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Costs of in- and outpatient respiratory disease and the seasonal influenza vaccination program in Armenia − 2020–2021

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Abstract

Background: Despite the substantial global impact of influenza, there are limited economic data to guide influenza vaccination programs investments in middle-income countries. We measured the costs of influenza and the costs of an influenza vaccination program in Armenia, using a societal perspective.

Methods: During December 2022 through March 2023, retrospective cost data were collected from case-patients and healthcare providers through structured questionnaires at 15 healthcare facilities selected through stratified sampling. Medical costs included medications, laboratory costs, laboratory and diagnostic tests, and routine health care service costs and direct and indirect societal costs were included. Vaccination program costs from the 2021–2022 influenza season were identified using accounting records and categorized as: planning, distribution, training, social mobilization and outreach, supervision and monitoring, procurement, and national- and facility-level administration and storage.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2024.05.055.

Results: The mean costs per episode for SARI and ILI case-patients were $US 823.6 and $US 616.57, respectively. Healthcare service costs were the largest direct expenses for ILI and SARI case-patients. Total costs of the 2021–2022 influenza vaccination program to the government were $US 4,353,738, with the largest costs associated with national- and facility-level administration and storage (30% and 65% respectively). The total cost per dose administered was $US 25.61 ($US 7.73 per dose for procurement and $US 17.88 for the marginal administration cost per dose).

Conclusions: These data on the costs of seasonal influenza prevention programs and the societal costs of influenza illness in Armenia may inform national vaccine policy decisions in Armenia and may be useful for other middle-income countries. Influenza vaccines, like other vaccine programs, are recognized as substantially contributing to the reduction disease burden and associated mortality and further driving economic growth. However, a formal cost-effectiveness analysis should be performed once burden of disease data are available.

Keywords

Armenia; Influenza; Vaccination; Vaccination program; Costing; Cost-effectiveness

1. Introduction

Influenza is a significant global concern due to its widespread transmission, substantial annual disease burden, and potential to cause pandemics. The World Health Organization (WHO) recommends yearly influenza vaccination, especially for high-risk and vulnerable groups such as health workers, children, the elderly, pregnant women, and people with chronic conditions [1–3]. The WHO estimates that over 44,000 people die annually of respiratory diseases associated with seasonal influenza in the WHO European Region [4]. Influenza surveillance in Armenia is conducted through laboratory testing and an established sentinel surveillance program. The National Center for Disease Control (NCDC) conducts specimen testing during influenza seasons with support from the NCDC laboratories and the US Centers for Disease Control and Prevention (CDC). This surveillance demonstrated that between 2017 and 2023, 20–43 % of influenza-like-illness (ILI) cases and 13–41 % of severe acute respiratory illness (SARI) cases were influenza positive using RT-PCR (Supplemental Materials, Figure 2). While these data demonstrate that influenza is a common cause of respiratory illnesses treated in clinics and hospitals, estimates of the rates of influenza in the population are lacking which limits estimates of national burden of disease and economic burden of disease in Armenia.

The seasonal influenza vaccination program was established in Armenia in 2010, after the 2009 A(H1N1) pandemic, and has been implemented since 2016 as a component of the National Immunization Program by the NCDC. During the 2021–2022 influenza season, quadrivalent inactivated vaccines were administered in Armenia. The Armenia National Immunization Program recommends vaccine for those at high risk for influenza and its complications, [5] so the national influenza vaccination program targeted pregnant women, health care workers, people with chronic disease, children under 5 years, adults ≥ 65 years, and special population groups, including children and service providers in orphanage homes, special educational institutions, residents and service providers in nursing homes, and members of the army. During the 2021–2022 vaccine campaign, 170,000 doses of

influenza vaccine were administered at government health facilities (150,000 procured by the Ministry of Health and 20,000 by the Partnership for Influenza Vaccine Introduction [PIVI]).

Despite the substantial global impact of influenza, there is a paucity of economic burden data to inform cost-effectiveness studies for influenza vaccine programs outside the United States. Furthermore, many economic studies have yet to analyze indirect costs or use laboratory-confirmed data on influenza-associated SARI or ILI cases to assess the cost of illness [6–10]. Like many other countries, Armenia requires cost of illness, and the cost of vaccine estimates to drive policy decisions. This evaluation was the first to assess the costs of influenza-associated illness in Armenia. The evaluation aimed to provide estimates of the societal costs of influenza-associated illness and the cost of conducting the seasonal influenza vaccination program for the Government of Armenia.

2. Methods

2.1. Healthcare service context in Armenia

Improving financial access to high-quality health care is essential to preventing morbidity and mortality from influenza in Armenia. However, influenza prevention and treatment are underfunded due to limited public resources, leading to high out-of-pocket payments for patients. While the right to health care is decreed in the Armenian Constitution, achieving universal health coverage in the country is a challenge due to donor funding transition, the COVID-19 pandemic, and regional conflicts. Armenia has a decentralized health care system, and the Ministry of Health is the single payer for publicly funded services covered under the Basic Benefits Package. There are three payment mechanisms for health care in Armenia, including services fully funded under the Basic Benefits Package, services partly subsidized by the state, and services paid fully out-of-pocket by the patient. As a share of total health spending, (84.8 % in 2019), out-of-pocket expenditures were the highest in the WHO European Region and far above the national average for European countries (28.7 %) and other UMICs worldwide (44.1 %) [11]. This results in low financial protection for vulnerable groups in the population. Data from the 2021 Integrated Living Conditions survey indicated that while there is adequate physical access to health services, financial accessibility remains a major issue for many Armenians [12].

Armenia reduced the total number of hospital beds and hospitals between 1990 and 2020 by 58 % and 32 %, respectively, due to funding challenges after the collapse of the Soviet Union. Rural hospitals were closed, and most general secondary hospitals were merged with outpatient polyclinics. Rural polyclinics function as structural departments of secondary hospitals and are permitted by State Order to “admit” ILI patients as daily patients. ILI patients sleep at their own homes and visit the polyclinic during the day for continued treatment as day inpatients. Therefore, the treatment costs of ILI patients are only slightly lower than the inpatient cost of a SARI patient who spends the night at a polyclinic throughout their treatment.

2.2. Sampling

Costs of medically attended influenza-associated illness were collected during the 2022–2023 influenza season using a stratified sampling approach. NCDC staff stratified enrolment and analysis by type of clinic (sentinel surveillance site vs. non-sentinel surveillance site) and further by case status of the patient (i.e., ILI vs. SARI). Data were collected from nine sentinel surveillance sites and six non-surveillance sites. The non-sentinel surveillance public sites were selected to capture a range of outpatient and inpatient costs across sites (patients at sentinel surveillance sites are assumed to incur lower costs per episode due to government subsidies, which would pose a challenge to capture the full cost per case-patient using retrospective data collection).

Patient-level costs data were collected primarily using a retrospective cohort method among individuals with SARI and ILI who sought medical treatment from the participating health care facilities. Patients from the surveillance and medical registry who received treatment for SARI or ILI during the 2022–2023 influenza season and whose signs and symptoms met the WHO case definitions (Supplemental Materials, Figure 1) were invited to participate in the survey after obtaining written consent or verbal assent. In some instances, while enumerators were checking the facility medical registries, they enrolled case-patients who were seen at the facility that day and met the case definition. Patients who had recovered from influenza during the current influenza season (2022–2023) were eligible for enrollment in the study. Since the amount of time that patients had recovered from influenza was not an eligibility criteria, the time since recovery for patients varied. Case-patients included those with ILI or SARI, and included both persons positive for influenza using RT-PCR testing and those not tested or found to be negative on testing. This was done to ensure sufficient samples size for the evaluation.

The sample size was determined based on equations in the WHO Manual of Estimating Economic Burden of Seasonal Influenza [13]. The number of sites and sample sizes within each site were determined based on desired precision of results (Z-score, 2.58; p, 0.05), resources available for data collection, the number of patients receiving treatment for SARI and ILI at each facility, and the expected variation in treatment costs among patients across facilities. Table 1 shows demographic and care-seeking behaviors of participants. Details on sampling are found in the Supplemental Materials.

Case-patients were sampled from three high-risk sub-populations within the total sample: children < 5 years, pregnant women, and adults > 65 years. The sample size was checked against key assumptions to ensure it was sufficiently powered to achieve the desired level of precision (see Supplemental Materials).

2.3. Data collection

Cost data were collected from December 2022 through March 2023 using standardized case-patient questionnaires to determine cost of illness and accounting records to assess the cost of Armenia’s vaccination program. The cost of illness per influenza-associated illness episode for inpatient ILI and SARI case-patients was evaluated separately and in aggregate.

NCDC staff interviewed case-patients by phone to collect direct and indirect medical and non-medical cost data.

Direct costs were defined as those incurred directly from seeking medical care for acute influenza-associated illness. Direct costs were categorized as medical and non-medical cost items. Medical costs included medications, laboratory costs, laboratory and diagnostic tests, and routine health care service costs (WHO-CHOICE estimate substituted for lack of patient recall of costs related to consultation and registration fees, hospital bed fees, hospital management costs, and any other routine health service costs incurred during visits to the health care facilities). Non-medical direct costs included transportation. Indirect costs were defined as productivity losses due to influenza illness of the case-patient and any household members, including caregivers (e.g., lost wages resulting from absenteeism). The questionnaire collected self-reported productivity losses for case-patients and their caregivers during the illness episode. These data are shown in Table 2.

Two questionnaires to capture inpatient and outpatient costs were adapted to fit the Armenian context from the WHO Manual for Estimating the Economic Burden of Seasonal Influenza [13]. A structured questionnaire was used to obtain health-seeking behavior information about the case-patient, socioeconomic information, and payment strategies for the treatment used by the household. Direct medical costs associated with inpatient care and direct medical costs incurred before and after hospital discharge were assessed; indirect costs were also assessed via the case-patient questionnaire (see Cost Analysis for a description of direct and indirect costs). Enumerators recorded all medications and laboratory tests that case-patients obtained during the illness episode. Interviews were also conducted with health care providers of each case-patient to collect information on direct medical costs of treatment that were either not listed in the medical registry or unavailable due to gaps in recall.

Additional data collection to determine the cost to the Government of Armenia for the 2021–2022 vaccination program was conducted from October 2022 through April 2023. Data was collected on costs incurred at national, province, municipal community, and health facility levels. Cost evaluation of the vaccine program from all public health care facilities that participated in the 2021–2022 vaccine program was conducted comprehensively (i.e., no sampling was performed). All 368 public facilities were included because costs were collected from the accounting records provided by the NCDC, no interviews with facility staff were conducted. Only costs incurred by the government were collected; private and faith-based health facilities were not included in the facility-level cost estimates for the vaccination program. This included financial expenditures made by the Armenian Ministry of Health, opportunity costs (i.e., the value of existing government resources used), and vaccine program-related donations, such as vaccine doses donated by the Task Force for Global Health's Partnership for Influenza Vaccine Introduction (PIVI) to the Ministry of Health.

2.4. Cost analysis

The cost per illness episode of medically attended ILI and SARI case-patients who sought care at public health facilities in Armenia was used to estimate the societal cost of

influenza-associated illness, including direct medical and non-medical costs, and indirect costs. Costs related to influenza surveillance were not included. Costs and productivity losses were evaluated as total days lost from work and school. The number of workdays lost by employed case-patients and caregivers due to illness or while caring for sick family members was collected. For daily-wage earners or homemakers, days lost because of illness or caring for sick family members were considered lost workdays.

Data analyses were aligned with the WHO Manual of Estimating Economic Burden of Disease and Choosing Interventions that are Cost Effective (WHO-CHOICE) [13,14]. Data on case-patient characteristics were described using proportions. Data for continuous variables (all costs) were described using means, standard deviations (SD), and ranges. Independent *t*-test or one-way analysis of variance were done to compare means, while medians were compared using Wilcoxon rank sum test or Kruskal-Wallis test as appropriate. Estimated means were calculated if the data were normally distributed (range or 95 % confidence interval (CI)); otherwise, medians (interquartile range (IQR)) were determined.

The cost per episode of influenza-associated illness was estimated as the sum of medical and non-medical costs, including costs of seeking health care prior to and after discharge from the current visit, and household loss of productivity. Out-of-pocket costs were estimated based on self-reported data from case-patients and caregivers at the time of interviews. Data on health care service costs (i.e., routine service delivery) were incomplete (i.e., most patients could not recall the cost), therefore WHO-CHOICE estimates were used in place of calculating routine health care service costs using actual data collected from the evaluation sites [14]. The human capital approach was used to calculate productivity loss for employed, daily wage earners, and homemaker case-patients and caregivers [15]. Total lost days were multiplied by the concurrent average monthly wage divided by 22 working days in a month to assign a monetary value to time and productivity losses. The average nominal wage rate for 2021–2022 in Armenia was 219,812 drams (or $US 477.85), according to the Statistical Committee of the Republic of Armenia [16]. The sum of productivity loss for each case-patient and caregiver was used to estimate the total indirect cost per episode for each case-patient. The total cost of each case of influenza was calculated as the sum of direct and indirect costs. Data from the case-patients and health facilities were entered into an Excel-based database and analyzed using STATA.

The cost of the vaccination program was calculated based on government expenditure to determine the economic cost of the program. Expenditures made by patients were excluded in the analysis of vaccination program costs. Vaccination program costs were assessed by program activity, including planning, distribution, training, social mobilization and outreach, supervision and monitoring, procurement, and national- and facility-level administration and storage. Each category included multiple cost elements, such as personnel, transportation, equipment, supplies, and materials. These aggregated categories were used by default, as a consequence of the cost categories in the retrospective cost data available from the NCDC and its accounting records. It was not possible to further disaggregate these costs.

Costs that were shared between influenza and other vaccine programs, such as refrigeration and storage and distribution costs, were divided by the proportion of the total number

of influenza vaccines procured. An allocation of 8.2 % of certain costs was calculated based on the number of influenza vaccines as a percentage of all vaccines procured in the country, including staff salary costs from the Department of Medical Immunobiological Preparations and electricity for refrigerators. A 5 % allocation was applied to other national storage costs. Facility-level vaccine administration and storage costs, which account for 65.1 % of the overall influenza vaccine program costs, included a per dosage allocation estimate of the cost of facility-level storage of vaccines, immunobiological preparations, electricity consumption, amortization of equipment, and salary costs of health care workers to administer influenza vaccines. The costs of planning, training, social mobilization, outreach, supervision, and monitoring were calculated based on the total spent on each program activity for the 2021–2022 influenza season. The total cost was used to calculate a unit cost per vaccine dose administered, with the number of influenza vaccine doses administered during the 2021–2022 season used as the denominator.

All costs were converted from their original currency (Armenian drams [AMD]) to 2022 US$ for analysis using a conversion rate of 392 AMD = $1 USD (average data collection period rate based on Central Bank of Armenia average foreign exchange rates from the data collection period (December 2022 to March 2023, the overlapping time horizon of the vaccine program cost data and the cost of illness data). The same exchange rate was used for the cost of illness data [17].

3. Results

3.1. Cost of influenza-associated illness

During the period of December 2022 to March 2023, a total of 915 case-patients were recruited into the evaluation and included in the final analysis. Case-patients had a median age of 4 (range of 0–99 years), and 48.4 % were female (Table 1). Among these 915 case-patients, 873 case-patients were SARI case-patients (<5 years old = 514, ≥65 years old = 107, pregnant women = 84, school-aged 5–7 years old = 115) and 42 ILI case-patients (<5 years old = 17, ≥ 65 years old = 2, school-aged 5–7 years old = 5). Approximately 50 % (n = 435) of SARI case-patients visited other health care providers before visiting the health care facilities included in this evaluation. The locations of the previous visit were public polyclinics (45.1 %), public hospitals (30.8 %), and pharmacies (19.8 %). Approximately 16 % (n = 150) of all case-patients had co-morbidities, the most common of which were hypertension (15 %), coronary heart disease (5 %), diabetes (4 %), and chronic obstructive pulmonary blockage (3 %).

The mean length of admission for SARI case-patients < 5 years old was 9.81 days (SD: 30.2) compared to 6.86 days (SD: 5.1) among case-patients ≥ 65 years old, and 13.2 days (SD: 40.3) among pregnant women. The mean length of admission for ILI case-patients < 5 years old was 7.82 days (SD: 3.3) compared to 6 days (SD: 4.2) among case-patients ≥ 65 years old. No pregnant ILI case-patients were included in the sample.

Among SARI case-patients, the mean number of case-patient workdays lost was 8.48 days (SD: 5.9), the mean number of caregivers' workdays lost due to the illness episode was 5.9 (SD: 4.48), and the mean number of case-patients' missed school days was 7.99 (SD:

5.97). The mean total value of total productivity lost, including the value of travel time, was $US 209.66 (SD: 145.87) for the SARI case-patient and $US 145.95 (SD: 110.71) for the caregiver. Among ILI case-patients, the mean number of case-patient workdays lost was 6.93 days (SD: 3.25), the mean number of caregivers' workdays lost due to the illness episode was 4.83 (SD: 1.17), and the mean number of case-patients' missed school days was 6.33 (SD: 4.08) (Table 2). The mean total value of total productivity lost, including the value of travel time, was $US 171.4 (SD: 80.28) for the ILI case-patient and $US 119.56 (SD: 28.92) for the caregiver.

All case-patients with influenza-associated illness incurred expenses (Table 3). The total mean cost to a SARI case-patient's household for influenza episode was $US 823.6 (SD: 2234.84), of which $US 779.89 were direct (SD: 2225.97) and $US 220.3 were indirect (SD: 192.57). The total mean cost to an ILI case-patient's household for influenza episode was $US 616.57 (SD: 279.76), of which $US 527.59 were direct costs (SD: 238.98) and $US 186.86 were indirect costs (SD: 86.66). Direct costs accounted for the largest proportion of total costs for both ILI and SARI case-patients. Health care service costs accounted for the largest proportion of direct costs, based on a product of days of admission and routine health facility service management costs estimated using WHO-CHOICE estimates. Only 42 of the 915 case-patients were ILI patients, which potentially lowers the accuracy of the cost per ILI episode result.

3.2. Vaccination program cost

The total cost of the 2021–2022 program including vaccine procurement was $US 4,353,738. The greatest proportion of costs was the facility-level administration and storage ($US 2,833,961 [65.09 %]) followed by national-level vaccine procurement ($US 1,314,530 [30.19 %]), and social mobilization and outreach ($US 120,438 [2.77 %]). The total unit cost per dose administered was $US 25.61. Since the average cost of purchase per vaccine (from the manufacturer) during the 2021–2022 influenza season was $US 7.73, the marginal administration cost per dose was $US 17.88. The total unit cost per dose administered $US 25.61 is the sum of the cost of planning ($US 0.03 per vaccine dose); distribution ($US 0.03 per vaccine dose); training ($US 0.09 per vaccine dose); social mobilization and outreach ($US 0.71 per vaccine dose); supervision and monitoring ($US 0.10 per vaccine dose); national-level vaccine administration and storage ($US 0.26 per vaccine dose); facility-level administration and storage ($US 16.67 per vaccine dose); and procurement ($US 7.73). As mentioned above, these aggregated categories were used by default, as a consequence of the cost categories in the retrospective cost data available from the NCDC and its accounting records. It was not possible to further disaggregate these costs. Table 4 shows the costs of the 2021–2022 influenza vaccination program to the Government of Armenia.

Based on vaccine coverage per risk group (Supplemental Materials, Table 3), the cost per vaccine dose per risk group is $3.84 per vaccine dose (for children aged from 6 months to 5 years), $0.03 per vaccine dose (for pregnant women); $7.25 per vaccine dose (for people over 65 years); $11.19 per vaccine dose (for people with underlying chronic medical conditions); $1.08 per vaccine dose (for healthcare providers); $0.74 per vaccine dose (for special groups of the population, including children and service providers in orphanages,

special educational institutions, residents of nursing homes and service personnel); and $1.15 per vaccine dose (for military recruits).

4. Discussion

The mean cost per illness episode for a SARI case-patient in Armenia is similar to those from other UMICs; however, the mean cost per illness episode for an ILI case-patient in Armenia is higher than those in other UMICs (which ranged from $US 7.24 to $US 322.62) [7,9]. This high cost is likely due to guidelines in Armenia that allow ILI case-patients to be treated as day inpatients, resulting in greater medical expenses and productivity losses due to work and school absenteeism for ILI case-patients and caregivers. The findings of this evaluation indicate that the costs to ILI case-patients and their households, both direct and indirect costs as well as productivity losses, are a substantial economic and social burden to the population of Armenia.

It is difficult to compare the total unit cost per influenza vaccine dose administered to other UMICs as only one other similar evaluation was reported in the *meta*-analysis published in 2023 (covering evidence from 2012 to 2021) [10]. However, in several studies included in the *meta*-analysis, vaccine procurement was the biggest contributor to overall costs, while the results from Armenia found that facility-level administration and storage were the highest contributing factor.

Cost of illness and vaccine delivery costing studies play an important role in providing policymakers with valuable evidence to inform vaccine introduction, resource allocation, introduction, and delivery. Global evidence suggests that influenza vaccines offer value-for-money [10]. These findings suggest that the influenza vaccine, at a cost of $25.61 per dose administered could offer a substantial cost-savings over influenza treatment, at a cost of over $616.57–823.6 per episode depending on level of severity. However, a formal cost-effectiveness analysis should be performed to estimate the cost-effectiveness in terms of cost per case averted once additional evidence on the burden of disease in Armenia is available.

The WHO Burden of Disease manual is being updated to include a chapter about how to estimate the disease burden averted through influenza vaccination [18]. In countries where influenza programs are in place, such as Armenia, estimates of the burden averted will demonstrate the value of existing vaccination programs, providing valuable information to economic evaluations such as the one presented in this paper. A newly developed tool to conduct this estimate, has been recently used to estimate averted illnesses from influenza vaccination in El Salvador, Panama, Peru, [19] and Kenya [20] between 2011–2023. This new evidence illustrates that influenza vaccination campaigns prevent hundreds of thousands of influenza-associated illnesses and hospitalizations (and related costs) [19,20].

A cost-effectiveness analysis (in terms of cost per case averted) would combine this data on cost of illness and cost of vaccination with disease burden and impact of the vaccine program. The cost of influenza vaccine delivery relative to the considerable costs borne by case-patients and their households observed in this evaluation underscores the

significance of ensuring access to affordable influenza vaccines in upper-middle-income countries (UMICs) such as Armenia to reduce economic and social losses resulting from influenza-associated illness.

This evaluation provides policymakers in Armenia with important knowledge about the economic benefits of seasonal influenza vaccination for consideration when allocating limited resources to public health programs and important inputs to calculate the cost-effectiveness or cost-benefit of the influenza vaccine. Cost per dose data from this evaluation can be used to inform program expansion in Armenia, particularly targeting high-risk groups susceptible to influenza-associated complications and hospitalizations. Furthermore, these results are highly relevant to investment decisions for vaccine programs in Armenia in the context of financial constraints resulting from the COVID-19 pandemic as well as co-circulation of influenza and COVID-19 and can inform the development of a comprehensive strategy to address both diseases. Further evaluation of shared costs of vaccine programs would provide crucial evidence on the efficiency and, ultimately, the cost-effectiveness of integrated vaccine program implementation and co-administration of influenza vaccine across the life course.

5. Limitations

The findings from this evaluation can be used to calculate the cost-effectiveness of the influenza vaccine in Armenia as part of a future investigation. This is an important evidence gap, a barrier to policy decision-making, and ultimately to vaccine use in LMICs and UMICs [10]. Nevertheless, a broad understanding of the societal cost of illness is an important step toward advocating for greater investment in influenza vaccines. Although the sampled facilities included a broad selection of both inpatient and outpatient facilities, due to practical constraints during data collection, 41 of the 42 ILI case-patients were collected from one facility. With any retrospective data collection there is a chance for recall bias. Though this was minimized as much as possible by enrolling patients who were recovered during the current influenza season to collect information on the type of care sought (where, from whom), and medical, and non-medical costs.

Additionally, NCDC staff assumptions of estimates of certain vaccine program cost elements were used, and these retrospective, subjective assumptions may have introduced biases and resulted in either over- or under-estimation of costs. However, estimates were provided by vaccine program management staff familiar with the resources needed to maintain the influenza vaccination program. Cost estimation did not include the costs associated with COVID-19 vaccine delivery; these costs were incomplete at the time of the evaluation as COVID-19 vaccine delivery occurred during this evaluation’s data collection period. Cost estimates may have been affected as a result. Despite these limitations, the evaluation findings provide valuable insights into the economic burden of seasonal influenza and the costs of vaccine delivery in Armenia.

6. Conclusion

The evaluation provides key evidence for policymakers to assess the cost-effectiveness of seasonal influenza vaccination programs in Armenia. Further, the findings may inform investment decisions and may be applicable not only to Armenia but informative for other UMICs facing similar challenges. Further research, including clear estimates of the national burden of influenza, would allow for more precise cost-effectiveness estimation and provide additional evidence to inform policy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

Data will be made available on request.

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Table 1

Demographic and care-seeking characteristics of respondents with influenza-associated illness in Armenia, December 2022-March 2023.

Variable	All data (N = 915)	ILI (N = 42)	SARI (N = 873)
Sex of case-patient, n (%)			
Male	472 (51.6 %)	33 (78.6 %)	439 (50.3 %)
Female	443 (48.4 %)	9 (21.4 %)	434 (49.7 %)
Age of case-patient or risk group, n (%)			
< 5 years	531 (58 %)	17 (40.5)	514 (58.9 %)
≥ 65 years	109 (11.9 %)	2 (4.8 %)	107 (12.3 %)
Pregnant women	84 (9.2 %)	–	84 (9.6 %)
Sought care prior to this hospitalization/outpatient visit, n (%)	436	1 (4.8 %)	435 (49.8 %)
Pharmacy		Not enough data	86/435 (19.8 %)
Private hospital			16/435 (3.7 %)
Public hospital			134/435 (30.8 %)
Public polyclinic			196/435 (45.1 %)
Traditional healer			3/435 (0.7 %)
Length of admission in days, mean (standard deviation)			
< 5 years	9.75 (29.7)	7.82 (3.3)	9.81 (30.2)
≥ 65 years	6.84 (5.04)	6.0 (4.2)	6.86 (5.1)
Pregnant women	13.2 (40.3)	–	13.2 (40.3)
Health care facility, n (%) of case-patients			
Arabkir MC, Yerevan			40 (4.6 %)
Armavir MC			90 (10.3 %)
Armenia RMC			50 (5.7 %)
Artashat MC			40 (4.6 %)
Ijevan Poliklinik			40 (4.6 %)
Ijevan MC			71 (8.1 %)
Kapan MC		41 (97.6 %)	79 (9 %)
Masis MC			50 (5.7 %)
Nairi MC			40 (4.6 %)
Poliklinik # 17			41 (4.7 %)
Poliklinik # 20		1 (2.4 %)	19 (2.2 %)
Surb Grigor Lusavorich MC			60 (6.9 %)
Surb Astvacamayr MC			100 (11.5 %)
Vanadzor MC			81 (9.3 %)
RIRHPOG			72 (8.2 %)

Table 2

Days lost from work and school of case-patients and caregivers (productivity losses $US).

	ILI			SARI		
Expenditure item	**n**	**Mean (SD)**	**Range**	**n**	**Mean (SD)**	**Range**
Case-patient missed workdays due to illness	14	6.93 (3.25)	(2 – 15)	82	8.48 (5.90)	(3 – 40)
Number of caregiver workdays lost due to illness	6	4.83 (1.17)	(3 – 6)	100	5.90 (4.48)	(1 – 30)
Case-patient missed school days due to illness	6	6.33 (4.08)	(3 – 14)	85	7.99 (5.97)	(0 – 25)
Value of total productivity lost to case-patient[1]	14	171.4 (80.28)	(49.47 – 371.06)	82	209.66 (145.87)	(74.21 – 989.5)
Value of total productivity lost to caregiver[2]	6	119.56 (28.92)	(74.21 – 148.42)	100	145.95 (110.71)	(24.74 – 742.12)

[1,2]Includes cost of missed work and value of travel time.

Table 3

Overall costs ($US), including direct and indirect costs for influenza-associated illness in Armenia, December 2022-March 2023.

		ILI			SARI		
Expenditure Item		**n**	**Mean (SD)**	**Range (min-max)**	**n**	**Mean (SD)**	**Range (min-max)**
Pre-visit costs	Health care prior to hospital/clinic visit	0	Not enough information	N/A	255	89.63 (269.60)	(1.28 – 3035.71)
Facility-based medical costs	Medications and laboratory costs[1]	21	62.56 (36.73)	(20.41– 178.57)	211	25.62 (69.82)[2]	(1.25 – 742.35)
	Transportation costs[3]	39	1.7 (0.76)	(0.26 – 4.1)	528	3.99 (4.6)	(0.01 – 42.09)
	Health care service costs[4]	42	493.23 (228.87)	(77.01 −1078.15)	873	739.03 (2230.9)	(77.01 – 28416.86)
	Other out-of-pocket costs	41	37.95 (19.32)	(12.62 – 102.04)	495	281.77 (309.82)	(2.55 – 2997.45)
Follow-up Costs	Health care after discharge from hospital/clinic visit (mean, SD)	1	Not enough information	N/A	220	47.42 (92.83)	(1.27 – 853.31)
Total direct cost		**42**	**527.59 (238.98)**	**(131.86 – 1115.14)**	**872**	**779.89 (2225.97)**	**(1.27 – 28482.68)**
Indirect cost [5]		**20**	**186.86 (86.66)**	**(59.32 – 444.9)**	**173**	**220.3 (192.57)**	**(29.66 – 2076.18)**
Total cost per illness episode		**42**	**616.57 (279.76)**	**(175.7 – 1263.43)**	**872**	**823.6 (2234.84)**	**(3.83 – 28601.31)**

*All costs presented in U.S. Dollars; 1 US$=392 Armenian drams (2022).

[1]Includes a combination of medications and laboratory fees and costs. In many cases these were not broken out per case-patient, so they have been combined to avoid duplication. The wide range seen here is mainly due to the difference in number of days of admission (and associated medication and laboratory costs per length of admission).

[2]The mean medications and laboratory costs were higher for ILI case-patients than SARI case-patients, which is expected due to higher visibility of these costs for ILI case-patients and reliance on self-reporting.

[3]Includes round-trip expense for case-patient from home to hospital and caregivers' travel expense for inpatient/hospital visits.

[4]Based on routine health facility service management costs (equipment maintenance, utilities, stationary, etc.) from WHO-CHOICE estimates. This estimate was substituted as many case-patients could not recall the consultation costs or other routine health service costs paid.

[5]Includes productivity losses (product of workdays loss), lost profits, and value of unpaid sick leave/cost of sick days.

Table 4

Cost of the 2021–2022 Influenza Vaccination Program ($US) to the Government of Armenia.

Program Activity	Cost (USD)	%	Cost per dose administered (USD)
Planning	5,096	0.12 %	0.03
Distribution	4,316	0.10 %	0.03
Training	15,737	0.36 %	0.09
Social mobilization & outreach	120,438	2.77 %	0.71
Supervision & monitoring	16,294	0.37 %	0.10
National-level administration & storage[1]	43,367	1 %	0.26
Facility-level administration & storage[2]	2,833,961	65.09 %	16.67
Procurement	$1,314,530	30.19 %	7.73
Total	4,353,738	100 %	25.61

[*] All costs presented in U.S. Dollars; 1 US$ = 392 Armenian drams (2022).

[**] Totals might not sum exactly to components due to rounding.

[1] Includes the marginal cost per dose for administration, storage, and distribution at the national level.

[2] Includes a per dosage estimate of the cost of facility-level storage of vaccines, immunobiological preparations, electricity consumption, amortization of equipment, and salary costs of health care workers to administer the vaccines.