EE527

The indirect costs and burden of vaccine-preventable cancers mortality in Middle East and North Africa (MENA) countries

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Background

- Cancer has a high clinical and economic burden, with ~10 million deaths globally in 2020.[1] In the Middle East and North Africa (MENA), cancer is the second-leading cause of death, with an economic cost ranging from USD $15-79 per capita.[2] Infections are responsible for approximately 13% of cancer cases worldwide. Human papillomavirus (HPV) and hepatitis B (HBV) are among the most important infections associated with cancer for which vaccines are now available. However, global vaccination rates for these cancer-causing infections remain low (~12% for HPV; 45% for HBV)[3,4]

Objectives

- To estimate the mortality impact and indirect cost of cancers potentially preventable by vaccination in selected MENA countries

Methods

Model structure

Inputs and assumptions

- A model was developed to estimate the indirect costs due to premature death associated with HPV- and HBV-related vaccine-preventable cancers. The model adopted a societal perspective for costs and only considered costs associated with productivity losses. Direct costs, such as treatment costs, were not considered. The model considered cancer-related deaths in a single year, with the potential costs considered up to the life expectancy
- The number of deaths and years of life lost (YLL) in 2019 from cancers associated with vaccine-preventable infections (ie, liver cancer caused by hepatitis B (ICD-10 C22), oral cavity (ICD-10 C00-08[a]), oropharynx (ICD-10 C09-10, C12-13[a]) and larynx cancer (ICD-10 C32), and cancer of the cervix uteri (ICD-10 C53) were sourced from the Institute for Health Metrics Evaluation (IHME) Global Burden of Disease.[5] Data from the IHME was stratified by country, age group, sex, and cancer type. All countries in the MENA region were included except for four countries (Kuwait, Occupied Palestinian Territory, Syria, and Yemen) due to data limitations
- Attributable fractions (AF) are the proportion of cancer-related deaths related to a specific infection and were applied to the number of deaths for each cancer type. AF for HPV-related cancers, stratified by cancer type, were sourced from de Martel et al.[6,7] Liver cancer mortality attributable to HBV infection was directly reported by IHME

[a]The ICD-10 codes provided reflect the disease areas covered by the original IHME mortality data. An additional modifier is applied to adjust the data to the subtype.

- Mortality due to oral cavity cancer in the IHME data set was aggregated with lip cancer, and oropharynx cancer mortality data aggregated with hypopharynx cancer. As lip cancer is not caused by HPV, lip cancer mortality was removed from the data using estimates on the global distribution of the cancer incidences from Shield et al.[8] In a similar manner, oropharynx data was adjusted using reporting from the WHO Cancer Today database[9,10]

Estimating the humanistic burden

- Mortality and YLL data was multiplied by the AF for each vaccine-preventable cancer based on published data to estimate the number of preventable deaths and preventable YLL
- Preventable YLL was divided by the number of preventable deaths to generate the average YLL/person (AYLL) to allow comparison between countries

Estimating the economic burden

- The value of productivity lost due to premature mortality was determined by calculating the value of YLL (VYLL), using the human capital approach. This was estimated by applying GDP per capita (World Bank; in USD) to YLL for each cancer, in each country. VYLL was discounted at a standard rate of 3% annually to obtain the present value of future costs

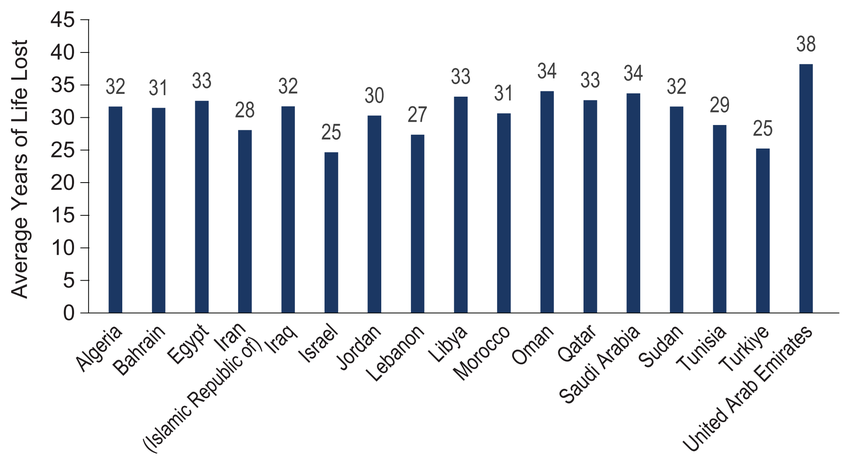
Scenario and sensitivity analysis

- Retirement ages, sourced from the World Bank,[11] were used to estimate the proportion of YLL that occurred when people would have been employed, had their death been prevented. This was applied to preventable YLL figures to determine years of productive life lost (YPLL). The value of YPLL (VYPLL) was then calculated in a similar manner to VYLL
- A deterministic sensitivity analysis (DSA) was performed to test the robustness of results to parameter uncertainty (GDP per capita and AF). Mortality and YLL inputs were also varied to their respective upper and lower bound estimates provided in the IHME data set

Results

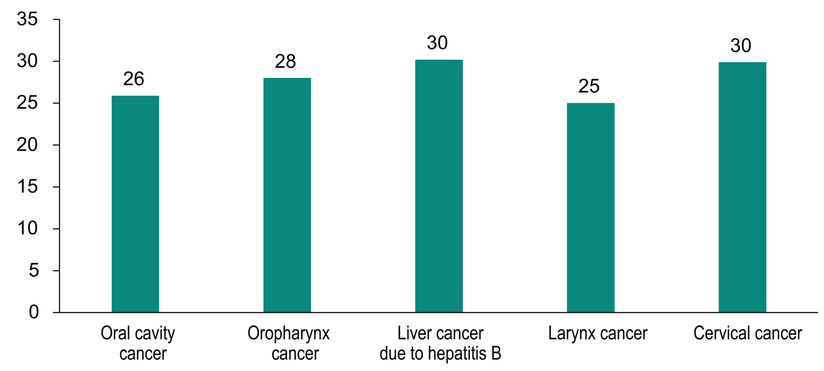
- In 2019, there were 11,645 vaccine-preventable cancer deaths and 348,632 YLL across MENA countries (**Table 1**). The estimated economic impact of premature mortality due to vaccine-preventable cancer deaths was over $1,688,821,605 across the MENA region, 76% of which was in the Middle East ($1,284,923,633). Liver cancer had the highest mortality burden (50% of total deaths), followed by cervical cancer (47% of total deaths)
- The United Arab Emirates (UAE) had the highest AYLL values (38), indicating the deaths caused by vaccine-preventable cancers in these regions occurred in younger age groups (**Figure 1**). This was followed by Oman and Saudi Arabia (34). Conversely, a low AYLL in Israel and Turkiye (25) indicate these deaths occurred in older age group

Figure 1. AYLL across all cancer indications, stratified by country



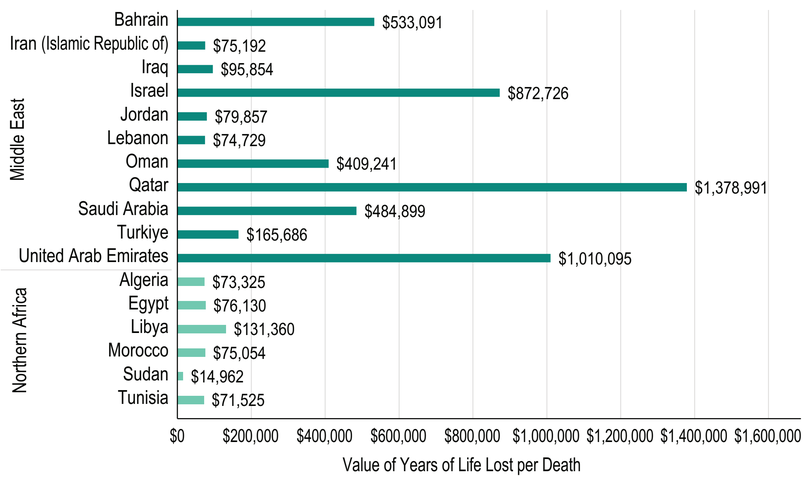
- AYLL by cancer indication (**Figure 2**), highlights liver cancer mortality as being associated with a higher burden of life-years lost per death, compared to other indications in this model

Figure 2. MENA AYLL per death, stratified by cancer type



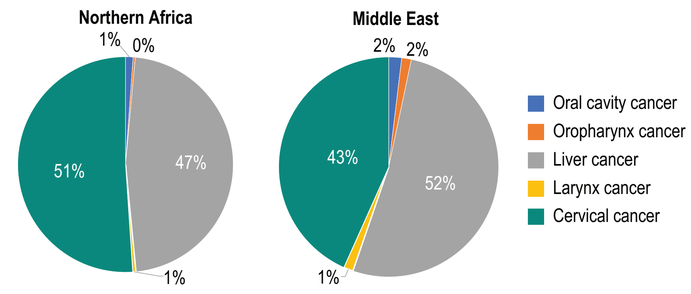
- The Middle East has a significantly higher VYLL per death compared to Northern Africa (**Figure 3**). The UAE, Qatar, Israel, and Bahrain in particular have much higher VYLL lost per death compared to countries in Northern Africa

Figure 3. Value of life lost per death, stratified by country



- The proportional burden of disease attributable to each cancer type was very similar between the Middle East and Northern Africa (**Figure 4**). In both regions, liver cancer led to the largest productivity loss (measured in VYLL) compared to other indications across MENA countries, closely followed by cervical cancer

Figure 4. Proportion of economic burden (measured in VYLL) imposed by each cancer type, stratified by MENA region



Scenario and sensitivity analysis

- The DSA showed that varying GDP per capita and AF resulted in a range of 10,329-12,279 deaths and $1.35-1.95 billion in productivity losses (VYLL) across MENA. Variations in MENA region deaths were driven by AFs, as the number of deaths was not dependent on GDP per capita
- When considering uncertainty in mortality and YLL inputs, a range of 6,988-18,093 deaths and indirect costs of $1.01-2.68 billion due to premature mortality were calculated
- When VYPLL was used, the economic burden due to HPV- and HBV-related cancer deaths in the MENA region was $246,884,477. This is a reduction of 85% in estimated costs across cancer indications

Table 1. Humanistic and economic burden of vaccine-preventable cancers, by country, in 2019

Region	Country	Deaths (total)	YLL (total)	AYLL	YPLL	VYLL ($)	VYPLL ($)
Middle East							
	Bahrain	25	798	31	106	$13,512,437	$2,518,105
	Iran (Islamic Republic of)	1,696	47,618	28	3,262	$127,555,185	$11,430,115
	Iraq	782	24,824	32	1,904	$74,987,402	$8,136,437
	Israel	195	4,814	25	723	$170,231,102	$32,260,684
	Jordan	115	3,486	30	239	$9,187,121	$866,587
	Lebanon	143	3,908	27	406	$10,671,554	$1,462,088
	Oman	58	1,973	34	233	$23,717,198	$4,084,781
	Qatar	47	1,533	33	31	$64,722,862	$1,809,130
	Saudi Arabia	482	16,244	34	1,850	$233,633,944	$39,120,315
	Turkiye	2,262	57,131	25	4,416	$374,843,784	$35,925,830
	United Arab Emirates	180	6,878	38	1,340	$181,861,043	$56,400,869
	Middle East total	**5,986**	**169,207**	**28**	**14,509**	**$1,284,923,633**	**$194,014,942**
Northern Africa							
	Algeria	967	30,630	32	2,676	$70,913,189	$8,869,176
	Egypt	2,256	73,433	33	6,542	$171,715,739	$21,889,397
	Libya	205	6,812	33	892	$26,946,220	$5,221,966
	Morocco	1,468	45,007	31	3,969	$110,183,817	$13,623,737
	Sudan	538	17,054	32	2,089	$8,052,259	$1,416,799
	Tunisia	225	6,489	29	556	$16,086,747	$1,848,459
	Northern Africa total	**5,659**	**179,425**	**32**	**16,723**	**$403,897,972**	**$52,869,535**
	MENA total	**11,645**	**348,632**	**30**	**31,232**	**$1,688,821,605**	**$246,884,477**

Discussion and conclusions

- Premature death from vaccine-preventable cancers leads to substantial YLL as well as productivity losses across included MENA countries. In 2019, ~32 people died per day due to potentially vaccine-preventable cancers, equating to a discounted productivity loss of over $4.63 million per day
- The Middle East was found to have a much greater productivity loss from potentially vaccine-preventable cancers than Northern Africa with 3 times greater VYLL per death. This difference is likely to be in part driven by GDP per capita. The AYLL for Northern Africa (32) was higher than for the Middle East (28), indicating that the age of death is younger in North Africa, and therefore that patients in the Middle East are likely to have access to more effective cancer care or have longer life expectancies
- While the conservative attitude to sexual behavior has generally contributed to the low prevalence of sexual infections, changing trends has yielded an increase in HPV infections across these countries in recent years.[12-14] In Northern Africa, cervical cancers accounted for 47% of the total productivity loss from vaccine-preventable cancers. These results combined with the changing trends in sexual infection and low vaccination rates emphasize the clear need for prioritizing HPV vaccination across MENA countries
- A relatively high coverage of HBV vaccination has been achieved across MENA countries, with a VCR of 77% or higher in all MENA countries for all three doses of the HBV vaccine.[15] Despite this, liver cancer due to HBV had a very high burden in Middle East and Northern African countries (47% and 52% of total VYLL, respectively). Although vaccines are effective in prevention of HBV and have led to a decrease in prevalence, there is a long delay until an effect in liver cancer reduction may be seen. Maintaining a high coverage rate is therefore essential to ensure a fall in liver cancer incidence over the coming decades
- The key strength of the model is the use of robust and publicly available data sets from reputable organizations used to parameterize this model. In addition, this model incorporates consideration of sex-dependent factors through GDP per capita, sex-specific retirement ages, and mortality YLL data stratified by sex. This supports valid and accurate modeling and increases the utility in guiding policy decisions. A scenario analysis was run to test the impact of only including productivity losses that accrued prior to retirement age. This approach was not taken in the base-case analysis, as GDP per capita is a productivity measure for everyone in the population (not just those of working age)
- The overall burden of disease is likely to be higher as several other HPV-related cancers (eg, anal or vaginal) were not included in this analysis. Furthermore, the model considers only costs related to productivity loss, and does not include direct medical costs involved in treating disease. Therefore, results presented here could be considered conservative of the total burden
- The model does not account for the impact of socio-demographic factors on disease incidence and burden. The model would therefore not reflect the impact of certain cancers being related to groups with higher/lower GDP per capita contributions on the economic value of productivity losses. In addition, the model does not account for the fact that patients diagnosed with cancer could be replaced in the workforce. While AYLL provides a useful measure for comparing countries with different levels of wealth, there is a wide range in life expectancy in the countries contained in the data set. Countries with higher life expectancy will naturally have a higher YLL lost per death even if the deaths are occurring at the same age
- The results of this analysis demonstrate the high mortality and economic burden associated with HBV- and HPV-related cancers, and the mortality and indirect costs that may be avoided by vaccination. These results may support decision-makers across the MENA region with prioritization of vaccination programs, due to the demonstrated cost offsets that may be achievable

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Disclosure

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