EE382

Burden and economic impact of vaccine-preventable cancer mortality in Europe

Bencina G[1]; Oliver E[2]; Brien H[2]; Meiwald A[2]; Hughes R[2]; Sabale U[3]; Ovcinnikova O[4]; Morais E[5]; Weston G[2]

[1]Center for Observational and Real-World Evidence, MSD Spain, Madrid, Spain; [2]Adelphi Values PROVE, Bollington, UK; [3]Center for Observational and Real-World Evidence, MSD Sweden, Stockholm, Sweden; [4]MSD (UK) Limited, London, UK; [5]MSD France, Lyon, France

Background

- Cancer has a high clinical and economic burden. In Europe, 1.3 million people died from cancer in 2020.[1] Annually, the cost of cancer in Europe has been estimated at €199 billion, with €50 billion from premature mortality[2]
- Global vaccination rates for hepatitis B virus (HBV) and human papillomavirus (HPV) remain low.[3,4] While effective vaccinations for HBV have existed for over 40 years, there were still 9,000 deaths due to HBV-related liver cancer in Europe in 2019.[5] Nine-valent HPV vaccines are available, providing the potential to protect against the 5% of all cancer cases that HPV is responsible for worldwide[6,7]

Objective

To support European policymakers in quantifying the burden associated with potentially vaccine-preventable cancers, and to help prioritize vaccination and increase vaccine uptake

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. Only costs associated with productivity losses were considered (no direct costs were included)
- The number of deaths and years of life lost (YLL) in 2019 from cancers associated with vaccine-preventable infections: 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 for 40 European countries.[8] Data from the IHME was stratified by country, age group, sex, and cancer type. The data from across Europe were categorized by sub-region: Eastern Europe, Northern Europe, Southern Europe, Western Europe[9]

[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.

- 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.[10,11] Liver cancer mortality attributable to HBV infection was directly reported by IHME
- The IHME mortality data aggregated oral cavity cancer with lip cancer, and oropharynx cancer with hypopharynx cancer. Lip cancer is not caused by HPV, so it was removed from the data using estimates on the distribution of the cancer incidence from Shield et al.[12] Oropharynx data was weighted based on WHO mortality data[13]

Estimating the humanistic burden

- Mortality and YLL data were multiplied by the AF for each vaccine-preventable cancer 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/death (AYLL) to allow comparison between regions

Estimating the economic burden

- The value of productivity lost due to premature mortality was determined by calculating the value of YLL (VYLL). GDP per capita (World Bank; in USD) was applied 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 (World Bank) 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 was performed by varying AFs and country GDP per capita together to understand the impact on results and identify key drivers of model estimates. Mortality and YLL inputs were also varied to their respective upper and lower bound estimates provided in the IHME data set

Results

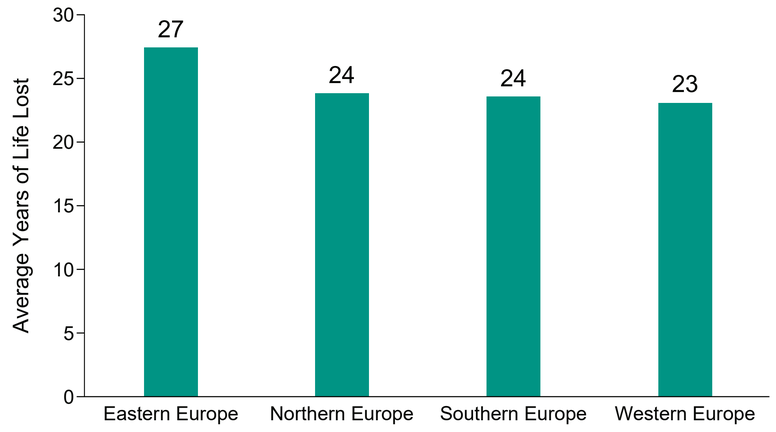
- In 2019, there were 31,906 vaccine-preventable cancer deaths and 790,893 YLL (30% in males) across European countries (**Table 1**). The estimated economic impact of premature mortality due to vaccine-preventable cancer deaths was €18,521,614,725, 45% of which was in Western Europe (€8,281,306,504). Cervical cancer had the highest mortality burden (61% of total deaths), followed by liver cancer (20% of total deaths)

Table 1. Humanistic and economic burden of vaccine-preventable cancers, in Europe by sub-region

Region	Deaths (total)	Deaths (% male/ female)	YLL (total)	YLL (% of total)	AYLL	YPLL	VYLL (€)	VYPLL (€)
Eastern Europe	11,253	26%/74%	308,179	39%	27	34,271	€2,994,074,392	€520,965,476
Northern Europe	4,088	27%/73%	97,238	12%	24	12,534	€3,775,450,059	€711,580,038
Southern Europe	7,446	34%/66%	175,322	22%	24	21,504	€3,470,783,770	€620,121,269
Western Europe	9,120	35%/65%	210,155	27%	23	26,666	€8,281,306,504	€1,501,819,982
European total	31,906	30%/70%	790,893	–	25	94,975	€18,521,614,725	€3,354,486,764

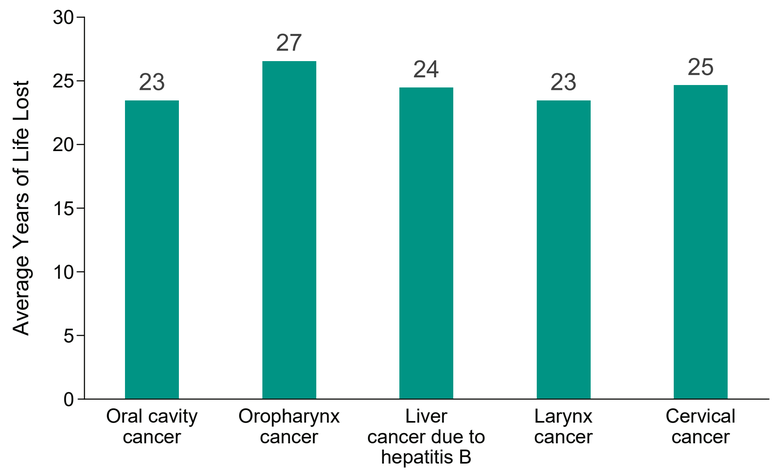
- Eastern Europe had the highest AYLL (27), indicating these deaths occurred at an earlier age on average than in Western Europe (23). Northern and Southern Europe also had similar AYLL values (24) (**Figure 1**)

Figure 1. AYLL due to vaccine-preventable cancers, stratified by European sub-regions



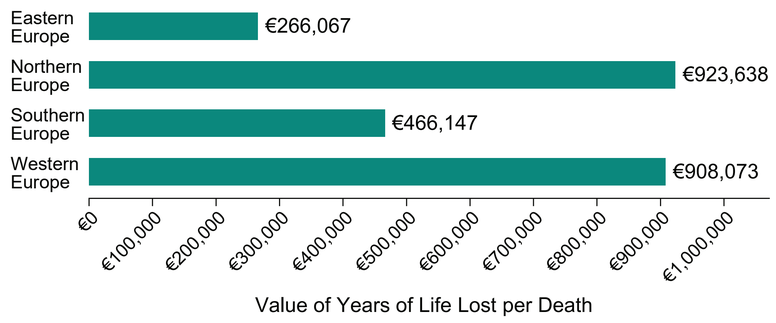
- Oropharynx cancer (**Figure 2**) had the highest AYLL (27) compared to other cancers

Figure 2. European AYLL, stratified by cancer type



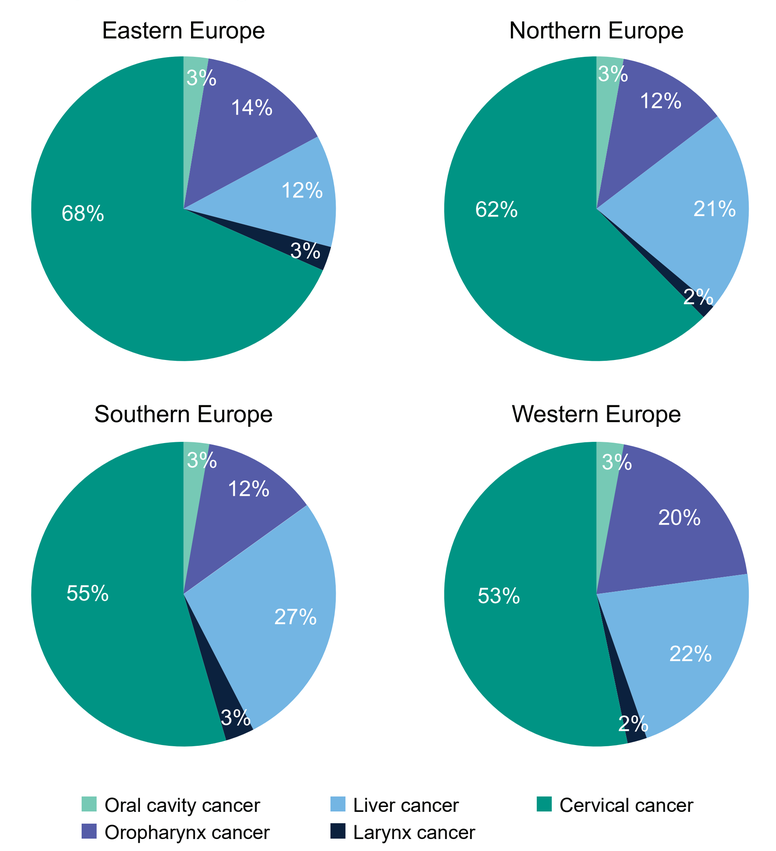
- Northern Europe and Western Europe had a significantly higher VYLL per death than the other two regions (**Figure 3**). While Western Europe had the highest VYLL overall, when this was standardized by the number of deaths, Northern Europe had the highest economic burden (€923,638 VLL/death)

Figure 3. Value of life lost per death, stratified by European sub-regions



- The proportion of disease attributable to each cancer type was very similar between the European sub-regions (**Figure 4**). In all sub-regions, cervical cancer led to the largest productivity loss (measured in VYLL) compared to other indications across European countries, closely followed by liver cancer. The proportional productivity loss associated with oropharynx cancer in Western Europe (20%) was much higher compared to other regions (12%-14%). There also was a large difference between the proportional productivity loss from cervical cancer in Eastern Europe (68%) and in Western Europe (53%)

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



Scenario and sensitivity analysis

- The DSA showed that varying GDP per capita and AF together led to a range of 26,314-34,179 deaths and €13.81-€21.82 billion in VYLL across European countries
- Consideration of upper/lower range of mortality inputs led to a range of 23,150-42,616 European deaths and a range in productivity cost of €13.68-€24.56 billion, due to premature mortality
- When VYPLL was used, productivity costs fell to €3,354,486,764 (82% reduction compared to VYLL)

Discussion and conclusions

- Premature death from potentially vaccine-preventable cancers led to substantial YLL and productivity losses across all European regions. In 2019, ~87 people died per day due to vaccine-preventable cancers, equating to a discounted productivity loss of over €50.74 million per day
- The Western and Northern European regions were found to have much higher VYLL/death than the other European sub-regions (**Figure 3**). This was likely driven by the higher GDP per capita associated with these regions. The AYLL for Western and Northern Europe occurred in older age groups compared to the other regions (**Figure 1**). Eastern Europe had a much higher AYLL; these deaths therefore likely occurred in younger age groups
- The results are reflective of the low HPV vaccination coverage found in the Eastern and Western European regions.[14] Eastern Europe had the highest number of deaths (11,253) and Western Europe had the highest productivity loss (€8,281,306,504). The model revealed a high burden of HBV-related liver cancer mortality (up to 27% of total productivity losses) despite the high coverage rate of HBV vaccination across Europe (91% for all three doses).[15] Although vaccines are effective in the prevention of HBV infection, there is a long delay until a reduction in liver cancer will be seen.[16] Maintaining high vaccination rates for both HPV and HBV across European countries should therefore be highly prioritized by policy makers
- This model relied on a robust and comprehensive data source from reputable organizations, maintaining reproducibility of results. Results were estimated for each of the 40 European countries included and then aggregated according to sub-region. This methodology avoided reliance on average economic inputs, increasing the validity of results. 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)
- Several other HPV-related cancers (eg, anal or vaginal) were not included in this analysis, so the economic burden will be underestimated. It should also be noted that these estimates could be considered a lower bound of the economic burden as the model focused on indirect costs – direct costs such as treatment were not captured – and only productivity costs accrued after death were considered
- The model relies on the AFs to estimate the number of deaths that could have been prevented with vaccination. Due to data limitations, case-related AFs were used (instead of mortality); this introduces the assumption that case-related and mortality-related AFs are equivalent. Furthermore, while this study seeks to provide a snapshot of the cost accumulated by vaccine-preventable cancers in 2019, the constantly changing landscape of vaccinated individuals and the pool of at-risk individuals prevents the model from capturing the true burden of disease
- The results of this analysis demonstrate the high mortality and economic burden associated with HBV- and HPV-related cancers in the European region. The implementation of effective vaccine uptake policies across Europe has the potential to lead to the elimination of HBV- and HPV-associated cancers

References

1. European Commission. A cancer plan for Europe. https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/promoting-our-european-way-life/european-health-union/cancer-plan-europe_en. Accessed September 18, 2023.
2. Hofmarcher T, et al. *Eur J Cancer.* 2020;129:41-49.
3. Spayne J, Hesketh T. *BMJ Open.* 2021;11(9):e052016.
4. World Health Organization. Immunization coverage. 2023. https://www.who.int/news-room/fact-sheets/detail/immunization-coverage. Accessed September 2023.
5. Cortesi PA, et al. *Lancet Public Health.* 2023;8(9):e701-e716.
6. de Sanjose S, et al. *JNCI Cancer Spectr.* 2018;2(4):pky045.
7. World Health Organization. Human papillomavirus and cancer. 2023. https://www.who.int/news-room/fact-sheets/detail/human-papilloma-virus-and-cancer#:~:text=HPV%20infection%20causes%20about%205,compared%20to%20women%20without%20HIV. Accessed September 18, 2023.
8. Institute for Health Metrics and Evaluation (IHME). Network GboD. Global Burden of Disease Study 2019 (GBD 2019). https://www.healthdata.org/research-analysis/about-gbd. Accessed April 28, 2023.
9. United Nations. Department of Economic and Social Affairs. Statistics Division: Geographic Regions. https://unstats.un.org/unsd/methodology/m49/. Accessed September 18, 2023.
10. de Martel C, et al. *Lancet Glob Health.* 2020;8(2):e180-e190.
11. de Martel C, et al. *Int J Cancer.* 2017;141(4):664-670.
12. Shield KD, et al. *CA Cancer J Clin.* 2017;67(1):51-64.
13. World Health Organization. Cancer Today: Estimated number of deaths in 2020, WHO Europe (EURO), both sexes, all ages (excl. NMSC). https://gco.iarc.fr/today/online-analysis-table?v=2020&mode=cancer&mode_population=who&population=900&populations=994&key=asr&sex=0&cancer=39&type=1&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&group_cancer=1&include_nmsc=0&include_nmsc_other=1#collapse-group-0-0. Published 2020. Accessed September 18, 2023.
14. Bruni L, et al. *Lancet Glob Health.* 2016;4(7):e453-e463.
15. World Health Organization. Hepatitis B vaccination coverage. 2022. https://immunizationdata.who.int/pages/coverage/HEPB.html. Accessed August 2023.
16. Al Zaabi M, et al. *EMJ Hepatol.* 2019. doi: 10.33590/emjhepatol/10313909.

Disclosure

This work was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Presented at ISPOR-EU; Copenhagen, Denmark; November 12-15, 2023.