

ORIGINAL RESEARCH

Cancer Incidence Trends From 1999 to 2015 And Contributions Of Various Cancer Types To The Overall Burden: Projections To 2030 And Extrapolation Of Economic Burden In Saudi Arabia

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Background: Cancer incidence in Saudi Arabia has increased for the last two decades, ratcheting up to global levels. The study aimed to analyze cancer trends and the contributions of various cancer types, forecast incidence, and estimate the economic burden in 2030.

Methods: A national-level cohort study utilizing the Data of Cancer Registry of patients who were diagnosed in 1999-2015. New cases in 2016-2030 were forecast and predicted based on 1999-2015 data. We used growth assumption and regression analysis to predict the trends of cancer cases. We assessed the contributions of cancer types to incidence trends. We carried forecasting of new cases and extrapolation of the potential economic burden. We conducted a sensitivity analysis of the cost of cancer with respect to changes in economic and epidemiologic factors.

Results: The findings suggest that the number of known cancer cases increased by 136% from 1999 to 2015 and is projected to rise by 63% in 2030. The forecast indicates female cases will account for higher number of cases and greater proportion increase. The future cost of all cancer types would be estimated at \$7.91 billion in 2015 value, of which \$3.76 billion will be attributable to care management and \$4.15 billion in lost productivity. With the assumption of growth of the aged-standardized incidence rate, the costs of care management and lost productivity are projected to be \$5.85 and \$6.47 billion, respectively in 2030, an increase of 56% in each component. The future undiscounted total estimated economic burden for the period 2015-2030 would be \$159.44 billion, of which 47.5% will be attributable to care management. Estimates were robust to uncertainty, but the 5-year prevalence of cancer survivorship would account for the greatest variability.

Conclusion: Our model showed an upsurge of cancer burden in terms of incidence and the potential economic burden, which may inform cancer control measures.

Keywords: cancer trends, the 2030 cancer burden projection, cancer economic burden, Saudi Arabia

Introduction

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Every sixth death in the world is due to cancer, making it the second leading cause of death after cardiovascular diseases. About 8.9 million people were estimated to have died from various forms of cancer in 2016.² Globally, breast cancer is the most prevalent form of cancer, followed by colon & rectum, and prostate cancer. While these are the top three cancer types across most countries, they tend to vary in their ranking across the world.

Cancer is ranked among the top four leading causes of death in the Eastern Mediterranean Region (EMR), with incidence expected to almost double by 2030.³ According to 2014 twelve-year cancer incidence report for the nationals of the Gulf Cooperation Council (GCC) States (1998–2009), Saudi Arabia accounted for three-quarters (75%) of cancer cases reported to Gulf Center for Cancer Control.⁴ According to Cancer Incidence Report of 2014, breast, colon, thyroid, and non-Hodgkin lymphoma were the most common in Saudi Arabia.⁵ According to various Saudi cancer incidence reports, cancer cases increased to 15,542 in 2015, a 137% increase from 1999 numbers.

Cancer incidence rates are increasing worldwide and are expected to further continue to rise over the next decades. The rate of increase in incidence and mortality varies across countries with a higher toll in the developing countries. Cancer remains a priority for intervention^{3,6} by the World Health Organization (WHO), the Regional Committee for the EMR, and national governments, including Saudi Arabia. While cancer incident rates in Saudi Arabia are lower than in Western countries, they are dramatically increasing owing, in part, to changes in lifestyle⁷ and the increasing use of tobacco.⁸ The dramatic increase in the incidence rates of cancer in Saudi Arabia is expected to ratchet up to global levels. Cancer trends and projection of future new cases will be of particular use in Saudi Arabia for informing budgetary, policy and development plans in line with Vision 2030, which aims to achieve major transformations in the Kingdom in all sectors especially health care. It is important to study the trends of the various types of cancer and the overall associated economic cost in order to provide an understanding of the extent of the burden and implications for the direct health and social care spending in Saudi Arabia. This study is expected to inform opportunities for current and future management of cancer. It is also expected to enlighten prospects for developing plans to innovate and organize efforts for control of cancer in terms of allocating resources, build capacity, and implement strategies to minimize the impact of the disease.

The purpose of this study is fourfold: 1) identify and analyze the overall cancer trends during the past three decades, 2) project cancer incidence in Saudi Arabia to 2030, 3) analyze the contributions of various cancer types to the overall burden, and 4) estimate economic burden of cancer by 2030. The overall future and present value of cancer cost in terms of both management care and lost productivity will by provide a perspective in order to

account for the share of total cancer cost in direct health and social care spending in Saudi Arabia.

Methods

This is a retrospective cohort study of patients of top cancer types and extrapolative forecasting of the future burden in Saudi Arabia using data from the Saudi Cancer Registry (SCR). SCR is a nationwide database and cases diagnosed between 1999 and 2015 were analyzed. Typically, the SCR reports accurate data as part of its mandate and serves as a resource for annual reports of new cases of cancer. All health facilities in the country periodically report newly detected cases of cancer to the SCR. The SCR reports data anonymously to comply with privacy, confidentiality, and protection of patients' rights. The data were publicly made available by SCR in aggregate form (webpage, www.chs.gov.sa). Although there may be underreporting of some cases, the SCR database is a population-based registry that is mandated by the law and the annual report will not be generated until all the hospitals reported their diagnosed cancer cases. Therefore, we believe the SCR data are the best available data to use for such an analysis.

We obtained ethical approval from King Abdullah International Medical Research Center, the Ministry of National Guard Health Affairs (MNGHA), and Alfaisal University, Riyadh, Saudi Arabia.

Statistical Analysis

Statistical analysis was carried out using the STATA statistical package (version 13, STATA Corporation, TX, USA) and Excel Version 10. We descriptively summarized the data. We used a constant growth of the cancer cases assumption to predict cancer cases estimates for the future years using linear regression analysis. Additionally, we carried out forecasting of new cases by predicting the 2016-2030 cases based on the 1999-2015 numbers. We modeled the new case in relation to year diagnosis by constructing a trend line because the reported cases showed an upward trend. Then, we forecast the existing by adding a trend line to existing data points to allow for extrapolation of future new cases. The forecast future values were based on the trend and the possibility of the regression line exhibiting other non-linearity characteristics were ruled out because of the linearity of data.

Extrapolation Of Cancer Costs

We used epidemiologic and economic data and assumptions from Saudi Arabia, comparable regional countries,

and international data to extrapolate, project, and estimate the costs of overall cancer cases. Extrapolations of the economic burden of diseases have been used in health economic evaluations. 9,10 In the absence of long-term data such as direct costs and lost productivity associated with a disease, temporal extrapolation over a longer time horizon is required.¹¹ We used purchasing power parity (PPP) for international comparison because it is a measure of the ratio of the prices in national currencies of the same good or service in different countries at the same point in time. 12 Typically, there is a PPP for every sector. However, PPP of health for Saudi Arabia was not available and therefore we used the general economy PPP. Integrating PPP into cost-of-disease studies provides a greater understanding of health care comparisons across countries.¹³ The United States often provides ideal data in these adjustments for international comparisons. Health expenditure per capita converted to the United States dollars (USD) PPPs are in fact among the most frequently quoted indicators for international comparisons and are usually presented in the form of a country ranking. 14 Additionally, the USA has predominantly privately produced health care system where purchases are not only relevant, but price indexes are used to create constant price-output measures for medical services. 13 Productivity changes are often ignored in countries where health care provided by the public sector. 13 Since health care in Saudi Arabia is largely financed by the public sector, the Kingdom will greatly benefit from such international comparisons.

Sensitivity Analysis

We used sensitivity analysis to assess the impact of a range of values of epidemiologic and economic factors on the future economic burden of cancer. These factors included aged-standardized incidence rate (ASR), non-health GDP per capita, the 5-year survival rate, health expenditure as a share of GDP, discount rate, and PPP. The absence of reliable standard data on which to base economic evaluation and the existence of a range of estimates for the aforementioned factors necessitates the accounting for uncertainty (13). Thus, sensitivity analysis is a methodology emphasized in health economic models (14).

Results

A total number of 15,542 new cancer cases were reported in 2015, up from 6592 cases in 1999, an increase of more than twofold (136%) over the 15-year period. Further analysis shows that the forecast of the known cancer

cases will increase to 19,460 by 2030, a rise of as much as 63% from the 2015 numbers. Over the same period, analyses of cases in terms of nationality and gender exhibit similar trends. For instance, the total number of known Saudi cases rose from 5076 in 1999 to 12,038 in 2015, an upsurge of 137% and this further projected to increase by 62% in 20,130. Similarly, the total known non-Saudi cases rose from 1516 in 1999 to 3504 in 2015, an upsurge of 131% and this further project to increase by 67% in 2030.

The total number of known male cases surged from 3367 in 1999 to 7270 in 2015, an upsurge of 116% and this is further projected to increase by 56% to 11,352 cases in 2030. The total number of known female cases increased from 3225 in 1999 to 8272 cases in 2015, a rise of 156% and this further projected to increase by 69% to 13,871 cases in 2030.

Although their absolute cases are much smaller than Saudis are, the forecast indicates a greater proportion increase for non-Saudis during the period 2016–2030. The forecast further indicates female cases (both Saudis and non-Saudis) will not only account for a significant number of cancer cases but also greater proportion increase during the period 2016–2030. There will be an increase in the known cancer cases of Saudis by as much as 63% in 2030 from the 2015 numbers. Figure 1 shows these analyses.

The analyses are limited to known cancer cases. Throughout the years, the known cases approximately represented 98.7% of all the reported cases. Therefore, the number of cases analyzed or projected is somewhat conservative and that the actual estimates could be slightly higher.

The Contribution Of Top ten Cancer Case By Type

The trend and projection for the top ten cancer cases are depicted in Figure 2. Although most cancer types are increasing in incidence, breast, colorectal, thyroid cancer, and non-Hodgkin's lymphoma account for the largest contributions to the increased rates. For instance, there were 2016 known new breast cancer cases reported in 2015, up from 578 cases in 1999. This was more than a threefold increase of 249% over the 15-year period. In 2030, breast cancer cases are projected to increase by 1.75 times from the 2015 numbers to 3539 cases.

For colorectal cancer, the known reported cases increased approximately 3.9 times from 376 cases in 1999 to 1465 in 2015. By 2030, the reported cases are further projected to rise

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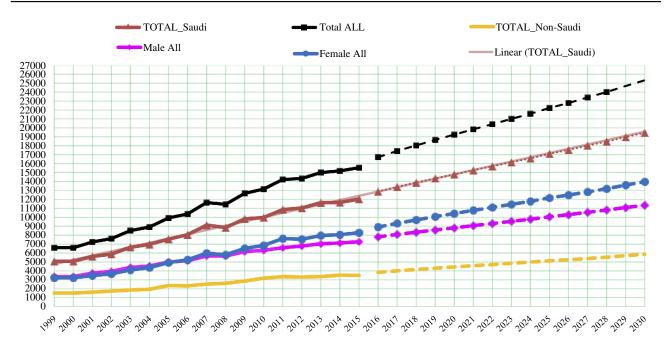


Figure 1 Total number of cancer cases by gender and nationality (1999–2030). The continuous lines are trends from 1999 to 2015. The dotted lines represent the projected cases (2016–2030).

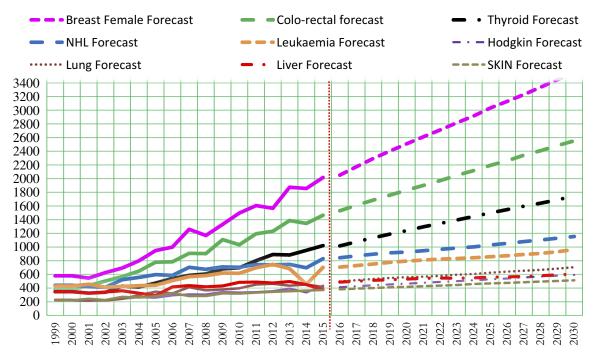


Figure 2 Top cancer cases by type (1999–2030). The continuous lines are trends from 1999 to 2015. The dotted lines represent the projected cases (2016–2030).

by 74% from the 2015 numbers. Although less dramatic, thyroid, and non-Hodgkin's lymphoma exhibit similar trends. The 1020 thyroid cases in 2015 represented a 194% increase from 347 cases in 1999. This is further projected to increase by 71% to 1746 cases in 2030. Non-Hodgkin's lymphoma cases increased by 88% in 2015, up from the 1999 numbers

and are projected to increase by an additional 39% in 2030. Figure 2 depicts these analyses.

The Economic Burden

In this section, we extrapolated the economic burden of all cancer cases using epidemiologic and economic factors

assumptions of the USA and Saudi Arabian data. The total economic burden of the top cancer types was estimated to be \$7.91 billion in 2015 values. Of this, \$3.76 billion was attributable to care management and \$4.15 billion in potential lost productivity. The estimated \$3.76 billion cost of cancer care management is the product of the ratio of the 5-year prevalence cancer survivorship per 100,000 populations, ratio of respective health care expenditure as share of gross domestic product (GDP), ratio of respective purchasing power parity (PPP), and \$147.2 billion, the 2015 USA cancer costs attributable to care management. The potential lost productivity of \$4.15 billion is a product of the ratio of respective non-health GDP per capita, the ratio of the respective 5-year prevalence cancer survivorship per 100,000 populations, the ratio of the respective purchasing power parity, and the 2015 USA cancer-related lost productivity of \$134.8 billion. Table 1 shows the parameterization and assumptions used.

Table 2 shows the future and present value estimated cost of top cancer types in terms of both care management and lost productivity. With the assumption of growth of ASR, the cost of all cancer attributable to care management is projected to be \$5.85 billion in 2030, up from \$3.76 billion in 2015. Similarly, potential lost productivity is expected to increase to \$6.47 billion in 2030, up from \$4.15 billion in 2015.

Based on the estimated cancer economic burden of 2015 and assumption of ASR growth, the total undiscounted future economic burden of top cancer types (combined cost of care management and lost productivity) in the period 2015–2030 would be \$159.44 billion (\$75.75 billion+\$83.69 billion) of which 48% is expected to be

related to care management and the rest in lost productivity. With 5% discount rate, the present value (PV) of these total future costs (2015–2030) is estimated at \$109.99 (\$52.25 billion+\$57.74 billion) billion, of which 48% is expected to be related to care management. PV is premised on the assumption of the time value of money.

Sensitivity Analysis

We conducted a sensitivity analysis to assess the impact of a range of values of the parameter assumptions used to compute the total base economic burden of 2015. These assumptions included ASR growth, non-health GDP per capita, the 5-year prevalence of cancer survivorship per 100,000 populations, health expenditure as a share of GDP, discount rate, and purchasing power parity (PPP) on the economic burden.

Table 3 shows the base case PV of the future economic burden of cancer (combined cost of care management and lost productivity), i.e. \$109.99 billion over the 2015–2030 horizons. A 20% reduction in the 5-year prevalence of cancer survivorship (per 100,000 populations), non-health GDP per capita, health GDP per capita, and ASR growth, would decrease the base total estimated burden by \$22 billion, \$11.55 billion, \$10.45 billion, and \$4.43 billion, respectively. A 20% increase in these parameters would symmetrically add the same amounts to the total burden during the same period.

Allowing PPP and discount rate to vary in similar fashion produce opposite effects. A 20% reduction in PPP and discount rate would increase the estimated PV economic burden by \$27.5 billion and \$7.84 billion, respectively. However, a 20% increase in these factors

Table I Computation Of Total Cancer-Related Economic Cost, Saudi Arabia (2015)

(i)	Future annual average ASR growth	3%
(ii)	Discount rate	5%
(iii)	Purchasing power parity USA	1
(iv)	Purchasing power parity, Saudi Arabia	1.378
(v)	Health expenditure as % GDP, United States	16.80%
(vi)	Health expenditure as % GDP, Saudi Arabia	5.80%
(vii)	Non-health GDP per capita, United States	\$46,908
(viii)	Non-health GDP per capita, Saudi Arabia	\$19,539
(ix)	Prevalence of cancer survivorship 5 years per 100,000 population, Saudi Arabia	192.8
(x)	Five-year prevalence of cancer survivorship per 100,000 population, United States	1,892.10
(xi)	Cancer costs attributable to care management. \$ billions, United States (2015)	\$147.20
(xii)	Cancer costs related to lost productivity \$ billions, United States (2015)	\$134.80
(xiii)	Estimated cancer costs attributable to care management. \$ billions, Saudi Arabia (2015)	\$3.76
(xiv)	Estimated cancer costs related to lost productivity \$ billions, Saudi Arabia (2015)	\$4.15
(xv)	Estimated total cancer cost, \$ billions (care management+lost productivity), Saudi Arabia	\$7.91

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Table 2 Future And Present Value Estimated Cost Of Top Cancer Types (Care Management And Lost Productivity)

Year		Cancer Care Managen	nent	Lost Productivity	Lost Productivity		
		Future Cost (\$ Billions) Undiscounted	Present Value Cost (\$ Billions) In 2015 Values	Future Cost (\$ Billions) Undiscounted	Present Value Cost (\$ Billions) In 2015 Values		
Beginning year=0	2015	3.76	3.76	4.15	4.15		
1	2016	3.87	3.69	4.28	4.07		
2	2017	3.99	3.62	4.40	4.00		
3	2018	4.11	3.55	4.54	3.92		
4	2019	4.23	3.48	4.67	3.84		
5	2020	4.36	3.41	4.81	3.77		
6	2021	4.49	3.35	4.96	3.70		
7	2022	4.62	3.28	5.11	3.63		
8	2023	4.76	3.22	5.26	3.56		
9	2024	4.90	3.16	5.42	3.49		
10	2025	5.05	3.10	5.58	3.43		
П	2026	5.20	3.04	5.75	3.36		
12	2027	5.36	2.98	5.92	3.30		
13	2028	5.52	2.93	6.10	3.23		
14	2029	5.68	2.87	6.28	3.17		
15	2030	5.85	2.82	6.47	3.11		
Total		75.75	52.25	83.69	57.74		

Table 3 Parameter Assumptions And Sensitivity And Adjusted Sensitivity Of The PV Economic Burden Of Cancer (\$ billions)

	Panel A	Panel A Parameter Assumptions								
		ASR Growth	Non-Health GDP Per Capita	Discount Rate	5-Year Prevalence Of Cancer Survivors/ 100,000	Health Expenditure % GDP	Purchasing Power Parity			
A	20% Reduction	2.4%	\$15,631	4.0%	154.24	4.6%	1.10			
В	Base scenario	3.0%	\$19,539	5.0%	192.8	5.8%	1.38			
С	20% Increase	3.6%	\$23,447	6.0%	231.36	7.0%	1.65			
	Panel B	Sensitivity Analysis Of PV Of Future Costs								
D	20% Reduction	\$105.56	\$98.44	\$117.83	\$87.99	\$99.54	\$137.49			
E	Base scenario	\$109.99	\$109.99	\$109.99	\$109.99	\$109.99	\$109.99			
F	20% Increase	\$114.66	\$121.54	\$102.94	\$131.99	\$120.44	\$91.66			
	Panel C	Adjusted Sensitivity Analysis								
G=(D-E)	20% Reduction	-\$4.43	-\$11.55	\$7.84	-\$22.00	-\$10.45	\$27.50			
Н	Base scenario									
I=(F–E)	20% Increase	\$4.67	\$11.55	-\$7.05	\$22.00	\$10.45	-\$18.33			
J=Abs (G-I)	Range	\$9.09	\$23.09	\$14.89	\$44.00	\$20.90	\$45.83			
K=Range of J	Rank	6	3	5	2	4	1			

would decrease the PV estimated burden by \$18.33 billion and \$7.05 billion, respectively during the same period.

It is evident from the above sensitivity analysis that when different parameter assumptions are taken into consideration (20% reduction and 20% increase), the burden

of all cancer appears to change. However, while there is a decrease or increase in the total costs below or above the base value, the changes do not significantly influence the actual estimates, suggesting that the results are robust to the different parameter assumptions.

Figure 3 shows the sensitivity of the estimated PV of the future economic burden of cancer (\$ billions) both in terms cost of care management and lost productivity with respect to epidemiologic and economic factors. The 5-year prevalence of cancer survivorship (per 100,000 populations), non-health GDP per capita, and health expenditure as a share of GDP would account for much of the variability, while lesser variability would be attributable to the discount rate and ASR growth.

Discussion

Utilizing reported data on all cancer cases between 1999 and 2015 Cancer Registry of Saudi Arabia, the purpose of this study was to identify and analyze the overall cancer trends, and project cancer incidence to 2030. Additionally, the study analyzed the contributions of various cancer types to the overall burden, and project economic burden of cancer by 2030. Generally, our results suggest increased cancer incidence over time in Saudi Arabia, with projections showing a significant increase by 2030. This result is consistent with the general global trends. For instance, the worldwide incidence of cancer could increase more than 75% by 2030, with the number of new cancer cases expected to double in the least developed countries, according to the results of a population-based study. 15 The rate of increase in cancer cases in the future varies across countries. Although rates of increase in incidence will be greater in Saudi Arabia, the trend is generally consistent with that of high-income countries such as

Germany¹⁶ by 2030. However, a study in Britain predicted that overall rates of cancer are projected to be stable or decline by 2030.¹⁷

For Saudi Arabia, these predictions are consistent with general trends reported in previous studies. ^{18,19} Our results further suggest that four types of cancer will contribute largest to the increases in incidence cases. Breast, colorectal, thyroid cancer, and non-Hodgkin's lymphoma account for the largest contributions to the increased incidence rates in Saudi Arabia in recent years. However, the latest global cancer incidence report indicates that lung, breast, and colorectal cancers were the top three types of cancers, contributing to 35.2% of all cancers. ²⁰ In terms, of prevalence, globally breast, colorectal, and prostate cancers are the most common and while these are the top three cancer types, however, they tend to vary in their ranking across the world. ²¹

The general increase in cancer over time is attributed to a variety of reasons, including increased caloric intake, ²² epidemiologic transitions, ^{23,24} and low screening at an early stage ²⁵ among other factors. In particular, breast cancer will remain the most common cancer diagnosed in the Kingdom and incidence will remain high, in part because of very low mammogram screening rates. ²⁶ Other factors include demographic shifts to the aging population, ²⁷ and modifiable lifestyle factors such as obesity, unhealthy diet, lack of exercise, and increasing prevalence of smoking. ²⁸

Our results suggest that the present value of the economic cost of cancer in Saudi Arabia in 2015 was estimated at \$7.91

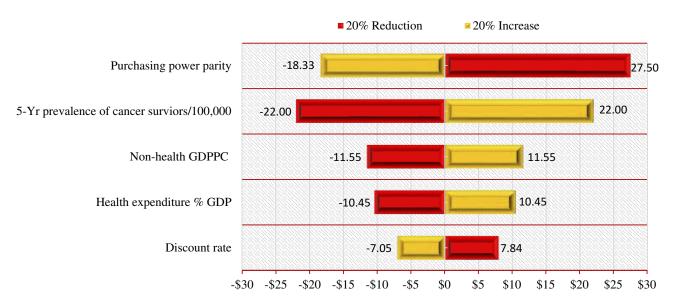


Figure 3 A tornado diagram depicting the sensitivity of present and future value of cost of cancer (management care and productivity lost) (\$ billion) with respect to epidemiologic and economic factors: 2015–2030.

billion of which \$3.76 in care management and \$4.15 billion in lost productivity. The economic cost of cancer is projected to increase by the year 2030 assuming growth of incidence rates. By the year 2025, the costs of cancer care management in Saudi Arabia would be projected to increase by 34% from the 2015 economic burden. By 2030, this is further projected to increase by 16% from the 2025 burden. These trends are consistent with the history and projections of developed countries such as the United States.²⁹ By comparison, a study³⁰ showed that in a 10-year period from 2010 to 2020, the costs of cancer care in the US were projected to increase to by 27%. That increase in cancer cost only reflected population changes, but when recent trends of declining incidence, improving survival, and increasing costs were assumed to continue, the estimated cost of cancer care would increase to by 39%.³⁰

Our analysis indicates that PV of the future economic burden of cancer in Saudi Arabia (in 2015 values) would account for 17% of direct health and social care spending of 2015. In comparison, a recent study on public health care financing and costs of cancer care across 28 EU member states indicated that the total cancer costs as a percentage of the total sum of public and private expenditure ranged from 3.9% to 7% with a mean of 6.06%.³¹ In the United States, cancer accounted for 7% of total expenditures in 2013.³² These analyses and comparisons indicate that the growth of the future economic burden of cancer in the decade and a half to come will outpace those in high-income countries.

Contributions And Limitations

The contribution of our study is that it simultaneously analyzed the overall cancer trends and contributions of various cancer types, projected cancer incidence and estimated the economic burden of cancer by 2030. This comprehensive analysis of the burden of all cancer types has not hitherto been carried out in Saudi Arabia consistent with Vision 2030. That said, it should be noted that the study has limitations. Our analysis utilized data from SCR where records may be prone to lack of harmonization from the various sources that feed the registry. The different sources might have led to underestimation of the incidence of the various types of cancer cases. Thus, there is a need to consider additional data from primary sources. Additionally, the extrapolation of the burden of all cancer in terms of both cost of care management care and lost productivity, was in part dependent on a variety of parameter assumptions derived from epidemiologic and economic data from comparable regional and international sources. In particular, using data from the USA

might have inflated projections on costs considering the high cost of health care compared to the Organization for Economic Cooperation and Development (OECD) countries owing to overdiagnosis and overtreatment. Although sensitivity analysis was carried out to apportion sources of uncertainty or variability in the data, extrapolation may yield more nuanced results, which require careful interpretation.

Conclusion

The purpose of this study was to identify and analyze the overall cancer trends from 1999 to 2015, project cancer incidence to 2030, analyze the contributions of various cancer types to the overall burden, and extrapolate the economic burden of cancer by 2030. Our findings suggest that total known cancer cases increased by 136% from 1999 to 2015 and are projected to rise by 63% in 2030. The forecast further indicates female cases (both Saudis and non-Saudis) will not only account for the total cancer cases but also greater proportion increase during the period 2016-2030. Although most cancer types increased over the period under study, breast, colorectal, thyroid cancer, and non-Hodgkin's lymphoma accounted for the largest contributions to the increased rates by as much as between two to more than threefolds. The costs of all cancer attributable to care management and potential lost productivity are estimated at \$3.76 billion and \$4.15 billion, respectively in 2015. With the assumption of growth of ASR, these costs are projected to reach \$5.85 billion and \$6.47, respectively in 2030, an increase of 56% for each component.

The dramatic increases in cancer cases and the enormous reported economic burden underscore the urgent need for containing cancer control and prioritization of research. Thus, the findings may provide a baseline for assessing the impact of public health interventions. The results may also inform current and future management of cancer and the development of plans to innovate and organize efforts for control of cancer in terms of allocating resources, build capacity, and implement strategies to minimize the impact of the disease.

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Disclosure

The authors report no conflicts of interest in this work.

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