

Analysis of productivity costs in cancer: a systematic review

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ABSTRACT

Introduction: The concept of indirect costs – or productivity losses to both patients and their informal caregivers arising from an illness – started to gain more importance two decades ago with the intention of strengthening cost estimates prior to evaluating, which historically was performed only with direct cost data.

Objective: The aim of this study is to explore the methodological differences in estimating productivity costs in studies of cancer diseases, as well as providing an updated and comprehensive overview of the worldwide relevance of productivity costs of cancer.

Methods: The study is conducted using a systematic literature review.

Results: The literature search resulted in 332 articles. After removing those not meeting eligibility criteria or duplicities, 27 articles were included in the qualitative analysis. It is observed that the weight of cost productivity is noticeable; in several cases, it may represent over 50% of the total. The most common method of estimation is the Human Capital method. However, certain heterogeneity is observed in the method of estimating, as well as in the resultant figures.

Conclusions: More efforts are needed to standardize calculations and allow for real comparisons between countries.

Keywords: Cancer, Friction cost, Human capital, Indirect costs, Productivity costs, Systematic review

Introduction

Quantifying productivity costs (in the case of economic evaluations of treatments for cancer and other diseases, productivity effects are usually computed in the form of benefits or costs savings) in health economics is under constant discussion among experts, focusing the debate on whether they should be considered and, if so, what methodologies should be adopted – an issue directly related to the perspective of the analysis and to the relevant effects that must be considered. In order to achieve the maximum possible standardization, and therefore facilitate the comparison (and even the transferability) between regions or countries it would be necessary to clearly define how productivity costs should be defined, measured and valued. The existence of different methodologies to estimate these costs renders the comparison of the different study findings less reliable. In the process of resource allocation, it is of high interest for decision makers to

properly address these methodological questions, due to the considerable relative weight that productivity costs represent for many diseases, for instance, cancer.

According to estimates by WHO (1) and its Globocan project, cancer is one of the leading causes of morbidity and mortality worldwide; the latest data for 2012 estimate 14 million new cases and 8.2 million cancer-related deaths. In addition, WHO has also foretold an increase of 70% of new cases in the next 20 years. In absolute numbers, this would mean an increase from 14 million annual cases of cancer in 2012 to 22 million in two decades. These high numbers also imply a high economic burden of disease. An estimate for the European Union (2) indicates that the total costs of cancer in 2009 reached €126.3 billion. Of this amount, 40% would consist of health-care costs, 42% would be productivity costs (lost work days caused by morbidity and premature mortality), and the remaining 18%, informal care costs.

Relevant scientific advances in oncology have taken place in recent years. Precision medicine and, lately, treatment strategies based on immune response have provided cancer patients with more tolerable drugs and better results, not only in terms of objective responses, but also in overall survival. Recent studies trying to compare personalized strategies with traditional chemotherapy in cancer patients have shown that current treatments based on precision medicine can be an independent predictor of better outcomes and fewer toxic deaths (3). In this setting, a significant reduction in productivity costs (due to fewer lost work days and to minor premature mortality),

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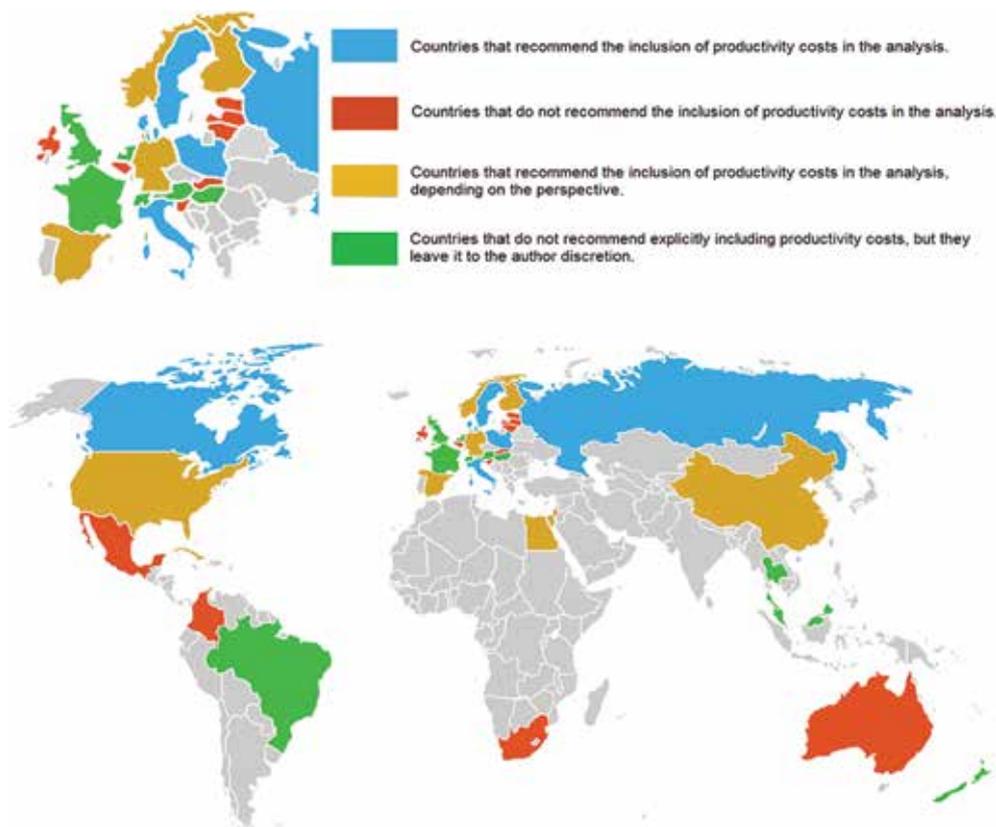


Fig. 1 - International recommendations on inclusion of productivity costs in Economic Evaluation Analysis (2007-2014).

either following a significant improvement in overall survival, or following a valuable reduction in toxic events for cancer treatment, could be more frequently found with personalized treatments than with traditional chemotherapy. It is clear that economic evaluations of new cancer drugs, based on these personalized strategies, will change significantly if they are carried out from a societal perspective instead of from a payer or National Health Service perspective.

Delving into productivity costs

The term productivity cost refers to the actual or potential production lost due to the time a person spends away from his job due to a health problem. The time when an individual is not being productive can be monetarized, and there are different methods to achieve this. The most widespread method, known as Human Capital approach, consists of estimating the production loss by means of the equivalent gross salary a target group of patients are failing to earn due to their illness. This method does not account for the fact that the patient's job duties will often be replaced by an unemployed colleague, and hence no actual reduction in production will take place; nor that there will be costs of hiring and training in case of permanent work absence (4). The Friction Costs method tries to address these problems by considering productivity costs from the employer's perspective. For the employer, productivity costs are the costs generated when a worker who is sick and absent from work has to be replaced – either temporarily or permanently (5). The Friction Costs method is also subject to criticism, due to its theoretical sustainability. Oliva (6)

underlines the non-compliance of the minimizing costs principle implicit in the approach, noting that a company would not have hired someone in first place for developing certain tasks that could be performed by a worker already on staff. Besides these two methods, there are other alternatives, such as including the productivity effects in the measurement of the QALYs (Quality Adjusted Life Years) gained, or the Willingness to Pay (WTP) approach. The QALY approach aims to reduce the indirect costs to “temporary costs” and other “additional frictional costs” (6), assuming the measurement of QALYs does already capture the productivity effects; the WTP approach leaves the judgment to the individuals to assess their own health in monetary terms (7).

Official positions

In the last 20 years, guides and recommendations for conducting economic evaluations have been published, where positioning in terms of productivity costs can be observed, and the change of tendencies over time. The Australian Guidelines for Pharmaceuticals published in 1995 (8) recommended the inclusion of direct costs only. Canada, through its CCOHTA, recommended in 1997 the inclusion of lost time due to an intervention, either work or leisure (9). The website of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) (www.ispor.org) (10) maintains the collection of most guidelines and recommendations that have been published by more than 30 countries; almost 70% of these countries consider productivity costs relevant (Fig. 1).

The aim of this literature review is to explore the methodological differences in estimating productivity costs by the Human Capital and Friction Costs methods in cost of illness/burden of illness studies of cancer diseases. A second objective is to provide an updated and comprehensive overview of the worldwide relevance of the productivity costs of cancer. This is to raise awareness among health policy makers on its dimension, and to ensure that it will be taken into account when making decisions about prioritization and choice of treatments for this disease.

Methods

Literature search

The electronic databases Medline (OVIDSP), WOS (Web of Science) and NHSeed were consulted, without limitation of time in antiquity, with a deadline of December 2014.

The following descriptors were used: medical economics, cost of illness, burden of disease, economic burden, indirect cost, work loss, productivity loss, rehabilitation cost, absenteeism, human capital societal cost, neoplasm, cancer and tumor. They were employed both in free text and controlled vocabulary.

An additional manual search was also performed to identify other potentially relevant studies.

Finally, a selection of articles was made through the titles and abstracts to full text analysis.

Criteria

Those relevant articles were identified within two inclusion criteria and two exclusion criteria:

Inclusion criteria

1. Target population comprising patients of any age with a diagnosis of neoplasia or any cause of cancer.
2. Articles involving analysis or description of the annual productivity costs in monetary terms, calculated using the Human Capital or Frictional Costs methods.

Exclusion criteria

1. Cost-effectiveness and cost-utility analyses.
2. Articles not written in English.

Data extraction and synthesis

A standardized "worksheet" was developed to extract and categorize the results of the articles. This extraction was carried out by one reader (JGM). The categorization and extraction process was performed following four steps:

- A first distinction according to the articles that met (or not) these three requirements: a) it contained original research, b) results were explicit or could be calculated using the data provided, and c) the analysis used the "Human Capital" method.

- A second classification was made regarding the type of results, distinguishing four sub-categories according to the cause of productivity costs: premature death, permanent disability, temporary disability and morbidity costs (which could be considered a sum of the previous two). Articles could present results in one or more subcategories.
- The recording of estimation details as the discount and growth factors, as well as the currency employed and the year used for updating costs.
- A final distinction was performed as to whether the costs were presented per patient or as aggregates.

Results

The literature search resulted in 332 articles, which were found in the electronic databases Medline (54 items), WOS (259 articles) and NHSeed (19 items). They were reduced to 262 after eliminating duplicates. Through the titles, abstracts and readings, 216 items were eliminated for not meeting eligibility criteria, leaving 46 studies selected for full text reading (Fig. 2).

The 46 articles were published from 1999 to 2014, most being in 2010 and 2013. There was a growing trend in the number of publications over time: over 50% were from 2010 and beyond.

Considering the study area, there were 23 publications on national cancer in the USA, 2 in Canada, 1 in Mexico and 1 in Puerto Rico. Twelve publications were from the European continent, highlighting Sweden with 4. There are 2 from Asia, one from South Korea and one from Japan. At the regional level, two publications covering the European region were obtained. There were also 2 more that included random countries without any geographical relationship. Finally, one publication talked about costs worldwide.

After complete reading, 17 publications were discarded for not having useful data due to approach limitations, such as being systematic reviews. Two publications that presented a cost estimation based on the Friction Costs method exclusively, were also discarded due to the large difference in each approach. The 27 remaining papers were included in the qualitative analysis. All the 27 publications present costs estimated through the Human Capital method (2 present results by the Friction Costs approach). The following results were presented in the 27 publications:

- Seven publications presented results for the three main productivity costs: premature death, permanent disability and temporary disability. One presents results per patient.
- Eight publications presented results for premature death and morbidity, considering it as a sum of permanent disability and temporary disability. Two papers presented results per patient.
- The remaining articles presented only a part of the productivity costs.

All results were converted to 2015 US\$ PPP (purchasing power parity), in order to compare them properly. In Tables I-VI this is shown in the last column of each table.

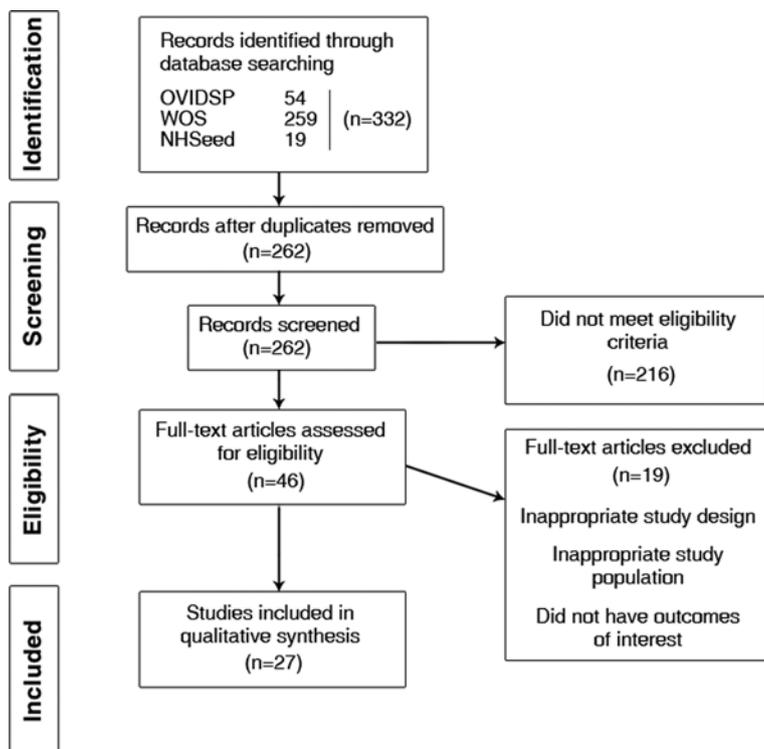


Fig. 2 - Results.

As seen in Tables I-IV, 15 articles present all types of productivity costs, (8 morbidity costs as the sum of permanent and temporary incapacity). Of these 15 articles, 13 are complete “cost of illness” studies, so all the direct costs are estimated. In Table VI, shows the percentages that each cost represents.

Discussion

Productivity costs, which are ignored in most of the cost estimations generated by a disease (due to a non-generation of an explicit expenditure), may represent more than two-thirds of total costs, as some of the “burden and total cost of disease” studies suggest (37). This magnitude is what compelled us to have an updated international look at the amounts of these productivity costs by country, the similarities and differences between measurement methods, as well as the increase in the number of such publications over time.

The results of our revision reaffirm the figures: indirect costs represent between 37% and 82% of the total costs of the disease (Tab. VI), providing the method used is the Human Capital method, and the perspective of society is taken into account. Even so, the amplitude of the interval (around 45 percentage points) calls for a deeper analysis of the heterogeneity. Productivity costs are basically constituted by three sub-costs; ordered by relative importance in the case of cancer, these sub-costs are regarding: (i) premature mortality, (ii) permanent disability, and (iii) temporary disability. It is clear that fluctuations in the value of productivity costs over total costs will first depend on which of these three sub-costs is being accounted for. If a study has an estimation of permanent and temporary disability, the total productivity cost will

be higher, and that will imply a higher relative weight of this type of cost on the totals.

There are other factors that explain the heterogeneity: for example, demographic aspects, as the specific incidence/prevalence of the population, which will be the determinant: the higher the incidence in a specific region, the higher the productivity cost will be (this also applies for the direct costs).

Furthermore, there are other specific factors that arise from the interpretation and application of the Human Capital method that each author makes in his/her productivity cost estimation. The method leaves the author with the choice of:

- The average salary imputed to the patients. The Human Capital approach quantifies all time lost by a population and multiplies it by a single salary (sometimes the national minimum, sometimes an average), or a stratified salary depending on the age of the patient/social class/gender, etc. Therefore, this is a particularly sensitive component for the final results.
- The sources of information where salaries, incidence, and other components are extracted. The quality of the data will depend on whether they come from official sources, private sources, sources of national, local (to then extrapolate the rest of the population), etc.

In any case, beyond the lack of methodological consistency, it is convenient that this type of cost has more presence in both “cost of the disease” studies and the subsequent economic evaluations, if looking at the high levels the figures can reach. Although it would still be more convenient that “cost of the illness” and “Economic Evaluation” studies have

TABLE I - Articles including all productivity costs, aggregate

| Author, year of publication | Cost discounting year, region | Type of cancer | Original currency | Type of cost | Results (thousands, original currency) | 2015 US\$, PPP (thousands) | | | | |
|---------------------------------|-------------------------------|-----------------|-------------------|---------------------------------|--|----------------------------|-----------------|----------------------|----------|-----------|
| Blomqvist et al, 2000 (11) | 1996, Sweden | Brain | US\$ | Premature death | 109,700.00 | 108,833.57 | | | | |
| | | | | Permanent disability | 28,800.00 | 28,572.53 | | | | |
| | | | | Temporary disability | 11,600.00 | 11,508.38 | | | | |
| | | | | TOTAL | 150,100.00 | 148,914.48 | | | | |
| Lidgren et al, 2007 (12) | 2002, Sweden | Breast | SEK | Premature death | 1.104.233.0 | 150,894.04 | | | | |
| | | | | Permanent disability | 380,641.0 | 52,014.80 | | | | |
| | | | | Temporary disability | 620,452.0 | 10,735.79 | | | | |
| | | | | TOTAL | 2.105.326.0 | 213,644.63 | | | | |
| Macioch et al, 2011 (13) | 2009, Poland | All cancers | € | Premature death | 1,571,839.0 | 4,259,579.55 | | | | |
| | | | | Permanent disability | 535,449.0 | 1,451,031.31 | | | | |
| | | | | Temporary disability | 504,328.0 | 1,366,695.46 | | | | |
| | | | | TOTAL | 2,611,616.0 | 7,077,306.32 | | | | |
| Reis et al, 2006 (14) | 2000, Germany | Lymphoma | € | Premature death | 429,068.3 | 663,676.58 | | | | |
| | | | | Permanent disability | 149,855.0 | 231,793.55 | | | | |
| | | | | Temporary disability | 90,076.6 | 139,329.19 | | | | |
| | | | | TOTAL | 669,000.0 | 1,034,799.32 | | | | |
| Selke et al, 2003 (15) | 1999, France | Colorectal | € | Premature death | 221,280.0 | 342,337.90 | | | | |
| | | | | Permanent disability | 256,510.0 | 396,841.54 | | | | |
| | | | | Temporary disability | 50,310.0 | 77,833.60 | | | | |
| | | | | TOTAL | 528,100.0 | 817,013.04 | | | | |
| Oliva et al, 2005 (16) | 2003, Spain | Breast | € | Premature death | 113,055.0 | 204,715.35 | | | | |
| | | | | Permanent disability | 159,295.0 | 288,444.85 | | | | |
| | | | | Temporary disability | 16,381.0 | 29,662.04 | | | | |
| | | | | TOTAL | 288,731.0 | 522,822.2 | | | | |
| | | | | Frictional cost approach | <i>Premature death</i> | <i>2,287.45</i> | <i>4,142.02</i> | | | |
| | | | | | <i>Permanent disability</i> | <i>5,452.92</i> | <i>9,873.92</i> | | | |
| | | | | | <i>Temporary disability</i> | <i>3,880.5</i> | <i>7,026.65</i> | | | |
| | | | | TOTAL | 11,620.9 | 21,042.65 | | | | |
| | | | | Oliva et al, 2005 (16) | 2003, Spain | Cervix | € | Premature death | 21,701.0 | 39,295.28 |
| | | | | | | | | Permanent disability | 20,565.0 | 37,238.26 |
| Temporary disability | 1,161.0 | 2,102.29 | | | | | | | | |
| TOTAL | 43,427.0 | 78,635.8 | | | | | | | | |
| Frictional cost approach | <i>Premature death</i> | <i>393.16</i> | <i>711.92</i> | | | | | | | |
| | <i>Permanent disability</i> | <i>310.80</i> | <i>562.78</i> | | | | | | | |
| | <i>Temporary disability</i> | <i>432.06</i> | <i>782.36</i> | | | | | | | |
| TOTAL | 1,136.03 | 2,057.08 | | | | | | | | |

PPP = purchasing power parity.



TABLE II - Articles including all productivity costs, aggregate (permanent and temporary disabilities presented as morbidity costs)

| Author, year of publication | Cost discounting year, region | Type of cancer | Original currency | Type of cost | Results (thousands, original currency) | 2015 US\$, PPP (thousands) |
|----------------------------------|-------------------------------|----------------|-------------------|-----------------|--|----------------------------|
| Haga et al, 2013 (17) | 2008, Japan | Stomach | Yen | Premature death | 806,400,000.0 | 7,424,064.44 |
| | | | | Morbidity costs | 54,000,000.0 | 497,147.17 |
| | | | | TOTAL | 860,400,000.0 | 7,921,211.6 |
| Byun et al, 2014 (18) | 2010, South Korea | Colorectal | KRW | Premature death | 1,027,311.000.0 | 1,226,106.69 |
| | | | | Morbidity costs | 132,348,000.0 | 157,958.76 |
| | | | | TOTAL | 1,159,659.000.0 | 1,384,065.5 |
| Morris et al, 2009 (19) | 2002, England | Skin | £ | Premature death | 98,167.0 | 189,024.16 |
| | | | | Morbidity costs | 20,859.0 | 40,164.77 |
| | | | | TOTAL | 119,026.0 | 229,188.9 |
| Tinghög et al, 2008 (20) | 2005, Sweden | Skin | € | Premature death | 53,275.0 | 67,040.16 |
| | | | | Morbidity costs | 9,528.0 | 11,989.84 |
| | | | | TOTAL | 62,803.0 | 79,030.0 |
| Wilson et al, 1999 (21) | 1996, US | Pancreas | US\$ | Premature death | 3,739,000.0 | 5,351,422.12 |
| | | | | Morbidity costs | 279,350.0 | 399,818.07 |
| | | | | TOTAL | 4,018,350.0 | 5,751,240.2 |
| Luengo-Fernandez et al, 2013 (2) | 2009, EU27 | All cancers | € | Premature death | 42,600,000.0 | 56,624,163.10 |
| | | | | Morbidity costs | 9,430,000.0 | 12,534,409.81 |
| | | | | TOTAL | 52,030,000.0 | 69,158,572.91 |

PPP = purchasing power parity.

TABLE III - Articles including all productivity costs, per patient

| Author, year of publication | Cost discounting year, region | Type of cancer | Original currency | Type of cost | Results (thousands, original currency) | 2015 US\$, PPP (thousands) | |
|---------------------------------|-------------------------------|----------------|-------------------|---------------------------------|--|----------------------------|---------------|
| Hanly et al, 2012 (22) | 2008, Ireland | Breast | € | Premature death | 84.49 | 101.72 | |
| | | | | Permanent disability | 82.58 | 99.42 | |
| | | | | Temporary disability | 26.36 | 31.74 | |
| | | | | TOTAL | 193.43 | 232.88 | |
| | | | | Frictional cost approach | Premature death | 1.16 | 1.4 |
| | | | | | Permanent disability | 1.01 | 1.22 |
| | | | | | Temporary disability | 5.93 | 7.14 |
| | | | | | TOTAL | 8.10 | 9.76 |
| | | | | | TOTAL | 201.59 | 251.86 |
| | | | | Hanly et al, 2012 (22) | 2008, Ireland | Prostate | € |
| Permanent disability | 75.04 | 90.35 | | | | | |
| Temporary disability | 13.41 | 16.14 | | | | | |
| TOTAL | 109.15 | 131.42 | | | | | |
| Frictional cost approach | Premature death | 0.37 | 0.445 | | | | |
| | Permanent disability | 1.52 | 1.83 | | | | |
| | Temporary disability | 6.32 | 7.61 | | | | |
| | TOTAL | 8.21 | 9.88 | | | | |
| | TOTAL | 117.36 | 141.30 | | | | |

PPP = purchasing power parity.

TABLE IV - Articles including all productivity costs, per patient (PD and TD presented as morbidity costs)

| Author, year of publication | Cost discounting year, region | Type of cancer | Original currency | Type of cost | Results (thousands, original currency) | 2015 US\$, PPP (thousands) |
|-----------------------------|-------------------------------|----------------|-------------------|-----------------|--|----------------------------|
| Broekx et al, 2011 (23) | 2010, Flanders | Breast | € | Premature death | 63.08 | 82.73 |
| | | | | Morbidity costs | 23.31 | 30.57 |
| | | | | TOTAL | 86.39 | 113.30 |
| Tingstedt et al, 2011 (24) | 2009, Sweden | Pancreas | € | Premature death | 226.43 | 290.55 |
| | | | | Morbidity costs | 60.77 | 77.98 |
| | | | | TOTAL | 287.20 | 368.53 |

PPP = purchasing power parity.

TABLE V - Rest of articles

| Presenting aggregate costs | | | | | | |
|---------------------------------|-------------------------------|---------------------------------------|-------------------|------------------------|--|-------------------------------|
| Author, year of publication | Cost discounting year, region | Type of cancer | Original currency | Type of cost estimated | Results (thousands, original currency) | 2015 US\$, PPP (thousands) |
| Binazzi et al, 2013 (25) | 2006, Italy | All cancers | € | Premature death | 354,195.30 | 540,265.27 |
| Bradley et al, 2008 (26) | 2005, US | All cancers | US\$ | Premature death | 115,831.272 | 138,230,161.69 |
| Bristow et al, 2013 (27) | 2011, US | Skin (melanoma) | US\$ | Premature death | 66,945.053 (for the period 1990-2008) | 71,133,695.28/ 3,743,878.7 |
| Ekweme et al, 2011 (28) | 2006, US | All cancers | US\$ | Premature death | 173,073.500 | 200,383,313.25 |
| Ekweme et al, 2011 (28) | 2006, US | Skin (melanoma) | US\$ | Premature death | 3,487.600 | 4,037,919.40 |
| Ekweme et al, 2008 (29) | 2003, US | All cancers | US\$ | Premature death | 133,531.973 | 169,002,966.92 |
| Ekweme et al, 2008 (29) | 2003, US | Associated with human papilloma virus | US\$ | Premature death | 3,629.826 | 4,594,041.03 |
| Insigna, 2006 (30) | 2000, US | Cervical | US\$ | Premature death | 1,300,000 | 1,742,736.94 |
| Li et al, 2010 (31) | 2007, US | Urogenital | US\$ | Premature death | 10,400.000 | 11,728,941.72 |
| Max et al, 2002 (32) | 1998, US | Prostate | US\$ | Premature death | 180,198 | 250,843.09 |
| Ortiz-Ortiz et al, 2010 (33) | 2004, Puerto Rico | All cancers | US\$ | Premature death | 64,200 | 79,079.39 |
| Tangka et al, 2013 (34) | 2010, US | All cancers | US\$ | Temporary disability | 115,900 | 125,693.25 |
| Presenting costs per patient | | | | | | |
| Müller-Nordhon et al, 2005 (35) | 2002, Germany | Pancreas | € | Permanent disability | 239 | 360.74 |
| | | | | Temporary disability | 2972 | 4485.81 |
| Sasser et al, 2005 (36) | 2000, US | Breast | US\$ | Permanent disability | 4,602 | 6169.29 |
| | | | | Temporary disability | 3,634 | 4871.62 |

PPP = purchasing power parity.



TABLE VI - Productivity costs versus direct costs

| Author, year of publication | Cost discounting year, region | Type of cancer | Type of cost | % of the total costs | % of the direct costs |
|-----------------------------------|-------------------------------|----------------|---------------------------------|----------------------|-----------------------|
| Blomqvist et al, 2000 (11) | 1996, Sweden | Brain | Premature death | 54.36% | 212.19% |
| | | | Permanent disability | 14.27% | 55.71% |
| | | | Temporary disability | 5.75% | 22.44% |
| | | | Total productivity costs | 74.38% | |
| | | | Total direct costs | 25.62% | |
| Lidgren et al, 2007 (12) | 2002, Sweden | Breast | Premature death | 36.81% | 123.41% |
| | | | Permanent disability | 12.69% | 42.54% |
| | | | Temporary disability | 20.68% | 69.34% |
| | | | Total productivity costs | 70.17% | |
| | | | Total direct costs | 29.83% | |
| Reis et al, 2006 (14) | 2000, Germany | Lymphoma | Premature death | 25.31% | 41.82% |
| | | | Permanent disability | 8.84% | 14.61% |
| | | | Temporary disability | 5.31% | 8.78% |
| | | | Total productivity costs | 39.47% | |
| | | | Total direct costs | 60.53% | |
| Selke et al, 2003 (15) | 1999, France | Colorectal | Premature death | 22.59% | 49.00% |
| | | | Permanent disability | 26.18% | 56.80% |
| | | | Temporary disability | 5.14% | 11.14% |
| | | | Total productivity costs | 53.90% | |
| | | | Total direct costs | 46.10% | |
| Haga et al, 2013 (17) | 2008, Japan | Stomach | Premature death | 72.38% | 317.86% |
| | | | Morbidity costs | 4.85% | 21.28% |
| | | | Total productivity costs | 77.23% | |
| | | | Total direct costs | 22.77% | |
| | | | | | |
| Byun et al, 2014 (18) | 2010, South Korea | Colorectal | Premature death | 32.93% | 52.41% |
| | | | Morbidity costs | 4.24% | 6.75% |
| | | | Total productivity costs | 37.17% | |
| | | | Total direct costs | 62.83% | |
| | | | | | |
| Morris et al, 2009 (19) | 2002, England | Skin | Premature death | 40.92% | 81.22% |
| | | | Morbidity costs | 8.70% | 17.26% |
| | | | Total productivity costs | 49.62% | |
| | | | Total direct costs | 50.38% | |
| | | | | | |
| Tinghög et al, 2008 (20) | 2005, Sweden | Skin | Premature death | 37.40% | 66.89% |
| | | | Morbidity costs | 6.9% | 11.96% |
| | | | Total productivity costs | 44.09% | |
| | | | Total direct costs | 55.91% | |
| | | | | | |
| Luengo-Fernandez et al, 2013 (2)* | 2009, EU27 | All cancers | Premature death | 41.35% | 83.54% |
| | | | Morbidity costs | 9.15% | 184.9% |
| | | | Total productivity costs | 50.50% | |
| | | | Total direct costs | 49.50% | |
| | | | | | |
| Wilson et al, 1999 (21) | 1996, US | Pancreas | Premature death | 76.04% | 415.91% |
| | | | Morbidity costs | 5.68% | 31.07% |
| | | | Total productivity costs | 81.72% | |
| | | | Total direct costs | 18.28% | |
| | | | | | |
| Broekx et al, 2011 (23)** | 2010, Flanders | Breast | Premature death | 63.85% | 508.70% |
| | | | Morbidity costs | 23.59% | 187.98% |
| | | | Total productivity costs | 87.45% | |
| | | | Total direct costs | 12.55% | |
| | | | | | |
| Tingstedt et al, 2011 (24) | 2009, Sweden | Pancreas | Premature death | 50.56% | 140.94% |
| | | | Morbidity costs | 13.57% | 37.83% |
| | | | Total productivity costs | 64.13% | |
| | | | Total direct costs | 35.87% | |
| | | | | | |

* This article also presents informal care costs. If those are included as productivity costs, the percentages change to: productivity costs: 59.61%; direct costs: 40.39%.

** This article presents "housekeeping activities" costs too. If those are included as productivity costs, the percentages change to: productivity costs: 88.50%; direct costs: 11.50%.

a greater presence, even as they are carried out nowadays (direct costs), between clinicians, planners, managers, politicians and other stakeholders involved. These kinds of studies are very useful in making better informed decisions in the allocation of resources, which are always scarce.

Looking on the positive side, it is encouraging to observe a growing interest in productivity cost estimations in recent years. More than 50% of the results found for our review were published from 2010. If the trend remains positive, it is logical to think that in the future it will be constituted as another input in the economic evaluation analysis. However, one must be cautious in this regard, since in the field of economic evaluation, there is still notable absence of consensus on the theoretical and conceptual framework (38).

In view of the results of this review, it is recommended to incorporate the loss of productivity, at least in premature mortality, as the most relevant component of the indirect cost, to economic analysis, when the analysis is performed from the point of view of society, and using a common method, a standardized Human Capital approach.

It is important to point out a limitation to this review. There are several types of articles in the scientific literature where costs are estimated for a particular pathology. The basic of these are called Cost of Illness (Col) or Cost of the disease. These studies can be found alone, or as the economic annex of more global studies, called "Burden of the Disease", where besides the economic weight, incidence, prevalence and other series of indicators are presented. "Col" studies can be performed through two different approaches: prevalence approach (pathology-associated total costs are estimated regardless of when it occurs, in a given territory, in a period of time also determined, normally of one year) and incidence approach (this method focuses on calculating the costs incurred by a patient who has the disease for the first time). In the economic evaluation studies, cost estimations of specific pathologies can also be found, as these compare different alternatives in terms of costs and consequences. These sub-variations in the type of studies were not taken into account in the systematic search planning, which implies a possible misinterpretation of the results as they are presented.

Conclusion

Although all estimates presented as results are made by the method of Human Capital, there are still methodological barriers that make it impossible to realistically compare results. More efforts to standardize calculations are needed, with the aim of making figures for productivity (or indirect) costs more consistent and therefore attractive; this has to be the first step towards drawing the attention of economic analysis demanders (agents who plan, provide, receive or pay for services), so that they begin to consider such costs as being important, and ideally, in the future, essential in the evaluations.

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