

# Burden of Disease Caused by Influenza in Germany: A Retrospective Claims Database Analysis

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## BACKGROUND

- In recent years, seasonal influenza epidemics have affected approximately 10% to 20% of the world's population.<sup>1</sup>
- The highest risk of a severe course of influenza and concomitant diseases is associated with children, the elderly, and individuals with a disease disposition.<sup>2</sup>
- Given the high annual morbidity, a substantial economic burden arises due to direct medical cost in the outpatient and inpatient sector and indirect costs caused by productivity losses due to incapacity to work.<sup>3</sup>
- Vaccinations can provide an effective tool for the containment of disease spread.<sup>4</sup>
- The number of patients affected by an influenza infection and seeking healthcare may serve as an indicator for the impact of the seasonal burden.<sup>5</sup>

## OBJECTIVES

- To assess the impact of influenza on the healthcare system and estimate the burden of disease caused by influenza in Germany during the 2012/2013 influenza season.

## METHODS

### STUDY SAMPLE

- We conducted a retrospective claims data analysis using the Health Risk Institute research database, which contains anonymized data of 3,953,260 individuals (approximately 4.9% of the German population).
- The study period comprised 1 October 2012 to 30 June 2013, and patients with a documented ICD-10-GM (International Classification of Diseases, 10th Revision, German Modification) code for influenza during the 2012/2013 influenza season were identified.
- Patients were defined as influenza patients if they had at least 1 outpatient or inpatient diagnosis with 1 of 3 influenza codes during the study period.
- The relative frequency of the most common concomitant diseases, otitis media and pneumonia, was evaluated and compared to individuals not infected with influenza.

### RESOURCE USE AND COST

- Healthcare resource utilization and costs were calculated from the perspective of the statutory health insurance (SHI) system.
- Direct costs were calculated separately for each domain (prescriptions, outpatient care, and inpatient care) based on influenza-specific resource utilization.
- Medicinal treatment was identified by assessing prescriptions based on Anatomical Therapeutic Chemical Classification (ATC) codes for analgesics, antibiotics, antitussives, M2-membrane protein inhibitor, neuraminidase inhibitor, and nose spray.<sup>6</sup>

### VACCINATION RATES

- The observation period comprised 1 July to 31 December 2012 and included all patients with at least 1 vaccination identified by codes (influenza: 89111 for standard vaccination, 89112 for other indications).
- On 31 December 2012, the total German population comprised about 80,523,700 individuals.<sup>7</sup>
- The extrapolation was calculated by multiplying the results with an extrapolation factor that was determined by dividing the German population by the specific study sample.
- Results were adjusted for the German SHI population by calculating an adjustment factor of 0.8656 based on the ratio of the SHI population of 69,704,0007 to the German population.

## RESULTS

- We observed 65,826 patients with a documented influenza diagnosis during the 2012/2013 influenza season.
- The highest rates are present in the age group of 2 to 6 years (3.2%). Overall, 1.7% of the SHI population had a documented influenza infection (Table 1).

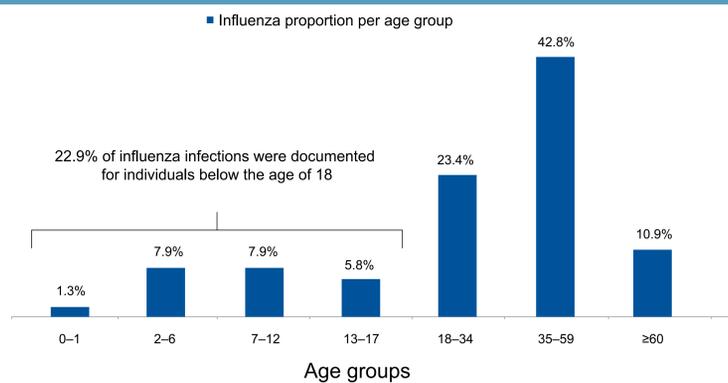
**Table 1. Rate of Identified Influenza Patients and Total Patient Counts Stratified by Age Groups**

Age Groups	Rate in Percent (95% CI)*	Total†
0–1	2.47% (2.31, 2.64)	14,952
2–6	3.17% (3.09, 3.26)	91,951
7–12	2.43% (2.36, 2.50)	91,457
13–17	1.93% (1.87, 1.99)	67,778
18–34	1.93% (1.90, 1.96)	271,339
35–59	1.89% (1.87, 1.92)	496,218
≥60	0.68% (0.66, 0.70)	126,951
<b>Total</b>	<b>1.67% (1.65, 1.68)</b>	<b>1,160,646</b>

\*Confidence intervals with 95% confidence level were calculated by applying the Clopper-Pearson Interval. †The extrapolation is based on a sample size of 3,961,887 and an extrapolation factor of 17.59, adjusted to the SHI population with 86.56%.

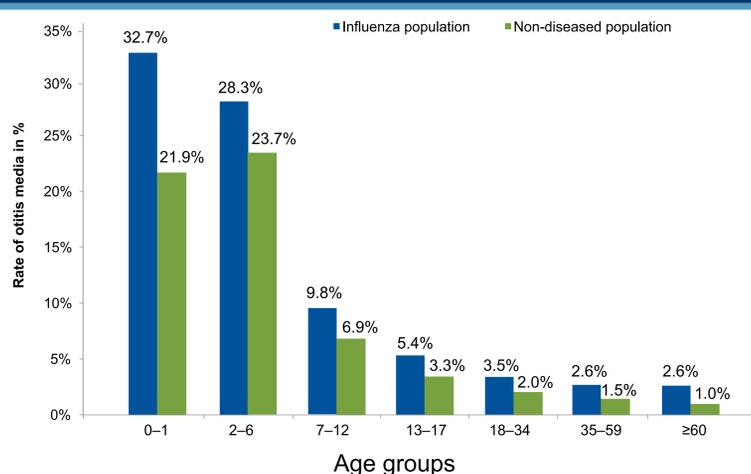
- Overall, 22.9% of influenza infections were documented for children aged between 0 and 17 years (Figure 1).

**Figure 1. Influenza Proportion per Age Group**



- The frequency of otitis media, which is generally highest for children aged between 0 and 6, is increased in individuals with documented influenza (Figure 2).

**Figure 2. Otitis Media Frequency Rate: Comparison Between Influenza Population and Non-diseased Population**



- A higher number of pneumonia cases was identified, with a relative frequency of 2.5% for the influenza population and 0.2% for the population not affected by influenza.
- Children between the ages of 0 and 1 had a relative frequency of 4.5% in the influenza population and 0.2% in the non-diseased population.
- The relative frequency of pneumonia was highest for children aged 0 to 1 (4.5%) and individuals above the age of 60 (5.5%) in the influenza population.

### RESOURCE USE AND COST

#### INPATIENT CARE

- Overall, 14,952 influenza-related hospitalizations were identified during the influenza season.
- Over 65% of the inpatient visits were caused mainly by influenza; for the group aged 2 to 17, the proportion of influenza principal diagnosis codes was over 80%.
- With influenza as a principal diagnosis, children aged between 0 and 1 were in the hospital for 5.2 days in comparison to individuals aged 60 and above, who averaged 10.4 days.
- Hospitalizations amounted to 150,436 days and a total cost of €87,202,485 for the SHI population, leading to cost per day of €579.66 for an influenza-related hospitalization.

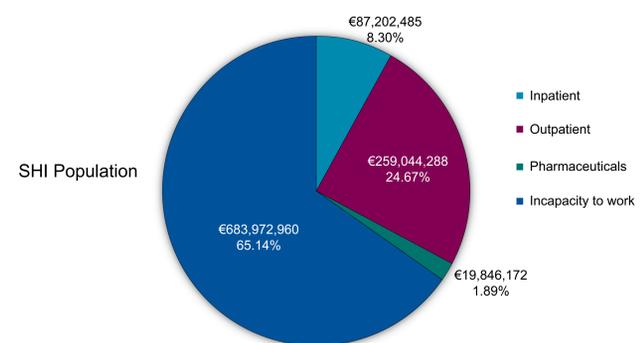
#### OUTPATIENT CARE

- Costs were highest for antibiotics (42% of influenza patients had a prescription) and analgesics; overall, the influenza-related pharmaceutical cost was €19,846,172 based on the SHI population in Germany.
- In total, 7,682,046 outpatient visits and a total cost of €259,044,288 for the extrapolated SHI influenza population were calculated.

#### SOCIETAL PERSPECTIVE

- Out of the influenza population, 36% of individuals had incapacity to work caused by influenza. In total, after extrapolation, this resulted in 3,886,210 days and a mean duration of incapacity to work of 8.15 days.
- The cost of incapacity to work resulted in €683,972,960 assuming cost per day of €176.<sup>8</sup>
- Distribution of total cost differed by sector, including the indirect cost of incapacity to work (Figure 3).

**Figure 3. Distribution of Total Cost per Sector**



### VACCINATION RATES

- Based on documented vaccinations during the third and fourth quarter of 2012, vaccination rates ranged between 1% and 37% for the different age groups.
- Children aged 0 to 1 had the lowest vaccination rate at 1.3%.
- Individuals above the age of 60, where an influenza vaccination is indicated, had the highest vaccination rate at 36.8%.
- The extrapolation resulted in 9,500,740 vaccinated individuals in the SHI population, with an overall vaccination rate of 13.6% (Table 2).

**Table 2. Vaccination Rates and Patient Counts**

Age Groups	Vaccination Rates (95% CI)*	Extrapolation of Individuals†
0–1	1.29% (1.18, 1.42)	7,812
2–6	2.80% (2.72, 2.89)	81,036
7–12	3.66% (3.58, 3.74)	137,354
13–17	2.82% (2.74, 2.89)	98,823
18–34	2.28% (2.24, 2.31)	319,729
35–59	7.51% (7.47, 7.55)	1,963,168
≥60	36.76% (36.65, 36.87)	6,892,817
<b>Total</b>	<b>13.63% (13.60, 13.66)</b>	<b>9,500,740</b>

\*Confidence intervals with 95% confidence level were calculated by applying the Clopper-Pearson Interval. †The extrapolation is based on a sample size of 3,961,887 and an extrapolation factor of 17.59, adjusted to the SHI population with 86.56%.

## DISCUSSION

- In Germany, direct and indirect medical costs of diseases caused by influenza viruses have been estimated to be 1 to 2.5 thousand million Euros.<sup>9</sup>
- The most recent data for the 2012/2013 influenza are based on the epidemiological report from the German influenza sentinel system (AGI) of the Robert Koch Institute (RKI).
- In total, based on Infection Protection Act (IfSG), 66,000 laboratory-confirmed acute influenza disease cases and 10,700 laboratory-confirmed inpatient cases were reported. As our method is based on verified diagnosis codes and not on laboratory-confirmed disease, we identified 65,826 influenza cases (1,160,646 after extrapolation), which are only partly comparable. The RKI states that only a small number of patients with influenza-similar symptoms are laboratory-checked and an underestimation based on the IfSG data is to be expected.<sup>10</sup> Sentinel estimations resulted in 7.7 million excess outpatient consultations, which is in line with our results (7.7 million influenza-related outpatient visits) and 4.3 million excess cases of incapacity to work/bed rest, whereas the lower number in our study population (3.9 million days) might be due to the fact that sick leave for schoolchildren or bed rest are not included.
- Additionally, the number of hospitalizations in our study (14,952) is almost half the amount as estimated by the AGI (32,000), which might be partially due to the fact that the AGI estimation is not based on inpatient claims but on information given by the physician if the patient was further transferred to the hospital.<sup>10</sup>
- Finally, the calculated relative frequency of otitis media in our study is in line with published literature.<sup>11-13</sup>

## LIMITATIONS

- Claims data are recorded for accounting purposes and not for clinical research. As a result, it is not possible to characterize patients by clinical parameters such as disease severity or to see the physician's intention for each intervention.
- Data on the incidence of influenza are limited by the difficulties inherent in distinguishing influenza from other influenza-like illnesses.<sup>14</sup>

## CONCLUSION

- The assessment of resource use and cost resulted in total cost for the 2012/2013 influenza season of €366,092,945 based on the SHI population. The highest direct costs were calculated for outpatient care (€259,044,288), followed by inpatient care (€87,202,485) and pharmaceuticals (€19,846,172).
- The results of our retrospective analysis suggest an increased disease burden of influenza for children aged between 0 and 17 years.
- In total, 22.9% of the influenza infections were documented for individuals below the age of 18.
- The relative frequency of otitis media was highest for children aged 0 to 6 years, whereas the pneumonia frequency was highest in individuals aged 60 and above and children aged 0 to 1.
- In comparison, calculated vaccination rates were relatively low, especially for the younger population.
- These results suggest that given the calculated low cost of influenza vaccination, a higher vaccination rate might lower the disease burden for children and individuals with a disease disposition and decrease the seasonal cost of influenza from a health insurance perspective.

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