

Supplementary Information: Quantifying the impact of norovirus transmission in the community on acute kidney injury hospitalisations in England: a mathematical modelling study

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S1. Transmission model and parameters

S1.1 Force of infection and additional model details

The force of infection (λ_i) is a function of the probability of transmission q_i , contact between age groups c_{ij} , the number of people symptomatically infected (I_s) and asymptotically infected (I_a), and a seasonal forcing term (κ). The probability of infection q_i is different for those <5 years old and ≥ 5 years old to reflect the higher incidence observed in children <5 in epidemiological and modelling studies (1–3). Symptomatic (I_{s_i}) and asymptomatic (I_{a_i}) individuals contribute to the force of infection. However, we assume that asymptomatic individuals are less infectious and this is reflected by a factor ρ ; reflecting the previously modelled and outbreak data suggesting reduced infectiousness of asymptomatic individuals (2,4).

In the force of infection there is a seasonal forcing term denoted κ . Similar to previously reported studies, the term for the seasonal amplitude is denoted $w1$ and a seasonal offset term denoted as $w2$ (2,3,5). The seasonal forcing term is applied to the contact matrix c_{ij} .

Fixed parameters were birth and death rate, contacts patterns, incubation period, duration of symptoms, duration of asymptomatic shedding, proportion of infections symptomatic, relative infectiousness during asymptomatic period. Estimated parameters from Bayesian inference were the duration of immunity, amplitude and offset of seasonal forcing, and the probability of transmission in the under 5's and over 5's. Table 2 lists the fixed and estimated parameters.

S1.2 Model equations

$$\frac{dS_i}{dt} = bN + \delta R_i - \lambda_i S_i - dS_i + \tau S_i;$$

$$\frac{dE_i}{dt} = \lambda_i S_i - \sigma \varepsilon E_i - \varepsilon(1 - \sigma)E_i - dE_i;$$

$$\frac{dI_{s_i}}{dt} = \sigma \varepsilon E_i - \psi I_{s_i} - dI_{s_i} + \tau I_{s_i};$$

$$\frac{dI_{a_i}}{dt} = (1 - \sigma)\varepsilon E_i + \psi I_{s_i} + \lambda_i R_i - \gamma I_{a_i} - dI_{a_i} + \tau I_{a_i};$$

$$\frac{dR_i}{dt} = \gamma I_{a_i} - \lambda_i R_i - \delta R_i + \tau R_i;$$

$$\lambda_i = q_i \kappa \sum_{j=1}^4 c_{ij} (I_{s_j} + \rho(I_{a_j})); \quad \text{force of infection}$$

$$\kappa = 1 + w1 \cos\left(\frac{2\pi t}{364} + w2\right) \quad \text{seasonal forcing}$$

i denotes age groups: 0-4; 5-14; 15-64; 65+

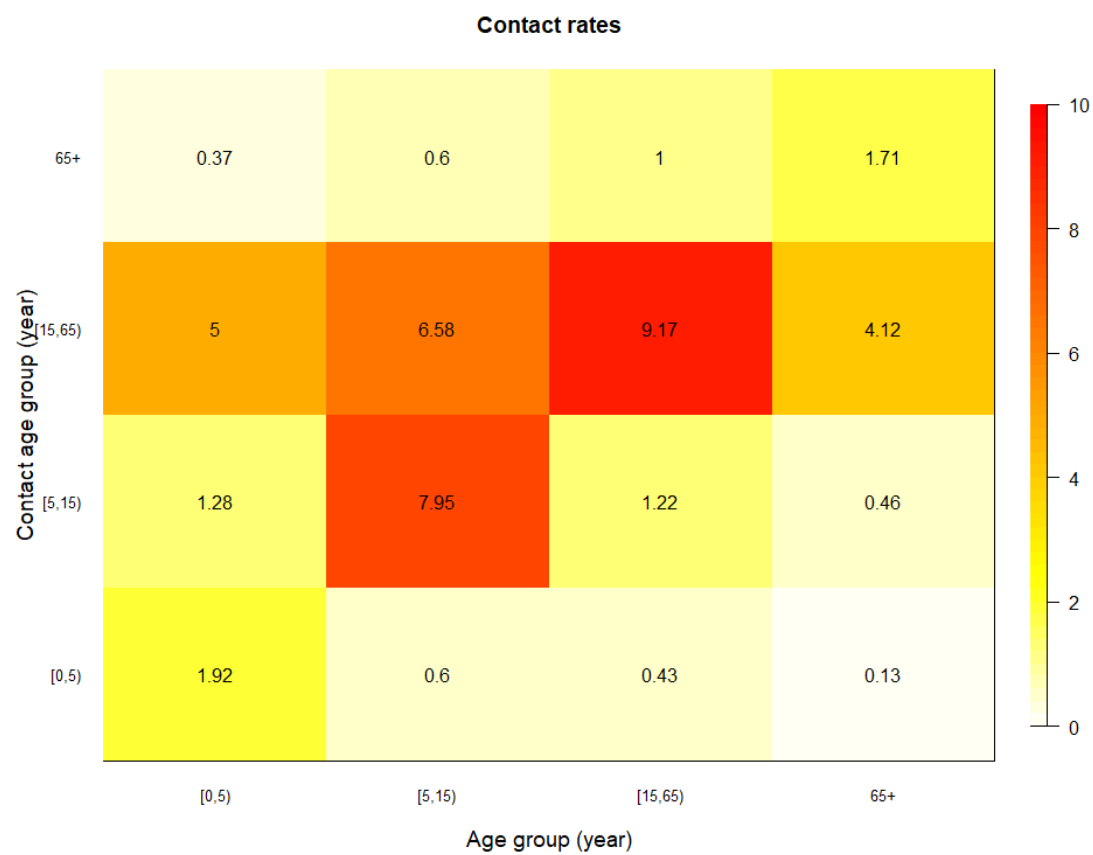
S , susceptible; E , exposed; I_s , infectious symptomatic; I_a , infectious asymptomatic; R , recovered, N , total population; transition parameters described in S1.3

Parameter	Symbol	Value	Prior	Source
Duration of symptoms (days)	$1/\psi$	2 days	-	(2,6,7)
Duration of asymptomatic shedding (days)	$1/\gamma$	10 days	-	(2,7,8)
Incubation period	$1/\varepsilon$	1 day	-	(2,6,7)
Aging	τ	1/365	-	
Birth rate	$1/b$	11.4 per 1000	-	(9)
Contact rate	c_{ij}	See S1.4		(10)
Relative infectiousness during asymptomatic period	ρ	0.05	-	(2,4)
Proportion of infections symptomatic	σ	Fitted	Normal; mean = 0.75; SD = 0.075	(5)
Duration of immunity (years)	$1/\delta$	Fitted	Uniform; 0.5-13	(2,11)
Seasonal amplitude term	$w1$	Fitted	Uniform; 0-0.1	-
Seasonal offset term	$w2$	Fitted	Uniform; 0-0.5	-
Probability of infection between under 5s	$q1$	Fitted	Normal; mean = 0.21; SD = 0.115	(2,12)
Probability of infection to over 5s	$q2$	Fitted	Normal; mean = 0.005; SD = 0.032	(2,12)
Underreporting to surveillance 0-4	χ_{0-4}	Fitted	Uniform; 0-0.01	(12,13)
Underreporting to surveillance 15-64	χ_{15-64}	Fitted	Uniform; 0-0.01	(12,13)
Underreporting to surveillance 65+ in the winter	$\theta_{winter,65+}$	Fitted	Uniform; 0-0.06	(12,13)
Underreporting to surveillance 65+ in the summer	$\theta_{summer,65+}$	Fitted	Uniform; 0-0.1	-
AKI hospitalisation in 65+ in the winter	$\theta_{AKI,winter,65+}$	Fitted	Uniform; 0-0.75	-
AKI hospitalisation in 65+ in the summer (week 27)	$\theta_{AKI,summer,65+}$	Fixed	0	-
Gastroenteritis hospitalisation in 65+ in the winter	$\theta_{Gastro,winter,65+}$	Fitted	Uniform; 0-0.5	(14,15)
Gastroenteritis hospitalisation in 65+ in the summer (week 27)	$\theta_{Gastro,summer,65+}$	Fixed	0	-
GP attendance for gastroenteritis in under 5s	ζ	Fitted	Uniform; 0-0.5	(13,14)

96 S1.4 Contact rates

97

98 We applied the following POLYMOD UK contact matrix



S2. Data sources

S2.1 Norovirus surveillance data

We fit to data from the UK Health Security Agency's Second Generation Surveillance System (SGSS), the national laboratory reporting system for positive laboratory tests for England (16). We used deduplicated counts of laboratory data positive for norovirus from faecal and lower gastrointestinal tract specimens over time. Norovirus is not a notifiable disease, therefore surveillance in England is passive (17). Given this, samples taken represent outbreaks in care homes and health care settings, and of individuals hospitalised with more severe disease (17).

S2.2 Second study of infectious intestinal disease in the community (IID2)

The second longitudinal study of infectious intestinal diseases in the UK (IID2) measured incidence of sporadic community cases of laboratory positive norovirus in a prospective community cohort followed up between 2008-2009 (13). The study involved 88 primary care practices and analysed data from 6,836 participants. Compared to the general population, participants were more likely to be older, female, less deprived, and living in rural areas (13). Rates of GP consultation and reports to national surveillance were also measured. We fit our model to age stratified incidence per 1000 person years estimated by the IID2 study. We also used rates of GP consultation and under reporting to national surveillance to assess suitability of estimated under reporting parameters from the data fitting process.

S2.3 Clinical Practice Research Datalink (CPRD) Aurum

CPRD Aurum is a primary care database collecting longitudinal electronic health data from participating GPs representing 46 million patients with 16 million currently registered and active individuals (18). Quality assured data on patients consultations and conditions are collected using Read codes, a standardised hierarchical coding structure. Contributing general practices cover 20% of practices in the UK and the data are representative of the UK population by age and sex (19). We extracted data on attendances for gastroenteritis by age. We defined a GP attendance for gastroenteritis where there was a recorded pathogen code (positive test for norovirus) or a diagnosis code (e.g. gastroenteritis) (Supplement S7.3). Symptom codes (e.g. diarrhoea and vomiting only) were not included as they were non-specific. Attendance counts were converted into incidence per 1000 person years. We took the denominator of each year as the number of patients who were registered in the midpoint (week 27) of each year.

S2.4 Hospital Episode Statistics (HES)

75% of CPRD Aurum is linked to Hospital Episode Statistics (HES), which contains data on hospital admissions in England, recorded using the International Classification of Diseases version 10 (ICD-10) classification (18,19). We extracted data from HES for community-acquired AKI, and gastroenteritis hospitalisations (Supplement S7.1). We defined community-acquired hospitalisations as an AKI code recorded in any position (primary, secondary, tertiary, etc.) in an episode within three days of admission, and refer to this definition as 'AKI hospitalisation' subsequently. We defined gastroenteritis hospitalisation as a relevant ICD-10 code in any position in HES, at any time during an admission. The denominator of each year was the number of patients who were registered in the midpoint (week 27) of each year.

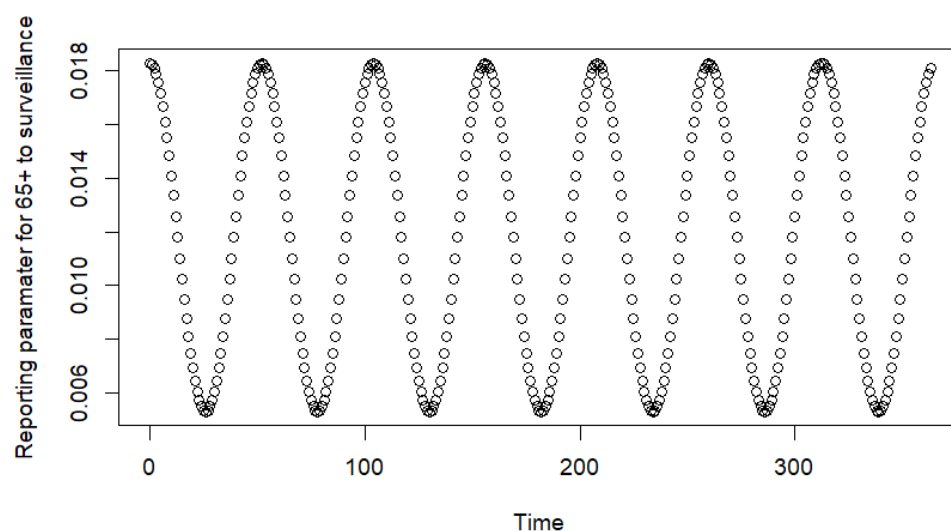
S3. Model fitting

S3.1 Observation model explanation

Observation model for surveillance data

We developed an observation model to link the incidence of norovirus infections to surveillance data. For age groups 0-4 and 15-64, we simply apply a reporting parameter that scales the number of infections we simulate from the model, implying a fraction are reported to surveillance systems. This scaling factor is estimated through the Bayesian inference process.

For surveillance data reported in the age group 65+, due to factors such as outbreaks in healthcare settings, higher burden in this is vulnerable patient population, and more testing, we assume better detection to surveillance systems in the winter than the summer. We implement this by applying a reporting parameter that scales the number of infections we simulate from the model, as a smooth cosine function depicted as follows:



Observation model for GP attendance

We developed an observation model to link the incidence of norovirus infections to GP attendances for gastroenteritis in age groups 0-4. We take into account secular trends in the GP attendance data with a B-spline function of time with three knots. A B-spline function was used due to its properties of modelling long term patterns smoothly (20). Three knots were chosen, in order to parsimoniously capture the overall secular trend but avoid capturing seasonality of the data. This secular trend is then applied to the model output of norovirus infections in children aged 0-4. In the 5-14, 15-64 and 65+ age group, we assumed that norovirus dynamics are poorly captured in GP attendance data, therefore we did not fit the model to GP attendances for gastroenteritis in these groups.

The model output, now with a secular trend applied from the observed data, is multiplied by a parameter which fits the model output to observed data of GP attendance for all-cause gastroenteritis. We interpret this parameter as a factor linking a norovirus infection to all cause gastroenteritis

diagnosis at a GP. This is strictly speaking not a parameter of the proportion of norovirus infections diagnosed at a GP as there are other causes of a GP attendance for gastroenteritis.

Observation model for hospitalisations

We developed an observation model to link the incidence of norovirus infections within the population with hospitalisations with gastroenteritis and AKI. For simplicity, we outline the process of fitting the AKI hospitalisation observation model. The method is the same for gastroenteritis hospitalisations and detailed in the visual explanation (Supplement S3.2).

Firstly, we assume that a fraction of hospitalisations are caused by norovirus infections. This is estimated through the Bayesian inference process by applying a parameter to the model output for each healthcare outcome. For example, we apply a parameter to estimate the number of norovirus infections in 65+ year olds linked to an AKI hospitalisation. However, this alone would not fit the model output to the data.

In order to link the model output to the different outcomes, we take into account additional factors influencing observations in EHR data. These factors include changes in coding practices and different disease-specific trends, all culminating in influencing non-specific disease syndromes such as AKI or gastroenteritis. To capture these trends we used a B-spline function of time with three knots on the observation data.

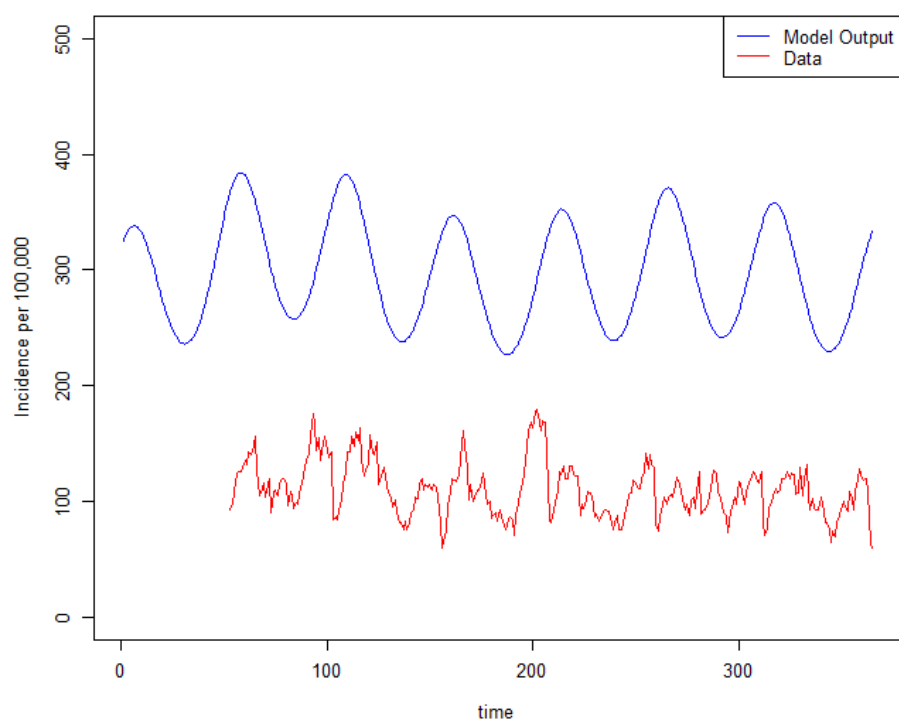
We then make an assumption that the sinusoidal seasonality in the AKI data is in part due to the observed seasonality in norovirus infections. In accounting for other causes of community acquired AKI, we simply add the changes in norovirus linked AKI hospitalisation incidence to the cubic spline (representing the secular trend of community acquired AKI hospitalisations). The parameter estimating the proportion of norovirus infections linked to AKI hospitalisations influences the amplitude of the model output fitting to the AKI hospitalisations data. Through Bayesian inference, we estimate the parameter values that gives the amplitude that best reflects the seasonality observed in the AKI hospitalisation data.

However, we assume that the proportion of norovirus infections linked to the AKI hospitalisation data is not a single fixed value. Due to winter factors such as outbreaks in healthcare settings, higher burden in vulnerable patient populations, we assume better detection and attribution of AKI or gastroenteritis hospitalisations to norovirus in the winter. Therefore the reporting parameter linking infection to hospitalisation data varies between the winter and summer, and the transition between seasons is captured using a smooth cosine function.

S3.2 Observation model visual explanation

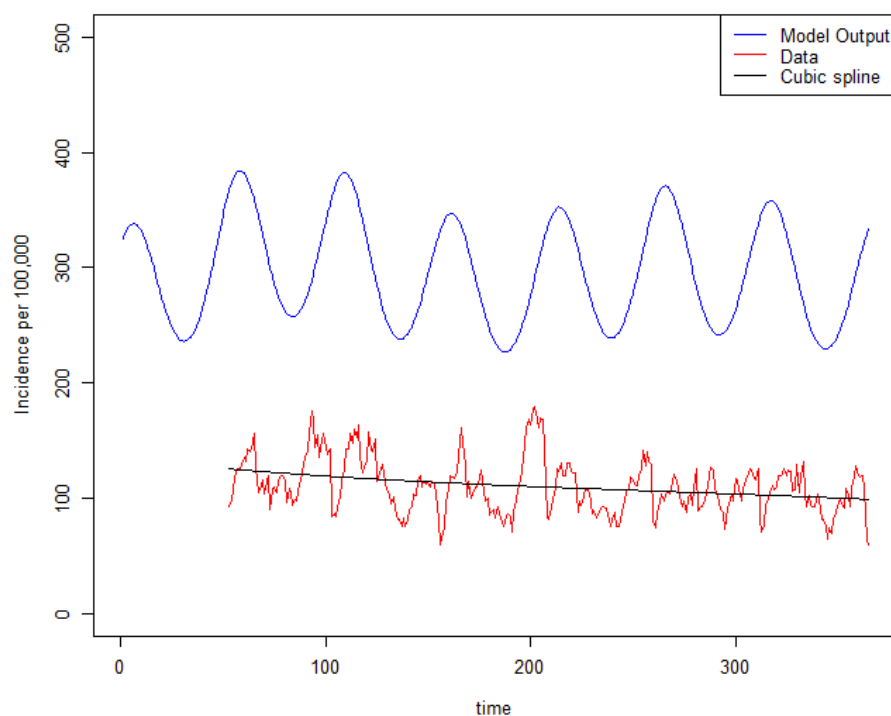
Observation model for GP attendance for gastroenteritis

We took the following steps in fitting the model output to the data on gastroenteritis attendances in general practice. The figure below depicts the model output of norovirus infections in the children aged 0-4, and data on GP attendance for gastroenteritis in children aged 0-4:



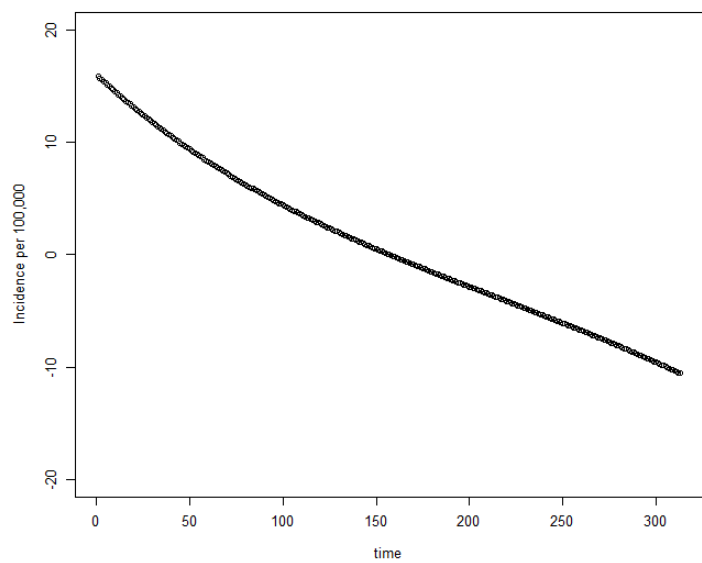
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268 Electronic health data has long term trends which reflect changes in coding practices as well as
 269 disease specific trends which are multi-factorial when using non-specific disease outcomes such as
 270 GP attendance for gastroenteritis. In order to fit the norovirus model infections to GP attendances for
 271 gastroenteritis first we capture the long terms trends in the GP attendance data with a spline function
 272 of time. We use a B-spline basis function with 3 knots to capture the long term trend:
 273



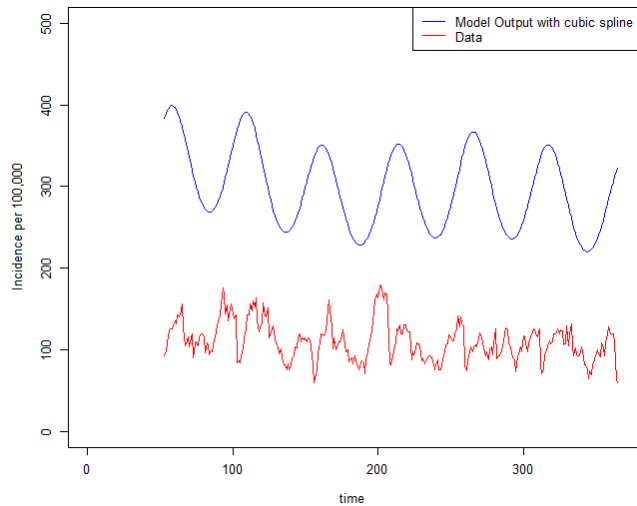
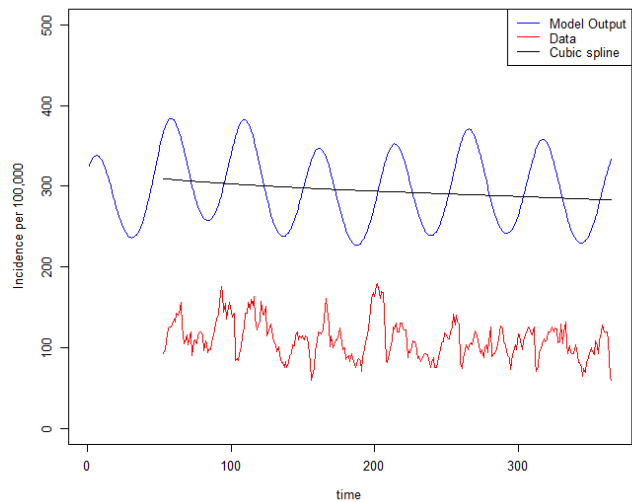
296

297 The output of the cubic spline is then added to the model output. In order to capture the changing
 298 incidence of the cubic spline over time, the median of the spline function is taken, and the difference
 299 between the spline function and the median is calculated to give an output as below:

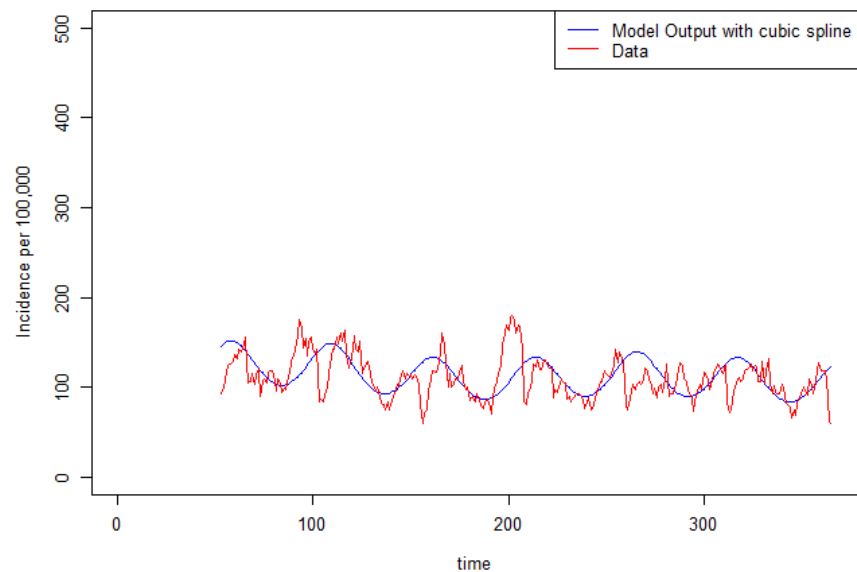


316

317 This spline function is then added to the model output to capture the long term trends observed in the
 318 GP attendance data.



The model output with the cubic spline is then multiplied by a reporting parameter which fits the model output to observed data of GP attendance for gastroenteritis.

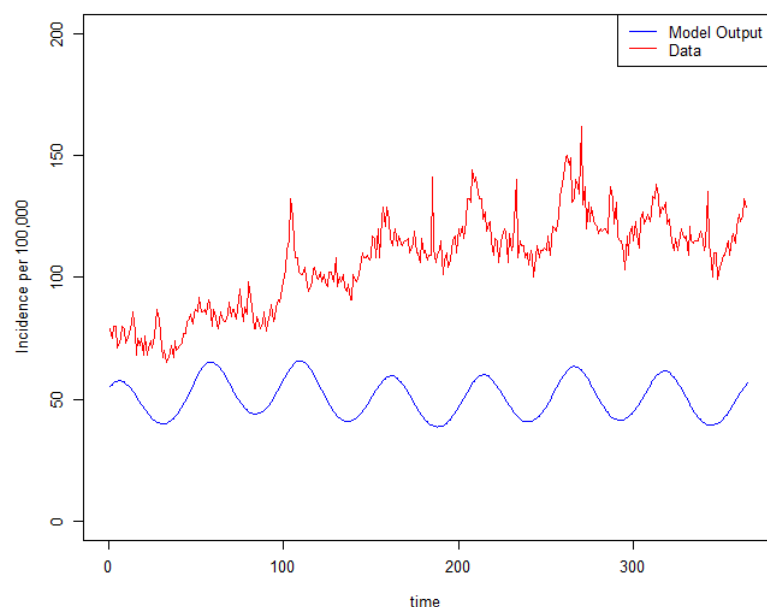


The reporting parameter is interpreted as a factor linking norovirus infections to all cause gastroenteritis diagnosis at a GP. This is strictly speaking not a parameter of the proportion of norovirus infections diagnosed at a GP as there are other causes of a GP attendance for gastroenteritis.

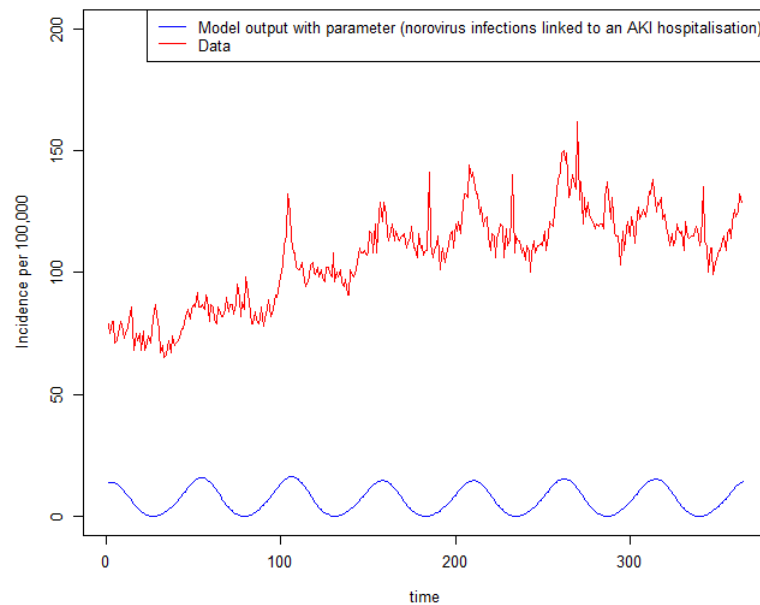
Observation model for acute kidney injury hospitalisations in people aged 65 years and above

We took the following steps in fitting the model output to the data on community acquired acute kidney injury hospitalisations.

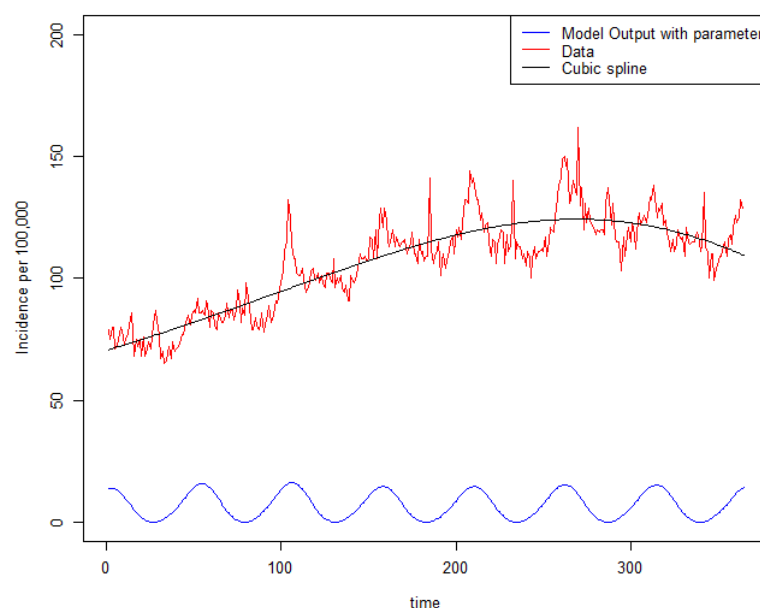
The figure below depicts the model output of norovirus infections in the adults aged 65+, and data on acute kidney injury hospitalisations:



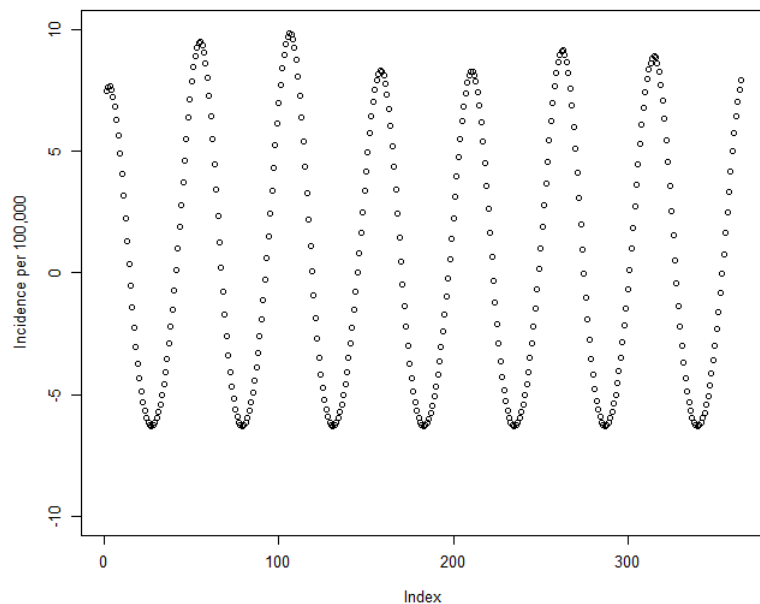
We assume that a fraction of AKI hospitalisations is caused by norovirus infections. Therefore applying a parameter, which estimates the number of norovirus infections in 65+ year olds linked to an AKI hospitalisation, we would expect the incidence of norovirus infections linked to AKI hospitalisations to be much lower than the overall incidence of community acquired AKI hospitalisations (which have many causes). We also assume that the proportion of norovirus infections linked to the AKI hospitalisation data is not a single fixed value. Due to winter factors such as outbreaks in healthcare settings, higher burden in vulnerable patient populations, we assume better detection and attribution of AKI hospitalisations to norovirus in the winter. Therefore the reporting parameter linking infection to hospitalisation data varies between the winter and summer, and the transition between seasons is captured using a smooth cosine function.



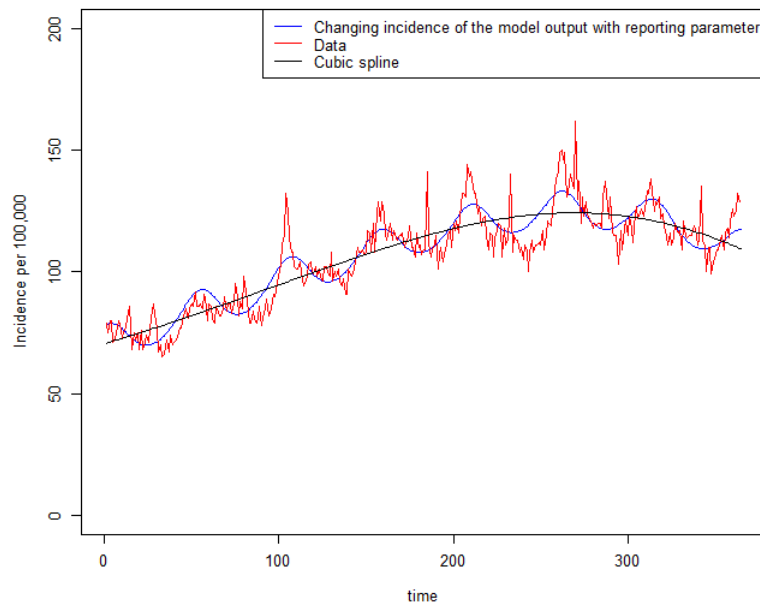
However, to fit the model output to the data on community acquired AKI hospitalisations, we need to incorporate the long term secular trend observed in the data and account for the other causes of community acquired AKI. First we capture the secular trend in the data with a B-spline basis function with 3 knots:

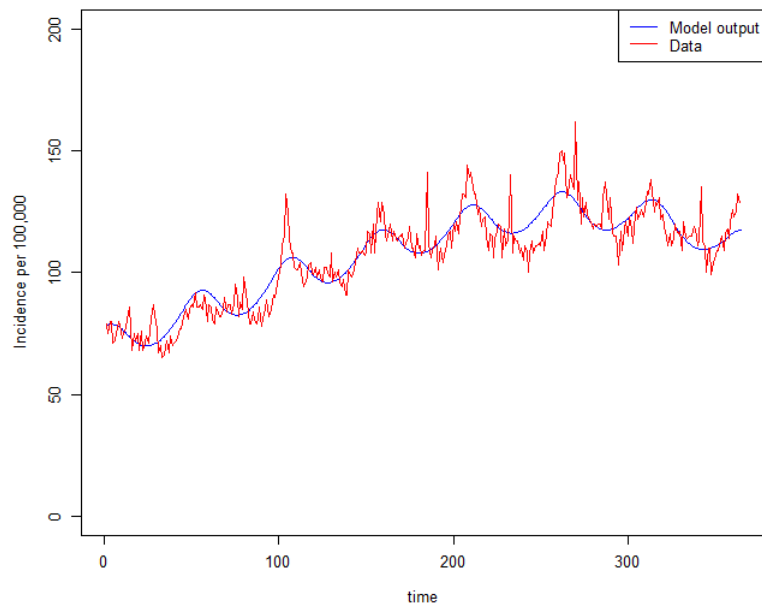


We then make an assumption that the sinusoidal seasonality in the AKI data is in part due to norovirus infections. In accounting for other causes of community acquired AKI, we simply add the changes in norovirus linked AKI hospitalisation incidence to the cubic spline (representing the secular trend of AKI hospitalisations, and community acquired AKI hospitalisations). The changes in the norovirus linked AKI hospitalisation incidence is calculated by taking the difference between the model output and the median of the model output to give an output as below.



Then added to the cubic spline to fit to the data time series.





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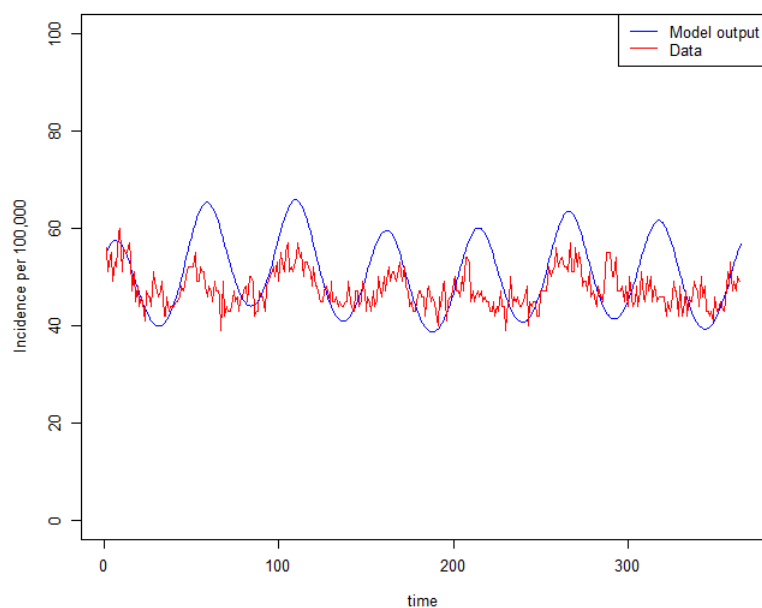
498 The parameter estimating the proportion of norovirus infections linked to AKI hospitalisations
 499 determines the amplitude of the model output fitting to the AKI hospitalisations data. Therefore
 500 assuming norovirus infections in part drives the sinusoidal seasonality observed in AKI, the larger
 501 proportion of norovirus linked AKI hospitalisation, then we would expect more extreme seasonality of
 502 the AKI data. Additionally, we assume that the fit between norovirus infections and all cause AKI.
 503 Through Bayesian inference, the parameter estimates the value giving the best fit to the AKI
 504 hospitalisation data.

505

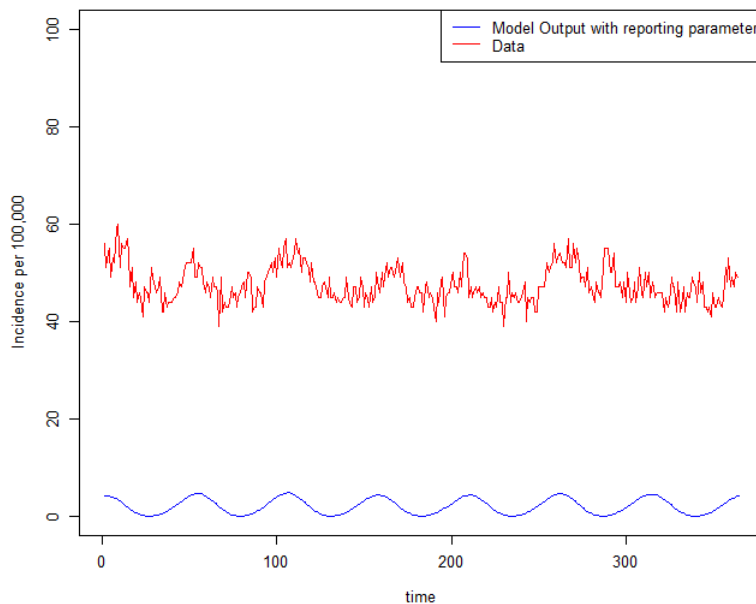
506 *Observation model for gastroenteritis hospitalisations in people aged 65 years and above*

507 We took the following steps in fitting the model output to the data on gastroenteritis hospitalisations.
 508 The figure below depicts the model output of norovirus infections in the adults aged 65+, and data on
 509 gastroenteritis hospitalisations:

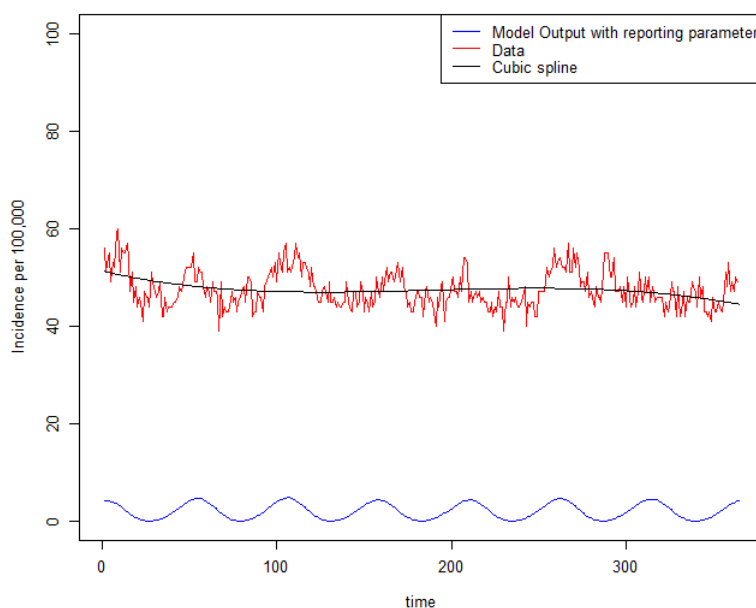
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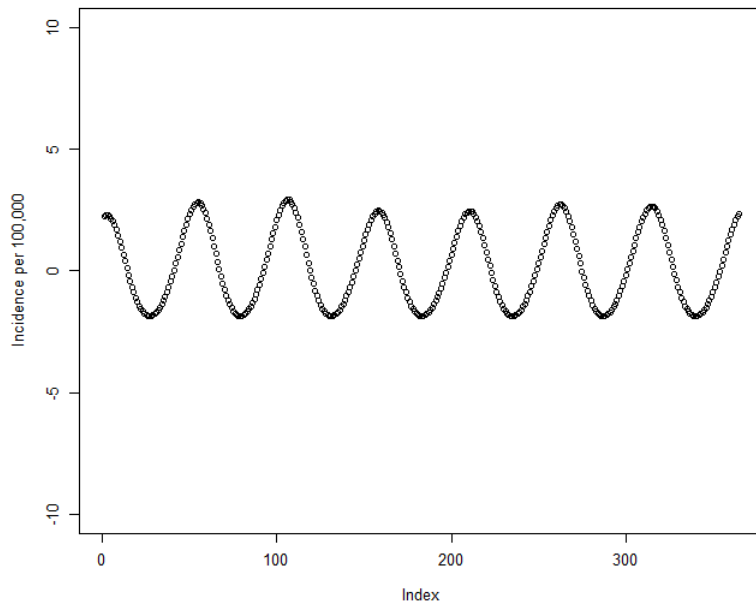
529 We assume that a fraction of gastroenteritis hospitalisations are caused by norovirus infections.
 530 Therefore applying a parameter, which estimates the number of norovirus infections in 65+ year olds
 531 linked to gastroenteritis hospitalisation, we would expect the incidence of norovirus infections linked
 532 to gastroenteritis hospitalisations to be much lower than the overall incidence of gastroenteritis
 533 hospitalisations (which have many causes). We also assume that the proportion of norovirus infections
 534 linked to the gastroenteritis hospitalisation data is not a single fixed value. Due to winter factors such
 535 as outbreaks in healthcare settings, higher burden in vulnerable patient populations, we assume better
 536 detection and attribution of gastroenteritis hospitalisations to norovirus in the winter. Therefore the
 537 reporting parameter linking infection to hospitalisation data varies between the winter and summer,
 538 and the transition between seasons is captured using a smooth cosine function.



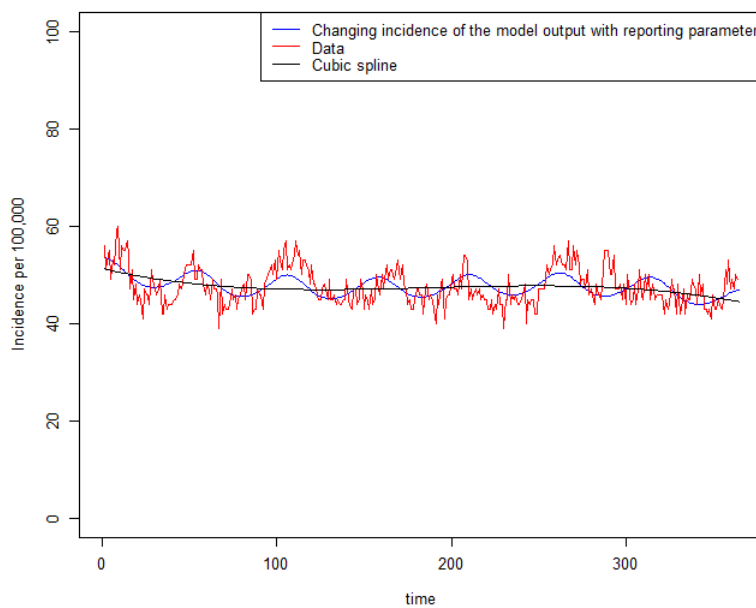
557 However, to fit the model output to the data on gastroenteritis hospitalisations, we need to incorporate
 558 the long term secular trend observed in the data and account for the other causes of gastroenteritis
 559 hospitalisations. First we capture the secular trend in the data with a B-spline basis function with 3
 560 knots:

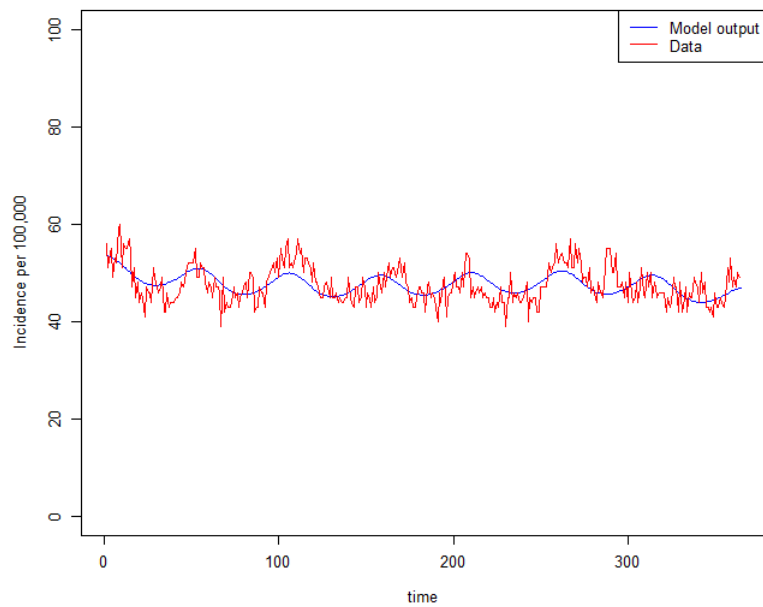


We then make an assumption that the sinusoidal seasonality in the gastroenteritis data is in part due to norovirus infections. In accounting for other causes of gastroenteritis hospitalisations, we simply add the changes in norovirus linked gastroenteritis hospitalisation incidence to the cubic spline (representing the secular trend of gastroenteritis hospitalisations, and other causes of gastroenteritis hospitalisations). The changes in the norovirus linked gastroenteritis hospitalisation incidence is calculated by taking the difference between the model output and the median of the model output to give an output as below.



Then added to the cubic spline to fit to the data time series.





648 The parameter estimating the proportion of norovirus infections linked to gastroenteritis
 649 hospitalisations determines the amplitude of the model output fitting to the gastroenteritis
 650 hospitalisations data. Therefore assuming norovirus infections in part drives the sinusoidal seasonality
 651 observed in gastroenteritis hospitalisations, the larger proportion of norovirus linked AKI
 652 hospitalisation, then we would expect more extreme seasonality of the data.
 653

S3.3 Observation model equations

S3.3.1 Fitting to surveillance data

Number of notifications to surveillance stratified by age groups (0-4 and 15-64)

$$A_i(t) = \theta_i I_{s_i}(t)$$

Number of notifications to surveillance for age group 65+

$$A_{65+}(t) = I_{s_i} \times \left[\left(\frac{1}{2} \left(1 + \cos \left(\frac{2\pi(w-1)}{52} \right) \right) \right) \times \theta_{winter,65+} + \left(\frac{1}{2} \left(1 - \cos \left(\frac{2\pi(w-1)}{52} \right) \right) \right) \times \theta_{summer,65+} \right]$$

Where:

- A denotes the number of notifications to surveillance
- i denotes age group (unless otherwise specified)
- I_s denotes the number of symptomatic infections simulated by the model
- w denotes the week number
- θ_i denotes the reporting parameter scaling the number of infections by age group
- $\theta_{winter,65+}$ denotes the peak of the reporting parameter scaling the number of infections in the 65+ age group in the winter (week 52)
- $\theta_{summer,65+}$ denotes the trough of the reporting parameter scaling the number of infections in the 65+ age group in the summer (week 27)

S3.3.2 B-spline function

$$spl(t) = B_k(t)$$

Where:

- k denotes the number of knots specified in the B-spline function
- t is the variable at which the B-spline function is evaluated i.e. the function is evaluated at each time point

S3.3.3 Fitting to AKI hospitalisation data in 65+

Model incidence of AKI hospitalisation = B

$$spl_{AKI\ hosp,65+}(t) = (t_1, x_{1,AKI\ hosp}), (t_2, x_{2,AKI\ hosp}), \dots, (t_n, x_{n,AKI\ hosp}) \sim spl(t);$$

$$\theta_{AKI,seasonal,65+}(t)$$

$$\begin{aligned} &= I_{s_{65+}} \\ &\times \left[\left(\frac{1}{2} \left(1 + \cos \left(\frac{2\pi(w-1)}{52} \right) \right) \right) \times \theta_{AKI,winter,65+} \right. \\ &\quad \left. + \left(\frac{1}{2} \left(1 - \cos \left(\frac{2\pi(w-1)}{52} \right) \right) \right) \times \theta_{AKI,summer,65+} \right]; \end{aligned}$$

$$B(t) = \left(\left(\left(\frac{Is_{65+}}{pop_{65}} \times 100,000 \right) \times \theta_{AKI,seasonal,65+}(t) \right) - median \left(\left(\frac{Is_{65+}}{pop_{65}} \times 100,000 \right) \times \theta_{AKI,summer,65+} \right) \right) + spl_{AKI hosp,65+}(t)$$

Where:

- B denotes the number of AKI hospitalisations (all cause)
- t denotes time
- $spl_{AKI hosp,65+}$ denotes the spline function fitted to AKI hospitalisation data in 65+
- $\theta_{AKI,seasonal,65+}(t)$ denotes the seasonal reporting parameter, representing the proportion of norovirus infections linked to an AKI hospitalisation in a given time t
- Is_{65+} denotes the number of symptomatic infections simulated by the model
- w denotes the week number
- $\theta_{AKI,winter,65+}$ denotes the peak of the parameter scaling the number of infections in the 65+ age group in the winter (week 52) linked to an AKI hospitalisation in a given time t
- $\theta_{AKI,summer,65+}$ denotes the trough of the parameter scaling the number of infections in the 65+ age group in the summer (week 27) linked to an AKI hospitalisation in a given time t
- pop_{65} denotes the population of the size of 65+ age group

S3.3.4 Fitting to gastroenteritis hospitalisation data in 65+

Model incidence of Gastroenteritis hospitalisation = C

$$spl_{Gastro hosp,65+}(t) = (t_1, x_{1,Gastro hosp}), (t_2, x_{2,Gastro hosp}), \dots, (t_3, x_{3,Gastro hosp}) \sim spl(t);$$

$$\begin{aligned} \theta_{Gastro,seasonal,65+}(t) &= Is_{65+} \\ &\times \left[\left(\frac{1}{2} \left(1 + \cos \left(\frac{2\pi(w-1)}{52} \right) \right) \right) \times \theta_{Gastro,winter,65+} \right. \\ &\left. + \left(\frac{1}{2} \left(1 - \cos \left(\frac{2\pi(w-1)}{52} \right) \right) \right) \times \theta_{Gastro,summer,65+} \right]; \end{aligned}$$

$$C(t) = \left(\left(\left(\frac{Is_{65}}{pop_{65}} \times 100,000 \right) \times \theta_{Gastro,seasonal,65+}(t) \right) - median \left(\left(\frac{Is_{65}}{pop_{65}} \times 100,000 \right) \times \theta_{Gastro,summer,65+} \right) \right) + spl_{Gastro hosp,65+}(t)$$

Where:

- C denotes the number of gastroenteritis hospitalisations (all cause)
- t denotes time
- $spl_{Gastro hosp,65+}$ denotes the spline function fitted to gastroenteritis hospitalisation data in 65+
- $\theta_{Gastro,seasonal,65+}(t)$ denotes the seasonal reporting parameter, representing the proportion of norovirus infections linked to a gastroenteritis hospitalisation in a given time t

- Is_{65+} denotes the number of symptomatic infections simulated by the model
- w denotes the week number
- $\theta_{Gastro,winter,65+}$ denotes the peak of the parameter scaling the number of infections in the 65+ age group in the winter (week 52) linked to a gastroenteritis hospitalisation in a given time t
- $\theta_{Gastro,summer,65+}$ denotes the trough of the parameter scaling the number of infections in the 65+ age group in the summer (week 27) linked to a gastroenteritis hospitalisation in a given time t
- pop_{65} denotes the population size of 65+ age group

S3.3.5 Fitting to Gastroenteritis attendance to GP in 0-4

Model incidence of Gastroenteritis GP attendance in 0 – 4 year olds = D

$$spl_{Gastro\ GP,0-4}(t) = (t_1, x_{1,Gastro\ GP}), (t_2, x_{2,Gastro\ GP}), \dots, (t_n, x_{n,Gastro\ GP}) \sim spl(t);$$

$$median\ spl_{Gastro\ GP,0-4}(t) = spl_{Gastro\ GP,0-4}(t) - median(spl_{Gastro\ GP,0-4}(t));$$

$$D(t) = \left(\frac{Is_{0-4}}{pop_{0-4}} \times 100,000 \right) + median\ spl_{Gastro\ GP,0-4}(t) \times \zeta$$

Where:

- D denotes the number gastroenteritis attendances in age group 0-4 (call cause)
- t denotes time
- $spl_{Gastro\ GP,0-4}$ denotes the spline function fitted to gastroenteritis GP attendances data in 0-4 age group
- ζ denotes the scaling parameter linking norovirus infections to the gastroenteritis GP attendances data in 0-4 age group
- Is_{0-4} denotes the number of symptomatic infections simulated by the model
- pop_{0-4} denotes the population size of 0-4 age group

S3.4 Likelihood calculation

To implement the Metropolis-Hastings algorithm we calculated an overall log likelihood for each value of θ . For each data source we calculated the likelihood assuming a quasi-Poisson distribution. For the age stratified incidence data a Poisson distribution was assumed. The log likelihood calculated for each source of data was then combined to give an overall log likelihood, which was used to estimate the posterior for each parameter (θ).

$$\log L_{norovirus\ surveillance}(\theta | x, \phi_{norovirus\ surveillance})$$

$$= \sum_{i=1}^n [x_i \log(\mu_i(\theta)) - \mu_i(\theta) - \log(x_i!)] / \phi_{norovirus\ surveillance}$$

$$\log L_{AKI\ hospitalisation}(\theta | x, \phi_{AKI\ hospitalisation})$$

$$= \sum_{i=1}^n [x_i \log(\mu_i(\theta)) - \mu_i(\theta) - \log(x_i!)] / \phi_{AKI\ hospitalisation}$$

$$\begin{aligned} & \log L_{\text{Gastroenteritis hospitalisation}}(\theta | x, \phi_{\text{Gastroenteritis hospitalisation}}) \\ &= \sum_{i=1}^n [x_i \log(\mu_i(\theta)) - \mu_i(\theta) - \log(x_i!)] / \phi_{\text{Gastroenteritis hospitalisation}} \end{aligned}$$

$$\begin{aligned} & \log L_{\text{Gastroenteritis GP attendance}}(\theta | x, \phi_{\text{Gastroenteritis GP attendance}}) \\ &= \sum_{i=1}^n [x_i \log(\mu_i(\theta)) - \mu_i(\theta) - \log(x_i!)] / \phi_{\text{Gastroenteritis GP attendance}} \end{aligned}$$

Where:

- L denotes the likelihood of each source of data
- θ denotes the parameters
- x_i denotes the observed value of the i -th data point in each source of data
- $\mu_i(\theta)$ denotes the expected value for the i -th data point as a function of parameters θ
- ϕ denotes the dispersion parameter for each source of data

$$\log L_{\text{IID2 age stratified incidence}}(\theta | x) = \prod_{i=1}^n \frac{e^{-\theta} \theta^{x_i}}{x_i!}$$

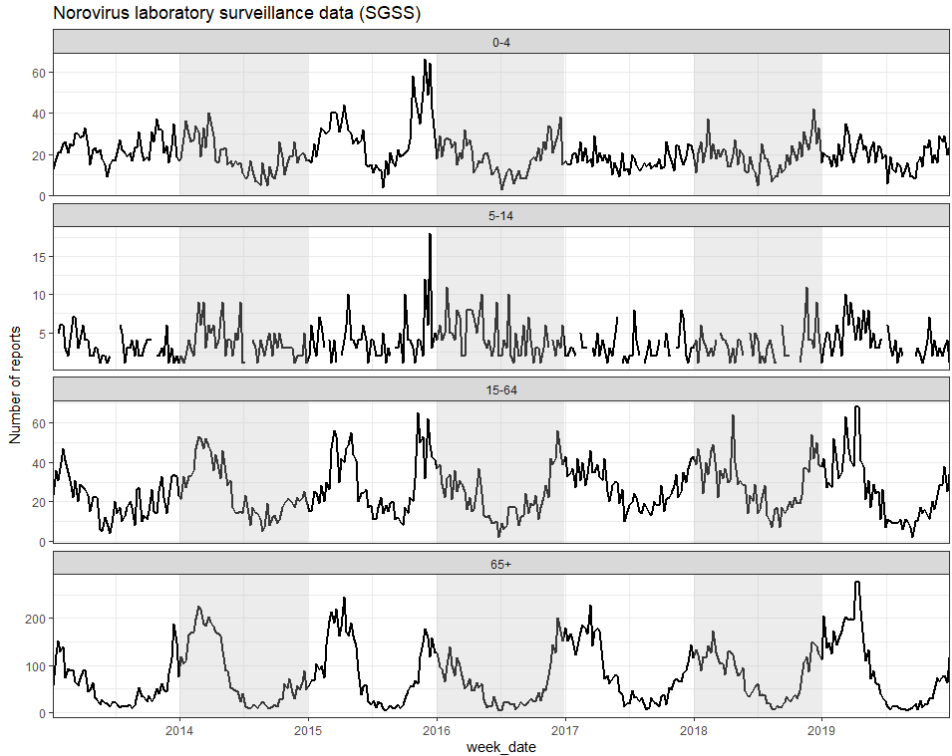
Where:

- L denotes the likelihood
- θ denotes the parameters
- x_i denotes the observed value of the i th data point

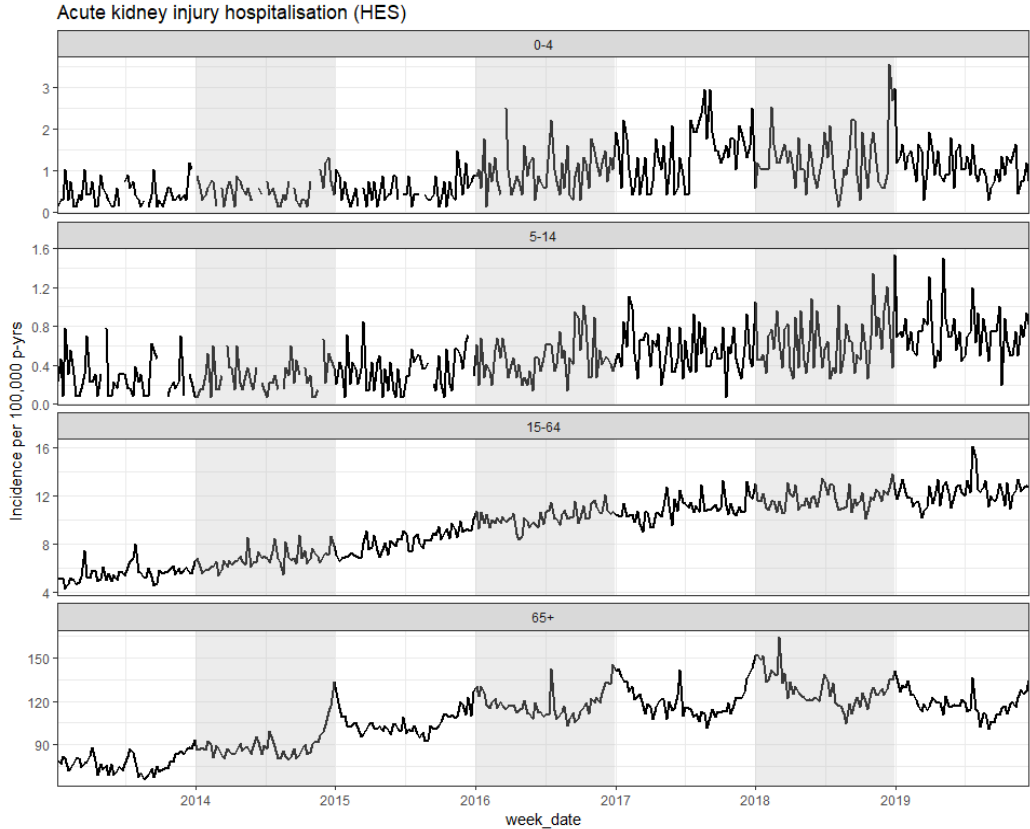
$$\begin{aligned} \log L_{\text{overall}} &= \log L_{\text{norovirus surveillance}} + L_{\text{AKI hospitalisation}} + L_{\text{Gastroenteritis hospitalisation}} \\ &+ L_{\text{Gastroenteritis GP attendance}} + L_{\text{IID2 age stratified incidence}} \end{aligned}$$

S4. Descriptive analysis

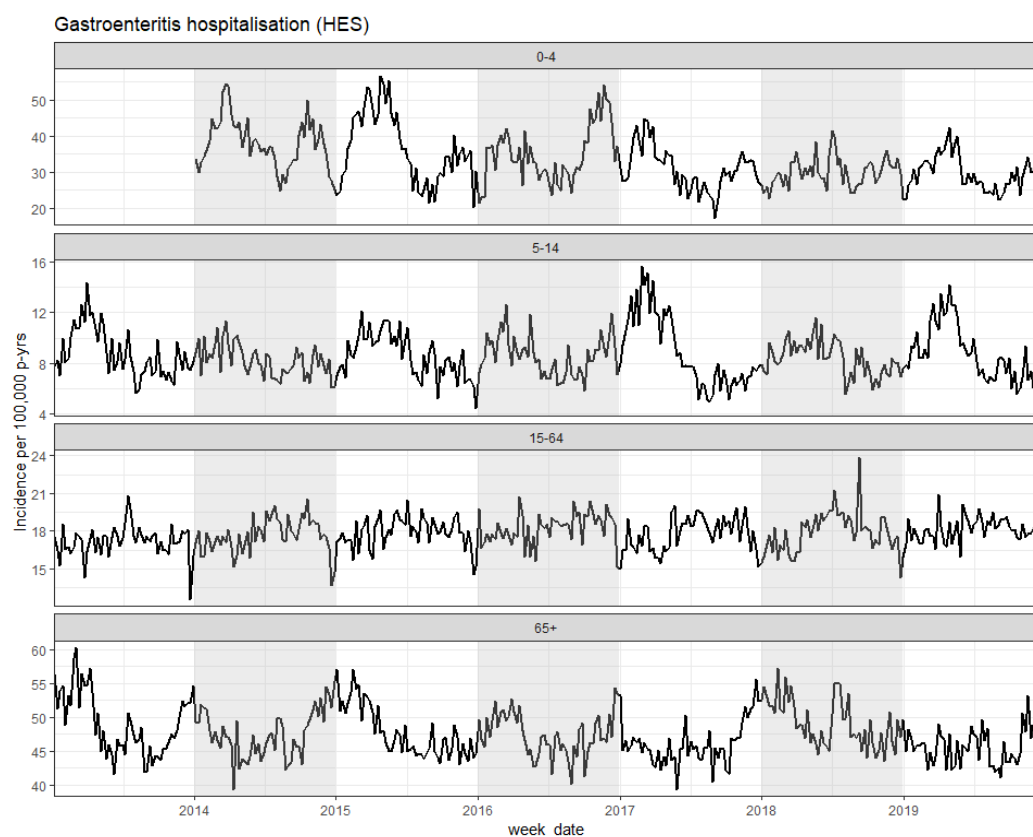
S4.1 Age stratified norovirus surveillance time series



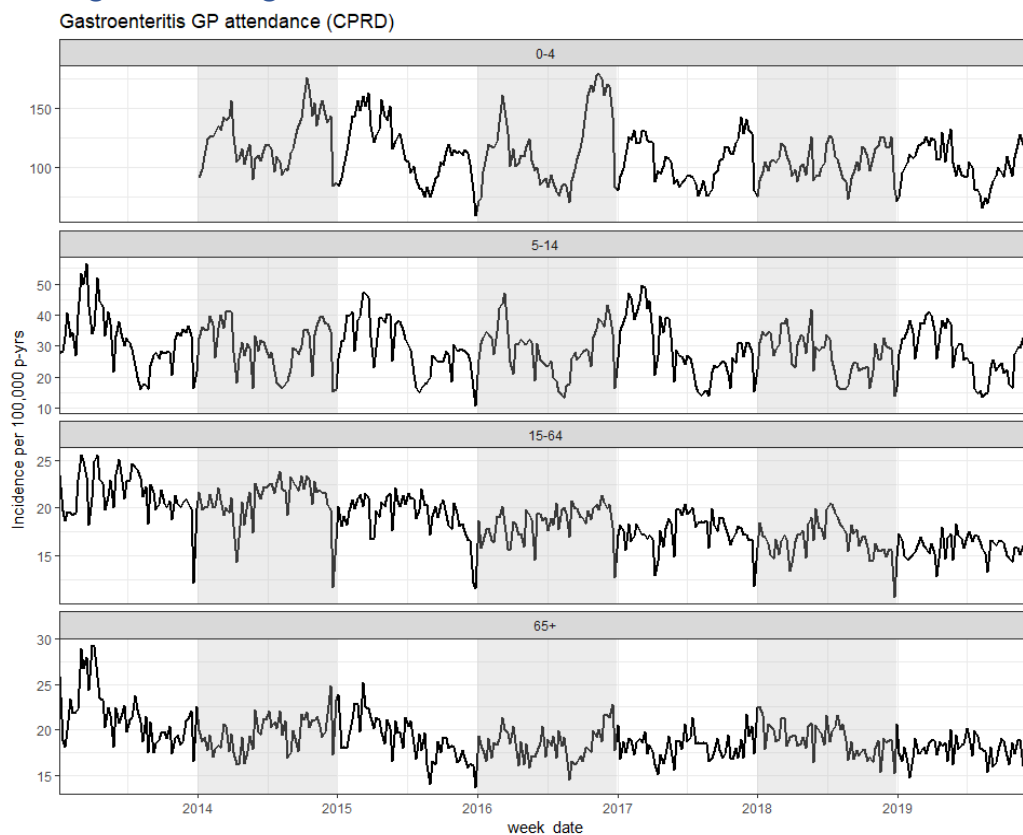
S4.2 Age stratified acute kidney injury hospitalisation time series



828 S4.3 Age stratified gastroenteritis hospitalisation time series

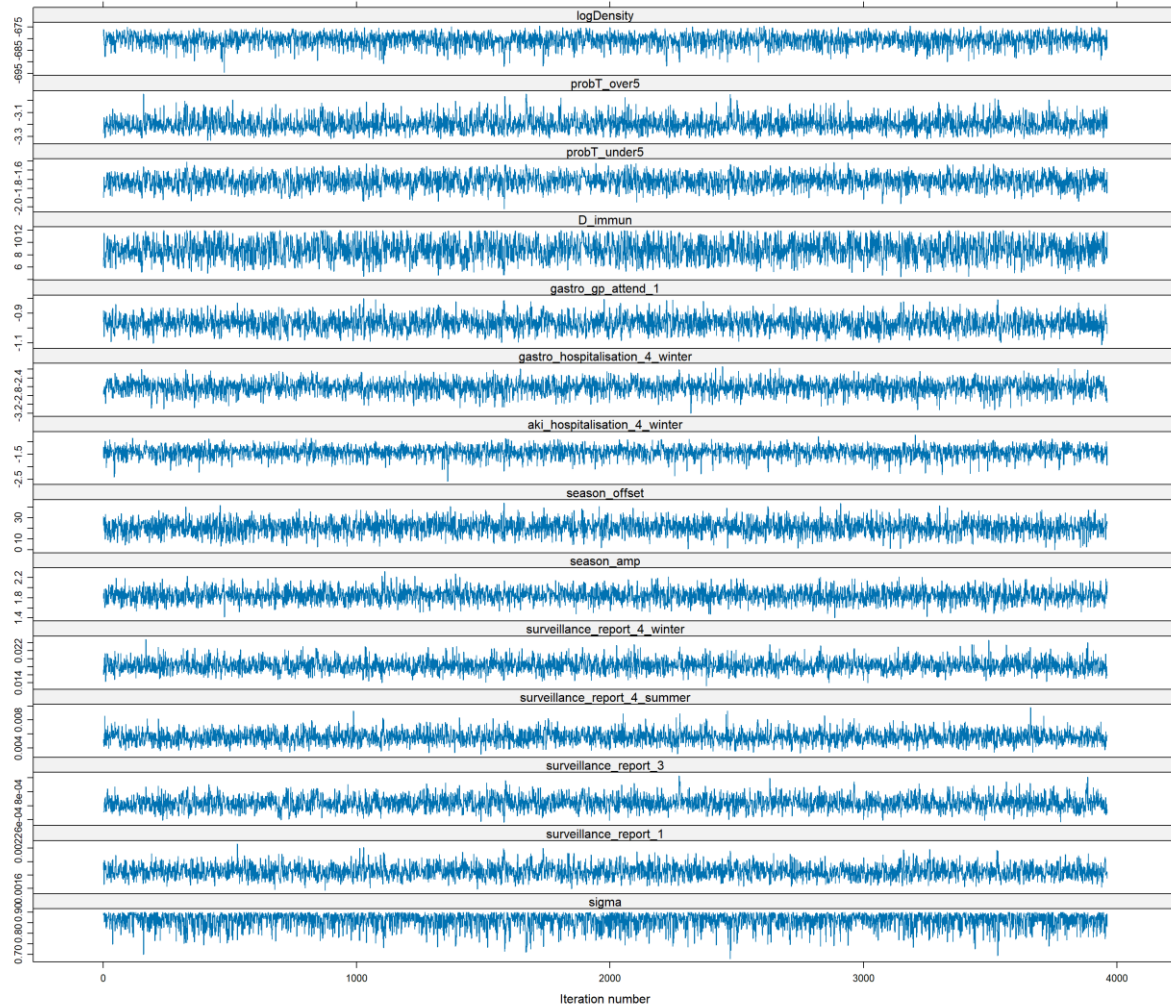


846 S4.4 Age stratified gastroenteritis GP attendance time series

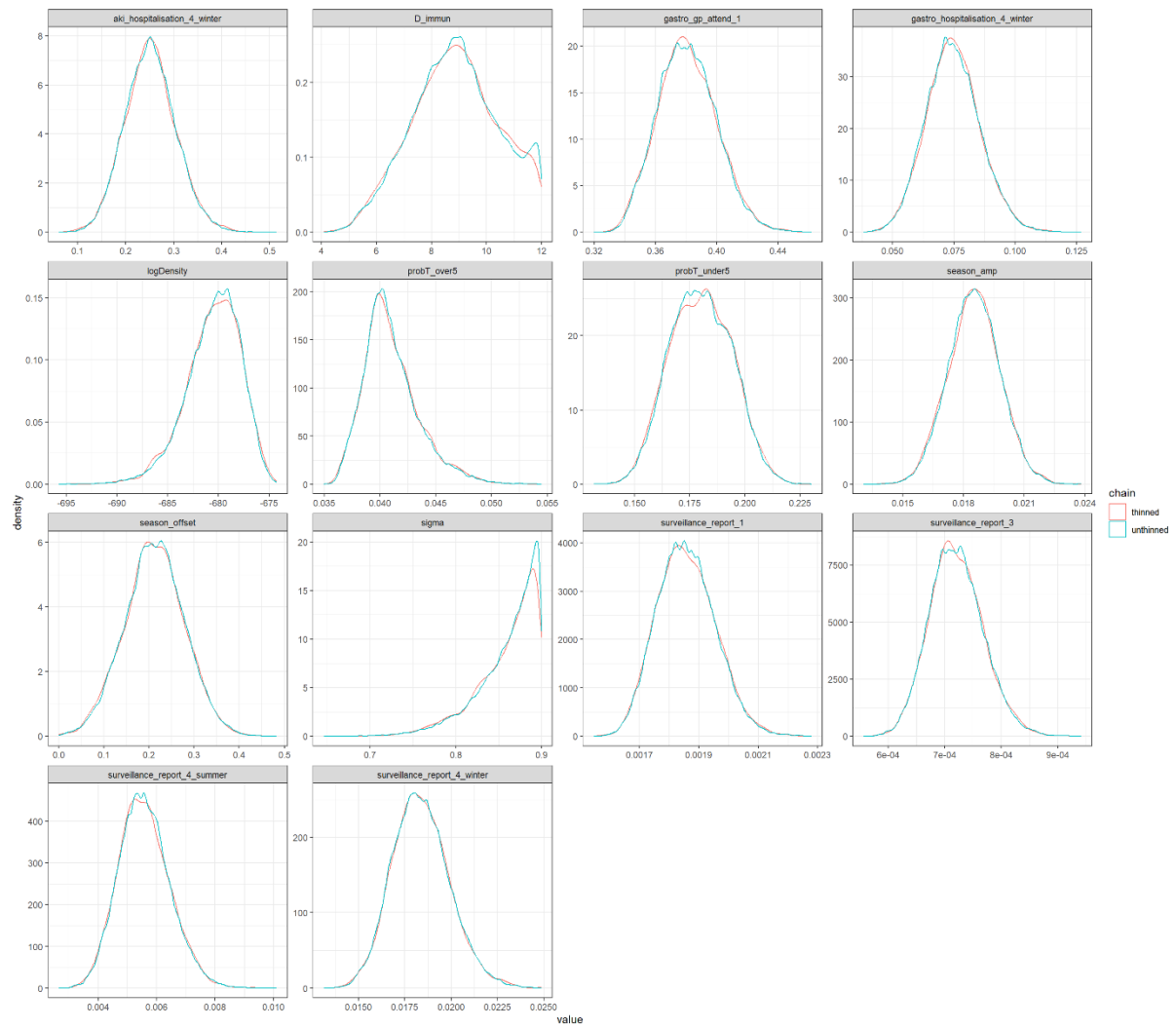


S5. Assessment of model fit

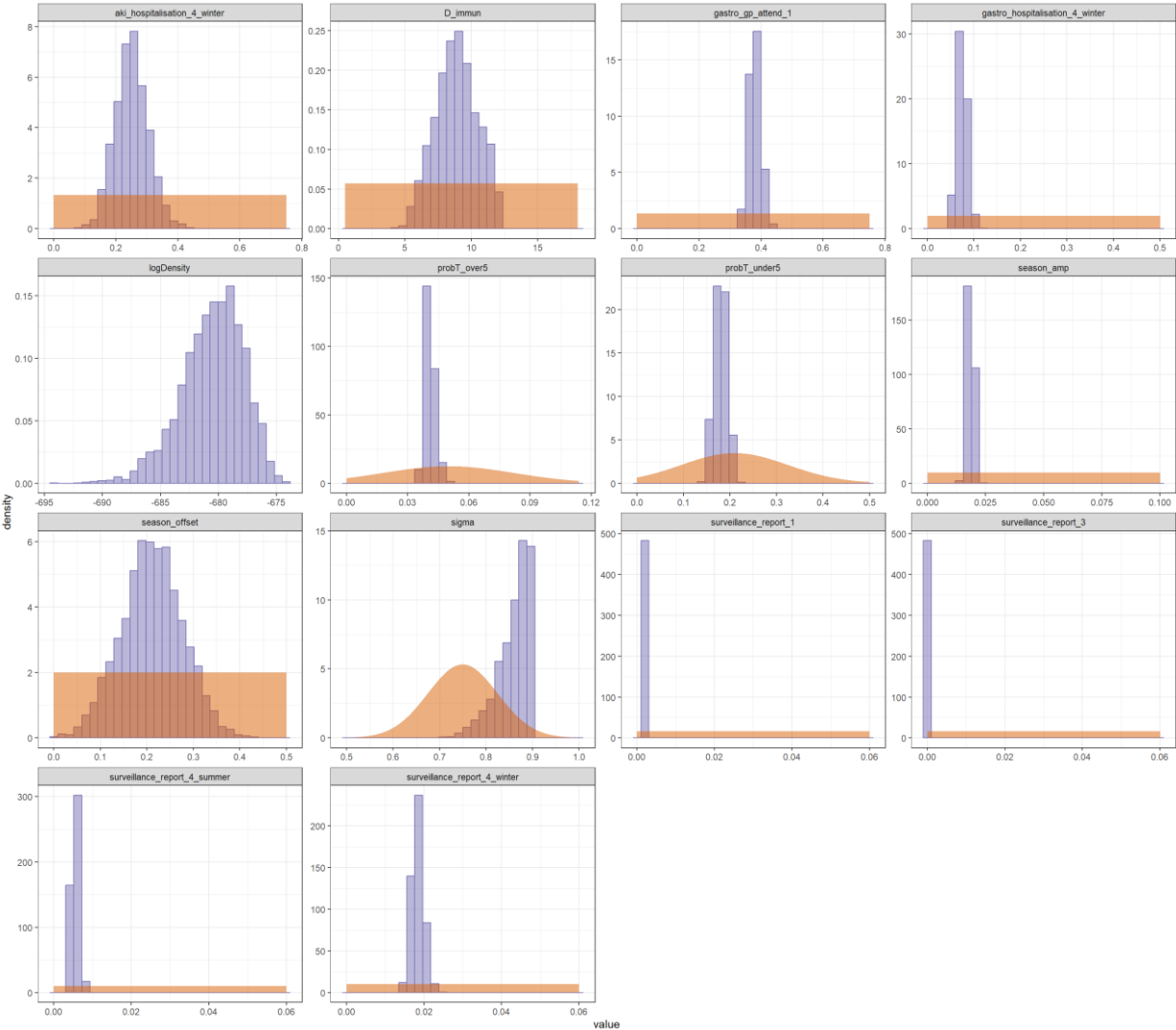
S5.1 Trace plots of estimated parameters



S5.2 Posterior distribution of parameters

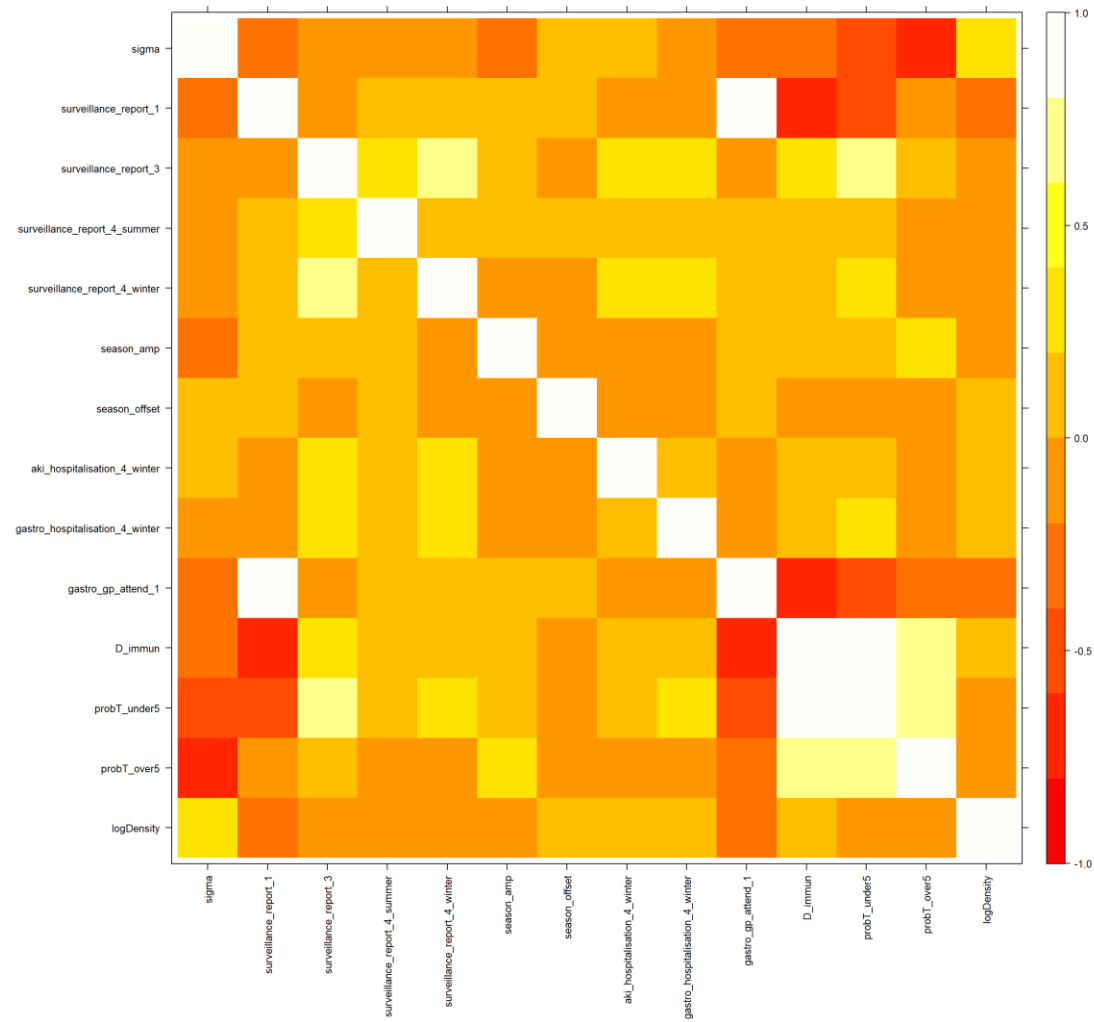


868

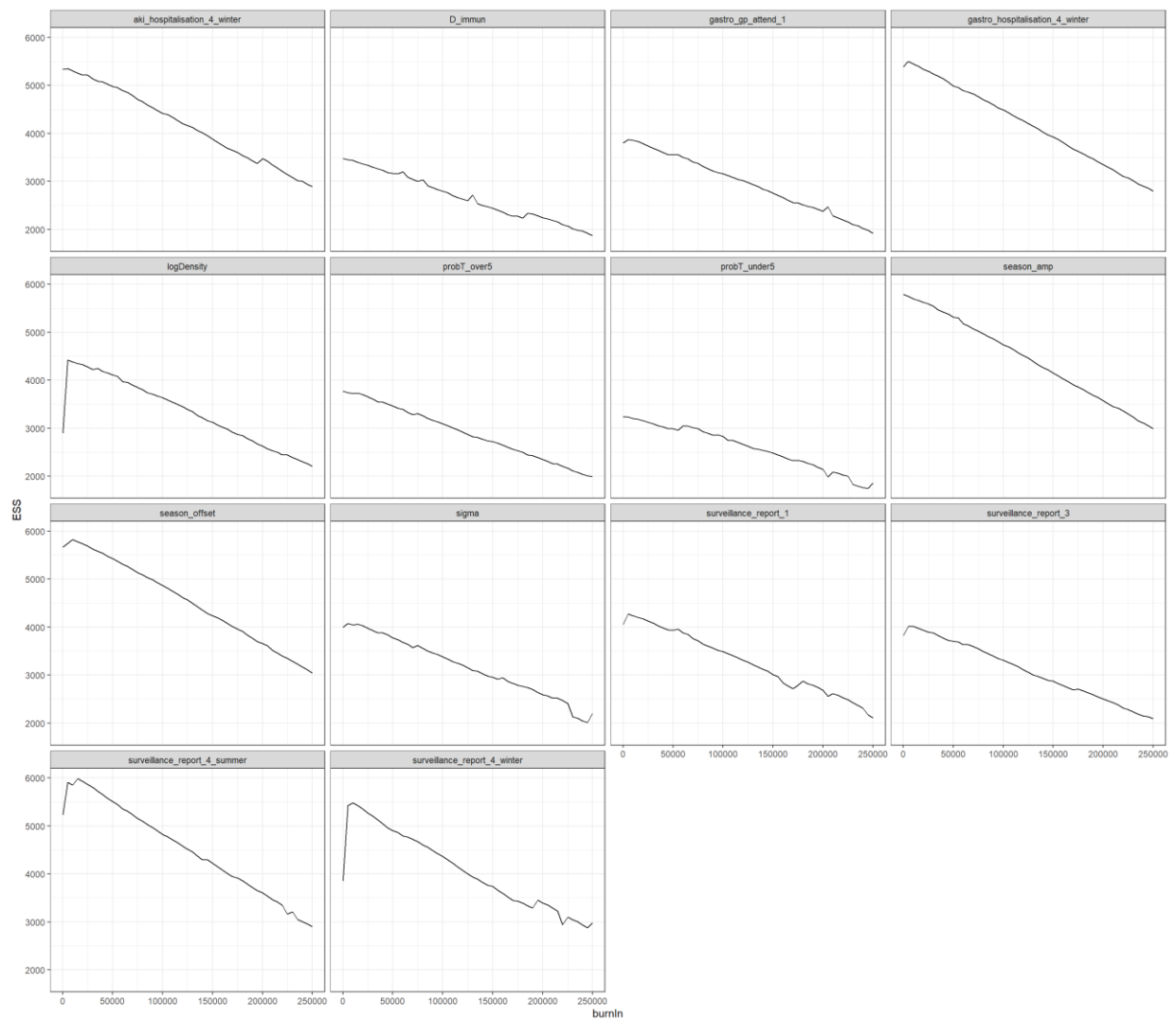


869

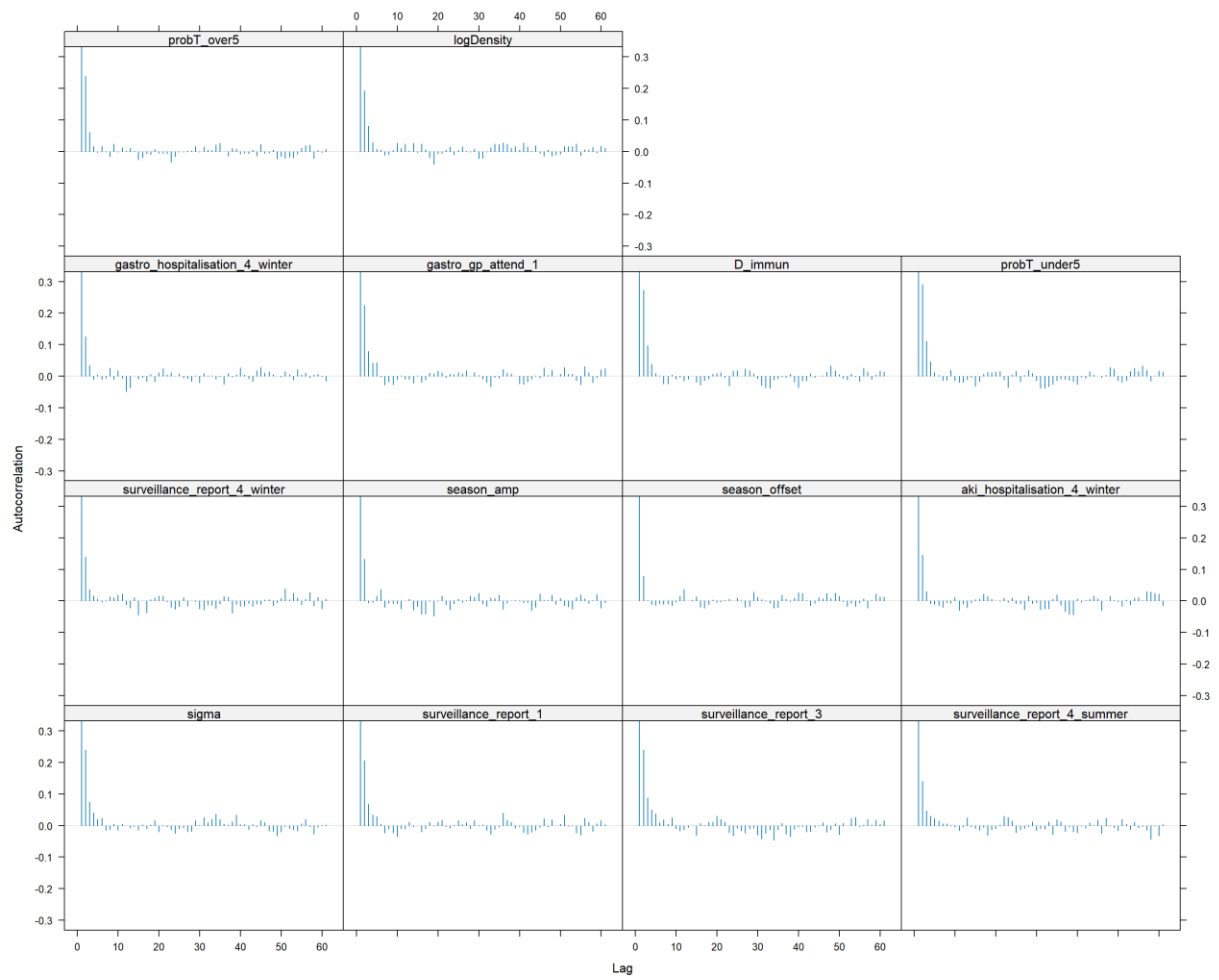
S5.4 Parameter correlations



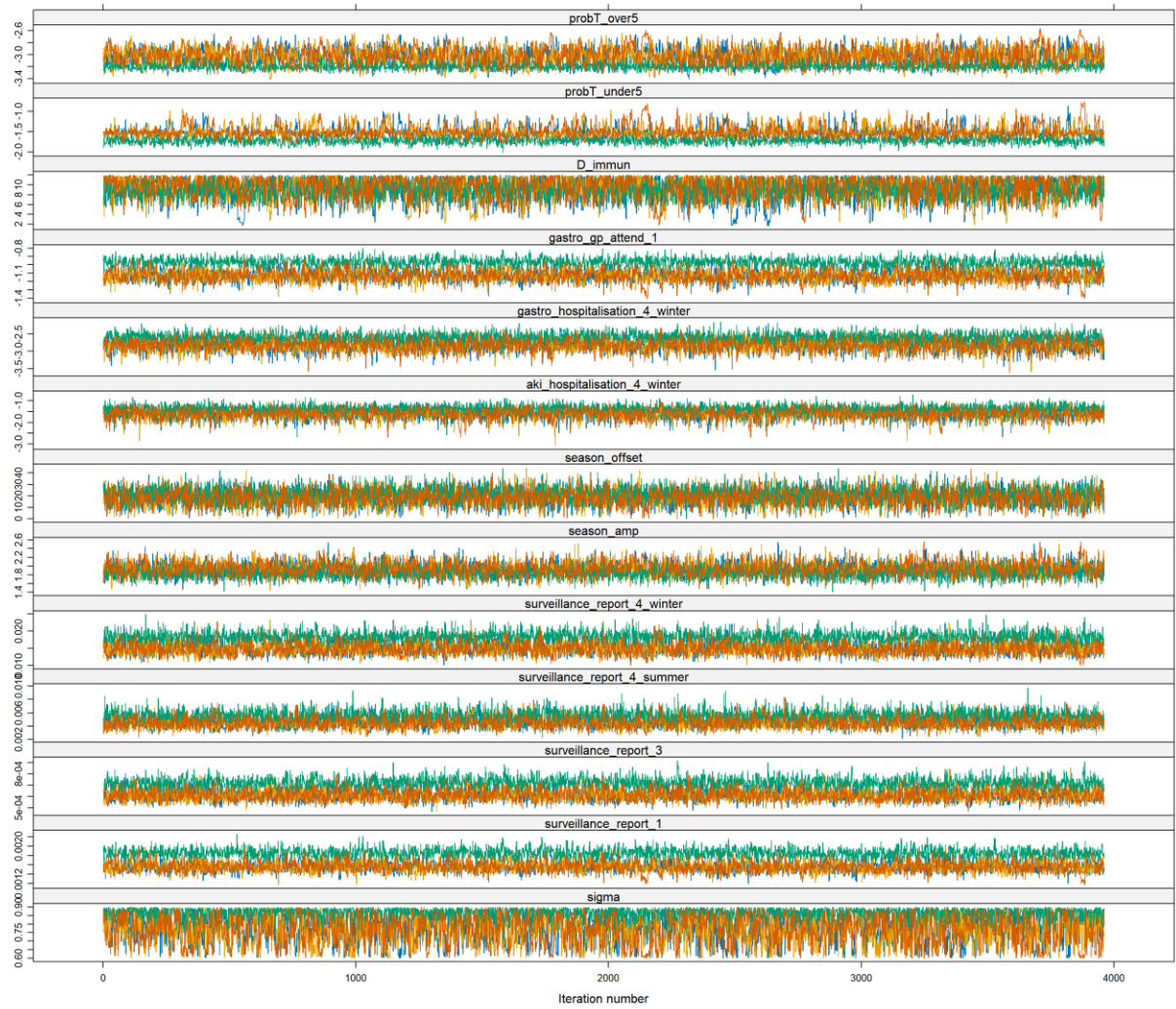
S5.5 Effective sample size



S5.6 Autocorrelation plots



S5.7 Multi chain plots



S5.8 Sensitivity analysis of AKI definition and spline knots

Parameter	AKI definition - AKI code in primary and secondary position only	AKI definition - AKI code any position and any time during admission	AKI definition 1 knot	AKI definition 2 knots
Proportion symptomatic	0.78 (0.61-0.89)	0.8 (0.62-0.89)	0.87 (0.76-0.9)	0.78 (0.62-0.89)
Duration of immunity	9.7 (4.2-12)	10 (5.1-12)	8.9 (5.9-12)	10 (5.2-12)
Probability of infection between under 5s	0.22 (0.18-0.31)	0.22 (0.18-0.3)	0.18 (0.16-0.21)	0.22 (0.18-0.3)
Probability of infection to over 5s	0.048 (0.038-0.064)	0.048 (0.039-0.062)	0.041 (0.037-0.048)	0.049 (0.039-0.061)
Seasonal amplitude term	0.019 (0.016-0.023)	0.02 (0.017-0.023)	0.019 (0.016-0.021)	0.02 (0.017-0.022)
Seasonal offset term	0.19 (0.06-0.31)	0.2 (0.067-0.34)	0.22 (0.082-0.34)	0.19 (0.057-0.32)
Norovirus associated AKI hospitalisation in 65+ in the winter	0.0023 (0.0011-0.014)	0.23 (0.14-0.32)	0.26 (0.17-0.37)	0.2 (0.13-0.3)
Norovirus associated hospitalisation in 65+ in the winter	0.065 (0.048-0.088)	0.063 (0.048-0.083)	0.08 (0.059-0.1)	0.063 (0.047-0.087)
Underreporting to surveillance 0-4	0.0016 (0.0014-0.0018)	0.0016 (0.0014-0.0018)	0.0019 (0.0017-0.002)	0.0015 (0.0014-0.0018)
Underreporting to surveillance 15-64	0.00062 (0.00053-0.00072)	0.00061 (0.00053-0.00072)	0.00072 (0.00064-0.00083)	6e-04 (0.00053-0.00071)
Underreporting to surveillance 65+ in the winter	0.015 (0.012-0.019)	0.015 (0.012-0.019)	0.018 (0.016-0.022)	0.015 (0.012-0.018)
Underreporting to surveillance 65+ in the summer	0.0045 (0.0032-0.0063)	0.0045 (0.0031-0.0064)	0.0055 (0.004-0.0074)	0.0044 (0.0031-0.0062)
GP attendance for all cause gastroenteritis in under 5s	0.32 (0.29-0.37)	0.32 (0.29-0.37)	0.38 (0.35-0.42)	0.32 (0.29-0.37)

S6. Cost analysis

S6.1 Elective inpatient and non-elective inpatient costs (21,22)

currency	currency_description	activity	unit_cost	total_cost	year	type
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	17	7,907.799	134,432.58	2013-2014	Elective Inpatients
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	59	7,241.908	427,272.57	2013-2014	Elective Inpatients
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	104	4,603.212	478,734.05	2013-2014	Elective Inpatients
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	34	4,168.357	141,724.14	2013-2014	Elective Inpatients
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	116	3,275.483	379,956.00	2013-2014	Elective Inpatients
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	310	2,585.044	801,363.60	2013-2014	Elective Inpatients
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	536	1,696.352	909,244.85	2013-2014	Elective Inpatients
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	18	7,902.517	142,245.30	2014-2015	Elective Inpatients
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	78	6,749.594	526,468.31	2014-2015	Elective Inpatients
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	175	3,869.496	677,161.87	2014-2015	Elective Inpatients
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	47	4,269.758	200,678.62	2014-2015	Elective Inpatients
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	127	2,532.303	321,602.43	2014-2015	Elective Inpatients
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	405	2,233.162	904,430.44	2014-2015	Elective Inpatients
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	616	1,402.640	864,026.21	2014-2015	Elective Inpatients
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	31	9,579.441	296,962.68	2015-2016	Elective Inpatients
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	92	7,569.423	696,386.94	2015-2016	Elective Inpatients
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	191	3,601.290	687,846.30	2015-2016	Elective Inpatients
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	27	3,354.564	90,573.24	2015-2016	Elective Inpatients
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	159	3,373.126	536,327.00	2015-2016	Elective Inpatients
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	510	2,087.279	1,064,512.47	2015-2016	Elective Inpatients
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	714	1,493.748	1,066,536.30	2015-2016	Elective Inpatients
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	17	8,612.242	146,408.12	2016-2017	Elective Inpatients
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	89	5,889.121	524,131.80	2016-2017	Elective Inpatients
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	212	3,956.070	838,686.89	2016-2017	Elective Inpatients
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	39	3,969.871	154,824.95	2016-2017	Elective Inpatients
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	161	2,874.770	462,837.89	2016-2017	Elective Inpatients
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	487	1,766.250	860,163.74	2016-2017	Elective Inpatients
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	792	1,359.246	1,076,522.95	2016-2017	Elective Inpatients
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	30	8,451.193	253,535.79	2017-2018	Elective Inpatients
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	107	5,647.583	604,291.42	2017-2018	Elective Inpatients
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	214	4,144.560	886,935.78	2017-2018	Elective Inpatients
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	34	4,432.709	150,712.09	2017-2018	Elective Inpatients
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	228	2,566.488	585,159.15	2017-2018	Elective Inpatients
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	571	1,773.467	1,012,649.40	2017-2018	Elective Inpatients
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	658	1,338.331	880,621.63	2017-2018	Elective Inpatients
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	41	9,189.626	376,774.68	2018-2019	Elective Inpatients
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	95	5,820.393	552,937.31	2018-2019	Elective Inpatients
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	216	3,879.436	837,958.10	2018-2019	Elective Inpatients
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	50	5,637.573	281,878.67	2018-2019	Elective Inpatients
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	227	3,284.832	745,656.87	2018-2019	Elective Inpatients

currency	description	activity	unit cost	total cost	year	type
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	527	1,879.562	990,529.08	2018-2019	Elective Inpatients
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	673	1,476.884	993,942.87	2018-2019	Elective Inpatients
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	895	6,433.694	5,758,156.50	2013-2014	Non-Elective Inpatients - Long Stay
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	2,597	4,812.611	12,498,349.94	2013-2014	Non-Elective Inpatients - Long Stay
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	2,194	3,512.228	7,705,828.44	2013-2014	Non-Elective Inpatients - Long Stay
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	2,024	3,663.807	7,415,544.72	2013-2014	Non-Elective Inpatients - Long Stay
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	8,304	2,891.999	24,015,163.76	2013-2014	Non-Elective Inpatients - Long Stay
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	17,213	2,224.495	38,290,238.27	2013-2014	Non-Elective Inpatients - Long Stay
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	10,939	1,746.525	19,105,234.75	2013-2014	Non-Elective Inpatients - Long Stay
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	1,062	6,587.701	6,996,138.57	2014-2015	Non-Elective Inpatients - Long Stay
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	3,140	5,016.299	15,751,179.57	2014-2015	Non-Elective Inpatients - Long Stay
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	3,059	3,784.718	11,577,452.98	2014-2015	Non-Elective Inpatients - Long Stay
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	2,343	3,786.669	8,872,166.49	2014-2015	Non-Elective Inpatients - Long Stay
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	9,321	2,953.558	27,530,112.62	2014-2015	Non-Elective Inpatients - Long Stay
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	19,564	2,227.329	43,575,473.89	2014-2015	Non-Elective Inpatients - Long Stay
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	11,622	1,785.630	20,752,588.57	2014-2015	Non-Elective Inpatients - Long Stay
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	1,221	6,720.552	8,205,794.33	2015-2016	Non-Elective Inpatients - Long Stay
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	3,580	4,995.541	17,884,034.99	2015-2016	Non-Elective Inpatients - Long Stay
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	3,220	3,779.535	12,170,102.11	2015-2016	Non-Elective Inpatients - Long Stay
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	2,725	3,871.695	10,550,369.31	2015-2016	Non-Elective Inpatients - Long Stay
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	10,601	2,893.770	30,676,855.83	2015-2016	Non-Elective Inpatients - Long Stay
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	20,202	2,163.854	43,714,177.99	2015-2016	Non-Elective Inpatients - Long Stay
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	11,837	1,812.846	21,458,652.46	2015-2016	Non-Elective Inpatients - Long Stay
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	1,365	6,714.072	9,164,708.20	2016-2017	Non-Elective Inpatients - Long Stay
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	3,817	4,670.266	17,826,406.75	2016-2017	Non-Elective Inpatients - Long Stay
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	3,304	3,605.986	11,914,178.21	2016-2017	Non-Elective Inpatients - Long Stay
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	3,184	3,608.385	11,489,096.70	2016-2017	Non-Elective Inpatients - Long Stay
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	11,257	2,751.746	30,976,403.09	2016-2017	Non-Elective Inpatients - Long Stay
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	20,236	2,107.993	42,657,350.23	2016-2017	Non-Elective Inpatients - Long Stay
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	11,525	1,662.109	19,155,807.55	2016-2017	Non-Elective Inpatients - Long Stay
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	1,679	6,294.697	10,568,796.64	2017-2018	Non-Elective Inpatients - Long Stay
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	3,417	4,609.432	15,750,430.18	2017-2018	Non-Elective Inpatients - Long Stay
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	2,960	3,581.195	10,600,335.91	2017-2018	Non-Elective Inpatients - Long Stay
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	4,424	3,564.853	15,770,908.05	2017-2018	Non-Elective Inpatients - Long Stay
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	11,354	2,703.707	30,697,884.53	2017-2018	Non-Elective Inpatients - Long Stay
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	18,525	2,074.279	38,426,016.52	2017-2018	Non-Elective Inpatients - Long Stay
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	9,889	1,808.682	17,886,054.36	2017-2018	Non-Elective Inpatients - Long Stay
LA07H	Acute Kidney Injury with Interventions, with CC Score 11+	2,015	5,655.508	11,395,847.69	2018-2019	Non-Elective Inpatients - Long Stay
LA07J	Acute Kidney Injury with Interventions, with CC Score 6-10	3,533	4,695.233	16,588,259.37	2018-2019	Non-Elective Inpatients - Long Stay
LA07K	Acute Kidney Injury with Interventions, with CC Score 0-5	2,724	3,692.976	10,059,667.71	2018-2019	Non-Elective Inpatients - Long Stay
LA07L	Acute Kidney Injury without Interventions, with CC Score 12+	5,666	3,512.503	19,901,842.32	2018-2019	Non-Elective Inpatients - Long Stay
LA07M	Acute Kidney Injury without Interventions, with CC Score 8-11	12,380	2,854.320	35,336,485.08	2018-2019	Non-Elective Inpatients - Long Stay
LA07N	Acute Kidney Injury without Interventions, with CC Score 4-7	18,948	2,313.415	43,834,581.94	2018-2019	Non-Elective Inpatients - Long Stay
LA07P	Acute Kidney Injury without Interventions, with CC Score 0-3	10,071	1,955.560	19,694,441.42	2018-2019	Non-Elective Inpatients - Long Stay

S7. Code list

S7.1 ICD-10 codes

ICD10 code	Code description
N17.0	Acute renal failure with tubular necrosis
N17.1	Acute renal failure with acute cortical necrosis
N17.2	Acute renal failure with medullary necrosis
N17.8	Other acute renal failure
N17.9	Acute renal failure, unspecified
N19	Unspecified kidney failure
A00.0	Cholera due to <i>Vibrio cholerae</i> 01, biovar cholerae
A00.1	Cholera due to <i>Vibrio cholerae</i> 01, biovar eltor
A00.9	Cholera, unspecified
A01.0	Typhoid fever
A01.1	Paratyphoid fever A
A01.2	Paratyphoid fever B
A01.3	Paratyphoid fever C
A01.4	Paratyphoid fever, unspecified
A02.0	Salmonella enteritis
A02.1	Salmonella sepsis
A02.2	Localized salmonella infections
A02.8	Other specified salmonella infections
A02.9	Salmonella infection, unspecified
A03.0	Shigellosis due to <i>Shigella dysenteriae</i>
A03.1	Shigellosis due to <i>Shigella flexneri</i>
A03.2	Shigellosis due to <i>Shigella boydii</i>
A03.3	Shigellosis due to <i>Shigella sonnei</i>
A03.8	Other shigellosis
A03.9	Shigellosis, unspecified
A04.0	Enteropathogenic <i>Escherichia coli</i> infection
A04.1	Enterotoxigenic <i>Escherichia coli</i> infection
A04.2	Enteroinvasive <i>Escherichia coli</i> infection
A04.3	Enterohaemorrhagic <i>Escherichia coli</i> infection
A04.4	Other intestinal <i>Escherichia coli</i> infections
A04.5	Campylobacter enteritis
A04.6	Enteritis due to <i>Yersinia enterocolitica</i>
A04.7	Enterocolitis due to <i>Clostridium difficile</i>
A04.8	Other specified bacterial intestinal infections
A04.9	Bacterial intestinal infection, unspecified
A05.0	Other bacterial foodborne intoxications, not elsewhere classified
A05.1	Botulism
A05.2	Foodborne <i>Clostridium perfringens</i> [<i>Clostridium welchii</i>] intoxication
A05.3	Foodborne <i>Vibrio parahaemolyticus</i> intoxication
A05.4	Foodborne <i>Bacillus cereus</i> intoxication
A05.8	Other specified bacterial foodborne intoxications
A05.9	Bacterial foodborne intoxication, unspecified
A06.0	Acute amoebic dysentery
A06.1	Chronic intestinal amoebiasis
A06.2	Amoebic nondysenteric colitis
A06.3	Amoeboma of intestine
A06.4	Amoebic liver abscess (K77.0*)
A06.5	Amoebic lung abscess (J99.8*)
A06.6	Amoebic brain abscess (G07*)
A06.7	Cutaneous amoebiasis
A06.8	Amoebic infection of other sites
A06.9	Amoebiasis, unspecified
A07.0	Balantidiasis
A07.1	Giardiasis [lambliasis]
A07.2	Cryptosporidiosis
A07.3	Isosporiasis
A07.8	Other specified protozoal intestinal diseases
A07.9	Protozoal intestinal disease, unspecified
A08.0	Rotaviral enteritis
A08.1	Acute gastroenteropathy due to Norwalk agent
A08.2	Adenoviral enteritis
A08.3	Other viral enteritis
A08.4	Viral intestinal infection, unspecified
A08.5	Other specified intestinal infections
A09	Other gastroenteritis and colitis of infectious and unspecified origin
A09.0	Other and unspecified gastroenteritis and colitis of infectious origin
A09.9	Gastroenteritis and colitis of unspecified origin

ICD10 code	Code description
K52.8	Other specified noninfective gastroenteritis and colitis
K52.9	Noninfective gastroenteritis and colitis, unspecified
R11	Nausea and vomiting
R19.7	Diarrhea, unspecified

S7.2 GP attendance medical codes for acute kidney injury

Medcode ID	Code description
2388721000000111	Acute kidney injury warning stage
2204191000000110	Acute kidney injury
354406016	Renal impairment
460091000006111	Acute renal failure
86957016	Nephrotic syndrome
2206791000000119	Acute kidney injury stage 1
354407013	Impaired renal function
259688011	Renal function tests abnormal
2206811000000118	Acute kidney injury stage 2
2206831000000114	Acute kidney injury stage 3
303943013	Impaired renal function disorder
459420012	Deteriorating renal function
619541000006116	Dialysis for renal failure
354320010	Nephropathy
303907019	Glomerulonephritis
303826014	Nephrotic syndrome with membranous glomerulonephritis
304058013	Nephritis, nephrosis and nephrotic syndrome NOS
677951000006111	Nephritis
354417015	Acute-on-chronic renal failure
303916015	Acute renal failure NOS
47940012	Acute interstitial nephritis
303806010	Nephritis, nephrosis and nephrotic syndrome
678061000006111	Nephropathy - chronic
303855018	Nephrotic syndrome NOS
396706011	Nephrotic syndrome with minimal change glomerulonephritis
303960015	Impaired renal function disorder NOS
303875010	Membranous glomerulonephritis
303905010	Interstitial nephritis
481692010	Acute renal failure due to rhabdomyolysis
396707019	Nephritis and nephropathy unspecified
677941000006114	Nephritis - chronic
303833014	Nephrotic syndrome, focal and segmental glomerular lesions
460151000006118	Acute tubular necrosis
14415811000006111	Acute kidney injury stage 1
2645796013	Acute renal failure due to ACE inhibitor
2732241000006113	Acute renal failure syndrome
886621000006112	Nephritis NOS
303834015	Nephrotic syndrome, diffuse membranous glomerulonephritis
461420012	Dialysis procedure
429641000006113	Tubulointerstitial nephritis
677461000006115	Nephrotic syndrome, diffuse mesangial proliferative glomerulonephritis
677561000006119	Nephrotic syndrome in systemic lupus erythematosus
354413016	Acute drug-induced renal failure
303846016	Nephrotic syndrome in diabetes mellitus
303915016	Other acute renal failure
349998013	Haemofiltration
303845017	Nephrotic syndrome in amyloidosis
14415821000006115	Acute kidney injury stage 2
14415831000006117	Acute kidney injury stage 3
1705781000006113	Acute renal failure due to obstruction
303839013	Nephrotic syndrome, diffuse crescentic glomerulonephritis
303832016	Nephrotic syndrome, minor glomerular abnormality
677471000006110	Nephrotic syndrome, diffuse mesangiocapillary glomerulonephritis
677621000006112	Nephrotic syndrome with membranoproliferative glomerulonephritis
481693017	Acute tubular necrosis
303825013	Nephrotic syndrome with proliferative glomerulonephritis
303844018	Nephrotic syndrome in diseases EC
3183501000006111	Renal failure syndrome
2184271000000115	Acute renal failure due to non-traumatic rhabdomyolysis
677981000006115	Nephritis unsp+OS membranoprolif glomerulonephritis lesion
886611000006116	Nephritis/nephrosis/neph syndr
678081000006118	Nephropathy induced by other drugs meds and biologl substncs
460081000006113	Acute renal cortical necrosis
303819014	Acute diffuse nephritis

Medcode ID	Code description
508913018	Necrotising renal papillitis
1221119015	ARF - Acute renal failure
405116017	Acute renal medullary necrosis
1230447010	Acute idiopathic interstitial nephritis
1847641000006114	Acute renal failure induced by non-steroidal anti-inflammatory drug
2191301000000116	Acute renal failure induced by radiographic contrast media
2198081000000118	Acute renal failure due to traumatic rhabdomyolysis
5986751000006115	Kidney biopsy sample
303853013	Nephrotic syndrome associated with another disorder
303951011	Renal function impairment with growth failure
8040791000006115	Acute renal failure
460121000006110	Acute renal failure following labour and delivery
678091000006115	Nephropathy induced by unspec drug medicament or biol subs
2615221000006111	Kidney biopsy
677971000006118	Nephritis unsp+membranoprolif glomerulonephritis lesion NOS
12717101000006112	Nephritis, nephrosis and nephrotic syndrome
355554015	Nephropathy NOS in pregnancy without hypertension
303838017	Nephrotic syndrome, dense deposit disease
2214211000000112	Acute renal failure induced by toxin
7954321000006110	Acute renal failure stage 1
5094041000006117	Acute renal impairment
303849011	Nephrotic syndrome in polyarteritis nodosa
303854019	Nephrotic syndrome with other pathological kidney lesions
405118016	Acute papillary necrosis
13485211000006111	Acute kidney injury due to disease caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)
304053016	Nephropathy induced by heavy metals
5966771000006111	Transient acute renal failure
5094071000006113	Nephrotoxic acute renal failure
305571011	Acute renal failure following abortive pregnancy
14057041000006114	Acute tubulointerstitial nephritis
303848015	Nephrotic syndrome in malaria
677481000006113	Nephrotic syndrome, diffuse endocapillary proliferative glomerulonephritis
2191151000000117	Acute renal failure induced by poison
7827241000006112	Acute kidney injury due to hypovolaemia
7829401000006116	Acute kidney injury due to sepsis
3136131000006110	Abnormal renal function
7214431000006112	Biopsy of kidney using ultrasound guidance
8425521000006110	Acute kidney injury due to acute tubular necrosis due to sepsis
5093891000006115	Membranous glomerulonephritis - stage IV
2180741000000113	Acute renal failure induced by aminoglycoside
2180861000000117	Acute renal failure induced by cisplatin
2180901000000112	Acute renal failure induced by cyclosporin A
7100101000006115	Acute renal failure due to acute cortical necrosis
6927831000006111	Tubulointerstitial nephritis with uveitis syndrome
4195491000006118	Hemolytic uremic syndrome
12704041000006118	Acute renal cortical necrosis
7879771000006116	Acute kidney injury due to trauma
8425491000006113	Acute kidney injury due to acute tubular necrosis due to hypovolaemia
13485231000006117	Acute kidney injury due to disease caused by Severe acute respiratory syndrome coronavirus 2
2185551000000111	Acute renal failure induced by animal toxin
2185591000000115	Acute renal failure induced by plant toxin
2185631000000115	Acute renal failure induced by heavy metal
2191381000000114	Acute renal failure induced by solvent
7954341000006115	Acute renal failure stage 2
7954361000006116	Acute renal failure stage 3
4789251000006116	Nephropathy associated with vesicoureteral reflux
7841561000006115	Acute renal insufficiency
5093831000006119	Membranous glomerulonephritis - stage I
7085691000006115	Tubulo-interstitial nephritis

S7.3 GP attendance medical codes for gastroenteritis

Medcode ID	Code description
317494018	Loose stools
317462011	[D]Nausea and vomiting NOS
451469011	[D]Projectile vomiting
317459013	[D]Emesis
317458017	Vomiting
317457010	[D]Nausea
317456018	Nausea and vomiting
79989019	Vomiting in newborn

Medcode ID	Code description
1816481000006111	Gastroenteritis and colitis of unknown origin
619781000006115	Diarrhoea - presumed non-infectious
72962011	Enterocolitis
42550011	Gastroenteritis
302640019	Persistent vomiting NOS
302638012	Cyclical vomiting
302636011	Persistent vomiting
301423018	Influenza with gastrointestinal tract involvement
2015181000006112	Norovirus infection
982731000006112	Diarrhoea/loose stools
854661000006115	Diarrhoea & vomiting
377011000006119	Gastroenteritis presumed infectious
287995017	[X]Other specified intestinal infections
287994018	Viral and ill-defined gastrointestinal infections
287993012	Viral enteritis
287990010	Amoebic infection
287987016	Amoebic infection
287986013	[X]Bacterial food-borne intoxication, unspecified
287985012	[X]Other specified bacterial food-borne intoxications
287984011	Bacterial enteritis
287983017	[X]Other specified bacterial intestinal infections
287982010	[X]Shigellosis, unspecified
287981015	[X]Other shigellosis
287980019	[X]Salmonella infection, unspecified
287979017	[X]Other specified salmonella infections
287977015	[X]Cholera, unspecified
347485016	Acanthamoeba keratitis
287944019	Acanthamoebiasis
123933019	Winter vomiting disease
123932012	Epidemic vomiting syndrome
633521000006119	E. coli infection
501778016	Escherichia coli infection
286213013	Intestinal tract infectious disease NOS
286212015	Other specified infectious diseases of intestinal tract
878891000006118	Specific GIT infectious dis.
785691000006115	Ill-defined intestinal infection
878931000006110	Viral + ill-defined GIT inf.
360012013	Infantile gastroenteritis
619761000006113	Infectious diarrhoeal disease
72144015	Diarrhoea of presumed infectious origin
286202010	Infectious diarrhoea NOS
179018017	Viral gastroenteritis
86701000006110	Traveler's diarrhoea
201288012	Epidemic diarrhoea
479228018	Infectious diarrhoea
572061000006117	Colitis, enteritis and gastroenteritis presumed infect NOS
1494813012	Gastroenteritis - presumed infectious origin
353405010	Suspected infectious enteritis
645721000006113	Enteritis presumed infectious
1495457013	Colitis - presumed infectious origin
473395016	Gastric flu
395323013	Colitis, enteritis and gastroenteritis presumed infectious
286182018	Gastrointestinal infection
878941000006117	Gastroenteritis - viral + NOS
21441016	Infectious gastroenteritis
91741012	Infectious enteritis
65964017	Infectious colitis
286180014	Infectious colitis, enteritis and gastroenteritis
1222445017	Ill-defined intestinal tract infections
799701000006116	Infectious disease of digestive tract
451427012	Infantile viral gastroenteritis
61191000006113	Viral gastroenteritis
799691000006116	Gastrointestinal tract infection specified organism NEC
286173012	Enteritis due to specified virus NOS
1174781000000115	Enteritis due to Norovirus
365356015	Viral vomiting
286172019	Enteritis due to rotavirus
365357012	Viral diarrhoea
1227968013	Enteritis due to enterovirus
501712011	Enteritis due to adenovirus
395321010	Enteritis due to specified virus
286165015	Unspecified bacterial enteritis
286164016	Other specified gastrointestinal tract infections NOS
286163010	Other specified other gastrointestinal infection

Medcode ID	Code description
1234534014	Enteritis due to Yersinia enterocolitica
533191000006119	Campylobacter intestinal infection
619811000006118	Diarrhoea due to Campylobacter jejuni
533201000006116	Enteric campylobacteriosis
619821000006114	Diarrhoea due to Pseudomonas pyocyanea
395320011	Pseudomonas gastrointestinal tract infection
619831000006112	Diarrhoea due to staphylococcal toxin
1773224011	Diarrhoea due to staphylococcus
395319017	Staphylococcal gastrointestinal tract infection
286141018	Bacterial intestinal infectious disease
286140017	Proteus gastrointestinal tract infection NOS
286139019	Proteus morgani gastrointestinal tract infection
286137017	Proteus mirabilis gastrointestinal tract infection
286136014	Proteus gastrointestinal tract infection
472961000006112	Gastrointestinal infection caused by Klebsiella aerogenes
286134012	Arizona paracolon gastrointestinal tract infection
360044012	Enterohaemorrhagic Escherichia coli infection
360051015	Enteroinvasive Escherichia coli infection
360040015	Enterotoxigenic Escherichia coli infection
360043018	Enteropathogenic Escherichia coli infection
365279016	Escherichia coli gastrointestinal tract infection
286129013	Intestinal infection due to other organisms
286128017	Protozoal intestinal diseases NOS
286127010	Other specified protozoal intestinal diseases
360073010	Cryptosporidiosis
572031000006114	Giardial colitis
802121000006117	Giardiasis
286119018	Protozoal intestinal disease
286117016	Amoebiasis NOS
91483015	Amoebic nondysenteric colitis
286104019	Acute amoebic dysentery
1490309018	Amoebiasis
286102015	Food poisoning NOS
1222370018	Foodborne Bacillus cereus intoxication
286100011	Other specified bacterial food poisoning
1234561014	Vibrio parahaemolyticus food poisoning
286099015	Other Clostridia causing food poisoning
569601000006113	Clostridium perfringens food poisoning
1234964014	Staphylococcal food poisoning
286096010	Other bacterial food poisoning
286095014	Shigellosis NOS
286094013	Other specified shigella infection
878911000006116	Bacillary dysentery
501911000006117	Bacillary dysentery Shigella sonnei
395316012	Shigella sonnei
286089013	Shigella boydii (group C)
286088017	Shigella flexneri
988691000006119	Bacillary dysentery
409836012	Bacillary dysentery
395315011	Shigella dysenteriae
353844012	Vomiting co-occurrent and due to infectious disease
60387019	Shigellosis
286084015	Salmonella infection
286083014	Other specified salmonella infection
286078018	Local salmonella infection unspecified
494811016	Localised Salmonella infection
443811013	Salmonella food poisoning
443815016	Salmonellosis
443812018	Salmonella gastroenteritis
124991010	Food poisoning
286071012	Other salmonella infections
109787018	Bacterial food poisoning
286066017	Typhoid and paratyphoid fevers
286065018	Cholera NOS
126156018	Vibrio cholerae
551671000006114	Cholera - Vibrio cholerae El Tor
551661000006119	Cholera - Vibrio cholerae
105789012	Cholera
222831000000115	Intestinal infectious disease
763991000006113	Food poisoning notification administration
264402018	Notification of food poisoning
261410016	Stool culture positive
261408018	Stool culture cryptosporidium positive
261251016	Sample salmonella cultured

Medcode ID	Code description
1539981000006116	Norovirus (small round-structured viruses) nucleic acid detn
1923531000006118	Rotavirus RNA (ribonucleic acid) detection assay
2335181000000114	Rotavirus nucleic acid detection assay
313311000000111	Rotavirus nucleic acid detection
1923481000006116	Norovirus RNA (ribonucleic acid) detection assay
2333361000000116	Norovirus nucleic acid detection assay
313191000000117	Norovirus nucleic acid detection
1488689010	Suspected food poisoning
372283012	Diarrhoea and vomiting
619771000006118	Diarrhoea and vomiting, symptom
397928013	Diarrhoea symptom
103081000006118	Toddler diarrhoea
1786047017	Loose stool
103578017	Diarrhoea
619741000006114	Diarrhoea
397927015	Diarrhoea symptoms
252622013	Vomiting NOS
2238541000000114	Frequency of vomiting
252620017	Bilious vomiting
372248013	Vomiting symptom
15155012	Projectile vomiting
100841000006111	Throwing up
2647992016	Emesis
2643931013	Vomiting
407086011	C/O - vomiting
63631000006119	Finding of vomiting
5730511000006110	Diarrhoea and vomiting after gastrointestinal tract surgery
5089301000006119	Diarrhoea due to ingestion of unabsorbable substances
13012291000006117	Gastroenteritis caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)
12990711000006115	Gastroenteritis caused by 2019-nCoV (novel coronavirus)
3512083018	Diarrhoea co-occurrent and due to carcinoid syndrome
6746021000006114	Norovirus
7303631000006118	Norovirus infection

S8. Supplement references

1. Harris JP, Iturriza-Gomara M, O'Brien SJ. Re-assessing the total burden of norovirus circulating in the United Kingdom population. *Vaccine*. 2017 Feb;35(6):853–5.
2. Simmons K, Gambhir M, Leon J, Lopman B. Duration of Immunity to Norovirus Gastroenteritis. *Emerg Infect Dis*. 2013 Aug;19(8):1260–7.
3. Steele MK, Remais JV, Gambhir M, Glasser JW, Handel A, Parashar UD, et al. Targeting pediatric versus elderly populations for norovirus vaccines: a model-based analysis of mass vaccination options. *Epidemics*. 2016 Dec;17:42–9.
4. Sukhrie FHA, Teunis P, Vennema H, Copra C, Thijs Beersma MFC, Bogerman J, et al. Nosocomial Transmission of Norovirus Is Mainly Caused by Symptomatic Cases. *Clin Infect Dis*. 2012 Apr 1;54(7):931–7.
5. Gaythorpe KAM, Trotter CL, Conlan AJK. Modelling norovirus transmission and vaccination. *Vaccine*. 2018 Sep;36(37):5565–71.
6. Glass RI, Parashar UD, Estes MK. Norovirus Gastroenteritis. *N Engl J Med*. 2009 Oct 29;361(18):1776–85.
7. Atmar RL, Opekun AR, Gilger MA, Estes MK, Crawford SE, Neill FH, et al. Norwalk Virus Shedding after Experimental Human Infection. *Emerg Infect Dis*. 2008 Oct;14(10):1553–7.
8. Wu Q song, Xuan Z liang, Liu J yi, Zhao X tao, Chen Y fang, Wang C xi, et al. Norovirus shedding among symptomatic and asymptomatic employees in outbreak settings in Shanghai, China. *BMC Infect Dis*. 2019 Dec;19(1):592.
9. Office for National Statistics. Vital statistics in the UK: births, deaths and marriages [Internet]. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/vitalstatisticspopulationandhealthreferencetables>
10. Mossong J, Hens N, Jit M, Beutels P, Auranen K, Mikolajczyk R, et al. Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases. Riley S, editor. *PLoS Med*. 2008 Mar 25;5(3):e74.
11. Parrino TA, Schreiber DS, Trier JS, Kapikian AZ, Blacklow NR. Clinical Immunity in Acute Gastroenteritis Caused by Norwalk Agent. *N Engl J Med*. 1977 Jul 14;297(2):86–9.
12. O'Reilly KM, Sandman F, Allen D, Jarvis CI, Gimma A, Douglas A, et al. Predicted norovirus resurgence in 2021–2022 due to the relaxation of nonpharmaceutical interventions associated with COVID-19 restrictions in England: a mathematical modeling study. *BMC Med*. 2021 Dec;19(1):299.
13. Tam CC, Rodrigues LC, Viviani L, Dodds JP, Evans MR, Hunter PR, et al. Longitudinal study of infectious intestinal disease in the UK (IID2 study): incidence in the community and presenting to general practice. *Gut*. 2012 Jan;61(1):69–77.
14. Verstraeten T, Cattaert T, Harris J, Lopman B, Tam CC, Ferreira G. Estimating the Burden of Medically Attended Norovirus Gastroenteritis: Modeling Linked Primary Care and Hospitalization Datasets. *J Infect Dis*. 2017 Nov 15;216(8):957–65.

15. Sandmann FG, Shallcross L, Adams N, Allen DJ, Coen PG, Jeanes A, et al. Estimating the Hospital Burden of Norovirus-Associated Gastroenteritis in England and Its Opportunity Costs for Nonadmitted Patients. *Clin Infect Dis*. 2018 Aug 16;67(5):693–700.
16. Public Health England. PHE National norovirus and rotavirus Report 09 April 2020 – Week 15 report (data to week 13) [Internet]. Available from: <https://www.gov.uk/government/statistics/norovirus-and-rotavirus-summary-of-surveillance-2019-to-2020>
17. Ondrikova N, Clough HE, Cunliffe NA, Iturriza-Gomara M, Vivancos R, Harris JP. Understanding norovirus reporting patterns in England: a mixed model approach. *BMC Public Health*. 2021 Dec;21(1):1245.
18. Clinical Practice Research Datalink [Internet]. 2021. Available from: <https://cprd.com/Data>
19. Wolf A, Dedman D, Campbell J, Booth H, Lunn D, Chapman J, et al. Data resource profile: Clinical Practice Research Datalink (CPRD) Aurum. *Int J Epidemiol*. 2019 Dec 1;48(6):1740–1740g.
20. Bhaskaran K, Gasparrini A, Hajat S, Smeeth L, Armstrong B. Time series regression studies in environmental epidemiology. *Int J Epidemiol*. 2013 Aug;42(4):1187–95.
21. NHS England and NHS Improvement. National Cost Collection for the NHS [Internet]. Available from: <https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/>
22. Department of Health and Social Care. NHS reference costs [Internet]. Available from: <https://www.gov.uk/government/collections/nhs-reference-costs>