data obtained.

We identified 57 experts, outstanding in the field of cancer research in their countries of origin (Austria, France, Luxembourg, Belgium, Germany, Netherlands, Denmark, Greece, Norway, Bulgaria, Hungary, Poland, Croatia, Ireland, Portugal, Cyprus, Italy, Romania, Czech Republic, Slovenia, Spain, Finland, Lithuania, Switzerland). We also contacted researchers in international organizations (WHO, IARC, WCRF). Finally, nine leading experts agreed to participate and take part in interviews. Seven of them preferred to answer by telephone, and two chose to answer written questions.

5.1.4 Interview findings

This analysis provides views about the impact of cancer research funding in Europe while identifying areas of unmet need to gain deeper insight into the main challenges that should be addressed for future research in ONCOL.

With regard to intervention programmes and impacts, it appears that while significant funding has been devoted to cancer programmes in the last decade, with major contributions made to cancer control, most efforts have been directed towards basic research and to interventions at a national level, as opposed to applied research and multinational interventions. It also appears that several publications show a decrease of academic clinical trials all over Europe. In addition, and despite the many positive impacts reported in the area of cancer in general and specifically in innovative fields such as tumour biology, it is suggested that care should be taken to ensure that benefits outweigh the risks of screening procedures and invasive tests.

A current issue which, according to respondents, needs to be addressed urgently, since it seems to constitute a major threat for the continuity of research, is the question of the specific consent requirement proposed as an amendment to the European General Data Protection Regulation. This could disable cancer registries and cancer research if approved. Indeed, information is key to cancer research and the concerns raised do seem to have substance if researchers fall inside the requirements of this regulation.

Another issue coming from the interviews is the apparent disparity in research funding allocation between communicable and non-communicable diseases, with non-communicable diseases receiving a tiny percentage of funding compared with their burden. Cancer on its own accounts for 20-29% of deaths in Europe *vs*. 1% of deaths from communicable diseases, according to data provided by a senior research interviewee. Cancer continues to be a leading cause of death and, consequently, respondents suggest there is a need for increasing funding for cancer research and prevention programmes in an effort to contribute to an overall reduction in cancer incidence and mortality. More specifically, this analysis demonstrates the need for more independent research since, amongst other consequences, commercial partnerships compromise intellectual property rights. There was a general recognition of the growing importance of personalised cancer medicine which several respondents considered to be the future of cancer research and, therefore, urged the European Union to prioritise it.

5.2 Downloading of papers and country outputs

5.2.1 Creation and calibration of the filter

The filter was first developed in consultation with Cancer Research UK, a leading charity, for the Science Citation Index on CD-ROM. It has since been extensively modified to make it apply to the Web of Science (WoS) with its different interface and software, and to take account of the additional

journals covered by the WoS, and ones added recently. It has also been amended to include newly-discovered genes that predispose a person to cancer, and new medicines. The list of title words also included the names of a large number of cancers. After several rounds of revision, with successive sets of papers being marked by our Spanish partners in the Escuela Andaluza de Salud Publica, the final values of precision and recall were **p = 0.95 and r = 0.98**.

5.2.2 Analysis of European and individual country outputs

The analysis began with a comparison of the European and world outputs in cancer research, and the determination of how much biomedical research was accounted for by oncology. For this purpose, we used a previously-developed filter based on biomedical address words, such as:

*an*esthe*, biophys, Cilag, dermatol*, epidem*, family, Genentech, hlth*, IRCCS*, Janssen*

which was found to give good discrimination between biomedical and non-biomedical papers in journals such as *Nature* and *Science*, and to provide virtually complete coverage of most biomedical journals. Table 38 shows the world outputs of biomedical research papers and ones in oncology, with the output of the 31 European countries as a group (integer counts) in biomedical research.

Table 38. Biomedical research outputs from the world and from the EUR31 country group (integer count), and the corresponding outputs in oncology.

Year	*BIOMED*			*ONCOL*			*ONCOL/BIOMED, %*	
	World	*EUR31*	*EUR %*	*World*	*EUR31*	*EUR %*	*World*	*EUR31*
2002	372134	158121	42.5	43473	17857	41.1	11.7	11.3
2003	387844	163324	42.1	46098	18908	41.0	11.9	11.6
2004	405565	168608	41.6	48023	19159	39.9	11.8	11.4
2005	425313	176562	41.5	51027	20550	40.3	12.0	11.6
2006	450141	185422	41.2	53941	21486	39.8	12.0	11.6
2007	484370	198119	40.9	58964	23334	39.6	12.2	11.8
2008	521430	209200	40.1	63670	24608	38.6	12.2	11.8
2009	545028	216739	39.8	66477	25110	37.8	12.2	11.6
2010	571067	225649	39.5	71168	26182	36.8	12.5	11.6
2011	605770	235267	38.8	74890	26862	35.9	12.4	11.4
2012	641615	248188	38.7	83025	28584	34.4	12.9	11.5
2013	665225	256864	38.6	87968	29414	33.4	13.2	11.5

So the European group of nations has diminished its presence more in cancer research (from 41% of the world to 33%) than in biomedical research overall (from 43% to 39%). The reduction is primarily because of the rise in output of China and other Asian nations such as South Korea, Taiwan and India. Cancer research represents just over one ninth of all European biomedical research output, but one eighth of world biomedical output.

For each of the original 31 countries, we determined the integer and fractional count totals, and the numbers in each of the 12 years; we also determined the annual average percentage growth rate (AAPG) based on fractional counts. [This was obtained from a plot of the logarithm of the number of papers each year.] Table 39 lists the results for ONCOL papers, with the total integer and fractional counts, the percentage of the foreign contribution and the annual average percentage growth rate. Since research output tends to be correlated with Gross National Product (rather than simply with population), we have plotted the countries' fractional paper counts against GDP for a representative year (Figure 35).

Table 39. Outputs of 31 European countries in cancer research (ONCOL), 2002-13 (12 years) in both the SCI and SSCI. Integer and fractional counts, the percent foreign contribution and the annual growth rate. *The countries are ranked by their fractional count outputs. For codes see Table 2.*

Country	*Int cts*	*Frac cts*	*% Int*	*AAPG*		*Country*	*Int cts*	*Frac cts*	*% Int*	*AAPG*
DE	60456	45436	24.8	2.6		IE	3367	2247	33.3	9.3
IT	48499	37876	21.9	4.8		PT	3136	2079	33.7	13.3
UK	52465	37541	28.4	2.4		HU	2855	1897	33.6	3.2
FR	40329	30127	25.3	4.1		HR	1720	1429	16.9	9.7
NL	23572	16068	31.8	4.5		RO	1748	1248	28.6	35.7
ES	21453	15654	27.0	7.6		SI	1298	898	30.8	10.6
SE	14881	9205	38.1	2.0		SK	1196	755	36.9	6.6
PL	9699	7543	22.2	10.0		BG	673	453	32.6	10.4
GR	9513	7243	23.9	3.8		LT	396	265	33.0	16.4
CH	12827	6837	46.7	4.1		IS	509	208	59.1	3.7
BE	10891	6253	42.6	2.9		LU	259	116	55.3	14.6
AT	8971	5563	38.0	1.1		EE	208	97	53.2	4.0
DK	7692	4713	38.7	8.0		LV	191	86	55.2	7.3
NO	6650	4054	39.0	6.2		CY	198	79	60.1	18.0
FI	6015	3721	38.1	0.0		MT	51	22	56.5	12.1
CZ	4422	3005	32.0	9.2						

This table shows that there are big differences in output, with more than three orders of magnitude between the largest (Germany) and the smallest (Malta). However, some of the smaller countries are expanding their output rapidly – notably Romania, whose fractional count output rose from only 7 papers in 2002 to over 250 in 2013.

It is also expected that researchers in the scientifically larger countries (*e.g.*, UK, Germany) would find it easier to work with a partner within the country that provided complementary expertise than researchers from small countries (*e.g.*, Estonia, Ireland) and would therefore tend to collaborate less internationally. However we might expect that international transnational links would be much weaker for the Member States in eastern Europe, and so Figure 36 has been plotted to show if this is the case. The figure shows that these "accession" Member States do indeed collaborate less than expected, whereas the five Scandinavian countries, with Belgium, Luxembourg and Switzerland, collaborate internationally more than the trend-line would suggest.

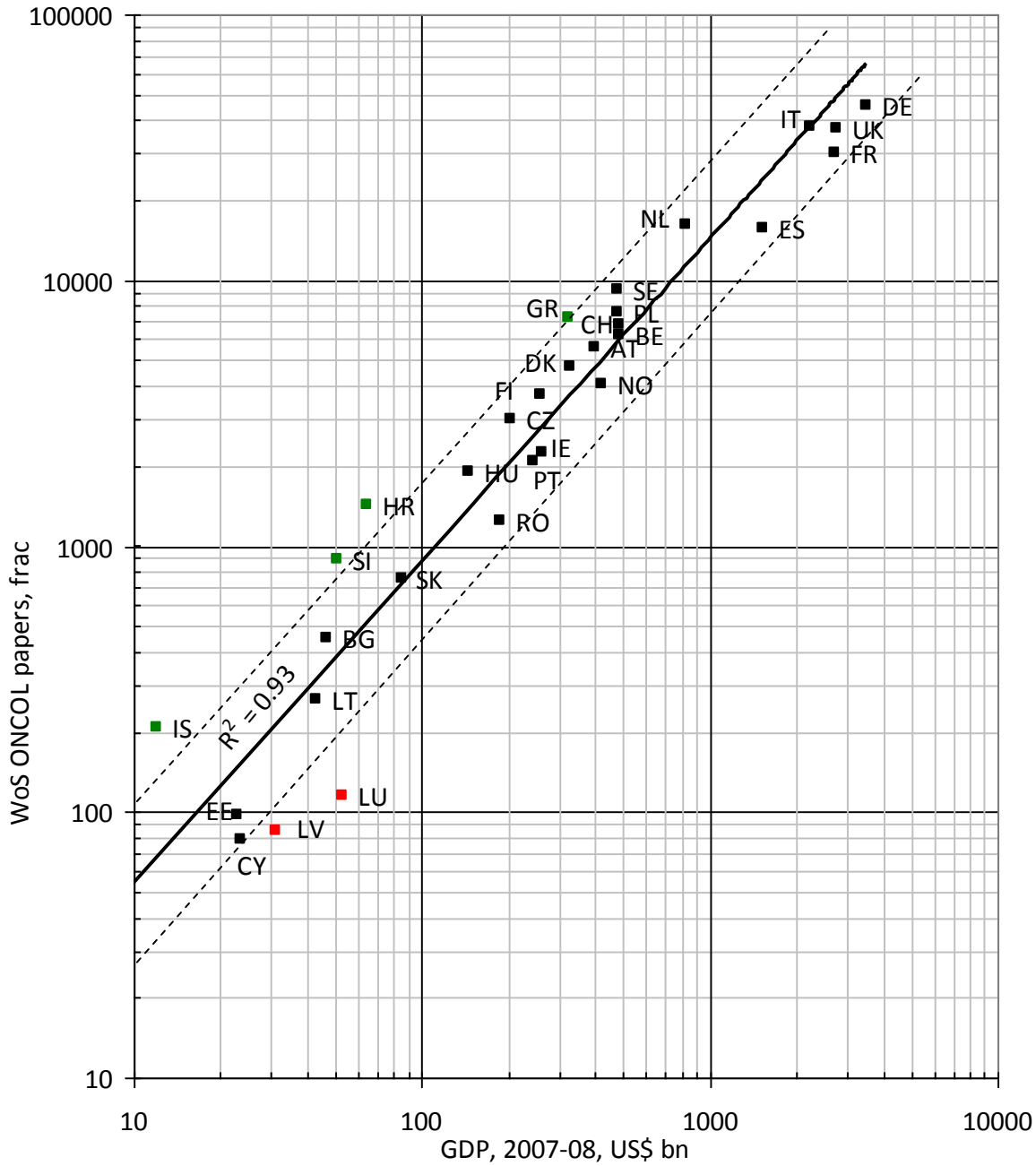

Figure 35. Plot of ONCOL paper output, 2002-13, against GDP for European countries. *Note: MT omitted. Dashed lines show values x2 or x0.5 relative to power trend-line. For codes, see Table 1.*

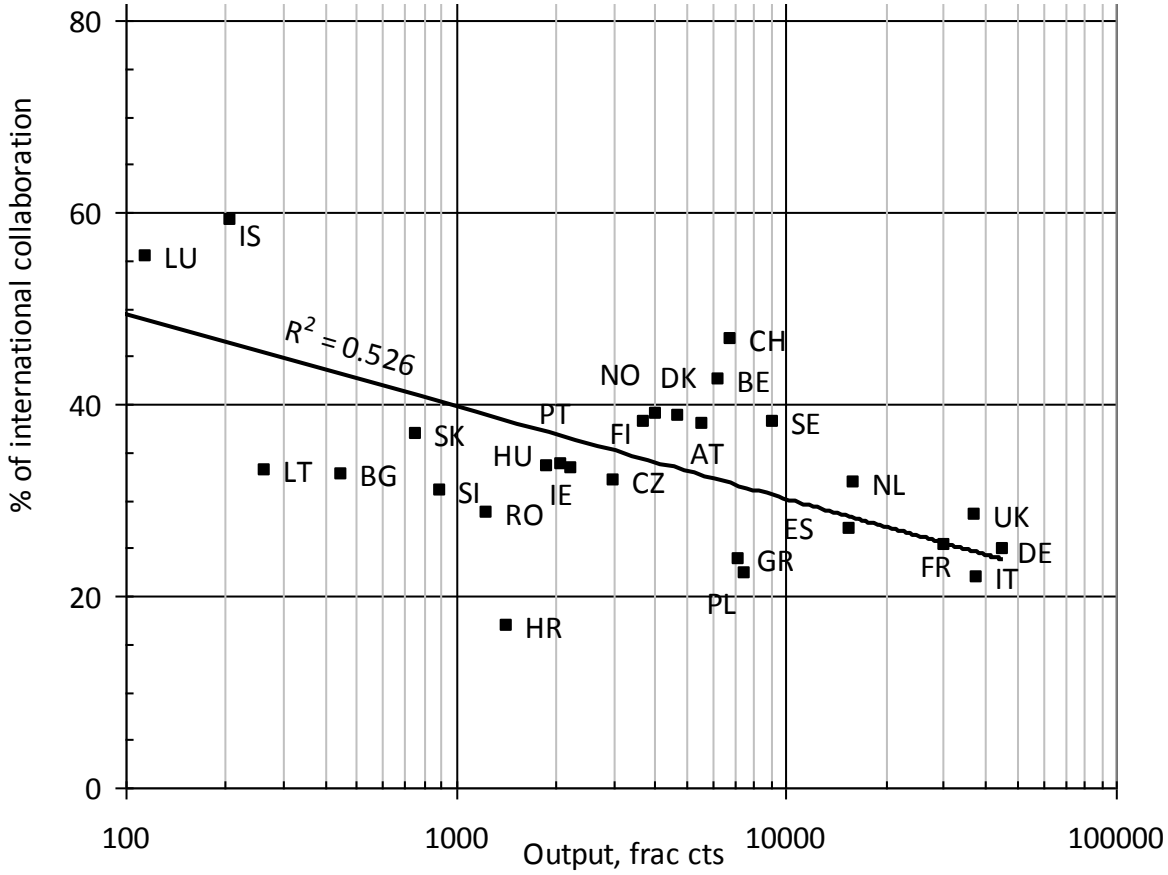

Figure 36. Percentages of international collaboration in cancer research (ONCOL), 2002-13, by European countries plotted against their output (fractional counts of papers). *For codes, see Table 1.*

5.3 Analysis of research level, citations and percentage of reviews

5.3.1 Research level of papers and journals

The research level of the papers decreased over the years from 2.05 to 1.87 (*i.e.*, they became more clinical). However the mean RLs of the journals in which the papers were published were rather more basic, with a mean of 2.1 on the scale 1 = clinical to 4 = basic research. This feature, that the European NCD research papers were more clinical than the mean for the journals in which they appeared, occurred in the other four NCD study areas.

5.3.2 Analysis of five-year citations to the ONCOL papers

Citation scores in ONCOL have been increasing slowly with time, in part because the WoS now covers more journals than previously, and also because authors are expected to be more punctilious in their acknowledgement of earlier work. Figure 37 shows the progression in ONCOL ACI scores from 2002 to 2009; the values for intermediate years (2003-08) for Europe are shown as three-year moving averages in order to smooth out annual fluctuations. The mean score for Europe was slightly below the world average in 2002-03, but since 2006 it has been slightly higher, probably because of the greatly increased world presence of China, whose papers tend to be less well cited than average.

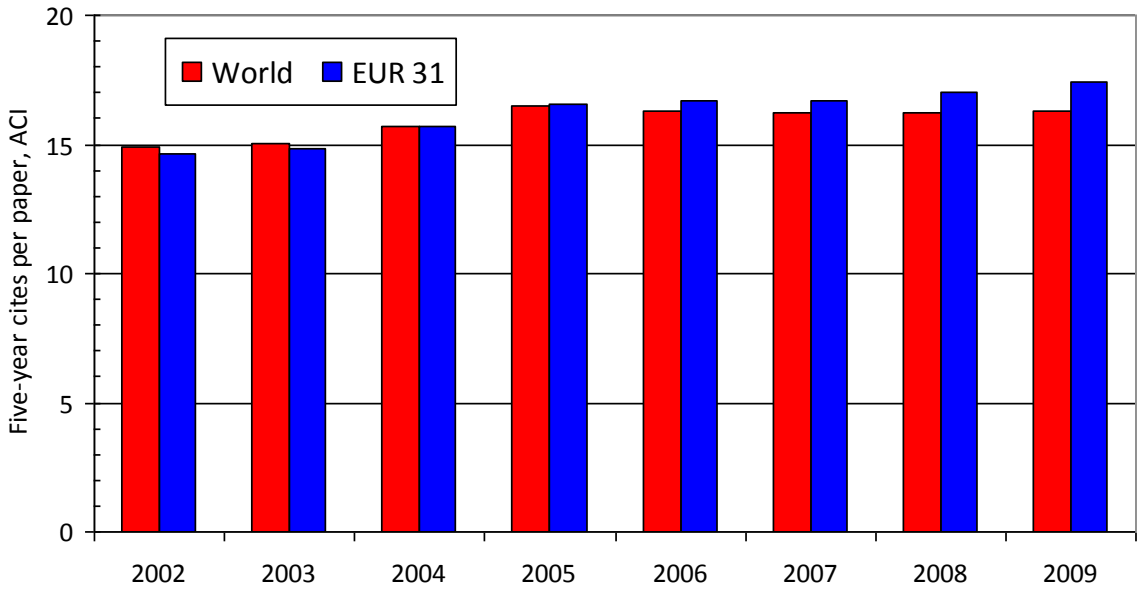

Figure 37. Chart showing the increase in mean citations per ONCOL paper with publication year, 2002-09, for world and for EUR31 papers.

The mean citations per paper for the EUR31 countries are shown in Table 40. This also shows how many of a country's papers received enough cites to put them in the top 5% of EUR31 papers in the eight-year period, for which the qualification was 53 cites. [There were actually 5.15% of European papers that achieved this number of citations.] This may be a better measure of how effective a country's research output is because it is normally the most influential papers that are really important to the development of a field.

Table 40. Citation performance of EUR31 countries in ONCOL in 2002-09, ranked by the % with 53 or more cites in the five years following publication (ACI) (Top 5%) rather than the mean value.

ISO	*Mean*	*Top 5%*	*%*		*ISO*	*Mean*	*Top 5%*	*%*		*ISO*	*Mean*	*Top 5%*	*%*
CH	19.1	280.1	6.67		FR	14.1	763.0	4.12		CZ	9.5	27.4	1.66
NL	19.4	603.1	6.17		ES	14.2	366.3	4.11		BG	6.3	3.3	1.27
UK	18.0	1469.1	6.14		IT	14.3	905.5	3.96		PL	7.9	50.9	1.25
IS	19.3	6.9	5.83		IE	13.8	47.0	3.74		RO	6.0	4.3	1.05
BE	17.2	216.6	5.44		NO	15.0	86.3	3.61		LT	5.8	1.2	1.05
DK	17.5	139.2	5.30		LV	9.4	1.5	3.25		SI	7.3	4.1	0.83
FI	16.6	117.4	4.74		PT	12.6	30.9	3.17		EE	8.5	0.3	0.60
SE	15.6	267.7	4.51		GR	9.5	89.9	1.93		MT	3.9	0.1	0.50
AT	15.0	158.0	4.37		CY	9.3	0.7	1.89		HR	5.1	3.7	0.47
LU	16.7	2.4	4.26		HU	9.3	21.7	1.81					
DE	14.3	1211.5	4.22		SK	8.9	7.7	1.75					

The mean ACI and percentage of citable papers in the top 5% are closely correlated (r^2 = 0.94) but they are different indicators of citation impact.

Figure 38 shows the effects of co-authorship with five extra-European countries for ten leading European countries. For each non-European country, the effects are quite striking. The biggest positive effect overall is seen for Australia, followed by Canada. Somewhat surprisingly, the effect of the USA being a partner was not as positive as might have been supposed, and for the 10 countries

examined and taken as a group, the mean ACI value (30.5 cites per paper) was only slightly above the values for China and Japan, and well below the values for Canada (36.6) and Australia (44.2).

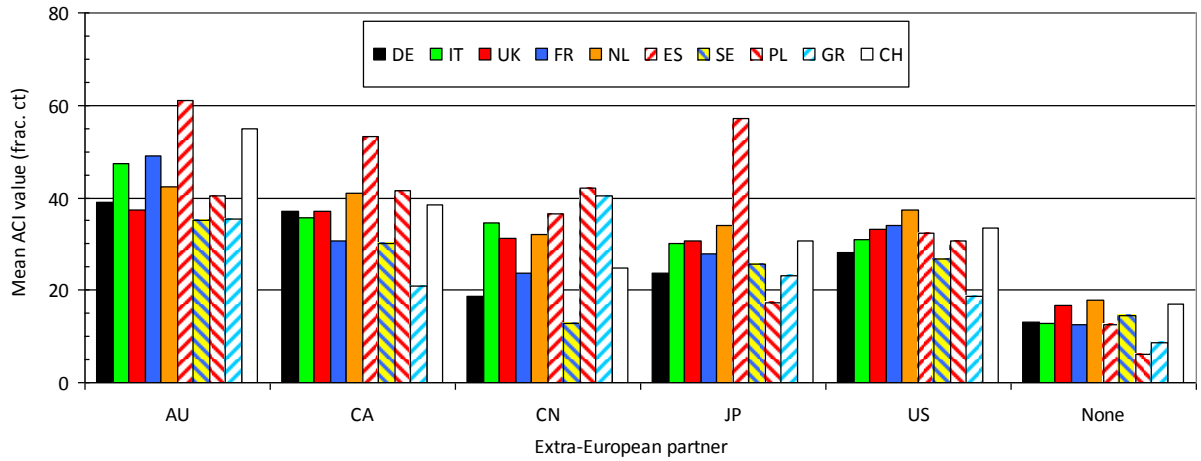

Figure 38. Mean ACI values for 10 leading European countries in cancer research, 2002-09, for their papers co-authored with a researcher from the five specified countries, or from none of 11 extra-European prospective partners. (*The others were Brazil, India, Israel, Russia, South Korea and Turkey.)*

5.3.3 The percentage of reviews

Another indicator of "quality", or more accurately the esteem with which a country's researchers are held, is the percentage of reviews (Lewison, 2009) which are usually invited by journal editors from senior scientists. Figure 39 shows this percentage, with the bars coloured according to the number of reviews published by the country in the 12-year period.

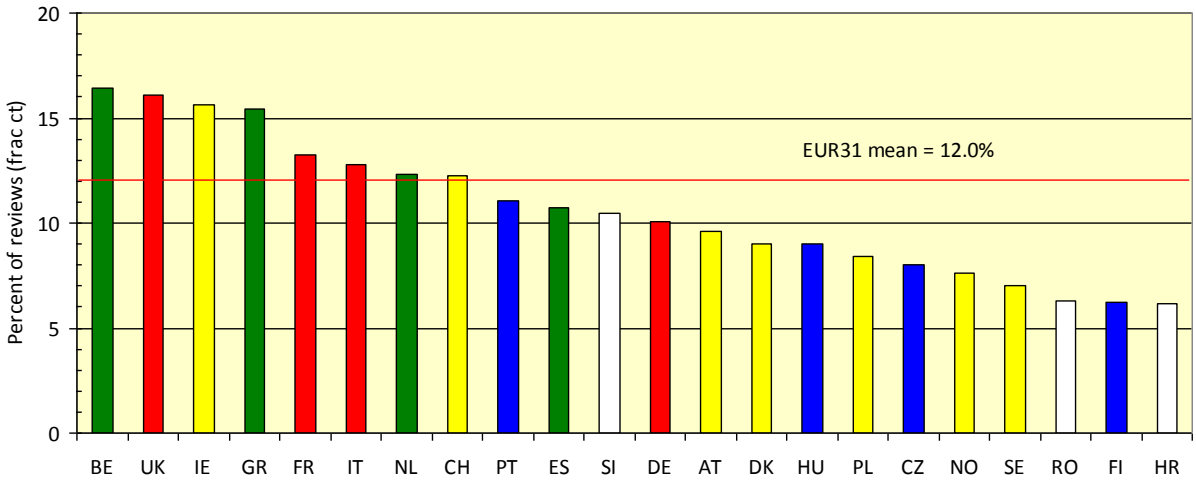

Figure 39. Chart showing the percentage of ONCOL reviews by 22 European countries with at least 50 papers classed as "reviews" in the WoS during 2002-13. *Red bars: > 3000 reviews (frac. cts); green bars: > 1000 reviews; yellow bars: > 300 reviews; blue bars: > 100 reviews; white bars: < 100 reviews.*

It is perhaps surprising that the five Scandinavian countries score relatively low on this indicator, whereas Greece performs highly and is in the top group, with > 15% of its papers classed as reviews.

5.4 Analysis by research type and by cancer site

5.4.1 Eleven research types and their definition

We had previously developed some 11 sub-filters to identify ONCOL papers of different research types. They are listed in Table 41 with their tetragraph (4-character) codes used in the tables that follow. Each of these sub-filters consisted of sets of strings searched for in the paper titles, and many of them also had strings sought in the names of the journals. An example is diagnosis, where the title strings are: *biopsies, biopsy, detect, diagnose* and the journal string is: *DIAGNOS*. Others are much more complex: the chemotherapy one lists the 151 different drugs used for this method of treatment. Some papers were identified as being of more than one research type but there were also many papers not classifiable in this way.

Table 41. List of research types in cancer research defined by sub-filters.

Research type	*Code*	*Research type*	*Code*	*Research type*	*Code*
Chemotherapy	CHEM	Palliative care	PALL	Radiotherapy	RADI
Diagnosis	DIAG	Pathology	PATH	Screening	SCRE
Epidemiology	EPID	Prognosis	PROG	Surgery	SURG
Genetics	GENE	Quality of life	QUAL		

For each of these research types, we determined the fractional count of each of the 31 countries, and these were then compared with the expected number (on the assumption that each country had the same research type profile) and the ratio of observed to expected calculated. Table 42 shows the numbers of papers and Table 43 the ratios of observed to expected numbers.

Table 42. Numbers of papers of 11 research types from each of 31 European countries in ONCOL research, 2002-13. Countries ranked by total output; fractional counts.

	CHEM	*DIAG*	*EPID*	*GENE*	*PALL*	*PATH*	*PROG*	*QUAL*	*RADI*	*SCRE*	*SURG*	*TOTAL*
DE	4483	2284	1590	8976	396	3738	4618	203	2331	376	5187	45436
IT	5701	1587	1712	6252	398	2755	3842	100	1314	381	4678	37876
UK	3514	1541	2100	6863	759	2572	4115	304	1748	675	4076	37541
FR	3737	1238	1432	4894	243	2000	2981	95.3	1687	364	3370	30127
NL	1769	739	1044	2969	264	1201	1952	195	1349	453	1814	16068
ES	1895	777	733	3362	173	1262	1766	65.9	451	198	1231	15654
SE	765	370	1055	2300	205	546	1296	95.7	474	146	651	9205
PL	769	338	361	1850	69.3	557	589	26.2	301	46.1	589	7543
GR	1148	314	290	1373	84.9	538	785	34.0	243	64.2	824	7243
CH	720	390	223	1118	63.1	559	670	22.9	400	56.8	665	6837
BE	723	222	175	906	57.9	418	543	18.6	441	96.3	627	6253
AT	665	300	180	1076	33.5	493	636	12.4	278	51.8	577	5563
DK	396	229	604	959	105	341	707	51.0	330	118	344	4713
NO	284	163	342	937	142	363	668	68.0	227	101	316	4054
FI	258	139	345	1071	35.0	335	606	19.6	115	124	237	3721
CZ	405	110	132	769	10.3	245	268	5.61	92.7	22.8	262	3005
IE	178	104	67.1	413	28.2	180	266	11.9	54.3	47.0	324	2247
PT	182	105	127	567	16.4	220	180	11.2	34.2	23.7	90.5	2079
HU	171	91.1	60.7	438	9.14	371	163	5.82	65.0	13.5	134	1897
HR	125	87.0	41.9	289	17.8	132	120	4.67	38.6	18.1	130	1429
RO	81.9	99.1	44.9	199	8.72	113	109	2.50	20.9	11.8	250	1248
SI	93.8	35.1	34.2	161	7.43	62.5	103	3.00	44.3	17.0	82.3	898
SK	71.5	21.7	39.4	199	5.98	40.4	47.4	2.89	11.2	6.10	28.4	755
BG	50.0	12.9	18.8	103	0.41	25.9	35.9	0.20	10.5	4.74	36.1	453
LT	15.9	14.3	17.9	44.6	4.27	15.1	39.7	0.00	14.9	1.94	33.7	265
IS	9.20	10.2	41.6	77.2	7.98	11.6	37.7	6.18	1.18	7.66	12.4	208
LU	7.08	1.50	3.30	25.4	0.25	6.30	7.88	0.17	0.05	4.80	4.15	116
EE	6.34	2.36	5.12	27.2	0.00	10.3	22.7	1.10	3.02	2.98	3.72	97
LV	4.86	6.21	8.45	24.2	1.00	4.24	8.39	0.00	2.15	2.98	4.40	86
CY	8.91	2.32	4.95	12.2	5.86	2.25	4.62	2.00	3.04	0.27	3.00	79
MT	2.95	0.01	2.21	4.04	0.00	1.50	1.32	0.00	0.20	0.01	0.14	22
EUR31	28240	11334	12836	48259	3152	19119	27189	1369	12085	3437	26585	252718
%	11.2	4.5	5.1	19.1	1.2	7.6	10.8	0.5	4.8	1.4	10.5	

Clearly, genetics is the dominant research type, followed by chemotherapy, prognosis and surgery. Very little research attention is evidently paid to quality of life, palliative care or screening.

Table 43. Ratio of observed to expected numbers of papers in 11 research types for the leading 18 European countries, 2002-13, with > 2000 papers. *Values > 2 tinted bright green; values > 1.41 tinted pale green; values < 0.71 tinted orange; values < 0.5 tinted pink.*

	CHEM	*DIAG*	*EPID*	*GENE*	*PALL*	*PATH*	*PROG*	*QUAL*	*RADI*	*SCRE*	*SURG*
DE	0.88	1.12	0.69	1.03	0.70	1.09	0.94	0.82	1.07	0.61	1.09
IT	1.35	0.93	0.89	0.86	0.84	0.96	0.94	0.49	0.73	0.74	1.17
UK	0.84	0.92	1.10	0.96	1.62	0.91	1.02	1.50	0.97	1.32	1.03
FR	1.11	0.92	0.94	0.85	0.65	0.88	0.92	0.58	1.17	0.89	1.06
NL	0.99	1.03	1.28	0.97	1.32	0.99	1.13	2.24	1.76	2.07	1.07
ES	1.08	1.11	0.92	1.12	0.89	1.07	1.05	0.78	0.60	0.93	0.75
SE	0.74	0.90	2.26	1.31	1.79	0.78	1.31	1.92	1.08	1.17	0.67
PL	0.91	1.00	0.94	1.28	0.74	0.98	0.73	0.64	0.83	0.45	0.74
GR	1.42	0.97	0.79	0.99	0.94	0.98	1.01	0.87	0.70	0.65	1.08
CH	0.94	1.27	0.64	0.86	0.74	1.08	0.91	0.62	1.22	0.61	0.92
BE	1.03	0.79	0.55	0.76	0.74	0.88	0.81	0.55	1.47	1.13	0.95
AT	1.07	1.20	0.64	1.01	0.48	1.17	1.06	0.41	1.05	0.68	0.99
DK	0.75	1.08	2.52	1.07	1.79	0.96	1.39	2.00	1.46	1.84	0.69
NO	0.63	0.90	1.66	1.21	2.81	1.18	1.53	3.10	1.17	1.83	0.74
FI	0.62	0.83	1.83	1.51	0.75	1.19	1.51	0.97	0.65	2.45	0.61
CZ	1.21	0.82	0.86	1.34	0.27	1.08	0.83	0.34	0.65	0.56	0.83
IE	0.71	1.03	0.59	0.96	1.01	1.06	1.10	0.98	0.51	1.54	1.37
PT	0.78	1.13	1.20	1.43	0.63	1.40	0.80	0.99	0.34	0.84	0.41

For each research type, the higher and lower ratios should balance, but not all the country ratios are given in Table 43, so that some research types appear to be over- or under-researched. There are some patterns emerging, such as the strength in palliative care of Scandinavian countries (but not Finland), and in epidemiology of all four and particularly of Iceland (ratio = 3.94).

5.4.2 Twenty two cancer manifestations (sites) and their definition

A similar set of sub-filters was created to identify ONCOL papers where the focus was on the cancer site of concern – again, some papers mentioned several sites and many more made no mention of any site. Table 44 lists the cancer sites, with their assigned trigraph codes.

Table 44. List of 22 cancer manifestations (body sites) for which sub-filters were developed to identify relevant ONCOL papers.

Site	*Code*	*Site*	*Code*	*Site*	*Code*
bladder	BLA	liver	LIV	pancreas	PAN
bone	BON	lung, trachea, bronchus	LUN	prostate	PRO
brain	BRA	lymphoma	LYM	stomach	STO
cervix	CER	breast	MAM	testicles	TES
colon / rectum	COL	melanoma	MEL	thyroid	THY
gallbladder	GAL	mouth (head & neck)	MOU	uterus	UTE
kidney	KID	oesophagus	OES		
leukaemia	LEU	ovaries	OVA		

Table 45. Ratio of observed to expected numbers of papers relevant to 13 main cancer sites for the leading 18 European countries, 2002-13, with > 2000 papers. Countries are ranked by total output, fractional counts. Cancer sites ranked from left to right by amount of research output, based on integer counts. *Values > 2 tinted bright green; values > 1.41 tinted pale green; values < 0.71 tinted orange; values < 0.5 tinted pink*.

	MAM	*COL*	*LEU*	*LYM*	*PRO*	*LUN*	*LIV*	*STO*	*BRA*	*MEL*	*MOU*	*KID*	*OVA*
DE	0.75	0.85	1.07	1.05	1.06	0.81	1.16	1.19	1.24	1.12	1.04	1.22	0.78
IT	0.92	0.93	1.08	1.09	0.89	1.15	1.34	1.03	1.10	1.04	0.82	0.90	1.06
UK	1.19	1.15	0.92	0.87	1.09	0.80	0.68	0.77	0.83	0.85	1.23	0.83	1.08
FR	0.92	0.89	1.00	1.14	0.99	1.14	1.24	0.92	0.99	0.89	0.61	1.35	0.85
NL	1.09	1.33	0.81	0.75	1.10	1.20	0.80	1.03	0.80	1.00	1.52	0.86	0.84
ES	0.99	1.10	0.99	1.25	0.78	1.24	1.18	0.97	1.00	0.95	1.19	1.05	0.69
SE	1.17	1.14	1.07	0.87	1.61	0.67	0.52	0.83	1.12	0.85	0.71	0.74	0.96
PL	1.01	0.93	1.43	0.71	0.47	1.19	0.62	1.16	0.83	1.07	0.64	0.96	1.93
GR	1.23	1.07	0.88	1.25	0.82	1.56	1.03	1.40	0.71	0.67	1.15	0.85	1.64
CH	0.84	0.72	0.73	1.20	0.90	1.01	0.94	0.65	1.22	1.38	1.28	0.81	0.63
BE	1.11	0.74	0.88	0.79	0.97	1.26	1.04	0.96	0.92	0.94	1.19	0.77	0.99
AT	1.00	0.75	1.26	1.06	1.28	0.67	1.03	0.66	1.12	1.39	0.92	1.33	1.19
DK	1.41	1.49	0.89	1.02	0.70	1.12	0.40	0.75	0.71	1.17	0.96	0.51	1.85
NO	1.32	1.42	0.89	0.86	1.07	0.92	0.47	0.86	1.08	0.94	0.83	0.33	1.84
FI	1.48	0.94	0.70	0.66	1.96	0.70	0.36	1.09	0.76	0.91	1.70	0.90	1.67
CZ	0.66	1.01	2.00	1.37	0.62	0.66	1.10	0.80	0.87	0.82	0.65	1.31	0.86
IE	1.59	1.35	0.51	0.57	1.37	1.03	0.54	1.08	0.66	0.76	0.90	1.30	0.67
PT	1.39	0.86	0.56	0.60	0.92	0.83	0.61	2.22	0.64	0.76	0.52	0.77	0.61

This table shows which countries are strong (relative to their overall ONCOL output) in research on the different cancer sites. There are actually relatively few marked differences from the European average (denoted by a score of unity), but liver cancer is little researched in Scandinavia, Ireland and the UK, whereas the reverse is true for breast cancer. Prostate cancer is strong in Finland but weak in Poland; the reverse is true for leukaemia.

5.5 The burden of disease from different cancers

5.5.1 Data on DALYs from the Global Burden of Disease

For cancer, data were provided in the GBD study (see Murray et al., 2012) on some 24 different manifestations, not all of which corresponded to our analysis of sites (see Table 44, above). However DALYs were given for all 13 of the sites listed in the columns of Table 45, and the percentages of total DALYs (all disease areas) for the 18 countries are shown in Table 46.

It is noticeable that the smaller countries are more likely to depart from the European mean in terms of burden of disease, though there is no particular reason why this should be so. In all countries, lung cancer imposes the greatest burden (though in Portugal colorectal cancer is almost as much), but since the cancer sites are ordered in terms of research output to make comparison with Table 45 easier, it is clear that it is not receiving the attention from researchers that it appears to warrant. Melanoma imposes an above-average burden in the Scandinavian countries (Norway, Sweden, Denmark and Iceland), probably because of their inhabitants' tendency to be fair-skinned.

Table 46. Percentages of all DALYs for 13 cancer sites (for codes, see Table 11) for 27 European countries in 2010. *Values > 2 x EUR31 average tinted pink; values > 1.41 x average tinted pale yellow; values < 0.71 x average tinted pale green; values < 0.5 x average tinted bright green.*

	MAM	COL	LEU	LYM	PRO	LUN	LIV	STO	BRA	MEL	MOU	KID	OVA
DE	1.57	2.12	0.66	0.47	0.89	3.59	0.56	0.91	0.61	0.26	0.28	0.67	0.49
IT	1.66	2.21	0.76	0.57	0.76	3.45	1.01	1.15	0.66	0.22	0.24	0.57	0.43
UK	1.76	1.94	0.58	0.63	0.87	3.65	0.36	0.56	0.60	0.31	0.21	0.46	0.55
FR	1.69	2.00	0.72	0.53	0.92	3.68	0.90	0.58	0.84	0.25	0.42	0.46	0.47
NL	1.87	2.51	0.65	0.57	0.92	4.63	0.32	0.68	0.77	0.44	0.19	0.61	0.55
ES	1.33	2.23	0.63	0.46	0.85	3.35	0.77	0.92	0.77	0.19	0.27	0.54	0.39
SE	1.30	1.88	0.57	0.50	1.34	2.50	0.47	0.52	0.77	0.42	0.18	0.58	0.55
PL	1.12	1.73	0.51	0.34	0.45	4.15	0.37	0.94	0.66	0.24	0.25	0.46	0.53
GR	1.43	1.46	0.73	0.26	0.79	3.96	0.57	0.92	0.85	0.12	0.13	0.44	0.37
CH	1.71	1.73	0.59	0.54	1.08	3.15	0.62	0.59	0.69	0.37	0.28	0.55	0.49
BE	1.82	2.04	0.60	0.53	0.93	4.07	0.42	0.59	0.67	0.25	0.29	0.56	0.46
AT	1.40	1.74	0.63	0.40	0.85	3.10	0.65	0.80	0.56	0.33	0.25	0.57	0.45
DK	1.73	2.35	0.58	0.51	1.10	4.33	0.40	0.51	0.88	0.41	0.25	0.65	0.60
NO	1.20	2.14	0.51	0.51	1.16	2.92	0.24	0.52	0.79	0.51	0.19	0.56	0.56
FI	1.31	1.37	0.51	0.60	0.87	2.50	0.49	0.68	0.70	0.29	0.18	0.58	0.44
CZ	1.24	2.60	0.62	0.39	0.69	3.75	0.57	0.83	0.63	0.31	0.30	0.85	0.54
IE	1.64	1.93	0.56	0.54	0.77	2.98	0.36	0.63	0.73	0.27	0.17	0.39	0.54
PT	1.44	2.45	0.63	0.50	0.93	2.46	0.59	1.70	0.81	0.16	0.32	0.29	0.30
HU	1.26	2.44	0.55	0.32	0.55	4.51	0.47	0.94	0.54	0.22	0.66	0.44	0.38
HR	1.30	2.25	0.53	0.37	0.63	3.75	0.58	1.07	0.71	0.28	0.33	0.46	0.35
RO	1.01	1.37	0.44	0.28	0.39	2.83	0.70	0.99	0.56	0.13	0.37	0.26	0.32
SI	1.44	2.35	0.56	0.43	0.78	3.60	0.58	1.10	0.60	0.42	0.26	0.48	0.49
SK	1.09	2.22	0.53	0.32	0.48	2.91	0.52	0.87	0.64	0.27	0.50	0.54	0.43
BG	1.06	1.68	0.40	0.21	0.44	2.73	0.63	1.04	0.62	0.12	0.21	0.28	0.22
LT	1.07	1.42	0.53	0.24	0.55	2.34	0.28	1.17	0.53	0.18	0.29	0.55	0.53
IS	1.29	1.48	0.52	0.46	1.18	3.21	0.29	0.48	0.85	0.37	0.18	0.75	0.38
LU	1.46	1.97	0.63	0.45	0.69	3.30	0.72	0.51	1.04	0.25	0.30	0.40	0.33

The correlation between the relative disease burden and the relative amount of research (Table 41) is mostly poor or very poor; only in Italy and France is it positive. This suggests that for most countries in Europe, the cancer research portfolio is not well adjusted to reflect their relative burden. For example, the high relative burden from melanoma in Scandinavia has not led to an above-average concentration of research effort on this manifestation of cancer. Figure 39 shows the overall situation, with a positive but rather small correlation between disease burden and research output, but it is apparent that lung cancer is under-researched and perhaps breast cancer over-researched.

This graph shows that the leading cancer disease burdens in Europe are from lung, colorectal and breast cancers, in that order. These three cancers were selected for the analysis of the references on clinical guidelines, of which some data on the first of these, lung cancer, are given in the next section.

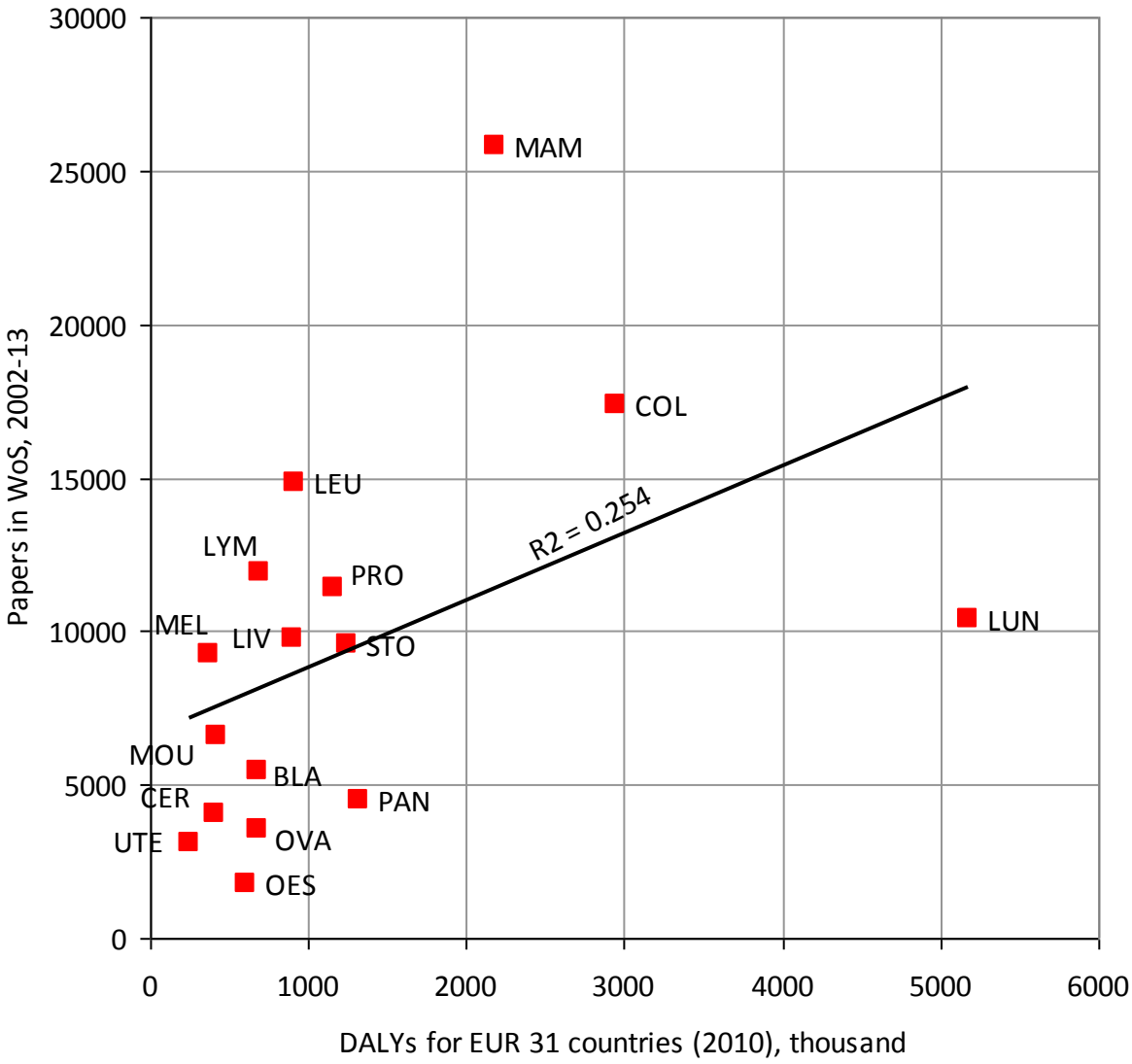

Figure 40. Scatter plot of European outputs of papers on research on different manifestations of cancer, 2002-13, as a function of the European burden of disease from the different cancer sites, 2010.

5.6 References on cancer clinical guidelines

5.6.1 Lung cancer clinical guidelines: preliminary study

The example chosen here is the set of 17 guidelines for lung cancer (almost always the most burdensome form of the disease) in five countries: France, Germany, Italy, Spain and the UK. There were a total of 3232 references, but only 2512 of them could be identified as papers in the WoS, and their parameters determined. Some of the papers were cited on more than one of the 17 guidelines, with one being cited on seven of them. Although the guidelines were all published in the years 2008-14, some of the cited papers appeared as long ago as the 1960s, and the inter-quartile range was from 1998 to 2006.

As expected, the large majority (78%) of the cited papers were in the sub-field of lung cancer research, and they were very clinical in character. Figure 41 shows that papers from European countries, and Canada, are relatively over-cited compared with their presence in lung cancer

research, but research from east Asian countries (China, South Korea and to a lesser extent, Japan) is almost ignored. This was found previously in a study of 43 UK cancer clinical guidelines (Lewison & Sullivan, 2008).

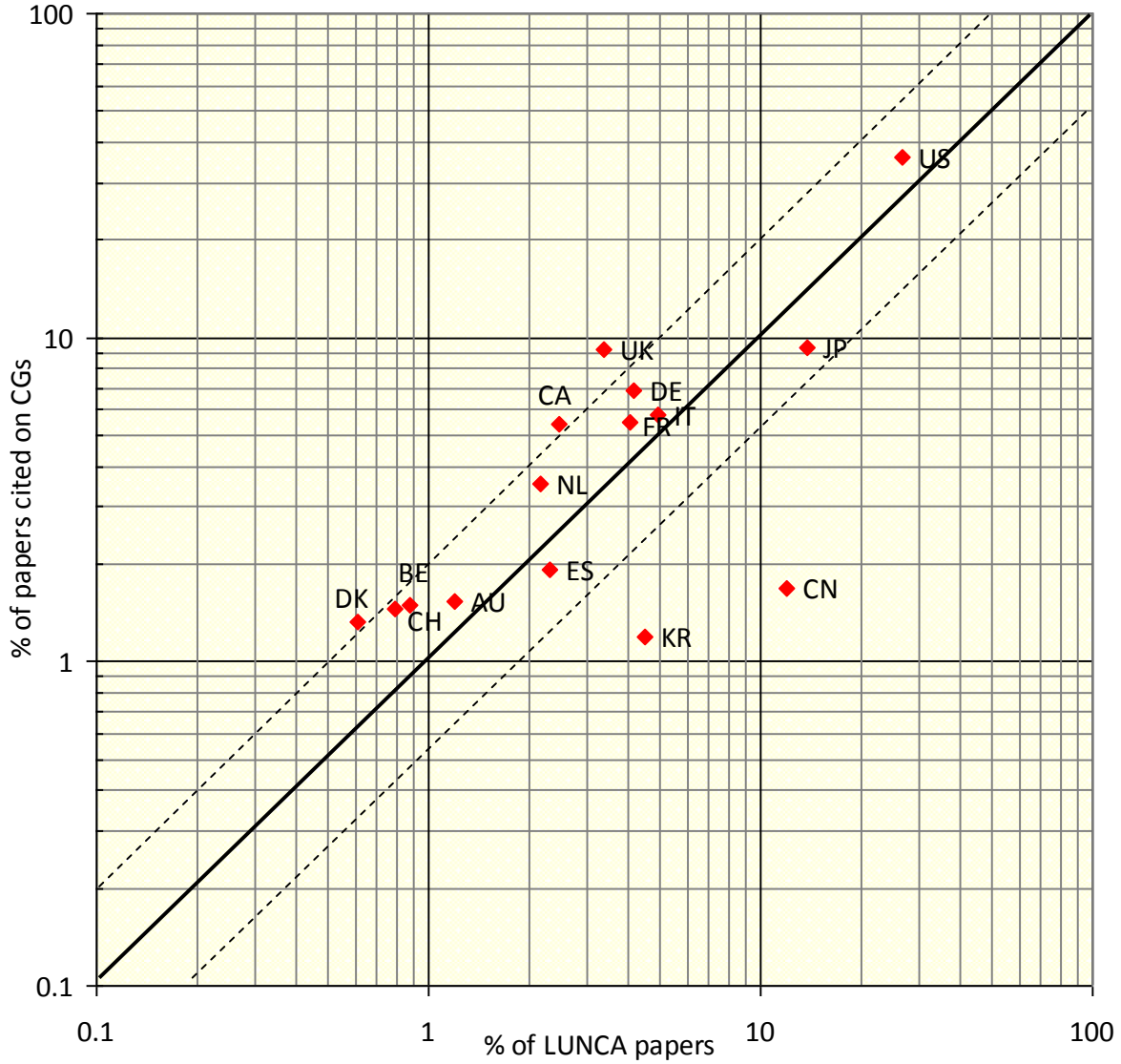

Figure 41. Comparison between presence of leading countries in the papers cited on 17 European clinical guidelines on lung cancer and their presence in lung cancer research, 2004-13, fractional counts. (Dashed lines indicate a factor of two, up or down.)

There is a big difference between the types of research cited on the 17 clinical guidelines and those forming the lung cancer *oeuvre*. This is shown in Figure 42. The evidence base for the clinical guidelines depends much more on the three treatment options (surgery, SURG; chemotherapy, CHEM; and radiotherapy, RADI) and much less on genetics (GENE). There is a contrast here, because papers of the different research types achieve very different levels of academic citations, with the most highly cited (genetics) obtaining more than twice the citation score of one of the least cited (surgery), see Figure 43. But as Figure 42 shows, surgery papers have the most influence on patient treatment, whereas genetics papers have very little. Genetics papers in lung cancer may obtain the most citations, and so may impress grant-giving bodies, but it is lung cancer surgery research that may actually benefit patients through its effect on clinical guidelines.

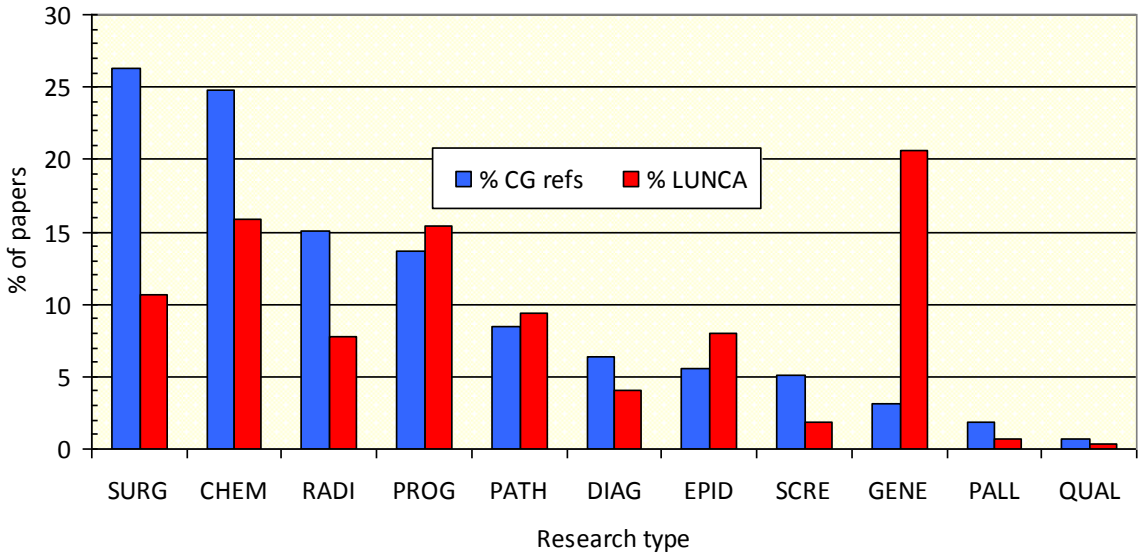

Figure 42. Chart showing the different types of research found in lung cancer, 2004-08, and in the papers cited on 17 European lung cancer clinical guidelines. *For codes see Table 41*.

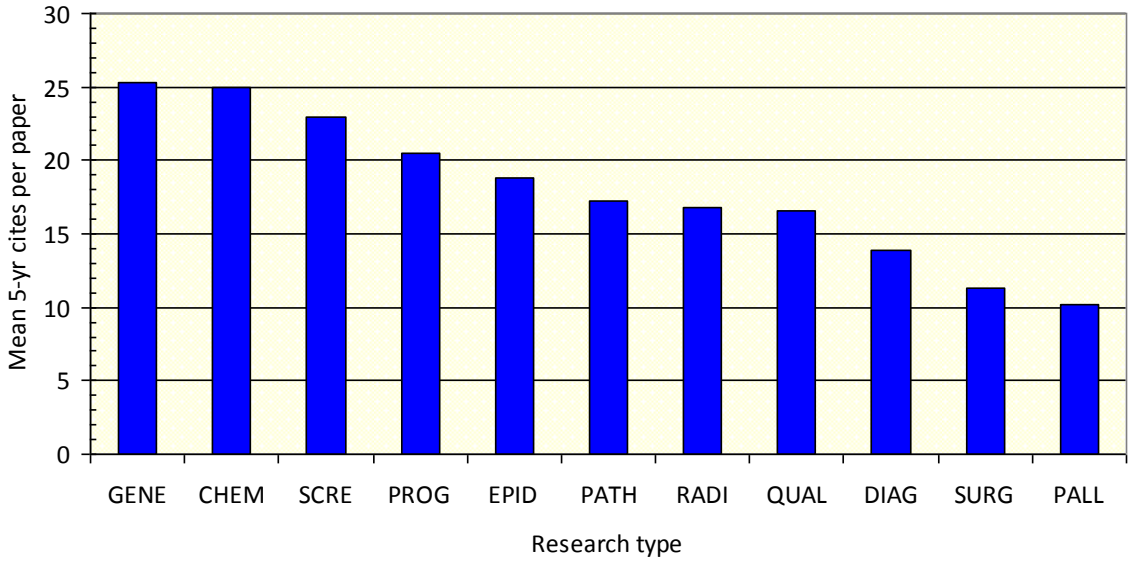

Figure 43. Mean five-year citation scores for European lung cancer papers, 2004-09, of different research types (for codes, see Table 2.)

6 Respiratory diseases research (RESPI)

6.1 Survey of funding organisations (London School of Economics)

6.1.1 Definitions of Chronic Respiratory Diseases (CRDs, RESPI)

CRDs are a group of illnesses that produce respiratory abnormalities under which breathing becomes slowed or forced. CRDs constitute a major public health problem across both the developed and the developing world. By 2020, the World Bank/World Health Organization projects that Chronic Obstructive Pulmonary Disease (COPD) will be the fifth highest disease in terms of the worldwide burden. The other prevalent conditions within the broader category of CRDs include: emphysema, chronic bronchitis, asthma, pulmonary arterial hypertension and cystic fibrosis with pulmonary manifestations. The conditions are outlined under the ICD-10 codes J44-J45, I27 and E84, and are listed below within these precise categories. For the purposes of data collection, research investment in RESPI was defined as 'research into causation, occurrence, clinical features, pathophysiology and treatment of non-communicable diseases affecting upper and lower airways and lung parenchyma'.

Table 47 ICD-10 Definitions (CRDs)

ICD-10	*Diseases*
J44	Chronic Obstructive Pulmonary Disease (COPD)
J44.1	COPD with acute exacerbation, unspecified
J44.8	Other specified COPD, Chronic bronchitis: asthmatic (obstructive) NOS, emphysematous NOS, obstructive NOS
J44.9	COPD, Chronic obstructive, airway disease NOS, lung disease NOS
J45	Asthma
J45.0	Predominantly allergic asthma
J45.1	Non allergic asthma
J45.8	Mixed asthma
J45.9	Asthma, unspecified, Asthmatic bronchitis NOS Late-onset asthma
I27	Pulmonary hypertension
E84	Cystic fibrosis with pulmonary manifestations

6.1.2 Data gathering from literature and the Web

We conducted a survey of research investment and funding flows for CRDs across the European area. The survey identified a total of 114 Research Funding Organizations (RFOs) investing in RESPI research. Of these 45 RFOs have a baseline research funding commitment of greater than € 0.1 million, which is broadly sufficient to influence the conduct of research within the disease category. Few of the 114 RFOs identified were devoted exclusively to RESPI research (n=10), and the overwhelming majority made research investments in other NCD disease areas.

As for the other NCDs, it is likely that the RESPI survey does not capture all research funding activity in the disease area. However, the reliability of the surveys across the NCD disease areas are affected by similar factors, but to different degrees. In the case of CRDs, the reliability of the results for the IA are limited by: (a) the public availability of data; (b) the cooperation of identified RFOs; (c) the general transparency of institutions operating in the area of CRDs; and (d) the arbitrary nature of the funding threshold.

The annual investment threshold varies across the five disease categories. In terms of CRDs, we manipulated the threshold given that it would otherwise privilege higher spending RFOs over lower spending RFOs. For example, above the € 0.5 million threshold, the study only identified 26 RFOs

across the whole of Europe. Consequently, the threshold was lowered to € 0.1 million to include an extra 19 RFOs. But, even at this low level, the study seemed to exclude RFOs from smaller MS. In order to ensure that these MSs were represented in the analysis, we included an additional 13 RFOs below the € 0.1 million threshold, the majority of which are from smaller MS.

Table 48 RESPI RFOs Annual Funding Threshold (2013) and amounts reported

Threshold	*N*	*Max*	*Min*	*Total reported*
> € 500K	26	€ 31,709,000.00	€ 525,000.00	€ 200 million
> € 100K	45	€ 31,709,000.00	€ 104,309.09	€ 214 million
< € 100K	13*	€ 98,012.68	€ 4,969.1	£ 0.6 million
Total with financial data 2013	58**			

**These RFOs were mostly located in MS that otherwise contained no relevant funding organizations.*
*** Represents the number of RFOs from the n=78 that actually provided financial data for 2013*

Unusually compared with the other NCDs the mid-sized RFOs contributed more than the large ones.

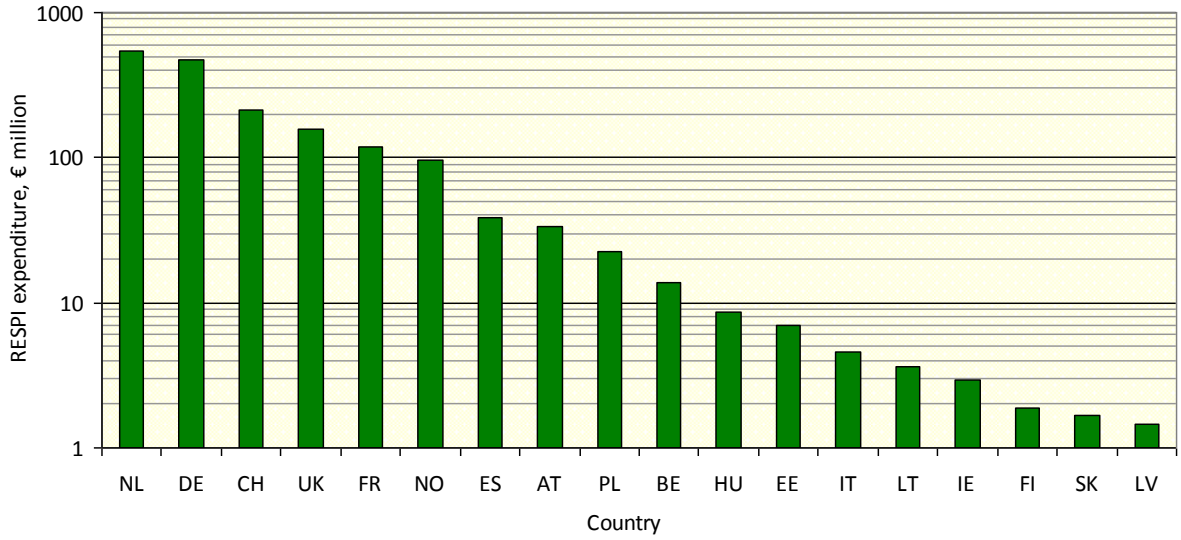

Figure 44. Annual expenditure by 18 European countries on RESPI research, € million. *Note: data not available from 12 countries, including Greece, Sweden.*

Having made a funding investment, CRD RFOs were asked about their goals, expectations and processes for monitoring investments. For example, what kinds of impacts did RFOs expect investments to make? Did they hope to deliver advances in drug therapies, improved access to new therapies, increased public and political attention, publication of academic papers and clinical guidelines? Results revealed that RFO expectations varied, and were distributed relatively evenly between four key deliverables: academic papers, improved access, therapeutic advances and increased attention. For many RFOs, the most important impacts were published academic papers (61 RFOs) and improving access to new therapies or care (60 RFOs). In most cases, RFOs did indeed require fund recipients to publish an academic article and final report within the lifetime of the project. Only 15% of the RFOs surveyed had different requirements, which are listed below as 'other'. Among this category, the most common expectations were the production of pharmaceutical patents and the commercial use of project results. Of additional interest is that only 12 RFOs listed legislative changes as an expected impact when most of surveyed RFOs were in fact public sector institutions.

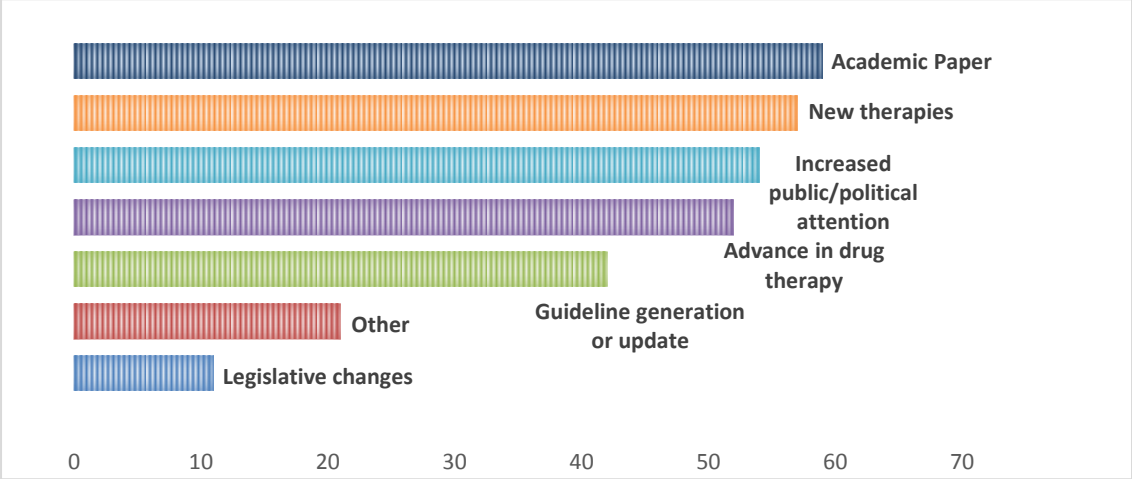

Figure 45. RFO Expected Impacts (n=82)* **The RFOs provided more than one answer. In addition, website enquires uncovered a range of expected impacts within single RFOs. Results combine data combined from survey and from online sources.*

6.1.3 Interviews: people contacted and methodology

While accurate mapping of RFOs and their funding activities *via* surveys and bibliometrics can assist government in identifying the most fruitful approaches to making in NCD investments research; policy makers must also take account of the often strong visions and firm priorities of leaders in the field of CRD research. To this end, we conducted semi-structured interviews as a means for eliciting the preferences and opinions of key CRD stakeholders. In this way, MAPPING_NCDs opens a dialogue with CRD researchers on the basis that qualitative interviews hold the potential to develop wider theory and hypothesis for both mapping CRD research funding, and also improving the relevance, efficiency and impact of CRD research investment.

Stakeholders were selected to reflect a range of factors including: expertise in RESPI research, geographic location and expertise in awarding research funding. For all stakeholders, interview questions explored (1) current threads of research; (2) future research areas; (3) types of collaboration; (4) working with collaborators; (5) working with the commercial sector ; (6) types of funding organizations; (7) working with funding organizations; (8) future strategies for funding NCD research. Personnel were selected to reflect a range of geographical regions across the EU. The aim was to solicit views and experiences of people involved in both the conduct and funding of research across the EU area. In total, 14 interviews were conducted. All interviews were recorded and transcribed. Consent was gained for all interview subjects and their anonymity. Transcripts were typed verbatim, proof read and corrected, while notes and comments were collected and made into memos. Transcripts were analyzed on a thematic basis, with responses collated under the most common themes. Some of the main findings are reported in the section below.

6.1.4 Interviews: main findings

Interviews with stakeholders revealed five major themes with regard to the future of research in the area of CRDs. There was a generalised recognition of the growing importance of stratified medicine, which several informants considered to be the future of research across the wider spectrum of NCDs. Other respondents emphasised the importance of directing research towards tackling individual CRDs such as COPD and asthma. For COPD, informants stressed that the future was both about non-clinical measures like smoking cessation, public health and health service delivery and about relieving the symptoms of COPD *via* pharmaceutical treatments. For asthma, our respondents suggested there was greater scope for developing innovative and game-changing pharmaceuticals

than for COPD. Across the broader spectrum of CRDs, and indeed all NCDs, respondents also suggested that there was a need to find new ways of working with the commercial sector.

Consistent with the academic literature, stakeholders emphasised that the model for drug discovery has changed and that pharmaceutical companies were less prepared to take risks with allocation of resources. Consequently, there was a need for academic institutions to pursue the basic science that pharmaceutical companies were no longer able to conduct for themselves. Other informants suggested that these new research requirements needed to fit within a wider strategic approach to the funding of NCD research that accommodated both the needs of researchers and the requirements of funders to demonstrate the effectiveness of their investments.

6.2 Downloading of papers and country outputs

6.2.1 Development and calibration of the filter

This subject area, and its definition, was discussed with Professor Tariq Sethi of Guy's Hospital, King's College London. It was agreed that it should include the major non-infectious respiratory diseases, such as allergic rhinitis, asthma, chronic obstructive pulmonary/respiratory disease, cystic fibrosis, and emphysema, but that it could also include the effects of infection if the primary problem was one of pulmonary insufficiency (*e.g.*, for environmental or genetic reasons). The filter was very short and listed four specialist journals and eight title words or phrases. It generated the smallest of the five NCD files, with just 18822 papers, of which 188 were in the SSCI only (1.0%). The calibration gave values for precision, **p = 0.939** and **recall, r = 0.884**.

6.2.2 Outputs of EUR31 countries

The world and European outputs, year by year, of RESPI research papers are given below.

Table 49. Outputs of respiratory disease research papers (RESPI) in the Web of Science from 2002 to 2013 from EUR31 group of countries, integer and fractional counts.

	RESPI					*RESPI/BIOMED, %*	
Year	*World*	*EUR31 Int*	*EUR31 frac*	*EUR %*	*Int'l %*	*World*	*EUR31*
2002	2104	1202	1128	57.1	6.2	0.57	0.76
2003	2123	1253	1150	59.0	8.2	0.55	0.77
2004	2177	1222	1122	56.1	8.2	0.54	0.72
2005	2429	1401	1273	57.7	9.1	0.57	0.79
2006	2635	1401	1280	53.2	8.6	0.59	0.76
2007	2771	1537	1399	55.5	9.0	0.57	0.78
2008	2889	1537	1384	53.2	10.0	0.55	0.73
2009	2990	1654	1479	55.3	10.6	0.55	0.76
2010	3108	1730	1546	55.7	10.6	0.54	0.77
2011	3293	1889	1646	57.4	12.9	0.54	0.80
2012	3482	1897	1663	54.5	12.3	0.54	0.76
2013	3628	2099	1838	57.9	12.4	0.55	0.82

In comparison with the other NCD results, RESPI shows a much greater European presence, averaging 56%, which is much higher than the percentages for the other four (38% for ONCOL, 42% for CARDI, 40% for DIABE and 35% for MENTH). The internationalism was initially lower than in the other NCDs, but has caught up and even surpassed some of them. But RESPI is a very small subject area, and even in Europe only averages 0.8% of the papers in biomedicine overall.

6.2.3 Outputs of individual European countries

The results for the individual European countries are shown in Table 50, overleaf. The UK has much the highest output, more than twice as high as the second country, France. Figure 46 shows that it is publishing almost twice as much as expected, as are Sweden and the Netherlands. On the other hand, Austria is publishing very little, and Germany, Norway and Switzerland are doing barely half of what might be expected from their wealth.

Table 50. Outputs of 31 European countries in respiratory disease research (RESPI), 2002-13 in both the SCI and SSCI. Integer and fractional counts, the percent foreign contribution and the annual growth rate. *The countries are ranked by their fractional count outputs. Codes are in Table 2.*

Country	*Int ct*	*Frac ct*	*% int*	*AAPG*		*Country*	*Int ct*	*Frac ct*	*% int*	*AAPG*
UK	5537	3924	29.1	3.1		AT	263	140	46.9	0.9
FR	2387	1870	21.7	0.1		HU	158	109	31.0	5.1
IT	2372	1847	22.1	4.1		CZ	131	77	41.4	7.5
DE	2474	1701	31.2	3.1		HR	88	77	13.0	12.5
NL	2065	1447	29.9	5.4		RO	85	61	28.0	19.2
ES	1742	1351	22.4	7.8		SK	64	45	28.9	17.6
SE	1407	886	37.1	3.0		SI	58	43	25.2	30.6
BE	990	617	37.7	6.3		IS	89	33	63.2	5.7
DK	792	487	38.5	8.8		LT	39	27	31.9	9.5
PL	580	454	21.7	13.2		BG	33	17	48.7	19.2
GR	510	383	25.0	10.1		EE	45	12	74.1	2.5
CH	695	353	49.2	4.1		CY	16	8	49.7	11.4
FI	489	342	30.1	1.9		MT	13	6	51.3	5.4
NO	458	267	41.6	7.0		LV	6	4	29.2	20.9
PT	225	164	26.9	19.4		LU	3	1	66.7	2.7
IE	239	155	35.3	13.5						

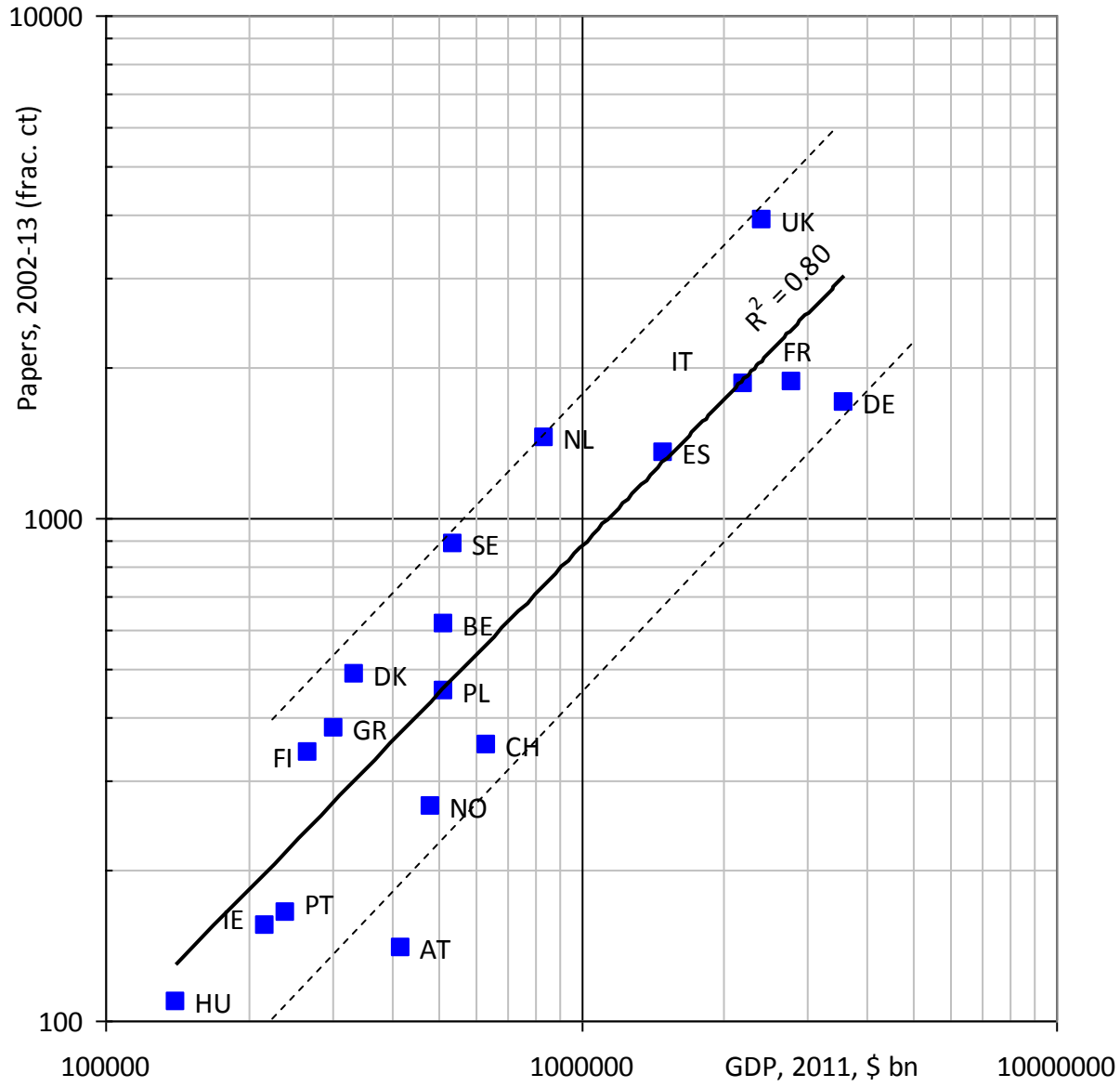

Figure 46. Plot of RESPI paper output, 2002-13, against GDP for 18 European countries with fractional counts above 100 papers. *Note: BG, CY, CZ, EE, HR, IS, LT, LU, LV, MT, RO, SI and SK omitted. Dashed lines show values x 2 or x 0.5 relative to power trend-line. For codes, see Table 2.*

The research level of the RESPI papers tended slightly to increase (*i.e.*, become more basic) over time, and the papers were noticeably more clinical than the average for the journals in which they were published. This rose from 1.72 to 1.82; not a big rise but in the other NCD areas the journals tended to become more clinical with time.

6.3 Analysis of citations and percentage of reviews

6.3.1 Five-year citation analysis

The citation scores (five-year cite scores, ACI) for the world and for the EUR31 countries are given in the figure below for the eight years, 2002-09.

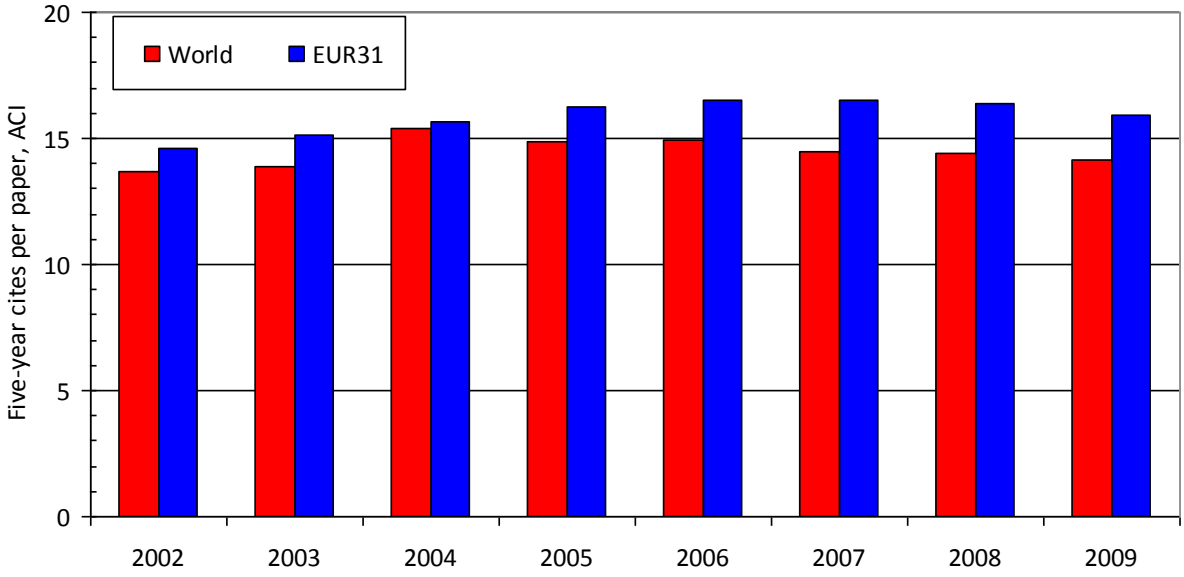

Figure 47. Chart showing the variation in mean citations per RESPI paper with publication year, 2002-09, for world (red) and for EUR31 (blue) papers.

The next table shows the citation scores (ACI) for individual countries and also the numbers of papers whose citations put them in the top 5% of the cohort in terms of citations, for which the qualifying numbers were 52 cites.

Table 51. Citation performance of 18 EUR31 countries in RESPI in 2002-09 with at least 50 citable papers, ranked by the percent with 52 or more cites in the five years following publication (ACI) (Top 5%) rather than the mean value.

ISO	*ACI*	*Top 5%*	*%*		*ISO*	*ACI*	*Top 5%*	*%*		*ISO*	*ACI*	*Top 5%*	*%*
UK	19.6	176.4	7.28		NO	14.7	5.4	3.80		FI	14.1	5.6	2.44
BE	18.2	24.8	6.74		ES	12.2	23.7	3.12		GR	10.1	3.6	1.65
DK	18.3	15.3	6.04		IT	12.9	35.1	3.08		HU	11.3	1.0	1.65
NL	17.9	45.1	5.32		IE	11.9	2.0	2.97		PL	8.5	3.9	1.59
CH	16.0	9.6	4.64		FR	9.8	34.9	2.80		AT	11.4	1.2	1.27
DE	13.9	43.9	4.04		SE	13.7	13.8	2.55		PT	8.3	0.3	0.33

6.3.2 Percentage of reviews

This is shown in Figure 48. The UK shows a much higher value than Belgium, the next country.

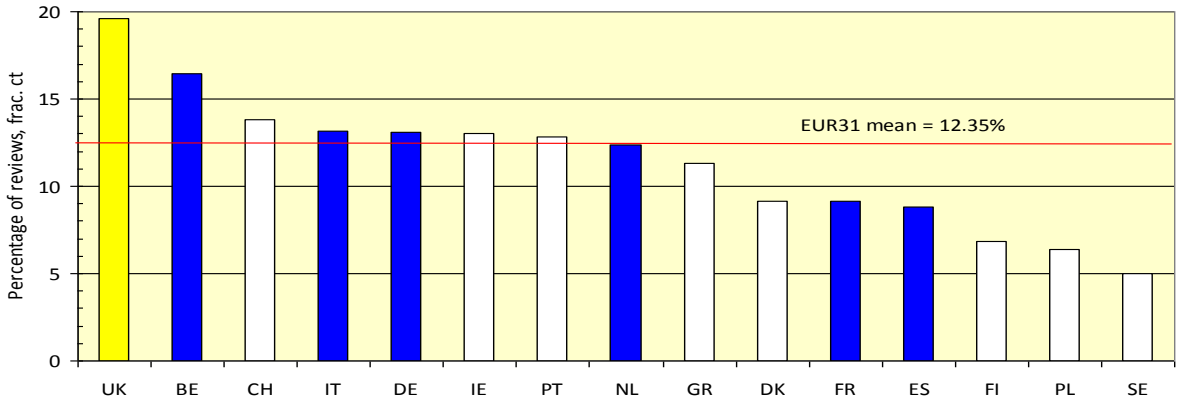

Figure 48. Percentage of reviews among RESPI papers from 15 European countries with at least 20 reviews in the WoS in 2002-13. *Yellow bar: > 300 reviews; blue bars: > 100 reviews*.

6.4 Outputs of research in different respiratory diseases

6.4.1 Outputs from individual countries and relative commitments

There were five diseases that the filter covered, and they were coded as follows: Allergic rhinitis, coded ALRH; Asthma, coded ASTH; Chronic Obstructive Pulmonary Disease, coded COPD; Cystic Fibrosis (Mucoviscidosis), coded CYFI; and Emphysema, coded EMPH. The numbers of papers relevant to each of these five disease areas and from each of the 31 European countries are given in the next table.

Table 52. Numbers of papers in five respiratory disease areas from each of the 31 European countries, 2002-13.

ISO	*ALRH*	*ASTH*	*COPD*	*CYFI*	*EMPH*	*RESPI*		*ISO*	*ALRH*	*ASTH*	*COPD*	*CYFI*	*EMPH*	*RESPI*
UK	108	1752	1070	914	77.1	3924		AT	10.1	64.1	38.7	21.2	7.1	140
FR	82.1	852	320	556	53.0	1870		HU	13.7	65.5	16.0	10.4	2.7	109
IT	166	750	564	361	77.3	1847		CZ	4.9	34.9	10.8	28.9	1.5	77
DE	123	693	365	414	79.3	1701		HR	4.1	48.0	21.4	2.0	0.0	77
NL	34.0	645	591	163	48.7	1447		RO	3.7	28.7	24.4	6.4	1.0	61
ES	79.3	512	586	143	35.5	1351		SK	5.3	16.7	19.5	2.8	0.0	45
SE	86.4	508	217	76	25.0	886		SI	0.0	24.1	20.5	2.7	0.0	43
BE	43.9	220	158	163	29.4	617		IS	0.5	19.3	12.4	0.5	0.0	33
DK	22.9	227	154	90	12.0	487		LT	2.2	15.9	11.0	1.6	0.0	27
PL	38.0	299	78.4	56.3	1.0	454		BG	1.2	10.4	4.2	2.2	0.0	17
GR	17.5	169	166	35.6	7.3	383		EE	1.8	5.2	3.3	0.1	0.3	12
CH	18.0	141	96.2	80.7	13.6	353		CY	1.0	6.0	0.0	0.0	2.0	8
FI	20.2	264	58.0	4.3	7.6	342		MT	0.0	6.3	0.0	0.0	0.0	6
NO	5.4	138	109	15.6	2.9	267		LV	0.0	0.2	4.0	0.0	0.0	4
PT	7.4	79.1	27.0	50.9	5.0	164		LU	0.0	0.8	0.3	0.0	0.0	1
IE	6.6	29.7	24.5	90.1	3.4	155		**EUR**	**858**	**7279**	**4585**	**3214**	**478**	**16248**

The relative commitment to these five disease areas by the 18 leading countries with at least 100 RESPI papers is shown in Table 53.

Table 53. Relative commitment to research on five respiratory diseases by 18 European countries, 2002-13, compared to outputs in RESPI overall. *Values > 2 tinted bright green; values > 1.41 tinted pale green; values < 0.71 tinted gold; values < 0.5 tinted pink.*

	ALRH	*ASTH*	*COPD*	*CYFI*	*EMPH*			*ALRH*	*ASTH*	*COPD*	*CYFI*	*EMPH*
UK	0.51	0.99	0.97	1.20	0.67		PL	1.56	1.46	0.61	0.64	0.08
FR	0.82	1.01	0.61	1.53	0.97		GR	0.85	0.98	1.53	0.48	0.65
IT	1.67	0.90	1.08	1.00	1.44		CH	0.95	0.88	0.96	1.17	1.32
DE	1.34	0.90	0.76	1.25	1.60		FI	1.10	1.72	0.60	0.06	0.77
NL	0.44	0.99	1.45	0.58	1.16		NO	0.38	1.15	1.45	0.30	0.38
ES	1.09	0.84	1.54	0.54	0.90		PT	0.84	1.07	0.58	1.59	1.04
SE	1.82	1.27	0.87	0.44	0.97		IE	0.80	0.43	0.56	2.99	0.75
BE	1.33	0.79	0.91	1.36	1.64		AT	1.35	1.02	0.98	0.78	1.74
DK	0.88	1.03	1.12	0.95	0.85		HU	2.34	1.33	0.52	0.49	0.83

6.5 Burden from different respiratory diseases

6.5.1 Burden of RESPI in individual countries and diseases (asthma and COPD)

These data have been taken from the WHO Global Burden of Disease study for 2010.

Table 54. Percentages of DALYs for the 31 European countries attributable to asthma, COPD and other lung diseases, 2010.

	ASTH	*COPD*	*Other*	*RESPI*			*ASTH*	*COPD*	*Other*	*RESPI*
UK	1.81	4.19	1.07	7.07		BG	0.40	3.47	0.64	4.52
CH	1.29	4.46	0.88	6.64		DE	1.05	2.94	0.48	4.47
DK	1.13	4.75	0.56	6.43		IT	0.98	2.64	0.55	4.17
IE	1.65	3.31	0.81	5.77		HU	0.46	3.43	0.28	4.16
BE	0.94	3.88	0.80	5.62		FR	1.46	2.10	0.59	4.15
GR	0.63	2.88	2.09	5.61		PL	0.85	2.71	0.41	3.97
CY	1.57	2.31	1.52	5.40		SI	0.63	2.82	0.42	3.87
NL	0.93	3.88	0.53	5.34		HR	0.58	2.88	0.33	3.79
PT	1.61	2.26	1.25	5.12		CZ	0.44	2.67	0.37	3.48
NO	1.27	3.32	0.46	5.05		FI	1.10	1.97	0.40	3.48
SE	1.56	2.93	0.52	5.01		RO	0.62	2.42	0.22	3.25
AT	0.90	3.51	0.39	4.80		SK	0.68	2.13	0.38	3.20
ES	0.83	2.65	1.30	4.77		LT	0.37	2.01	0.24	2.62
IS	1.37	2.70	0.57	4.64		LV	0.43	1.42	0.27	2.11
LU	0.88	3.10	0.61	4.59		EE	0.53	1.21	0.23	1.97
MT	1.09	2.78	0.67	4.55						

The range of values is fairly narrow, but it is clear that the UK tops the list. The three small Baltic countries suffer the least from these diseases.

6.6 The funding of RESPI research

6.6.1 Basic parameters

This NCD was the first of the five to be analysed in accordance with the methodology described above. The file consisted of 18,822 papers, of which 9269 were published during the last five years, 2009-13. Of these, 775 or 8.4% had a conflict of interest statement, and needed to be examined individually in order to check the funding bodies listed in the FU column of the spreadsheet, and redact them if necessary. Some papers originally crediting funding bodies were found not to be funded explicitly, and others had the number sharply reduced; a very few should have had additional funders credited. After the redaction, 5451 papers had one or more funders (59%) and the remaining 41% had none. Figure 49 shows the percentages of papers with given numbers of funders or more.

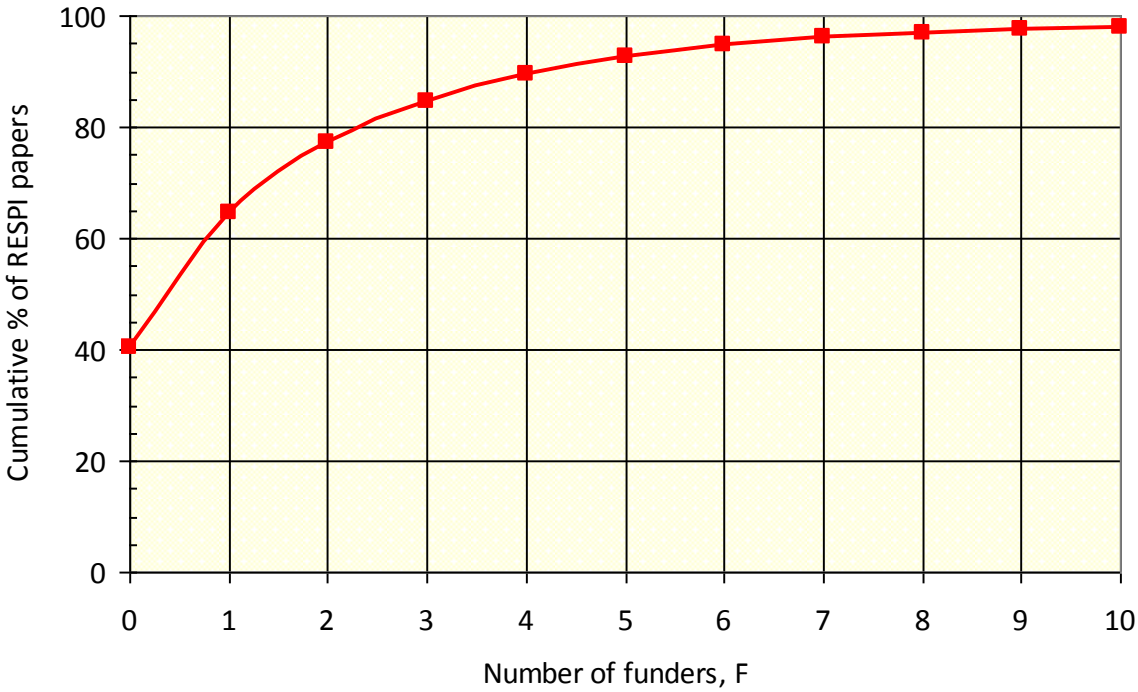

Figure 49. Cumulative percentage of numbers of RESPI papers with different numbers of funders, 2009-13.

6.6.2 Overall analysis and breakdown by country

The first analysis was in terms of the mean number of funders per country, and there was a big variation, with the Scandinavian countries having the most and (of the major countries) Poland and Greece the least, see Figure 50 below. The number of funders has been calculated on a fractional count basis. The analysis by main sector, using fractional counts of sectors for each paper and fractional country counts, is shown in Figure 51. Overall, the public sector and the private-non-profit sector each contributed just over 19% of the total, industry 14% and the EU 2.6%. Some 45% of the contributions were "none", that is the papers were funded by institutional sources - universities and hospitals. But for these leading countries, the PNP sector contributed slightly more than the public sector: 19.7% compared with 18.3%.

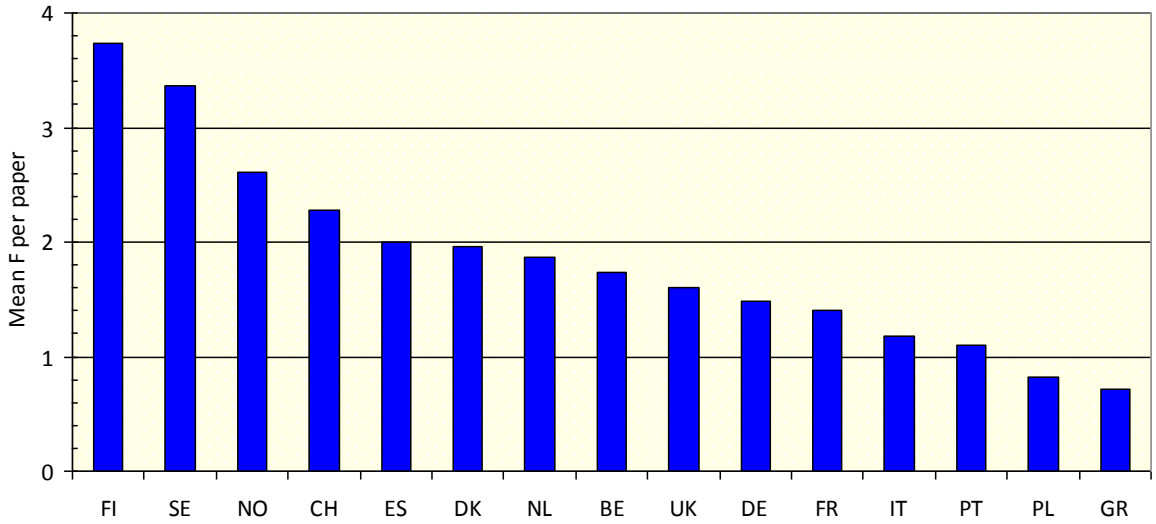

Figure 50. Mean number of funders per paper for RESPI papers, 2009-13, fractional count basis, for countries with at least 100 papers.

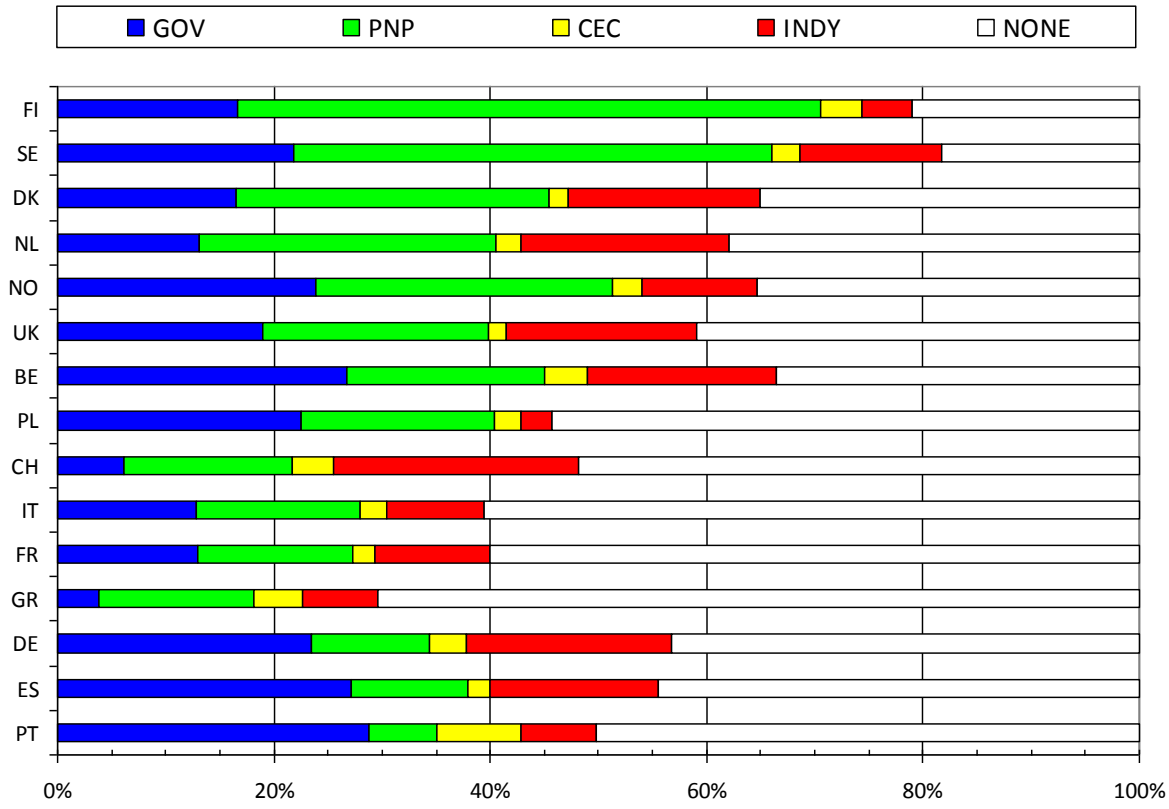

Figure 51. Analysis of funding sources for RESPI papers from 15 leading European countries, 2009-13, based on fractional country counts and also on fractional funding counts for each paper. *The countries are ranked by the percentage of private-non-profit funded papers.*

The above figure shows that the Scandinavian countries depended heavily on the private-non-profit sector, with 38.5% on average compared with 19.8% from the public sector. On the other hand, the 11 former Communist countries of Eastern Europe depended much more on their public sector for support of RESPI research: 28% compared with 13.5% from the PNP sector. They also received little support from industry: only 3.8% compared with 14% for Europe as a whole. They did, however,

obtain relatively more support from the EU: 4.0% compared with 2.5% for the top 15 countries shown in Figure 51. Nevertheless, support from the EU went largely to the leading Member States in Western Europe, see Table 55.

Table 55. European Union support for respiratory disease research, 2009-13: numbers of papers (N) and percent of papers for individual countries (%).

Country	*N*	*Country*	*N*		*Country*	*%*	*Country*	*%*
UK	32.0	SE	10.6		LV	47.1	BE	4.0
DE	25.6	GR	9.3		SK	23.7	FI	3.9
IT	21.6	PT	8.5		CZ	11.1	CH	3.7
FR	16.0	CH	6.5		PT	7.9	EE	3.7
NL	15.9	PL	6.3		AT	5.6	HU	3.4
ES	14.5	SK	5.4		GR	4.6	DE	3.3
BE	12.8	FI	5.2		IS	4.1	CY	3.0

Finally, Table 56 shows the list of the leading individual funders of respiratory disease research in Europe in the five years of the study.

Table 56. List of leading funders of European respiratory disease research, 2009-13, with fractional counts of numbers of papers and percentage of European output (8173 papers).

Funder name	*Contribution*	*% of EUR31*
GlaxoSmithKline plc	223.0	2.73
European Union	207.5	2.54
UK Department of Health (and NIHR)	167.5	2.05
AstraZeneca plc	130.9	1.60
DE Deutsche Forschungsgesellschaft - DFG	119.6	1.46
Novartis Pharma AG	113.1	1.38
NL Stichting Astma Bestrijding	84.9	1.04
UK Medical Research Council	80.6	0.99
ES Instituto Carlos III	80.6	0.99
UK The Wellcome Trust	78.7	0.96
Boeringer-Ingleheim AG	74.3	0.91
FR Association Vaincre la Mucoviscidose	55.2	0.68
Pfizer Inc.	51.3	0.63
ES miscellaneous non-profits	49.8	0.61
SE Swedish Heart Lung Foundation	47.8	0.58
Polish Universities	44.6	0.55
BE Agency for Innovation by Science and Technology	43.9	0.54
Takeda	41.0	0.50

It is striking that the pharma industry plays such a prominent role, with six out of the top 16 individual funders of RESPI research in Europe.

6.6.3 Analysis by research level, subject area and number of authors

The RESPI database was divided up by five disease areas: asthma (AST), bronchiectasis (BRO), chronic obstructive pulmonary disease (COPD, COP), cystic fibrosis (CYF) and emphysema (EMP). Figure 52 shows the numbers of funders and the mean research level of the papers in each area.

Cystic fibrosis is the most basic, followed by emphysema, but asthma, followed by COPD, receives the most funding (in terms of numbers of funders per paper).

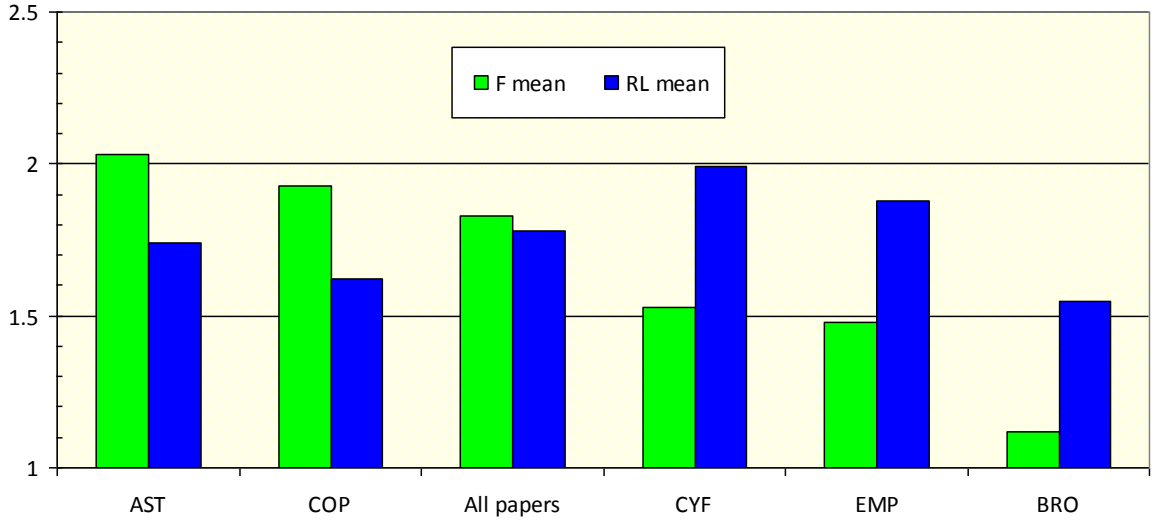

Figure 52. Mean number of funders per paper (F) and mean research level (RL) on a scale from 1 = clinical to 4 = basic research for all RESPI papers and those in five disease areas, 2009-13.

Overall, papers in clinical journals tend to give fewer funding acknowledgements than ones in basic journals. This also holds true for papers with clinical title words compared with ones containing basic title words, see Table 57.

Table 57. Numbers of funding bodies per paper for RESPI papers, 2009-13, in journals of different RL (RL 1 is clinical; RL4 is basic) and containing clinical and/or basic title words. *N = total number of papers in each group; F = 0 is number with no funding acknowledgements.*

RL (J)	*F*	*N*	*F = 0*	*% fund*		*Title words*	*F*	N	*F = 0*	*% fund*
1.0 to 1.5	1.36	4487	2284	49.1		Clinical not basic	1.06	1051	593	43.6
1.5 to 2.0	1.92	2023	734	63.7		All clinical	1.14	1168	633	45.8
2.0 to 2.5	2.53	1155	348	69.9		Clinical and basic	1.81	117	40	65.8
2.5 to 3.0	2.33	815	212	74.0		All basic	2.11	255	81	68.2
3.0 to 3 .5	2.62	480	106	77.9		Basic not clinical	2.36	138	41	70.3
3.5 to 4 .0	3.24	281	36	87.2						

It is not surprising that the average number of funders per paper rises with the number of authors, A, as the additional authors may be expected to be able to tap extra funding sources, and papers with many authors are likely to be international and attract funding from different countries, but nevertheless the correlation is striking, see Figure 53.

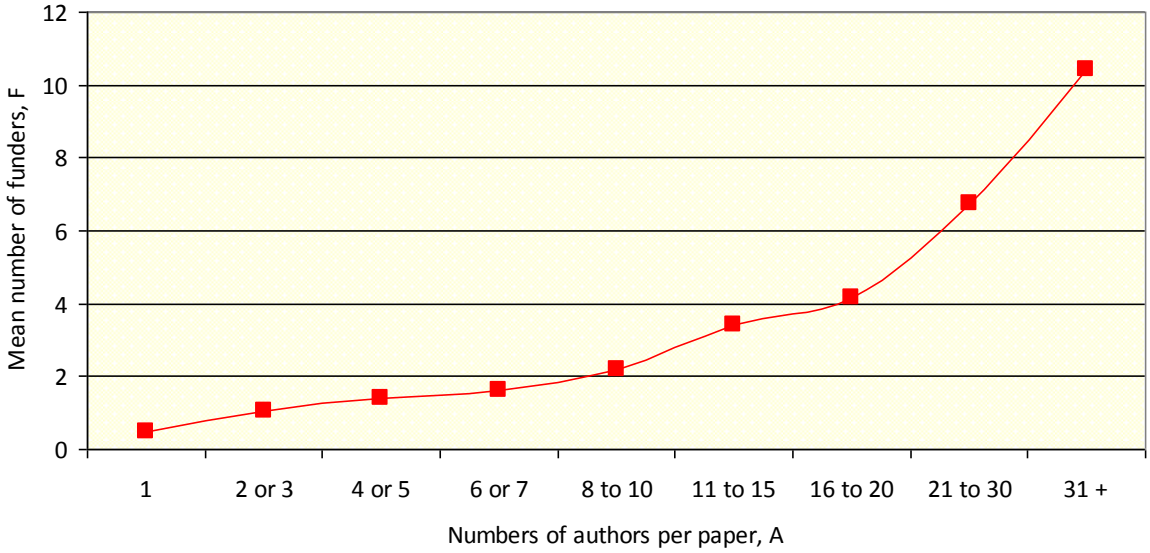

Figure 53. Mean number of funding bodies per paper for RESPI papers, 2009-13, as a function of the numbers of authors.

6.6.4 Correlation of funding with citation scores for 2009 papers

In confirmation of the statement in section 1.6.1 of this report, we found that, for 2009 papers, the numbers of funding bodies correlated positively with the mean citation score, see Figure 54. The increase in actual citation impact (ACI) for papers with many funding acknowledgements is very clear, and the relationship will be expected to hold even when account is taken of factors such as the papers tending to be basic and having more authors (Lewison & Dawson, 1998; Roe *et al.*, 2010). The effects of other factors will be explored in detail later, when 2010 citation data are available and in other disease areas where there are many more papers.

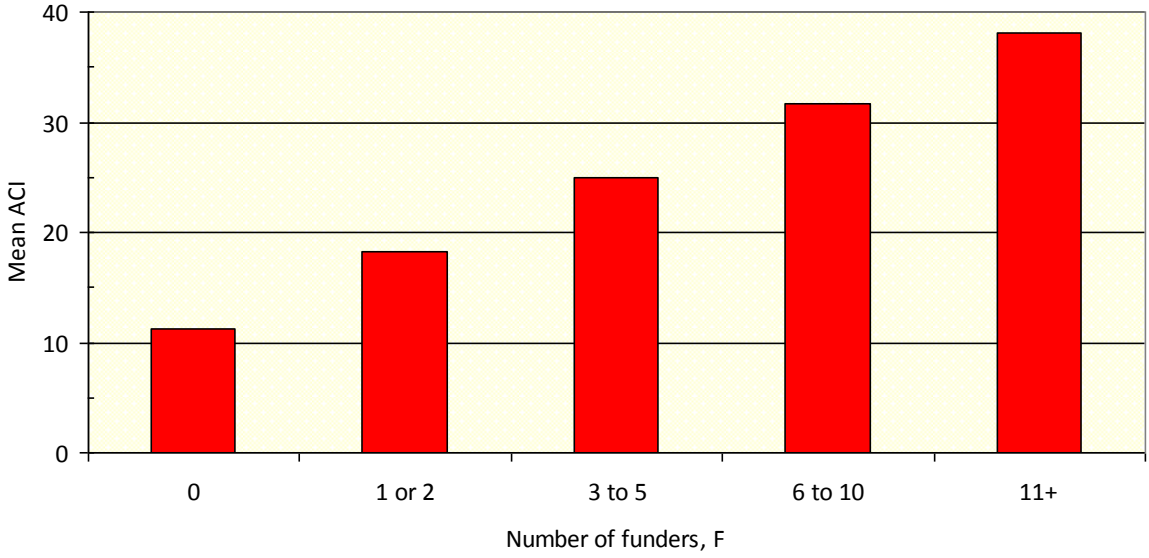

Figure 54. Mean five-year citation count (ACI) for groups of 2009 RESPI papers with different numbers of funding acknowledgements.

7 Research by members of health advisory committees

7.1 Committees and members in EUR31 countries, and outputs

7.1.1 Countries whose health policy advisory committees were analysed

We were not able to find lists of committee members for all the 31 European countries, and some did not appear to have them, so the analysis was confined to 21 countries out of the 31, shown in Table 58.

Table 58. List of European countries used in this study with their digraph ISO codes.

Country	*Code*		*Country*	*Code*		*Country*	*Code*
Austria	AT		Finland	FI		Luxembourg	LU
Bulgaria	BG		France	FR		Netherlands	NL
Croatia	HR		Germany	DE		Poland	PL
Cyprus	CY		Hungary	HU		Portugal	PT
Czech Republic	CZ		Ireland	IE		Spain	ES
Denmark	DK		Italy	IT		Switzerland	CH
Estonia	EE		Lithuania	LT		United Kingdom	UK

7.1.2 Outputs of papers

The numbers of papers found by members of these committees, on both integer and fractional counts, are shown in Table 59, overleaf. The numbers of papers do not correspond in any way to the scientific size of the countries, but rather the composition and number of their health advisory committees. For example, in the UK there were only two (out of more than 30) that were concerned with one of the five NCDs considered here. The total number of papers was 12,854 articles and reviews, but when these were matched to the five NCD files for the years 2009-13, there were only 5713 papers, or 44% of the original total.

These papers were, as expected, rather clinical with a mean RL (p) of 1 49 and a mean RL (j) of 1 .74. These values are higher than those obtained for papers cited on DIABE clinical guidelines (see section 3.7.3), and varied somewhat by subject area and country, see Figure 55.

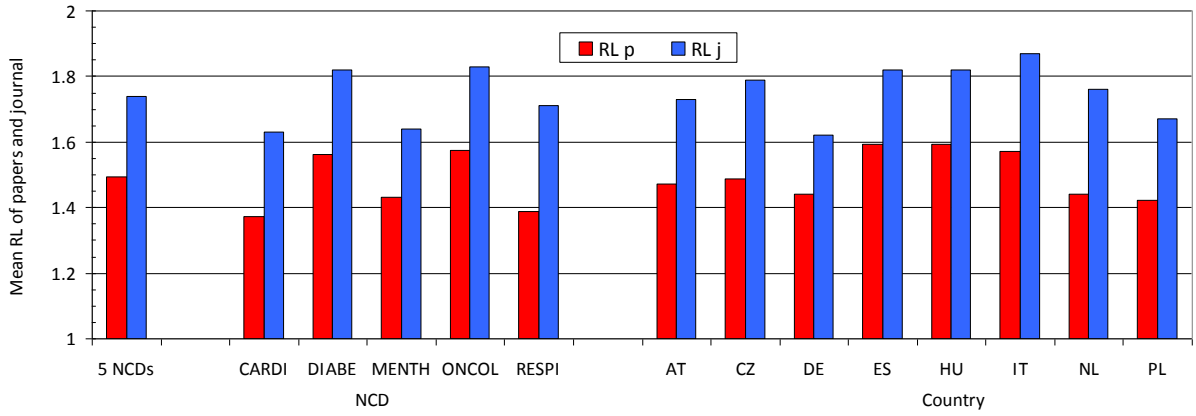

Figure 55. Mean Research Level (RL) of papers from members of health advisory committees in five NCDs and from eight EU Member States

Cancer and diabetes research were the most basic, as was that of the advisers in Italy, Spain, Hungary and the Czech Republic.

Table 59. Outputs of papers by health advisory committee members in various European countries (for ISO codes, see Table 2). EUR = 31 countries; ROW = rest of the world.

Country	*Cttees*	*Memb.*	*Papers*	*Frac*	*Other EUR*	*EUR, %*	*ROW*	*ROW, %*
NL	5	83	2554	1949	397	15.5	208	8.2
DE	5	125	2010	1715	142	7.1	153	7.6
AT	4	189	1384	976	276	19.9	132	9.5
HU	5	247	1311	921	246	18.8	144	11.0
ES	1	46	1179	1053	60.5	5.1	65.3	5.5
CZ	4	51	969	732	176	18.2	60.7	6.3
IT	4	107	965	808	94.2	9.8	62.7	6.5
PL	3	60	794	671	71.6	9.0	51.3	6.5
UK	2	35	403	340	29.8	7.4	33	8.2
EE	2	106	347	188	123	35.4	36.5	10.5
FR	3	46	294	233	38.5	13.1	22.8	7.8
LT	9	89	145	119	21.2	14.6	4.5	3.1
CH	3	39	141	63.1	64.6	45.8	13.3	9.4
DK	2	42	111	95.7	12	10.8	3.3	3.0
FI	1	16	100	65	15.1	15.1	19.9	19.9
PT	1	16	51	48.9	2.1	4.1	0	0.0
HR	1	19	39	25	12.6	32.3	1.4	3.6
CY	3	26	36	18.4	13.7	38.1	3.9	10.8
IE	2	49	10	5.85	3.22	32.2	0.93	9.3
BG	1	9	7	7	0	0.0	0	0.0
LU	1	31	4	1.58	2.22	55.5	0.2	5.0

7.2 Comparison with research and disease burdens

7.2.1 Comparison of the five NCDs with research in Europe and disease burdens

We next examined how well the five NCDs were represented among these advisers' portfolios. The papers in the file were all matched against the NCD output files, and the numbers in each of the five NCDs are shown in Table 60, where they are compared with overall European research outputs and the European disease burden from the five NCDs.

It appears from Table 60 that there is less research experience than would be merited in cardiovascular and respiratory diseases and as a corollary, more than proportionate in diabetes and cancer. But this is for Europe as a whole, and the situation is different for individual countries. It is only worth performing this analysis for countries with a large number of papers, and we have limited it to countries with at least 700 papers, *i.e.*, the top eight in Table 59.

Table 60. Numbers of papers in the advisers' overall portfolio of research in each of the five NCDs, and comparison with EUR31 research output in 2009-13, and disease burden in 2010 in EUR31 countries (thousand DALYs).

NCD	*Advisers*	*Percent*	*EUR31 papers*	*EUR31, %*	*DALYs, k*	*DALYs, %*
CARDI	1345	*23.0*	101212	*29.9*	28573	*34.2*
DIABE	489	*8.4*	20018	*5.9*	3610	*4.3*
MENTH	1217	*20.8*	71437	*21.1*	19290	*23.1*
ONCOL	2540	*43.4*	136152	*40.3*	25193	*30.2*
RESPI	256	*4.4*	9269	*2.7*	6854	*8.2*
Sum	5847	*100.0*	338088	*100.0*	83520	*100.0*

Table 61. Comparison of the size of health advisers' research portfolios in eight European countries in five NCDs with the countries' relative disease burden from these NCDs. *(CARDI = cardiovascular diseases, DIABE = diabetes, MENTH = mental disorders, ONCOL = cancer, and RESPI = respiratory diseases.) Cells in lower left section tinted pink if % of research < 0.5 x % of DALYs; pale yellow if < 0.71 x % of DALYs; pale green if > 1.41 x % of DALYs; bright green if > 2 x % of DALYs.*

	Papers by committee members					*kDALYs in 2010*				
Nos	*CARDI*	*DIABE*	*MENTH*	*ONCOL*	*RESPI*	*CARDI*	*DIABE*	*MENTH*	*ONCOL*	*RESPI*
AT	102	45	143	371	15	411	72	321	361	109
CZ	185	40	101	288	6	758	79	313	583	110
DE	174	22	284	587	15	4630	638	3169	4268	1068
ES	116	36	91	263	39	1783	395	1644	1934	526
HU	165	68	185	293	42	994	106	329	661	155
IT	94	22	33	245	8	3008	516	2109	3010	678
NL	241	136	144	149	108	608	84	725	829	229
PL	137	55	67	169	8	2838	303	1394	1953	476
%	*CARDI*	*DIABE*	*MENTH*	*ONCOL*	*RESPI*	*CARDI*	*DIABE*	*MENTH*	*ONCOL*	*RESPI*
AT	15.1	6.7	21.2	54.9	2.2	32.3	5.7	25.2	28.3	8.6
CZ	29.8	6.5	16.3	46.5	1.0	41.1	4.3	17.0	31.6	6.0
DE	16.1	2.0	26.2	54.3	1.4	33.6	4.6	23.0	31.0	7.8
ES	21.3	6.6	16.7	48.3	7.2	28.4	6.3	26.2	30.8	8.4
HU	21.9	9.0	24.6	38.9	5.6	44.3	4.7	14.7	29.4	6.9
IT	23.4	5.5	8.2	60.9	2.0	32.3	5.5	22.6	32.3	7.3
NL	31.0	17.5	18.5	19.2	13.9	24.6	3.4	29.3	33.5	9.3
PL	31.4	12.6	15.4	38.8	1.8	40.8	4.4	20.0	28.0	6.8

The last table generally confirms the findings for Europe mentioned above, but there are some exceptions. In diabetes Germany is under-represented and in oncology the Netherlands is; on the other hand it is over-represented in respiratory diseases. Italy is under-represented in mental disorders, as is the Netherlands, but Hungary is over-represented here.

7.2.2 Comparison of outputs with six cancer site research outputs and burdens

The numbers of papers are great enough to allow an analysis of the main cancer sites (manifestations) and types of research. We confined the analysis to the eight countries in Table 61,

to six leading cancer sites: colorectal (COL), lung (LUN), breast (MAM), pancreas (PAN), prostate (PRO) and stomach (STO); to three treatment methods: chemotherapy (CHEM), radiotherapy (RADI) and surgery (SURG); and to two other research types, genetics (GENE) and pathology (PATH). Figure 56 compares the disease burden from the individual cancers with the output of research by the advisers, relative to all cancers, and Table 62 shows the analysis of the outputs of the advisers in the eight countries.

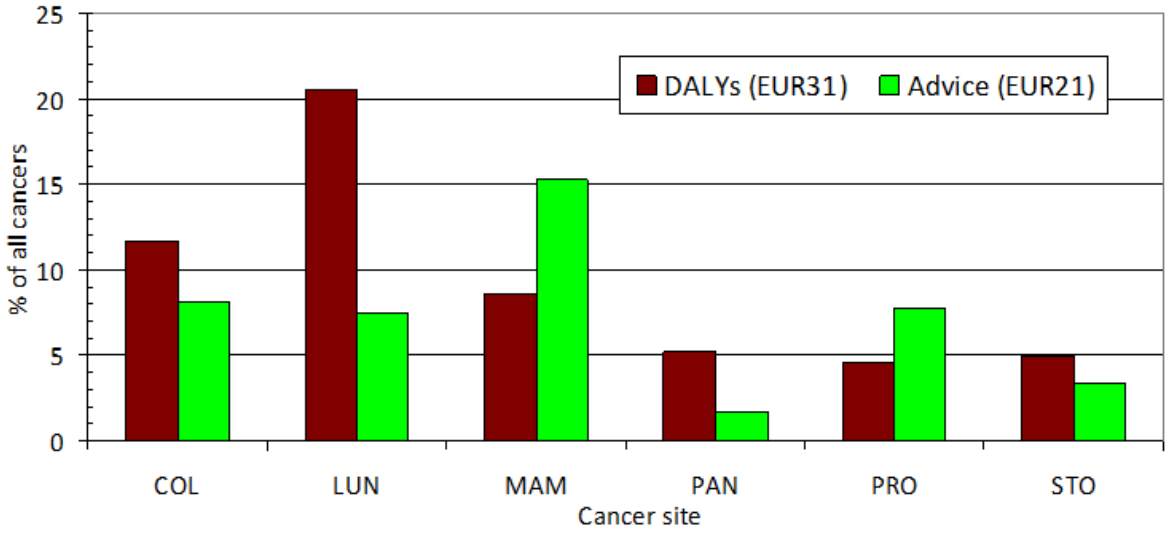

Figure 56. Comparison of disease burden from six common cancers in EUR31, 2010, with the amount of research from the health committee advisers in EUR21 countries, 2009-13.

This shows the frequently-found imbalance for lung and breast cancers – the former is under-researched and the latter over-researched, in relation to all cancers – but also that pancreatic cancer does not get as much attention from the advisers as it would appear to merit, whereas prostate cancer receives proportionately more attention.

Table 62. Numbers of cancer papers on six leading sites and of five research types published by health committee advisers in eight European countries, 2009-13. *Cells tinted pink if numbers of papers < 0.5 x European average for cancer; pale yellow if nos. < 0.71 x average; pale green if > 1.41 x average; bright green if > 2.0 x average.*

Papers	*COL*	*LUN*	*MAM*	*PAN*	*PRO*	*STO*	*CHEM*	*RADI*	*SURG*	*GENE*	*PAT*	*All*
AT	10	19	100	2	35	4	58	23	18	103	33	371
CZ	21	5	29	6	12	10	25	14	48	78	29	288
DE	35	27	50	18	115	22	87	34	153	83	48	587
ES	42	26	27	4	12	17	51	18	16	61	26	263
HU	26	47	70	2	16	4	52	21	21	86	76	293
IT	11	3	35	2	2	7	45	11	59	35	25	245
NL	14	3	42	0	1	6	4	4	18	20	5	149
PL	13	49	11	8	0	11	31	8	24	44	11	169
EUR22	206	191	389	43	197	86	370	138	377	537	259	254

There is much less variation in the disease burden from these six cancers across Europe, except that prostate cancer is relatively less of a burden in the three eastern European countries (Poland and Hungary, and to a less extent the Czech Republic), perhaps because the life expectancy of their men is lower, so the lack of expertise among advisory committee members is understandable. Hungary and Poland suffer relatively more from lung cancer, and their advisers' expertise in the subject is

clearly extensive and relevant. There are some surprising differences in expertise in different research types, with Germany and Italy strong in surgery, but the Netherlands rather weak in several treatment types.

7.2.3 Comparison with mental disorders in eight countries

The second sub-field analysis that we conducted was of different manifestations of mental disorders. These differ greatly from one another, and there is likely to be less carry-across of expertise in the different manifestations than for some other disease areas. Figure 57 shows the percentages of DALYs and of research for six different mental disorders, both as fractions of the total due to mental disorders. These are addiction (ADD), alcoholism (ALC), Alzheimer's disease and other dementias (ALZ), anxiety and panic disorders (ANX), unipolar depression (DEP) and schizophrenia (SCH). The addictions, alcoholism, anxiety disorders and depression appear to be receiving less attention than they need, but schizophrenia has much research experience among the advisers compared with its burden.

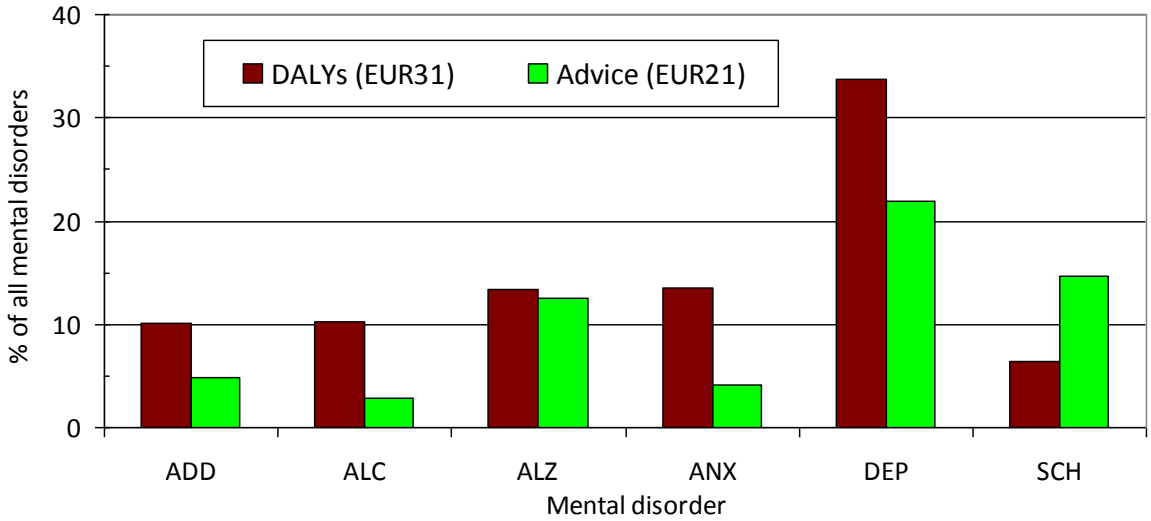

Figure 57. Comparison of disease burden from six mental disorders in EUR31, 2010, with the amount of research from the health committee advisers in EUR21 countries, 2009-13.

Table 63. Comparison of disease burden from six mental disorders with the research outputs of health committee advisers in eight European countries. *Cells tinted pink if numbers of papers < 0.5 x European average for mental disorders; pale yellow if nos. < 0.71 x average; pale green if > 1.41 x average; bright green if > 2.0 x average.*

	% of all DALYs							*Papers by advisers*						
	ADD	*ALC*	*ALZ*	*ANX*	*DEP*	*SCH*	*MENTH*	*ADD*	*ALC*	*ALZ*	*ANX*	*DEP*	*SCH*	*All*
AT	1.7	1.6	1.7	1.4	4.9	0.8	14.1	23	3	19	3	13	44	143
CZ	0.7	0.7	1.0	1.9	3.2	0.8	10.0	3	0	20	0	17	26	101
DE	1.1	1.5	2.3	1.8	4.6	0.8	13.6	2	11	15	10	85	58	284
ES	1.9	0.8	2.7	1.2	4.8	1.0	14.4	6	2	29	4	6	9	91
HU	0.6	1.0	1.7	1.6	2.6	0.7	9.3	8	2	21	8	38	25	185
IT	1.4	0.4	0.9	1.4	4.8	0.8	11.4	2	1	16	0	3	4	33
NL	1.0	1.1	0.9	2.0	7.8	0.8	15.4	7	8	17	8	34	8	144
PL	1.0	2.1	0.7	1.9	3.5	0.8	11.4	2	2	9	3	32	3	67
EUR	1.3	1.3	1.7	1.7	4.3	0.8	12.9	59	35	153	50	266	178	1217

The numbers of papers are much smaller than for cancer, and some countries in this table appear to have unbalanced advice from their health committee advisers if it is based on their research experience. The dementias are well researched by the advisers in Spain, Italy and the Czech Republic, and schizophrenia in Austria. But in some countries there is almost no research experience in mental disorders among its advisers, notably Italy (except for dementia).

7.2.4 Comparison with cardiovascular diseases in eight countries

The third analysis was of cardiovascular diseases, including cerebrovascular disease (stroke). The definitions that we used to create sub-fields of CARDI do not correspond accurately to the data for disease burden, but it is instructive first to see how the percentages of papers from advisers compare with the overall disease burden from cardiovascular diseases, which varies much more than that from cancer. The data are in Table 61, and are presented as a chart in Figure 58.

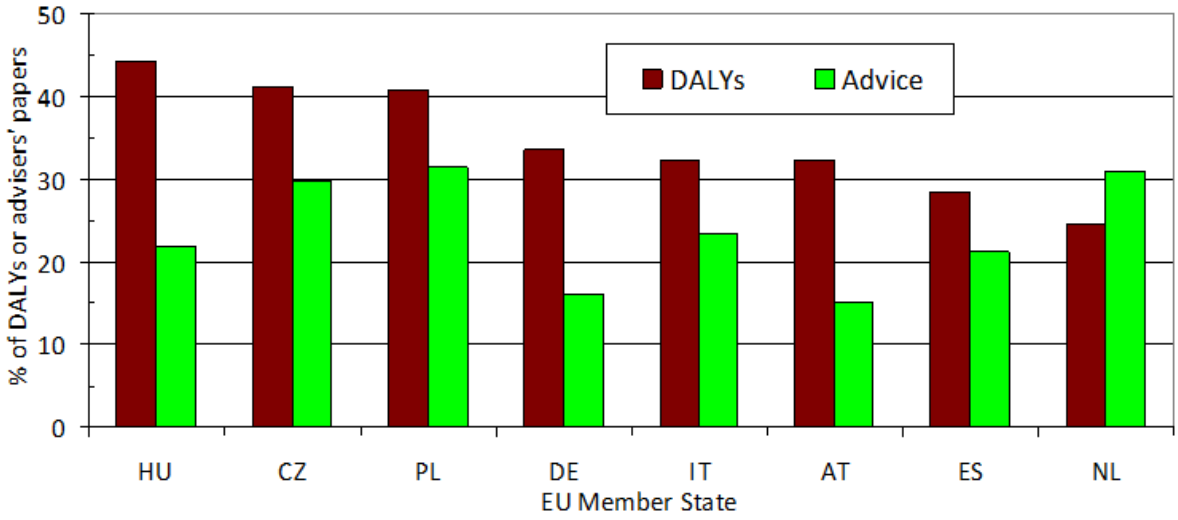

Figure 58. Comparison of disease burden from cardiovascular disease (as a percentage of the five NCDs) in 2010 and the corresponding percentage of advisers' CARDI papers, 2009-13.

The three eastern European "accession" countries which were socialist until 1989 and joined the EU in May 2004 clearly have much higher levels of cardiovascular disease than the others, but the correlation between DALYs and papers shown in Figure 58 is almost nil ($r^2 = 0.02$). The Netherlands is the only one of the eight countries that has more research experience among its health advisers than cardiovascular disease would warrant, and contrasts with Germany and Hungary which have less than half as much as would be proportionate.

Table 64 shows the distribution of papers between six leading subject areas, with 150 or more papers from all the countries. The subjects are arterial disease including atherosclerosis and aortic aneurysms (ART); cerebrovascular disease (stroke, CER); ischaemic heart disease including acute myocardial infarction (ISC); arrythmias, including atrial fibrillation (ARR); hypertension (HYP); and heart failure (FAI).

The distribution of cardiac expertise is very unbalanced, with Austria showing to advantage in hypertension (HYP) and cerebrovascular disease (CER) but not in heart failure (FAI), and Italy relatively very strong in arterial disease (ART) but weak elsewhere.

Table 64. Research outputs in six subject areas within cardiovascular diseases from health committee advisers in eight EU Member States, 2009-13. *Cells tinted pink if numbers of papers < 0.5 x European average for all cardiovascular disease; pale yellow if nos. < 0.71 x average; pale green if > 1.41 x average; bright green if > 2.0 x average.*

Subject:	*ART*	*CER*	*ISC*	*ARR*	*HYP*	*FAI*	*All*
AT	16	33	12	7	27	1	102
CZ	19	44	19	48	23	24	185
DE	35	13	29	10	25	42	174
ES	20	18	20	25	21	10	116
HU	34	16	31	42	14	16	165
IT	50	13	10	1	3	3	94
NL	41	36	32	18	41	36	241
PL	15	25	20	14	7	11	137
EUR21	252	227	197	176	176	153	1345

7.2.5 Comparison with respiratory diseases in eight countries

The final analysis is of two respiratory diseases, asthma (AST) and chronic obstructive pulmonary disease, COPD (COP). These account for 1.1% and 2.9% of all European DALYs, so the latter is much more serious but receives less research attention (Begum *et al*., 2016). There are also fewer research papers on COPD from the advisers (107) than ones on asthma (131). In Table 65 the comparison is with the total numbers of papers from each country in the five NCDs because respiratory medicine is dominated by these two diseases – the main other one being cystic fibrosis but there are only 12 papers on this disease in the database. There is a relative lack of research expertise in respiratory diseases generally, and particularly in COPD with the conspicuous exceptions of the Netherlands and Spain. Spain has a lower relative disease burden from these two diseases together than any other country in "western" Europe except for Finland and this may be as a result of having much expertise in COPD (but not in asthma). However the Netherlands is not so well placed and is as high as sixth (out of 31 countries) in its relative burden from the two diseases.

Table 65. Numbers of papers from health advisory committee members in eight European Member States in asthma (AST) and COPD (COP), and comparison with total output in all five NCDs. *Cells tinted pink if numbers of papers < 0.5 x European average; pale yellow if nos. < 0.71 x average; pale green if > 1.41 x average; bright green if > 2.0 x average.*

Country	*AST*	*COP*	*All RESPI*	*Total*		*Country*	*AST*	*COP*	*All RESPI*	*Total*
AT	8	9	15	673		IT	1	4	8	394
CZ	5	1	6	605		NL	67	38	108	749
DE	3	6	15	1054		PL	3	3	8	416
ES	8	33	39	537		EUR21	131	107	256	5713
HU	30	8	42	744						

7.3 Discussion and conclusions

We have examined a new indicator and compared the research outputs of members of European countries' health advisory committees with their countries' disease burdens. There is an implicit assumption that there should be a correlation, namely that these advisers should be selected on the basis that their expertise should match the clinical needs of the countries. That means that diseases

that cause a relatively greater burden should be matched by the presence of expert advisers who know about these diseases (or mental disorders). This would allow them to argue for better treatment facilities for patients. There is also a parallel assumption that a country's biomedical research portfolio should reflect its disease burden, so that it will be better able to treat patients and to take steps to reduce the diseases' incidence.

However, the inverse may also be the case, that is that if a country has invested heavily in research on a particular disease for some years, and has health policy advice stemming from this research, this should have led to an improvement in the situation, with fewer patients and better outcomes. This is a kind of "holy grail" of medical research: more research leads to better health. Of course, the links are far more complex than that, and many steps are needed to translate research findings, usually from many different sources, into better treatment for patients and for less illness, see Figure 59.

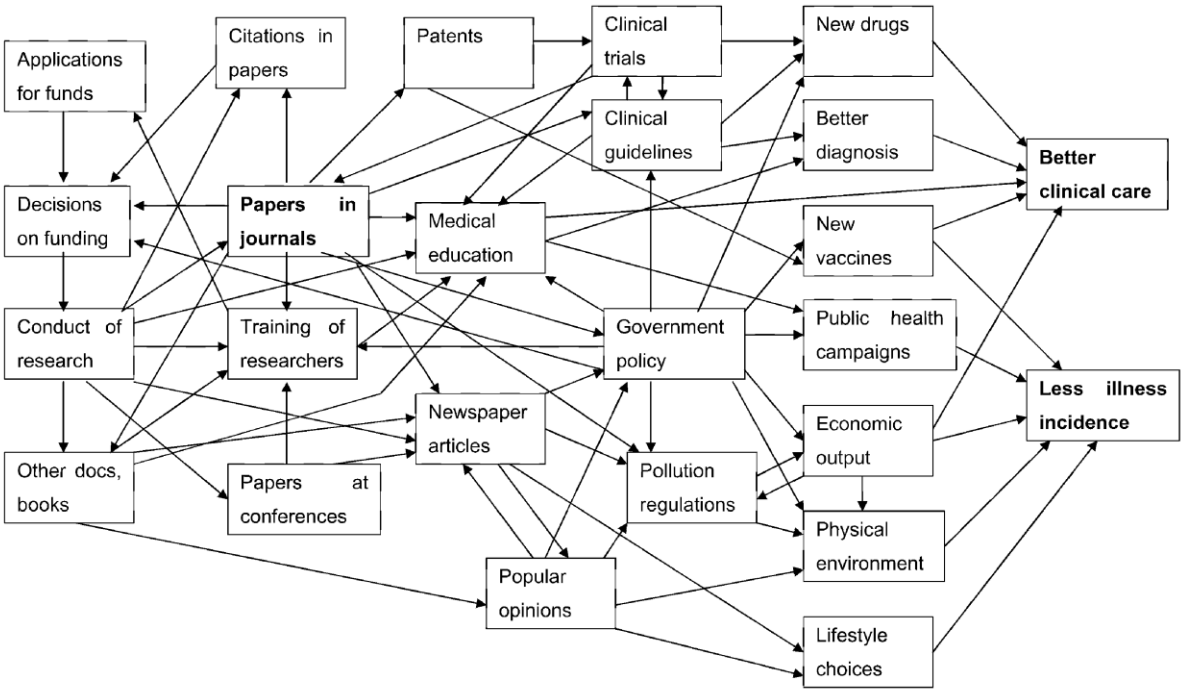

Figure 59. Diagram showing the many linkages between biomedical research and better health.

This diagram (Lewison, 2005) shows how central "Government policy" is to the provision of better health and wealth, and how dependent it is on many different sources. [This diagram omits the role of advisory committees, but governments have been known to reject the advice of experts or even to dismiss them if their views are unpalatable (Nutt, 2009).] Better health is not just a matter of better clinical care, but economic, regulatory and organisational policies play a major role, too, particularly in the reduction of communicable, maternal and nutritional diseases through better housing, clean air and water, and good food supplies. In Europe, most of these are available to most of the population (but by no means all) and attention is increasingly being paid to the improvement of "lifestyle choices", such as the reduction of smoking, more exercise and better food choices. Health advisory committees can assist with the selection of government policies that affect all of these, though to date there has been success on a wide scale only for the discouragement of smoking. This may reflect the focus of advisory committees more on the physical than the social determinants of disease. Their membership may need to alter to reflect the changing pattern of disease in the different countries, and how it can be managed, and this paper offers a first step in the collection of evidence that can guide this process.

8 Research cited by newspaper stories

8.1 Analysis of data from Belgian newspaper *Le Soir*

8.1.1 Introduction

At the time of writing, the results from many of the newspapers had been assembled, but the analysis had not started as we were awaiting the data from several other newspapers that would provide a fuller picture of how European research was being presented to the public. In particular, two UK newspapers, *Daily Mail* and *The Guardian* were still being processed, together with one Irish newspaper, the *Irish Times*. As an example of the analysis that is possible with newspaper stories (and the papers that they cite), we present here the results for one Francophone Belgian newspaper, *Le Soir*. (The examination of the archive and assembly of the database was carried out by Gabrielle Emanuel, a bi-lingual King's College graduate student.)

8.1.2 Analysis of the stories

There were a total of 994 stories on NCD research in *Le Soir*. However, the file of newspaper stories only continued until the end of February 2013, so the output of stories has been increased for the last year to scale up to 12 months of output. The numbers of stories on the five NCDs, and their variation with time, are shown in Figure 60.

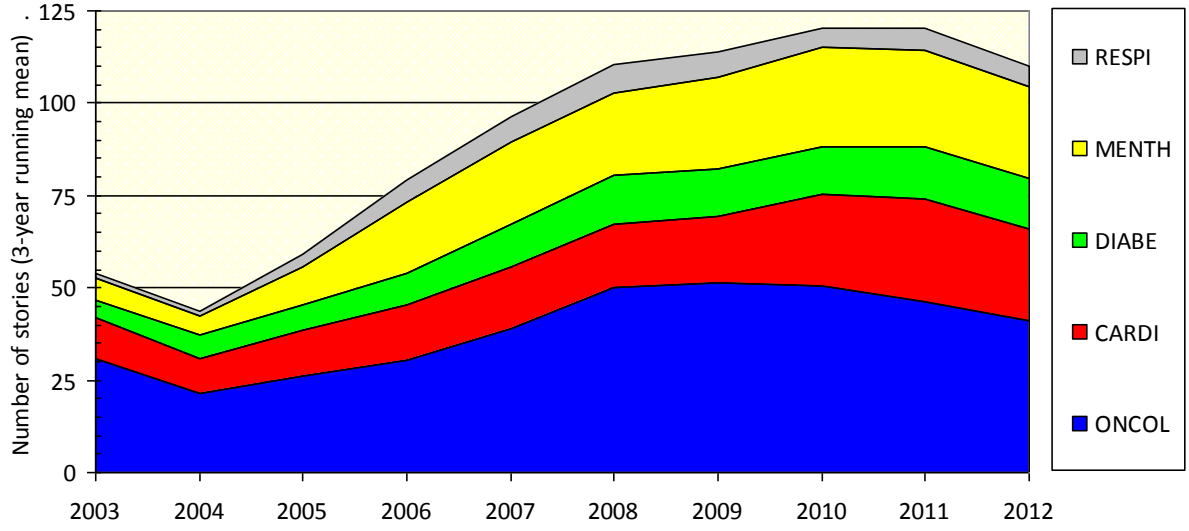

Figure 60. The numbers of stories on NCD research in Le Soir, 2002-13 (three-year running means).

Evidently, there has been a steady rise from 2004 to a maximum in about 2010-11, and then a small decline. Cancer, followed by mental disorders and cardiovascular research, is the main NCD area being reported, and the amount of coverage of the different NCDs correlates quite well with the relative disease burden and the amount of research in Belgium, see Figure 61.

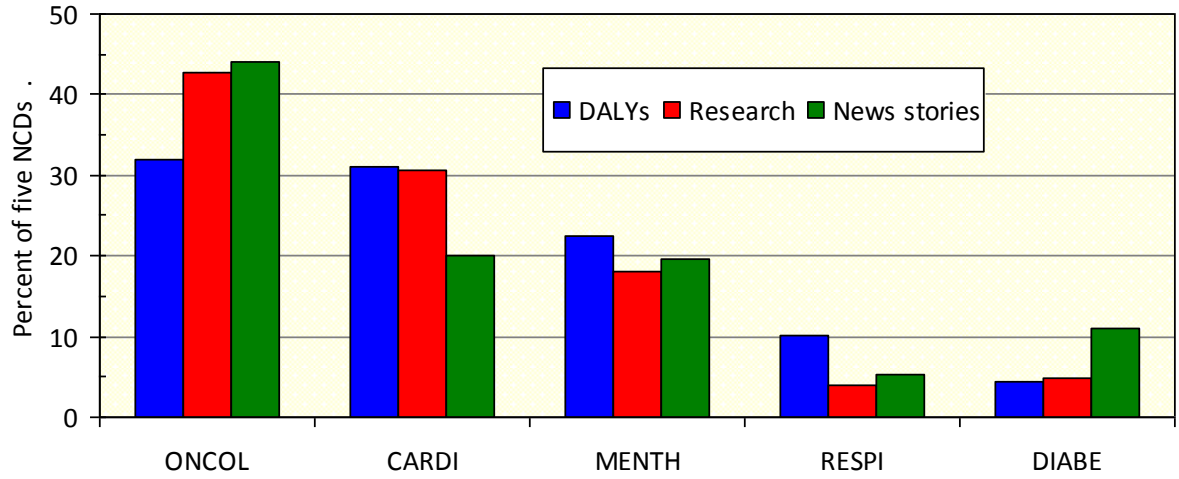

Figure 61. Chart showing the correlation between the disease burden in Belgium (Disability-Adjusted Life Years, DALYs, in 2010), the amount of research (percentage of all biomedical research) and the number of stories in Le Soir in 2002-13.

Relative to the disease burden, cancer is over-researched and reported; cardiovascular diseases are under-reported; respiratory diseases are under-researched and under-reported, and diabetes is over-reported.

8.1.3 Manifestations of cancer research and newspaper stories

We also examined the breakdown of stories of cancer and mental disorders research by disease area. For cancer, the correlation was best with the amount of research in Belgium, with a correlation factor $r^2 = 0.78$, see Figure 62.

As expected (see Lewison *et al*., 2008) breast cancer gets the most coverage, but it is interesting that lung cancer research, which is sometimes regarded as rather a neglected subject, is second, and its coverage is proportionately more than that given to breast cancer research by *Le Soir*. However, mouth and stomach cancer are barely noticed, and there were no stories about thyroid cancer although it accounted for almost 1% of cancer DALYs in Belgium in 2010.

8.1.4 Mental disorders and newspaper stories

The different mental disorders are shown in Figure 63 for their Belgian disease burden, amount of research and coverage in the 203 stories in *Le Soir*. It is striking how much coverage is given to dementia (ALZ), but very little to bipolar (BIP) and eating (EAT) disorders. There are also relatively fewer stories on unipolar depression than the disorder would warrant, but the coverage in *Le Soir* at 20% is more than twice that in stories in the British Broadcasting Corporation (BBC) web archive (Lewison *et al*., 2012).

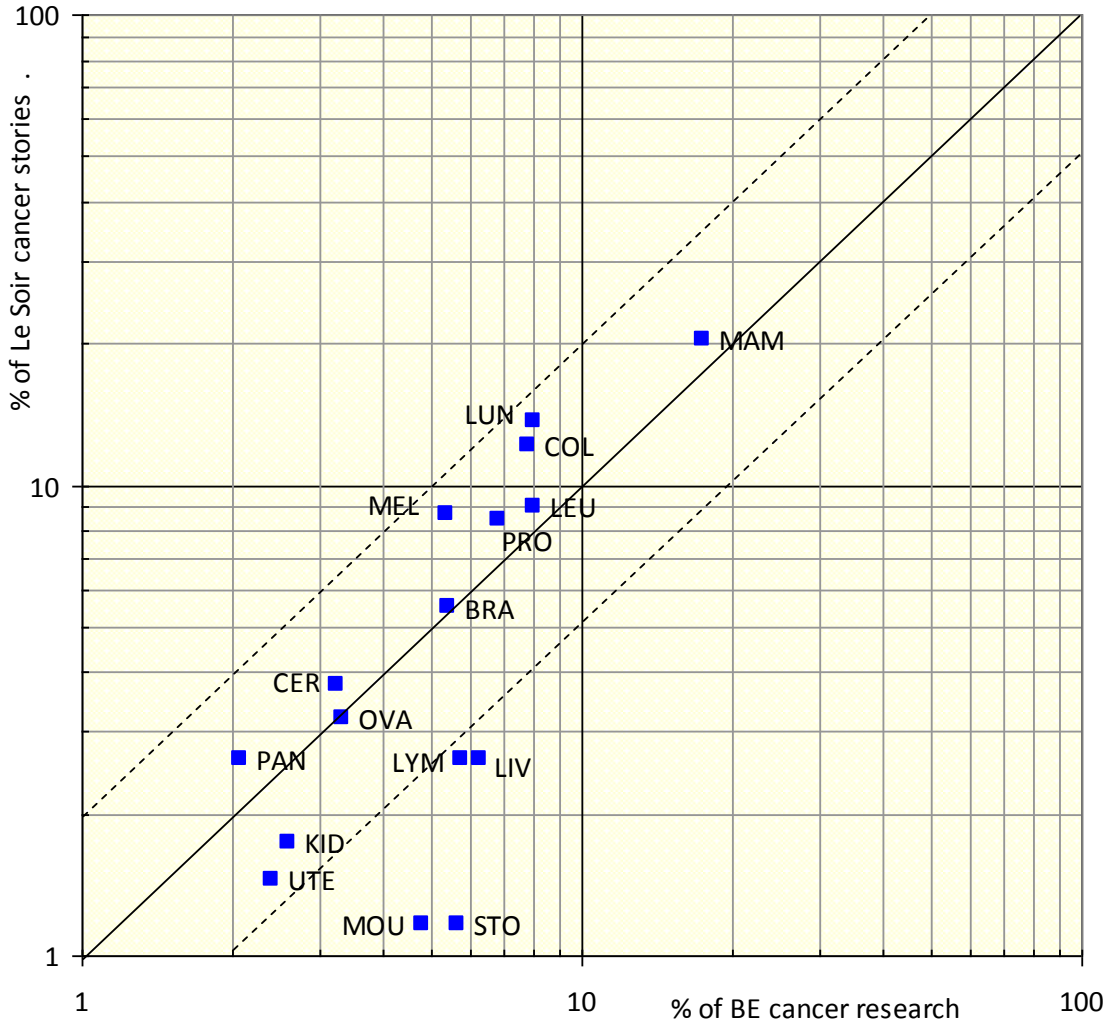

Figure 62. Comparison of the newspaper coverage in Le Soir of research on different cancers and the amount of Belgian cancer research, 2002-13; integer counts. *For codes, see Table 44.*

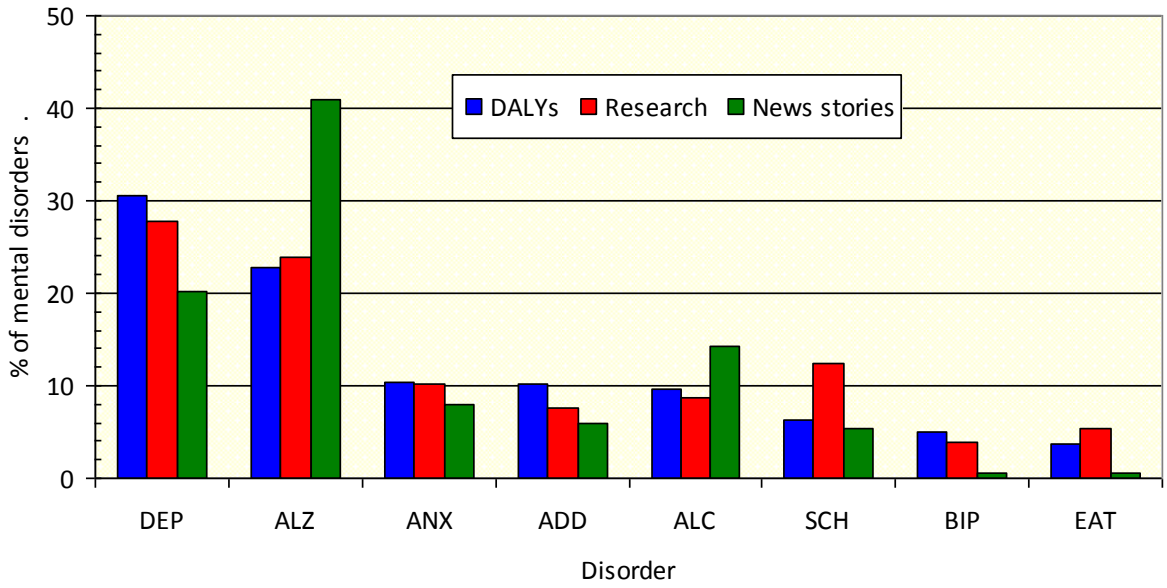

Figure 63 Coverage of different mental disorders in Belgium: disease burden (DALYs), research output, and coverage in stories in Le Soir. *For codes, see Table 34*.

8.1.5 Analysis of the cited research papers

The next analysis presented here is of the nationality of the research cited in *Le Soir*. By comparison with previous work on cancer (Lewison *et al*., 2008) we would expect that a Belgian newspaper would over-cite research from Belgium by a bigger factor than for the UK in UK newspapers, and Figure 64 shows that this is indeed the case, with an over-citation ratio of x 7.6, compared with x 2.7 for the UK in mental disorders research and x 6 in cancer. French research is also over-cited, by x 3.1, slightly more than that from the Netherlands (x 2.5). There is also substantial over-citation of research from the Scandinavian countries: Sweden x 2.6, Finland x 2.9, Denmark x 3.2, Norway x 3.5 and Iceland an astonishing x 22 (involving 14 papers, though the fractional count was much lower).

8.1.6 Analysis of the journalists in *Le Soir*

Altogether *Le Soir* used the services of 24 different journalists, but three of them (Frédéric Soumois, Jacques Poncin and Christian du Brulle) wrote two thirds of the stories. Wire services were also used, notably Agence France Presse (78 stories) and Belga (22 stories). Medical research reporting in this newspaper seems to be dominated by men who contributed 77% of the stories compared with only 10% from women. During the last four years, women's contribution declined to just 5%. By contrast, 55% of BBC reports of cancer research are written by women, and there is a similar proportion of mental disorders research stories written by UK newspaper journalists.

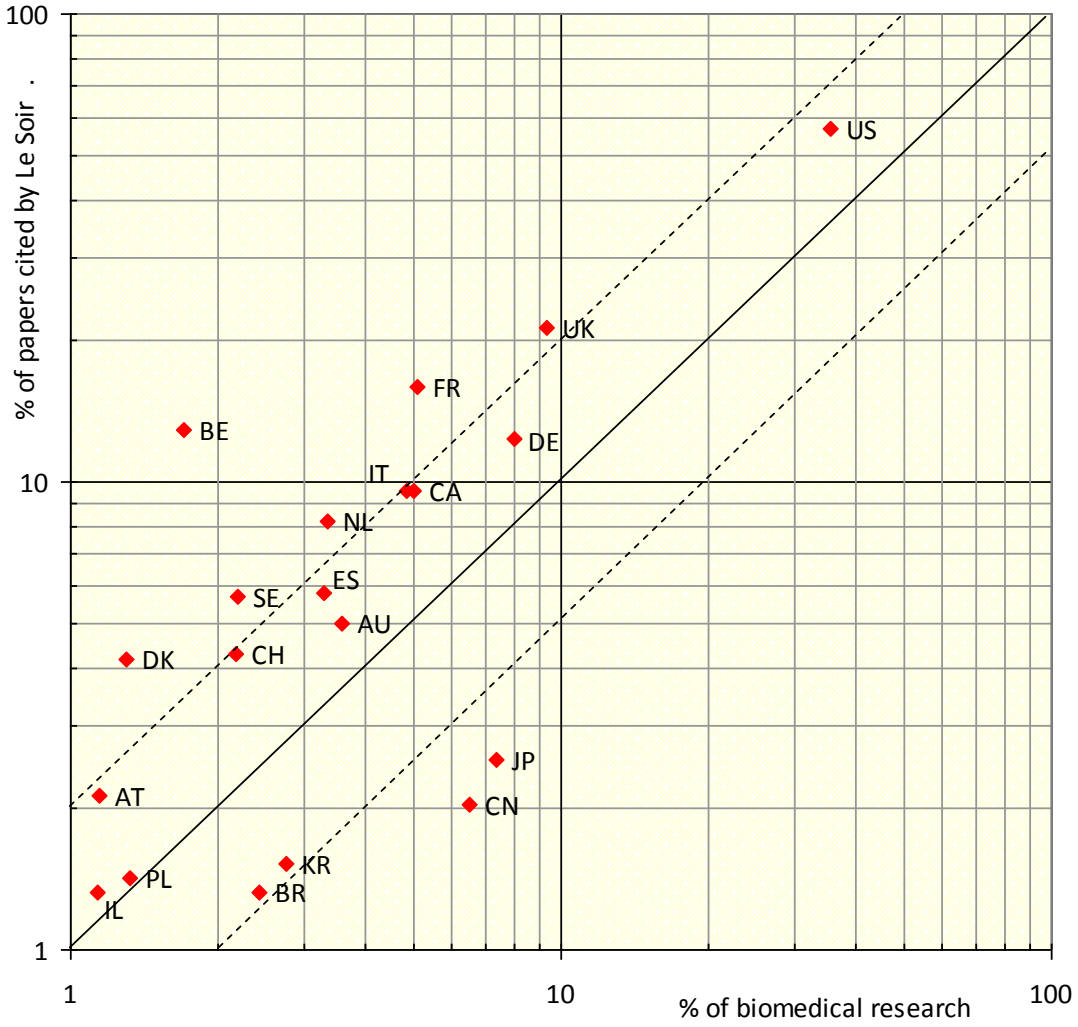

Figure 64. Countries represented among papers cited by stories on NCD research in Le Soir compared with their presence in biomedical research in the WoS, 2002-13; integer counts. *For codes, see Table 1.*

8.1.7 Analysis of the commentators on the research

Our last analysis was of the commentators on the significance of the results being described in the stories. These people are often seen as authoritative and can put the new work in context. In the UK, both newspapers and broadcasters (Lewison *et al.,* 2008; Lewison *et al.,* 2012) turn frequently to representatives of the medical research charities, who usually downplay the hype associated with discoveries and imply that donations are still needed to convert results from rodents to routine clinical practice. However in Belgium, only 126 (13%) of the stories in *Le Soir* had a commentator at all, and the largest numbers were from universities (44%) and hospitals (25%). There was only one charity commentator, and he was from a US charity, the American Heart Association. This may partly explain why the UK public are generally so supportive of medical research charities compared with Belgium.

9 Conclusions and recommendations

9.1 More research or better-directed research?

9.1.1 Comparison of countries

The volume of research papers has been compared with individual countries' wealth in a series of log-log plots (CARDI: Figure 3; DIABE: Figure 11; MENTH: Figure 28; ONCOL: Figure 35; and RESPI: Figure 46). These show whether countries are doing more or less research in a particular disease than would be expected on the basis of their wealth. Some countries are clearly doing relatively more than expected, and others (necessarily) are doing less than the trend-line would suggest. The results are collected together in Table 66.

Table 66. List of apparently over-performing and under-performing countries in research in the five NCDs in comparison with the EUR31 trend-line relating research outputs to GDP.

NCD	*High-performing countries*	*Low-performing countries*
CARDI	Greece, Netherlands	Bulgaria, Romania
DIABE	Denmark, Finland, Sweden, UK	Norway, Portugal, Romania
MENTH	Croatia, Finland, Netherlands, Sweden	Bulgaria, France, Romania, Slovakia
ONCOL	Croatia, Greece, Iceland, Slovenia	Cyprus, France, Latvia, Luxembourg
RESPI	Netherlands, Sweden, UK	Austria, Germany

Some of these high-performing countries are doing so because their disease burden from these NCDs is higher than average (for example, for the UK in RESPI), but there are other cases where it does appear that there is not the immediate clinical need (for example, for the UK in DIABE). In some of these cases, resources might be better directed to other diseases. It would not be practical to suggest that disease-specific medical charities change their remits, but it might be possible for major state funding bodies, or foundations with a diverse portfolio, to reduce their research spend to allow for this. For example, the Wellcome Trust in the UK has a long-standing policy of not funding clinical cancer research as it regards it as being satisfactorily supported by the numerous cancer research charities.

9.1.2 Comparison of the five NCDs

There appears to be an imbalance, as was pointed out by one of the respondents to our partners' survey (see section 5.1.4) between the amount of research in Europe on communicable and non-communicable diseases, in view of the latter imposing 85% of the total burden (in DALYs). This was borne out by our results, as research outputs in the five NCDs totalled only 28% of the European biomedical research output whereas the five NCDs together accounted for 55% of the total DALY burden. This suggests that some re-balancing of the overall biomedical research portfolio would be in order, although some biomedical research is rather basic and could yield long-term benefits for many different diseases.

Another aspect of this is the balance of research effort between the five NCDs. The overall situation is shown in Figure 65, overleaf. (The amount of research has been scaled up so that the totals for the five NCDs are the same.) MENTH appears to have an appropriate amount of research - though this may not be the case for some countries, see above - but ONCOL appears to attract somewhat more than enough support whereas RESPI is clearly under-funded. [We noted this in the analysis of funding: over 40% of the RESPI papers had no specific acknowledgement to a funder compared with 30% of DIABE papers.] In particular, we saw that COPD was under-funded compared with asthma.

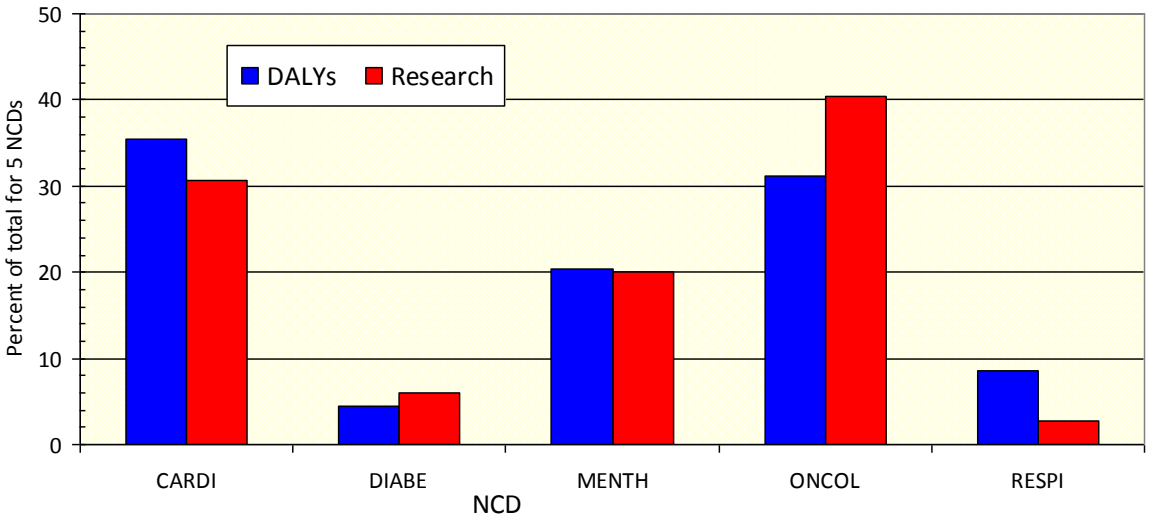

Figure 65. Comparison between disease burden and research outputs (EUR31 countries) for five NCDs.

9.1.3 Comparison of research types

At present we only have data for cancer research, but it seems likely that some of the lessons from this NCD might be applicable to other disease areas. The most striking lesson to emerge from our study of the references on lung cancer clinical guidelines was that surgery research was the leading research type cited as evidence for the guidelines, whereas it took a relatively modest place in overall research output, and was very little cited in the serial academic literature. Research funders should probably take more account of other ways in which research can have an impact on the practice of medicine than simply counting citations.

9.2 Who is funding NCD research in Europe and who should do it

9.2.1 The three main sectors

Results from both DIABE and RESPI (Figures 18 and 51, respectively) show that there are big differences between countries in their sources of support for research, and this was also shown in the previous surveys of cancer research funding n Europe (Eckhouse *et al.*, 2005; Sullivan *et al.*, 2008). Northern European countries enjoy a wide range of private-non-profit funders (especially collecting charities and endowed foundations) but these hardly exist in eastern Europe. It would be very desirable to investigate what fiscal or other disincentives exist in eastern Europe to the development of the charitable sector and what more might be done to encourage it. There may also be lessons for charities and foundations in western and northern Europe on the situation in each others' countries, with respect to:

- how they raise money
- how they spend it
- the fiscal regime
- publicity, such as commenting on newspaper stories.

We have investigated in our funding analysis of DIABE and RESPI the commercial sector, but it is not practicable for us to comment on their funding strategies. We note in passing that much research funded by the commercial sector involves multiple companies working together to support individual projects.

9.2.2 The future

One of the conclusions that we have drawn is that the overall portfolio of research outputs, and that of individual countries, may need some adjustment. Since it is clear from our partners' surveys that most research funders act in responsive mode, and claim to be funding "the best", there is little scope for changing this portfolio in response to a perceived need to alter the balance. There is bound also to be a high degree of inertia in the system, with the top researchers continuing their own work, attracting able students, and so perpetuating the *status quo*. Methods need to be explored of how best to change the system. Ring-fencing subject areas in need of more attention has been tried, but it may not succeed as it could lead to the funding of lower quality research proposals attracted by the pot of money on offer. One possibility is for major research funders to seek out and import high-quality teams from other countries if there is no cadre of researchers in their own country on whom they could build.

Another possibility is for the European Commission to support short- and medium-term (from a few weeks to a few months) visits between Member States to help those who are not doing enough in particular areas of need to learn from their European neighbours. We noted, for example, that in cancer palliative care research seems to be almost neglected in some countries, and this must be causing great distress among terminally-ill patients who are not receiving the most up-to-date care to relieve their suffering. There would also appear to be scope to encourage more exchange of surgeons, as surgical research is clearly not a priority for some countries.

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