Predicting the Impact of Childhood Vaccines: Health & Economics

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Biological Background[1,2]

Measles
- Infectious period lasts 6-7 days and recovery takes 7-10 days
- Airborne: contained in droplets (survives on surfaces for hours)
- Severe cold-like symptoms, red eyes, sensitivity to light, fever, rash
- Serious complications: pneumonia, encephalitis (babies < 1 year old, children with weakened immune system)
- Risks during pregnancy include miscarriage, stillbirth, premature birth

Mumps
- Infectious period lasts 4-8 days (airborne) and recovery takes 1 to 2 weeks.
- Most common symptom is swelling of the parotid glands
- Headaches, joint pain, high temperature
- Can be passed on by infected people who have no obvious symptoms
- Serious complications: viral meningitis, swelling of testicles/ovaries if gone through puberty, encephalitis

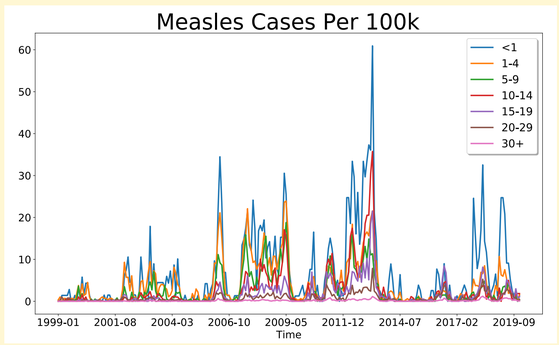
Rubella
- Infectious period lasts 11-12 days (airborne) and recovery takes about 3 days
- Symptoms include a red/pink spotty rash, joint pain, and flu-like symptoms
- Serious complications: encephalitis, low platelet count, ear infection
- If caught early during pregnancy can lead to miscarriage or baby born with Congenital Rubella Syndrome (CRS)
- Babies with CRS may spread the virus for more than a year

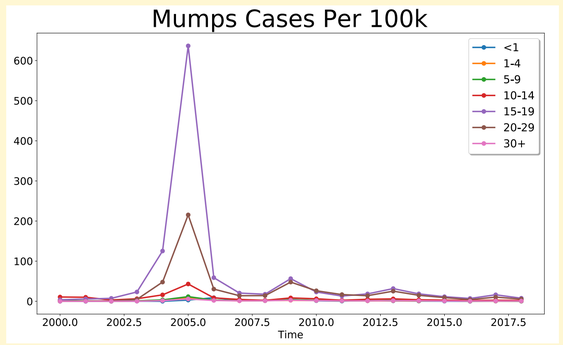
MMR Vaccine

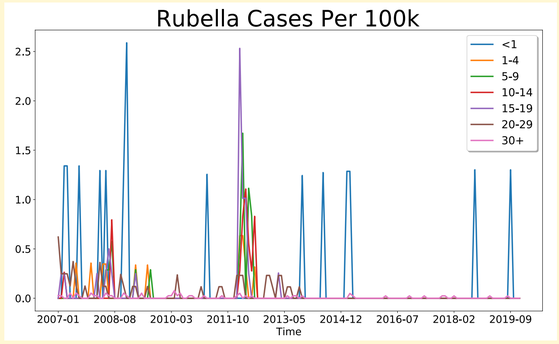
2 doses
1 year old *(Newborn babies have antibodies passed on from their mother at birth which make the MMR vaccine less effective. Antibodies are almost gone by the age of 1.)*
3 years and 4 months old *(before child goes to school)*
99% of people protected against measles and rubella and 88% against mumps

Side Effects
Area around needle injection might get red, swollen, and sore.
7 to 11 days after injection babies or young children may feel unwell for about 2-3 days.

Data Sources







- **New reported cases:** epidemiological data for MMR diseases are available as age standardised rates from the ECDC Surveillance Atlas of Infectious Diseases dataset
  Measles: monthly data, 1999-2019 ***Mumps:*** annual data, 2000-2017
  Rubella: monthly data, 2007-2019

- **Demographics:** collected from the Office for National Statistics
  Birth rate: per million, from 1888 ***Death rate:*** by single age, from 1974 to 2018
  Annual mid-population: from 1971

- **Vaccination rate:** from Public Health England
  MMR vaccine coverage: 1985-2013

ODE Model for Diseases[3,4]

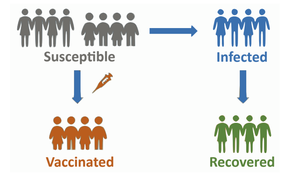
Let us define a k-age group compartmental SIRV model for the infection dynamics of the diseases covered by the MMR vaccine:

$$\frac{dS_i}{dt} = \delta_{i1}B - \sum_{j=1}^{k} \beta_i c_{ij} S_i I_j - v_i S_i - d_i S_i + \delta(t - t_{\text{end}}) a_{i-1} S_{i-1} - \delta(t - t_{\text{end}}) a_i S_i$$

$$\frac{dI_i}{dt} = \sum_{j=1}^{k} \beta_i c_{ij} S_i I_j - \gamma_i I_i - d_i I_i + \delta(t - t_{\text{end}}) a_{i-1} I_{i-1} - \delta(t - t_{\text{end}}) a_i I_i$$

$$\frac{dR_i}{dt} = \gamma_i I_i - d_i R_i + \delta(t - t_{\text{end}}) a_{i-1} R_{i-1} - \delta(t - t_{\text{end}}) a_i R_i$$

$$\frac{dV_i}{dt} = v_i S_i - d_i V_i + \delta(t - t_{\text{end}}) a_{i-1} V_{i-1} - \delta(t - t_{\text{end}}) a_i V_i$$



where $i = 1,\ldots, k$ and S_i, I_i, R_i, V_i are an i-age group of the proportion of Susceptible, Infected, Recovered, and Vaccinated people.

B = Birth rate
β_i = Age-based force of Infection
v_i = Age-based Vaccination rate
d_i = Age-based (natural) death rate
γ_i = Age-based Recovery rate
a_i = Aging rate ($a_0 = a_k = 0$)
c_{ij} = Average number of contacts from j-age group to i-age group *(Who Interacts With Who)*

$$\delta(t - x) = \begin{cases} 0 & \text{if } t \neq x \\ \infty & \text{if } t = x \end{cases}$$

and $\int_{x-\epsilon}^{x+\epsilon} \delta(t - x) dt = 1$

$$\delta_{ij} = \begin{cases} 0 & \text{if } i \neq j \\ 1 & \text{if } i = j \end{cases}$$

Economic Evaluation[5]

Cost-effectiveness analysis: Compares costs with natural biomedical units of outcomes i.e. number of cases, life years gained or quality-adjusted life years (QALY). Current threshold for treatments, suggested by NICE, is £20,000 to £30,000 per QALY.
Cost-benefit analysis: Attaches monetary values to the measure of effect.
Cost-utility analysis: Focuses more on the financial aspect, applied to pharmacoeconomics.

We look at compendia and NHS reference costs for:
- Direct costs (direct labour, materials, medicines, facilities etc.)
- Indirect/societal costs (volunteer services, cost of work loss etc.)
- Costs associated to immunisation
- Benefits of vaccination

Calculation:

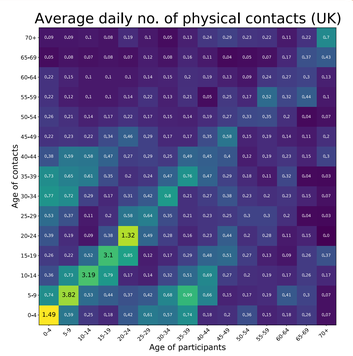
Net Present Value (NPV):
to analyse profitability of a project; considers time value of money.

$$\text{NPV} = \sum_{t=0}^{T} \frac{R_t}{(1 + r)^t}$$

R_t = Net cash inflow−outflows during a single time period, t
r = Discount rate (rate of inflation)
t = Time period in years
T = Number of time periods under consideration

Future Work

- **Modelling**
  - Having defined the model and identified suitable data sources, the next step is to attempt to fit the model and evaluate how well it fits the data.
  - Addition of temporal forcing.
- **Health Economics of MMR Vaccinations**
  - Modelling impact of alternative vaccination policies
  - Pricing of MMR vaccination policies.
- **Parameter Estimation**
  - Using different *Who Interacts With Who* matrices (e.g. BBC pandemic) instead of the current POLYMOD (see heatmap)



References
1. NHS. www.nhs.uk. **2.** Anderson, Roy M., B. Anderson, and Robert M. May. *Infectious diseases of humans: dynamics and control.* Oxford university press, 1992. **3.** Bolker, Ben M., and Grenfell, Bryan T. "Chaos and biological complexity in measles dynamics." *Proceedings of the Royal Society of London. Series B: Biological Sciences* 251.1330 (1993): 75-81. **4.** Bolker, B., and Grenfell, Bryan T. "Space, persistence and dynamics of measles epidemics." *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences* 348.1325 (1995): 309-320. **5.** Zhou, Fangjun, et al. "Economic evaluation of the routine childhood immunization program in the United States, 2009." *Pediatrics* 133.4 (2014): 577-585.