Economic and Clinical Burden of Paediatric Influenza in Nine European Countries

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BACKGROUND

- A substantial body of evidence is available describing the clinical and economic burden of influenza in the United States (US), particularly in young children.[1-3] A high incidence of paediatric hospitalisations and outpatient consultations translates into a significant cost burden. The magnitude of paediatric influenza burden in Europe is unclear.
- In 2008, the US Advisory Committee on Immunization Practices extended their vaccination recommendations to include all children aged 6 months to 18 years.[3]
- Evidence-based vaccination policies have also been recommended for other countries, including Austria, Canada, China, Estonia, Finland, Hong Kong, Israel, Korea, Latvia, Slovakia, Slovenia, Singapore, Taiwan, and several Latin American countries.[4-6]
- The burden of influenza is an important consideration when considering the introduction of national vaccination policies.[7]

OBJECTIVE

- To identify available data regarding the economic and clinical burden associated with influenza in a paediatric population in nine countries in Europe (Austria, Finland, France, Germany, Italy, The Netherlands, Spain, Sweden, and the United Kingdom [UK]).

METHODS

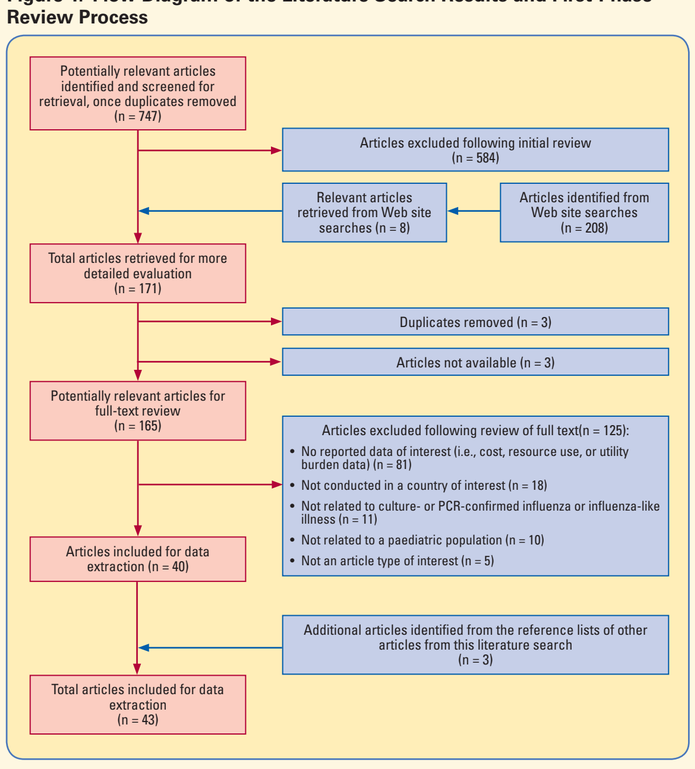
- A structured and comprehensive literature search was performed in compliance with the QUOROM guidelines using the following electronic databases and Internet sites:
  - PubMed
  - EMBASE
  - The Cochrane Library
  - Relevant health technology assessment (HTA) appraisals of influenza vaccination (e.g., National Institute for Health and Clinical Excellence [NICE], Scottish Medicines Consortium [SMC], Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen [IQWIG]).
- Search terms included combinations of free text and Medical Subject Headings:
  - Health condition of interest (disease): Terms for influenza (including polymerase chain reaction [PCR] or culture-confirmed infection, and influenza-like illness (ILI).
  - Study type(s): Terms for cost, economic or burden analyses (e.g., cost-effectiveness analysis and cost-of-illness studies), quality of life (QOL), absenteeism, and productivity.
  - Limits:
    - Published from 1970 to March 2009
    - Excluded editorials, letters, meta-analyses, practice guidelines, and comments
    - Restricted to paediatric patients (aged ≤ 18 years) and to studies conducted in humans
    - Restricted to Austria, Finland, France, Germany, Italy, Spain, Sweden, The Netherlands, and the UK.
- Relevant data of the following types were extracted from included articles:
  - Health care use
  - Costs, including direct costs, indirect costs, and nonmedical direct costs
  - Absenteeism and productivity losses in patients and their household contacts
  - QOL and utility data
  - Types and incidence of complications from influenza
  - Incidence and prevalence of confirmed influenza infection and ILI

RESULTS

Articles Identified

- The literature was systematically assessed following the Quality of Reporting of Meta-Analyses (QUOROM) guidelines. (Figure 1).
- Of the 43 articles identified, 15 studies reported data relating specifically to laboratory-confirmed influenza, with the remaining studies reporting data related to influenza-like illness. A total of 13 articles reported data specifically relating to laboratory-confirmed influenza in children.

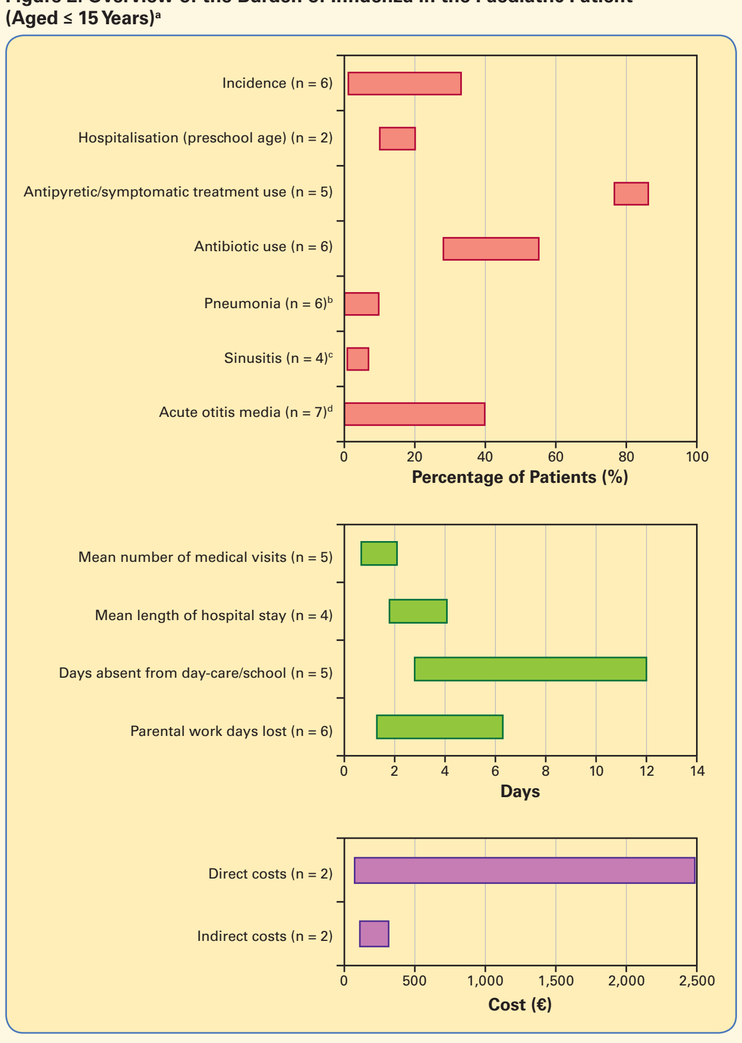
Figure 1. Flow Diagram of the Literature Search Results and First-Phase Review Process



Overall Summary of Clinical and Economic Burden

- Studies provided a sizeable range in the burden of illness (Figure 2).

Figure 2. Overview of the Burden of Influenza in the Paediatric Patient (Aged ≤ 15 Years)[a]



n = number of articles reporting these data.

[a] The bars represent the range of values reported in the studies identified in the literature review, from the minimum reported value to the maximum reported value.

[b] Six studies, which included a total of 12 data points for different age groups.

[c] One study, which included a total of four different age groups.

[d] Seven studies, which included a total of 13 data points for different age groups.

Health Care Resource Use

- Nineteen articles reported health care resource use data in children, eight of which specifically reported data for laboratory-confirmed influenza.
- Children were reported to incur substantial resource use, requiring hospitalisation in 10% to 20% of cases for an average of 2 to 4 days and up to two medical visits per case (Figure 2).
- Antibiotic use was required in 28% to 55% of cases, and antipyretic/symptomatic treatment in 76% to 86% of cases (Figure 2).
- Household contacts of infected children also required hospitalisation (0.3% to 0.4%), additional medical visits (10% to 14%), antibiotics (5% to 8%), and antipyretics (13% to 16%).
- A further 11 studies reported health care resource use data associated with ILI in children, which also supported the substantial burden of influenza (data not shown).

Costs

- A single article reported cost data specifically for children with laboratory-confirmed influenza.[8] The 2002 study was conducted in children aged 0 to 3 years and presented costs associated with laboratory-confirmed influenza in Germany, as well as costs of lower respiratory tract infections.
- Direct costs, driven mainly by hospitalisation costs, formed the largest proportion of costs in hospitalised cases (€2,597), whereas indirect costs formed the largest proportion of the costs of office-based cases (€223).
- A further nine articles reported cost data associated with ILI in children, reporting a similar magnitude of costs as for laboratory-confirmed influenza (data not shown).

Absenteeism

- Seven articles reported absenteeism data specifically for children with laboratory-confirmed influenza.
- Children were reported to have 3 to 12 days of absence from day care or school (Figure 2).
- Parents of sick children reported 1 to 6 days of absence from work to care for their children or because of their own illness contracted from their children (Figure 2).
- A further four articles reported absenteeism data associated with ILI in children. These articles reported a similar length of absence from school/day care, ranging from 0.5 to 13.8 days, and a shorter length of absence from work in parents of children with ILI, ranging from 0.5 to 2.9 days.

QOL

- A single article reported QOL data specifically for children with laboratory-confirmed influenza.[9]
- The article reported a trial comparing inactivated vaccine with no vaccine specifically in children (6-18 years) with asthma, using the Paediatric Asthma Quality of Life Questionnaire (range of possible scores: 1-7, with 7 indicating the highest QOL).
- Influenza reduced the overall QOL score from baseline (6.16) in both groups, although the impact was smaller in vaccinated children (5.87) compared with non-vaccinated children (5.47).
- Respiratory symptoms were also measured and found to be more severe in the upper respiratory tract than the lower respiratory tract, and the symptoms were less severe in vaccinated children compared with nonvaccinated children.
- A further three articles reported QOL data associated with ILI in children (data not shown).

Incidence Rates of Confirmed Influenza and ILI

- Data on the rates of confirmed influenza and of ILI were identified in 21 of the 43 articles extracted. Of these, 15 articles provided incidence data specifically for the paediatric population.
- Of those studies that confirmed influenza by laboratory methods, a greater proportion of cases was confirmed in young children (aged ≤ 3 years) compared with the overall population (53.4% vs. 38.7%) (Table 1).
- There were also differences in incidence rates between influenza A and influenza B. Seven of the eight studies stratifying data in children for influenza A and influenza B, reported a greater proportion of influenza infections to be influenza A (data not shown).

Table 1. Incidence of ILI and Laboratory-Confirmed Influenza Reported in the Included Studies

Age Group	Mean (Range) Incidence (%) Averaged Over All Studies		
	ILI	Laboratory-Confirmed Influenza (% of Suspected Influenza/ILI)	Laboratory-Confirmed Influenza (% of Total Population)
Overall population (not restricted to a specific age range)	8.9 (0.1-27.1)	38.7 (14.0-65.0)	No studies
≤ 15 years	12.3 (0.1-37.7)	36.0 (9.3-51.8)	15.7 (1.1-33.0)
≤ 3 years[a]	No studies	53.4 (42.4-68.9)	16.0 (1.1-33.0)

[a] The studies included for the age group ≤ 3 years were a subset of the studies included for the age group ≤ 15 years

Complications of influenza

- Eight of the 43 included articles reported data on complications, specifically related to laboratory-confirmed influenza in children.
- Frequently reported complications of influenza included acute otitis media (up to 40%), pharyngitis (31% to 48%), rhinopharyngitis (46% to 54%), febrile seizures/convulsions (up to 45%), and pneumonia (up to 10%) (Figures 3 and 4).

Incidence (Percentage Range) of Influenza Complications Reported Within the Included Articles in All Paediatric Patients (≤ 15 Years)

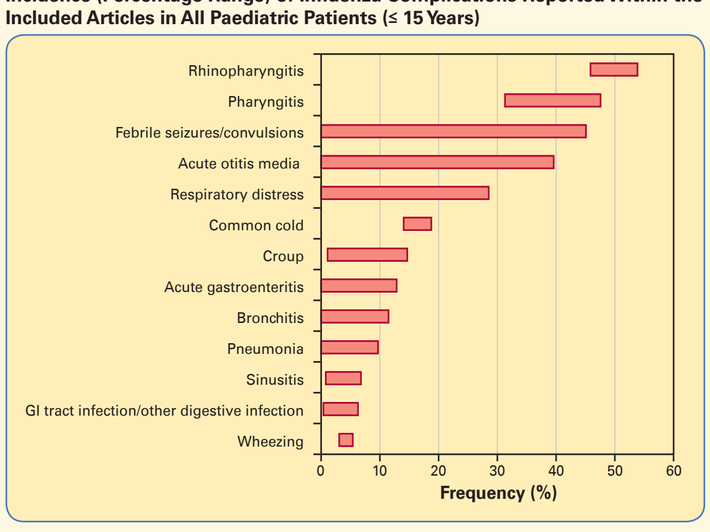
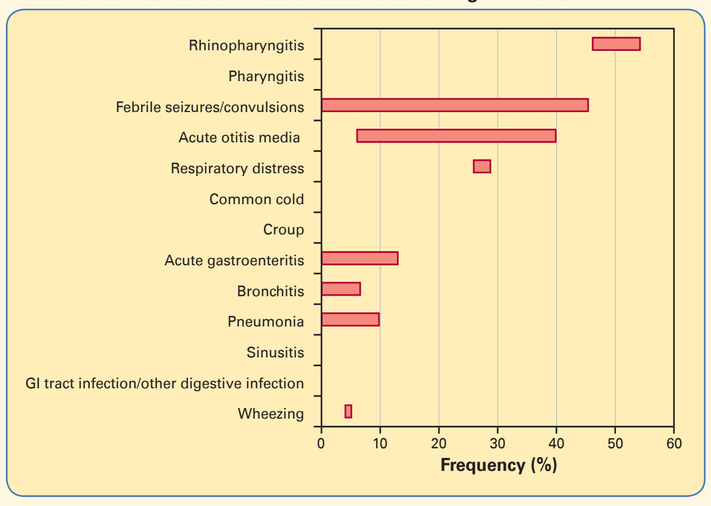


Figure 4. Incidence (Percentage Range) of Influenza Complications Reported Within the Included Articles in Paediatric Patients Aged ≤ 3 Years



DISCUSSION

- The burden of paediatric influenza in Europe is substantial, in terms of incidence, resource use, absenteeism, and the associated direct and indirect economic burden.
- In addition to children themselves being affected, household contacts, including parents and siblings, also incurred increase resource use and/or absence from work, as a result of contracting influenza from or caring for sick children.
- The duration of absenteeism from work and hospitalisation rates associated with laboratory-confirmed influenza, incidence of ILI, and complication rates reported in our literature review were in line with data from previous publications.[10-12]

Limitations

- Note that this review was designed to investigate the economic burden of influenza in terms of resource use, cost, impact on QOL, and productivity. The clinical endpoints reported were obtained from the economic-related literature. Additional research may be necessary to better quantify the clinical burden of paediatric influenza in Europe.

Conclusions

- Multiple studies have examined the burden of influenza illness in children. These data should be considered by policy bodies when formulating future recommendation for vaccination coverage of healthy children in European Union.

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