

# Summary Report

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May 27, 2020

# 1 Model

Let us define a  $k$ -age group compartmental SIRV model for the infection dynamics of the diseases covered by the MMR vaccine. This model takes the form of a system of four vectorised ordinary differential equations. Each of the  $k$  vector entries then corresponds to a given age subgroup with span  $a_i$ ,  $i \in 1 \dots k$ . Each equation then governs the dynamics what proportion of the subpopulations is susceptible, infected, recovered, or of those who have been vaccinated.

The model can either be represented in matrix form

$$\begin{aligned} \frac{ds}{dt} &= (\mathbf{I} - \mathbf{V})\mathbf{b} - (\mathbf{V} + \mathbf{D})\mathbf{s} - \mathbf{s} * (\boldsymbol{\beta}(t)\mathbf{C}\mathbf{i}) + \delta_{t_{end}}(t)(\mathbf{L} - \mathbf{I})\mathbf{A}\mathbf{s} \\ \frac{di}{dt} &= \mathbf{s} * (\boldsymbol{\beta}(t)\mathbf{C}\mathbf{i}) - (\mathbf{D} + \boldsymbol{\gamma})\mathbf{i} + \delta_{t_{end}}(t)(\mathbf{L} - \mathbf{I})\mathbf{A}\mathbf{i} \\ \frac{dr}{dt} &= \boldsymbol{\gamma}\mathbf{i} - \mathbf{D}\mathbf{r} + \delta_{t_{end}}(t)(\mathbf{L} - \mathbf{I})\mathbf{A}\mathbf{r} \\ \frac{dv}{dt} &= \mathbf{V}(\mathbf{s} + \mathbf{b}) - \mathbf{D}\mathbf{v} + \delta_{t_{end}}(t)(\mathbf{L} - \mathbf{I})\mathbf{A}\mathbf{v} \end{aligned}$$

$\mathbf{s} * \mathbf{i}$  Denotes the elementwise product

$\mathbf{L}$ ,  $(L)_{ij} = \delta_{i,j+1}$  Denotes the lower shift matrix

Where:

$\mathbf{s}, \mathbf{i}, \mathbf{r}, \mathbf{v} \in \mathbb{R}^k$	k-age group compartment vectors
$\mathbf{b} := (b, 0, \dots, 0)$	Birth rate
$\mathbf{V} := \text{diag}(v_1, \dots, v_k)$	Vaccination rates
$\mathbf{D} := \text{diag}(d_1, \dots, d_k)$	Death rates due to other causes
$\boldsymbol{\beta}(t) := \text{diag}(\beta_1(t), \dots, \beta_k(t))$	Age-based force of infection
$\boldsymbol{\gamma} := \text{diag}(\gamma_1, \dots, \gamma_k)$	Recovery rates
$\mathbf{C} \in \mathbb{R}^{k \times k}$ , $\mathbf{C} := (c)_{ij}$	Who Interacts With Who matrix
$\mathbf{A} \in \mathbb{R}^{k \times k}$	The age group transition matrix

where  $\mathbf{A}$  has the structure

$$\mathbf{A} = \begin{bmatrix} a_1^{-1} & & & & \\ & a_2^{-1} & & & \\ & & \ddots & & \\ & & & a_{k-1}^{-1} & \\ & & & & 0 \end{bmatrix}$$

Or in indexed form

$$\begin{aligned}
\frac{dS_i}{dt} &= \delta_{1,i}(1 - v_1)b + \delta_{t_{end}}(t)a_{i-1}S_{i-1} - \sum_{j=1}^k \beta_i c_{ij} S_i I_j - (d_i + \delta_{t_{end}}(t)a_i + v_i)S_i \\
\frac{dI_i}{dt} &= \delta_{t_{end}}(t)a_{i-1}I_{i-1} + \sum_{j=1}^k \beta_i c_{ij} S_i I_j - (d_i + \gamma_i + \delta_{t_{end}}(t)a_i)I_i \\
\frac{dR_i}{dt} &= \delta_{t_{end}}(t)a_{i-1}R_{i-1} + \gamma_i I_i - (d_i - \delta_{t_{end}}(t)a_i)R_i \\
\frac{dV_i}{dt} &= \delta_{1,i}v_1b + \delta_{t_{end}}a_{i-1}V_{i-1} + v_i S_i - d_i V_i - \delta_{t_{end}}(t)a_i V_i
\end{aligned}$$

Where  $i = 1 \dots k$  and  $a_0 = a_k = 0$ .  
 $I_0 = S_0 = R_0 = V_0 = 0$

## 2 Data

### 2.1 Immunisation Rates

Immunisation is available from the NHS COVER reports [4].

### 2.2 Between Group Contact Rates

As a starting point for *Who Interacts With Who* matrices, the POLYMOD study [6] can be utilised. This matrix will then further be weighted by force of infection for each age group, to be inferred from data.

### 2.3 Epidemiologic Data

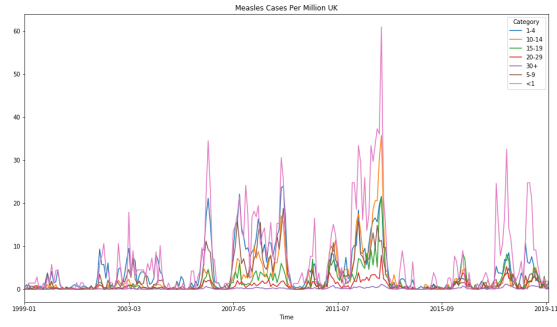
There are several sources of age-structured epidemiologic data for MMR diseases available.

By far the highest temporal resolution for measles and rubella is offered by the ECDC Surveillance Atlas of Infectious Diseases dataset [9], which offers age standardised rates with monthly resolution, spanning years 1999-2019 for measles, and 2007-2019 for rubella. Unfortunately for mumps this dataset only offers yearly resolution for years 2000-2017.

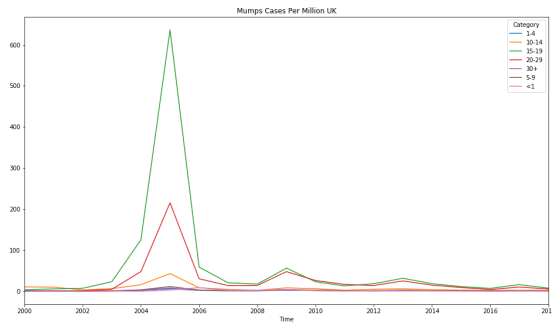
Further recent age-structured data with yearly temporal resolution is available from Public Health England (PHE) reports [5, 7, 8]

Historic age-structured data can be obtained from the Health Protection Agency (HPA) archives [2, 3, 1]. These datasets span years 1989-2012, and offer yearly temporal resolution. This data offers an insight into situation when vaccination rate too low to confer herd immunity.

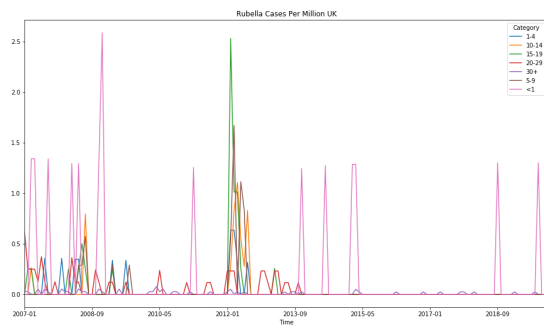
This data should be sufficient to parametrise and fit an age-stratified SIRV model for years 1998-2019, as well as to confirm that the compound behaviour of this model under low vaccination rates corresponds to real data.



(a)



(b)



(c)

Figure 1: ECDC Age Standardised rates for the UK plotted against time 1a Measles data 1b Mumps data 1c Rubella data

## 2.4 Population Structure

Consider a situation where a constant population size is desired, and the following is given:

$\alpha^*$	age distribution
$\mathbf{b}$	birth rate per capita
$\mathbf{N}$	total population size

It is then required to estimate the matrix consisting of the total proportions of each age group that die every year  $\mathbf{X} = \text{diag}(x_1, \dots, x_n)$ , such that:

$$\alpha^* = (\alpha^* + \mathbf{b}/N) + (\mathbf{I} - \mathbf{L})\mathbf{A}\mathbf{D}(\alpha^* + \mathbf{b}/N)$$

then:

$$\begin{aligned} \alpha^* &= (\mathbf{I} + (\mathbf{I} - \mathbf{L}))\mathbf{A}\mathbf{X}(\alpha^* + \mathbf{b}/N) \\ \Rightarrow \quad \mathbf{M}^{-1}\alpha^* &= \mathbf{X}\mathbf{q} \\ \Rightarrow \quad \langle \mathbf{M}^{-1}\alpha^*, \mathbf{e}_j \rangle &= \langle \mathbf{X}\mathbf{q}, \mathbf{e}_j \rangle \\ \Rightarrow \quad \langle \mathbf{M}^{-1}\alpha^*, \mathbf{e}_j \rangle &= x_j q_j \\ \Rightarrow \quad x_j &= \frac{\langle \mathbf{M}^{-1}\alpha^*, \mathbf{e}_j \rangle}{q_j} \end{aligned}$$

Where:

$$\begin{aligned} \mathbf{M} &=: (\mathbf{I} + (\mathbf{I} - \mathbf{L}))\mathbf{A} \\ \mathbf{q} &=: \alpha^* + \mathbf{b}/N \end{aligned}$$

and  $\mathbf{e}_j$  is the  $j$ -th basis vector.

Furthermore  $\mathbf{M}$  is invertible as  $(\mathbf{I} - \mathbf{L})\mathbf{A}$  is singular, positive-semidefinite, and  $\mathbf{M}$  it's spectral shift away from zero.

Finally, to obtain death rates  $d_j$ , we note that these relate to the total proportion of a given age group that dies every year through:

$$x_j \alpha_j^* = \int_0^1 d_j a \, da, \quad a(0) = \alpha_j^*$$

Therefore:

$$\log(x_j + 1) = d_j$$

## References

- [1] [ARCHIVED CONTENT] HPA - *Mumps Notifications in England and Wales (England only), by Age Group, 1989 - 2012*. URL: [https://webarchive.nationalarchives.gov.uk/20140505193443/http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb\\_C/1195733844620](https://webarchive.nationalarchives.gov.uk/20140505193443/http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733844620) (visited on 04/07/2020).
- [2] [ARCHIVED CONTENT] HPA - *Notifications, by Age Group, 1989 - 2012*. URL: [https://webarchive.nationalarchives.gov.uk/20140505192945/http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb\\_C/1195733802298](https://webarchive.nationalarchives.gov.uk/20140505192945/http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733802298) (visited on 04/07/2020).
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- [6] Joël Mossong et al. "Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases". In: *PLOS Medicine* 5.3 (Mar. 25, 2008). Publisher: Public Library of Science, e74. ISSN: 1549-1676. DOI: 10.1371/journal.pmed.0050074. URL: <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0050074> (visited on 04/02/2020).
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- [8] *Rubella: confirmed cases in England and Wales by age and region, 2012 to 2019*. GOV.UK. Library Catalog: [www.gov.uk](http://www.gov.uk). URL: <https://www.gov.uk/government/publications/rubella-confirmed-cases/rubella-confirmed-cases-in-england-and-wales-by-age-and-region-2012-to-2013> (visited on 04/07/2020).
- [9] *Surveillance Atlas of Infectious Diseases*. URL: <https://www.ecdc.europa.eu/en/surveillance-atlas-infectious-diseases> (visited on 04/02/2020).