

Received:
25 November 2017
Revised:
17 May 2018
Accepted:
23 May 2018

Cite as: Omar B. Da'ar,
Ashraf El-Metwally,
Raghib Abu-Saris,
Abdul Rahman Jazieh. A
finite and stable exponential
growth-adjusted indirect cost
of cancer associated with
discounted years of life lost in
Saudi Arabia.
Heliyon 4 (2018) e00637.
doi: [10.1016/j.heliyon.2018.
e00637](https://doi.org/10.1016/j.heliyon.2018.e00637)



A finite and stable exponential growth-adjusted indirect cost of cancer associated with discounted years of life lost in Saudi Arabia

Omar B. Da'ar^{a,b,*}, Ashraf El-Metwally^{a,c}, Raghib Abu-Saris^a,
Abdul Rahman Jazieh^{d,e}

^a College of Public Health & Health Informatics, King Saud Bin Abdulaziz University for Health Sciences, National Guard Health Affairs (NGHA), Riyadh, Saudi Arabia

^b Graduate School of Professional Studies, St. Mary's University of Minnesota, USA

^c University of Tampere, Tampere, Finland

^d Oncology Department, King Abdulaziz Medical City, National Guard Health Affairs Hospital, Riyadh, Saudi Arabia

^e College of Medicine, King Saud bin Abdulaziz University for Health Sciences, National Guard Health Affairs (NGHA), Riyadh, Saudi Arabia

* Corresponding author.

E-mail addresses: odaar@smumn.edu, obdaar@hotmail.com (O.B. Da'ar).

Abstract

Background: The risk of getting cancer before full life expectancy and mortalities per year are on the rise in Saudi Arabia. Yet, evidence of economic burden of cancer in the country remains largely unknown. In order to provide evidence, we attempted to estimate the economic burden in terms of indirect cost associated with premature cancer deaths among the active or potentially economically active population aged 15–60 years in Saudi Arabia.

Method: Within the framework of the World Health Organization guide of identifying the economic consequences of disease and injury, our method employs cost-of-illness approach. This approach is based on a macroeconomic model that estimates the indirect cost of cancer in terms of total non-health gross domestic product resource loss associated with a disease. We used epidemiological, health

system, and macroeconomic data for our estimation. We discounted the net loss at 3% and computed an extension of the loss with a finite and stable upper limit proxied by non-health gross domestic product per capita. We carried out separate analyses for male and female. We conducted sensitivity analyses to account for uncertainties of epidemiological and economic factors on the robustness of the estimated economic burden. We varied the proportion of total cancer deaths, discount rate, and value of health expenditure per capita by $\pm 20\%$. We further determined which of these factors or parameters had the greatest uncertainty or variation on the net present value total non-health gross domestic product resource loss per Capita.

Results: Our results indicate the indirect cost associated with cancer deaths among Saudi population aged 15–60 years to be Int\$ 2.57 billion of which Int\$ 1.46 billion (57%) was accounted for by females. The total indirect loss of cancer deaths increased by 8% to Int\$ 2.77 billion when the loss is allowed to grow with a finite and stable upper limit proxied by non-health gross domestic product per capita over the discounted years of life lost per a death among female and male respectively. Much of the uncertainty in the determination of the value of the loss was accounted for by the proportion of total cancer deaths and discount rate, while health expenditure per capita was responsible for the least variability.

Conclusion: Our findings reveal evidence of indirect cost associated with cancer premature deaths in Saudi Arabia. In order to develop cancer control actions, the results of this study can inform health system policymakers not only of the extent of the enormous economic burden but also drawing attention to epidemiological and economic factors that explain the variability of the burden.

Keywords: Economics, Public health

1. Introduction

There is a growing concern about the escalating burden of non-communicable diseases (NCDs) from both the public health and economic perspectives [1, 2]. Two-thirds of deaths associated with NCDs comprise mainly of cardiovascular diseases, cancers, diabetes, and chronic lung diseases. One-fourths of these global deaths take place before the age of 60 [3].

Globally, 17.5 million cancer cases and 8.7 million deaths were reported in 2015. Between 2005 and 2015, cancer cases increased by 33%, with population aging contributing half of the increase [4]. Incident cancer cases in the Eastern Mediterranean Region (EMR) increased on average by 46.1% from 495 thousand in 2005 to 723 thousand cases in 2015 [5]. In 2015, cancer caused on average 379 thousand deaths and 11.7 million disability-adjusted life years (DALYs) in EMR of which 3% were attributable to years lived with disabilities (YLDs) and 97% to years of

life lost (YLLs) [5]. The total economic impact of premature death and disability of cancer is approaching trillions of dollars, which by far accounts for the largest drain on the global economy [3, 6]. Many studies have examined the mortality costs associated with premature death from cancer across the globe [7, 8, 9, 10, 11, 12, 13]. This impact is indicative of the shift in the global burden of disease towards NCDs. The World Health Organization (WHO) considers the burden of disease as a combination of premature death and disability [14].

Cancer was globally the second-leading cause of death behind cardiovascular diseases in 2015 [4]. Cancer is ranked among the top four leading causes of death in the Eastern Mediterranean Region (EMR) [15]. In EMR, incident cancer cases increased on average by 46.1% from 495 thousand in 2005 to 723 thousand cases in 2015 [5]. A 2013 WHO report indicated that the incidence is expected to almost double by 2030 [15].

Given this alarming trend and the substantial contribution of cancer to the disease burden in EMR countries, cancer control has to be among the top health policy priorities [5]. In an attempt to curtail the burden of cancer, WHO regional bodies like Regional Committee for the EMR, and national governments have identified cancer as a priority for intervention [15, 16]. However, lack of scientific evidence has hindered efforts to control cancer.

Gulf Cooperation Council (GCC) countries have been shown to bear huge indirect cost associated with cancer, running into billions of dollars [17]. According to 2014 twelve-year cancer incidence report for the nationals of the GCC countries (1998–2009), Saudi Arabia accounted for 75% of cancer cases reported to Gulf Center for Cancer Control [18]. The country has relatively large population aged 15–64. Of concern to policymakers is that cancer scourge affects active or potentially economically active population. Nearly 21.2 million (69%) of the estimated 30.9 million Saudi population in 2014 were aged 15–64. Of this, 12.6 million (59%) were male and 8.6 million (41%) were female. There were 17,522 cancer incidences of which 12,012 (69%) occurred among those aged 15–64 according to GLOBOCAN 2012. During the same period, 9,134 cancer mortalities were reported of which 4,845 (53%) aged 15–64.

The aforementioned statistics indicate that cancer is hitting harder among crucial population of the country's current or potential workforce. In addition, cancer poses serious current and future burden, exacting pressure on healthcare resources and system [16, 17, 18, 19]. However, evidence of economic burden remains a significant challenge, limiting not only decision-making in health systems but also the very efforts directed at the development of cancer control actions.

This paper is therefore to contribute to documenting evidence of economic burden, especially the indirect cost associated with premature deaths due to cancer in Saudi

Arabia, where the need for cancer evidence is a high priority area for research. The absence of evidence in this context may be seen as part of the recognition of the dearth of knowledge and application of economic analyses in the country [20]. The paper raises the pertinent questions: what is the economic burden or indirect cost associated with premature cancer deaths among active or potentially economically active population (15–60 years) in Saudi Arabia? How do uncertainties about epidemiological and economic factors affect the magnitude and robustness of the economic burden associated with cancer? We restrict our analysis to population aged 15–60 years due to limitation of data.

2. Methods

2.1. Conceptual framework

Our method involves estimation of the indirect cost of cancer using a macroeconomic model of *cost-of-illness* (COI) method. We follow recommendations of reporting economic evaluations according to WHO guideline for identifying the economic consequences of disease and injury [21]. We computed discounted years of life lost due to premature death and non-health gross domestic product per capita (GDPPC) loss. We then use this information to estimate the total non-health resource loss associated with cancer deaths among economically active or potentially active population in Saudi Arabia.

Previous studies have used similar approaches of COI method to estimate the impact of deaths associated with a disease on non-health components of the future gross domestic product (GDP) [22, 23, 24]. As reported in [23, 24], the impact of deaths associated with disease on the non-health components of GDP is the ‘quantity of interest’ when capturing indirect cost of a burden of a disease because the use of health services or goods does not generate utility or welfare *per se* [25]. GDP, that is, the total value of all marketed final goods and services produced in an economy during a year is also considered one of the measures of the market production forgone due to the ultimate burden of a disease [20]. Since medical care and health expenditures actually form part of GDP [23], a more appropriate quantity of interest would be the impact of disease or injury on the non-health components of GDP [22].

2.2. Total non-health macroeconomic loss of cancer model and specification

We follow the framework of previous studies [22, 23, 24] in measuring the indirect cost by computing discounted total non-health GDP loss due to disease deaths according to equations 2.1, 2.2, and 2.3. However, we augment the approaches of the previous studies both substantively and contextually. First, we add a modified

exponential growth component with a finite and stable upper limit proxied by non-health GDPPC to the COI model. Reason for doing so is to dispel the notion that it is conceivable for the cancer-related non-health GDP per capita loss to the economy to exceed the GDP per capita in any given year. Additionally, our study is the first of its kind, at least according to our knowledge to estimate the indirect cost of cancer in the context of Saudi Arabia.

The extension of the model takes into account the future value of non-health resources with continuous but finite stable growth over the years of life lost (YLL). The future value relies on the underlying concept of time value of money, which is the notion that a current sum of money, or unit of account is worth more today than the same amount at a future date. Time value of money is also consistent with the concept of the value of life where the value of preventing a human’s death is the present value of expected earnings [26]. Value of life can be measured in terms of the extra consumption that individuals enjoy because of surviving. The social objective that justifies this measure is the maximization of gross national product (GNP), [27] a similar measure to GDP but which accounts for net income receipt less net payments from abroad.

The net present value non-health GDP per capita loss of the economy for the target population is given by:

$$n_{(15-60)} = n_{F(15-60)} + n_{M(15-60)} \tag{2.1}$$

where $n_{(15-60)}$ is the net present value of total non-health GDP loss due to cancer deaths for both female and male population aged 15–60 years (NPVTNHGDP); n_F is net present value of non-health GDP loss due to cancer deaths for female aged 15–60 years ($NPVNHGDPPC_{F(15-60)}$); n_M is net present value of non-health GDP loss due to cancer deaths for male aged 15–60 years ($NPVNHGDPPC_{M(15-60)}$);

$$\begin{aligned}
 n_{F(15-60)} &= \frac{1}{(1+r)^1} \times n_1 \times tcd_{F(15-60)} + \frac{1}{(1+r)^2} \times n_2 \times tcd_{F(15-60)} + \frac{1}{(1+r)^3} \times n_3 \times tcd_{F(15-60)} \\
 &\quad \cdot \\
 &\quad \cdot \\
 &\quad \cdot \\
 &\quad + \frac{1}{(1+r)^T} \times n_T \times tcd_{F(15-60)} \\
 &= \sum_{t=1}^T \left\{ \frac{1}{(1+r)^t} \times n_t \times tcd_{F(15-60)} \right\}
 \end{aligned} \tag{2.2}$$

and

$$\begin{aligned}
 n_{M(15-60)} &= \frac{1}{(1+r)^1} \times n_1 \times tcd_{M(15-60)} + \frac{1}{(1+r)^2} \times n_2 \times tcd_{M(15-60)} + \frac{1}{(1+r)^3} \times n_3 \times tcd_{M(15-60)} \\
 &\quad \cdot \\
 &\quad \cdot \\
 &\quad \cdot \\
 &\quad + \frac{1}{(1+r)^T} \times n_T \times tcd_{M(15-60)} \\
 &= \sum_{t=1}^T \left\{ \frac{1}{(1+r)^t} \times n_t \times tcd_{M(15-60)} \right\}
 \end{aligned}
 \tag{2.3}$$

where $NPVTNHGDPPC_{(15-60)}$ is the net present value of total non-health GDP loss due to cancer deaths; n_t is the growth-adjusted non-health GDP per capita loss due to cancer deaths among population aged 15–60 years at time, t ; $n_t = GDPPC - a^t(GDPPC - n_0)$; a is a growth parameter depicting the proportion of initial non-health GDP per capita loss (n_0) to GDP per capita; $n_0 \leq n_t < GDPPC$ by assumption; $1/(1+r)^t$ is the discount factor; $\sum_{t=1}^T$ depicts the summation from year t to T ; t represents the first year of life lost to cancer and T is the terminal year, i.e. the final year of all years of life lost per cancer death, which can be computed by taking the difference between average age at death (AAD) from cancer and average life expectancy at birth; $tcd_{F(15-60)}$ is the total number of cancer deaths that occur among female population aged 15–60 years in 2014, while $tcd_{M(15-60)}$ is the total number of cancer deaths that occurred among male population aged 15–60 years in Saudi Arabia.

3. Results

3.1. Computing non-health GDP loss due to cancer

We computed the net present value of current and future non-health GDP loss due to cancer deaths as the sum of non-health GDP loss among female and male populations aged 15–60 years. The non-health GDPPC loss attributable to cancer deaths among the female and male population of this age group was estimated by multiplying the total number of discounted years of life lost (which is equivalent to the sum of the discount factors) by the non-health GDP per capita and the total number of cancer deaths in the age group.

The basic premise of discounting is that losses occurring in the future are less of a burden than losses occurring in the present period. Thus, losses occurring in different periods need adjustment for their time value. Discounting future health outcomes have been addressed in previous studies [28, 29]. As reported in a previous study [23], there exists a small level of uncertainty of survival in a society that increases monotonically over time [14]. More generally, an important reason for discounting future costs and benefits in economics is ‘time preference’, which refers to the desire

to enjoy benefits in the present while deferring any negative effects of doing so [30]. In fact, failure to discount effects even when costs are counted for can lead to inconsistent or misleading results in health and medical practices [31].

Non-health GDPPC loss due to cancer deaths among Saudi female population aged 15–60 years was estimated by multiplying the total discounted years of life lost by the non-health GDP per capita and the total cancer deaths in that population group. For example, in Saudi Arabia, 38.3 and 34.7 undiscounted YLL were lost per a death among female and male aged between 15–60 years respectively. These values represent the difference between the average life expectancy at birth (LE) of a Saudi Female and AAD from cancer ($77.3 - 39 = 38.3$ and $73.7 - 39 = 34.7$). With an assumption of 3% discount rate, this yielded about 23.1 and 21.7 discounted years of life lost per a death among female and male aged less than 15–60 years respectively. AAD for both male and female were estimated to be 39 years while the LE at birth for Saudis is 73.7 for men and 77.3 for women according to health data we gleaned from WHO updates, World Bank, United Nations for Population [32].

3.2. Baseline results

We first present baseline results without the assumption of future growth. Non-health GDP per capita for Saudi population for 2011 was Int\$ 15,939, which is per capita GDP of Int\$ 17,800 less total health expenditure per capita of Int\$ 1,861. Estimated total cancer deaths (ETCD) aged <65 were 10,101 in 2011. Nearly 70.2% of the total cancer deaths or 7,091 ($0.702 \times 10,101$) deaths were aged 15–60 years. Of these deaths, 55% were female translating to 3,897 females and 3194 males. At 3%, the estimated discounted YLL is 23.1 for female and 21.7 for male respectively. Thus, the net present value of non-health GDP lost due to cancer deaths among Saudi female population aged 15–60 years is approximately Int\$ 1,460,339,286, which is obtained by multiplying 23.1, the discounted years lost, by Int\$ 15,939, the per capita non-health GDP, and the 3,897 cancer deaths. On the other hand, the net present value of non-health GDP lost due to cancer deaths among Saudi male population aged 15–60 years is Int\$ 1,107,004,886, which is approximately obtained by multiplying 21.7, the discounted years lost, by Int\$ 15,939, the per capita non-health GDP, and the 3,194 cancer deaths. See Table 1 for an illustration of cancer-related indirect cost in terms of total non-health GDP lost using actual data from Saudi Arabia. Table 2 further reveals the variables and data sources for our study.

3.3. Results with growth assumption

Taking into account the growth of NPVNHGDP loss with a finite and stable upper limit proxied by non-health GDPPC, the loss of cancer deaths is estimated to increase by 8% to Int\$ 1.576 billion, up from Int\$ 1.460 for females. For males, the value increases to Int\$ 1.91 billion, up from Int\$ 1.107 billion. These values were generated

Table 1. Computation of cancer-related total non-health GDP loss in Saudi Arabia.

(i)	Estimated Total Cancer Deaths <65 year	10,101
(ii)	Proportion Total cancer deaths (PTCD), Age Group, 15–60 years (Total)	0.702
(iii)	Proportion Age Group Female (15–60 years)	0.55
(iv)	Proportion Age Group Male (15–60 years)	0.45
(v)	Estimated Total Cancer Deaths (Female & Male) 15–60 = 0.702 × 10,101	7,091
(vi)	Estimated Total Cancer Deaths, $ETCD_F (15-60) = 0.55 \times 7091$	3,897
(vii)	Estimated Total Cancer Deaths, $ETCD_M (15-60) = 0.45 \times 7091$	3,194
(viii)	Average age at death for female, $AAD_F (15-60)$	39
(ix)	Average age at death for male, $AAD_M (15-60)$	39
(x)	Saudi Average female LE at birth, LE_F	77.3
(xi)	Saudi Average male LE at birth, LE_M	73.7
(xii)	Gross domestic product (GDP) per capita ($GDPPC_{Int\$}$)	17,800
(xiii)	Health expenditure per capita, $HEPC_{Int\$}$	1,861
(xiv)	Initial non-health $GDPPC_{Int\$} (N_0) = GDPPC_{Int\$} - HEPC_{Int\$}$	15,939
(xv)	Proportion of $NHGDPPC_{Int\$}$ to $GDPPC_{Int\$}$	0.895
(xvi)	Discount rate, r	3%
(xvii)	Undiscounted $YLL_F (15-60) = LE_F - AAD_F (15-60)$	38.3
(xviii)	Undiscounted $YLL_M (15-60) = LE_M - AAD_M (15-60)$	34.7
(xix)	Discounted $YLL_F (15-60)$	23.1
(xx)	Discounted $YLL_M (15-60)$	21.7
(xxi)	NPV Un-adjusted non-health GDPPC loss, female ($NPVUNHGDPPCL_F (15-60)$) = Discounted $YLL_F (15-60) \times N_{0_Int\$} \times ETCD_F (15-60)$	\$1,460,339,286
(xxii)	NPV Un-adjusted non-health GDPPC loss, male ($NPVUNHGDPPCL_M (15-60)$) = Discounted $YLL_M (15-60) \times N_{0_Int\$} \times ETCD_M (15-60)$	\$1,107,004,886
(xxiii)	NPV Un-adjusted total non-health GDPPC loss ($NPVUTNHGDPPCL_T (15-60)$) = $NPVUNHGDPPCL_F (15-60) + NPVUNHGDPPCL_M (15-60)$	\$2,567,344,172
(xxiv)	* NPV growth-adjusted non-health GDPPC loss, female ($NPVgNHGDPPCL_F (15-60)$) = Discounted $YLL_F (15-60) \times N_{t_Int\$} \times ETCD_F (15-60)$	\$1,575,521,485
(xxv)	* NPV growth-adjusted non-health GDPPC loss, male ($NPVgNHGDPPCL_M (15-60)$) = Discounted $YLL_M (15-60) \times N_{t_Int\$} \times ETCD_M (15-60)$	\$1,191,187,510
(xxx)	* NPV growth-adjusted total non-health GDPPC loss ($NPVgTNHGDPPCL_T (15-60)$) = $NPVgNHGDPPCL_F (15-60) + NPVgNHGDPPCL_M (15-60)$	\$2,766,708,995

*With growth-adjusted assumption where $n_t = GDPPC - d'(GDPPC - n_0)$.

Table 2. Variables and Data sources.

	Variable	Data Sources
1.	Saudi Average female LE at birth	World Health Organization (WHO), World Bank, United Nations for Population
2.	Saudi Average male LE at birth	World Health Organization (WHO), World Bank, United Nations for Population
3.	Undiscounted YLL for female (15–60)	Authors' computation
4.	Undiscounted YLL for male (15–60)	Authors' computation
5.	Discounted YLL for female (15–60)	Authors' computation
6.	Discounted YLL for male (15–60)	Authors' computation
7.	Total cancer deaths	Saudi Arabia Cancer Organizations and Resources
8.	Probability of dying between 15 and 64 years female (per 1 000 population)	Saudi Arabia Cancer Organizations and Resources
9.	Total cancer deaths among female (15–60) $TCD_M (15-60)$	Authors' computation
10.	Total cancer deaths among male (15–60) $TCD_F (15-60)$	Authors' computation
11.	Average age at death for female (15–60) – $AAD_F (15-60)$ AAD	World Health Organization (WHO)
12.	Average age at death for male (15–60) – $AAD_M (15-60)$	World Health Organization (WHO)
13.	Gross domestic product per capita (GDPPC)	World Bank
14.	Health expenditure per capita (HEPC (Int\$))	World Bank
15.	Non-Health expenditure GDP per capita (NHGDPPC)	Authors' computation
16.	Average inflation growth of HEPC (i)	Central Department of Statistics & Information of Saudi Arabia
17.	Continuous compounding factor for NHGDPPC (Female)	Authors' computation
18.	Continuous compounding factor for NHGDPPC (Male)	Authors' computation
19.	Discount rate, (r)	World Health Organization (WHO)

over the 23.1 and 21.7 discounted YLL respectively. Fig. 1 shows the growth-adjusted non-health GDP per capita loss due to cancer deaths among population aged 15–60 years.

Fig. 2 shows the discounted growth-adjusted non-health GDP per capita loss due to cancer deaths among population aged 15–60 years.

3.4. Sensitivity analysis

Our analysis presents useful relationships and interactions between various epidemiological and economic factors and reports a single summary outcome of

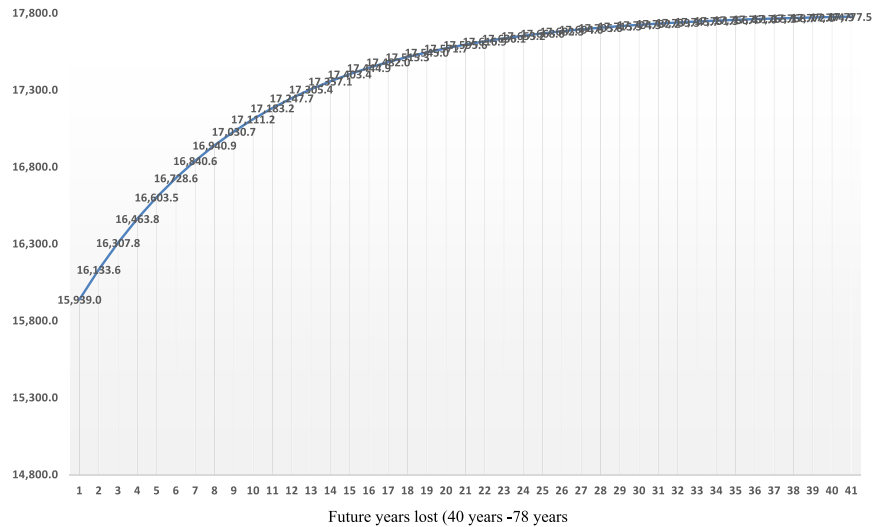


Fig. 1. Growth-adjusted Non-health GDP per capita Loss associated with future years of life lost (from 40 years to 78 years).

NPVNHGDPPC loss of cancer deaths. However, the interpretation of these results depends on the level of uncertainty in those factors [33]. Thus, it is important to account for uncertainty in health economic models [29]. The absence of reliable standard data on which to base economic evaluation and the existence of a range of estimates for the factors or parameter used compels one to account for uncertainty [34]. Thus, it is customary to establish whether various factors affect evaluation results or indirect cost. Table 3 shows sensitivity analysis where some of the factors

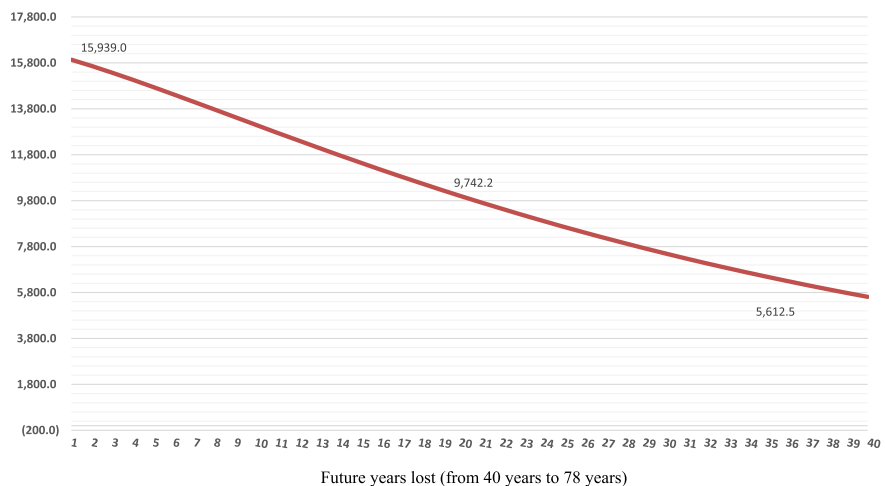


Fig. 2. Discounted growth-adjusted Non-health GDP per capita Loss (Int\$) associated with future years of life lost (from 40 years to 78).

Table 3. Input base factors.

	20% Reduction	Base (100%)	20% Increase
Discount rate, r	2.4%	3.0%	3.6%
PTCD	0.562	0.702	0.842
HEPC	\$1,489	\$1,861	\$2,233

considered in the computation are varied by $\pm 20\%$ in order to ascertain the robustness of cancer-related NHGDPPC loss to the economy.

This analysis assessed the impact of a range of values such as the proportion of total cancer deaths (PTCD_{15–60}), discount rate, and the value of health expenditure per capita (HEPC) on the model's outputs. We do so by demonstrating the relationship between the input values and the model's results using a threshold analysis.

Table 4 reveals the base case of \$2.767 billion NPVNHGDPPC Loss. While the reduction of PTCD by 20% reduced the indirect cost to \$2.213 billion, the increase of PTCD 20% raised the loss to \$3,320 billion. However, reduction of discount rate and HEPC by 20% increased the indirect cost to \$3.024 and \$2.773 billion respectively, representing a rise of 9% and 0.2% above the base case of \$2.767 billion. Fig. 3 depicts a threshold analysis and graphically illustrates the results of Table 4.

Table 5 further depicts adjusted sensitivity with the ranking of the parameters according to changes in NPVNHGDPPC loss when the different parameters are increased or reduced by 20%. The results reveal that PTCD_{15–60} exhibits symmetric range such that the absolute deviations from the base on either side are the same. In other words, 20% reduction or increase in the base rate of PTCD_{15–60}, for example, yields symmetric range, that is, the absolute value of the reduction in total loss equals to the absolute value of the increase in the loss. However, growth in the discount rate and HEPC better reveal reality given that a 20% reduction or increase results in asymmetric range.

In both cases, the absolute value of the reduction in total loss is greater than the absolute value of the increase in the loss. For instance, NPV NHGDPPC loss increases by \$258 million when discount rate was reduced by 20% compared to a reduction of \$225 million resulting from 20% increase in the rate (see Table 5).

Table 4. NPVNHGDPPC Loss with base factors loss (Int\$ millions).

	20% Reduction	Base (100%)	20% Increase
Discount rate, r	\$3,024	\$2,767	\$2,541
HEPC	\$2,773	\$2,767	\$2,762
PTCD rate	\$2,213	\$2,767	\$3,320

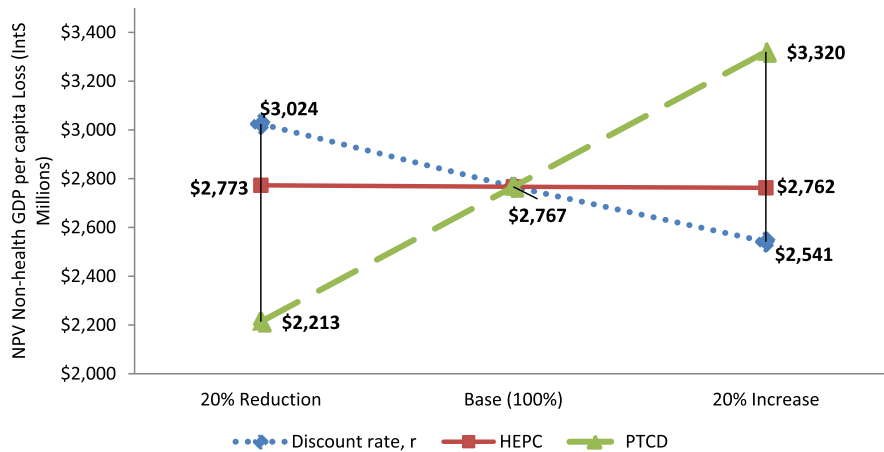


Fig. 3. NPV Non-Health GDP per Capita Loss Sensitivity (Int\$ millions).

Fig. 4 is a pictorial representation of Table 5 and depicts results of the impact of standardized range on NPV Non-Health GDP per Capita Loss. It is evident that ranking of the parameters according to changes in NPV NHGDPPC loss change when the different parameter assumptions are taken into consideration (20% reduction and 20% increase). Thus, sensitivity analysis of taking into consideration the assumption of 20% reduction or increase in the different parameters merely decrease or increase the value and magnitude of the loss below or above the base value by 1%–20%. However, it does not significantly reduce the loss or turn it into benefits, suggesting that the results are robust to the different parameter assumptions in estimating the loss to the economy.

The foregoing sensitivity analysis revealed that the results are sensitive but robust with respect to changes in the different factors or parameters assumptions used in estimating the loss to the economy. The deterministic tornado diagram (Fig. 5) shows the factors or parameters whose uncertainty drove the greatest effect on the NPV Non-Health GDP per Capita Loss.

Fig. 5 shows that much of the uncertainty in the determination of the value of the loss was accounted for by PTCD, while HEPC was responsible for the least variability. Thus, PTCD and discount rate or time preference are important in the computation of discounted YLL and hence total cancer-related non-health GDP per capita loss to the

Table 5. Adjusted Sensitivity with ranking of factors.

	20% Reduction	Base (100%)	20% Increase	Range	Rank
Discount rate, r	\$258	—	−\$225	\$483	2
HEPC	\$6	—	−\$4	\$10	3
PTCD	−\$553	—	\$553	\$1,107	1

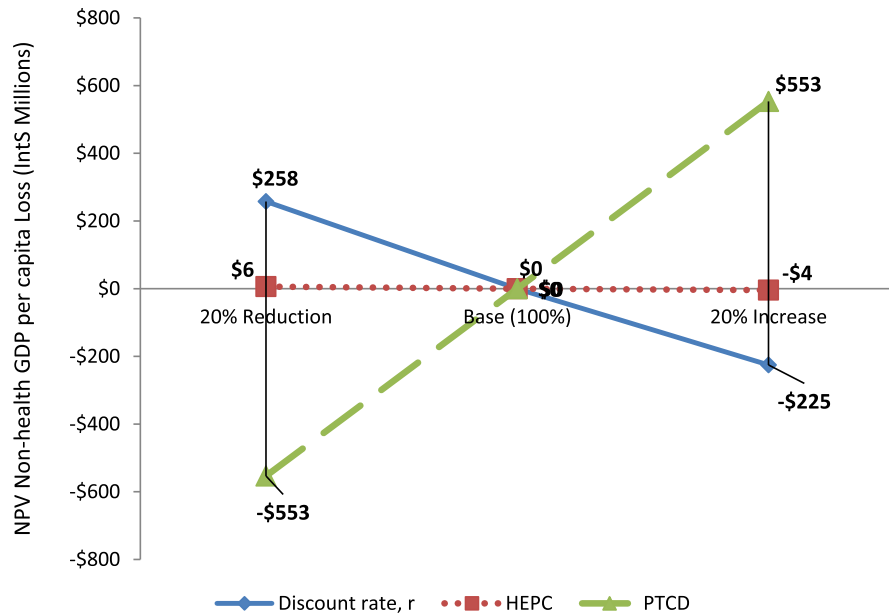


Fig. 4. NPV Non-Health GDP per Capita Loss Sensitivity (Int\$ millions).



Fig. 5. A Tornado Diagram depicting the sensitivity of NPV Non-Health GDP per Capita Loss (Int\$) with respect to epidemiological and economic factors.

economy. However, they should draw more attention from policymakers given that their impact on the loss associated with cancer also bears greater uncertainty.

4. Discussion

This paper presented the indirect cost of cancer in Saudi Arabia, that is, mortality indirect costs associated with lost productivity or burden related to YLL due to premature death among Saudi population aged 15–60 years. First, we estimated the net

present value of non-health GDP loss due to cancer deaths among Saudi population aged 15–60 years to be Int\$ 2.57 billion of which Int\$ \$1.46 billion (57%) was accounted for by females. However, when growth of NPVNHGDP loss with a finite and stable upper limit proxied by non-health GDPPC is taken into account over the discounted YLL per a death among female and male respectively, the total NPVNHGDPPC loss of cancer deaths was estimated to increase by 8% to Int\$ 2.767 billion of which Int\$ 1.576 billion (57%) was accounted for by females.

Our findings that the indirect cost cancer associated with lost productivity or burden related to YLL due to premature death are consistent with studies that examined the relationship between mortality costs and premature deaths from cancer across the globe, implying cancer deaths burden economies [7, 8, 9, 10, 11, 12, 13]. Our results are also consistent with studies showing growing burden for national systems attributable to cancer as major cause of disability, morbidity, and mortality [35].

In addition, these findings are consistent with the challenge of the shift in global burden of disease towards NCDs [36, 37, 38]. We also showed that the results are sensitive but robust to uncertainties in the considered epidemiological and economic factors, affirming the need for sensitivity analysis as expected in health economic models [33, 34].

Our analysis makes a unique contribution to evidence of economic burden, especially the indirect cost of premature deaths associated with cancer in Saudi Arabia. In particular, we monetize potential lost productivity or burden related to YLL due to premature death. Measuring the indirect cost of cancer in this manner is significant in that it informs cancer intervention from early screening, diagnosis, and better treatment, potentially minimizing mortality. Thus, the contribution of this paper is in documenting evidence of economic burden of cancer and might assist efforts directed at the development of cancer control actions in order to combat the scourge.

It is important to note several limitations, however. First, given monetary transactions do not reflect indirect cost associated with lost opportunities and productivity, there is need to treat NPV TNHGDPPC loss as an approximation. Second, the reported COI or indirect cost of cancer is a partial evaluation because the analysis did not include the morbidity costs, that is, the value of losses in productivity or output for people who are ill or disabled and cannot go about their productive lives. Third, the study excluded the direct costs associated with cancer intervention which for practical reasons mostly included in cancer costs along with mortality and morbidity [39].

5. Conclusion

Despite the data and measurement limitations mentioned, the results of this paper are expected contribute to evidence of economic burden, especially the indirect cost

associated with premature deaths due to cancer in Saudi Arabia. The results of this study can inform health system policymakers on the extent of the economic burden and development of cancer control actions and the wider debate on the shifting burden of disease. The huge indirect cost associated cancer deaths underscore the enormous economic loss associated with NCDs for the GCC [17] and urgent need for containing cancer controls and to fully implement recommendations of WHO Report on the Regional meeting on cancer control and research priorities [2].

Declarations

Author contribution statement

Omar Da'ar: Conceived and designed the experiments, analyzed and interpreted the data, wrote the paper.

Ashraf El-Metwally: Analyzed and Interpreted the data.

Raghib Abu-Saris: Contributed reagents, materials, analysis tools or data.

Abdul Rahman Jazieh: Conceived and designed the experiments, contributed reagents, materials, analysis tools or data.

Funding statement

This work was supported by King Abdullah International Medical Research (KAIMRC) under the umbrella of cost of cancer evaluation (Protocol # RC17/114/R).

Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

- [1] D. Bloom, D. Chisholm, E. Llopis, K. Prettnner, A. Stein, A. Feigl, From Burden to “Best Buys”: reducing the Economic Impact of Non-communicable Disease in Low-and Middle-income Countries. Program on the Global Demography of Aging, 2011 Oct. <http://ideas.repec.org/p/gdm/wpaper/7511.html>.

- [2] World Health Organization. Report on the Regional Meeting on Cancer Control and Research Priorities Doha, Qatar 20–22 October 2013. http://apps.who.int/iris/bitstream/handle/10665/116205/IC_Meet_Rep_2013_EN_15211.pdf?sequence=1.
- [3] A. Alwan, D.R. MacLean, L.M. Riley, E.T. d'Espaignet, C.D. Mathers, G.A. Stevens, D. Bettcher, Monitoring and surveillance of chronic non-communicable diseases: progress and capacity in high-burden countries, *Lancet* 376 (9755) (2010 Nov 27) 1861–1868.
- [4] C. Fitzmaurice, C. Allen, R.M. Barber, L. Barregard, Z.A. Bhutta, H. Brenner, D.J. Dicker, O. Chimed-Orchir, R. Dandona, L. Dandona, T. Fleming, Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the global burden of disease study, *JAMA Oncol.* 3 (4) (2017 Apr 1) 524–548.
- [5] C. Fitzmaurice, Burden of cancer in the Eastern Mediterranean Region, 2005–2015: findings from the global burden of disease 2015 study, *Int. J. Publ. Health* (2017 Aug) 1–4.
- [6] R. John, H. Ross, The Global Economic Cost of Cancer, in: C. American (Ed.), American Cancer Society, Atlanta, USA: Livestrong, 2010, pp. 6–17. Google Scholar.
- [7] K.R. Yabroff, C.J. Bradley, A.B. Mariotto, M.L. Brown, E.J. Feuer, Estimates and projections of value of life lost from cancer deaths in the United States, *J. Natl. Cancer Inst.* 100 (24) (Dec 17 2008) 1755–1762.
- [8] C.J. Bradley, K.R. Yabroff, B. Dahman, E.J. Feuer, A. Mariotto, M.L. Brown, Productivity costs of cancer mortality in the United States: 2000-2020, *J. Natl. Cancer Inst.* 100 (24) (Dec 17 2008) 1763–1770.
- [9] D.U. Ekwueme, H.W. Chesson, K.B. Zhang, A. Balamurugan, Years of potential life lost and productivity costs because of cancer mortality and for specific cancer sites where human papillomavirus may be a risk factor for carcinogenesis-United States, 2003, *Cancer* 113 (10 Suppl) (Nov 15 2008) 2936–2945.
- [10] C. Li, D.U. Ekwueme, S.H. Rim, F.K. Tangka, Years of potential life lost and productivity losses from male urogenital cancer deaths—United States, 2004, *Urology* 76 (3) (Sep 2010) 528–535.
- [11] W. Max, D.P. Rice, H.Y. Sung, M. Michel, W. Breuer, X. Zhang, The economic burden of prostate cancer, California, 1998, *Cancer* 94 (11) (Jun 1 2002) 2906–2913.

- [12] W. Max, D.P. Rice, H.Y. Sung, M. Michel, W. Breuer, X. Zhang, The economic burden of gynecologic cancers in California, 1998, *Gynecol. Oncol.* 88 (2) (Feb 2003) 96–103. Pubmed. PMID: 12586586.
- [13] T. Kitazawa, K. Matsumoto, S. Fujita, K. Seto, S. Hanaoka, T. Hasegawa, Cost of illness of the prostate cancer in Japan-a time-trend analysis and future projections, *BMC Health Serv. Res.* 15 (1) (2015) 453.
- [14] Murray CJ, Lopez AD, World Health Organization. The Global Burden of Disease: a Comprehensive Assessment of Mortality and Disability From Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020: Summary. <http://www.hup.harvard.edu/catalog.php?isbn=9780674354487>.
- [15] World Health Organization. Report on the Regional Meeting on Cancer Control and Research Priorities Doha, Qatar 20–22 October 2013.
- [16] World Health Organization, Global Status Report on Noncommunicable Diseases 2010, World Health Organization, Geneva, 2011. http://www.who.int/nmh/publications/ncd_report2010/en.
- [17] G. Chahine, J. Bitar, P. Assouad, S. AbiChaker, The \$68 Billion Challenge, Quantifying and Tackling the Burden of Chronic Diseases in the GCC, 2013. <https://www.strategyand.pwc.com/reports/the-68-billion-dollar-challenge>.
- [18] Gulf Centre for Cancer Registration Cancer Incidence Report: Gulf Cooperation Council Countries, GCCR, Riyadh (Saudi), 2014.
- [19] E. Ibrahim, S.B. Bin, L. Banjar, S. Awadalla, M.S. Abomelha, Current and future cancer burden in Saudi Arabia: meeting the challenge, *Hematol. Oncol. Stem Cell Ther.* 1 (4) (Oct-Dec 2008) 210–215. Pubmed. PMID: 20058475.
- [20] O.B. Da'ar, A.M. Al Shehri, Towards integration of health economics into medical education and clinical practice in Saudi Arabia, *Med. Teach.* 37 (Suppl. 1) (2015) S56–S60.
- [21] World Health Organization, WHO Guide to Identifying the Economic Consequences of Disease and Injury, World Health Organization, Geneva, 2009. Google Scholar.
- [22] D. Chisholm, A.E. Stanciole, T.T. Edejer, D.B. Evans, Economic impact of disease and injury: counting what matters, *BMJ* 340 (2010) c924. Pubmed. PMID: 20197323.
- [23] J.M. Kirigia, G.M. Mwabu, J.N. Orem, R.D. Muthuri, Indirect cost of maternal deaths in the WHO African Region in 2010, *BMC Pregnancy Childbirth* 14 (2014) 299.

- [24] J.M. Kirigia, F. Masiye, D.G. Kirigia, P. Akweongo, Indirect costs associated with deaths from the Ebola virus disease in West Africa, *Infect. Dis. Poverty* 4 (2015) 45.
- [25] M. Grossman, On the concept of health capital and demand for health, *J. Polit. Econ.* 80 (1972) 223–255.
- [26] B.A. Weisbrod, Costs and benefits of medical research: a case study of poliomyelitis, *J. Polit. Econ.* 79 (3) (1971) 527–544.
- [27] R.W.A. Sugden, *The Principles of Cost-benefit Analysis*, Oxford University Press, Oxford, 1985.
- [28] G.B. Chapman, A.S. Elstein, Valuing the future: temporal discounting of health and money, *Med. Decis. Making* 15 (4) (Oct-Dec 1995) 373–386.
- [29] W.S. Cartwright, in: Michael F. Drummond, Bernie O'Brien, Greg L. Stoddart, George W. Torrance (Eds.), *Methods for the Economic Evaluation of Health Care Programmes*, second ed., Oxford University Press, Oxford, 1997. *J Ment Health Policy Econ.* Mar 1 1999;2(1):43.
- [30] D.J. Torgerson, J. Raftery, Economic notes. Discounting, *BMJ* 319 (7214) (Oct 2 1999) 914–915. Pubmed. PMID: PMC1116731.
- [31] M.C. Weinstein, W.B. Stason, Foundations of cost-effectiveness analysis for health and medical practices, *N. Engl. J. Med.* 296 (13) (Mar 31 1977) 716–721.
- [32] World Development Indicators, The World Bank, 2014. <http://data.worldbank.org/data-catalog/world-development-indicators>. <https://datacatalog.worldbank.org/dataset/world-development-indicators>.
- [33] M. Taylor, *What Is Sensitivity Analysis?* Consortium YHE: University of York, 2009, pp. 1–8. Google Scholar.
- [34] H.M. Levin, P.J. McEwan, *Cost-effectiveness Analysis: Methods and Applications*, second ed., Sage, Thousand Oaks, CA, 2001.
- [35] M. Jakovljevic, C. Malmose-Stapelfeldt, O. Milovanovic, N. Rancic, D. Bokonjic, Disability, work absenteeism, sickness benefits, and cancer in selected European OecD countries—forecasts to 2020, *Front. Public Health* 5 (2017 Feb 27) 23.
- [36] S.R. Shrivastava, P.S. Shrivastava, J. Ramasamy, World Health Organization Recommends cost-effective interventions to control the rise in incidence of noncommunicable diseases in low-resource settings, *Int. J. Prev. Med.* 7 (2016) 54.

- [37] A.H. Mokdad, M.H. Forouzanfar, F. Daoud, et al., Global burden of diseases, injuries, and risk factors for young people's health during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013, *Lancet* 387 (10036) (June 11 2016) 2383–2401.
- [38] D.E. Bloom, E. Cafiero, E. Jané-Llopis, S. Abrahams-Gessel, L.R. Bloom, S. Fathima, A.B. Feigl, T. Gaziano, A. Hamandi, M. Mowafi, D. O'Farrell, The Global Economic Burden of Noncommunicable Diseases. Program on the Global Demography of Aging, 2012 Jan. http://www3.weforum.org/docs/WEF_Harvard_HE_GlobalEconomicBurdenNonCommunicableDiseases_2011.pdf.
- [39] P. Greenwald, J.W. Cullen, D. Weed, Cancer prevention and control, *Semin. Oncol.* 17 (4) (Aug 1990) 383–390.