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News & Views

Cancer research funding in Europe

Janet Fricker

Europe is awash with small cancer studies, funded by the governments and charitable institutions of individual European countries that are failing to realise their full potential. ''The problem with Europe is there's no one place to go for big cancer research funding, apart from the European Commission,'' said Philippe Autier, from the International Agency for Research on Cancer (IARC) (Lyon, France). ''We're seeing a fragmented picture where there is little knowledge about who funds what, and a duplication of effort. Overall European cancer funding lacks any real co-ordination. But the blame can't totally be laid at the doors of the European Commission – member states need to be taking some responsibility.''

Françoise Meunier

In reality the European Commission has been a bit part player in cancer research – the Framework 6 Programme provided a miserly 6% of the total yearly cancer research spend in Europe. The derisory budget for cancer research had been laid down by the EC member states. Securing funds from the Commission is an extraordinarily bureaucratic process, where cancer investigators compete with investigators from all other scientific fields for limited funds. There are innumerable rules and regulations that disqualify worthwhile projects and discourage investigators from applying. The Commission put out calls for proposals on topics specified within the Framework agreement, a practice they have justified as the need to build ''critical mass'' in priority areas. ''Such approaches block the life blood to innovation. Brilliant ideas that aren't from predefined areas have been totally stuck,'' said Volker Diehl, from the Comprehensive Cancer Centre in Heidelberg (Germany).

Additional layers of bureaucracy deterring scientists have included investigators being required to form consortiums to meet guidelines about involving a specified number of countries, requirements to include at least one small or medium enterprise (SME) in the application, and a stipulation that all organizations should be new. The result is that networks that have been in existence for years are automatically disqualified, or need to create a new organization. Last issue Fatima Cardoso (Institute Jules Bordet, Brussels, Belgium) told how TRANSBIG was created as a new consortium out of BIG to get around this requirement.

The Commission fails even to adequately support the world-class European Organization for Research and Treatment of Cancer (EORTC), a 45-years-old institution promoting, conducting and co-ordinating pan-European clinical cancer trials on an independent basis. The EORTC cobbles together its money from the EORTC Charitable Trust (via an assortment of European Cancer Leagues), other private funds and the pharmaceutical industry, with money from the European Commission only received on a project basis, despite years

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of attempting to persuade the Commission to provide core funding for a pan-European clinical research infrastructure. It is ironic, many find, that the EORTC has received a core grant from the National Cancer Institute (NCI) in the USA since 1973.

The Commission has countered that clinical trials are too expensive for public funding and should be financed by cancer charities, national government and the pharmaceutical industry. This, said Françoise Meunier, Director General of the EORTC, represents failure to recognize that many clinical trials do not concern drugs at all. A major component of the EORTC program consists of non-sponsored academic trials regarding surgical methods, radiotherapy regimes, and systemic therapy with combinations of drugs to define new standards of care. "Typically, it's impossible to get pharmaceutical sponsorship for such studies as they involve combinations of drugs that may have been available for several years and the studies are not aiming at registration of new compounds," said Meunier.

Richard Sullivan

Charitable support does not provide the solution for international collaborations, since national charities are often reluctant to see the money they have raised cross European borders. The European Prospective Investigation of Cancer (EPIC) study, the largest study on diet and health ever undertaken, is a case in point. Initiated in 1993, EPIC set out to determine how diet and lifestyle factors interact with genetics to influence people's risk of cancer. The study now possesses a unique data resource on the diet and lifestyle of 500,000 people from all over Europe, who are being followed through to see who develops cancer. Key findings have included corroboration of the hypothesis that fibre intake reduces colorectal cancer. But this project, which has the potential to reveal a myriad of additional useful is threatened by lack of funding.

Initially EPIC was funded by the European Commission's Europe against Cancer Programme, but now is no longer supported by the Commission. "To keep EPIC alive we're having to deal with 30 to 40 funding bodies from 10 different countries who are willing largely only to fund research in their own countries," said Elio Riboli, the principal investigator, from Imperial College (London, UK). "Co-ordinating so many donors requires a huge effort, taking a considerable amount of time that detracts from our research."

The received wisdom in most European countries, said Richard Sullivan from Cancer Research UK, is that fund raising should be for cancer research in that country alone. "Governments are also in competition and believe the money should be spent in driving forward the wealth of their nation through science and technology rather than being distributed through Europe."

Philippe Autier

Such national tendencies and lack of support from the Commission result in many studies recruiting subjects at national levels as data are not readily applicable to other countries, leading to a considerable loss of credibility. Take the Million Women Study, initiated in the UK in 1997, which has shown that current users of oestrogen–progestagen hormone replacement therapy are more likely to develop breast cancer. "Other European countries are resisting the findings, saying the UK is not representative of the rest of Europe. They are now planning to repeat the studies in their own settings, leading to much unnecessary duplication of effort," said Autier.

Difficulties facing European research funding have been compounded by the introduction of the European Clinical Trials Directive (EUCTD), which came into force in May 2004. This directive introduces a further raft of bureaucratic, financial and legal obligations. The EUCTD, originally intended as a way of simplifying and harmonizing pharmaceutical clinical trials throughout Europe by creating a single legal framework, with the aim of increased protection to the patients, has also been applied to non-commercial clinical trials carried out by academic researchers. Each trial is now obliged to have a 'sponsoring' research body or institution who is required to pay for every drug or device used by every patient enrolled in the trial (including fully licensed drugs normally be funded by the health service) and to meet the costs of any inspections. The amount of information to be provided in the application dossier has significantly increased and the investigational products have to be specially labeled, packaged, stored, and handled – even if it is a drug that has been in common use for years. All this places a heavy financial and administrative burden on non-commercial sponsors.

A recent survey of directors of eight clinical trial units (CTUs) in the UK, published in *EJC* (2007, 42: 8–13), revealed

that the clinical trials directive has doubled the cost of running non-commercial cancer clinical trials in the UK, and resulted in substantial delays in starting trials of between 6 and 12 months. Costs associated with additional administrative and pharmacovigilance support alone were estimated at £50,000 for each trial. Moreover, the study found that far be it from facilitating European interactions, the EUCTD was responsible for making CTUs unable or unwilling to open trials in non-UK centers due to different interpretations by different member states.

The effects are reverberating throughout Europe. In Spain and Poland, the directive has totally killed clinical trials. The EORTC, partly as a result of the directive, now only opens 10 new trials a year, opposed to 20 a few years ago, reported Meunier.

Everyone agrees that to move on Europe requires good quality data providing a baseline of who exactly funds what. The European Cancer Research Managers (ECRM) Forum study, published in March 2005, was the first attempt to get a handle on the non-commercial funding of cancer research in Europe. It revealed a disturbing picture of cancer research funds that were in short supply both centrally from the EU and from individual states. The study revealed a ''heterogenous'' mis-mash of funding that varied enormously between different countries, with research in Europe surviving largely on the philanthropy of charitable institutions.

The survey found:

- The USA spent five times more per person (€17.63 compared to €3.76), and four times more as a percentage of GDP (0.0578% compared to 0.0163%), on cancer research than the 15 countries that were members of the EU before May 2004. When USA spending was compared to the 25 current EU members, the gap widened to seven times more per person (€17.63 versus €2.56) and four times more as a percentage of GDP.
- Government agencies accounted for only half of the total European spend of €1.43 billion, the rest came from charities, with 65 major charities across 23 countries contributing around €667.3 million to cancer research. The European Commission contributed around €90 million.
- Spending on cancer research varied widely across Europe. The UK spent the most (€388 million), followed by Germany and France; while Malta spent nothing. When spending was analyzed as a proportion of GDP, the UK spent the most (0.0267%), followed by Sweden, Germany, France and the Netherlands.
- The Government charity split varied between different countries. In eight countries, there was no cancer research spending by charitable organisations, while in three countries, there was no spending by governments. One of the most extreme examples was Sweden with a €6.43 per capita spend on cancer research (ranking second only after the UK), but only €0.56 of this came from government. More than 90% of Swedish research money is contributed by Swedish cancer charities. At the other extreme was Greece, where nearly all research funding came from government.
- The EU concentrates a large proportion of its spending on basic scientific research at the expense of preventative and clinical research. Biology received 41% of all cancer research funding, compared with 20% for treatment and just 4% for prevention. In contrast, the USA spent 25% on biology, 25% on treatment and 9% on prevention.

At the time Richard Sullivan, chair of the European Cancer Research Managers Forum, concluded: ''The EU is massively behind the USA in its support of non-commercial cancer research. …Also threatened is the ability to recruit and retain clinicians and scientists to work in cancer research, as well as the commercial attractiveness of the EU.''

Gordon McVie, senior consultant to the European Institute of Oncology, believes under funding has major implications for the quality of patient care in Europe, estimating that up to 20,000 more lives could be saved each year if funding for cancer research was increased. ''Innumerable studies have shown that patients treated in clinical trials do better, whether they are entered into the experimental or control arm,'' he said.

One criticism of the Research Manager's study was that it failed to include infrastructure money used in European labs, whereas the US comparative data included this money, indicating that differences between the US and Europe may not have been as great as suggested. A follow-up survey, due out Autumn 2007, addresses these issues by introducing bibliometric analysis ''It's a much more robust methodology involving a process of reverse engineering where we identified cancer research publications which allow us to estimate the actual spend per country much more accurately,'' explained Sullivan. Such methods add to the first study where European Cancer Research Managers Forum members were asked to identify sources of cancer research funding in their countries, and organisations were then contacted to provide their latest available figures for annual direct cancer research spending (Figure 1).

''The latest results are real eye opener dramatically changing our perspective on the funding of European cancer research,'' said Sullivan, adding that the results revealed real improvements in both the direct per capita spend and percentage of GDP.

Sullivan believes that this is partly because the first survey achieved its aim of helping to ''act as a clarion call'' to generate action, and was instrumental in persuading research organisations to step up to the mark. ''We were quoted in 70 per cent of European cancer policy documents. If countries see for the first time how badly they compare to the rest of Europe it creates a real incentive to try to do better. New charities have been launched on the back of the report.''

There are welcome signs that the EC wants change, and is now directing greater resources towards biotechnology research. In 2001 the European Council launched the Lisbon agenda with the objective of making the EU ''the most competitive place in the world to do business''. Part of the strategy requires Europe to boost its R&D spending from 1.9% of the gross domestic product in 2000 to 3% by 2010.

In FP7 the Commission appears to be putting its money where its mouth is. FP7, running from 2007 to 2013, has a budget of €53.2 billion, representing a 63% increase from FP6 at current prices. The EC also appears to have taken note of criticisms, and is making real attempts to reduce bureaucracy in its funding system and stall the brain drain to both the US and the Far East.

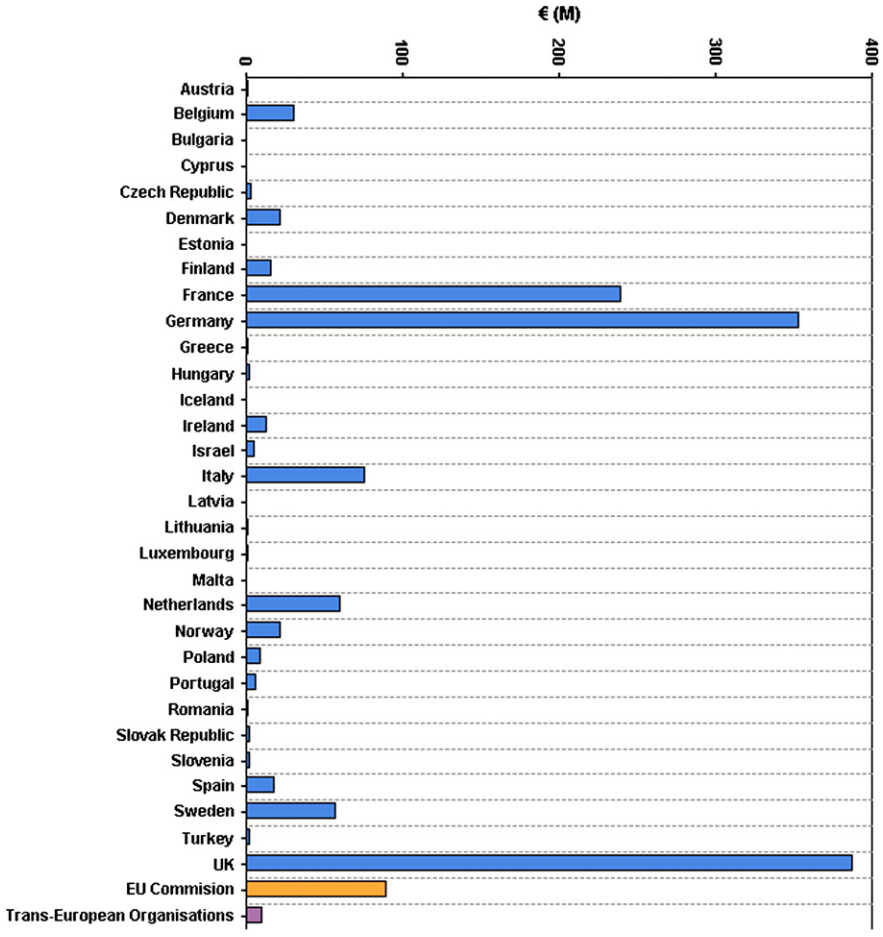

Figure 1 – Direct Cancer Research Spending by Country, including European Commission and Trans-European Organisations. From: Eckhouse, S., Sullivan, R. A survey of public funding of cancer research in the European Union. PLOS Medicine 3(7), e267.

The European Research Council, officially launched as part of FP7 in February 2007 to support basic research, is being heralded as the first pan-European funding body to support investigator driven research, from a ''bottom up perspective''. The ERC allows researchers to identify new opportunities and directions rather than priorities being set by politicians, with excellence being the sole criteria for selection. The ERC will provide starting grants for post docs and other young scientists worth up to £2 million over 5 years and advanced grants to established researchers worth up to £2.5 million over 5 years. At the launch Science and Research Commissioner Janez Potočnik said he hoped the ERC would generate a ''snowball'' effect, with greater competition leading to better research. ''Better research will lead to more private investment in research. More investment will lead to better facilities and better facilities will attract and retain better researchers.''

Another innovation, supported by the 7th Framework, designed to stall brain drain is the Marie Curie programme that will devote money to employing and training researchers and facilitating cross-border moves.

The pharmaceutical industry is being brought firmly on board through the Innovative Medicines Initiative (IMI), where companies will commit to match public resources invested by the European Commission to award research grants for European Private–Public partnerships. The focus will be on the principle causes of delays or ''bottlenecks'' in discovery and the development of medicines, with individual companies being encouraged to share data in circumstances that do not comprise commercial confidentiality. It is estimated that the EU will invest €1 billion in IMI from 2008 to 2013, leveraging an additional €1 billion investment from the pharmaceutical industry.

The EC have also funded the Eurocan + Plus project, an initiative from IARC looking to improve the co-ordination of cancer research in Europe. ''What's needed is one reference point, an organization that can co-ordinate activities critical for accomplishing high quality cancer research in Europe and achieve consensus about the main priorities. It would allow us to get an idea of what is currently being funded to avoid duplication and fragmentation and allow vital links to be fostered between academics and industry,'' said Autier, who is involved with the Eurocan + Plus project.

The hope must be that if all the stakeholders – the Commission, pharmaceutical industry and individual EU country governments and charities – could be brought together this would enable the Lisbon dream to be realized.