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Burden of seasonal influenza in the Swiss adult population during the 2016/2017–2018/2019 influenza seasons

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Abstract

Background: Evidence on the burden of seasonal influenza in Switzerland is scarce, yet it is critical for the design of effective prevention and control measures. The objective of this study was to assess influenza-related resource utilization, health care expenditures and quality-adjusted life-years (QALYs) lost in Switzerland across the 2016/2017–2018/2019 influenza seasons.

Methods: We retrospectively analyzed multiple real-world data sources to calculate epidemiological and health outcomes, QALYs lost, and direct medical costs due to influenza in the Swiss adult population. Subgroups included residents 18–49, 50–64, and 65+ years of age. The observation period was Week 26, 2016, to Week 25, 2019.

Results: Across the three seasons, we estimated seasonal averages of 203,090 (se ± 26,717) general practitioner (GP) visits for influenza-like illness (ILI) 4944 (se ± 785) influenza-attributable hospitalizations and 1355 (se ± 169) excess deaths attributable to influenza. We estimated a total loss of 8429 (2016/2017), 11,179 (2017/2018), and 7701 (2018/2019) QALYs due to influenza. On average, 88% of the loss in QALYs was attributed to premature deaths due to influenza.

The total direct medical costs amounted to 44.4 (2016/2017), 77.3 (2017/2018), and 64.5 (2018/2019) million euros. On average, 79.6% of the total costs arose due to hospitalizations.

Conclusions: In Switzerland, the burden of influenza on patients and payers is significant and particularly high in the elderly population. Policy interventions to increase vaccination rates and the uptake of more effective vaccines among the elderly are needed to reduce the burden of influenza.

KEYWORDS
burden of disease, epidemiology, human, influenza

1 | INTRODUCTION

Seasonal influenza imposes a large burden on populations and health-care systems worldwide. Recent global estimates have shown an annual average of 389,000 deaths (95% confidence interval: 294,000–518,000) from respiratory complications alone, 67% of which were observed among individuals 65 years of age and older.[1] Influenza's burden expands beyond respiratory complications, including but not limited to cardiovascular, renal, and neurological complications and morbidity.[2]

Although many influenza disease burden studies have been conducted worldwide,[3–10] evidence on the burden of seasonal influenza in Switzerland is scarce and limited in scope. Muery et al.[11] previously described clinical characteristics among a small sample ($n = 60$) of children and adolescents hospitalized with influenza infection in a University Children's Hospital in Switzerland during the 2002/2003 and 2003/2004 seasons. Brinkhof et al.[12] used Poisson regression modeling to estimate influenza-attributable mortality among Swiss residents in 1969–1999 among adults 60 years of age and older. Mombelli et al.[13] assessed the epidemiology and outcomes of influenza in a Swiss nationwide cohort of transplant recipients during eight consecutive influenza seasons. The latest estimate of the direct medical costs of influenza in Switzerland dates back to 2003 and heavily relies on expert input and a global burden of illness model instead of local data.[14] A recent study assessed the lost production due to influenza in Switzerland but did not estimate direct medical costs.[15] To our knowledge, no study has used local real-world data and combined multiple data sources to describe the burden of influenza in Switzerland among the overall adult population.

Comprehensive, locally representative, and accurate data are key to informing policy and public health decisions for the treatment and prevention of influenza. To improve the understanding of influenza burden in Switzerland, we conducted a retrospective analysis of real-world data to describe the burden of influenza among Swiss adult residents over three influenza seasons (2016/2017–2018/2019), including epidemiological outcomes, health outcomes, healthcare resource utilization, quality-adjusted life-years (QALYs) lost due to influenza, and associated direct medical costs.

2 | METHODS

We retrospectively analyzed multiple real-world data sources to calculate epidemiological and health outcomes, QALYs lost, and direct medical costs due to influenza in the Swiss adult population (overall and stratified by age: 18–49, 50–64, and 65+ years) over three influenza seasons: 2016/2017, 2017/2018, and 2018/2019. Due to the nature of this study, no approval from an ethics committee was needed. A season was defined as the period between Week 26 of the first year and Week 25 of the second year. First, we estimated epidemiological outcomes, health outcomes, and healthcare utilization for the treatment of influenza (see Section 2.2). Second, we estimated life-years (LYs) lost at premature death due to influenza and QALYs lost at premature death due to influenza and during influenza episodes (see Section 2.3). Third, we estimated the unit costs of medical services used and total direct medical costs. We assessed the uncertainty of the results using probabilistic sensitivity analysis (see the Probabilistic sensitivity analysis section in Appendix S1 for details) and scenario analysis (see the Scenario analysis section in Appendix S1 for details). The results of the probabilistic sensitivity analysis are reported as expected values and 95% credible intervals (CIs).

2.1 | Data sources

We obtained data on the permanent resident population by age and life tables from the Swiss Federal Statistical Office.[16] Data on weekly incidence rates of general practitioner (GP) visits for influenza-like illness (ILI) as well as weekly virology data of cases that were analyzed at the National Reference Laboratory for Influenza in Geneva were obtained from the Swiss Sentinel monitoring system.[17] The system includes information from 150–250 volunteer GPs and pediatricians who may change every season. Data on risk factors and vaccination rates were obtained from the Swiss Health Survey[18] and the Statistics of Sociomedical Institutions.[19] We obtained data on hospitalizations with a main diagnosis of influenza from the Medical Statistics of Hospitals.[20] The Medical Statistics of Hospitals is a complete registry of all inpatient stays in acute care, rehabilitation, and psychiatric hospitals in Switzerland. Data on the cost of hospitalizations were obtained from the SwissDRG batchgrouper.[21] Weekly data on the total number of deaths were obtained from the Causes of Death Statistics.[22] Daily temperature measurements used in the statistical analysis of influenza-related excess deaths were obtained from the Swiss Federal Office of Meteorology and Climatology.[23]

2.2 | Epidemiological and health outcomes and quantity of services used

We combined the estimates of total GP visits for ILI from Swiss Sentinel monitoring with Swiss case-to-visit ratios of 57.7% (2016/2017), 62.46% (2017/2018), and 63.79% (2018/2019) from Richard et al.[24] to estimate the total number of ILI cases. While these case-to-visit ratios were collected in a population that is not representative of the Swiss population,[24] we still believe that local data are more meaningful than foreign estimates. We used these estimates of ILI cases to estimate the number of influenza cases using an ILI to laboratory-confirmed influenza ratio of 33% from Belazi et al.[25] To estimate the expenditures for antiviral medications prescribed during GP visits, we used proportions of GP visits for ILI with antiviral medications of 1.8% (2016/2017), 1.0% (2017/2018), and 2.2% (2018/2019) from the annual reports on the influenza season by the Swiss Federal Office of Public Health.[26–28] Because these proportions were only reported for all visits combined, we assumed identical proportions for all age groups. To identify the proportion of residents at high risk of influenza complications, we extracted medical risk factors from published literature and vaccine recommendations.[29–31] The prevalence of risk factors in the population was estimated using the prevalence of medical risk factors in the Swiss Health Survey (see Appendix S1 for detailed results on risk factors). The estimated proportion of the population at high risk of influenza complications was used in the calculation of costs of GP visits for ILI as clinical experts suggested that these visits included more services for high-risk individuals (see Tables 6 and 7 in Appendix S1). The Swiss Health Survey was also used to estimate the proportion of individuals who were vaccinated in the last 12 months. We validated these self-reported results by previous Swiss estimates of vaccination uptake. The total number of hospitalizations with influenza was estimated using the Medical Statistics of Hospitals.[20] We identified cases of seasonal influenza by ICD-10-GM main diagnoses J10 and J11. The ICD-10-GM is the German modification of the ICD-10 classification.[32] We excluded cases with ICD-10-GM main diagnosis J09 and/or secondary diagnoses U6920 or U6921, as these identify zoonotic or pandemic influenza cases in the ICD-10-GM classification.[*] We further used the Medical Statistics of Hospitals to identify the proportion of acute care hospitalizations with inpatient rehabilitation, follow-up GP visits, in-hospital death, emergency department (ED) admission, intensive-care unit stay, and respiratory, cardiac, or cardiorespiratory complications. Total influenza-related excess mortality was estimated using a negative-binomial regression analysis of weekly all-cause mortality from the Causes of Death Statistics.[22] Explanatory variables included weekly numbers of GP visits for ILI as a proxy for influenza activity, weekly temperature data, and lagged all-cause mortality. The independent variable of interest was GP visits for ILI. The dependent variable was weekly all-cause mortality. The model was specified and fitted according to prespecified criteria and statistical tests. Specifically, we ran a modified Park test and modified Hosmer–Lemeshow tests and specified the right-hand side based on the Akaike information criterion (see Appendix S1 for a detailed description of the methods used). The number of excess deaths was estimated as the difference between model predictions with observed GP visits for ILI and model predictions with GP visits for ILI set to zero. A sieve bootstrap[33] was used to assess the uncertainty of influenza-related excess mortality.

2.3 | LYs lost and QALYs lost

We used life tables from the Swiss Federal Statistical Office to estimate age-specific life expectancies at premature death due to influenza based on the area under the curve of extrapolated, half-cycle corrected overall survival curves over years since premature death.[34] The average life expectancy was calculated as the average of age-specific life expectancies weighted by the observed numbers of deaths at each age in the general population. This approach assumes that the relative increase in the probability of death due to influenza is constant across age and that the absolute risk of dying from influenza increases with age. The estimation of QALYs lost followed the same approach as total LYs lost, but each annual survival probability was weighted by the EQ-5D utilities in the Swiss population, which we obtained from Perneger et al.[35] Future QALYs were discounted at 3% per annum. We estimated QALYs lost during an influenza episode for healthy adults and elderly and high-risk individuals based on data from Turner et al.[36] who pooled multiple randomized controlled trials comparing oseltamivir with a placebo. The average utility loss was calculated as the cumulative difference between daily quality of life and the last value at Day 21 as a proxy for pre-influenza quality of life as no pre-influenza quality of life was available from the pooled randomized controlled trials. This approach ignored long-term decreases in quality of life after influenza episodes. Total LYs and QALYs lost because of premature death due to influenza were obtained by multiplying the estimated number of excess deaths by the average amount of LYs and QALYs lost in cases of premature death. The total amount of QALYs lost during influenza episodes was computed as the product of influenza episodes and average QALYs lost during an influenza episode.

2.4 | Direct medical costs

All costs were computed in Swiss francs at 2022 prices and tariff rates and converted to euros using an exchange rate of 0.9767 euro per Swiss franc.[37] We estimated the unit cost of GP visits for ILI based on two sample invoices that we created based on expert input using the Swiss fee-for-service outpatient tariff system TARMED.[38] As the TARMED tariff system has special rates for examinations of elderly and comorbid patients, one invoice was compiled for patients younger than 75 years of age who are not at high risk of influenza complications and one for patients over 75 years of age or patients of any age who are at high risk of influenza complications (the sample invoices can be found in Appendix S1). The cost of a follow-up GP visit for ILI after hospitalization was assumed to be identical to the cost of an initial GP visit for a low-risk patient. We multiplied the population in each age group by incidence rates of GP visits for ILI, the proportion of positive sample from GP visits for ILI, the proportion of the population at high risk, and the cost of the appropriate sample invoice to obtain the total direct costs of GP visits for influenza.

The price of antiviral medication during a GP visit for ILI was set to the oseltamivir sales price of EUR 55.34 for ten 75 mg capsules.[39] Oseltamivir had not been on the Swiss list of pharmaceutical specialties during the observation period of our study. This price is very similar to the last list price of Tamiflu® (EUR 54.37) before it was taken off the list of pharmaceutical specialties on March 1, 2010. We multiplied the estimated number of GP visits for ILI by the proportion of GP visits for ILI with an antiviral prescription and the price of antiviral drug medication to obtain the total direct medical costs of antiviral prescriptions. We assumed that all patients who received antiviral medication had influenza and not just ILI.

The cost of hospitalizations with a main diagnosis of influenza was estimated based on the SwissDRG per-case payment system as the product of a case-specific cost weight and the treating hospital's base rate. Case-specific cost weights were obtained by uploading the dataset of cases with a main diagnosis of influenza to the SwissDRG batchgrouper.[21] The base rates were taken from the canton of Zurich in 2022.[40] We included the costs for inpatient rehabilitation, calculated as the product of length of stay in inpatient rehabilitation with an influenza main diagnosis and an average per diem rate in the Canton of Zurich in 2022.[40]

*ICD-10-GM diagnosis codes J09 constituted only 3.0% of all influenza main hospital diagnoses in the 2018/2019 season, and the exclusion of these cases does not lead to a large underestimation of the number of inpatient cases if J09 was also used for seasonal influenza.

The total direct medical costs were obtained by summing the estimated total costs of GP visits for influenza, antiviral prescription medications, and hospitalizations.

3 | RESULTS

3.1 | Epidemiological and health outcomes

Over all three seasons, we estimated an average of 203,090 (se ± 26,717) GP visits for ILI, 331,270 (se ± 40,691) ILI cases, and 109,319 (se ± 13,428) influenza cases (Table 1 and Figure 1) per season. Per-season results can be found in Appendix S1. We found an average of 4944 (se ± 785) hospitalizations per season. On average, 93% (4598) of these hospitalizations were admitted through the ED, 73% (3605) had respiratory complications, 14.7% (727) had cardiorespiratory complications, 1.8% (90) had cardiac complications, 5% (675) received intensive care, 2% died in the hospital (342), 6.7% (331) were discharged to inpatient rehabilitation, and 13% (1886) of inpatient cases received a recommendation for a follow-up GP visit. We further estimated an average of 3207 (se ± 380) antiviral medication prescriptions and 1355 (se ± 169) excess deaths per season. The 2016/2017 and 2018/2019 seasons were A-dominant, with 96.05% and 99.5% of all tested strains being A-type, while the 2017/2018 season was B-dominant, with 70.51% of all tested strains belonging to the B-type. Estimated vaccination rates were 6.4% (234,006) in the 18–49 age group, 11.4% (200,509) in the 50–64 age group, and 35.8% (555,607) in the 65+ age group.

Incidence rates of GP visits for ILI and hospitalizations and excess deaths varied considerably across seasons (for additional information, see the Detailed results section in Appendix S1). The 2017/2018 season had the highest incidence of GP visits for ILI, with 3684 visits per

TABLE 1 Average per-season results across all three influenza seasons.

Age group	18–49	50–64	65+	Total
Epidemiology, *n* (per 100,000 residents)				
Population	3,656,353	1,755,775	1,550,242	6,962,370
Vaccinated	234,006 (6400)	200,509 (11,420)	555,607 (35,840)	978,213 (14,050)
At high risk of complications	375,873 (10,280)	339,567 (19,340)	579,170 (37,360)	1,294,610 (18,594)
GP visits for ILI	119,161 (3258)	53,317 (3036)	30,611 (1975)	203,090 (2917)
ILI cases	194,332 (4314)	86,925 (4953)	50,013 (3230)	331,270 (4759)
Influenza cases	64,130 (1754)	28,685 (1634)	16,504 (1065)	109,319 (1570)
Hospitalizations	476 (13)	729 (41)	3739 (241)	4944 (213)
ED admissions	450	696	3452	4598
Respiratory complications	374	562	2669	3605
Cardiorespiratory complications	7	74	646	727
Cardiac complications	1	9	80	90
Intensive care	26	52	146	225
In-hospital deaths	2	7	105	114
Antiviral medication prescriptions	1891 (52)	835 (48)	481 (31)	3207 (46)
Post-discharge GP visits	234 (6)	347 (20)	1305 (84)	1886 (27)
Excess deaths	57 (2)	66 (4)	1232 (79)	1355 (19)
Costs (million EUR)				
GP visits for ILI	3.17	1.56	1.31	6.04
Antiviral medications	0.10	0.05	0.03	0.18
Hospitalizations	4.07	7.26	38.36	49.69
Post-discharge GP visits	0.01	0.02	0.06	0.09
Total costs	7.36	8.89	39.75	56.01
Quality-adjusted life-years (QALYs) lost				
Life-years lost premature death	2547	1774	9520	13,841
Discounted life-years lost premature death	1371	1180	7857	10,408
Discounted QALYs lost premature death	1122	933	5936	7991
QALYs lost influenza episode	651	292	168	1111
Total QALYs lost	1774	1225	6105	9103

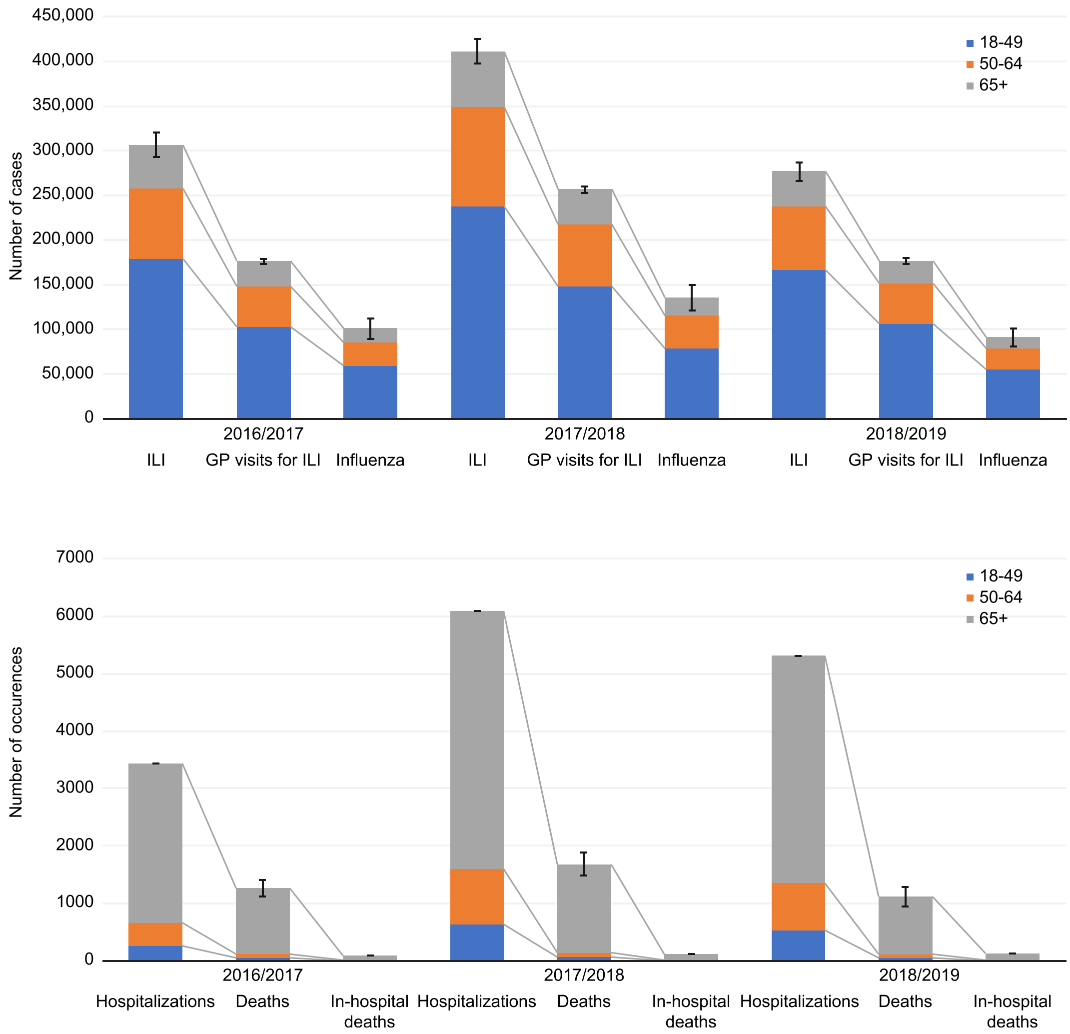

FIGURE 1 (A) Total cases of influenza-like illness (ILI) and general practitioner (GP) visits for ILI and influenza per age group and season. (B) Total hospitalizations, excess deaths and in-hospital deaths per age group and season. Error bars show ±1 standard deviation of total cases.

100,000 residents compared with 2551 and 2515 in the 2016/2017 and 2018/2019 seasons, respectively. The 2017/2018 season had 6088 hospitalizations compared with 3441 and 5303 in the 2016/2017 and 2018/2019 seasons, respectively. Estimated excess deaths were also highest in the 2017/2018 season, with 1683 compared with 1262 and 1120 in the 2016/2017 and 2018/2019 seasons, respectively.

While the incidence of GP visits for ILI was comparatively low in the 65+ age group, the incidence of hospitalizations, cardiac and cardiorespiratory complications, and excess deaths was higher than in the other age groups. The average estimated incidence of GP visits for ILI was 1975 in the 65+ age group compared with 3258 and 3036 in the 18–49 and 50–64 age groups, respectively. Hospitalizations per 100,000 residents were much higher in the 65+ age group with 241 compared with 13 and 41 in the 18–49 and the 50–64 age groups. The same is true for excess deaths, with an average of 1232 (65+) excess deaths per season compared with 57 and 66 in the 18–49 and 50–64 age groups, respectively. Cardiac and cardiorespiratory complications also varied between age groups with a combined rate of 19.27% (65+), 11.27% (50–64), and 1.29% (18–49).

3.2 | LYs lost and QALYs lost

Average discounted QALYs lost amounted to 9103 (95% CI 5605; 10,339) per season, 88% of which were attributed to premature deaths and 12% to impaired quality of life during influenza episodes.

The number of QALYs lost due to premature death was highest in the 2017/2018 season, with 9801 (95% CI 8007; 12,783) QALYs compared with 7401 (95% CI 6071; 9630) and 6773 (95% CI 5450; 8890) in the 2016/2017 and 2018/2019 seasons, respectively

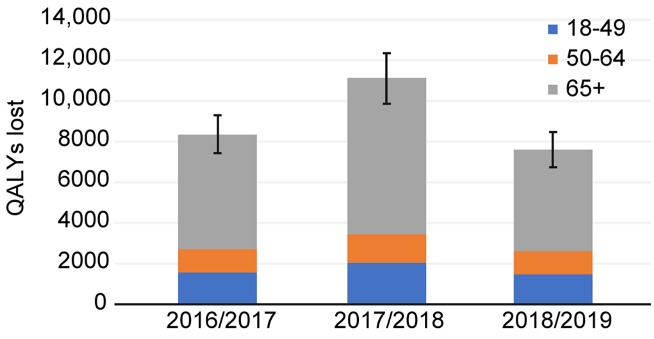

FIGURE 2 Quality-adjusted life-years (QALYs) lost by age group and season. The error bars show ±1 standard deviation of the total QALYs lost.

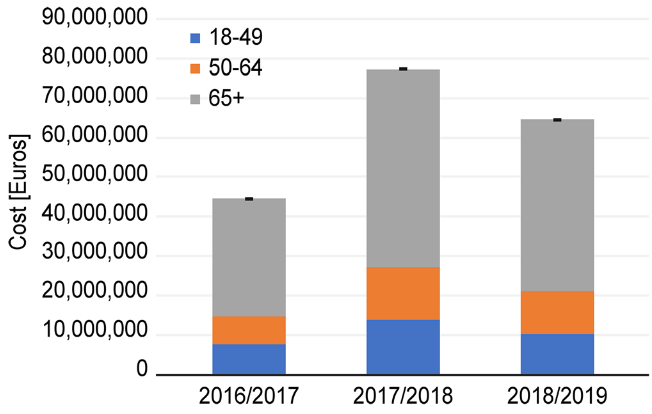

FIGURE 3 Direct medical costs in euros by age group and season. The error bars show ±1 standard deviation of the total direct medical costs.

(Figure 2). Loss of quality of life during influenza episodes was also comparatively high in the 2017/2018 season, with a total loss of 1378 (95% CI 915; 1996) QALYs compared with 1028 (95% CI 683; 1487) and 928 (95% CI 608; 1342) QALYs in the 2016/2017 and 2018/2019 seasons, respectively.

Most of the QALYs lost due to premature death occurred in the 65+ age group with an average of 5936 (95% CI 3760; 6945) QALYs lost compared with 1122 (95% CI 814; 1305) and 933 (95% CI 528; 1183) QALYs lost in the 18–49 and 50–64 age groups, respectively. The probabilistic sensitivity analysis showed that the uncertainty about the total amount of QALYs lost was quite high. The scenario analysis showed that the main driver of overall uncertainty was variability in the number of influenza-related excess deaths (detailed results of the scenario analysis can be found in Appendix S1).

3.3 | Direct medical costs

The total direct medical costs across all three seasons amounted to 168.0 (95% CI 167.8; 168.8) million euros (Figure 3). A total of 18.1 (95% CI 17.9; 18.9) million euros were spent on GP visits for influenza; 0.5 (95% CI 0.46; 0.60) million euros on antiviral medication; 149.1 (95% CI 149.1; 149.1[†]) million euros on hospitalizations, including acute care and rehabilitation; and 0.27 (95% CI 0.27; 0.27) million euros on follow-up GP visits (see the Detailed results section in Appendix S1). Our estimates of medical expenditures are equivalent to EUR 5.64 (2016/2017), EUR 10.17 (2017/2018), and EUR 8.29 (2018/2019) per resident.

Medical expenditures for hospitalizations and GP visits for ILI were higher in the 2017/2018 season than in the other seasons. A total of 61.8 (95% CI 61.8; 61.8 [see footnote †]) million euros were spent on hospitalizations in the 2017/2018 season compared with 33.6 (95% CI 33.6; 33.6 [see footnote †]) and 53.7 (95% CI 53.7; 53.7 [see footnote †]) million euros in the 2016/2017 and 2018/2019 seasons, respectively. GP visits for influenza cost 8.8 (95% CI 8.6; 9.3) million euros in the 2017/2018 season compared with 5.1 (95% CI 4.9; 5.5) and 4.1 (95% CI 3.9; 4.4) million euros in the 2016/2017 and 2018/2019 seasons, respectively.

Most of the costs were accrued in the 65+ age group, accounting for an average of 66.34% of total direct medical costs.

4 | DISCUSSION

This study is the first in 20 years to estimate the burden of influenza on health care payers and patients in Switzerland and to use such a wide range of data sources.[14] We obtained most input parameters from de novo analyses of Swiss real-world data sources and combined the results to obtain a comprehensive assessment of the health effects and costs of influenza in the Swiss adult population. Notably, our findings highlight the significant disease burden among older adults aged 65+ years, the group for whom rates of hospitalizations and deaths were consistently the highest across the three observed seasons. Moreover, we also found elevated disease burden among the 50–64-year-old population versus the younger adult population (<50 years of age), where rates of hospitalizations were approximately three-fold greater. Loss of QALYs and increased direct medical costs further demonstrate the impact of this increased disease burden.

Our epidemiological results are largely similar to estimates for other European countries. Paternoster et al.[41] reported 3486 (2016/2017), 4041 (2017/2018), and 3379 (2018/2019) ILI cases per 100,000 residents in France, which is similar to our results. However, our estimates for influenza incidence are considerably smaller than the reported estimates of 1949 (2016/2017), 2492 (2017/2018), and 2162 (2018/2019) per 100,000 residents from the same study due to different positivity rates. However, our estimates of influenza incidence are similar to values reported by Scholz et al.[7] for Germany in earlier seasons, which range from 800 to 1790 influenza cases per 100,000 insured individuals. Our estimates of influenza-related excess

[†]Hospitalization costs have a very low uncertainty because the Medical Statistic of Hospitals includes every case that was hospitalized and the SwissDRG batch grouper provides the actual cost weights that were used to reimburse the hospitals.

deaths are generally lower than estimates from other countries. An analysis of influenza-related excess mortality in the area of Vienna (Austria) finds an average number of 140.1 excess deaths per 100,000 residents over 60 years of age in the 1999/2000–2008/2009 seasons, which is quite high in comparison to our estimates.[42] Because the present study covers different seasons, it is not clear if these differences in excess deaths are driven by actual differences in mortality, different modeling decisions, or occur simply because of differences in timing and settings.

Total medical expenditures varied considerably across seasons and accounted for 0.04% to 0.09% of total Swiss healthcare expenditures[43] or 0.47% to 1.07% of medical expenditures for communicable diseases.[44] The largest proportion of medical expenditures was observed among residents aged 65+ who exhibited much higher hospitalization rates than younger patients.

In addition to the financial burden, influenza causes a significant humanistic burden. Premature death was the main driver of QALYs lost, and most deaths occurred in individuals aged 65+.

The strengths of our study include the combination of a wide range of data sources. This leads to a multitude of outcomes that can serve as a first step in continuous monitoring of the burden of influenza in Switzerland. This seems especially relevant given the uncertainty on the epidemiology of influenza after the COVID-19 pandemic.

However, this study also has limitations. First, the study focuses on the adult Swiss resident population and does not include minors. This focus on the adult population was prespecified based on a preliminary assessment of the available data and its external validity for the Swiss population. We decided that a study for both adult and minor populations using the same data sources and data analytic approaches would have limited the external validity, and we deemed it more robust to focus on adults and tailor the methods to this population. Second, the estimates of influenza incidence are uncertain because they depend on projected numbers of GP visits for ILI and published results from the literature. However, our results seem plausible compared with results from other countries. Third, the estimation of excess deaths related to influenza relies heavily on modeling decisions, and our estimates might not exactly capture the true values. Nevertheless, we specified the regression model in an empirical manner based on prespecified procedures and achieved a better fit with our model than with alternative models. Fourth, the identification of influenza-related hospitalizations by influenza main diagnoses led to an underestimation of the costs of hospitalizations as cases who were hospitalized for influenza-related secondary acute events were not classified as influenza-related hospitalizations. However, the inclusion of all cases with influenza secondary diagnoses and attribution of the full hospitalization costs to influenza would have led to a considerable overestimation of the hospitalization costs, and we decided to focus on influenza main diagnoses in favor of a conservative approach. This decision only affected hospitalization incidence and costs but not influenza epidemiology which was obtained from the Sentinel monitoring system. Fifth, the calculation of LYs lost at premature death due to influenza assumed that patients who die due to influenza have the same life expectancy as members of the general population of the same age. This might lead to an overestimation of LYs lost if individuals who die due to influenza are more vulnerable than members of the general public. We counteracted this overestimation of LYs lost by invoking the assumption that influenza has a proportional effect on age-specific mortality rates. Sixth, we are only able to detect hospitalizations that are coded with the specified ICD-10-GM diagnoses. Thus, we may underestimate the true number of hospitalizations due to influenza. Seventh, the samples tested at the National Reference Laboratory for Influenza were not randomly selected and might not reflect the true proportion of GP visits for ILI that actually were influenza.

5 | CONCLUSION

Our results show that seasonal influenza poses substantial burden on the Swiss healthcare system and population. Policy interventions to increase vaccination rates and uptake of more effective vaccines are needed to reduce influenza burden in future seasons. Continuous monitoring of the burden of influenza for the directing of public health interventions is particularly important as well in the uncertainty of the years following the COVID-19 pandemic.

AUTHOR CONTRIBUTIONS

Daniel Ammann: Conceptualization; data curation; formal analysis; investigation; methodology; validation; visualization; writing—original draft; writing—review and editing. **Jana Bilger:** Conceptualization; data curation; formal analysis; investigation; methodology; validation; visualization; writing—original draft; writing—review and editing. **Matthew M. Loiacono:** Conceptualization; funding acquisition; writing—review and editing. **Susanne G. Oberle:** Conceptualization; funding acquisition; writing—review and editing. **Andreas Dounas:** Conceptualization; funding acquisition; writing—review and editing. **Oriol Manuel:** Investigation; methodology; writing—review and editing. **Mark Pletscher:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing—original draft; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

D.A., J.B., and M.P. report grants from Sanofi, during the conduct of the study. O.M. has participated in advisory boards for Takeda, Biotest, and MSD. M.M.L., S.G.O., and A.D. are employees of Sanofi and may hold shares and/or stock options in the company.

ETHICS STATEMENT

No ethics approval was needed for this study.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/irv.13218.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Swiss Federal Statistical Office, the Swiss Federal Office of Meteorology and Climatology, and the Swiss Sentinel monitoring system. Restrictions apply to the availability of these data, which were used under license for this study.

PATIENT CONSENT STATEMENT

No patient consent was needed for this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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