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A REVIEW ON CANCER RESEARCH FUNDING

Mioara Calipsoana MATEI[1], Valeriu CHIRICA[2], Doina AZOICAI[3]

Abstract

Cancer is one of the major causes of illness worldwide and the second most important cause of death. The burden of this disease goes beyond the individuals and their families to health caregivers and society. Many actors contribute to the management of cancer in a specific society, and one of the most important issues related to this is cancer research funding, which provides the opportunity for advances in cancer Biology, Etiology, Prevention, Early Detection, Treatment, Cancer Control and Scientific Model Systems. In this paper we presented a literature review on cancer research funding. We analysed the amount of money invested in cancer research in different regions, the type of funding organizations, the distribution of cancer research funding by percentage of Gross Domestic Product, by Common Scientific Outline categories and by cancer site. The results show that USA and Europe had the major spending in cancer research, followed by Canada, Australia, and Asia (especially Japan and China). Among European countries United Kingdom has allocated the largest funds for cancer research. The major funders for oncological research were the governmental organizations in USA, Canada, Australia, and both, governmental and charities, in Europe. In recent years China made impressive progress in cancer research funding, but is still far behind the Western countries. For all regions the majority of funding for cancer research was directed to Biology and Treatment, and less oriented to Prevention and Cancer control. However, in order to direct the funding for cancer research accordingly to burden of disease in different populations and societies, further research is needed.

Keywords: cancer, research, funding, expenditure, investment, charity.

[1] Grigore T. Popa University of Medicine and Pharmacy, Faculty of Medicine, Discipline of Primary Health Care and Epidemiology, Iasi Clinical Epidemiology Unit, Department of Oncogenetics, Iasi, ROMANIA. E-mail: mioara.matei@umfiasi.ro

[2] Grigore T. Popa University of Medicine and Pharmacy, Faculty of Medicine, Discipline of Primary Health Care and Epidemiology, Department of Oncogenetics, Iasi, ROMANIA. E-mail: valeriu.chirica@yahoo.com (corresponding author).

[3] Grigore T. Popa University of Medicine and Pharmacy, Faculty of Medicine, Discipline of Primary Health Care and Epidemiology, Iasi Clinical Epidemiology Unit, Department of Oncogenetics, Iasi, ROMANIA. E-mail: doina.azoicai@umfiasi.ro

Introduction

Cancer is one of the main causes of illness globally with an estimated number of 14.1 million new cases identified in the year 2012 and a total of 32.6 million people living with cancer, diagnosed over a period of five years (Ferlay *et al.*, 2013; GLOBOCAN, 2012). Also, cancer is the second most important cause of death worldwide, with 7.6 million deaths in 2008 (representing around 13% of all deaths) (Bloom *et al*., 2011) rising to 8.2 million deaths in 2012 (accounting for 22 % of all deaths determined by non-communicable diseases) (Ferlay *et al.*, 2013; World Health Organization, 2015). Also, in 2012 the most commonly diagnosed cancers worldwide were: lung cancer (13% of total), breast cancer (11.9%), and colorectal cancer (9.7%); the top three causes of cancer deaths were: lung cancer (19.4%), liver (9.1%), and stomach (8.8%) (Ferlay *et al.*, 2013). So, "one in three will develop cancer within their lifetime, and one in four will die from it" (Eckhouse *et al*., 2007).

There are few studies and reports that provide information about cancer research funding in different regions and a very small number tried to take into consideration more than one region or to present the situation at the global level. There are many types of sources for cancer research funds, including governmental agencies, state governments, supranational institutions or other big organizations (such as European Commission, National Institutes of Health etc), industry or charity. Also, according to Common Scientific Outline (CSO) classification, there are seven different areas of scientific interest in cancer research that help to improve the comparison among research portfolio of public, nonprofit, and governmental research agencies: Biology; Etiology; Prevention; Early detection, diagnosis and prognosis; Treatment; Cancer control, survivorship, and outcomes research; Scientific model systems (International Cancer Research Partnership, 2014). The aim of this paper is to provide information and support for decision making actors in cancer research funding for the major benefit of cancer patients and society.

Methods

We performed a scientific literature search within the PubMed, Science Direct and OVID MEDICAL databases, using different combinations of the following key words: "cancer (or neoplasm or malignancy) AND research AND funding (or expenses or expenditure or costs)".

In *PubMed*, a total of 14,332 articles (including duplicates) were obtained. Also, another search was performed using the following combinations: "cancer research funding in Europe" (1,366 articles); "cancer research funding in Asia" (541 articles); "cancer research funding in Australia" (431 articles); "cancer research funding in Canada" (579 articles) and "cancer research funding in USA" (3,708 articles).

In *Science Direct*, a total number of 41,209 articles (including duplicates) were obtained. A second search was performed using the following combinations: "cancer research funding in Europe" (7,596 articles); "cancer research funding in Asia" (3,150 articles); "cancer research funding in Australia" (6,399 articles); "cancer research funding in Canada" (8,838 articles) and "cancer research funding in USA" (20,368 articles).

In *OVID MEDICAL* [Ovid MEDLINE (R) 1946 to February Week 4, 2015] a total of 2,396 articles (including duplicates) were obtained. Also, a second search was performed using the following combinations: "cancer research funding in Europe" (1,203 articles); "cancer research funding in Asia" (351 articles); "cancer research funding in Australia" (600 articles); "cancer research funding in Canada" (701 articles) and "cancer research funding in USA" (366 articles). After duplicate removal, the titles and abstracts of the remaining papers were evaluated according to the following inclusion criteria: (1) published between 2005 and 2014; (2) worldwide; (3) published in English; (4) full text; (5) humans as subjects. A secondary literature search was performed using the references cited in the selected papers. A total of 22 papers were identified, for which the full-text version were obtained.

Results

A total of 17 studies reported in 22 papers were reviewed. These scientific articles reporting on cancer research funding, were developed in the following geographical regions: Europe (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2005; Eckhouse *et al*., 2007; Fricker, 2007; Torjesen, 2014; Institute National du Cancer, 2010; Kanavos *et al*., 2014; Illman, 2005; Watson, 2005; Eckhouse *et al*., 2008), USA (Gillum *et al*., 2011; Brown, 2007; Chow & Itagaki, 2010; International Cancer Research Partnership, 2012), Australia (Cancer Australia, 2014; Shirazee *et al*., 2011a; Shirazee *et al*., 2011b), Canada (Canadian Cancer Research Alliance, 2014; Canadian Cancer Research Alliance, 2012; Gotay, 2013) and Asia (Cheng, 2007; Hong & Dong, 2014) (*Table 1*).

This review presents the following data: the studies' characteristics (Table 1), the amount of money spent on cancer research (Table 2, Table 4, Table 5, Table 6), values by source and type of funding organisations (Table 3), by CSO categories (Table 7), and by cancer site (Table 8). Also, there is information about the methodology to collect data on cancer research funding, types of reported results, values about cancer research funding by countries, and by GDP (Gross Domestic Product) / per capita.

Overview of the methods used in the literature in order to collect data on cancer research funding

The studies identified in the literature used different methods to collect data about cancer research expenditure: questionnaires / letters sent to the relevant Institutions/ Organizations (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2005; Eckhouse *et al*., 2007; Gillum *et al.*, 2011; Shirazee *et al*., 2011a; Shirazee *et al*., 2011b; Kanavos *et al*., 2010; Eckhouse *et al.*, 2008; Cancer Australia, 2014) or to leading cancer researchers (Shirazee *et al*., 2011a; Shirazee *et al.*, 2011b; Eckhouse *et al.*, 2008), information from institutional websites (where available) (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2005; Eckhouse *et al*., 2007; Shirazee *et al*., 2011a; Shirazee *et al*., 2011b; Kanavos *et al*., 2010; Eckhouse *et al.*, 2008; Cancer Australia, 2014), interrogation of the most relevant databases regarding the data on cancer research papers (the outputs of cancer work) (Eckhouse *et al.*, 2008; Eckhouse *et al*., 2007, Gillum *et al.*, 2011; Hong & Dong, 2014) or interrogation of common databases regarding cancer research funding (Eckhouse *et al.*, 2008; Kanavos *et al*., 2014; International Cancer Research Partnership, 2012).

Table 1. Studies included in the current analysis

No. crt	Authors	Year of publication	Region	Period of analysis
1	Eckhouse S. et al.	2005	Europe	2002-2003
2	Illman J	2005	Europe	2002-2003
3	Watson R	2005	Europe	2002-2003
4	Eckhouse S, Sullivan R.	2006	Europe	2002-2003
5	Brown H.	2007	USA	1996-2005
6	Cheng MH	2007	Asia (Japan, China, South Korea, Singapore)	2005-2006 2008-2009
7	Eckhouse S. et al.	2007	Europe	2004
8	Fricker J	2007	Europe	2005 2007-2013
9	Eckhouse S. et al.	2008	Europe; USA	2006-2007
10	Chow DS, Itagaki MW	2010	USA; Asia (Japan, China)	2009
11	Kanavos P	2010	Europe; USA	2006-2007
12	*** Institute National du Cancer	2010	France	2009-2010
13	Gillum LA et al.	2011	USA	2004-2006
14	Shirazee N et al. (a)	2011	Australia	2008-2010
15	Shirazee N et al. (b)	2011	Australia	2008-2010
16	*** Canadian Cancer Research Alliance	2012	Canada	2005-2009
17	*** International Cancer Research Partnership	2012	Europe (France, UK, Netherlands); USA; Australia ; Asia (Japan)	2005-2008
18	Gotay C	2013	Canada	2005-2010
19	Hong W, Dong E	2014	Asia (China)	
20	Torjen J	2014	UK	2013
21	*** Canadian Cancer Research Alliance	2014	Canada	2011
22	*** Cancer Australia	2014	Australia; Canada; UK; USA	2003-2005 2006-2011

The most used method was the “top-down” approach (Inmon, 2005; Kimball & Ross, 2002) which means the collection of data from organizations that fund

cancer-related research or from organizations that administer cancer-related projects and programs. This method offers a high response rate (62-96%) compared with "bottom-up" approach, which means to directly contact the leading cancer researchers (27-42%) (Cancer Australia, 2014; Eckhouse *et al.*, 2008; Shirazee *et al*., 2011b). Other method used with good results to evaluate the cancer research funding was the interrogation of a common database. Some authors checked the RADiUS (Research and Development in the United States) database to assess the direct spend for governmental agencies which did not report it in published documents or as additional source of data (Eckhouse *et al*., 2007; Eckhouse *et al*., 2008; Kanavos *et al*., 2010). Also, the International Cancer Research Partnership (ICRP) analysed the data regarding cancer research funding, reported by its Member Organizations to a common database that covers a significant proportion of global cancer research funding, outside the industrial sector, and includes an important part of the cancer research in North America and Europe (International Cancer Research Partnership, 2012).

The majority of these studies assessed the direct spending for oncological research. However, some of them have also provided data regarding indirect funding ("hidden spend"), which comes into cancer research via overall budgets (health services or universities budgets) (Eckhouse *et al*., 2007; Eckhouse *et al*., 2008; Kanavos *et al*., 2010). The bibliometric method for the evaluation of cancer research expenditure was taken into consideration for the assessment of direct (Eckhouse *et al*., 2007; Eckhouse *et al*., 2008; Gillum *et al.*, 2011;) or indirect costs (Eckhouse *et al*., 2007; Eckhouse *et al*., 2008).

Some authors conducted their own research, while others used data from existing studies carried out by other people /institutions (Gotay, 2013; Fricker, 2007; Watson, 2005). For example, in the former category were included: the two surveys of European Cancer Research Managers Forum (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2005), and a survey conducted in WA (Shirazee *et al*., 2011b). In these surveys there are data on cancer research expenditure, in general, but some of the papers refer to a specific type (site) of cancer (Hong & Dong, 2014) or to a specific area of research (interventional oncology [Chow & Itagaki, 2010] or drug development [Kanavos *et al*., 2010]).

Other issues related to data collection are the currency conversion (which allows the comparison between countries/regions), the rate of inflation, and the "hidden spending". Some studies used adjustment for inflation (Eckhouse *et al*., 2007), other did not (Cancer Research Alliance, 2012; International Cancer Research Partnership, 2012; Shirazee *et al*., 2011b). A number of studies did not included in their analysis the indirect costs (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2007; Shirazee *et al*., 2011b; Cancer Australia, 2014), those existing in universities/hospitals for infrastructure (in Europe, for example, it was estimated an amount of €1,589 million for indirect cancer research funding in 2006-2007) (Kanavos *et al.*, 2010) or scholarships/fellowships. So, the interpretation of data has to be done with caution.

Evidences on cancer research expenses

The spending on cancer research is covered from public and private sources. Among public funders there are: Governmental agencies (national/federal and regional/provincial Governments), charitable organizations (annual fundraisers and endowed charities) and supranational organizations (eg. European Commission). The private sector is dominated by Pharmaceutical and Biotechnology industries. However, an important progress for the cancer research funding is the public-private partnership.

Europe

In 2002-2003, the non-commercial funding for cancer research in Europe was €1.43 billion (Eckhouse & Sullivan, 2006) and increased by 38% until 2004, at the level of €1.97 billion (Eckhouse *et al*., 2007; Shirazee *et al*., 2011a). In 2004, the indirect spending to support cancer research in Europe contributed with €1.3 billion and the Global public sector cancer research spending (including indirect sources) was €14.03 billion (Eckhouse *et al*., 2007; Eckhouse *et al*., 2008). For the period 2006-2007 Europe has increased the funding for cancer research from both governmental and charity sources (Eckhouse *et al*., 2008), the direct spending being €2.79 billion and indirect spending, €1.58 billion (Kanavos *et al*., 2010) (*Table 2*).

Across Europe there are huge differences between countries regarding the funds directed to oncological research. The leader in cancer research funding was United Kingdom (UK), with €388 million in 2002-2003 (Eckhouse & Sullivan, 2006), and with an important increase at €1,104 million in 2007 (Kanavos *et al*., 2010). After UK, Germany (€426 million - 2007), France (€389 million - 2007), and Italy (€233 million - 2007) spent the highest amount of money on cancer research in Europe (Kanavos *et al*., 2010).

Table 2. The amount of money spent on cancer research in Europe

No. crt	Authors	Year of publication	Types of funding organisations	Amount of money spent for cancer research	Year spanning
1	Eckhouse S., Sullivan R.	2006	-Non-commercial	- EU = €1.43 billion - USA (US National Cancer Institute) = €3.60 billion	2002-2003
2	Eckhouse S. et al.	2007	- Governmental agencies - Charity - Pharmaceutical industry	- ***Non-commercial (public) funding organisations***: • **EUROPE** = €1,971 million on direct funding, 38% increase since the last survey • **USA** = €5,158 million, relatively static since the last survey - In addition – ***money from national healthcare systems and universities*** (indirect funding) to support cancer research: • **EUROPE** = €1,364 million • **USA** = €109 million - ***Global public sector cancer research spending*** (including indirect sources) = €14,030 million - ***Direct spending*** by top 18 ***pharmaceutical companies*** = €3,095 million (does not include all industry) - **EUR** = 52% of total cancer research publications (1.3 papers/billion euro GDP) - **USA** = 48% of total output (1.4 papers/billion euro GDP) - Total ***major Pharmaceutical companies*** spend contributing to public domain (2004) = €3.1 billion (estimated from bibliometric method) = 8% of the worldwide Bio-Pharmaceutical Industry R&D expenditure (= €39.6 billion)	2004
3	Shiraze N. et al.	2011	- Public funding	- Western Australia - €2 billion = AU$3.2 billion, 38% increase in spending from 2002	2004
4	Eckhouse S. et al.	2008	- Charity - Governmental funding	- The ***total global spend*** (excluding industry) = €11 billion - In addition, the ***top 24 pharma companies*** – spent = €3 billion (does not include development, registration clinical trial or marketing costs) - **Europe** has increased its funding of cancer research through both: • ***philanthropic funders***, from €21.5 million to €27.5 million/ year • ***Governmental sources***, from €21.4 million to 31 million. - Increase in ***philanthropic funds,*** partly due to Portugal and UK - Increase in ***governmental funding,*** from Ministries and/or Research Councils (but not including infrastructure funding through healthcare and university systems) - 9 out of 32 countries have an imbalance between charitable and governmental funding	2004-2005 2006-2007

No. crt	Authors	Year of publication	Types of funding organisations	Amount of money spent for cancer research	Year spanning
5.	Shiraze N. et al.	2011	- Public funding	- Western Australia - €2 billion = AU$3.2 billion, 38% increase in spending from 2002	2004
6	Eckhouse S. et al.	2008	- Charity - Governmental funding	- The ***total global spend*** (excluding industry) = €11 billion - In addition, the ***top 24 pharma companies*** – spent = €3 billion (does not include development, registration clinical trial or marketing costs) - **Europe** has increased its funding of cancer research through both: • ***philanthropic funders***, from €21.5 million to €27.5 million/ year • ***Governmental sources***, from €21.4 million to 31 million. - Increase in ***philanthropic funds,*** partly due to Portugal and UK - Increase in ***governmental funding,*** from Ministries and/or Research Councils (but not including infrastructure funding through healthcare and university systems) - 9 out of 32 countries have an imbalance between charitable and governmental funding	2004-2005 2006-2007
5	Kanavos P.	2010	- *Public sector*: • national governments or regional authorities • annual fundraisers or endowed charities • supranational organizations (European Commission) - *Private sector (commercial funding)* - *Public-private partnership*	***I. Direct funding:*** - In 2007 ***public funding*** organisations across ***Europe and USA*** = €8.6 billion invested in cancer research - ***Private sector*** across ***Europe and USA*** = €6 billion invested in cancer research - ***Europe:*** • Total spend = €2,792 million • Drug development = €603 million ***II. Estimated indirect cancer research funding:*** - ***Europe:*** • Total spend = €1,589 million • Drug development = €488 million - ***Cumulative spending*** for ***cancer drug development*** in Europe and USA = €2.8 billion in 2007-2008 - ***USA:*** • direct spend = 60% • indirect spend = 2% - ***Europe:*** • direct spend = 21% • indirect spend = 17%	2006-2007

6	Institute National du Cancer	2010	- *Governmental funding* - *Charity*	- France - overall cancer research expenditure = €56.02 million ***1. Open calls (76%):*** - Translational research = 16% - Biology research = 22% - Clinical research = 33% - Human and social science, epidemiology and public health = 5% ***2. Projects specific to one type of cancer*** = 9.7% ***3. Platforms / resources / infrastructure*** = 7.3% ***4. Support for doctors / researchers / young teams / training*** = 3.6% ***5. Projects directed to a specific re-search issue*** = 3.1% ***6. International*** = 0.4% - ***Charitable cancer organizations*** – mainly the National League Against Cancer and the French Cancer Research Association = €55 million for cancer research.	2009

Over the time Malta reports €0 for research related to cancer and Bulgaria did not provide any report (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2008; Kanavos *et al*., 2010). Romania spent €0.95 million for cancer research in 2004 (Eckhouse *et al*., 2007) and €1.6 million in 2007 (Kanavos *et al*., 2010). Across European Union (including European Commission and Trans-European Organizations) the average spend *per capita* for oncological research was €2.56 (2002-2003) (Eckhouse & Sullivan, 2006), and €18.34 (2007) (Kanavos *et al*., 2010) (*Table 3*).

Table 3. Values of cancer research funding by type of funding organizations, in Europe

No. crt	Authors	Year of publication	Value by type of funding organizations	
			Charities	**Governmental**
1	Eckhouse S., Sullivan R.	2006	- > 50% - 65 charities organisations from 23 countries - ? €667.3 million - average amount spent = €21.5 million - 8 countries = no cancer spending by charities - 11 countries spent more than government	- < 50% - 65 governmental sources of cancer research funding from 28 countries - ? €662.3 million - average amount spent = 21.4 million - 3 countries = no cancer spending by governments
2	Eckhouse S. et al.	2007	- = 47% of total = €879 million - 75 charities (14 charities = responsible for 80% of all charity = 36% of the total identified in Europe) - Charities increased their spending with 24% = €209 million - 7 countries = no spending from charities for cancer research - the average charity spend = €27.5 million - UK = the largest increase in charity and governmental funding from 2003 as absolute value - Greece = the largest % change in governmental - Iceland = 78% decrease in charity - Poland = 97% decrease in charity	- = 53% of total = €992 million - 79 governmental agencies (29 governmental agencies = responsible for 80% of all government spend = 40% of the total identified in Europe) - 3 countries = no spending from governmental agencies for cancer research - the average governmental spend = €31 million - Luxemburg = 59% decrease in governmental funding

No. crt	Authors	Year of publication	Value by type of funding organizations	
			Charities	Governmental
3	Eckhouse S. et al.	2008	- Greece and Spain had under-developed philanthropic funding	- Sweden and Denmark had low governmental spend
4	Kanavos P.	2010	- Investment in drug development by philanthropic organizations in Europe = €301 million - Investment in drug development by philanthropic organizations in the USA = €231 million	- Investment in drug development by governmental organizations in Europe = €298.7 million - Investment in drug development by governmental organizations in the USA = €1,447 million

As a percentage of GDP, the average cancer research spending for Europe in 2007 was 0.0143% of GDP, which means a decrease of 19.2% from 2004 figures. The European expenditure for cancer research is driven by the UK with 0.072% of GDP, followed by Sweden with 0.048% of GDP (Kanavos *et al*., 2010). In 2004, the public spending on cancer research in Europe (as a whole) was shared between charity (47% = €879 million) and governmental organizations (53% = €992 million) (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2007), but at the individual level, there were 3 countries with no cancer research funding from governmental agencies and 7 countries without money from charity for oncological research (Eckhouse *et al*., 2007).

USA

The total spending (including federal, industry and non-profit organizations) on cancer research in the USA, in 1996-1997, was US$5.16 billion, with the major contribution from federal agencies (US$3.06 billion) (Eckhouse & Sullivan, 2006) (*Table 4*).

Table 4. The amount of money spent in cancer research in USA

No. crt	Authors	Year of publication	Types of funding organisations	Amount of money spent in cancer research	Year spanning
1	Eckhouse S. Sullivan R.	2006	- Federal - Industry - Non-profit organisations	-**Total USA amount** = US$5.16 billion -**Federal funding (**the major contribution from **National Cancer Institute)** = US$3.06 billion - **Industry funding** = US$1.6 billion -**Non-profit organisations** = US$305 million - 2002 = doubling of funds since 1997 – just **National Cancer Institute** = US$4,192 billion	1996-1997
2	Eckhouse S. et al.	2007	- Non-commercial - Governmental funding - Charitable organizations	- **Non-commercial cancer research spend** = €5,168 million - the largest contributor = Federal Government (Department of Health and Human Services, of which the **National Cancer Institute** = major division = €3,252 million -**Governmental funding** = 94% of overall USA 2004 spend -**Charitable organizations** = 6%	2004

3	Gillum LA et all.	2011	- Governmental	- NIH budget in 2006 = US$28.5 billion - NIH budget for the 29 conditions included in the current study = US$11.9 billion -7 from 29 conditions studied were cancers = US$1.82 billion = 15.3% of total	2006
4	Brown H	2007	- Governmental	- NCI budget: 1996 = US$2.25 billion; 2001 = US$2.75 billion; 2003 = US$3.75 billion; 2005 = US$4.62 billion; 2006 = US$4.82 billion	1996-2006
5	Shiraze N. et al	2011	- Governmental funds (National Cancer Institute)	- US$4.7 billion / year = AU$5.2 billion / year = 14% increase from 2002	2004-2006
6	Kanavos P.	2010	- *Public sector* (national or regional authorities; annual fundraisers or endowed charities; supranational organizations) - *Private sector (commercial funding)* - *Public-private partnership*	***I. Direct funding:*** - ***USA:*** • Total spend = €5,799 million • Drug development = €1,678 million. ***II. Estimated Indirect funding:*** - ***USA:*** • Total spend = €477 million • Drug development = €44 million.	2006-2007

In 2004 the non-commercial cancer research spending was US$5,168 million (from which National Cancer Institute – NCI – contributed with US$3,252 million). However, the amount of money came from governmental agencies (94%) and from charitable organizations (6%) (Eckhouse *et al*., 2007). Between 2004 and 2006 the USA spent US$4.7 billion/year from governmental funding (especially NCI) (Shirazee *et al*., 2011a). In 2006-2007 the direct funding was US$5,799 million and the indirect expenditure accounted for US$477 million (Kanavos *et al*., 2010). The NCI budget in 2006 was US$4.82 billion (Brown, 2007).

Australia

In 2004 the cancer research funding from Australian Government was AU$68 million. In 2007 this contribution reached AU$ 118.6 million (174% increases from 2004) (Shirazee *et al*., 2011b). Between 2008 and 2010, the Australian Government spent AU$35.8 million for cancer research in Western Australia (from which AU$28.5 million as competitive funding and AU$7.3 million as non-competitive funding). The amount of money spent for competitive funding increased over the period, from AU$7.7 million in 2008 to AU$10.92 million in 2010, but the total rose from AU$11.36 million in 2008 to AU$12.58 million and decreased in 2010 to a level of AU$11.84 million (Shirazee *et al*., 2011b). From 2003-2005 to 2009-2011, the total direct funding for cancer research in Australia was AU$1.3 billion, with an upward trend from AU$292 million in 2003-2005 to AU$596 million in 2009-2011 (Cancer Australia, 2014) (*Table 5*).

Regarding the source and type of funding organizations for cancer research in Australia, the major funders in 2006-2011 were: National Health and Medical Research Council (NHMRC) - AU$568 million = 56% of total funding (1,060 research projects and programs), other Australian governmental sources - AU$96.9 million = 10 % of total funding (279 research projects and programs), and Cancer councils - AU$95.7 million = 9% of total funding (616 research projects and programs) (Cancer Australia, 2014).

Table 5. The amount of money spent on cancer research in Australia

No. crt	Authors	Year of publication	Types of funding organisations	Amount of money spent on cancer research	Year spanning
1.	Shiraze N. et al.	2011	- Australian Governmental funds (National Health and Medical Research Council - NHMRC)	- AU$68 million	2004
				- AU$118.6 million = 174% increase from 2004	2007
			- 66% of this funds = provided by Commonwealth Government - 2% = state and territory governments - 9% = state and territory Cancer Council	- AU$291.5 million from which 6% was for Western Australia (WA)	2003-2005
			1. Commonwealth Government funding 2. State Government	- AU$40 million – New South Wales - AU$1.8 million – New South Wales	2001-2003
			1. Commonwealth Government funding 2. State Government 3. Charitable and non-profit organization funding 4. Industry and foreign government funding	- AU$67.7 million – New South Wales - AU$25 million – New South Wales - Remained stable – New South Wales - Decrease during this period – New South Wales	2004-2006
			1. Australian Government (NHMRC; Australian Research Council; Cancer Australia) 2. Western Australia Cancer Council 3. Western Australia State Government	- AU$35.8 million (249 grants) from which: • AU$28.5 million = ***competitive funding*** (half of which from Australian Government and 3% from State Government) • AU$7.3 million = ***non-competitive funding*** (79% from State Government) - 2008 = AU$11.36 million (from which AU$7.57 million = competitive funding) - 2009 = AU$12.58 million (from which AU$9.99 million = competitive funding) - 2010 = AU$11.84 million (from which AU$10.92 million = competitive funding)	2008-2010
2	Cancer Australia	2014	- Australian Government (NHMRC; Cancer Australia) - State and territory Governments - Cancer foundations - Cancer Councils - International funders - Other sources	- direct funding = AU$1.01 billion - 3,106 cancer research projects and research programs - From 2003-2005 to 2009-2011 = the total direct funding for cancer research = AU$1.3 billion - 2003-2005 = AU$292 million (1,332 projects) - 2006-2008 = AU$413 million (1,596 projects) - 2009-2011 = AU$596 million (2,100 projects) - The total direct funding for cancer research increased for all states and territories, with the exception of the Australian Capital Territory - The number of cancer research projects and programs increased for all states and territories	2006-2011

If we look at the States and Territories between 2005 and 2011, we can observe that Victoria was by far the most funded for cancer research (AU$417 million for 1,070 cancer research projects and programs), followed by New South Wales (AU$293 million for 906 cancer research projects and programs). The lowest level of funding was received by Northern Territory (AU$1.8 million – 5 projects) (Cancer Australia, 2014).

Canada

In 2009 in Canada there were three sources of funding for cancer research: the government ($409.99 million = 75.2%), voluntary organizations ($95.72 million = 17.5%), and other sources ($39.76 million = 7.3%) (Canadian Cancer Research Alliance, 2012) (*Table 6*).

Table 6. The amount of money spent on cancer research in Canada

No. crt	Authors	Year of publication	Types of funding organisations	Amount of money spent in cancer research	Year spanning
1	Canadian Cancer Research Alliance	2014	-Federal government agencies -Provincial government organizations -Voluntary organizations	-2011 - $548.3 million (the highest investment level in the 7 years captured in the survey) -The 2011 investment = 47% higher (33% when adjusted for inflation) than 2005.	2005-2011
2	Gotay C.	2012	- Government (74%) - Voluntary (18%) - Other (partnered/leveraged) = 9%	- $536.1 million = an increase of 43% in cancer research investment from 2005 to 2010 - The largest overall funder was Canadian Institutes of Health Research = $136.9 million, followed by the Ontario Institute for Cancer Research = $49.9 million - The single largest funder in the voluntary sector remained the Canadian Cancer Society = $41.7 million	2010
3	Canadian Cancer Research Alliance	2012	- Governmental funding - Voluntary - Other	- Overall cancer research investment: • ***2005*** = $372.2 million • ***2006*** = $389.6 million • ***2007*** = $426.5 million • ***2008*** = $471.1 million • ***2009*** = $545.5 million = an increase of 46.6%. - After correcting for inflation by adjusting to 2009 dollar, the overall increase in investment from 2005 to 2009 was 35.9% - Total cancer research investment from sources ***NOT INCLUDED*** in the Canadian Cancer Research Survey, 2005-2009 = less than $1,770.5 million - Research investment grew for all sectors from 2005 to 2009 – the highest average rate – for provincial government sector	2005-2009

The federal government was the most important funder for oncological research ($172.1 million in 2005 and $ 253.2 million in 2010) (Gotay, 2013), but the provincial governments presented the most important increase in cancer-related investment during 2005-2010 (from $94.4 million in 2005 to $142.5 million in 2010) (Gotay, 2013; Canadian Cancer Research Alliance, 2014). In 2011 the cancer research funding in Canada reached the highest level ($548.3 million) in the seven years captured in the Canadian survey (2005-2011). It was a 47% increase in oncological research funding from 2005 to 2011 (Canadian Cancer Research Alliance, 2014). The major funder of the cancer research activity was the Government (Canadian Institutes of Health Research) (74% in 2010) (Gotay, 2013). The total investment in cancer research from sources not included in the Canadian Cancer Research Survey was less than $ 1,770.5 million (Canadian Cancer Research Alliance, 2012).

Asia

There is one paper identified in our scientific literature search that presents data on cancer research funding in Asia, globally (Cheng, 2007) and one paper that refers to breast cancer research funding in China (Hong & Dong, 2014).

Among Asian nations, Japan has a long history of private support, but also local research (Cheng, 2007). In one study was showed that the value spent *per capita*, for the fiscal year 2004-2005, for cancer research in Japan was €7.88 (Eckhouse *et al*., 2007; Eckhouse *et al*., 2008) and the amount of money spent, calculated using the bibliometric approach, was €1,004 million (Eckhouse *et al*., 2007). South Korea placed the responsibility for cancer funding on the public sector. The principal funder of cancer research in Singapore was the Singapore Cancer Syndicate, which was created in 2002 and had a 5-year budget (S$75 million for infrastructure and human resources / research teams and S$15.9 million for research grants) (Cheng, 2007).

In mainland China, the central government invested in research and development for all Biological Sciences, investment which steadily increase towards a level comparable with EU countries. Also, there were specific university-based projects and programs funded by public sector, through the Research Grant Council. This agency offered an important financial support (HK$ 1 million for a period of three years), but the chances to gain a grant were about 30%. In 2007, in this region, Pharmaceutical companies did not funded clinical trials and the private investment was practically inexistent (Cheng, 2007).

Whilst the big Pharma started to give more consideration to the mainland China, Hong Kong was the place where the Pharmaceutical companies carried out their clinical trials. In the latter the private sector and the philanthropic organizations were important sources for oncological research. One of the most important funder, the Hong Kong Cancer Fund, invested HK$10.8 million between 2002 and 2007 (Cheng, 2007).

Over the time, the investment in breast cancer research in China increase with the number of research projects (before 2011 = US$49,000 and after 2011 = US$130,000). The translational research on breast cancer was funded by Pharma industry, which supports also the majority of clinical trials. Philanthropic organizations rarely direct funds for clinical trials (Hong & Dong, 2014).

Global

At the global level, there was an upward trend in the funding provided by the non-commercial organizations, from $4.76 billion in 2005 to $4.83 billion in 2008 (International Cancer Research Partnership, 2012).

The scientific paper published by Eckhouse et al in 2007 showed that, using the bibliometric approach, the funding of cancer research worldwide (Global Public Sector) was about €11,035 million, from which: USA = €5,277 million, Europe = €3,335 million, Japan = €1,004 million, Canada = €276 million, Australia = €162 million, and the Rest of the World = €981 million. In the USA the most significant funder for oncological research was the Government (€4,712 million), followed by Charity (€456 million) and healthcare systems and universities (€109 million), whilst in the EU was the universities and healthcare systems (€1,364 million), followed by Government (€992 million), and, Charity (€872 million) (Eckhouse et al., 2007).

A comparison on cancer research funding

Common Scientific Outlines (CSO) coding is an internationally recognized classification that defines seven broad areas of cancer research: Biology; Etiology; Prevention; Early detection, diagnosis and prognosis; Treatment; Cancer control, survivorship, and outcomes research; Scientific model systems, which allows the comparison between countries/regions (International Cancer Research Partnership, 2014).

The distribution of cancer research funding by CSO categories could be an indicator to highlight the strengths in cancer field and the potential barriers to cancer research progress. Also, it helps the decision making factors to know and understand which actually the priorities in oncological research funding are.

We present the distribution of cancer research funding by CSO categories in different regions, according to the scientific papers included in the review (*Table 7*).

Generally, at the global level there was the same pattern of cancer research funding according CSO classification, irrespective of the analysed period, with the predominance for Biology and Treatment and less funds for cancer control and prevention. The most important percentage for Biology (41%) has been seen in Europe during 2002-2003 (Eckhouse & Sullivan, 2006). The same value was identified in the UK during 2006-2011. Canada (36%) and Australia (35%)

contributed with important funds to cancer Biology research, during 2006-2011 (Cancer Australia, 2014). During 2002-2003, USA invested 25% in Biology (Eckhouse & Sullivan, 2006). In 2009, in France, Biology was the second most funded area with 24%, after Treatment (35%) (Institute National du Cancer, 2010).

Table 7. Values about cancer research funding by CSO categories

No. crt	Authors	Publication year	CSO categories							
			Region / year	Cancer biology (%)	Etiology (%)	Prevention (%)	Early detection, diagnosis, prognosis (%)	Treatment (%)	Cancer control (%)	Scientific model systems (%)
1	Eckhouse S., Sullivan R.	2006	**EU / 2002-2003**	41	14	4	9	20	5	6
			USA / 2002-2003	25	17	9	12	25	9	3
2	Shiraze N. et al	2011	**Western Australia / 2008-2010**	40	6	6	8	23	12	5
3	Canadian Cancer Research Alliance	2014	**Canada / 2005**	43	11	2	10	24	8	1
			Canada / 2011	30	14	2	14	30	10	< 1
4	Gotay C.	2012	**Canada / 2005**	43.1	11.3	1.7	10.5	24.5	8.1	0.8
			Canada / 2010	31.5	13.3	2.6	12.3	29.8	10.3	0.2
5	International Cancer Research Partnership	2012	**Global level / 2005**	22.1	17.9	7.9	11.9	25.9	10.5	3.8
			Global level / 2008	24.9	13.8	6.8	13.3	26.7	10.5	3.9
6	Eckhouse S. et al.	2008	**Europe / fiscal year 2002-2003**	41	14	4	10	20	5	6
			USA / fiscal year 2002-2003	25	17	9	12	25	9	3
			Canada / fiscal year 2004-2005	45	10	2	8	22	12	1
7	Canadian Cancer Research Alliance	2012	**Canada / 2005**	42.9	11.4	1.7	10.5	24.5	8.1	0.9
			Canada / 2009	32.9	12.4	2.5	13.4	28.2	10.2	0.3
8	Cancer Australia	2014	**Australia / 2003-2005**	51	7	5	8	19	9	1
			Australia / 2006-2008	38	10	2	13	27	7	3
			Australia / 2009-2011	32	8	2	16	28	9	4
			Australia / 2006-2011	35	9	2	15	28	8	4
			Canada / 2006-2011	36	12	2	13	27	10	< 1
			UK / 2006-2011	41	10	3	11	25	6	3
9	Institute National du Cancer	2010	**France / 2009**	24.29	5.34	0.09	24.3	34.72	9.25	2.01

In general Treatment was the second area towards which the investments were directed. In 2002-2003, USA spent a greater percentage in Treatment (25%) than Europe (20%) (Eckhouse & Sullivan, 2006). In 2009, France invested 35% for cancer Treatment research (Institute National du Cancer, 2010). During 2006-2011, Australia spent 28% in Treatment, Canada – 27% and UK – 25% (Cancer Australia, 2014). Even if the cost of prevention is lower, in general, than that of treatment and the quality of life of the individual will be better, this review identified that cancer Prevention received one of the lowest level of funding. Among studies which were analysed in the review, USA contributed with the highest percentage (9% in 2002-2003) and was followed by Europe (4% in the same period) (Eckhouse & Sullivan, 2006), UK (3% in 2006-2011), Australia and Canada (2% each during 2006-2011) (Cancer Australia, 2014) and France (0.09% in 2009) (Institute National du Cancer, 2010). The Scientific Model Systems received the lowest amount of money in all regions (Eckhouse & Sullivan, 2006; Canadian Cancer Research Alliance, 2014; International Cancer Research Partnership, 2012; Cancer Australia, 2014).

Regarding the distribution of cancer research funding by cancer site, at the Global level, in 2008, the most funded was breast cancer (20.6%), followed by haematological malignancies (11.7%) and prostate cancer (8.7%) (International Cancer Research Partnership, 2012). But the assessment of the allocation of the funding for oncological research by CSO categories and by cancer site can help the identification of the areas which are underfunded or overfunded, for a specific type of cancer, in a specific country/region. This analysis showed huge differences in cancer research spending (*Table 8*). For example, for breast cancer, Biology, Treatment and Early Detection were the most funded CSO categories, while for colorectal cancer, Cancer control, followed by Treatment and Early Detection received the most important amount of money. For prostate cancer, another frequent malignancy, Treatment, Biology and Early Detection absorbed the majority of funds. For haematological malignancies, Treatment and Biology, followed by Etiology were on top (International Cancer Research Partnership, 2012). A different distribution has been seen for lung cancer, where Treatment and Cancer control received almost the same amount of money, followed by Prevention, Early Detection and Biology (International Cancer Research Partnership, 2012).

Table 8. Values about cancer research funding by cancer site and by CSO categories, at the Global level, in 2008 (adapted by ICRP, 2012)

No crt	CSO categories	Value by cancer site (USD mil. dollars)									
		Melanoma	Breast	Colon and rectum	Haematological malignancies	Lung	Ovary	Prostate	Other sites	Not site-Specific or basic science	TOTAL (USD mil. dollars)
1	Biology	22.7	238.4	49.1	153.2	37.2	24.5	90.3	139.1	402.1	**1203.6**
2	Etiology	16.1	133.7	65.7	83	42.7	20.2	47.2	144.4	74.5	**667.5**
3	Prevention	8.5	53.3	49.1	10.4	44.2	7.6	35.8	58.2	51.6	**329.6**
4	Early detection	17.4	168.7	50.2	43	43.3	31.6	70	104.1	82.7	**645.4**
5	Treatment	53.3	226.1	60.9	227	60.7	54.4	117.7	205.8	214.9	**1291.7**
6	Cancer control	4.3	141.5	66.2	27.6	59.4	8,1	47.4	70.9	69.7	**510.1**
7	Scientific model systems	6.0	38.8	11.2	23.4	11.4	5.2	12.3	36	41.6	**190.9**
	Total 2008	**128.2**	**995.7**	**352.5**	**567.5**	**298.7**	**151.7**	**420.7**	**758.5**	**937.2**	**4838.8**

One of the major outputs of the cancer research funding is the oncological research publication, which is a surrogate marker of the overall cancer research activity. Using the bibliometric approach, the cancer research productivity (publications) was slightly greater in Europe (43%) compared with USA (38%), with an upward trend towards more applied (clinical) outputs (Eckhouse *et al.,* 2008). The cancer research publications from USA were more basic than the outputs from Europe (Eckhouse *et al*., 2007). Japan and China published more clinical trials than USA (Chow & Itagaki, 2010).

Discussions

As a result of a continue increase of cancer burden on healthcare budgets and society, funding the cancer research should become a priority worldwide. The understanding of cancer research funding mechanism will help to create a stable environment for oncological research and will support the management of cancer, which is a very important and complex issue in every society, but also at the global level. This literature review has presented the available evidence on oncological research funding in different regions.

The majority of studies included in this review showed that Europe is the second power in terms of cancer research funding, behind USA (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2008; Watson, 2005; Kanavos *et al.*, 2010; Eckhouse *et al*., 2007; Shirazee *et al*., 2011b), which was the world leader for many years, but the lack of commitment to cancer research could lead to the loss of

this position in the future (Brown, 2007). Among the European countries, UK, Italy, Germany, and France had the major financial contribution to cancer research in absolute terms, whilst in *per capita*, the Netherlands and Sweden were the leading funders, and the newest European Union Member States were the weakest (Eckhouse & Sullivan, 2006; Kanavos *et al.*, 2010).

Europe has considerably risen its funding since 2004, reflecting an increased political interest (at the economic and social level) in cancer research (Kanavos *et al.*, 2010). Also there are countries which will increase their investment in cancer research in the next 5 to 10 years (UK) (Torjesen, 2014). But in many other European countries there is still a need to promote the development of national cancer priorities and strategies and to increase their Governmental financial contribution to cancer research (Eckhouse *et al*., 2007; Eckhouse & Sullivan, 2006; Kanavos *et al.*, 2010). By contrast, in USA, Canada and Australia the majority of oncological research investment derived from Governmental sources (Eckhouse *et al*., 2007; Canadian Cancer Research Alliance, 2014; Cancer Australia, 2014).

Although the European Commission could provide greater funds for oncological research, because of the bureaucratic process in reality most of the European cancer funding falls mainly into the responsibility of the governments of the Member States and charitable institutions, which can realise only small cancer studies, with no overall co-ordination (Fricker, 2007). While in the USA, the progress of oncological research was slowed down because of funding cuts (Brown, 2007), in Europe, over management and bureaucracy were serious threats for cancer research (Eckhouse *et al*., 2007). Efforts were putted together to simplify and harmonize procedures in Europe and to overpass the era of cutting cancer research funds in USA.

In cancer research policy, indirect and charitable funding should be seen as additional sources to the global effort (Governments and industry). Particularly in Europe these types of investments could be significant. Unlike USA, cancer research in Europe was supported by a strong charitable sector, but still underexploited (Eckhouse & Sullivan, 2006; Eckhouse *et al*., 2008). Charities account for around half of cancer research funding in Europe, also with important disparities among countries (Ilman, 2005; Kanavos *et al*., 2010).

Little data were published on cancer research funding in Asia, but from this literature it was highlighted that the development of clinical trials in China can be the result of China's economic growth and the application of the global-standard regulations, but also can be due to collaboration with Pharma industry in China and overseas researchers. Although significant progress has been made, China is still far behind many Western countries in conducting clinical trials (Hong & Dong, 2014).

The contribution of the oncological research funders from private sector was estimated to Ľ of total global research expenditure and was directed mainly to USA and Europe. Asia also registered important progress in funding of clinical trials, because of China, which appears attractive for private investors (larger population and smaller costs).

Eckhouse et al. showed that basic research dominates the majority of global research funding during 2004-2005 (Eckhouse *et al*., 2007), but there are tendencies to change this strategy towards more translational / clinical research (Gotay, 2013). In basic research, where the long-term public benefits overpass the private interests, the role of Government is very important. However, there is a global belief that clinical trials are too expensive for public funding alone and should be sustained jointly by cancer charities, national governments and Pharma industry (Kanavos *et al*., 2010; Fricker, 2007; Eckhouse *et al.,* 2008).

A significant issue in oncological research worldwide is the uncoordinated and fragmented cancer research efforts, with duplication in some areas and insufficiencies in others (Ilman, 2005; Cancer Australia, 2014; Kanavos, 2010; Gotay, 2012; Eckhouse *et al.*, 2008; International Cancer Research Partnership, 2012; Fricker, 2007). A possible solution to this situation could be the Shared Resources model, the national and international cooperation, which allows access to complementary expertise and facilities that are not widely available to individual researchers. The public-private partnership is another strategy to support cancer research. The collaboration of industry with academia could reduce the economic risk and flatten the operational process. Almost all major recent policy on oncological research funding have emphasized the public-private partnership direction, that represent more than a half of all cancer research in Europe and the USA at this time.

The public interest could also influence the funding level through lobbying efforts, additional funding support from private foundations and by directly stimulating the interest of investigators. There are many social and political decisions that still need to be made on what research projects or programs should be funded, who will pay the research, and who will benefit from it.

Conclusions

The scientific literature regarding cancer research expenditure is still insufficient with many gaps for different regions and countries, but national and international cooperation and public-private partnership could contribute to a better management of financial support for oncological research. The two big sources of cancer research funding at the global level are USA and Europe, followed by Canada and Australia. Asia has made important progress in this field due to the economic development and the increasing interest in cancer research in China. The most important cancer research funders in Europe are UK, Germany, France and Italy, with well-established policies and strategies regarding the funding of oncological research, but the European Commission could have an important contribution, providing they will find a way to give money with less bureaucracy, encouraging national and international collaborations to avoid research duplication and fragmentation. There is a need for improving investment in cancer research in small countries like Bulgaria, Estonia, Latvia, Lithuania, Romania, Slovenia etc., where less research projects and programs were implemented, and

also for a better publication of the research results. For these countries proper strategies and regulations are very important in order to better manage the small funds available for research in general, and for cancer research in particular. Through this review, we were able to identify areas where further research is needed, the most important being the evaluation of the relation between cancer research funding and the burden of this disease on the population and society. This analysis will allow a more efficient distribution of funds for the benefit of those affected by cancer (patients, caregivers, and society).

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Authors' contributions

MCM and LO conceived the questions to be studied. MCM and VC conducted the literature review. MCM produced the draft of the paper. MCM, DA, LO were involved in the writing of the final form of this paper. All authors read and approved the final manuscript.

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