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Investments in cancer research awarded to UK institutions and the global burden of cancer 2000-2013: a systematic analysis

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3 **Investments in cancer research awarded to UK institutions and the global burden of cancer 2000-**
4 **2013: a systematic analysis**

5
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49 and development
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3 **What this study adds:**
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6 **What is already known on this subject:**
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9 Prior to this study, we were unable to identify any studies investigating cancer research investment
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11 by the UK over time or any centralised database detailing public and philanthropic cancer research
12
13 investment.
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16 **What this study adds:**
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19 We systematically compiled a comprehensive database for UK research funding for the period 2000-
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21 2013. We identify 4,299 awards with a total research investment of UK£2.4 billion. We generated a
22
23 compound metric to capture cancer research investment relative to disease burden. We identify
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25 several potential investment “gaps”, for example, funding towards surgery and radiotherapy are
26
27 comparatively neglected considering their utility in the cancer care pathway
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ABSTRACT**Objectives**

We sought to systematically categorise cancer research investment awarded to UK institutions in the period 2000-2013 and to estimate research investment relative to disease burden as measured by mortality, disability-adjusted life years (DALYs), and years lived with disability (YLDs).

Design

Systematic analysis of all open access data.

Setting and participants

Public and philanthropic funding to all UK cancer research institutions, 2000-2013

Main outcome measures

Number and financial value of cancer research investment reported in 2013 UK pounds. Mortality, DALYs and YLDs data was acquired from the Global Burden of Diseases Study. A compound metrics was adapted to estimate research investment relative to disease burden as measured by mortality, DALYs, and YLDs.

Results

We identified 4,299 funded studies with a total research investment of UK£2.4 billion. The highest funding by sites were haematological, breast, prostate, colorectal, and ovarian cancers. Relative to disease burden as determined by a compound metric combining mortality, DALYs and YLDs, gender-specific cancers were found to be highest funded - the five sites that received the most funding were prostate, ovarian, breast, mesothelioma, and testicular cancer; the least well-funded sites were liver, thyroid, lung, upper GI and bladder. Pre-clinical science accounted for 66.2% of award numbers and 62.2% of all funding. The top five areas of primary research focus by funding were pathogenesis, drug therapy, diagnostic, screening and monitoring, women's health, and immunology. The largest

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3 individual funder was the Medical Research Council. In combination, the five lowest funded site
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5 specific cancers relative to disease burden account for 47.9%, 44.3% and 20.4% of worldwide cancer
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7 mortality, DALYs and YLDs.
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10 **Conclusions**

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12 Current and projected global cancer disease burden may be a consideration in the allocation of
13
14 limited research funding. Funding agencies and industry need to openly document their research
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16 investment to enable the development of transparent and objective methods to allocate funding.
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20 **Strengths and limitations of this study:**

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- 23 • We systematically analyse UK investment in cancer research and identify areas of relative
24 neglect.
 - 25 • Our findings will inform funders and contribute towards policy discussions to prevent
26 inequity in the allocation of limited resources
 - 27 • However, it is not possible to equate gaps in funding with areas of neglect without
28 consideration of other influences.
 - 29 • Our study is dependent on the accuracy of original investment data from the funding bodies
 - 30 • Assignment of disease categories and allocation of studies according to these categories is
31 subjective.
 - 32 • We could not openly access data of private sector research funding, nor were we able to
33 obtain disaggregated award data from CRUK.
 - 34 • Disease burden measures are typically an estimate and are subject to the potential
35 introduction of bias.
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Introduction

Cancers account for a high burden of morbidity and mortality worldwide. The Global Burden of Disease (GBD) Study estimates that cancer of all types resulted in 8,235,700 deaths in 2013[1]. Being predominantly a disease of older age, prevalence of cancers has historically fallen among high-income countries. However as low-income countries experience economic maturation, we are seeing an expanded distribution of this disease burden. Further deaths from cancer are projected due to global population growth and ageing[2,3]. Between 1990 and 2013, the proportion of all deaths that was attributable to cancer rose from 11.9% to 15.0%, largely among low- and middle-income countries and site-specific cancers accounted for 9 of the 50 leading causes of death, worldwide[1].

The socioeconomic impact of cancer, both in terms of direct costs involved in medical management as well as indirect costs resulting from productivity loss, on patients and caregivers are substantial. Direct health-related costs of cancer have been estimated to incur €51.0 billion within in the European Union[4] and \$124.5 billion in the United States[5]. Indirect costs are estimated to account for additional losses of €75.2 billion and \$115.8 billion, respectively. Economic evaluation of the impact of cancer outside of these two geographical regions has been lacking.

Investment in research and development (R&D) for cancers produces global public benefits that have a positive effect both locally and worldwide, irrespective of the site of the work or the location of the institution receiving an award, bringing substantial health, social, and economic benefit.

There are several national and international funding bodies that make cancer research investments along the R&D pipeline, from population health research, pre-clinical studies through to clinical trials and applied research. The UK remains one of the world's leading investors and producers of global biomedical and health research. Previous analyses by the Research Investments in Global Health study (ResIn, www.researchinvestments.org) has systematically analysed public and philanthropic

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3 awards totalling £3.7 billion to UK institutions for infectious disease from 1997 to 2013, and
4
5 evaluated funding against global disease burden[6,7] and publications and citations as a marker of
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7 research output[8]. Tracking investments in R&D provides information and evidence to inform
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9 funding decisions and priority setting. Here, we present a systematic analysis of cancer-related
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11 research awarded by public and philanthropic funders to UK institutions from 2000 to 2013,
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13 categorise the data against a range of cancer-specific and cross-cutting disease areas, and assess the
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15 award data against global measures of mortality, disability-adjusted life years (DALYs), and years
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17 lived with disability (YLD) across three time points.
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20 21 **Methods**

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23 Our methods build on those developed for the infectious disease research investment analysis,
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25 which are described in detail elsewhere[6,7] and adapted in subsequent peer-reviewed publications
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27 (www.researchinvestments.org/publications).
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31 We systematically examined funding awards from a number of public and philanthropic funding
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33 bodies (including the Medical Research Council, Department of Health, Biotechnology and Biological
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35 Sciences Research Council, Engineering and Physical Science Research Council, Wellcome Trust,
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37 European Commission, as well as 9 members of the Association of Medical Research Charities)
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39 between 2000 and 2013. Information was obtained by downloading openly-accessible information
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41 on the funder website, contacting the funder to request the information, or searching existing
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43 funding databases. For each award, the title and abstract, where available, were individually
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45 screened for relevance to cancer research. We excluded awards that were i) not obviously or
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47 immediately relevant to oncology; ii) led by a non-UK institution; iii) not considered to be for R&D
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49 activity. Unfunded studies were also excluded. Private sector data were not available to evaluate at
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51 the same level of detail as public and philanthropic research award data, and were therefore
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53 excluded from this analysis. Cancer Research UK (CRUK) would not provide their award data and so
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55 could not be included in the main analysis. There is some description of individual CRUK awards
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3 without grant amounts available at <https://europepmc.org/>. We report total number of studies in
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5 this analysis.
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8 Where awards were described in currencies other than UK pounds, these were converted to UK
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10 pounds using the mean exchange rate in the year of the award. All included awards were adjusted
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12 for inflation and reported in 2013 UK pounds.
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15 Each study in the dataset was reviewed by one author (either CDZ, GJG, MAE-H, MGH) and assigned
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17 to as many of 14 cross-cutting categories as appropriate. The 14 association categories were
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19 paediatric, geriatric, infection-associated, women's health, men's health, occupational health,
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21 pathogenesis, diagnostic/screening/monitoring, drug therapy, radiotherapy, surgery, immunology,
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23 psychosocial and global health. Awards were defined as global health if they were considered to
24
25 pursue a clear non-UK focus (e.g. 'thyroid cancer in Kenya'). The other category was only used when
26
27 none of the aforementioned categories were deemed to be appropriate. Studies were also allocated
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29 to one of five categories along the R&D pipeline: pre-clinical; phase I, II, or III clinical trials; product
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31 development (including phase IV activity); public health; and cross-disciplinary research. The cross-
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33 disciplinary category was defined as an award containing significant components across two distinct
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35 areas along the R&D pipeline (such as pre-clinical research leading directly into a phase I trial).
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39 Provisional datasets were circulated to all authors for review and comment with checks by second
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41 authors on sections of the data and any disagreements settled by consensus. Final datasets were
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43 then again circulated for further review by all authors. Microsoft Excel 2010 and 2013 and Stata
44
45 (V13) software were used for data analysis.
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49 Global data on mortality, disability-adjusted life years (DALYs) and years lived with disability (YLDs)
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51 were available at time points 2005, 2010 and 2013. All burden data were sourced from the findings
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53 of the Global Burden of Disease (GBD) study, for 2013[1,9,10] and for 2010[11,12]. Burden data from
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55 2005 were obtained directly from colleagues at the Institute for Health Metrics and Evaluation, USA.
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57 As defined by the GBD study, YLDs for a disease or injury are the sum of the YLDs for each sequela
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3 associated with the disease or injury[10]. DALYS are the product of adding YLLs and YLDs for each
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5 age–sex–country group[9].
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8 In order to allow direct comparison of relative investment with global health metrics across disease
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10 areas and between different time periods, metrics were adapted from the infectious disease
11
12 analyses to estimate the ‘investment per mortality/DALY/YLD observed [7]’. The metrics were
13
14 created using the following equation –
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$$\frac{\text{Total research investment up to the year before the time point} / \text{number of deaths, DALYs or YLD at} \\ \text{time point}}{\text{number of years of investment included}}$$

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22 For example, for assessment of breast cancer mortality at the 2013 time point, we took the sum of
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24 breast cancer research investment 2000-2012 (£124,305,716) and divided that by number of deaths
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26 reported in 2013 (471000), and divided the result by the number of years of investment included
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28 (13) to get an ‘investment per mortality observed’ metric of £20.30.
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31 These metrics were applied for research relating to 16 site-specific cancers, where there was
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33 comparable data in both the ResIn and GBD studies. We defined lung cancer by aggregating
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35 ‘tracheal, bronchus and lung cancer’ burden data from the GBD study. Similarly, we defined skin
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37 cancer by aggregating ‘malignant skin melanoma’ and ‘non-malignant skin cancer’, and we defined
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39 upper gastrointestinal (GI) cancer by aggregating ‘oesophageal’ and ‘stomach cancer’. The use of
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41 total investment and the division by number of years included aimed to reduce the impact of the
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43 volatility of annual research funding and the relatively short periods between time points. Ranking
44
45 scores of the investment metrics were developed for the 16 sites of cancer against 2013 burdens.
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47 Cancers were ranked in order of relative investment against burden from high to low and assigned a
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49 score (from 1 to 16). The mean ranking scores across mortality, DALYs and YLDs were used to
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51 illustrate an overall relative level of investment against 2013 global disease burden.
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55 56 **Patient involvement** 57 58 59 60

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There was no patient involvement in this study.

For peer review only

Results

We identified 4,299 funded studies that met our inclusion criteria (Table 1). The funding for these studies represented a total research investment of almost £2.4 billion. The mean award amount for each study was £555,513 (standard deviation (SD) £1,429,510) and median was £231,559 (inter-quartile range £114,619 – 487,063). 2,416 awards (56.2% of total) were designated towards a named site-specific cancer (Table 1), equating to £1.0 billion (40.3% of total). The top five cancer sites in terms of award number were haematological, breast, colorectal, prostate, and skin; the bottom five were testicular, bone, bladder, thyroid, and cholangiocarcinoma (Table 1). The top five cancer sites in terms of total funding were haematological, breast, prostate, colorectal and ovarian; the bottom five were testicular, mesothelioma, thyroid, bladder and chlangiocarinoma. Mean funding per award varied greatly between sites with prostate cancer receiving the most (£1.47 million) and bladder cancer the least (£117,385).

The top five areas of primary research focus, by number of awards, were drug therapy, diagnostic, screening and monitoring, women's health, immunology, and pathogenesis; the bottom five areas were men's health, surgery, occupational health, global health and geriatrics (Table 2). In terms of net funding, the top five areas of research were pathogenesis, drug therapy, diagnostic, screening and monitoring, women's health, and immunology; the bottom five were surgery, psychosocial, global health, occupational health, and geriatrics.

The majority of awards were focused on pre-clinical science, accounting for 66.2% of award numbers and 62.2% of all funding (Table 3). In terms of award number, this was followed by public health, cross-disciplinary, phase I-III, and product development. This order was reflected in terms of net investment, although cross-disciplinary studies ranked ahead of public health studies. Phase I-III clinical trials received the highest mean funding per award, at £736,172 (SD £3,361,312), whilst public health research received the least, at £496,744 (SD £1,000,757).

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3 The largest individual funder of cancer research of the studies identified was the Medical Research
4 Council, accounting for 35.1% of all funding (Table 4). The charitable sector was responsible for
5 39.5% of all awards (excluding CRUK) but 17.4% of funding. The European Commission was
6 responsible for the largest mean grant per award (£1.58 million).
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12 We generated a compound ranking score for the 16 sites of cancer against 2013 global disease
13 burdens, across mortality, DALYs, and YLDs (table 5). We identified the five sites that received the
14 most funding relative to disease burden as prostate, ovarian, breast, mesothelioma and testicular
15 cancer. The least well-funded sites relative to disease burden were cancers of the liver, thyroid, lung,
16 upper GI, and bladder.
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23 We were able to obtain some disaggregated data for 3,284 CRUK research grants during the period
24 of interest but this excluded individual award data. Compared to the aggregation of all other
25 funders, CRUK placed more of a focus on funding towards cancers of the prostate, ovary and liver –
26 by study number these sites accounted for 6.9%, 3.4% and 2.7% of CRUK funded studies compared
27 to 2.1%, 1.1% and 0.9% of all studies in our quantitative database, respectively. CRUK preferentially
28 funded research investigating pathogenesis, which accounted for 51.0% of all grants awarded. In
29 comparison, only 5.3% of all awards in our quantitative database were identified as primarily
30 focused on pathogenesis.
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41 **Discussion**

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43 We identified 4,299 funded studies, with a total research investment of £2.4 billion. We performed
44 qualitative analysis on a further 3,284 CRUK funded awards. The vast majority of all awards awarded
45 were investigating at least one of pathogenesis, diagnosis, monitoring and screening and drug
46 therapy. In the absence of CRUK data, the Medical Research Council and the Department of Health
47 were the two leading funding sources. Preclinical research accounted for £1.5 billion (62.2%) of total
48 R&D investment. Four of the five highest funded cancer sites relative to global disease burden were
49 gender-specific – namely prostate, ovarian, breast, and testicular cancers. Cancer research with a
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3 clear focus on women's health accounted for 640 studies (14.9%) and £199.5 million (8.4%) of
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5 investment. In comparison, 111 studies (2.6%) and £143.3 million (6.0%) of investment had a clear
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7 link with men's health. This may reflect the successes of various institutions and charities that have
8
9 sought to increase awareness of these sex-specific cancers. Breast cancer, the most commonly
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11 diagnosed cancer in the UK and the leading cause of cancer death in women, and prostate cancer,
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13 the second most frequently diagnosed cancer and the sixth leading cause of cancer death among
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15 men, were found to be relatively well funded[1,13].
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19 We highlight several cancer sites where there might be underinvestment, namely that of liver,
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21 thyroid, lung, upper GI tract, and bladder. In our analysis cancer of the upper GI tract combines
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23 oesophageal and stomach cancer. These site-specific cancers identified to be relatively underfunded
24
25 account for a substantial proportion of global cancer burden. Globally, these sites account for 47.9%,
26
27 44.3% and 20.4% of the global mortality[1], DALYs[9] and YLDs[10] of all cancers, respectively. The
28
29 disparity between YLDs and DALYs demonstrates the poor prognosis and high mortality of these
30
31 particular sites when compared against all neoplastic disease. Lung, liver, stomach and oesophagus
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33 are the first, second, third and fifth, leading sites of neoplastic mortality worldwide[1].
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37 With regard to interventions research, there is heavy investment in drug-based modalities. £620.9
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39 million (26.0%) was invested in novel drug therapies and £194.1 million (8.1%) was invested in the
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41 emergent role of immunomodulation. In comparison, funding towards radiotherapy and surgical
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43 interventions accounted for £88.2 million (3.7%) and £37.9 million (1.6%), respectively. In high-
44
45 income settings, around half of new cancer diagnoses will undergo a course of radiotherapy
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47 treatment during their clinical management; roughly a quarter will receive two or more
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49 courses[14,15]. Globally, over 80% of cancer cases will warrant surgical intervention, where it has
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51 preventative, diagnostic, curative, supportive, palliative, and reconstructive roles[16].
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55 Analysis by R&D pipeline showed that research investment in the UK places a heavy emphasis on
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57 pre-clinical research, but relatively little investment towards phase I-III clinical trials or product
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3 development, and this is line with previous research in infectious disease investment[6]. This may
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5 reflect the strengths of UK institutions in preclinical science, but also could suggest a need to
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7 strengthen research capacity further down the R&D chain. It would be useful to determine whether
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9 investment reflects the priorities of funding agencies and whether this is comparable to research
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11 investment in other countries. We noted a lack of readily available data from the pharmaceutical
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13 industry and this is likely to leave a data gap in particular for sum totals of investment in clinical trials
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15 of pharmaceutical products.
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18 Our findings contribute to the development of transparent and objective methods to couple the
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20 allocation of limited research funds with disease burden. Previous studies have suggested that
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22 financial investment might appropriately be coupled with DALYs as a measure of burden[17–20].
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24 Furthermore, previous UK research suggests that publicly funded cancer research offers substantial
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26 rates of return in terms of both health and monetary benefit [21]. We have further sought to
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28 incorporate mortality rates and YLDs into the consideration of cancer research investment.
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30 However, defining an appropriate amount of research investment for each site specific cancer is
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32 challenging since cancers of similar disease burdens may warrant different levels of investment to
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34 develop cost-effective interventions. Decisions may be influenced by any of a number of factors, for
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36 example due to exceptional need, as may be the case in mesothelioma, or due to public awareness
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38 and third-party lobbying, as may be the case with regards to the gender-specific cancers.
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42 A variety of factors contribute towards the difficulty in tracking net cancer research investment
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44 within the UK. Fragmentation of data from a large number of diverse public and private sources of
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46 funding, poorly designed donor accounting structures, where available, and the paucity of
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48 information from the private sector limit the evidence base to inform policy in real-time. In our
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50 study, we were unable to obtain quantitative data from CRUK, the world's largest cancer research
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52 charity and a leader in cancer research. They do not routinely publish or make available
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54 disaggregated investment data which is, in our experience across the infection and cancer analyses,
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3 unique amongst the more high-profile UK funders who are universally more transparent in their
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5 award decisions. Transparency in the tracking and monitoring of cancer research financing is
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7 essential to enable accountability and equity in resource allocation and to facilitate further future
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9 research in this area.
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12 In this study we systematically analyse UK investment in cancer research and identify areas of
13
14 relative neglect. Although the competitive application process used by most funders to allocate
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16 research grants ensure a portfolio of high quality, the absence of explicit resource allocation criteria
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18 could contribute towards inequalities in R&D by disease burden. Funding agencies will have
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20 particular areas of focus, and UK funders may have considered the focus of international agencies in
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22 their own research strategies. As a result, international data is essential to complete the mapping of
23
24 cancer research investment. Nevertheless, our findings will inform funders and contribute towards
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26 policy discussions to prevent inequity in the allocation of limited resources.
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30 By demonstrating the relationship between disease burden and research funding, we enable the
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32 identification of potential investment gaps. However, it is not possible to equate gaps in funding
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34 with areas of neglect without consideration of other influences such as the feasibility of research,
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36 costs of technologies, infrastructure and skill requirements, political and social considerations, and
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38 the accuracy of disease burden estimates.
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41 There are several potential limitations to our study. We are dependent on the accuracy of original
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43 investment data as sourced from the funding bodies. Although checks were made on any obvious
44
45 discrepancies or errors, interpretation of these original data may contain errors. We made no
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47 attempt to investigate the contribution of any indirect or estate costs. Currency conversions were
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49 averaged across each financial year and any intra-year fluctuations may not have been captured.
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51 Unless clearly documented, we were unable to assess how funding was distributed from lead
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53 institutions to collaborative partners. We considered individual awards, rather than number of
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55 studies.
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3 Furthermore, assignment of disease categories and allocation of studies according to these
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5 categories is subjective, and there might be disagreements regarding certain inclusion criteria.
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8 We could not openly access data of private sector research funding, nor were we able to obtain
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10 disaggregated award data from CRUK. Whilst our analysis did demonstrate that CRUK funding (with
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12 some exceptions) broadly reflected the findings of our quantitative database, it is likely that
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14 substantial awards towards particular areas of research could skew results; for example, the CRUK
15
16 accounts for 2014/15 suggest £394 million was invested into research or research-related activity,
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18 and we hypothesise that much of that would have met our inclusion criteria for this analysis[22].
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21 Disease burden measures are typically an estimate and are subject to the potential introduction of
22
23 bias from missing or unobtainable data as well as from differences in classification and diagnosis.
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26 Our report presents the latest investment data on cancer research awarded to UK institution between
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28 2000 and 2013. Cancers of the liver, thyroid, lung, upper GI tract, and bladder as well as research
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30 towards radiotherapy and surgical techniques in particular may warrant increased rates of
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32 investment. We will make the entire database and associated figures available online
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34 (www.researchinvestment.org) to assist policy makers, funding organisations, and researchers in the
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36 identification of investment gaps. We further encourage funding organisations to make their
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38 investment portfolios openly accessible to facilitate future research.
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41 We hope that open funding data in this area can contribute to redressing the misalignments in
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43 investments for cancer research. Cancer research can improve the clinical course of disease and
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45 offer tangible improvements in health outcomes[21]. Both policy makers and the scientific
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47 community need to ensure that limited resources are allocated appropriately to most effectively
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49 alleviate the morbidity and mortality associated with cancer.
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Contributions

MM and MGH are the guarantors of this study. MM, MGH, JRF and RA conceived and designed the study. MGH, CDZ, BJG and MAE-H obtained the data. MM and MGH conducted data formatting and statistical analysis. All authors helped interpret the findings. MM, MGH and CDZ wrote the first draft of the manuscript with input from RR, JRF and RA; all authors provided input to subsequent drafts. All authors had full access to all of the data in the study and take responsibility for its integrity and the accuracy of data analysis.

Transparency declaration

MM affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Funding

No funding was received for this study

Competing interests

All authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

Not required

Data sharing

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All data used is publicly available. Entire database and associated figures are permanently available with open access online (www.researchinvestment.org) to assist policy makers, funding organisations, and researchers.

For peer review only

References

- 1 Naghavi M, Wang H, Lozano R, *et al*. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;**385**:117–71.
- 2 Jemal A, Bray F, Center MM, *et al*. Global Cancer Statistics: 2011. *CA Cancer J Clin* 2011;**61**:69–90.<http://www.ncbi.nlm.nih.gov/pubmed/21296855>
- 3 Torre LA, Bray F, Siegel RL, *et al*. Global Cancer Statistics, 2012. *CA a cancer J Clin* 2015;**65**:87–108.<http://onlinelibrary.wiley.com/doi/10.3322/caac.21262/abstract>
- 4 Luengo-Fernandez R, Leal J, Gray A, *et al*. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol* 2013;**14**:1165–74.<http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24131614>
- 5 Yabroff KR, Lund J, Kepka D, *et al*. Economic Burden of Cancer in the United States: Estimates, Projections, and Future Research. *Cancer Epidemiol Biomarkers Prev* 2011;**20**:2006–14.<Go to ISI>://WOS:000295717900003
- 6 Head MG, Fitchett JR, Cooke MK, *et al*. UK investments in global infectious disease research 1997-2010: A case study. *Lancet Infect Dis* 2013;**13**:55–64.
- 7 Head MG, Fitchett JR, Nageshwaran V, *et al*. Research Investments in Global Health: A Systematic Analysis of UK Infectious Disease Research Funding and Global Health Metrics, 1997–2013. *EBioMedicine* 2016;**3**:180–90.<http://dx.doi.org/10.1016/j.ebiom.2015.12.016>
- 8 Head MG, Fitchett JR, Derrick G, *et al*. Comparing research investment to United Kingdom institutions and published outputs for tuberculosis, HIV and malaria: a systematic analysis across 1997-2013. *Health Res Policy Syst* 2015;**13**:63.<http://www.health-policy-systems.com/content/13/1/63>
- 9 Murray CJL, Barber RM, Foreman KJ, *et al*. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015;**386**:2145–91.
- 10 Vos T, Barber RM, Bell B, *et al*. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;**386**:743–800.
- 11 Murray CJ, Vos T, Lozano R, *et al*. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2197–223.<http://www.ncbi.nlm.nih.gov/pubmed/23245608>
- 12 Lozano R, Naghavi M, Foreman K, *et al*. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2095–128.

- 1
2
3 13 Jemal A, Bray F, Center MM, Ferlay J, Ward E FD. Global cancer statistics. *Cancer J Clin*
4 2011;**61**:69–90.
5
6 14 Barton MB, Frommer M, Shafiq J. Role of radiotherapy in cancer control in low-income and
7 middle-income countries. *Lancet Oncol* 2006;**7**:584–95.[http://ac.els-](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aab0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
8 [cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aab0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
9 [11e3-a45c-0000aab0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aab0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
10
11
12 15 Barton MB, Jacob S, Shafiq J, *et al.* Estimating the demand for radiotherapy from the
13 evidence: a review of changes from 2003 to 2012. *Radiother Oncol* 2014;**112**:140–4.
14
15 16 Sullivan R, Alatiser OI, Anderson BO, *et al.* Global cancer surgery: Delivering safe, affordable,
16 and timely cancer surgery. *Lancet Oncol*. 2015;**16**:1193–224.
17
18 17 Gross CP, Anderson GF, Powe NR. The relation between funding by the National Institutes of
19 Health and the burden of disease. *N Engl J Med* 1999;**340**:1881–7.
20
21 18 Lopez FC, Martin EA, Maleras RG, *et al.* Relationship between Research Funding in the
22 Spanish National Health System and the Burden of Disease. *Rev Esp Salud Publica*
23 2009;**83**:137–51.<Go to ISI>://WOS:000266635200011
24
25
26 19 Mitchell RJ, McClure RJ, Olivier J, *et al.* Rational allocation of Australia’s research dollars: does
27 the distribution of NHMRC funding by National Health Priority Area reflect actual disease
28 burden? *Med J Aust* 2009;**191**:648.
29
30 20 Lamarre-Cliche M, Castilloux AM, LeLorier J. Association between the burden of disease and
31 research funding by the Medical Research Council of Canada and the National Institutes of
32 Health. A cross-sectional study. *Clin Invest Med* 2001;**24**:83–
33 9.<http://www.ncbi.nlm.nih.gov/pubmed/11368150>
34
35
36 21 Glover M, Buxton M, Guthrie S, *et al.* Estimating the returns to UK publicly funded cancer-
37 related research in terms of the net value of improved health outcomes. *BMC Med*
38 2014;**12**:1.
39
40 22 CRUK. Annual report and accounts 2014/15. 2015.
41 [http://www.cancerresearchuk.org/sites/default/files/annual_report_and_accounts_2014-](http://www.cancerresearchuk.org/sites/default/files/annual_report_and_accounts_2014-15.pdf)
42 [15.pdf](http://www.cancerresearchuk.org/sites/default/files/annual_report_and_accounts_2014-15.pdf)
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Table Legends

Table 1: Cancer research investment awards and funding by site. All investment reported in 2013 UK pounds.

Table 2: Cancer research investment awards and funding by cross-cutting theme. All investment reported in 2013 UK pounds.

Table 3: Cancer research investment awards and funding by type of science. All investment reported in 2013 UK pounds.

Table 4: Cancer research investment awards and funding by funding agency (excluding CRUK). All investment reported in 2013 UK pounds.

Table 5: Compound ranking score for cancer research investment against 2013 global disease burdens, across mortality, DALYs, and YLDs, by cancer site.

Site of cancer	All funders where investment data was available						Cancer Research UK	
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Breast	571	13.3%	£137,960,107	5.8%	241611 (414584)	135752 (25000-216673)	273	8.3%
Haematological	1158	26.9%	£381,008,394	16.0%	329022 (476943)	186813 (120437-272324)	225	6.9%
Colorectal	147	3.4%	£77,279,857	3.2%	525713 (674881)	251800 (102078-819866)	205	6.2%
Prostate	92	2.1%	£135,290,779	5.7%	1470552 (6156372)	333757 (155227-721037)	123	3.7%
Ovarian	48	1.1%	£44,709,938	1.9%	931457 (3380145)	226764 (131990-627401)	112	3.4%
Lung	82	1.9%	£24,263,280	1.0%	295893 (556278)	146123 (66701-242934)	89	2.7%
Skin	87	2.0%	£22,179,011	0.9%	254931 (453726)	85406 (69629-248603)	84	2.6%
Brain	22	0.5%	£9,994,255	0.4%	454284 (498933)	401046 (196928-528008)	83	2.5%
Upper GI and	18	0.4%	£19,094,230	0.8%	1060791 (1448010)	788850 (80964-1296962)	80	2.4%
Head and neck	20	0.5%	£18,250,632	0.8%	912531 (1003091)	389751 (167358-1602465)	68	2.1%
Renal	19	0.4%	£13,885,496	0.6%	730815 (678732)	479197 (244075-1252574)	48	1.5%
Bladder	10	0.2%	£1,173,856	0.0%	117385 (106902)	94520 (29264- 173855)	48	1.5%
Cervical	26	0.6%	£14,328,402	0.6%	551092 (877250)	210179 (88934-368402)	43	1.3%
Pancreatic	16	0.4%	£9,453,577	0.4%	590848 (519850)	276237 (191804-1033948)	40	1.2%
Bone	13	0.3%	£17,242,183	0.7%	1326322 (1604685)	685853 (243559-1999907)	29	0.9%
Liver	37	0.9%	£25,037,541	1.0%	676690 (847151)	319082 (177974-776480)	20	0.6%
Mesothelioma	30	0.7%	£4,476,088	0.2%	149202 (101201)	137103 (95895-205500)	11	0.3%
Cholangiocarcinoma	2	0.0%	£582,405	0.0%	n/a	n/a	11	0.3%
Testicular	14	0.3%	£5,949,990	0.2%	424999 (507277)	242175 (102938-411010)	11	0.3%
Thyroid	4	0.1%	£1,375,881	0.1%	n/a	n/a	7	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

Cross-cutting theme	All funders where investment data was available						Cancer Research UK	
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Pathogenesis (mechanism)	227	5.3%	£1,374,387,838	57.6%	543881 (955710)	248573 (135752-506232)	1674	51.0%
Drug Therapy	1104	25.7%	£620,961,060	26.0%	562464 (1910050)	202342 (105622-436559)	935	28.5%
Diagnostic, Screening and Monitoring	681	15.8%	£359,618,823	15.1%	528074 (1155156)	205728 (102672-513836)	404	12.3%
Women's Health	640	14.9%	£199,534,693	8.4%	311773 (1041520)	153845 (56515-227202)	287	8.7%
Immunology (inc. biologics)	451	10.5%	£194,086,617	8.1%	430347 (760955)	240052 (125669-466250)	212	6.5%
Radiotherapy	112	2.6%	£88,262,353	3.7%	788056 (2413445)	243333 (106175-439419)	209	6.4%
Psychosocial	117	2.7%	£23,445,835	1.0%	200391 (352410)	87463 (27317-239059)	122	3.7%
Men's Health	111	2.6%	£143,392,908	6.0%	1291828 (5617919)	285203 (126037-700353)	120	3.7%
Paediatrics	175	4.1%	£62,641,938	2.6%	357953 (547484)	183099 (89522-322261)	118	3.6%
Surgery	72	1.7%	£37,900,334	1.6%	526393 (684908)	235413 (97890-761651)	95	2.9%
Infection-associated	129	3.0%	£56,819,379	2.4%	440460 (798013)	231836 (134693-439378)	48	1.5%
Global Health	12	0.3%	£6,434,960	0.3%	536246 (1089118)	129738 (77519-459274)	12	0.4%
Geriatrics	7	0.2%	£1,616,394	0.1%	230913 (254925)	121623 (76421-262167)	8	0.2%
Occupational Health	18	0.4%	£2,576,841	0.1%	143157 (116928)	137103 (33857-199998)	8	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

Type of science	All funders where investment data was available						Cancer Research UK	
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Pre-clinical	2845	66.2%	£1,485,997,379	62.2%	522318 (1006600)	240974 (132188-490872)	1809	55.1%
Phase I-III	303	7.0%	£223,060,276	9.3%	736172 (3361312)	178535 (70934-502399)	647	19.7%
Product development	172	4.0%	£104,214,364	4.4%	605897 (2213394)	193051 (75270-360813)	52	1.6%
Cross-disciplinary	441	10.3%	£315,145,351	13.2%	714615 (1586882)	238523 (126589-703764)	328	10.0%
Public health	512	11.9%	£254,333,282	10.6%	496744 (1000757)	209364 (82870-383623)	443	13.5%
Unable to specify	26	0.6%	£5,401,666	0.2%	n/a	n/a	5	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

All funders where investment data was available						
Funder	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)
MRC	768	17.9%	£837,649,875	35.1%	1090690 (1770533)	504606 (305375-1153374)
Charity (excluding Wellcome and CRUK)	1,699	39.5%	£415,189,093	17.4%	244372 (391813)	151912 (81000-223244)
Department of Health	586	13.6%	£413,421,823	17.3%	705498 (2675223)	232173 (102391-471236)
BBSRC	511	11.9%	£223,651,002	9.4%	437673 (388793)	373356 (267848-501592)
EPSRC	356	8.3%	£201,861,623	8.5%	567027 (972696)	306906 (144056-604016)
Wellcome	193	4.5%	£140,425,805	5.9%	727594 (1679370)	226761 (164547-427455)
European Commission (inc ERC)	50	1.2%	£78,757,447	3.3%	1575149 (731858)	1409678 (1252574-1830017)
Other	136	3.2%	£77,195,650	3.2%	567615 (1901202)	129944 (69309-263613)
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)

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	Research investment (UK pound) by burden observed, 2013			
Disease	Mean ranking across all burden metrics	Mortality	Years lived with disability	Disability-adjusted life years
Prostate	2.7	2	4	2
Ovarian	3.0	4	2	3
Mesothelioma	4.0	6	1	5
Breast	4.0	3	5	4
Testicular	4.7	1	3	10
Skin	5.0	5	9	1
Colorectal	6.7	7	7	6
Renal	8.3	8	10	7
Cervical	9.7	9	12	8
Pancreatic	10.0	12	6	12
Brain	11.0	11	11	11
Thyroid	11.3	10	15	9
Liver	11.3	13	8	13
Lung	13.7	14	13	14
Upper GI	14.7	15	14	15
Bladder	16.0	16	16	16

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Investments in cancer research awarded to UK institutions and the global burden of cancer 2000-2013: a systematic analysis

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3 **Investments in cancer research awarded to UK institutions and the global burden of cancer 2000-**
4 **2013: a systematic analysis**

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ABSTRACT

Objectives

We sought to systematically categorise cancer research investment awarded to UK institutions in the period 2000-2013 and to estimate research investment relative to disease burden as measured by mortality, disability-adjusted life years (DALYs), and years lived with disability (YLDs).

Design

Systematic analysis of all open access data.

Setting and participants

Public and philanthropic funding to all UK cancer research institutions, 2000-2013

Main outcome measures

Number and financial value of cancer research investment reported in 2013 UK pounds. Mortality, DALYs and YLDs data was acquired from the Global Burden of Diseases Study. A compound metric was adapted to estimate research investment relative to disease burden as measured by mortality, DALYs, and YLDs.

Results

We identified 4,299 funded studies with a total research investment of UK£2.4 billion. The highest funding by sites were haematological, breast, prostate, colorectal, and ovarian cancers. Relative to disease burden as determined by a compound metric combining mortality, DALYs and YLDs, gender-specific cancers were found to be highest funded - the five sites that received the most funding were prostate, ovarian, breast, mesothelioma, and testicular cancer; the least well-funded sites were liver, thyroid, lung, upper GI and bladder. Pre-clinical science accounted for 66.2% of award numbers and 62.2% of all funding. The top five areas of primary research focus by funding were pathogenesis, drug therapy, diagnostic, screening and monitoring, women's health, and immunology. The largest

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3 individual funder was the Medical Research Council. In combination, the five lowest funded site
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5 specific cancers relative to disease burden account for 47.9%, 44.3% and 20.4% of worldwide cancer
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7 mortality, DALYs and YLDs.
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10 **Conclusions**

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12 Current and projected global cancer disease burden may be a consideration in the allocation of
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14 limited research funding. Funding agencies and industry need to openly document their research
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16 investment to enable the development of transparent and objective methods to allocate funding.
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20 **Strengths and limitations of this study:**

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- 23 • We systematically analyse UK investment in cancer research and describe trends by cancer
24 site and type of science along the research pipeline.
 - 25 • We consider cancer research investments alongside the global burden of disease to provide
26 pragmatic commentary about areas of UK research strength and relative neglect to inform
27 funder strategy and contribute towards policy discussions.
 - 28 • Our study is dependent on the accuracy of original investment data from the funding bodies
 - 29 • We could not openly access data of private sector research funding, nor were we able to
30 obtain disaggregated award data from CRUK.
 - 31 • Disease burden measures are typically an estimate and are subject to the potential
32 introduction of bias; other variable influence funding decisions beyond the burden of
33 disease.
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Introduction

Cancers account for a high burden of morbidity and mortality worldwide. The Global Burden of Disease (GBD) Study estimates that cancer of all types resulted in 8,235,700 deaths in 2013[1]. Being predominantly a disease of older age, prevalence of cancers has historically fallen among high-income countries. However as low-income countries experience economic maturation, we are seeing an expanded distribution of this disease burden. Further deaths from cancer are projected due to global population growth and ageing[2,3]. Between 1990 and 2013, the proportion of all deaths that was attributable to cancer rose from 11.9% to 15.0%, largely among low- and middle-income countries and site-specific cancers accounted for 9 of the 50 leading causes of death, worldwide[1].

The socioeconomic impact of cancer, both in terms of direct costs involved in medical management as well as indirect costs resulting from productivity loss, on patients and caregivers are substantial. Direct health-related costs of cancer have been estimated to incur €51.0 billion within in the European Union[4] and \$124.5 billion in the United States[5]. Indirect costs are estimated to account for additional losses of €75.2 billion and \$115.8 billion, respectively. Economic evaluation of the impact of cancer outside of these two geographical regions has been lacking.

Investment in research and development (R&D) for cancers produces global public benefits that have a positive effect both locally and worldwide, irrespective of the site of the work or the location of the institution receiving an award, bringing substantial health, social, and economic benefit.

There are several national and international funding bodies that make cancer research investments along the R&D pipeline, from population health research, pre-clinical studies through to clinical trials and applied research. The UK remains one of the world's leading investors and producers of global biomedical and health research. Previous analyses by the Research Investments in Global Health study (ResIn, www.researchinvestments.org) has systematically analysed public and philanthropic

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3 awards totalling £3.7 billion to UK institutions for infectious disease from 1997 to 2013, and
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5 evaluated funding against global disease burden[6,7] and publications and citations as a marker of
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7 research output[8]. Tracking investments in R&D provides information and evidence to inform
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9 funding decisions and priority setting. Here, we present a systematic analysis of cancer-related
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11 research awarded by public and philanthropic funders to UK institutions from 2000 to 2013,
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13 categorise the data against a range of cancer-specific and cross-cutting disease areas, and assess the
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15 award data against global measures of mortality, disability-adjusted life years (DALYs), and years
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17 lived with disability (YLD) across three time points.
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20 21 **Methods**

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23 Our methods build on those developed for the infectious disease research investment analysis,
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25 which are described in detail elsewhere[6,7] and adapted in subsequent peer-reviewed publications
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27 (www.researchinvestments.org/publications).
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31 We systematically examined funding awards from a number of public and philanthropic funding
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33 bodies (including the Medical Research Council, Department of Health, Biotechnology and Biological
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35 Sciences Research Council, Engineering and Physical Science Research Council, Wellcome Trust,
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37 European Commission, as well as 9 members of the Association of Medical Research Charities)
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39 between 2000 and 2013. Information was obtained by downloading openly-accessible information
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41 on the funder website, contacting the funder to request the information, or searching existing
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43 funding databases. For each award, the title and abstract, where available, were individually
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45 screened for relevance to cancer research. We excluded awards that were i) not obviously or
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47 immediately relevant to oncology; ii) led by a non-UK institution; iii) not considered to be for R&D
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49 activity. Studies that were completed without funding were also excluded. Private sector data were
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51 not available to evaluate at the same level of detail as public and philanthropic research award data,
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53 and were therefore excluded from this analysis. Cancer Research UK (CRUK) would not provide their
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55 funding data at individual award level, as in accordance with their organisational policy, and so could
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3 not be included in the main analysis. There is some description of individual CRUK awards without
4 grant amounts available at <https://europepmc.org/>. We report total number of studies in this
5 analysis.
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10 Where awards were described in currencies other than UK pounds, these were converted to UK
11 pounds using the mean exchange rate in the year of the award. All included awards were adjusted
12 for inflation and reported in 2013 UK pounds.
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16 Each study in the dataset was reviewed by one author (either CDZ, GJG, MAE-H, MGH) and assigned
17 to as many of 14 cross-cutting categories as appropriate. The 14 association categories were
18 paediatric, geriatric, infection-associated, women's health, men's health, occupational health,
19 pathogenesis, diagnostic/screening/monitoring, drug therapy, radiotherapy, surgery, immunology,
20 psychosocial and global health. Awards were defined as global health if they were considered to
21 pursue a clear non-UK focus (e.g. 'thyroid cancer in Kenya'). The other category was only used when
22 none of the aforementioned categories were deemed to be appropriate. Studies were also allocated
23 to one of five categories along the R&D pipeline: pre-clinical; phase I, II, or III clinical trials; product
24 development (including phase IV activity); public health; and cross-disciplinary research. The cross-
25 disciplinary category was defined as an award containing significant components across two distinct
26 areas along the R&D pipeline (such as pre-clinical research leading directly into a phase I trial).
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40 Provisional datasets were circulated to all authors for review and comment with checks by second
41 authors on sections of the data and any disagreements settled by consensus. Final datasets were
42 then again circulated for further review by all authors. Microsoft Excel 2010 and 2013 and Stata
43 (V13) software were used for data analysis.
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50 Global data on mortality, disability-adjusted life years (DALYs) and years lived with disability (YLDs)
51 were available at time points 2005, 2010 and 2013. All burden data were sourced from the findings
52 of the Global Burden of Disease (GBD) study, for 2013[1,9,10] and for 2010[11,12]. Burden data from
53 2005 were obtained directly from colleagues at the Institute for Health Metrics and Evaluation, USA.
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3 As defined by the GBD study, YLDs for a disease or injury are the sum of the YLDs for each sequela
4 associated with the disease or injury[10]. DALYS are the sum of YLLs and YLDs for each age–sex–
5 country group[9].
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10 In order to allow direct comparison of relative investment with global health metrics across disease
11 areas and between different time periods, metrics were adapted from the infectious disease
12 analyses to estimate the ‘investment per mortality/DALY/YLD observed [7]’. The metrics were
13 created using the following equation –
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$$\text{(Total research investment up to the year before the time point / number of deaths, DALYs or YLD at time point) / number of years of investment included}$$

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24 For example, for assessment of breast cancer mortality at the 2013 time point, we took the sum of
25 breast cancer research investment 2000-2012 (£124,305,716) and divided that by number of deaths
26 reported in 2013 (471000), and divided the result by the number of years of investment included
27 (13) to get an ‘investment per mortality observed’ metric of £20.30.
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33 These metrics were applied for research relating to 16 site-specific cancers, where there was
34 comparable data in both the ResIn and GBD studies. We defined lung cancer by aggregating
35 ‘tracheal, bronchus and lung cancer’ burden data from the GBD study. Similarly, we defined skin
36 cancer by aggregating ‘malignant skin melanoma’ and ‘non-malignant skin cancer’, and we defined
37 upper gastrointestinal (GI) cancer by aggregating ‘oesophageal’ and ‘stomach cancer’. The use of
38 total investment and the division by number of years included aimed to reduce the impact of the
39 volatility of annual research funding and the relatively short periods between time points. Ranking
40 scores of the investment metrics were developed for the 16 sites of cancer against 2013 burdens.
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3 **Patient involvement**
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6 There was no patient involvement in this study.
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For peer review only

Results

We identified 4,299 funded studies that met our inclusion criteria (Table 1). The funding for these studies represented a total research investment of almost £2.4 billion. The mean award amount for each study was £555,513 (standard deviation (SD) £1,429,510) and median was £231,559 (inter-quartile range £114,619 – 487,063). 2,416 awards (56.2% of total) were designated towards a named site-specific cancer (Table 1), equating to £1.0 billion (40.3% of total). The top five cancer sites in terms of award number were haematological, breast, colorectal, prostate, and skin; the bottom five were testicular, bone, bladder, thyroid, and cholangiocarcinoma (Table 1). The top five cancer sites in terms of total funding were haematological, breast, prostate, colorectal and ovarian; the bottom five were testicular, mesothelioma, thyroid, bladder and chlangiocarinoma. Mean funding per award varied greatly between sites with prostate cancer receiving the most (£1.47 million) and bladder cancer the least (£117,385).

The top five areas of primary research focus, by number of awards, were drug therapy, diagnostic, screening and monitoring, women's health, immunology, and pathogenesis; the bottom five areas were men's health, surgery, occupational health, global health and geriatrics (Table 2). In terms of net funding, the top five areas of research were pathogenesis, drug therapy, diagnostic, screening and monitoring, women's health, and immunology; the bottom five were surgery, psychosocial, global health, occupational health, and geriatrics.

The majority of awards were focused on pre-clinical science, accounting for 66.2% of award numbers and 62.2% of all funding (Table 3). In terms of award number, this was followed by public health, cross-disciplinary, phase I-III, and product development. This order was reflected in terms of net investment, although cross-disciplinary studies ranked ahead of public health studies. Phase I-III clinical trials received the highest mean funding per award, at £736,172 (SD £3,361,312), whilst public health research received the least, at £496,744 (SD £1,000,757).

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3 The largest individual funder of cancer research of the studies identified was the Medical Research
4 Council, accounting for 35.1% of all funding (Table 4). The charitable sector was responsible for
5 39.5% of all awards (excluding CRUK) but 17.4% of funding. The European Commission was
6 responsible for the largest mean grant per award (£1.58 million).
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11 We generated a compound ranking score for the 16 sites of cancer against 2013 global disease
12 burdens, across mortality, DALYs, and YLDs (table 5). The amount of investment per unit disease
13 burden (£ per death/DALY/YLD) were used to compile this compound ranking score. The data for all
14 site-specific cancers measured here are presented in the supplementary information (Supplemental
15 Tables 1-3, Supplemental Figures 1-3). We identified the five sites that received the most funding
16 relative to disease burden as prostate, ovarian, breast, mesothelioma and testicular cancer. The
17 least well-funded sites relative to disease burden were cancers of the liver, thyroid, lung, upper GI,
18 and bladder.
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30 We were able to obtain some disaggregated data for 3,284 CRUK research grants during the period
31 of interest but this excluded individual award data. Compared to the aggregation of all other
32 funders, CRUK placed more of a focus on funding towards cancers of the prostate, ovary and liver –
33 by study number these sites accounted for 6.9%, 3.4% and 2.7% of CRUK funded studies compared
34 to 2.1%, 1.1% and 0.9% of all studies in our quantitative database, respectively. CRUK preferentially
35 funded research investigating pathogenesis, which accounted for 51.0% of all grants awarded. In
36 comparison, only 5.3% of all awards in our quantitative database were identified as primarily
37 focused on pathogenesis.
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48 Discussion

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50 We identified 4,299 funded studies, with a total research investment of £2.4 billion. We performed
51 qualitative analysis on a further 3,284 CRUK funded awards. The vast majority of all awards awarded
52 were investigating at least one of pathogenesis, diagnosis, monitoring and screening and drug
53 therapy. In the absence of CRUK data, the Medical Research Council and the Department of Health
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3 were the two leading funding sources. Preclinical research accounted for £1.5 billion (62.2%) of total
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5 R&D investment. Four of the five highest funded cancer sites relative to global disease burden were
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7 gender-specific – namely prostate, ovarian, breast, and testicular cancers. Cancer research with a
8
9 clear focus on women’s health accounted for 640 studies (14.9%) and £199.5 million (8.4%) of
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11 investment. In comparison, 111 studies (2.6%) and £143.3 million (6.0%) of investment had a clear
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13 link with men’s health. This may reflect the successes of various institutions and charities that have
14
15 sought to increase awareness of these sex-specific cancers. Breast cancer, the most commonly
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17 diagnosed cancer in the UK and the leading cause of cancer death in women, and prostate cancer,
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19 the second most frequently diagnosed cancer and the sixth leading cause of cancer death among
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21 men, were found to be relatively well funded[1,13].
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25 We highlight several cancer sites where there might be underinvestment, namely that of liver,
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27 thyroid, lung, upper GI tract, and bladder. In our analysis cancer of the upper GI tract combines
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29 oesophageal and stomach cancer. These site-specific cancers identified to be relatively underfunded
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31 account for a substantial proportion of global cancer burden. Globally, these sites account for 47.9%,
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33 44.3% and 20.4% of the global mortality[1], DALYs[9] and YLDs[10] of all cancers, respectively. The
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35 disparity between YLDs and DALYs demonstrates the poor prognosis and high mortality of these
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37 particular sites when compared against all neoplastic disease. Lung, liver, stomach and oesophagus
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39 are the first, second, third and fifth, leading sites of neoplastic mortality worldwide[1].
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43 Two previous studies have compared UK cancer funding with years of life lost (YLLs). Burnett et al
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45 [14] reported the relative over-funding of breast cancers and leukaemia. Carter et al [15] likewise
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47 reported higher levels of funding than their burden suggests of testicular, leukaemia, Hodgkin’s
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49 lymphoma, breast, cervical, ovarian, prostate cancer with relative underfunding of gallbladder, lung,
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51 nasopharyngeal, intestine, stomach, pancreatic, thyroid, oesophageal, liver, kidney, bladder, and
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53 brain/central nervous system. Although our site-specific classifications differed slightly, our findings
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55 are consistent with these previous studies. The slight differences that we report are likely due to our
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3 metrics which seek to capture mortality (global mortality and DALYs) and life burden (DALYs and
4 YLDs) rather than just mortality, and also different included components in the respective datasets.
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8 With regard to interventions research, there is heavy investment in drug-based modalities. £620.9
9 million (26.0%) was invested in novel drug therapies and £194.1 million (8.1%) was invested in the
10 emergent role of immunomodulation. In comparison, funding towards radiotherapy and surgical
11 interventions accounted for £88.2 million (3.7%) and £37.9 million (1.6%), respectively. In high-
12 income settings, around half of new cancer diagnoses will undergo a course of radiotherapy
13 treatment during their clinical management; roughly a quarter will receive two or more
14 courses[16,17]. Globally, over 80% of cancer cases will warrant surgical intervention, where it has
15 preventative, diagnostic, curative, supportive, palliative, and reconstructive roles[18].
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19 Analysis by R&D pipeline showed that research investment in the UK places a heavy emphasis on
20 pre-clinical research, but relatively little investment towards phase I-III clinical trials or product
21 development, and this is line with previous research in infectious disease investment[6]. This may
22 reflect the strengths of UK institutions in preclinical science, but also could suggest a need to
23 strengthen research capacity further down the R&D chain. It would be useful to determine whether
24 investment reflects the priorities of funding agencies and whether this is comparable to research
25 investment in other countries. We noted a lack of readily available data from the pharmaceutical
26 industry and this is likely to leave a data gap in particular for sum totals of investment in clinical trials
27 of pharmaceutical products.
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31 Our findings contribute to the development of transparent and objective methods to couple the
32 allocation of limited research funds with disease burden. Previous studies have suggested that
33 financial investment might appropriately be coupled with DALYs as a measure of burden[19–22].
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35 Furthermore, previous UK research suggests that publicly funded cancer research offers substantial
36 rates of return in terms of both health and monetary benefit [23]. We have further sought to
37 incorporate mortality rates and YLDs into the consideration of cancer research investment.
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3 We have chosen to compare cancer research funding to global rather than domestic UK disease
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5 burden. Due to increasing globalization, the emergence of non-communicable disease burden in
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7 resource poor settings, the internationalization of healthcare, the flow of people across national
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9 borders and the role of the UK as an international centre of biomedical research, we believe this
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11 approach to be justified.
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14 However, defining an appropriate amount of research investment for each site specific cancer is
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16 challenging since cancers of similar disease burdens may warrant different levels of investment to
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18 develop cost-effective interventions. Decisions may be influenced by any of a number of factors, for
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20 example due to exceptional need, as may be the case in mesothelioma, or due to public awareness
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22 and third-party lobbying, as may be the case with regards to the gender-specific cancers.
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26 A variety of factors contribute towards the difficulty in tracking net cancer research investment
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28 within the UK. Fragmentation of data from a large number of diverse public and private sources of
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30 funding, poorly designed donor accounting structures, where available, and the paucity of
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32 information from the private sector limit the evidence base to inform policy in real-time. In our
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34 study, we were unable to obtain quantitative data from CRUK, the world's largest cancer research
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36 charity and a leader in cancer research. They do not routinely publish or make available
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38 disaggregated investment data which is, in our experience across the infection and cancer analyses,
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40 unique amongst the more high-profile UK funders who are universally more transparent in their
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42 award decisions[24]. Transparency in the tracking and monitoring of cancer research financing is
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44 essential to enable accountability and equity in resource allocation and to facilitate further future
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46 research in this area.
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50 In this study we systematically analyse UK investment in cancer research and identify areas of
51
52 relative neglect. Although the competitive application process used by most funders to allocate
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54 research grants ensure a portfolio of high quality, the absence of explicit resource allocation criteria
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56 could contribute towards inequalities in R&D by disease burden. Funding agencies will have
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3 particular areas of focus, and UK funders may have considered the focus of international agencies in
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5 their own research strategies. As a result, international data is essential to complete the mapping of
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7 cancer research investment. Nevertheless, our findings will inform funders and contribute towards
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9 policy discussions to prevent inequity in the allocation of limited resources.
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12 By demonstrating the relationship between disease burden and research funding, we enable the
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14 identification of potential investment gaps. However, it is not possible to equate gaps in funding
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16 with areas of neglect without consideration of other influences such as the feasibility of research,
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18 costs of technologies, infrastructure and skill requirements, political and social considerations, and
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20 the accuracy of disease burden estimates.
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23 There are several potential limitations to our study. We are dependent on the accuracy of original
24
25 investment data as sourced from the funding bodies. Although checks were made on any obvious
26
27 discrepancies or errors, interpretation of these original data may contain errors. We made no
28
29 attempt to investigate the contribution of any indirect or estate costs. Currency conversions were
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31 averaged across each financial year and any intra-year fluctuations may not have been captured.
32
33 Unless clearly documented, we were unable to assess how funding was distributed from lead
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35 institutions to collaborative partners. We considered individual awards, rather than number of
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37 studies.
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41 Furthermore, assignment of disease categories and allocation of studies according to these
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43 categories is subjective, and there might be disagreements regarding certain inclusion criteria. As
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45 YLLs were not included in our analysis, we may underrepresent the disease burden of cancers that
46
47 occur disproportionately in the young and which are associated with poor survival, notably cancers
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49 of the ovary, cervix and CNS [14]. However, we would expect any additional information offered by
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51 YLL analysis to be predominantly captured by use of DALYs.
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55 We could not openly access data of private sector research funding, nor were we able to obtain
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57 disaggregated award data from CRUK. Whilst our analysis did demonstrate that CRUK funding (with
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3 some exceptions) broadly reflected the findings of our quantitative database, it is likely that
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5 substantial awards towards particular areas of research could skew results; for example, the CRUK
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7 accounts for 2014/15 suggest £394 million was invested into research or research-related activity,
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9 and we hypothesise that much of that would have met our inclusion criteria for this analysis[25].

10
11 Disease burden measures are typically an estimate and are subject to the potential introduction of
12
13 bias from missing or unobtainable data as well as from differences in classification and diagnosis.

14
15 Our report presents the latest investment data on cancer research awarded to UK institution
16
17 between 2000 and 2013. Cancers of the liver, thyroid, lung, upper GI tract, and bladder as well as
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19 research towards radiotherapy and surgical techniques in particular may warrant increased rates of
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21 investment. We will make the entire database and associated figures available online
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23 (www.researchinvestment.org) to assist policy makers, funding organisations, and researchers in the
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25 identification of investment gaps. We further encourage funding organisations to make their
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27 investment portfolios openly accessible to facilitate future research.
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31 We hope that open funding data in this area can contribute to redressing the misalignments in
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33 investments for cancer research. Cancer research can improve the clinical course of disease and
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35 offer tangible improvements in health outcomes[23]. Both policy makers and the scientific
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37 community need to ensure that limited resources are allocated appropriately to most effectively
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39 alleviate the morbidity and mortality associated with cancer.
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Contributions

MM and MGH are the guarantors of this study. MM, MGH, JRF and RA conceived and designed the study. MGH, CDZ, BJG and MAE-H obtained the data. MM and MGH conducted data formatting and statistical analysis. All authors helped interpret the findings. MM, MGH and CDZ wrote the first draft of the manuscript with input from RR, JRF and RA; all authors provided input to subsequent drafts. All authors had full access to all of the data in the study and take responsibility for its integrity and the accuracy of data analysis.

Transparency declaration

MM affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Funding

No funding was received for this study

Competing interests

All authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

Not required

Data sharing

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All data used is publicly available. Entire database and associated figures are permanently available with open access online (www.researchinvestment.org) to assist policy makers, funding organisations, and researchers.

For peer review only

References

- 1 Naghavi M, Wang H, Lozano R, *et al*. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;**385**:117–71.
- 2 Jemal A, Bray F, Center MM, *et al*. Global Cancer Statistics: 2011. *CA Cancer J Clin* 2011;**61**:69–90.<http://www.ncbi.nlm.nih.gov/pubmed/21296855>
- 3 Torre LA, Bray F, Siegel RL, *et al*. Global Cancer Statistics, 2012. *CA a cancer J Clin* 2015;**65**:87–108.<http://onlinelibrary.wiley.com/doi/10.3322/caac.21262/abstract>
- 4 Luengo-Fernandez R, Leal J, Gray A, *et al*. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol* 2013;**14**:1165–74.<http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24131614>
- 5 Yabroff KR, Lund J, Kepka D, *et al*. Economic Burden of Cancer in the United States: Estimates, Projections, and Future Research. *Cancer Epidemiol Biomarkers Prev* 2011;**20**:2006–14.<Go to ISI>://WOS:000295717900003
- 6 Head MG, Fitchett JR, Cooke MK, *et al*. UK investments in global infectious disease research 1997-2010: A case study. *Lancet Infect Dis* 2013;**13**:55–64.
- 7 Head MG, Fitchett JR, Nageshwaran V, *et al*. Research Investments in Global Health: A Systematic Analysis of UK Infectious Disease Research Funding and Global Health Metrics, 1997–2013. *EBioMedicine* 2016;**3**:180–90.<http://dx.doi.org/10.1016/j.ebiom.2015.12.016>
- 8 Head MG, Fitchett JR, Derrick G, *et al*. Comparing research investment to United Kingdom institutions and published outputs for tuberculosis, HIV and malaria: a systematic analysis across 1997-2013. *Health Res Policy Syst* 2015;**13**:63.<http://www.health-policy-systems.com/content/13/1/63>
- 9 Murray CJL, Barber RM, Foreman KJ, *et al*. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015;**386**:2145–91.
- 10 Vos T, Barber RM, Bell B, *et al*. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;**386**:743–800.
- 11 Murray CJ, Vos T, Lozano R, *et al*. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2197–223.<http://www.ncbi.nlm.nih.gov/pubmed/23245608>
- 12 Lozano R, Naghavi M, Foreman K, *et al*. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2095–128.

- 1
2
3 13 Jemal A, Bray F, Center MM, Ferlay J, Ward E FD. Global cancer statistics. *Cancer J Clin*
4 2011;**61**:69–90.
- 5
6 14 Burnet NG, Jefferies SJ, Benson RJ, *et al*. Years of life lost (YLL) from cancer is an important
7 measure of population burden--and should be considered when allocating research funds. *Br*
8 *J Cancer* 2005;**92**:241–5.
- 9
10 15 Carter AJR, Delarosa B, Hur H. An analysis of discrepancies between United Kingdom cancer
11 research funding and societal burden and a comparison to previous and United States values.
12 *Heal Res Policy Syst* 2015;**13**:62.<http://www.health-policy-systems.com/content/13/1/62>
- 13
14 16 Barton MB, Frommer M, Shafiq J. Role of radiotherapy in cancer control in low-income and
15 middle-income countries. *Lancet Oncol* 2006;**7**:584–95.[http://ac.els-](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aab0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
16 [cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aab0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
17 [11e3-a45c-0000aab0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aab0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
- 18
19 17 Barton MB, Jacob S, Shafiq J, *et al*. Estimating the demand for radiotherapy from the
20 evidence: a review of changes from 2003 to 2012. *Radiother Oncol* 2014;**112**:140–4.
- 21
22 18 Sullivan R, Alatisse OI, Anderson BO, *et al*. Global cancer surgery: Delivering safe, affordable,
23 and timely cancer surgery. *Lancet Oncol*. 2015;**16**:1193–224.
- 24
25 19 Gross CP, Anderson GF, Powe NR. The relation between funding by the National Institutes of
26 Health and the burden of disease. *N Engl J Med* 1999;**340**:1881–7.
- 27
28 20 Lopez FC, Martin EA, Maleras RG, *et al*. Relationship between Research Funding in the
29 Spanish National Health System and the Burden of Disease. *Rev Esp Salud Publica*
30 2009;**83**:137–51.<Go to ISI>://WOS:000266635200011
- 31
32 21 Mitchell RJ, McClure RJ, Olivier J, *et al*. Rational allocation of Australia’s research dollars: does
33 the distribution of NHMRC funding by National Health Priority Area reflect actual disease
34 burden? *Med J Aust* 2009;**191**:648.
- 35
36 22 Lamarre-Cliche M, Castilloux AM, LeLorier J. Association between the burden of disease and
37 research funding by the Medical Research Council of Canada and the National Institutes of
38 Health. A cross-sectional study. *Clin Invest Med* 2001;**24**:83–
39 9.<http://www.ncbi.nlm.nih.gov/pubmed/11368150>
- 40
41 23 Glover M, Buxton M, Guthrie S, *et al*. Estimating the returns to UK publicly funded cancer-
42 related research in terms of the net value of improved health outcomes. *BMC Med*
43 2014;**12**:1.
- 44
45 24 Fitchett JRA, Sharara N, Head MG, *et al*. Transparency and availability of data for cancer
46 research. *Lancet* 2016;**388**:866–7.[http://dx.doi.org/10.1016/S0140-6736\(16\)31427-1](http://dx.doi.org/10.1016/S0140-6736(16)31427-1)
- 47
48 25 CRUK. Annual report and accounts 2014/15. 2015.
49 [http://www.cancerresearchuk.org/sites/default/files/annual_report_and_accounts_2014-](http://www.cancerresearchuk.org/sites/default/files/annual_report_and_accounts_2014-15.pdf)
50 [15.pdf](http://www.cancerresearchuk.org/sites/default/files/annual_report_and_accounts_2014-15.pdf)
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Table Legends

Table 1: Cancer research investment awards and funding by site. All investment reported in 2013 UK pounds.

Site of cancer	All funders where investment data was available						Cancer Research UK	
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Breast	571	13.3%	£137,960,107	5.8%	241611 (414584)	135752 (25000-216673)	273	8.3%
Haematological	1158	26.9%	£381,008,394	16.0%	329022 (476943)	186813 (120437-272324)	225	6.9%
Colorectal	147	3.4%	£77,279,857	3.2%	525713 (674881)	251800 (102078-819866)	205	6.2%
Prostate	92	2.1%	£135,290,779	5.7%	1470552 (6156372)	333757 (155227-721037)	123	3.7%
Ovarian	48	1.1%	£44,709,938	1.9%	931457 (3380145)	226764 (131990-627401)	112	3.4%
Lung	82	1.9%	£24,263,280	1.0%	295893 (556278)	146123 (66701-242934)	89	2.7%
Skin	87	2.0%	£22,179,011	0.9%	254931 (453726)	85406 (69629-248603)	84	2.6%
Brain	22	0.5%	£9,994,255	0.4%	454284 (498933)	401046 (196928-528008)	83	2.5%
Upper GI and	18	0.4%	£19,094,230	0.8%	1060791 (1448010)	788850 (80964-1296962)	80	2.4%
Head and neck	20	0.5%	£18,250,632	0.8%	912531 (1003091)	389751 (167358-1602465)	68	2.1%
Renal	19	0.4%	£13,885,496	0.6%	730815 (678732)	479197 (244075-1252574)	48	1.5%
Bladder	10	0.2%	£1,173,856	0.0%	117385 (106902)	94520 (29264- 173855)	48	1.5%
Cervical	26	0.6%	£14,328,402	0.6%	551092 (877250)	210179 (88934-368402)	43	1.3%
Pancreatic	16	0.4%	£9,453,577	0.4%	590848 (519850)	276237 (191804-1033948)	40	1.2%
Bone	13	0.3%	£17,242,183	0.7%	1326322 (1604685)	685853 (243559-1999907)	29	0.9%
Liver	37	0.9%	£25,037,541	1.0%	676690 (847151)	319082 (177974-776480)	20	0.6%
Mesothelioma	30	0.7%	£4,476,088	0.2%	149202 (101201)	137103 (95895-205500)	11	0.3%
Cholangiocarcinoma	2	0.0%	£582,405	0.0%	n/a	n/a	11	0.3%
Testicular	14	0.3%	£5,949,990	0.2%	424999 (507277)	242175 (102938-411010)	11	0.3%
Thyroid	4	0.1%	£1,375,881	0.1%	n/a	n/a	7	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

Table 2: Cancer research investment awards and funding by cross-cutting theme. All investment reported in 2013 UK pounds.

Cross-cutting theme	All funders where investment data was available						Cancer Research UK	
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Pathogenesis (mechanism)	227	5.3%	£1,374,387,838	57.6%	543881 (955710)	248573 (135752-506232)	1674	51.0%
Drug Therapy	1104	25.7%	£620,961,060	26.0%	562464 (1910050)	202342 (105622-436559)	935	28.5%
Diagnostic, Screening and Monitoring	681	15.8%	£359,618,823	15.1%	528074 (1155156)	205728 (102672-513836)	404	12.3%
Women's Health	640	14.9%	£199,534,693	8.4%	311773 (1041520)	153845 (56515-227202)	287	8.7%
Immunology (inc. biologics)	451	10.5%	£194,086,617	8.1%	430347 (760955)	240052 (125669-466250)	212	6.5%
Radiotherapy	112	2.6%	£88,262,353	3.7%	788056 (2413445)	243333 (106175-439419)	209	6.4%
Psychosocial	117	2.7%	£23,445,835	1.0%	200391 (352410)	87463 (27317-239059)	122	3.7%
Men's Health	111	2.6%	£143,392,908	6.0%	1291828 (5617919)	285203 (126037-700353)	120	3.7%
Paediatrics	175	4.1%	£62,641,938	2.6%	357953 (547484)	183099 (89522-322261)	118	3.6%
Surgery	72	1.7%	£37,900,334	1.6%	526393 (684908)	235413 (97890-761651)	95	2.9%
Infection-associated	129	3.0%	£56,819,379	2.4%	440460 (798013)	231836 (134693-439378)	48	1.5%
Global Health	12	0.3%	£6,434,960	0.3%	536246 (1089118)	129738 (77519-459274)	12	0.4%
Geriatrics	7	0.2%	£1,616,394	0.1%	230913 (254925)	121623 (76421-262167)	8	0.2%
Occupational Health	18	0.4%	£2,576,841	0.1%	143157 (116928)	137103 (33857-199998)	8	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

Table 3: Cancer research investment awards and funding by type of science. All investment reported in 2013 UK pounds.

	All funders where investment data was available						Cancer Research UK	
Type of science	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Pre-clinical	2845	66.2%	£1,485,997,379	62.2%	522318 (1006600)	240974 (132188-490872)	1809	55.1%
Phase I-III	303	7.0%	£223,060,276	9.3%	736172 (3361312)	178535 (70934-502399)	647	19.7%
Product development	172	4.0%	£104,214,364	4.4%	605897 (2213394)	193051 (75270-360813)	52	1.6%
Cross-disciplinary	441	10.3%	£315,145,351	13.2%	714615 (1586882)	238523 (126589-703764)	328	10.0%
Public health	512	11.9%	£254,333,282	10.6%	496744 (1000757)	209364 (82870-383623)	443	13.5%
Unable to specify	26	0.6%	£5,401,666	0.2%	n/a	n/a	5	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

Table 4: Cancer research investment awards and funding by funding agency (excluding CRUK). All investment reported in 2013 UK pounds.

Funder	All funders where investment data was available					
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)
MRC	768	17.9%	£837,649,875	35.1%	1090690 (1770533)	504606 (305375-1153374)
Charity (excluding Wellcome and CRUK)	1,699	39.5%	£415,189,093	17.4%	244372 (391813)	151912 (81000-223244)
Department of Health	586	13.6%	£413,421,823	17.3%	705498 (2675223)	232173 (102391-471236)
BBSRC	511	11.9%	£223,651,002	9.4%	437673 (388793)	373356 (267848-501592)
EPSRC	356	8.3%	£201,861,623	8.5%	567027 (972696)	306906 (144056-604016)
Wellcome	193	4.5%	£140,425,805	5.9%	727594 (1679370)	226761 (164547-427455)
European Commission (inc ERC)	50	1.2%	£78,757,447	3.3%	1575149 (731858)	1409678 (1252574-1830017)
Other	136	3.2%	£77,195,650	3.2%	567615 (1901202)	129944 (69309-263613)
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)

Table 5: Compound ranking score for cancer research investment against 2013 global disease burdens, across mortality, YLDs, and DALYs, by cancer site.

Disease	Research investment (UK pound) by burden observed, 2013			
	Mean ranking across all burden metrics	Mortality	Years lived with disability	Disability-adjusted life years
Prostate	2.7	2	4	2
Ovarian	3.0	4	2	3
Mesothelioma	4.0	6	1	5
Breast	4.0	3	5	4
Testicular	4.7	1	3	10
Skin	5.0	5	9	1
Colorectal	6.7	7	7	6
Renal	8.3	8	10	7
Cervical	9.7	9	12	8
Pancreatic	10.0	12	6	12
Brain	11.0	11	11	11
Thyroid	11.3	10	15	9
Liver	11.3	13	8	13
Lung	13.7	14	13	14
Upper GI	14.7	15	14	15
Bladder	16.0	16	16	16

Supplementary Table 1: Investment per mortality observed for all site-specific cancers

	Number of deaths			Investment per mortality observed		
	2005	2010	2013	2005	2010	2013
Bladder	156385	170700	173900	£0.03	£0.26	£0.49
Brain	177191	195500	203900	£0.00	£2.02	£2.76
Breast	407108	438700	471000	£5.35	£18.20	£20.30
Cervical	221578	225400	235700	£2.93	£5.63	£4.50
Colorectal	644648	714600	771000	£3.54	£5.45	£6.77
Liver	715141	752100	818000	£0.04	£1.00	£1.45
Lung	1391577	1527100	1639600	£0.15	£0.57	£1.08
Mesothelioma	22128	n/a	33700	£0.81	?	£8.33
Ovarian	134354	160500	157800	£23.00	£20.98	£19.79
Pancreatic	276753	310200	352400	£0.56	£0.86	£1.67
Prostate	225081	256000	292700	£53.92	£45.19	£34.22
Renal	113048	162100	133800	£0.00	£2.27	£5.96
Skin	?	79700	96100	?	£14.20	£16.30
Testicular	7547	7700	8300	£7.27	£44.69	£55.14
Thyroid	29092	36000	33700	£0.00	£1.70	£3.14
Upper GI and oesophageal	1229320	1130100	1281200	£0.93	£1.18	£1.03

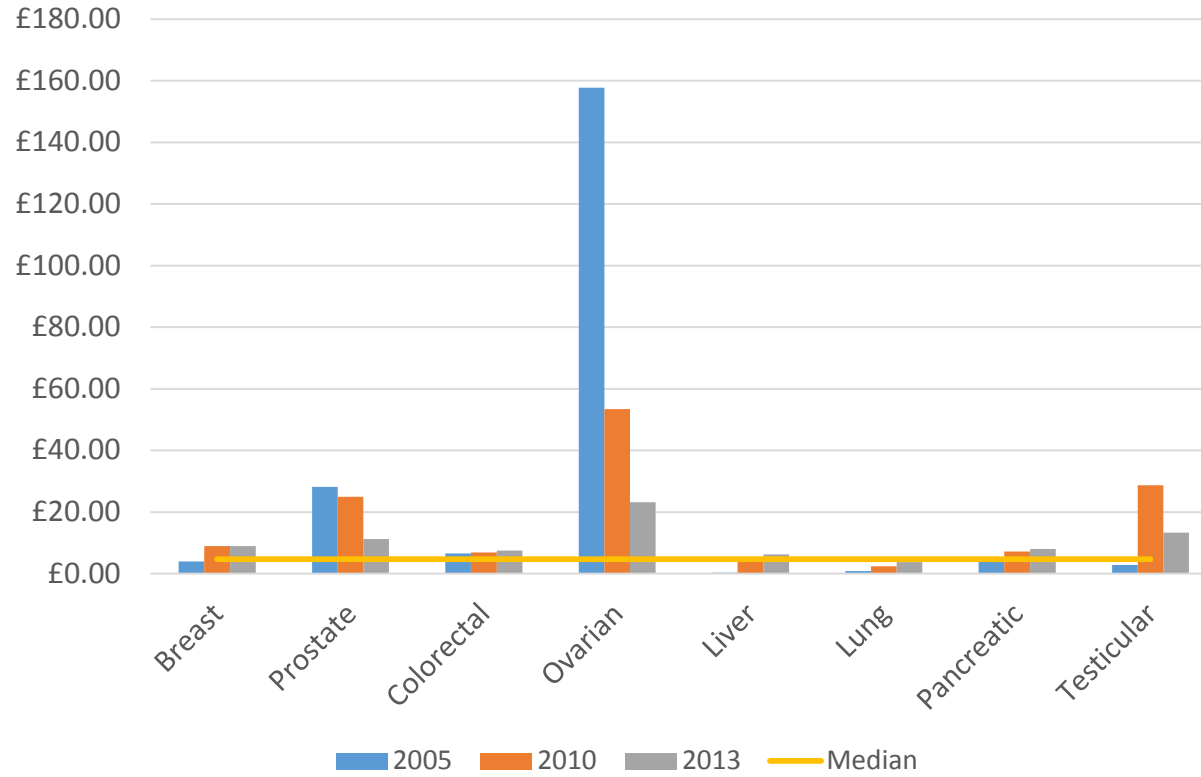
Supplementary Table 2: Investment per YLD observed for all site-specific cancers

	YLD			Investment per YLD observed		
	2005	2010	2013	2005	2010	2013
Bladder	153647	125000	179800	£0.05	£0.35	£0.47
Brain	105126	94000	121900	£0.00	£4.20	£4.61
Breast	885550	898000	1068200	£3.93	£8.89	£8.95
Cervical	242359	111000	243800	£4.28	£11.44	£4.35
Colorectal	561019	564000	701900	£6.50	£6.91	£7.44
Liver	160071	140000	190600	£0.29	£5.39	£6.24
Lung	388206	355000	467400	£0.86	£2.44	£3.78
Mesothelioma	7109	n/a	10800	£4.04	?	£25.98
Ovarian	31339	63000	134900	£157.75	£53.44	£23.15
Pancreatic	57317	37000	73600	£4.35	£7.18	£8.01
Prostate	690602	464000	893700	£28.12	£24.93	£11.21
Renal	112449	79000	139200	£0.00	£4.66	£5.72
Skin	?	300000	264100	?	£3.77	£5.93
Testicular	31339	12000	34300	£2.80	£28.67	£13.34
Thyroid	109078	48000	127600	£0.00	£1.27	£0.83
Upper GI and oesophageal	382757	304000	416100	£4.77	£4.39	£3.17

Supplementary Table 3: Investment per DALY observed for all site-specific cancers

	Global DALYs			Investment per DALY observed		
	2005	2010	2013	2005	2010	2013
Bladder	2987377	3015000	3139900	£0.00	£0.01	£0.03
Brain	6163358	6060000	6692200	£0.00	£0.07	£0.08
Breast	11762493	12018000	13258700	£0.19	£0.66	£0.72
Cervical	6775622	6440000	6914700	£0.10	£0.20	£0.15
Colorectal	13747947	14422000	15794100	£0.17	£0.27	£0.33
Liver	19175329	19111000	20888700	£0.00	£0.04	£0.06
Lung	30791630	32405000	34732900	£0.01	£0.03	£0.05
Mesothelioma	504037	n/a	763500	£0.04	?	£0.37
Ovarian	3541657	4118000	4056500	£0.87	£0.82	£0.77
Pancreatic	5704661	6161000	7029100	£0.03	£0.04	£0.08
Prostate	3812057	3787000	4768800	£3.18	£3.05	£2.10
Renal	2810156	3676000	3150300	£0.00	£0.10	£0.25
Skin	?	1967000	237200	?	£0.58	£6.61
Testicular	354875	313000	3787700	£0.15	£1.10	£0.12
Thyroid	764526	836000	851900	£0.00	£0.07	£0.12
Upper GI and oesophageal	27964269	25356000	27749600	£0.04	£0.05	£0.05

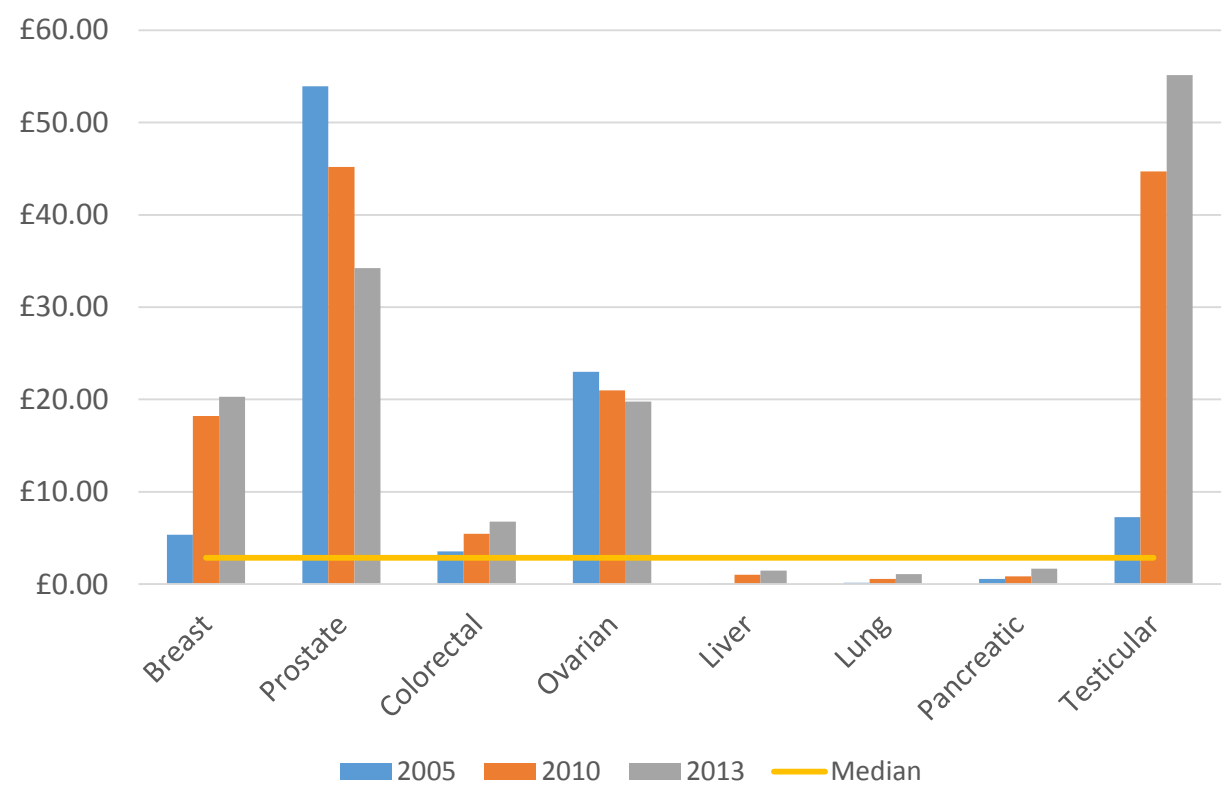
Supplementary Figure 1: Investment per YLD (£/YLD) for 8 indicator site-specific cancers



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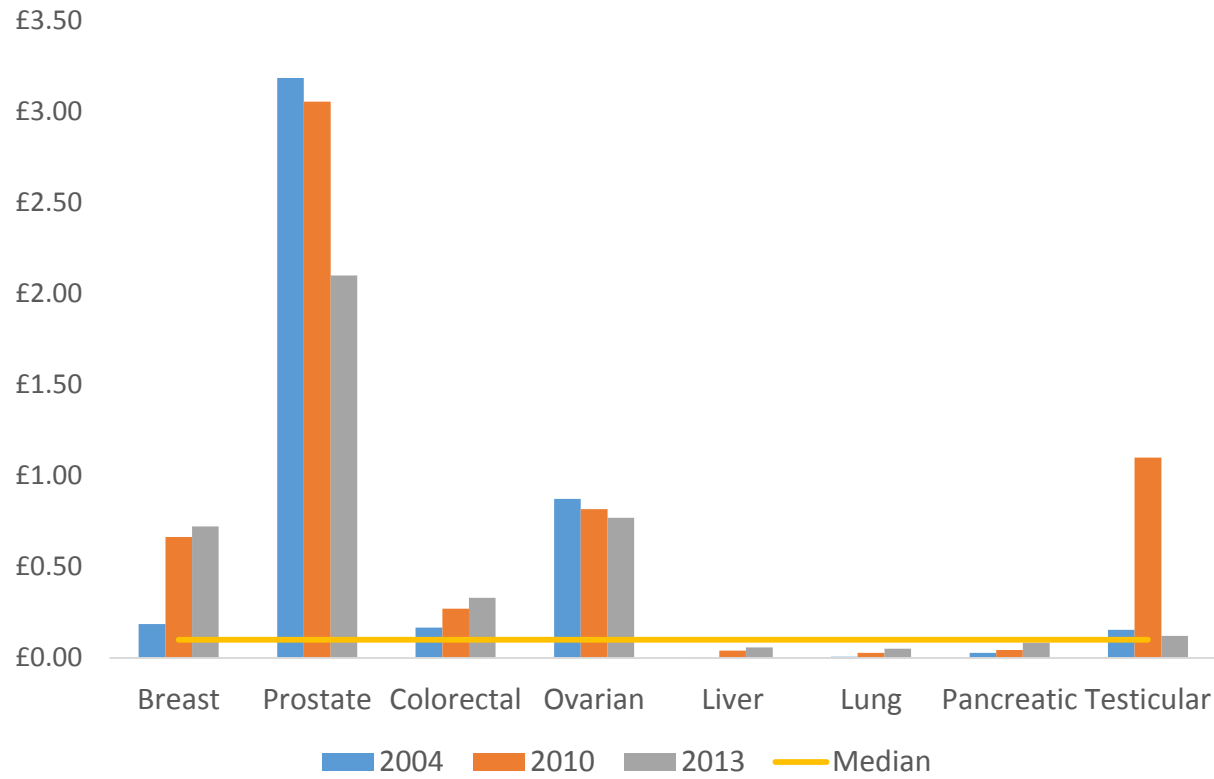
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Supplementary Figure 1: Investment per death (£/death) for 8 indicator site-specific cancers



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Supplementary Figure 1: Investment per DALY (£/DALY) for 8 indicator site-specific cancers



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Investments in cancer research awarded to UK institutions and the global burden of cancer 2000-2013: a systematic analysis

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3 **Investments in cancer research awarded to UK institutions and the global burden of cancer 2000-**
4 **2013: a systematic analysis**

5
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49 and development
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ABSTRACT

Objectives

We sought to systematically categorise cancer research investment awarded to UK institutions in the period 2000-2013 and to estimate research investment relative to disease burden as measured by mortality, disability-adjusted life years (DALYs), and years lived with disability (YLDs).

Design

Systematic analysis of all open access data.

Setting and participants

Public and philanthropic funding to all UK cancer research institutions, 2000-2013

Main outcome measures

Number and financial value of cancer research investment reported in 2013 UK pounds. Mortality, DALYs and YLDs data was acquired from the Global Burden of Diseases Study. A compound metric was adapted to estimate research investment relative to disease burden as measured by mortality, DALYs, and YLDs.

Results

We identified 4,299 funded studies with a total research investment of UK£2.4 billion. The highest funding by sites were haematological, breast, prostate, colorectal, and ovarian cancers. Relative to disease burden as determined by a compound metric combining mortality, DALYs and YLDs, gender-specific cancers were found to be highest funded - the five sites that received the most funding were prostate, ovarian, breast, mesothelioma, and testicular cancer; the least well-funded sites were liver, thyroid, lung, upper GI and bladder. Pre-clinical science accounted for 66.2% of award numbers and 62.2% of all funding. The top five areas of primary research focus by funding were pathogenesis, drug therapy, diagnostic, screening and monitoring, women's health, and immunology. The largest

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3 individual funder was the Medical Research Council. In combination, the five lowest funded site
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5 specific cancers relative to disease burden account for 47.9%, 44.3% and 20.4% of worldwide cancer
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7 mortality, DALYs and YLDs.
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10 **Conclusions**

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12 The cancer sites which we identify as receiving higher levels of funding relative to disease burden are
13
14 broadly consistent with those reported in previous studies. Funding agencies and industry need to
15
16 openly document their research investment to enable the development of transparent and objective
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18 methods to allocate funding.
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21 **Strengths and limitations of this study:**

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- 24 • We systematically analyse UK investment in cancer research and describe trends by cancer
25 site and type of science along the research pipeline.
 - 26 • We consider cancer research investments alongside the global burden of disease to provide
27 pragmatic commentary about areas of UK research strength and relative neglect to inform
28 funder strategy and contribute towards policy discussions.
 - 29 • Our study is dependent on the accuracy of original investment data from the funding bodies
 - 30 • We could not openly access data of private sector research funding, nor were we able to
31 obtain disaggregated award data from CRUK, which impedes discussion around the equity of
32 investment decisions.
 - 33 • Disease burden measures are typically an estimate and are subject to the potential
34 introduction of bias; other variable influence funding decisions beyond the burden of
35 disease.
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Introduction

Cancers account for a high burden of morbidity and mortality worldwide. The Global Burden of Disease (GBD) Study estimates that cancer of all types resulted in 8,235,700 deaths in 2013[1]. Being predominantly a disease of older age, prevalence of cancers has historically fallen among high-income countries. However as low-income countries experience economic maturation, we are seeing an expanded distribution of this disease burden. Further deaths from cancer are projected due to global population growth and ageing[2,3]. Between 1990 and 2013, the proportion of all deaths that was attributable to cancer rose from 11.9% to 15.0%, largely among low- and middle-income countries and site-specific cancers accounted for 9 of the 50 leading causes of death, worldwide[1].

The socioeconomic impact of cancer, both in terms of direct costs involved in medical management as well as indirect costs resulting from productivity loss, on patients and caregivers are substantial. Direct health-related costs of cancer have been estimated to incur €51.0 billion within in the European Union[4] and \$124.5 billion in the United States[5]. Indirect costs are estimated to account for additional losses of €75.2 billion and \$115.8 billion, respectively. Economic evaluation of the impact of cancer outside of these two geographical regions has been lacking.

Investment in research and development (R&D) for cancers produces global public benefits that have a positive effect both locally and worldwide, irrespective of the site of the work or the location of the institution receiving an award, bringing substantial health, social, and economic benefit.

There are several national and international funding bodies that make cancer research investments along the R&D pipeline, from population health research, pre-clinical studies through to clinical trials and applied research. The UK remains one of the world's leading investors and producers of global biomedical and health research. Previous analyses by the Research Investments in Global Health study (ResIn, www.researchinvestments.org) has systematically analysed public and philanthropic

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3 awards totalling £3.7 billion to UK institutions for infectious disease from 1997 to 2013, and
4
5 evaluated funding against global disease burden[6,7] and publications and citations as a marker of
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7 research output[8]. Tracking investments in R&D provides information and evidence to inform
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9 funding decisions and priority setting. Here, we present a systematic analysis of cancer-related
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11 research awarded by public and philanthropic funders to UK institutions from 2000 to 2013,
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13 categorise the data against a range of cancer-specific and cross-cutting disease areas, and assess the
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15 award data against global measures of mortality, disability-adjusted life years (DALYs), and years
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17 lived with disability (YLD) across three time points and in the wider literature.
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20 21 **Methods**

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23 Our methods build on those developed for the infectious disease research investment analysis,
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25 which are described in detail elsewhere[6,7] and adapted in subsequent peer-reviewed publications
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27 (www.researchinvestments.org/publications).
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31 We systematically examined funding awards from a number of public and philanthropic funding
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33 bodies (including the Medical Research Council, Department of Health, Biotechnology and Biological
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35 Sciences Research Council, Engineering and Physical Science Research Council, Wellcome Trust,
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37 European Commission, as well as 9 members of the Association of Medical Research Charities)
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39 between 2000 and 2013. Information was obtained by downloading openly-accessible information
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41 on the funder website, contacting the funder to request the information, or searching existing
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43 funding databases. For each award, the title and abstract, where available, were individually
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45 screened for relevance to cancer research. We excluded awards that were i) not obviously or
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47 immediately relevant to oncology; ii) led by a non-UK institution; iii) not considered to be for R&D
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49 activity. Studies that were completed without funding were also excluded. Private sector data were
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51 not available to evaluate at the same level of detail as public and philanthropic research award data,
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53 and were therefore excluded from this analysis.
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3 Cancer Research UK (CRUK) would not provide their funding data at individual award level and so
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5 could not be included in the main analysis. There is some description of individual CRUK awards
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7 without grant amounts available at <https://europepmc.org/>. We report total number of studies in
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9 this analysis.
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12 Where awards were described in currencies other than UK pounds, these were converted to UK
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14 pounds using the mean exchange rate in the year of the award. All included awards were adjusted
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16 for inflation and reported in 2013 UK pounds.
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19 Each study in the dataset was reviewed by one author (either CDZ, GJG, MAE-H, MGH) and assigned
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21 to as many of 14 cross-cutting categories as appropriate. The 14 association categories were
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23 paediatric, geriatric, infection-associated, women's health, men's health, occupational health,
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25 pathogenesis, diagnostic/screening/monitoring, drug therapy, radiotherapy, surgery, immunology,
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27 psychosocial and global health. Awards were defined as global health if they were considered to
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29 pursue a clear non-UK focus (e.g. 'thyroid cancer in Kenya'). The other category was only used when
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31 none of the aforementioned categories were deemed to be appropriate. Studies were also allocated
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33 to one of five categories along the R&D pipeline: pre-clinical; phase I, II, or III clinical trials; product
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35 development (including phase IV activity); public health; and cross-disciplinary research. The cross-
36
37 disciplinary category was defined as an award containing significant components across two distinct
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39 areas along the R&D pipeline (such as pre-clinical research leading directly into a phase I trial).
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41 Provisional datasets were circulated to all authors for review and comment with checks by second
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43 authors on sections of the data and any disagreements settled by consensus. Final datasets were
44
45 then again circulated for further review by all authors. Microsoft Excel 2010 and 2013 and Stata
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47 (V13) software were used for data analysis.
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52 Global data on mortality, disability-adjusted life years (DALYs) and years lived with disability (YLDs)
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54 were available at time points 2005, 2010 and 2013. All burden data were sourced from the findings
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56 of the Global Burden of Disease (GBD) study, for 2013[1,9,10] and for 2010[11,12]. Burden data from
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2005 were obtained directly from colleagues at the Institute for Health Metrics and Evaluation, USA.

As defined by the GBD study, YLDs for a disease or injury are the sum of the YLDs for each sequela associated with the disease or injury[10]. DALYS are the sum of YLLs and YLDs for each age–sex–country group[9].

In order to allow direct comparison of relative investment with global health metrics across disease areas and between different time periods, metrics were adapted from the infectious disease analyses to estimate the ‘investment per mortality/DALY/YLD observed [7]’. The metrics were created using the following equation –

$$\left(\frac{\text{Total research investment up to the year before the time point} / \text{number of deaths, DALYs or YLD at time point}}{\text{number of years of investment included}} \right)$$

For example, for assessment of breast cancer mortality at the 2013 time point, we took the sum of breast cancer research investment 2000-2012 (£124,305,716) and divided that by number of deaths reported in 2013 (471000), and divided the result by the number of years of investment included (13) to get an ‘investment per mortality observed’ metric of £20.30.

These metrics were applied for research relating to 16 site-specific cancers, where there was comparable data in both the ResIn and GBD studies. We defined lung cancer by aggregating ‘tracheal, bronchus and lung cancer’ burden data from the GBD study. Similarly, we defined skin cancer by aggregating ‘malignant skin melanoma’ and ‘non-malignant skin cancer’, and we defined upper gastrointestinal (GI) cancer by aggregating ‘oesophageal’ and ‘stomach cancer’. The use of total investment and the division by number of years included aimed to reduce the impact of the volatility of annual research funding and the relatively short periods between time points. Ranking scores of the investment metrics were developed for the 16 sites of cancer against 2013 burdens. Cancers were ranked in order of relative investment against burden from high to low and assigned a score (from 1 to 16). The mean ranking scores across mortality, DALYs and YLDs were used to illustrate an overall relative level of investment against 2013 global disease burden.

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6 There was no patient involvement in this study.
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Results

We identified 4,299 funded studies that met our inclusion criteria (Table 1). The funding for these studies represented a total research investment of almost £2.4 billion. The mean award amount for each study was £555,513 (standard deviation (SD) £1,429,510) and median was £231,559 (inter-quartile range £114,619 – 487,063). 2,416 awards (56.2% of total) were designated towards a named site-specific cancer (Table 1), equating to £1.0 billion (40.3% of total). The top five cancer sites in terms of award number were haematological, breast, colorectal, prostate, and skin; the bottom five were testicular, bone, bladder, thyroid, and cholangiocarcinoma (Table 1). The top five cancer sites in terms of total funding were haematological, breast, prostate, colorectal and ovarian; the bottom five were testicular, mesothelioma, thyroid, bladder and chlangiocarinoma. Mean funding per award varied greatly between sites with prostate cancer receiving the most (£1.47 million) and bladder cancer the least (£117,385).

The top five areas of primary research focus, by number of awards, were drug therapy, diagnostic, screening and monitoring, women's health, immunology, and pathogenesis; the bottom five areas were men's health, surgery, occupational health, global health and geriatrics (Table 2). In terms of net funding, the top five areas of research were pathogenesis, drug therapy, diagnostic, screening and monitoring, women's health, and immunology; the bottom five were surgery, psychosocial, global health, occupational health, and geriatrics.

The majority of awards were focused on pre-clinical science, accounting for 66.2% of award numbers and 62.2% of all funding (Table 3). In terms of award number, this was followed by public health, cross-disciplinary, phase I-III, and product development. This order was reflected in terms of net investment, although cross-disciplinary studies ranked ahead of public health studies. Phase I-III clinical trials received the highest mean funding per award, at £736,172 (SD £3,361,312), whilst public health research received the least, at £496,744 (SD £1,000,757).

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3 The largest individual funder of cancer research of the studies identified was the Medical Research
4 Council, accounting for 35.1% of all funding (Table 4). The charitable sector was responsible for
5 39.5% of all awards (excluding CRUK) but 17.4% of funding. The European Commission was
6 responsible for the largest mean grant per award (£1.58 million).
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11 We generated a compound ranking score for the 16 sites of cancer against 2013 global disease
12 burdens, across mortality, DALYs, and YLDs (table 5). The amount of investment per unit disease
13 burden (£ per death/DALY/YLD) were used to compile this compound ranking score. The data for all
14 site-specific cancers measured here are presented in the supplementary information (Supplemental
15 Tables 1-3, Supplemental Figures 1-3). We identified the five sites that received the most funding
16 relative to disease burden as prostate, ovarian, breast, mesothelioma and testicular cancer. The
17 least well-funded sites relative to disease burden were cancers of the liver, thyroid, lung, upper GI,
18 and bladder.
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30 We were able to obtain some disaggregated data for 3,284 CRUK research grants during the period
31 of interest but this excluded individual award data. Compared to the aggregation of all other
32 funders, CRUK placed more of a focus on funding towards cancers of the prostate, ovary and liver –
33 by study number these sites accounted for 6.9%, 3.4% and 2.7% of CRUK funded studies compared
34 to 2.1%, 1.1% and 0.9% of all studies in our quantitative database, respectively. CRUK preferentially
35 funded research investigating pathogenesis, which accounted for 51.0% of all grants awarded. In
36 comparison, only 5.3% of all awards in our quantitative database were identified as primarily
37 focused on pathogenesis.
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48 Discussion

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50 We identified 4,299 funded studies, with a total research investment of £2.4 billion. We performed
51 qualitative analysis on a further 3,284 CRUK funded awards. The vast majority of all awards awarded
52 were investigating at least one of pathogenesis, diagnosis, monitoring and screening and drug
53 therapy. In the absence of CRUK data, the Medical Research Council and the Department of Health
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3 were the two leading funding sources. Preclinical research accounted for £1.5 billion (62.2%) of total
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5 R&D investment. Four of the five highest funded cancer sites relative to global disease burden were
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7 gender-specific – namely prostate, ovarian, breast, and testicular cancers. Cancer research with a
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9 clear focus on women’s health accounted for 640 studies (14.9%) and £199.5 million (8.4%) of
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11 investment. In comparison, 111 studies (2.6%) and £143.3 million (6.0%) of investment had a clear
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13 link with men’s health. This may reflect the successes of various institutions and charities that have
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15 sought to increase awareness of these sex-specific cancers. Breast cancer, the most commonly
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17 diagnosed cancer in the UK and the leading cause of cancer death in women, and prostate cancer,
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19 the second most frequently diagnosed cancer and the sixth leading cause of cancer death among
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21 men, were found to be relatively well funded[1,13].
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25 We highlight several cancer sites where there might be underinvestment, namely that of liver,
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27 thyroid, lung, upper GI tract, and bladder. In our analysis cancer of the upper GI tract combines
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29 oesophageal and stomach cancer. These site-specific cancers identified to be relatively underfunded
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31 account for a substantial proportion of global cancer burden. Globally, these sites account for 47.9%,
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33 44.3% and 20.4% of the global mortality[1], DALYs[9] and YLDs[10] of all cancers, respectively. The
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35 disparity between YLDs and DALYs demonstrates the poor prognosis and high mortality of these
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37 particular sites when compared against all neoplastic disease. Lung, liver, stomach and oesophagus
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39 are the first, second, third and fifth, leading sites of neoplastic mortality worldwide[1].
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43 Two previous studies have compared UK cancer funding with years of life lost (YLLs). Burnett et al
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45 [14] reported the relative over-funding of breast cancers and leukaemia. Carter et al [15,16] likewise
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47 reported higher levels of funding than their burden suggests of testicular, leukaemia, Hodgkin’s
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49 lymphoma, breast, cervical, ovarian, prostate cancer with relative underfunding of gallbladder, lung,
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51 nasopharyngeal, intestine, stomach, pancreatic, thyroid, oesophageal, liver, kidney, bladder, and
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53 brain/central nervous system. Furthermore, they show that these broad discrepancies between
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55 cancer burden and research investment are also reflected in US data. Over the past decade in the
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3 UK, there has generally been a transition of increased funding towards previously underfunded
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5 cancers with one notable exception being breast cancer. Although our site-specific classifications
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7 differed slightly, our findings are broadly consistent with these previous studies with the
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9 identification of haematological and sex-specific cancers being relatively well-funded. We are unable
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11 to account exactly for the slight differences in our findings (such as cervical and colorectal cancers);
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13 however, they are likely due to our metrics which seek to capture mortality (global mortality and
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15 DALYs) and life burden (DALYs and YLDs) rather than just mortality, and also different included
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17 components in the respective datasets.
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21 With regard to interventions research, there is heavy investment in drug-based modalities. £620.9
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23 million (26.0%) was invested in novel drug therapies and £194.1 million (8.1%) was invested in the
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25 emergent role of immunomodulation. In comparison, funding towards radiotherapy and surgical
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27 interventions accounted for £88.2 million (3.7%) and £37.9 million (1.6%), respectively. In high-
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29 income settings, around half of new cancer diagnoses will undergo a course of radiotherapy
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31 treatment during their clinical management; roughly a quarter will receive two or more
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33 courses[17,18]. Globally, over 80% of cancer cases will warrant surgical intervention, where it has
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35 preventative, diagnostic, curative, supportive, palliative, and reconstructive roles[19].
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39 Analysis by R&D pipeline showed that research investment in the UK places a heavy emphasis on
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41 pre-clinical research, but relatively little investment towards phase I-III clinical trials or product
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43 development, and this is line with previous research in infectious disease investment[6]. This may
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45 reflect the strengths of UK institutions in preclinical science, but also could suggest a need to
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47 strengthen research capacity further down the R&D chain. It would be useful to determine whether
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49 investment reflects the priorities of funding agencies and whether this is comparable to research
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51 investment in other countries. We noted a lack of readily available data from the pharmaceutical
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53 industry and this is likely to leave a data gap in particular for sum totals of investment in clinical trials
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55 of pharmaceutical products.
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3 Our findings contribute to the development of transparent and objective methods to couple the
4 allocation of limited research funds with disease burden. Previous studies have suggested that
5 financial investment might appropriately be coupled with DALYs as a measure of burden[20–23]. In
6 recent years, whilst net UK governmental and charitable cancer investment has increased [24], there
7 has been a proportional reduction compared to that of total funding towards cancer, coronary heart
8 disease, dementia and stroke – in keeping with the health and social care costs attributable to each
9 disease [25]. Furthermore, previous UK research suggests that publicly funded research offers
10 substantial rates of return in terms of both health and monetary benefit both in the case of cancer
11 specifically [24] and biomedical sciences as a whole [26]. We have further sought to incorporate
12 mortality rates and YLDs into the consideration of cancer research investment. These analyses, when
13 considered together, provide convincing pragmatic evidence of UK research strength and types of
14 cancer where research investment has been particularly lacking.

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30 We have chosen to compare cancer research funding to global rather than domestic UK disease
31 burden. Due to increasing globalization, the emergence of non-communicable disease burden in
32 resource poor settings, the internationalization of healthcare, the flow of people across national
33 borders and the role of the UK as an international centre of biomedical research, we believe this
34 approach to be justified.

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However, defining an appropriate amount of research investment for each site specific cancer is
challenging since cancers of similar disease burdens may warrant different levels of investment to
develop cost-effective interventions. Decisions may be influenced by any of a number of factors, for
example due to exceptional need, as may be the case in mesothelioma, or due to public awareness
and third-party lobbying, as may be the case with regards to the gender-specific cancers.

A variety of factors contribute towards the difficulty in tracking net cancer research investment
within the UK. Fragmentation of data from a large number of diverse public and private sources of
funding, poorly designed donor accounting structures and the paucity of disaggregated information

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3 from the private sector limit the quality of the evidence base and thus the ability to inform policy in
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5 real-time. In our study, we were unable to obtain disaggregated investment data from CRUK. Despite
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7 requests across 2014 and 2015, CRUK refused to make available disaggregated investment data. This
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9 is in spite CRUK policy and representatives seemingly welcoming and encouraging the expansion of
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11 data-sharing and promoting the availability, accessibility and discoverability of such data [27,28]. In
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13 our experience across the ResIn infection and cancer analyses, this reluctance to be transparent is
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15 unique amongst more than 200 high-profile research funders in the UK and USA [29]. The lack of
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17 data liberation across non-communicable diseases impedes open scrutiny and hinders timely and
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19 effective response to this growing global disease burden [29,30]. Transparency in the tracking and
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21 monitoring of cancer research financing is essential to enable accountability and equity in resource
22
23 allocation and to facilitate further future research in this area. We would encourage CRUK to be
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25 more open in providing data on funding.
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29 In this study we systematically analyse UK investment in cancer research and identify areas of
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31 relative neglect. Although the competitive application process used by most funders to allocate
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33 research grants ensure a portfolio of high quality, the absence of explicit resource allocation criteria
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35 could contribute towards inequalities in R&D by disease burden. Funding agencies will have
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37 particular areas of focus, and UK funders may have considered the focus of international agencies in
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39 their own research strategies. As a result, international data is essential to complete the mapping of
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41 cancer research investment. Nevertheless, our findings will inform funders and contribute towards
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43 policy discussions that reduce inequities in the allocation of limited financial resources.
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47 By demonstrating the relationship between disease burden and research funding, we enable the
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49 identification of potential investment gaps. However, it is not possible to fully equate gaps in funding
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51 with areas of neglect without consideration of other influences such as the feasibility of research,
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53 costs of technologies, infrastructure and skill requirements, political and social considerations, and
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55 the accuracy of disease burden estimates.
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3 There are several potential limitations to our study. We are dependent on the accuracy of original
4 investment data as sourced from the funding bodies. Although checks were made on any obvious
5 discrepancies or errors, interpretation of these original data may contain errors. We made no
6 attempt to investigate the contribution of any indirect or estate costs. Currency conversions were
7 averaged across each financial year and any intra-year fluctuations may not have been captured.
8 Unless clearly documented, we were unable to assess how funding was distributed from lead
9 institutions to collaborative partners. We considered individual awards, rather than number of
10 studies.

11
12 Furthermore, assignment of disease categories and allocation of studies according to these
13 categories is subjective, and there might be disagreements regarding certain inclusion criteria. As
14 YLLs were not included in our analysis, we may underrepresent the disease burden of cancers that
15 occur disproportionately in the young and which are associated with poor survival, notably cancers
16 of the ovary, cervix and CNS [14]. However, we would expect any additional information offered by
17 YLL analysis to be predominantly captured by use of DALYs.

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19 We could not openly access data of private sector research funding, nor were we able to obtain
20 disaggregated award data from CRUK. Whilst our analysis did demonstrate that CRUK funding (with
21 some exceptions) broadly reflected the findings of our quantitative database, it is likely that
22 substantial awards towards particular areas of research could skew results; for example, CRUK are
23 particularly keen to fund clinical trials, an area typically not covered to such an extent by other
24 public and philanthropic funders. In 2014/15 CRUK invested £394 million into research or research-
25 related activity, and we hypothesise that much of that would have met our inclusion criteria for this
26 analysis [31]. Disease burden measures are typically an estimate and are subject to the potential
27 introduction of bias from missing or unobtainable data as well as from differences in classification
28 and diagnosis.

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3 Our report presents the latest investment data on cancer research awarded to UK institution
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5 between 2000 and 2013. Cancers of the liver, thyroid, lung, upper GI tract, and bladder as well as
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7 research towards radiotherapy and surgical techniques in particular may warrant increased rates of
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9 investment. We will make the entire database and associated figures available online
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11 (www.researchinvestment.org) to assist policy makers, funding organisations, and researchers in the
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13 identification of investment gaps. We further encourage funding organisations to make their
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15 investment portfolios openly accessible to facilitate future research.
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18 We hope that open funding data in this area can contribute to redressing the misalignments in
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20 investments for cancer research. Cancer research can improve the clinical course of disease and
21
22 offer tangible improvements in health outcomes[24]. Access to open data across all funders,
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24 including CRUK is essential and transparency can assist policy makers and the scientific community in
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26 ensuring that limited resources are allocated appropriately and thus most effectively alleviate the
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28 extensive mortality and morbidity associated with cancer.
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Contributions

MM and MGH are the guarantors of this study. MM, MGH, JRF and RA conceived and designed the study. MGH, CDZ, BJG and MAE-H obtained the data. MM and MGH conducted data formatting and statistical analysis. All authors helped interpret the findings. MM, MGH and CDZ wrote the first draft of the manuscript with input from RR, JRF and RA; all authors provided input to subsequent drafts. All authors had full access to all of the data in the study and take responsibility for its integrity and the accuracy of data analysis.

Transparency declaration

MM affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Competing interests

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Ethical approval

Not required

Data sharing

All data used is publicly available. Entire database and associated figures are permanently available with open access online (www.researchinvestment.org) to assist policy makers, funding organisations, and researchers.

For peer review only

References

- 1 Naghavi M, Wang H, Lozano R, *et al*. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;**385**:117–71.
- 2 Jemal A, Bray F, Center MM, *et al*. Global Cancer Statistics: 2011. *CA Cancer J Clin* 2011;**61**:69–90.<http://www.ncbi.nlm.nih.gov/pubmed/21296855>
- 3 Torre LA, Bray F, Siegel RL, *et al*. Global Cancer Statistics, 2012. *CA a cancer J Clin* 2015;**65**:87–108.<http://onlinelibrary.wiley.com/doi/10.3322/caac.21262/abstract>
- 4 Luengo-Fernandez R, Leal J, Gray A, *et al*. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol* 2013;**14**:1165–74.<http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24131614>
- 5 Yabroff KR, Lund J, Kepka D, *et al*. Economic Burden of Cancer in the United States: Estimates, Projections, and Future Research. *Cancer Epidemiol Biomarkers Prev* 2011;**20**:2006–14.<Go to ISI>://WOS:000295717900003
- 6 Head MG, Fitchett JR, Cooke MK, *et al*. UK investments in global infectious disease research 1997-2010: A case study. *Lancet Infect Dis* 2013;**13**:55–64.
- 7 Head MG, Fitchett JR, Nageshwaran V, *et al*. Research Investments in Global Health: A Systematic Analysis of UK Infectious Disease Research Funding and Global Health Metrics, 1997–2013. *EBioMedicine* 2016;**3**:180–90.<http://dx.doi.org/10.1016/j.ebiom.2015.12.016>
- 8 Head MG, Fitchett JR, Derrick G, *et al*. Comparing research investment to United Kingdom institutions and published outputs for tuberculosis, HIV and malaria: a systematic analysis across 1997-2013. *Health Res Policy Syst* 2015;**13**:63.<http://www.health-policy-systems.com/content/13/1/63>
- 9 Murray CJL, Barber RM, Foreman KJ, *et al*. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015;**386**:2145–91.
- 10 Vos T, Barber RM, Bell B, *et al*. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;**386**:743–800.
- 11 Murray CJ, Vos T, Lozano R, *et al*. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2197–223.<http://www.ncbi.nlm.nih.gov/pubmed/23245608>
- 12 Lozano R, Naghavi M, Foreman K, *et al*. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2095–128.

- 1
2
3 13 Jemal A, Bray F, Center MM, Ferlay J, Ward E FD. Global cancer statistics. *Cancer J Clin* 2011;**61**:69–90.
4
5
6 14 Burnet NG, Jefferies SJ, Benson RJ, *et al*. Years of life lost (YLL) from cancer is an important
7 measure of population burden--and should be considered when allocating research funds. *Br*
8 *J Cancer* 2005;**92**:241–5.
9
10
11 15 Carter AJR, Delarosa B, Hur H. An analysis of discrepancies between United Kingdom cancer
12 research funding and societal burden and a comparison to previous and United States values.
13 *Heal Res Policy Syst* 2015;**13**:62.<http://www.health-policy-systems.com/content/13/1/62>
14
15 16 Carter AJR, Nguyen CN. A comparison of cancer burden and research spending reveals
16 discrepancies in the distribution of research funding. *BMC Public Health*
17 2012;**12**:526.<http://dx.doi.org/10.1186/1471-2458-12-526>
18
19 17 Barton MB, Frommer M, Shafiq J. Role of radiotherapy in cancer control in low-income and
20 middle-income countries. *Lancet Oncol* 2006;**7**:584–95.[http://ac.els-](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aabb0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
21 [cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aabb0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
22 [11e3-a45c-0000aabb0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251](http://ac.els-cdn.com/S1470204506707598/1-s2.0-S1470204506707598-main.pdf?_tid=41dac6b8-7fa0-11e3-a45c-0000aabb0f27&acdnat=1389981382_3394f8c1d926c07e5acaad4254556251)
23
24
25 18 Barton MB, Jacob S, Shafiq J, *et al*. Estimating the demand for radiotherapy from the
26 evidence: a review of changes from 2003 to 2012. *Radiother Oncol* 2014;**112**:140–4.
27
28 19 Sullivan R, Alatise OI, Anderson BO, *et al*. Global cancer surgery: Delivering safe, affordable,
29 and timely cancer surgery. *Lancet Oncol*. 2015;**16**:1193–224.
30
31 20 Gross CP, Anderson GF, Powe NR. The relation between funding by the National Institutes of
32 Health and the burden of disease. *N Engl J Med* 1999;**340**:1881–7.
33
34 21 Lopez FC, Martin EA, Maleras RG, *et al*. Relationship between Research Funding in the
35 Spanish National Health System and the Burden of Disease. *Rev Esp Salud Publica*
36 2009;**83**:137–51.<Go to ISI>://WOS:000266635200011
37
38 22 Mitchell RJ, McClure RJ, Olivier J, *et al*. Rational allocation of Australia’s research dollars: does
39 the distribution of NHMRC funding by National Health Priority Area reflect actual disease
40 burden? *Med J Aust* 2009;**191**:648.
41
42 23 Lamarre-Cliche M, Castilloux AM, LeLorier J. Association between the burden of disease and
43 research funding by the Medical Research Council of Canada and the National Institutes of
44 Health. A cross-sectional study. *Clin Invest Med* 2001;**24**:83–
45 9.<http://www.ncbi.nlm.nih.gov/pubmed/11368150>
46
47 24 Glover M, Buxton M, Guthrie S, *et al*. Estimating the returns to UK publicly funded cancer-
48 related research in terms of the net value of improved health outcomes. *BMC Med*
49 2014;**12**:1.
50
51 25 Luengo-Fernandez R, Leal J, Gray A. UK research spend in 2008 and 2012: comparing stroke,
52 cancer, coronary heart disease and dementia. *BMJ Open* 2015;**5**:e006648.<http://dx.doi.org/>
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59
60

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3 26 Sussex J, Feng Y, Mestre-Ferrandiz J, *et al.* Quantifying the economic impact of government
4 and charity funding of medical research on private research and development funding in the
5 United Kingdom. *BMC Med* 2016;**14**:32.<http://dx.doi.org/10.1186/s12916-016-0564-z>
6
7 27 Teperek M. In conversation with Wellcome Trust and Cancer Research UK. Published Online
8 First: 2016.<https://unlockingresearch.blog.lib.cam.ac.uk/?p=528>
9
10 28 Teperek M. Charities' perspective on research data management and sharing. Published
11 Online First: 2016.<https://unlockingresearch.blog.lib.cam.ac.uk/?p=525>
12
13 29 Fitchett JRA, Sharara N, Head MG, *et al.* Transparency and availability of data for cancer
14 research. *Lancet* 2016;**388**:866–7.[http://dx.doi.org/10.1016/S0140-6736\(16\)31427-1](http://dx.doi.org/10.1016/S0140-6736(16)31427-1)
15
16 30 Davies J, Yudkin JS, Atun R. Liberating data: the crucial weapon in the fight against NCDs.
17 *Lancet Diabetes Endocrinol* 2016;**4**:197–8.[http://dx.doi.org/10.1016/S2213-8587\(16\)00037-1](http://dx.doi.org/10.1016/S2213-8587(16)00037-1)
18
19 31 CRUK. Annual report and accounts 2014/15. 2015.
20 http://www.cancerresearchuk.org/sites/default/files/annual_report_and_accounts_2014-
21 15.pdf
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Table Legends

Table 1: Cancer research investment awards and funding by site. All investment reported in 2013 UK pounds.

Site of cancer	All funders where investment data was available						Cancer Research UK	
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Breast	571	13.3%	£137,960,107	5.8%	241611 (414584)	135752 (25000-216673)	273	8.3%
Haematological	1158	26.9%	£381,008,394	16.0%	329022 (476943)	186813 (120437-272324)	225	6.9%
Colorectal	147	3.4%	£77,279,857	3.2%	525713 (674881)	251800 (102078-819866)	205	6.2%
Prostate	92	2.1%	£135,290,779	5.7%	1470552 (6156372)	333757 (155227-721037)	123	3.7%
Ovarian	48	1.1%	£44,709,938	1.9%	931457 (3380145)	226764 (131990-627401)	112	3.4%
Lung	82	1.9%	£24,263,280	1.0%	295893 (556278)	146123 (66701-242934)	89	2.7%
Skin	87	2.0%	£22,179,011	0.9%	254931 (453726)	85406 (69629-248603)	84	2.6%
Brain	22	0.5%	£9,994,255	0.4%	454284 (498933)	401046 (196928-528008)	83	2.5%
Upper GI and	18	0.4%	£19,094,230	0.8%	1060791 (1448010)	788850 (80964-1296962)	80	2.4%
Head and neck	20	0.5%	£18,250,632	0.8%	912531 (1003091)	389751 (167358-1602465)	68	2.1%
Renal	19	0.4%	£13,885,496	0.6%	730815 (678732)	479197 (244075-1252574)	48	1.5%
Bladder	10	0.2%	£1,173,856	0.0%	117385 (106902)	94520 (29264- 173855)	48	1.5%
Cervical	26	0.6%	£14,328,402	0.6%	551092 (877250)	210179 (88934-368402)	43	1.3%
Pancreatic	16	0.4%	£9,453,577	0.4%	590848 (519850)	276237 (191804-1033948)	40	1.2%
Bone	13	0.3%	£17,242,183	0.7%	1326322 (1604685)	685853 (243559-1999907)	29	0.9%
Liver	37	0.9%	£25,037,541	1.0%	676690 (847151)	319082 (177974-776480)	20	0.6%
Mesothelioma	30	0.7%	£4,476,088	0.2%	149202 (101201)	137103 (95895-205500)	11	0.3%
Cholangiocarcinoma	2	0.0%	£582,405	0.0%	n/a	n/a	11	0.3%
Testicular	14	0.3%	£5,949,990	0.2%	424999 (507277)	242175 (102938-411010)	11	0.3%
Thyroid	4	0.1%	£1,375,881	0.1%	n/a	n/a	7	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

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Table 2: Cancer research investment awards and funding by cross-cutting theme. All investment reported in 2013 UK pounds.

Cross-cutting theme	All funders where investment data was available						Cancer Research UK	
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Pathogenesis (mechanism)	227	5.3%	£1,374,387,838	57.6%	543881 (955710)	248573 (135752-506232)	1674	51.0%
Drug Therapy	1104	25.7%	£620,961,060	26.0%	562464 (1910050)	202342 (105622-436559)	935	28.5%
Diagnostic, Screening and Monitoring	681	15.8%	£359,618,823	15.1%	528074 (1155156)	205728 (102672-513836)	404	12.3%
Women's Health	640	14.9%	£199,534,693	8.4%	311773 (1041520)	153845 (56515-227202)	287	8.7%
Immunology (inc. biologics)	451	10.5%	£194,086,617	8.1%	430347 (760955)	240052 (125669-466250)	212	6.5%
Radiotherapy	112	2.6%	£88,262,353	3.7%	788056 (2413445)	243333 (106175-439419)	209	6.4%
Psychosocial	117	2.7%	£23,445,835	1.0%	200391 (352410)	87463 (27317-239059)	122	3.7%
Men's Health	111	2.6%	£143,392,908	6.0%	1291828 (5617919)	285203 (126037-700353)	120	3.7%
Paediatrics	175	4.1%	£62,641,938	2.6%	357953 (547484)	183099 (89522-322261)	118	3.6%
Surgery	72	1.7%	£37,900,334	1.6%	526393 (684908)	235413 (97890-761651)	95	2.9%
Infection-associated	129	3.0%	£56,819,379	2.4%	440460 (798013)	231836 (134693-439378)	48	1.5%
Global Health	12	0.3%	£6,434,960	0.3%	536246 (1089118)	129738 (77519-459274)	12	0.4%
Geriatrics	7	0.2%	£1,616,394	0.1%	230913 (254925)	121623 (76421-262167)	8	0.2%
Occupational Health	18	0.4%	£2,576,841	0.1%	143157 (116928)	137103 (33857-199998)	8	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

Table 3: Cancer research investment awards and funding by type of science. All investment reported in 2013 UK pounds.

Type of science	All funders where investment data was available						Cancer Research UK	
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)	Number of awards	Percentage of all oncology research awards
Pre-clinical	2845	66.2%	£1,485,997,379	62.2%	522318 (1006600)	240974 (132188-490872)	1809	55.1%
Phase I-III	303	7.0%	£223,060,276	9.3%	736172 (3361312)	178535 (70934-502399)	647	19.7%
Product development	172	4.0%	£104,214,364	4.4%	605897 (2213394)	193051 (75270-360813)	52	1.6%
Cross-disciplinary	441	10.3%	£315,145,351	13.2%	714615 (1586882)	238523 (126589-703764)	328	10.0%
Public health	512	11.9%	£254,333,282	10.6%	496744 (1000757)	209364 (82870-383623)	443	13.5%
Unable to specify	26	0.6%	£5,401,666	0.2%	n/a	n/a	5	0.2%
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)	3284	

Table 4: Cancer research investment awards and funding by funding agency (excluding CRUK). All investment reported in 2013 UK pounds.

Funder	All funders where investment data was available					
	Number of awards	Percentage of total	Sum investment (£)	Percentage of total	Mean award, £ (SD)	Median award, £ (IQR)
MRC	768	17.9%	£837,649,875	35.1%	1090690 (1770533)	504606 (305375-1153374)
Charity (excluding Wellcome and CRUK)	1,699	39.5%	£415,189,093	17.4%	244372 (391813)	151912 (81000-223244)
Department of Health	586	13.6%	£413,421,823	17.3%	705498 (2675223)	232173 (102391-471236)
BBSRC	511	11.9%	£223,651,002	9.4%	437673 (388793)	373356 (267848-501592)
EPSRC	356	8.3%	£201,861,623	8.5%	567027 (972696)	306906 (144056-604016)
Wellcome	193	4.5%	£140,425,805	5.9%	727594 (1679370)	226761 (164547-427455)
European Commission (inc ERC)	50	1.2%	£78,757,447	3.3%	1575149 (731858)	1409678 (1252574-1830017)
Other	136	3.2%	£77,195,650	3.2%	567615 (1901202)	129944 (69309-263613)
Total	4299		£2,388,152,318		555513 (1429510)	231559 (114619-487063)

Table 5: Compound ranking score for cancer research investment against 2013 global disease burdens, across mortality, YLDs, and DALYs, by cancer site.

Disease	Research investment (UK pound) by burden observed, 2013			
	Mean ranking across all burden metrics	Mortality	Years lived with disability	Disability-adjusted life years
Prostate	2.7	2	4	2
Ovarian	3.0	4	2	3
Mesothelioma	4.0	6	1	5
Breast	4.0	3	5	4
Testicular	4.7	1	3	10
Skin	5.0	5	9	1
Colorectal	6.7	7	7	6
Renal	8.3	8	10	7
Cervical	9.7	9	12	8
Pancreatic	10.0	12	6	12
Brain	11.0	11	11	11
Thyroid	11.3	10	15	9
Liver	11.3	13	8	13
Lung	13.7	14	13	14
Upper GI	14.7	15	14	15
Bladder	16.0	16	16	16

Supplementary Table 1: Investment per mortality observed for all site-specific cancers

	Number of deaths			Investment per mortality observed		
	2005	2010	2013	2005	2010	2013
Bladder	156385	170700	173900	£0.03	£0.26	£0.49
Brain	177191	195500	203900	£0.00	£2.02	£2.76
Breast	407108	438700	471000	£5.35	£18.20	£20.30
Cervical	221578	225400	235700	£2.93	£5.63	£4.50
Colorectal	644648	714600	771000	£3.54	£5.45	£6.77
Liver	715141	752100	818000	£0.04	£1.00	£1.45
Lung	1391577	1527100	1639600	£0.15	£0.57	£1.08
Mesothelioma	22128	n/a	33700	£0.81	?	£8.33
Ovarian	134354	160500	157800	£23.00	£20.98	£19.79
Pancreatic	276753	310200	352400	£0.56	£0.86	£1.67
Prostate	225081	256000	292700	£53.92	£45.19	£34.22
Renal	113048	162100	133800	£0.00	£2.27	£5.96
Skin	?	79700	96100	?	£14.20	£16.30
Testicular	7547	7700	8300	£7.27	£44.69	£55.14
Thyroid	29092	36000	33700	£0.00	£1.70	£3.14
Upper GI and oesophageal	1229320	1130100	1281200	£0.93	£1.18	£1.03

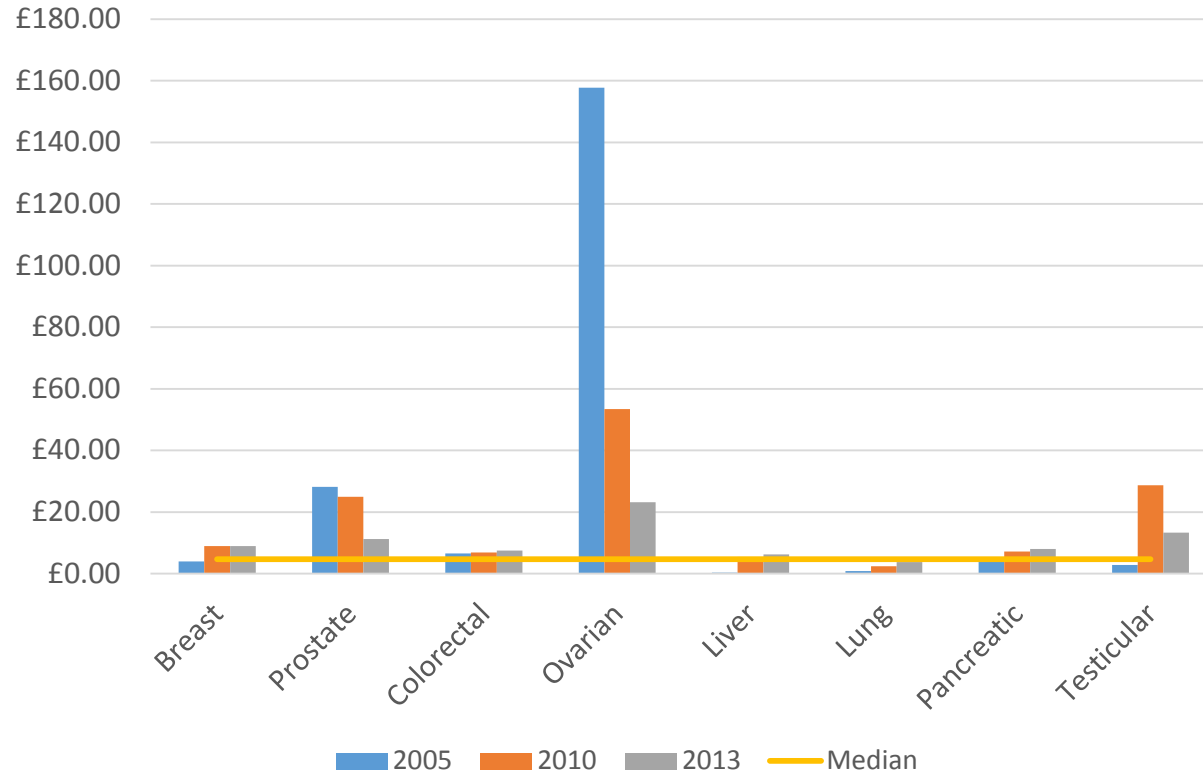
Supplementary Table 2: Investment per YLD observed for all site-specific cancers

	YLD			Investment per YLD observed		
	2005	2010	2013	2005	2010	2013
Bladder	153647	125000	179800	£0.05	£0.35	£0.47
Brain	105126	94000	121900	£0.00	£4.20	£4.61
Breast	885550	898000	1068200	£3.93	£8.89	£8.95
Cervical	242359	111000	243800	£4.28	£11.44	£4.35
Colorectal	561019	564000	701900	£6.50	£6.91	£7.44
Liver	160071	140000	190600	£0.29	£5.39	£6.24
Lung	388206	355000	467400	£0.86	£2.44	£3.78
Mesothelioma	7109	n/a	10800	£4.04	?	£25.98
Ovarian	31339	63000	134900	£157.75	£53.44	£23.15
Pancreatic	57317	37000	73600	£4.35	£7.18	£8.01
Prostate	690602	464000	893700	£28.12	£24.93	£11.21
Renal	112449	79000	139200	£0.00	£4.66	£5.72
Skin	?	300000	264100	?	£3.77	£5.93
Testicular	31339	12000	34300	£2.80	£28.67	£13.34
Thyroid	109078	48000	127600	£0.00	£1.27	£0.83
Upper GI and oesophageal	382757	304000	416100	£4.77	£4.39	£3.17

Supplementary Table 3: Investment per DALY observed for all site-specific cancers

	Global DALYs			Investment per DALY observed		
	2005	2010	2013	2005	2010	2013
Bladder	2987377	3015000	3139900	£0.00	£0.01	£0.03
Brain	6163358	6060000	6692200	£0.00	£0.07	£0.08
Breast	11762493	12018000	13258700	£0.19	£0.66	£0.72
Cervical	6775622	6440000	6914700	£0.10	£0.20	£0.15
Colorectal	13747947	14422000	15794100	£0.17	£0.27	£0.33
Liver	19175329	19111000	20888700	£0.00	£0.04	£0.06
Lung	30791630	32405000	34732900	£0.01	£0.03	£0.05
Mesothelioma	504037	n/a	763500	£0.04	?	£0.37
Ovarian	3541657	4118000	4056500	£0.87	£0.82	£0.77
Pancreatic	5704661	6161000	7029100	£0.03	£0.04	£0.08
Prostate	3812057	3787000	4768800	£3.18	£3.05	£2.10
Renal	2810156	3676000	3150300	£0.00	£0.10	£0.25
Skin	?	1967000	237200	?	£0.58	£6.61
Testicular	354875	313000	3787700	£0.15	£1.10	£0.12
Thyroid	764526	836000	851900	£0.00	£0.07	£0.12
Upper GI and oesophageal	27964269	25356000	27749600	£0.04	£0.05	£0.05

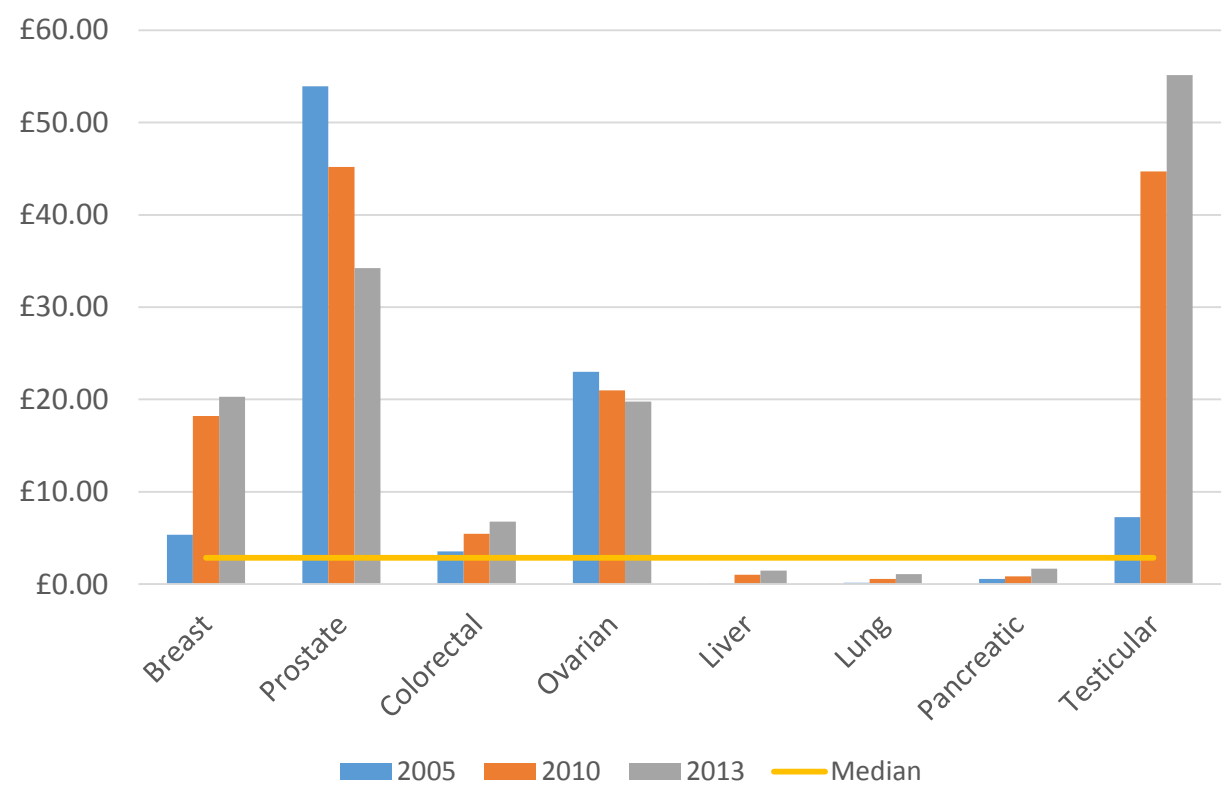
Supplementary Figure 1: Investment per YLD (£/YLD) for 8 indicator site-specific cancers



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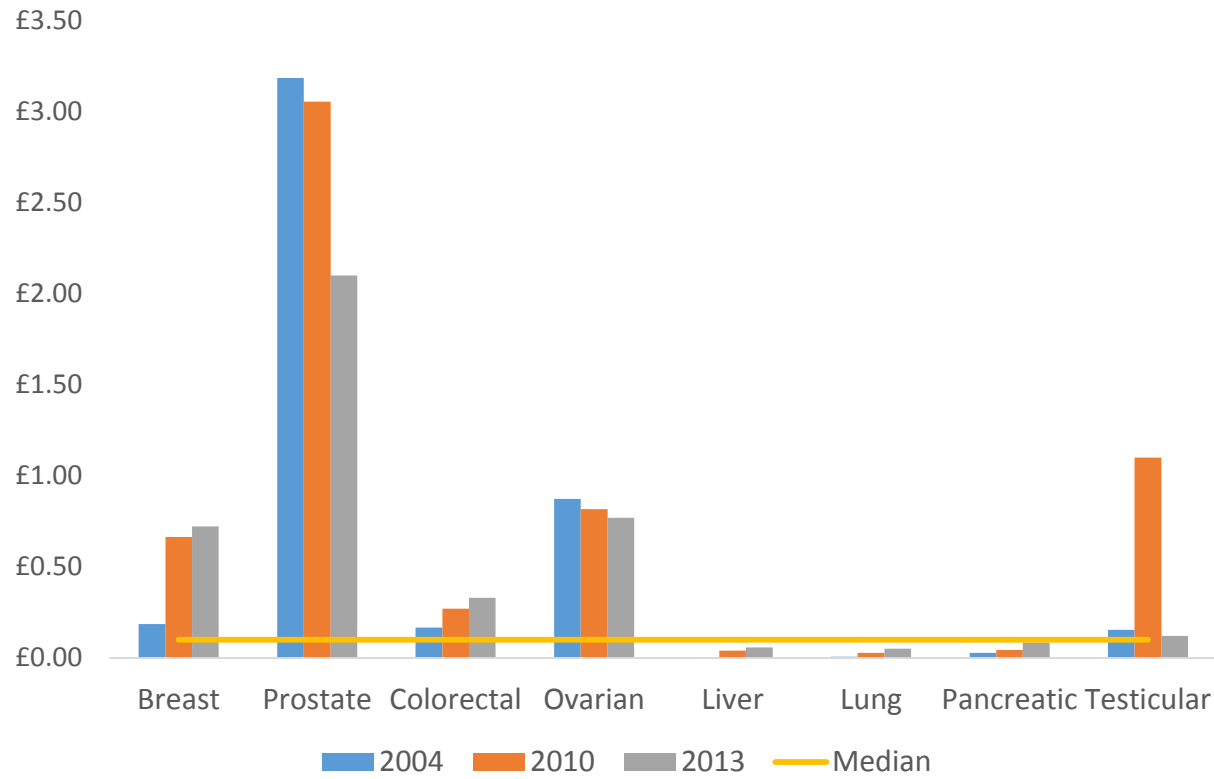
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Supplementary Figure 1: Investment per death (£/death) for 8 indicator site-specific cancers



only

Supplementary Figure 1: Investment per DALY (£/DALY) for 8 indicator site-specific cancers



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