Development of a dynamic transmission/cost effectiveness model for influenza A and B

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Background & Objectives: Economic modelling of childhood influenza vaccination

Conventional Pharmacoeconomic models for infectious diseases may underestimate the impact of vaccination

- Influenza and other infectious diseases are transmitted in the community from those who are infected to those who are not infected
- Force of infection is not static but changes dynamically in a non-linear fashion
- Children are major spreaders of disease. Paediatric vaccination may induce indirect protection effects (‘herd immunity’) in the wider population

Objectives

- To create a childhood influenza A/B economic model that incorporates dynamic transmission and indirect protection (herd immunity) effects
- To examine model behaviour using an investigational influenza vaccine, LAIV for children in the United Kingdom
Methods: Dynamic transmission simulations

- Children are the major transmitters of influenza in the population

- ‘Who Acquires Infection From Whom’ (WAIFW) contact matrix\(^1\) central in model

- Dynamics of transmission coded in Fortran and described by a set of linked differential equations forming a standard SEIRS model, such as has been previously published\(^2\)

- Seasonality of influenza emulated by sine wave function

- Age-stratified structure offering opportunity to capture indirect protection effects in unvaccinated age bands of the wider community

- The dynamic transmission model for influenza A/B served as the foundation for the UK (NHS focus) economic model built in Excel

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Methods: Basic construct of ‘hybrid’ CE model

Infectious model state is the link to the CE module

Estimates of UK influenza burden

UK ‘influenza like illness’ data
Methods: Linking influenza incidence to costs and outcomes

Influenza attributable resource use/costs and mortality are key

- UK databases – Influenza-like-illness (ILI) attributed GP visits/medication (GPRD), hospitalization (HES) and mortality (ONS), laboratory confirmed infection data (LabBase)
- Multiple regression analysis\(^1\) to estimate the influenza attributable proportion of ILI attributed outcomes
- Simulated age-stratified incidence of influenza A/B combined with regression analysis of burden to produce probabilities of an incident influenza infection leading to a GP consultation, Hospitalization or death
- Costs and QALY decrements based on estimates from 2003 HTA report\(^2\) (costs inflated to 2009 prices)

1. Pitman RJ et al, J Infect. 2007; 54: 530-8
Methods: Model Assumptions

- Vaccination scenarios use FDA indicated label for live-attenuated influenza vaccine (LAIV), which is approved in the U.S. for ages 2 – 49, but is not yet approved in U.K.
  - Target population: children age 2 – 18

- The Model:
  - Does not factor in vaccine adverse event costs
  - Does not incorporate costs of medications such as anti-virals
  - Does not incorporate indirect or productivity costs (Health service perspective)
  - Assumes GP vaccination and does not incorporate school based vaccination
Methods: Key Parameter Values

The values of these parameters are illustrative

- Who Acquires Infection From Whom (WAIFW) matrix¹
- Transmission coefficient
- Duration of
  - Latency, 2 days
  - Infectiousness, 2 days
  - Immunity, Influenza A: 6 years, B: 12 years
- Basic reproductive rate (Ro) of 1.8
- Discount rate 3.5%
- Time horizon 15 years

¹ Mossong J et al, PloS Medicine 2008; 5: 381-391
Results: Cases of Influenza by Vaccination Scenario

- **Influenza A**
  - No childhood vaccination ~ base case
  - 2 - 4 yr olds vaccinated ~ 4% population
  - 2 - 18 yr olds vaccinated ~ 20% population

- **Influenza B**
  - No childhood vaccination ~ base case
  - 2 - 4 yr olds vaccinated ~ 4% population
  - 2 - 18 yr olds vaccinated ~ 20% population

- **Initiation Vaccination 65+**
  - 2000 – 2024 / UK policy / 'mainstay' vaccine efficacy

- **Initiation Childhood vaccination**
  - 2000 – 2024 / potential labeling / LAIV 80% coverage
Results: Exploratory vaccination scenarios

Averted infectious influenza cases
**Results: model behaviour and validation**

Changes in resource use/costs, QALYs and mortality parallel simulated indirect protection effects increasing in size with

- Age range of vaccination
- Higher vaccination rate
- Greater vaccine effectiveness

*Model predictions are in line with published UK burden information*¹

¹ Pitman RJ et al, J Infect. 2007; 54: 530-8
Results: *Exploratory* model behaviour in CE plane

![Graph showing model behaviour in CE plane](image)

**Indirect protection (Herd immunity)**

- **80% vaccination 2-18 yrs**
- **50% vaccination 2-18 yrs**
- **10% vaccination 2-18 yrs**
- **80% vaccination 2-4 yrs**
- **80% vaccination 2-18 yrs excluding herd immunity effects**

<table>
<thead>
<tr>
<th>65+ age group</th>
<th>75% vaccination</th>
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<tbody>
<tr>
<td>Costing</td>
<td>Ibid.</td>
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<tr>
<td>Time frame</td>
<td>15 year cumulative</td>
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Limitations

- Model incidence calibrated against Tecumseh data (1970s, US data)

- Ability to benchmark model simulations against actual influenza epidemiological data, including infection rates (European data). Obtaining such data will help reduce uncertainty within the parameter estimates
Conclusions

- The age-stratified influenza model simulates indirect protection effects of childhood influenza vaccination in the population
- Conventional cost-effectiveness modelling for infectious diseases could significantly underestimate the benefits and value of vaccination strategies
- Dynamic transmission modelling is needed to accurately estimate the value of vaccine strategies

Future Model Directions

- Model consolidation by calibration with recent epidemiological data
- Influenza CE evaluations using the consolidated model