The relationship between school holidays and transmission of influenza in England and Wales

Web appendix

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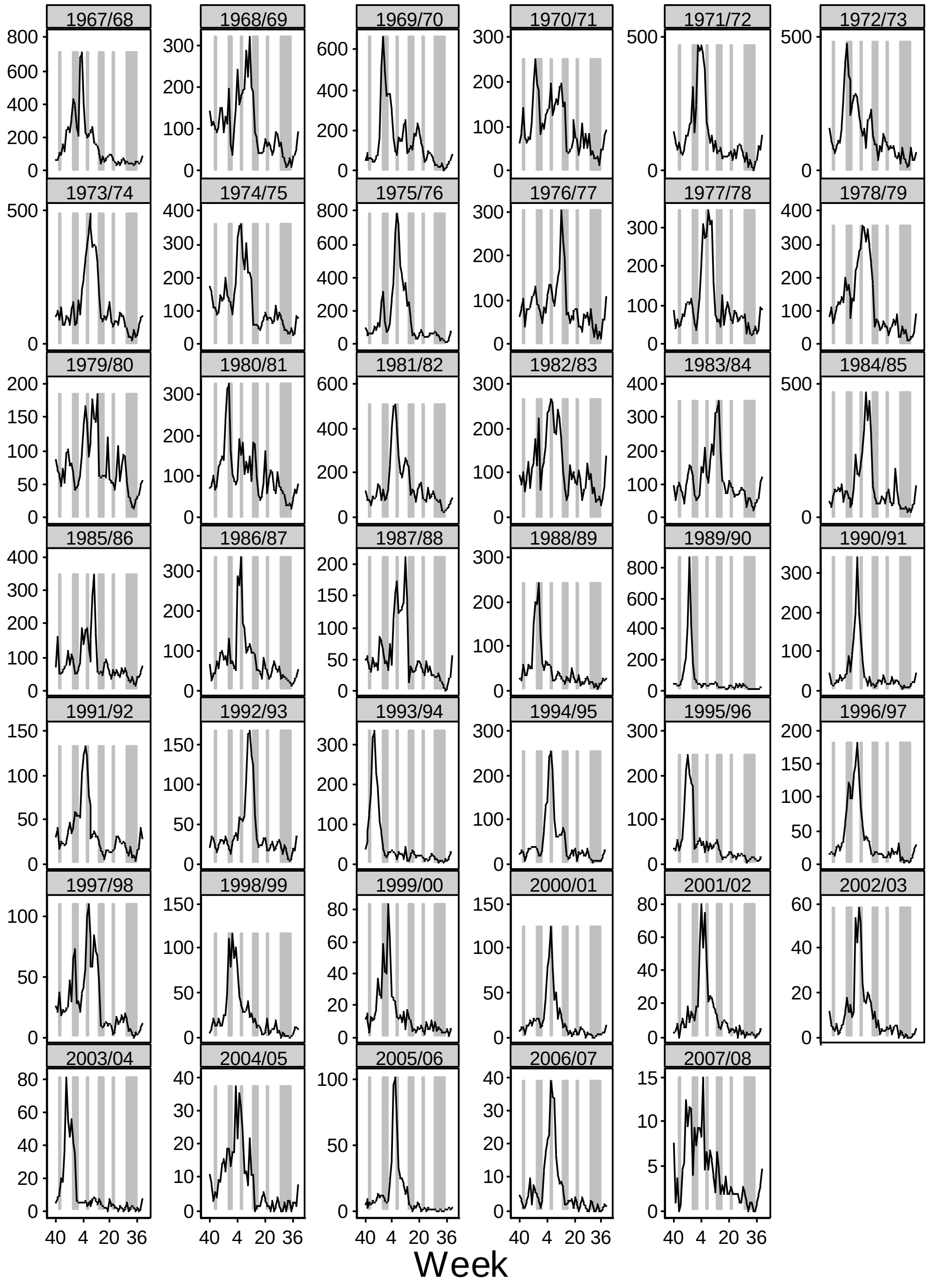
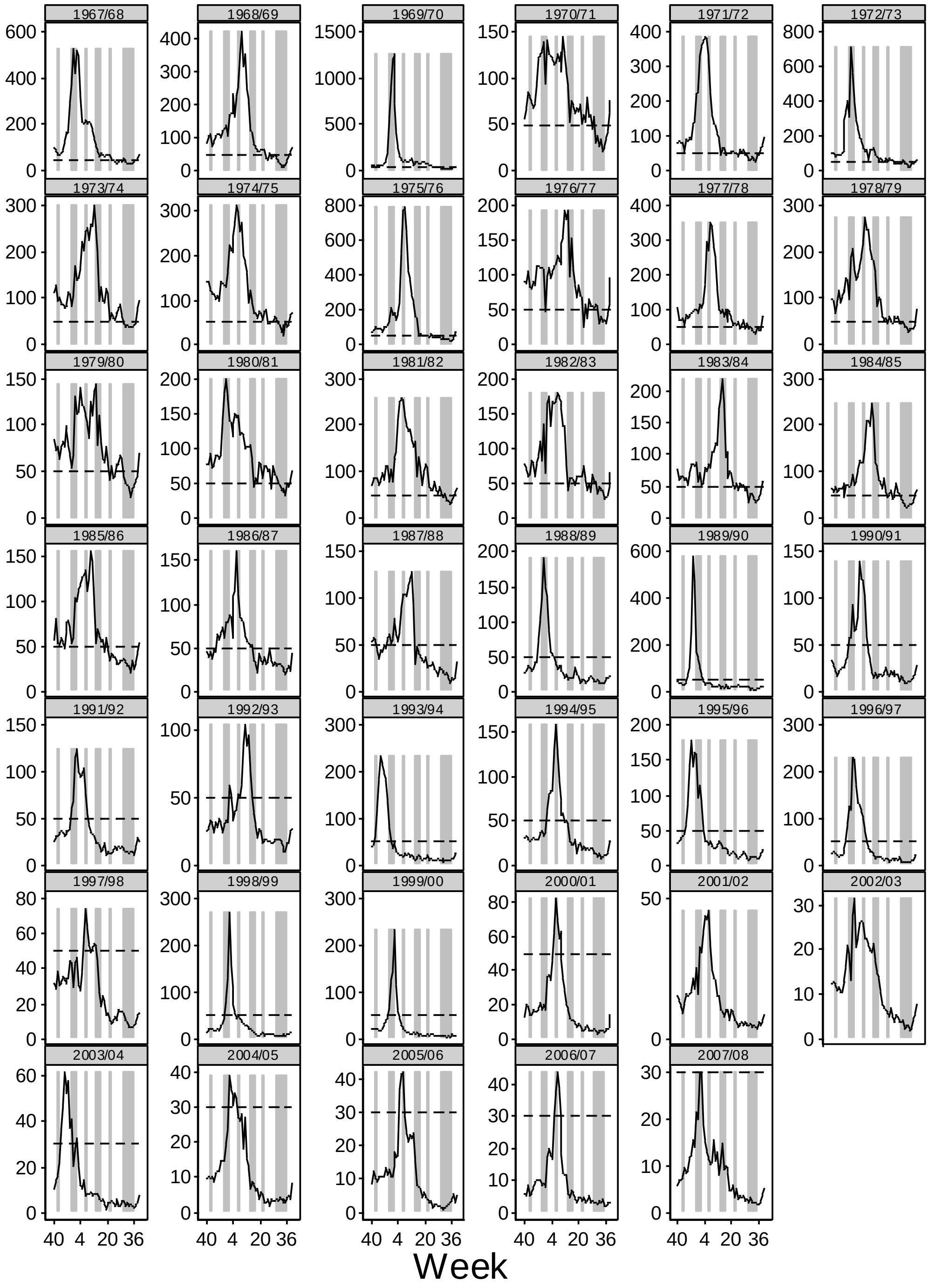


Web Figure 1.2: ILI consultation rates for all ages, 1967/68 to 2007/08 influenza years. An influenza season is defined as week 40 of one year to week 39 of the following year. Grey bars show the approximate timing of school holidays; horizontal dashed lines show the epidemic threshold of 50 consultations per 100,000 per week (before 2003/04) or 30 per 100,000 per week (from 2003/04 onwards) for years in which this was exceeded. Note the differing y axis scales.



Web Table 1.1: Circulating influenza viruses and sources of data for the proportion of the population susceptible at the start of each season (the latter proportion is shown in Figure 1 in the main text).

Season	**Circulating virus(es)**	**Population in serological study**	**Definition of seropositivity**	**Comments**
1967-68	A/England/68 (H2N2), A/Tokyo/67, B (1)	NA	NA	No suitable data found for this season
1968/69	A/Hong Kong/68 (H3N2) (2)	270 serum samples (of which 79 were from children); adult specimens were from blood donors, antenatal clinics and samples sent for Wasserman tests, child specimens from children admitted to hospital for accidents or burns and samples submitted for antistreptolysin O testing (3).	HI antibody titre ≥1:6	

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1969/70	A/Hong Kong/68 (H3N2), B/England/68 (2)	“Randomly collected serum specimens from persons of all ages…in Sheffield” (4)	HI antibody titre ≥1:10	The proportion seropositive each year is provided in 10 year age bands, without age-specific or overall denominators. Therefore the proportions used in the model are approximate. Tests were against A/HK/68.
1970/71	A/Hong Kong/68 (H3N2), B/England/68 (2)	“Randomly collected serum specimens from persons of all ages…in Sheffield” (4)	HI antibody titre ≥1:10	As 1969/70.
1971/72	A/Hong Kong/68 (H3N2) (2)	As 1969/70 for 5-14 year olds (4). For the “all ages” group, samples were from antenatal clinics, samples sent for antistreptolysin O tests (2).	HI antibody titre ≥1:10 for 5-14 year olds. HI antibody titre ≥1:40 for the all ages group.	As 1969/70 for 5-14 year olds. Both sources refer to tests against A/HK/68.

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1972/73	A/England/42/72 (H3N2), B/England/68, B/Hong Kong/72, B/Intermediate (2)	As 1971/72.	As 1971/72.	As 1969/70 for 5-14 year olds. The source for the all ages data provides figures separately for A/HK/68 and A/Eng/42/72; the latter were used as this was one of the dominant strains in 1972/73.
1973/74	A/Port Chalmers/73 (H3N2), B/Hong Kong/72, B/Intermediate (2)	As 1971/72.	As 1971/72.	As 1969/70 for 5-14 year olds. The source for the all ages data provides figures separately for A/HK/68, A/Eng/42/72 and A/PC/73; the latter were used as this was one of the dominant strains in 1973/74.

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1974/75	A/Port Chalmers/73 (H3N2), A/Scotland/74, A/Intermediate, B/Hong Kong/72 (2)	As 1971/72.	As 1971/72.	As 1969/70 for 5-14 year olds. The source for the all ages data provides figures separately for A/HK/68, A/Eng/42/72 and A/PC/73; the latter were used as this was one of the dominant strains in 1974/75.
1975/76	A/Victoria/75 (H3N2), A/England/864/75 (H3N2), B/Hong Kong/72 (2)	As 1971/72 for all ages. For 5-14 year olds, "Approximately 50 sera were collected…from normal persons and patients not having suffered recently from acute respiratory disease" in Sheffield (5).	As 1971/72 for all ages. HI antibody titre ≥1:30 for 5-14 year olds.	As 1969/70 for 5-14 year olds. The source for the all ages data provides figures separately for A/HK/68, A/Eng/42/72, A/PC/73 and A/Vic/2/75; the latter were used as this was one of the dominant strains in 1975/76.

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1976/77	A/Victoria/75 (H3N2) (6)	As 1975/76.	As 1975/76.	The source for the all ages data provides figures separately for A/HK/68, A/Eng/42/72, A/PC/73 and A/Vic/2/75; the latter were used as this was one of the dominant strains in 1976/77.
1977/78	A/Texas/1/77 (H3N2), A/USSR/90/77 (H1N1) (6)	As 1971/72	HI antibody titre ≥1:30	The estimate for all ages is an approximation (in the absence of age-specific denominators). Tests were against A\Victoria\75.
1978/79	B/Hong Kong/8/73 (6)	As 1977/78	As 1977/78	As 1977/78

Season	**Circulating virus(es)**	**Population in serological study**	**Definition of seropositivity**	**Comments**
1979/80	Intermediate between A/England/496/80 and A/Texas/1/77 (H3N2), B/Singapore/222/79 (6)	As 1977/78	As 1977/78	As 1977/78
1980/81	A/England/496/80 (H3N2), A/England/333/80 (H1N1) (6)	As 1977/78	As 1977/78	As 1977/78
1981/82	A/Belgium/1/81 (H3N2) (7)	As 1977/78	As 1977/78	As 1977/78

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1982/83	A/Belgium/1/81 (H3N2), A/England/333/80 (H1N1) (7)	"Sera were provided by several laboratories in different parts of the country [the UK]. The sera were obtained from patients of all ages bled during the summer months for a variety of routine clinical pathological tests." (7)	HI antibody titre ≥1:10	Data are provided separately for B/Singapore/222/79, A/England/496/80 and A/England/333/80; the latter were used as this was one of the dominant strains in 1982/83.
1983/84	A/Chile/1/84 (H1N1), B/USSR/100/83 (7)	As 1982/83	As 1982/83	Data are not presented for 1983/84; there is a statement that "similar patterns were obtained in 1983".

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1984/85	A/Philippines/2/82 (H3N2), B/USSR/100/83 (7)	As 1982/83	As 1982/83	Data are not presented for 1984/85; there is a statement that “sera taken in the summer of 1984 showed little change in the patterns of antibodies compared to the previous year.”
1985/86	A(H3N2), B (8)	As 1982/83	Single radial haemolysis ≥3mm.	Data are provided for 4 subtypes of A(H3N2) without an indication of which dominated the season. Seroprevalence is similar for the four types for those aged under 17.
1986/87	A(H1N1) (9)	NA	NA	No suitable data found for this season

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1987/88	A(H3N2), A(H1N1)(10)	NA	NA	No suitable data found for this season
1988/89	A(H1N1), A(H3N2) (10)	NA	NA	No suitable data found for this season
1989/90	A/Shanghai/11/87 (H3N2) (11)	149 participants (aged 17 to >60 years) in a vaccine trial in Italy (12).	HI antibody titre ≥1:40 in pre-vaccination sera.	No suitable data found for 5-14 year olds for this season. Data are provided separately for H1N1, H3N2 and B; the data for H3N2 were used as this was the dominant strain in 1989/90. Tests were against A/Shanghai/11/87.
1990/91	B (10)	NA	NA	No suitable data found for this season

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1991/92	A(H3N2) (10)	NA	NA	No suitable data found for this season
1992/93	B (10)	NA	NA	No suitable data found for this season
1993/94	A/Beijing/32/92 (H3N2) (11)	NA	NA	No suitable data found for this season
1994/95	B (10)	NA	NA	No suitable data found for this season

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1995/96	A(H3N2) (10)	39 individuals (not in risk groups) attending a general practice in Birmingham for influenza vaccination, in autumn 1995 (13).	HI antibody titre ≥1:40 in pre-vaccination sera.	Age range not stated but assumed to be adults. No suitable data found for 5-14 year olds for this season. Data are provided separately for H1N1, H3N2 and B; the data for H3N2 were used as this was the dominant strain in 1995/96. Tests were against A/Johannesburg/33/94.
1996/97	A/Wuhan/359/95 (H3N2) (11)	NA	NA	No suitable data found for this season
1997/98	A(H3N2) (14)	NA	NA	No suitable data found for this season

Season	Circulating virus(es)	Population in serological study	Definition of seropositivity	Comments
1998/99	Not identified	NA	NA	No suitable data found for this season
1999/00	Not identified	NA	NA	No suitable data found for this season

Dates of school holidays

In England and Wales, school holiday dates are not set nationally but are decided by local organisations known as Local Authority Districts (LADs). Typically, schools open for a new school year in September. Holidays lasting approximately 2 weeks occur over the Christmas and New Year period and around Easter. The summer holiday usually begins in late July and lasts approximately 6 weeks. Each term (autumn, spring and summer) is divided in two by a one-week half term break.

To identify typical school holiday dates, the names of all 326 LADs in England were downloaded from the website of the Office for National Statistics (15). Each LAD was assigned to one of the nine regions used at the time of analysis by the Health Protection Agency (now Public Health England), using maps of Government Office Regions (16) and LADs (17). Three LADs were randomly selected from each region. The websites of these 27 LADs were accessed to identify current and, where possible, historical dates of school holidays. Dates of school terms were also available for the Inner London Education Authority (ILEA) for 1952/53 to 1979/80, although these did not include half term dates (ILEA, unpublished data). Finally, term dates for the 13 modern LADs which were formed from the abolition of ILEA in 1990 (18) were identified.

Web Tables 1.2 and 1.3 summarise the median week numbers identified for the major holidays and half term breaks, respectively. The dates of the Christmas holiday were consistent between LADs and over time, beginning in week 51 and ending in week 1. The dates of the summer holiday also varied relatively little, beginning in week 29-30 (late July) and ending in week 35-36 (early September). The timing of the Easter holiday varied somewhat between LADs in the same year, but more markedly between years (consistent with the timing of Easter itself). The autumn half term usually took place in week 43 (late

October), the spring half term in week 7 (mid to late February) and the summer half term in week 22 (the beginning of June). Based on these results, we treated the following calendar weeks as school holidays: 1, 7, 14-16, 22, 30-35, 43 and 51-52.

Web Table 1.2: *Week numbers of median holiday dates (week 1 is the week of 1 January).*

LAD(s) and time period	**Number of LADs**	**Christmas holiday**		**Easter holiday**		**Summer holiday**	
		Start week	End week	Start week	End week	Start week	End week
ILEA, 1955/56 - 1979/80	1	51	1	14	17	30	36
ILEA, 2009/10	5	51	1	14	16	30	35
ILEA, 2010/11	13	51	1	15	17	30	36
ILEA, 2011/12	11	51	1	13	16	30	---
Non-ILEA, 2002/03	1	51	1	15	17	30	35
Non-ILEA, 2003/04	1	51	1	14	16	29	35
Non-ILEA, 2004/05	1	51	1	13	15	30	36
Non-ILEA, 2005/06	2	51	1	14	16	29	36
Non-ILEA, 2006/07	4	51	1	13	16	29	36
Non-ILEA, 2007/08	6	51	1	13	15	30	35
Non-ILEA, 2008/09	6	51	1	14	16	29	36
Non-ILEA, 2009/10	14	51	1	14	16	30	35
Non-ILEA, 2010/11	26	51	1	15	17	30	36
Non-ILEA, 2011/12	25	51	1	13	16	29	---

Web Table 1.3: Week numbers of median half term dates (week 1 is the week of 1 January).

LAD(s) and time period	**Number of LADs**	**Autumn**		**Spring**		**Summer**	
		Start week	End week	Start week	End week	Start week	End week
ILEA, 2009/10	5	43	44	7	8	22	23
ILEA, 2010/11	13	43	44	8	9	22	23
ILEA, 2011/12	11	43	44	7	8	22	24
Non-ILEA, 2002/03	1	42	43	7	8	21	22
Non-ILEA, 2003/04	1	43	44	7	8	22	23
Non-ILEA, 2004/05	1	43	44	7	8	22	23
Non-ILEA, 2005/06	2	43	44	7	8	22	23
Non-ILEA, 2006/07	4	43	44	7	8	21	23
Non-ILEA, 2007/08	6	42	44	7	8	21	22
Non-ILEA, 2008/09	6	43	44	7	8	21	22
Non-ILEA, 2009/10	14	43	44	7	8	22	23
Non-ILEA, 2010/11	26	43	44	8	9	22	23
Non-ILEA, 2011/12	25	43	44	7	8	22	24

Web Appendix 2: Further details of the SIR model fitted to the data

Description of the model

Web Table 2.4 summarizes the definitions of variables and parameters used in the age-structured model. The model used the following differential equations to describe the number of susceptible, infectious and recovered individuals in each of two age groups (0-14 and ≥15 years), denoted by the subscript *i*:

$$\frac{dS_i(t)}{dt} = -\lambda_i(t)S_i(t)$$

$$\frac{dI_i(t)}{dt} = \lambda_i(t)S_i(t) - fI_i(t)$$

$$\frac{dR_i(t)}{dt} = fI_i(t)$$

where $\lambda_i(t) = \beta_{i1}(t)I_1(t) + \beta_{i2}(t)I_2(t)$

The equations for the model without age-structure are analogous.

The equations for both the age-structured and the model without age structure were solved using the Euler method, implemented in the programming language C and using a time step of 1/16 days. For simplicity, the equations were set up using a population size with 100,000 individuals, and the model predictions of numbers of cases that were reported in each age group were calculated by scaling up the appropriate model predictions to the actual population size in the RCGP population accordingly.

Each model was run for each influenza year separately. For each influenza year, we fitted the model using each of 20 sets of starting values for the parameters that were being estimated. For each set of starting values, we used the Nelder and Mead algorithm to find the best fit parameter estimates as measured by the log likelihood deviance. In addition, the implemented Nelder-Mead algorithm includes a local-restart procedure where following convergence, a new combination of parameters (simplex) is initialised from the local optima and the search is repeated. This restart procedure was repeated 10 times for each initial set of starting values. We then compared the deviance between the 20 sets of starting values to identify the starting parameters which led to the lowest value; we report the fitted estimates from this run.

Relationship between the contact parameters and elements of the Next Generation Matrix

Contact between individuals was assumed to differ between the two age groups in the model, according to the following matrix of "Who Acquires Infection From Whom":

$$\begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_3 \end{pmatrix}$$

whereby 0-14 year olds effectively contact each other at a rate β_1, the rate at which ≥15 year olds and 0-14 year olds effectively contact each other equals β_2, and the rate at which ≥15 year olds contact each other equals β_3. β_1, β_2, β_3 were calculated from the corresponding elements of the Next Generation Matrix, R_{ij}, using the following equations:

$$\beta_1 = \frac{R_{11}}{N_1} f$$

$$\beta_2 = \frac{R_{21}}{N_1} f$$

$$\beta_3 = \frac{R_{22}}{N_2} f$$

The elements of the Next Generation Matrix that were estimated by fitting model predictions to the data were therefore R_{11}, R_{21} and R_{22}. The final element of the Next Generation Matrix that was required to calculate R_0 was R_{12}, which was calculated using the equation:

$$R_{12} = \frac{R_{21} N_2}{N_1}$$

Web Table 2.4: Summary of variables and parameters used in fitting the models to the consultation data.

Symbol	Definition
$S_i(t)$	Number of susceptible individuals in age group *i* at time *t*
$I_i(t)$	Number of infectious individuals in age group *i* at time *t*
$R_i(t)$	Number of recovered individuals in age group *i* at time *t*
N_i	Total population in age group *i*, assumed to stay fixed
$\beta_{ij}(t)$	The per capita rate of effective contact between two specific individuals in age groups *i* and *j* at time *t*, allowed to differ between term and holiday time and estimated by fitting to the data.
$\lambda_i(t)$	Force of infection among individuals in group *i* at time *t*.
ρ_i	Reporting fraction in age group *i* (proportion of infections that are reported to the surveillance system); estimated by fitting to the data*
I_{i0}	Number of infectious individuals in age group *i* present at the start of the season (i.e. when the epidemic threshold is reached); estimated by fitting to the data*
S_{i0}	Number of susceptible individuals in age group *i* present at the start of the season (i.e. when the epidemic threshold is reached); estimated by fitting to the data*
f	Rate of recovery from being infectious (= 1/infectious period); infectious period assumed to be 3.5 days (2 or 4 days in sensitivity analyses).
R_{ij}	Elements of the Next Generation Matrix, used to calculate the basic reproduction number. R_{ij} reflects the number of secondary infectious people in age category *i* generated by each infectious person in age category *j* in a totally susceptible population.

* Estimated separately for ages 0-14 and ≥15 years in the age-structured models.

Fitting the SIR model to the data

The expression for the log likelihood deviance is as follows:

$$-2\sum_{i}\sum_{w}\mathrm{C}_{\mathrm{i,w}} - \hat{\mathrm{C}}_{\mathrm{i,w}} + \mathrm{C}_{\mathrm{i,w}}\ln(\hat{\mathrm{C}}_{\mathrm{i,w}}) - \mathrm{C}_{\mathrm{j,w}}\ln(\mathrm{C}_{\mathrm{i,w}})$$

where $C_{i,w}$ is the observed number of cases in age group *i* reported in week *w and* $\hat{\mathrm{C}}_{\mathrm{i,w}}$ is the model prediction of the number of cases in age group *i* reported in week *w*. The latter was given by the following equation:

$$\hat{\mathrm{C}}_{\mathrm{i,w}} = \frac{N_{i,obs}}{N_{i,\mathrm{mod}}}\sum_{t_{w_0}}^{t_{w_f}}\rho_i I_i(t)$$

where t_{w_0} and t_{w_f} are the times at the start and ends of week *w*, and $N_{i,\mathrm{mod}}$ and $N_{i,obs}$ are the modelled and observed population sizes in age group *i*.

The fitting was carried out using an algorithm based on the simplex method of Nelder and Mead (19). To increase the probability that the values selected by the fitting routine were globally optimum, we started the fitting process for 20 different starting values. The starting values were selected to span the range of plausible parameter values. In addition, the implemented Nelder-Mead algorithm includes a local-restart procedure where following convergence, a new simplex is initialised from the local optima and the search repeated. This restart procedure was repeated 10 times for each initial starting value.

Web Appendix 3: Further details of the mass action model

The following equations were used to estimate weekly values of the contact parameter, β_t:

$$S_t = S_{t-1} - I_t \qquad \text{(Equation A3.1)}$$

$$I_{t+1} = \beta_t I_t S_t \qquad \text{(Equation A3.2)}$$

Here, S_t and I_t are the number of susceptible and infectious individuals, respectively, in week t, and were estimated from the data. Weekly values of the contact parameter, β_t, were estimated using Equation A3.3, obtained by rearranging Equation A3.2:

$$\beta_t = \frac{I_{t+1}}{I_t S_t} \qquad \text{(Equation A3.3)}$$

The number of infectious individuals each week was estimated by scaling up the reported rate of ILI consultations by the reporting fraction (the proportion of infections that are reported). For a given value of the number susceptible at the start of the influenza year (S_0,), the number of susceptible individuals in week 1 was estimated by substituting the value for the estimated number of infectious individuals in week 1 into Equation A3.1. The numbers of susceptible individuals in weeks 2, 3, ...t were then estimated similarly by substituting the values for I_2, I_3...I_t into Equation A3.1.

Web Appendix 4: Estimating the reporting fraction for the simple mass action model

The reporting fraction (for all ages combined) was estimated by comparing the cumulative reported attack rate for each influenza year in the RCGP data with that estimated via an iterative method. With this approach, the following equation (20):

$$R_0 = \frac{\ln s_f - \ln s_0}{s_f - s_0} \qquad \text{(Equation A4.5)}$$

was first rearranged to obtain an equation for the proportion susceptible at the end of each influenza year (s_f) in terms of the proportion susceptible at the beginning of each year (s_0) and the basic reproduction number:

$$s_f = \exp(R_0(s_f - s_0) + \ln s_0) \qquad \text{(Equation A4.6)}$$

Using season-specific serological data (or assuming a value of 0.3 for s_0 for years in which no suitable data were identified), and assuming that the basic reproduction number during the season was either 1.2, 1.5 or 1.8, s_f was estimated iteratively, with a starting value (s_{f0}) ranging between 0.1 and 0.9, using the following equation:

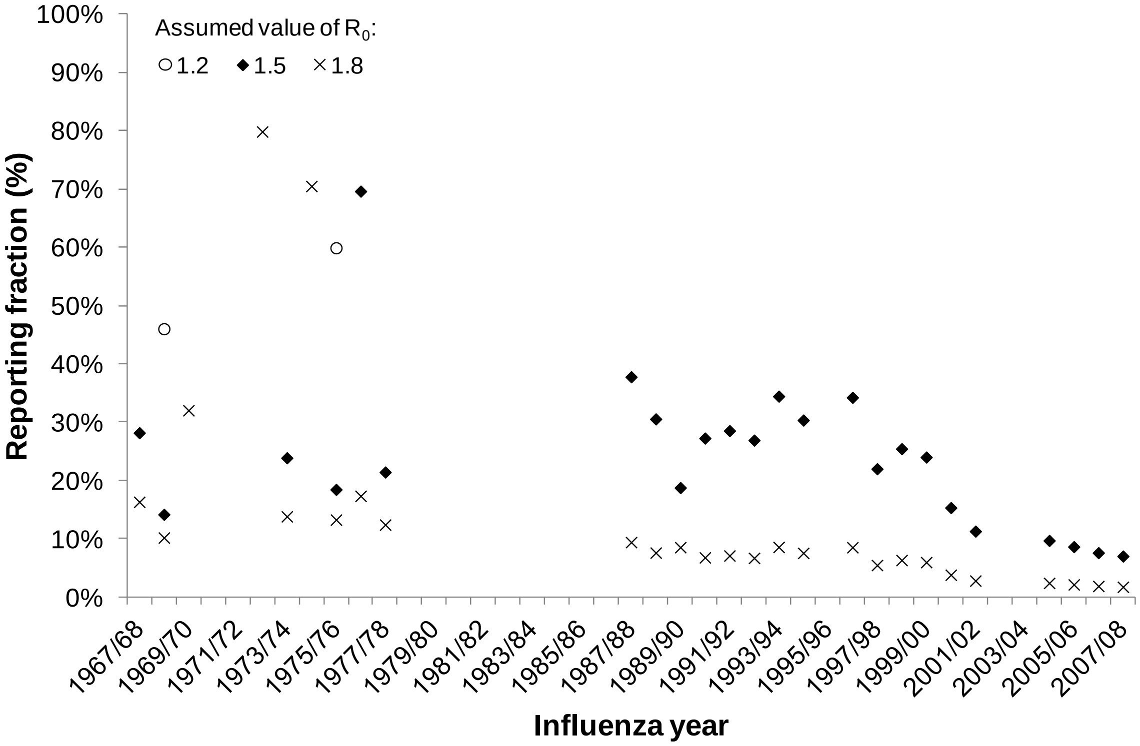
:

$$s_{f_{n+1}} = \exp(R_0(s_{f_n} - s_0) + \ln s_0)$$

The assumed values of R_0 are consistent with those reported in the literature (21, 22). The iterative process involves substituting s_{f0} into the right hand side of the above equation to obtain a value for s_{f_1}; the value for s_{f_1} is then substituted into the right-hand side of the equation to obtain s_{f_2}, and so on. The process was repeated n times until s_{f_n} equals $s_{f_{n+1}}$ and the value for s_{f_n} is assumed to equal the proportion susceptible at the end of the season. The value of s_f to which the estimates converged was used to estimate the cumulative attack rate for the respective influenza year, as $s_0 - s_f$. An alternative rearrangement, $s_f = (R_0 s_0 - \ln s_0 + \ln s_f)/R_0$, was also used instead of Equation A4.6, but did not give plausible estimates: the estimate of s_f often converged to the value of s_0, or was greater than s_0.

The reporting fraction was estimated as (cumulative reported attack rate in the RCGP data) / (estimated cumulative attack rate). Estimates were not possible in all seasons (especially as the starting value ($s_{f\,0}$) increased), and were implausibly low or high in others. For R_0 = 1.5 and with $s_{f\,0}$ = 0.25, the plausible estimates were typically around 20-40% (Web Figure 4.3). The estimated reporting fraction for R_0 = 1.8 was usually <10%.

Web Figure 4.3: Estimated season-specific reporting fractions for all ages in the RCGP data.



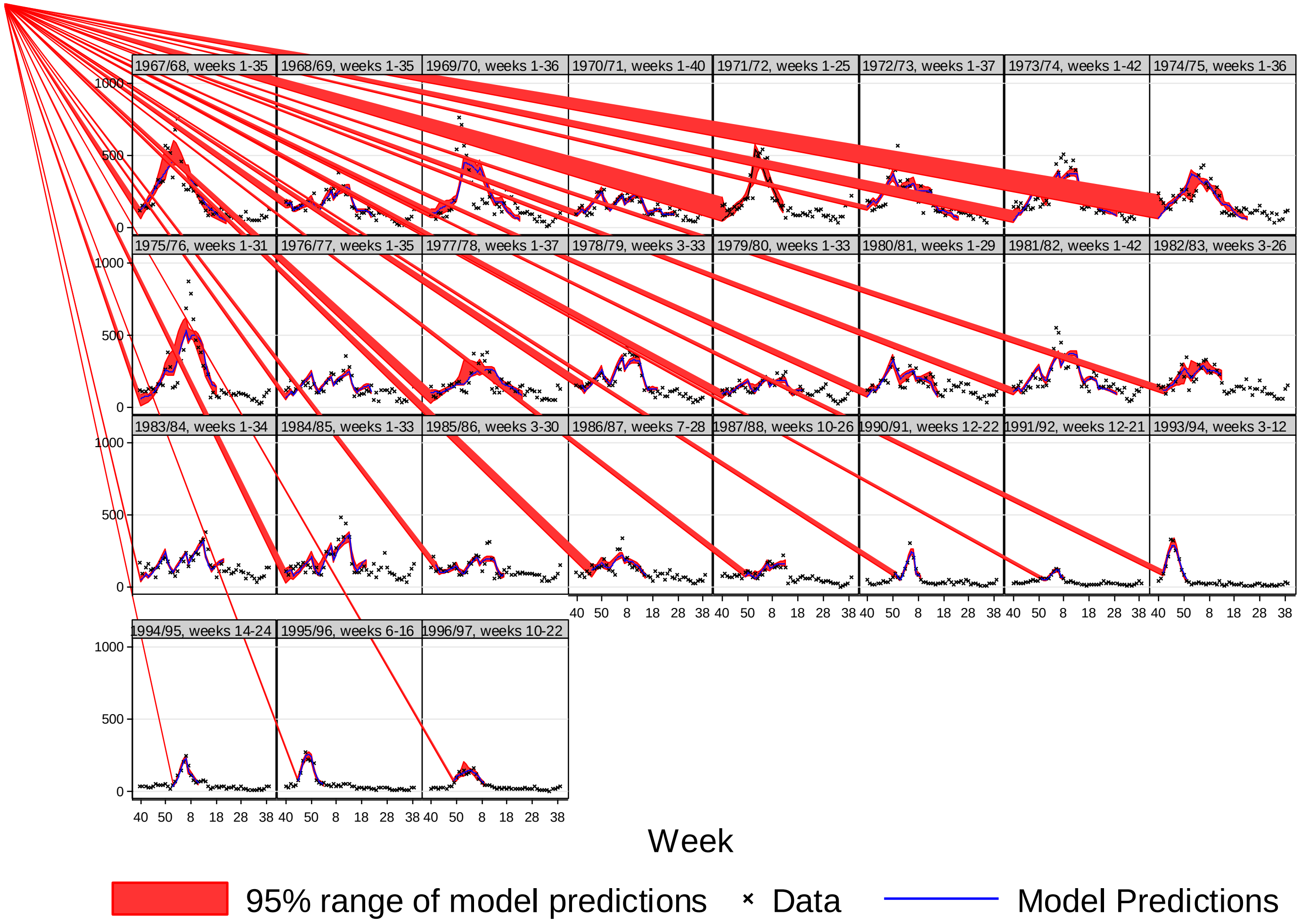
Based on the results assuming a basic reproduction number of 1.5, which suggested that a reporting fraction of ~20-40% was compatible with the data, we assumed a reporting fraction of 30% in all ages combined in the RCGP data. Assuming a reporting fraction of 30% for 5-14 year olds generated some negative estimates of the contact parameter, therefore we also assumed a higher reporting fraction (50%) for this age group. This is plausible, as children with ILI may be more likely than adults to consult a GP.

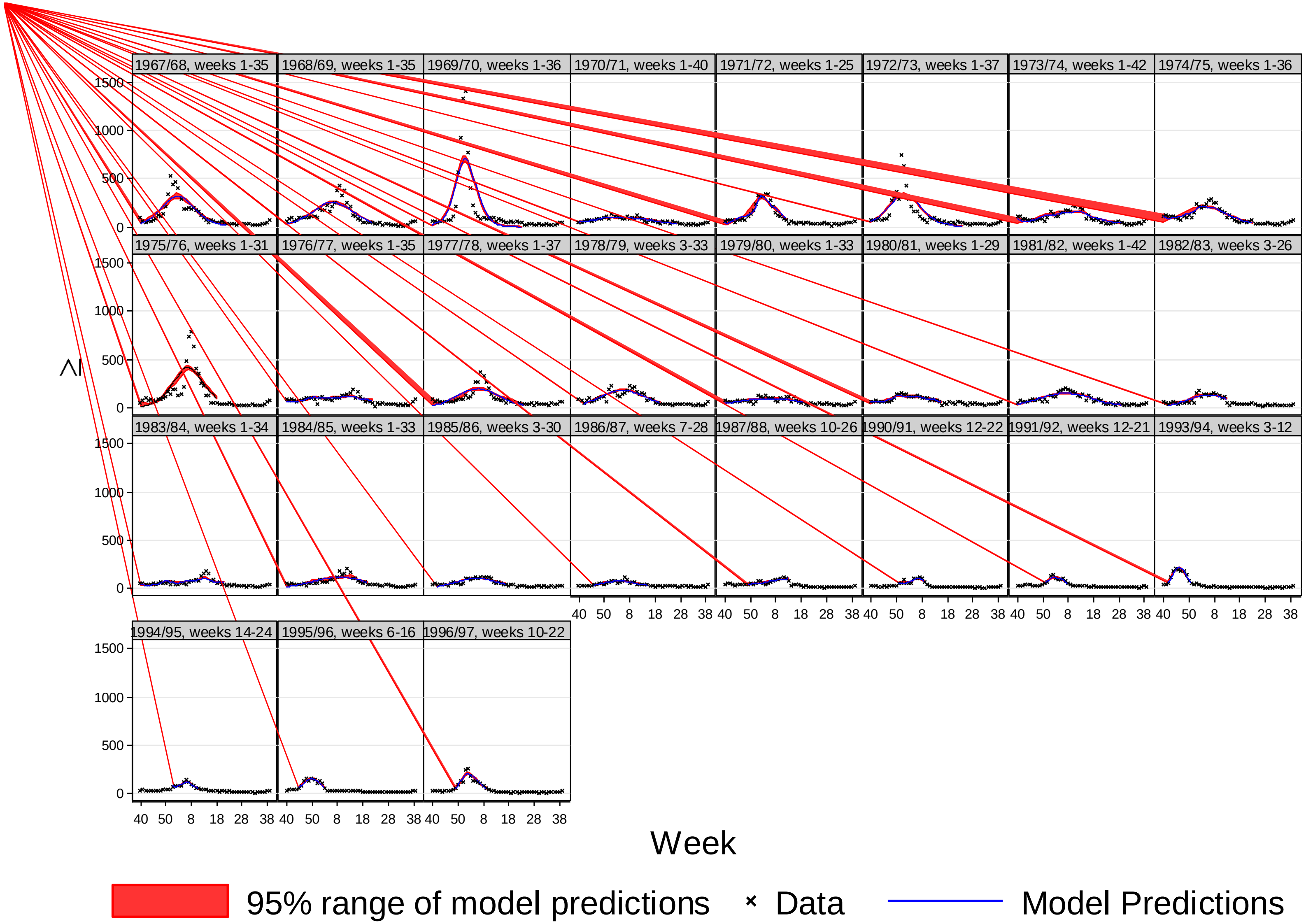
Web Appendix 5: Supplementary results

Results from fitting the age-structured model to the data

The predictions from the best-fitting models are shown together with the observed data in Web Figure 5.4. Web Table 5.5 summarises the estimates of the reporting fractions, proportions immune at the start of each influenza season, numbers of infectious individuals at the start of each season, and the basic reproduction number, from the age-structured model.

Web Figure 5.4: Predicted weekly ILI consultation rates per 100,000, by age group, from the best-fitting age-structured model for each influenza season, with observed consultation rates and 95% range of bootstrapped datasets. The infectious period was assumed to be 3.5 days.




1967/68, weeks 1-35
1968/69, weeks 1-35
1969/70, weeks 1-36
1970/71, weeks 1-40
1971/72, weeks 1-25
1972/73, weeks 1-37
1973/74, weeks 1-42
1974/75, weeks 1-36
1975/76, weeks 1-31
1976/77, weeks 1-35
1977/78, weeks 1-37
1978/79, weeks 3-33
1979/80, weeks 1-33
1980/81, weeks 1-29
1981/82, weeks 1-42
1982/83, weeks 3-26
1983/84, weeks 1-34
1984/85, weeks 1-33
1985/86, weeks 3-30
1986/87, weeks 7-28
1987/88, weeks 10-26
1990/91, weeks 12-22
1991/92, weeks 12-21
1993/94, weeks 3-12
1994/95, weeks 14-24
1995/96, weeks 6-16
1996/97, weeks 10-22
0
500
1000
1500
ΛI
40
50
8
18
28
38
Week
🟥 95% range of model predictions
× Data
Model Predictions

Web Table 5.5: Parameter estimates obtained by fitting the age-structured model to the RCGP consultation data. 95% CIs from the bootstrapped datasets are shown in brackets. The infectious period was assumed to be 3.5 days. Numbers are rounded.

Year	Reporting fraction (0-14 year olds), %	Reporting fraction (≥15 year olds), %	Proportion immune at start* (0-14 year olds)	Proportion immune at start* (≥15 year olds)	Number infectious at start* (0-14 year olds)	Number infectious at start* (≥15 year olds)	R_0	Log likelihood deviance (degrees of freedom)
1967/68	66 (42, 100)	28 (27, 100)	0.10 (1.5×10^{-5}, 0.65)	2.5×10^{-5} (7.7×10^{-6}, 0.62)	5 (0, 6)	43 (15, 97)	1.20 (1.08, 3.16)	1104 (25)
1968/69	100 (100, 100)	33 (31, 34)	8.5×10^{-4} (4.8×10^{-6}, 0.30)	3.4×10^{-5} (8.8×10^{-7}, 0.017)	7 (5, 8)	33 (30, 36)	1.09 (1.09, 1.44)	1015 (25)
1969/70	68 (64, 79)	99 (36, 100)	0.0071 (6.3×10^{-7}, 0.07)	0.75 (0.29, 0.77)	6 (4, 7)	6 (4, 20)	4.72 (1.66, 5.15)	6140 (26)
1970/71	95 (76, 100)	100 (39, 100)	0.0012 (1.6×10^{-6}, 0.22)	0.61 (9.1×10^{-4}, 0.60)	3 (2, 4)	21 (19, 53)	2.56 (1.06, 2.55)	195 (30)
1971/72	30 (28, 100)	100 (18, 100)	0.0017 (1.7×10^{-6}, 0.28)	0.19 (9.2×10^{-7}, 0.30)	5 (0, 16)	39 (24, 124)	1.11 (1.07, 1.41)	460 (15)
1972/73	86 (74, 99)	32 (32, 100)	0.042 (1.5×10^{-6}, 0.15)	0.11 (0.081, 0.73)	6 (5, 7)	60 (16, 61)	1.25 (1.21, 4.17)	1985 (27)
1973/74	69 (64, 100)	100 (38, 100)	9.0×10^{-8} (2.3×10^{-7}, 0.15)	0.19 (4.8×10^{-7}, 0.24)	1 (0, 4)	47 (36, 65)	1.17 (1.07, 1.36)	737 (32)
1974/75	46 (44, 100)	100 (36, 100)	0.0013 (3.7×10^{-7}, 0.21)	1.5×10^{-4} (4.7×10^{-7}, 0.13)	4 (1, 12)	67 (48, 102)	1.06 (1.05,1.31)	794 (26)
1975/76	100 (35, 100)	32 (31, 100)	0.50 (5.3×10^{-7}, 0.52)	2.8×10^{-4} (6.3×10^{-7}, 0.23)	2 (0, 3)	16 (13, 45)	2.13 (1.14, 2.22)	3185 (21)

Year	Reporting fraction (0-14 year olds), %	Reporting fraction (≥15 year olds), %	Proportion immune at start* (0-14 year olds)	Proportion immune at start* (≥15 year olds)	Number infectious at start* (0-14 year olds)	Number infectious at start* (≥15 year olds)	R_0	Log likelihood deviance (degrees of freedom)
1976/77	85 (71, 100)	99 (99, 100)	0.0060 (6.2×10^{-7}, 0.051)	3.0×10^{-4} (4.4×10^{-7}, 0.040)	2 (2, 4)	44 (35, 52)	1.07 (1.06, 1.11)	507 (25)
1977/78	100 (36, 100)	28 (26, 100)	0.041 (1.30×10^{-6}, 0.24)	0.030 (1.2×10^{-6}, 0.49)	4 (0, 5)	39 (27, 84)	1.12 (1.06, 1.91)	1179 (27)
1978/79	100 (94, 100)	28 (27, 31)	0.13 (1.2×10^{-5}, 0.30)	0.0041 (1.5×10^{-6}, 0.084)	5 (4, 7)	71 (63, 75)	1.13 (1.08, 1.42)	421 (21)
1979/80	100 (60, 100)	41 (34, 100)	3.2×10^{-6} (1.9×10^{-7}, 0.012)	0.033 (1.6×10^{-6}, 0.12)	4 (2, 5)	59 (53, 67)	1.07 (1.04, 1.18)	305 (23)
1980/81	44 (41, 100)	100 (24, 100)	8.4×10^{-4} (1.2×10^{-6}, 0.22)	0.032 (5.6×10^{-6}, 0.72)	7 (5, 7)	55 (31, 109)	1.10 (1.09, 3.78)	277 (19)
1981/82	100 (100, 100)	35 (33, 37)	1.4×10^{-5} (7.0×10^{-8}, 0.0012)	0.0018 (1.2×10^{-6}, 0.058)	4 (3, 6)	55 (50, 61)	1.07 (1.06, 1.12)	642 (32)
1982/83	81 (52, 100)	20 (17, 100)	0.37 (7.5×10^{-4}, 0.58)	0.045 (3.3×10^{-6}, 0.33)	5 (1, 7)	69 (30, 95)	1.67 (1.04, 2.52)	325 (14)
1983/84	81 (72, 91)	100 (100, 100)	4.7×10^{-5} (4.6×10^{-7}, 0.024)	2.4×10^{-4} (1.6×10^{-7}, 0.0043)	1 (1, 2)	36 (26, 46)	1.09 (1.08, 1.11)	622 (24)
1984/85	100 (48, 100)	32 (24, 100)	0.0058 (1.53×10^{-6}, 0.15)	0.19 (9.9×10^{-7}, 0.18)	4 (0, 5)	35 (35, 67)	1.31 (1.07, 1.34)	695 (23)

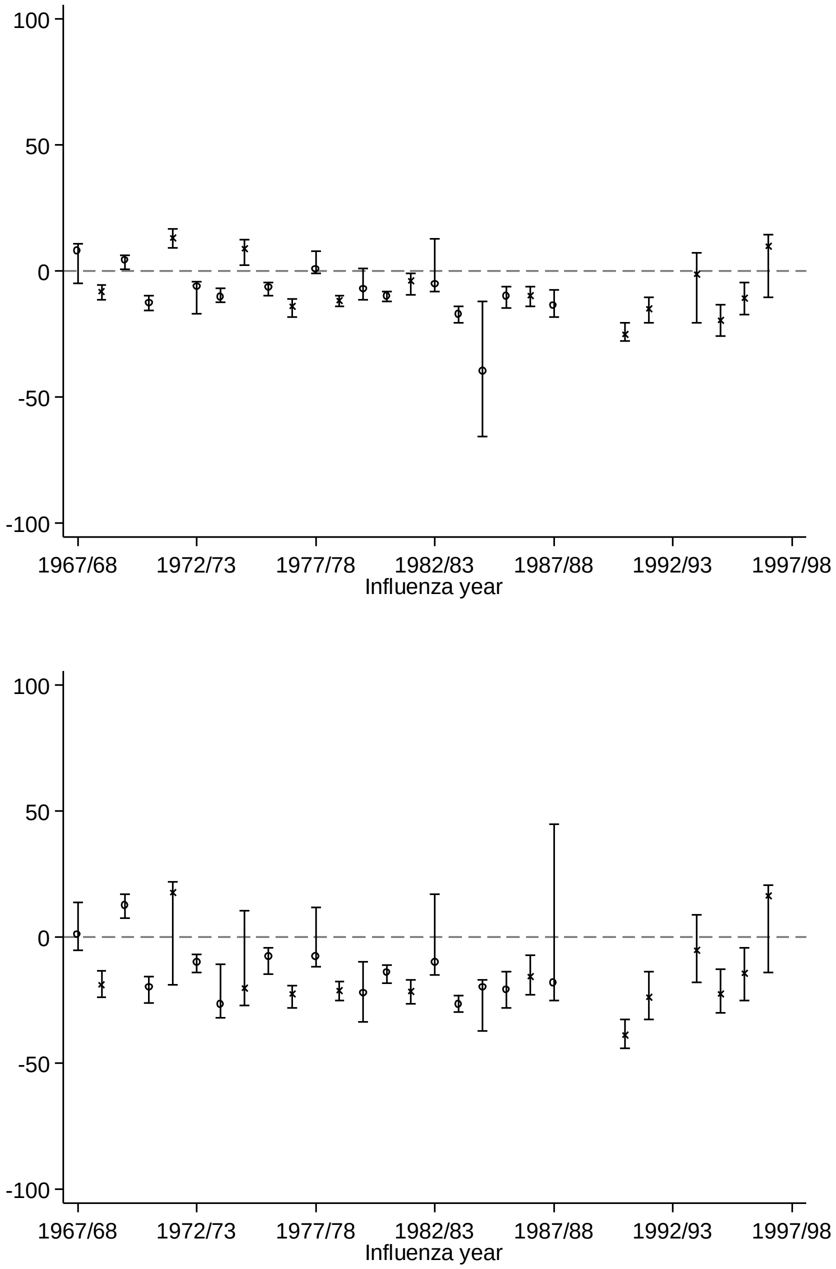
Year	Reporting fraction (0-14 year olds), %	Reporting fraction (≥15 year olds), %	Proportion immune at start* (0-14 year olds)	Proportion immune at start* (≥15 year olds)	Number infectious at start* (0-14 year olds)	Number infectious at start* (≥15 year olds)	R_0	Log likelihood deviance (degrees of freedom)
1985/86	100 (99, 100)	16 (14, 17)	0.29 (3.4×10^{-5}, 0.56)	6.1×10^{-4} (1.3×10^{-6}, 0.040)	6 (4, 7)	86 (77, 92)	1.31 (1.08, 2.20)	267 (18)
1986/87	100 (22, 100)	18 (9, 97)	0.66 (2.4×10^{-4}, 0.74)	0.46 (6.5×10^{-5}, 0.76)	4 (3, 12)	122 (56, 230)	2.74 (1.10, 4.40)	202 (12)
1987/88	15 (12, 100)	100 (28, 100)	3.3×10^{-6} (2.6×10^{-6}, 0.53)	0.27 (4.8×10^{-6}, 0.58)	22 (8, 26)	40 (35, 96)	1.30 (1.05, 2.69)	152 (7)
1990/91	14 (6, 25)	100 (45, 100)	0.73 (0.35, 0.85)	0.92 (0.73, 0.94)	65 (40, 156)	63 (51, 142)	11.3 (4.17, 15.5)	156 (1)
1991/92	11 (4, 24)	70 (23, 100)	0.61 (1.2×10^{-4}, 0.82)	0.95 (0.84, 0.97)	77 (33, 235)	130 (69, 441)	23.9 (7.12, 38.8)	120 (0)
1993/94	9 (5, 99)	100 (9, 100)	0.47 (0.11, 0.96)	0.90 (0.57, 0.95)	99 (5, 140)	0 (0, 1055)	3.58 (1.84, 31.1)	100 (0)
1994/95	6 (3, 7)	100 (56, 100)	0.33 (1.5×10^{-6}, 0.46)	0.95 (0.92, 0.96)	71 (51, 116)	154 (130, 276)	19.2 (10.4, 24.5)	90 (1)
1995/96	98 (17, 100)	13 (7, 43)	0.96 (0.73, 0.97)	0.65 (0036, 0.89)	4 (2, 37)	721 (210, 1288)	30.7 (5.4, 35.4)	159 (1)
1996/97	6 (5, 13)	68 (28, 100)	1.64×10^{-6} (3.0×10^{-6}, 0.55)	0.93, (0.66, 0.95)	115 (46, 116)	74 (10, 506)	15.1 (1.24, 24.0)	322 (3)

* First week in which the epidemic threshold was exceeded.

Alternative assumptions about the infectious period in the age-structured model

In the age-structured model assuming an infectious period of 2 days, the estimated percentage difference in the contact parameter amongst 5-14 year olds during holidays compared to termtime ranged from a reduction of 39% (95% CI 12, 66%) to an increase of 13% (95% CI 9, 17%) (Web Figure 5.5). For an infectious period of 4 days the corresponding range was from a reduction of 39% (95% CI 33, 44%) to an increase of 18% (95% CI 19% reduction to 22% increase).

Web Figure 5.5: Sensitivity of the estimated percentage difference in the contact parameter during termtime compared to holidays to the assumed duration of infectiousness. Estimated percentage difference in the contact parameter (amongst 0-14 year olds) for influenza during holidays compared to termtime based on fitting the age-structured model to ILI consultation data, assuming that the infectious period was 2 days (top) or 4 days (bottom). Crosses: single dominant subtype; Circles: more than one subtype circulating; Squares: unknown number of subtypes circulating. Error bars show 95% CIs.



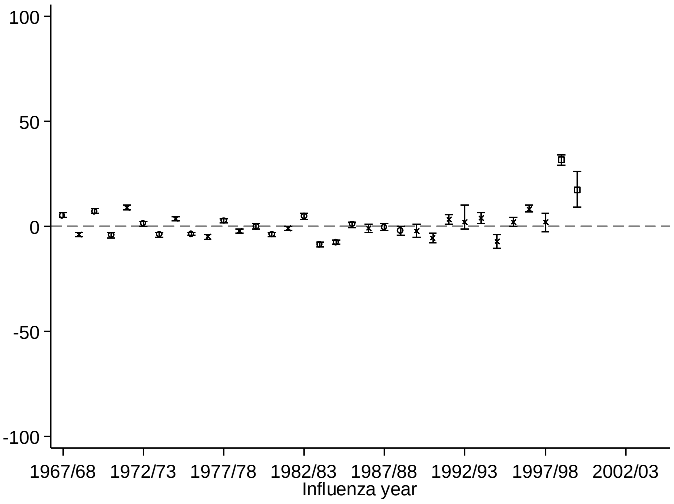
Results from fitting the model without age structure to the data

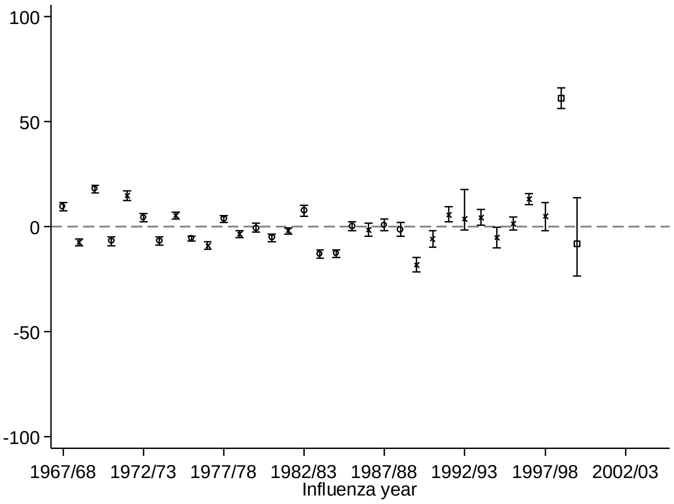
From the model without age structure and assuming an infectious period of 3.5 days, the estimated percentage difference in the contact parameter during holidays compared to termtime ranged from a reduction of 18% (95% CI 15, 22%) to an increase of 61% (95% CI 56, 66%) (Web Figure 5.6). In 13 years, the estimates were negative and had a 95% CI which excluded zero.

The corresponding range assuming an infectious period of 2 days was a reduction of 8% (95% CI 7, 10%) to an increase of 32% (95% CI 29, 34%); estimates for 11 years were negative and their 95% CI excluded zero. Assuming an infectious period of 4 days, the estimates ranged from a reduction of 22% (95% CI 19, 26%) to an increase of 71% (95% CI 66, 77%). Estimates for 13 years were negative with a 95% CI which excluded zero (Web Figure 5.6).

The estimates of the difference in the contact parameter comparing holidays to termtime were highly heterogeneous ($I^2 > 95\%$ in all cases) so were not combined in meta-analysis.

Web Figure 5.6: Estimated percentage difference in the contact parameter for influenza during holidays compared to termtime based on fitting the model to ILI consultation data for all ages combined. Crosses: single dominant subtype; Circles: more than one subtype circulating; Squares: unknown number of subtypes circulating. Error bars show 95% confidence intervals. The infectious period was assumed to be 2 days (top), 3.5 days (middle) or 4 days (bottom).


100
50
0
-50
-100
1967/68
1972/73
1977/78
1982/83
1987/88
1992/93
1997/98
2002/03
Influenza year


100
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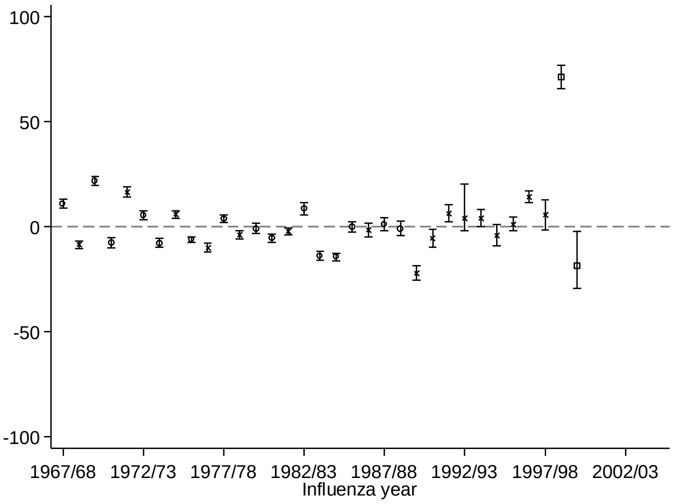
1967/68
1972/73
1977/78
1982/83
1987/88
1992/93
1997/98
2002/03
Influenza year


100
50
0
-50
-100
1967/68
1972/73
1977/78
1982/83
1987/88
1992/93
1997/98
2002/03
Influenza year

The estimates of the other parameters obtained by fitting the model without age structure to the data are summarised in Web Table 5.6.

Web Table 5.6. Parameter estimates from fitting the model without age structure to the RCGP data for all ages combined. 95% confidence intervals are given in brackets.

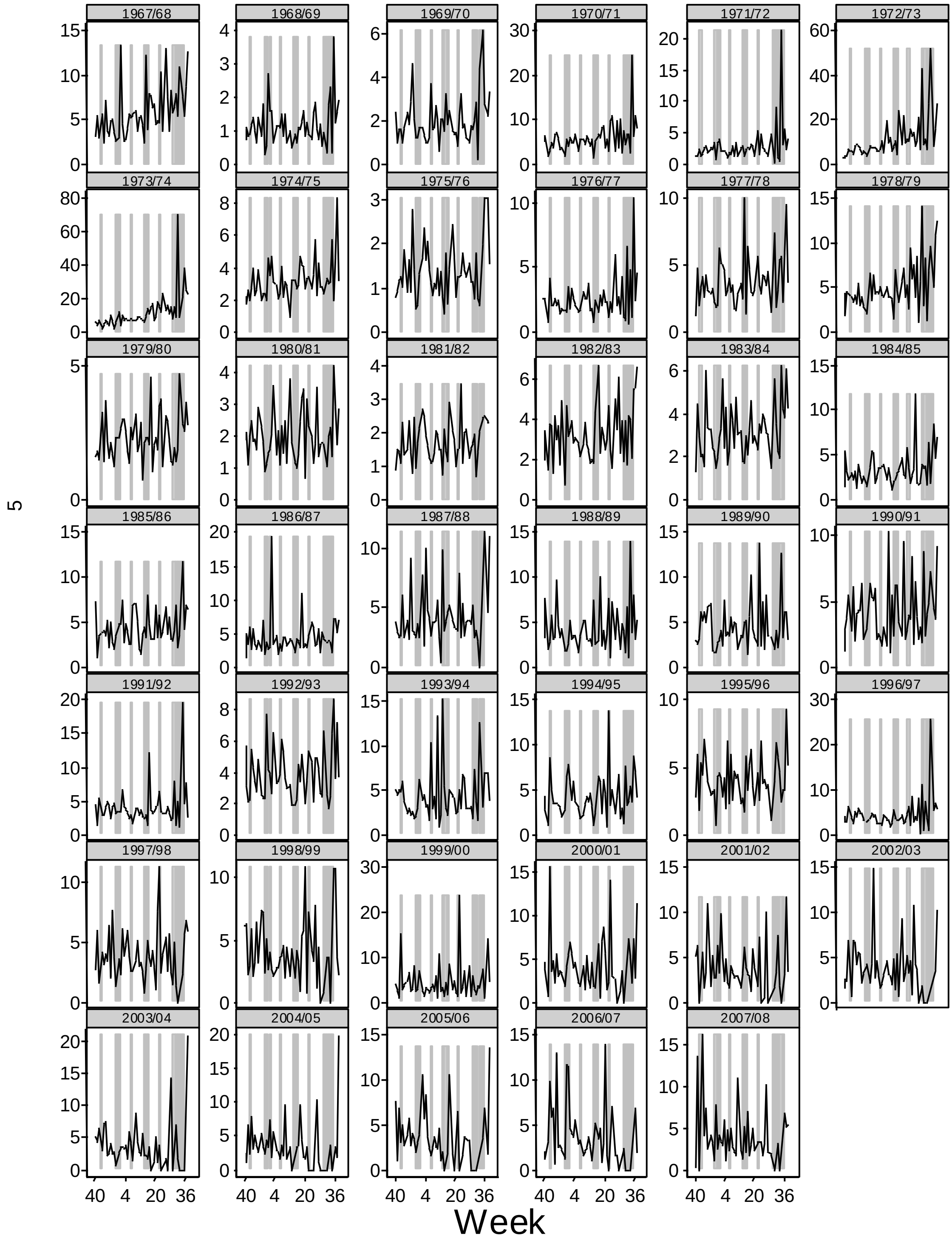
Year	Reporting fraction (%)	Proportion immune at start of season	Number infectious at start (per 100,000)	R_0	Log likelihood deviance (degrees of freedom)
1967/68	89 (35, 98)	0.60 (6.8×10^{-4}, 0.63)	32 (29, 81)	2.67 (1.07, 2.93)	828 (30)
1968/69	41 (39, 90)	0.031 (2.1×10^{-4}, 0.56)	41 (19, 44)	1.13 (1.10, 2.47)	984 (30)
1969/70	42 (36, 96)	0.16 (8.3×10^{-3}, 0.63)	69 (30, 80)	1.28 (1.09, 2.91)	6732 (31)
1970/71	58 (49, 95)	0.11 (2.0×10^{-4}, 0.45)	48 (29, 56)	1.18 (1.05, 1.91)	137 (35)
1971/72	27 (25, 97)	0.045 (6.5×10^{-4}, 0.74)	66 (18, 72)	1.12 (1.07, 4.04)	381 (20)
1972/73	90 (38, 99)	0.57 (0.0051, 0.61)	43 (39, 101)	2.52 (1.08, 2.79)	1905 (32)
1973/74	59 (51, 87)	0.10 (2.3×10^{-4}, 0.37)	39 (28, 46)	1.20 (1.07, 1.70)	667 (37)
1974/75	77 (44, 99)	0.42 (3.0×10^{-4}, 0.55)	45 (35, 78)	1.81 (1.05, 2.32)	692 (31)
1975/76	41 (35, 55)	0.12 (3.4×10^{-4}, 0.35)	17 (13, 21)	1.29 (1.14, 1.75)	3075 (26)
1976/77	96 (81, 100)	0.032 (4.7×10^{-6}, 0.11)	32 (30, 36)	1.08 (1.05, 1.18)	379 (30)
1977/78	34 (33, 90)	0.0055 (4.8×10^{-4}, 0.62)	50 (19, 52)	1.07 (1.07, 2.81)	1067 (32)
1978/79	36 (35, 99)	0.012 (0.0013, 0.64)	70 (26, 72)	1.09 (1.08, 2.97)	370 (26)
1979/80	58 (47, 91)	0.11 (2.0×10^{-4}, 0.43)	48 (31, 57)	1.17 (1.03, 1.82)	263 (28)
1980/81	49 (31, 96)	0.32 (2.8×10^{-4}, 0.65)	52 (27, 79)	1.58 (1.07, 3.10)	184 (24)
1981/82	49 (46, 97)	0.020 (3.1×10^{-4}, 0.50)	46 (24, 49)	1.08 (1.06, 2.12)	576 (37)
1982/83	52 (33, 91)	0.31 (0.0015, 0.61)	46 (26, 69)	1.50 (1.04, 2.66)	158 (19)
1983/84	98 (76, 100)	0.057 (2.0×10^{-5}, 0.15)	20 (19, 24)	1.13 (1.06, 1.25)	579 (29)
1984/85	41 (37, 70)	0.021 (3.4×10^{-4}, 0.40)	30 (19, 32)	1.12 (1.09, 1.83)	597 (28)
1985/86	32 (21, 80)	0.31 (5.7×10^{-4}, 0.73)	50 (20, 74)	1.54 (1.07, 3.89)	234 (23)
1986/87	34 (19, 83)	0.60 (0.26, 0.83)	62 (27, 111)	2.66 (1.47, 6.16)	161 (17)
1987/88	100 (53, 100)	0.0018 (2.6×10^{-6}, 0.12)	24 (21, 43)	1.03 (1.03, 1.17)	101 (12)
1988/89	19 (9, 76)	0.87 (0.73, 0.97)	110 (28, 226)	9.80 (4.75, 39.2)	36 (4)
1989/90	20 (11, 68)	0.79 (0.62, 0.94)	72 (22, 131)	6.90 (3.85, 23.3)	505 (4)

Year	Reporting fraction (%)	Proportion immune at start of season	Number infectious at start (per 100,000)	R_0	Log likelihood deviance (degrees of freedom)
1990/91	37 (13, 84)	0.86 (0.60, 0.94)	62 (27, 176)	8.02 (2.81, 18.7)	181 (6)
1991/92	22 (12, 83)	0.80 (0.65, 0.95)	99 (26, 170)	5.57 (3.17, 21.6)	74 (5)
1992/93	80 (6, 100)	0.31 (2.7×10^{-5}, 0.96)	30 (22, 345)	1.37 (0.93, 28.3)	2 (2)
1993/94	65 (13, 84)	0.94 (0.70, 0.96)	33 (25, 175)	21.8 (4.24, 28.8)	47 (5)
1994/95	9 (12, 71)	0.59 (0.67, 0.95)	238 (30, 192)	2.89 (3.56, 22.7)	129 (6)
1995/96	12 (14, 89)	0.65 (0.70, 0.95)	203 (27, 169)	3.46 (4.07, 26.3)	142 (6)
1996/97	82 (18, 86)	0.91 (0.60, 0.92)	33 (32, 150)	12.6 (2.75, 13.1)	147 (8)
1997/98	98 (86, 100)	0.031 (1.08×10^{-6}, 0.19)	77 (70, 88)	0.90 (0.86, 1.07)	15 (3)
1998/99	100 (100,100)	1.7×10^{-4} (1.03×10^{-6}, 0.03)	23 (20, 26)	0.80 (0.79, 0.83)	22 (2)
1999/00	7 (4, 47)	0.75 (0.57, 0.96)	144 (29, 214)	6.22 (3.99, 32.2)	128 (2)

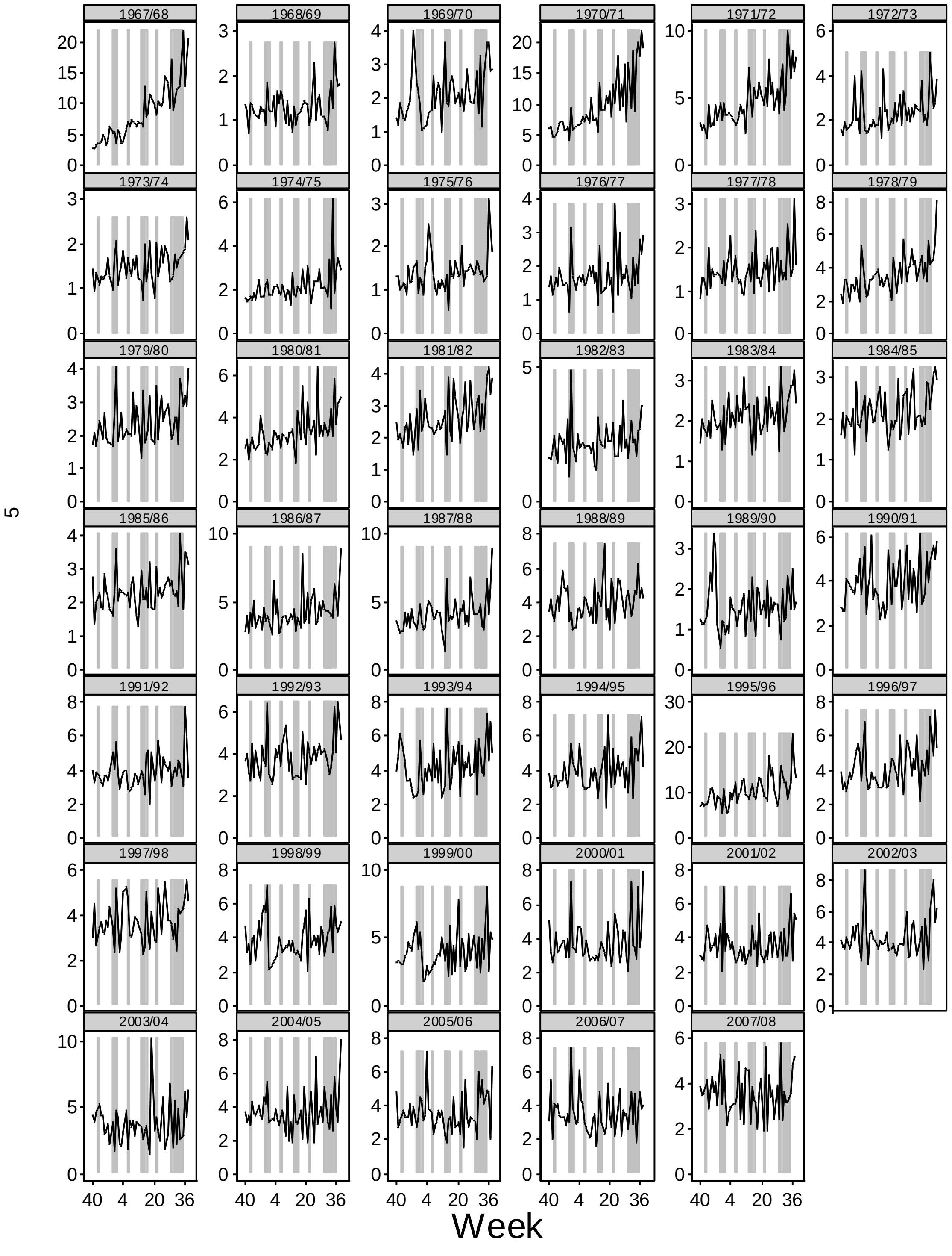
Estimates of the contact parameter from the simple mass action models

Weekly estimates of the contact parameter for 5-14 year olds and for all ages combined, as estimated using the simple mass action model, are shown in Web Figures 5.7 and 5.8.

Web Figure 5.7: Estimated weekly values of the contact parameter for influenza from the simple mass action model, based on RCGP data for 5-14 year olds, 1967/68 to 2007/08 influenza years. The reporting fraction was assumed to be 50% in all years; the proportion susceptible at the start of each year was based on season-specific serological data where possible. Grey rectangles show the approximate timing of school holidays.



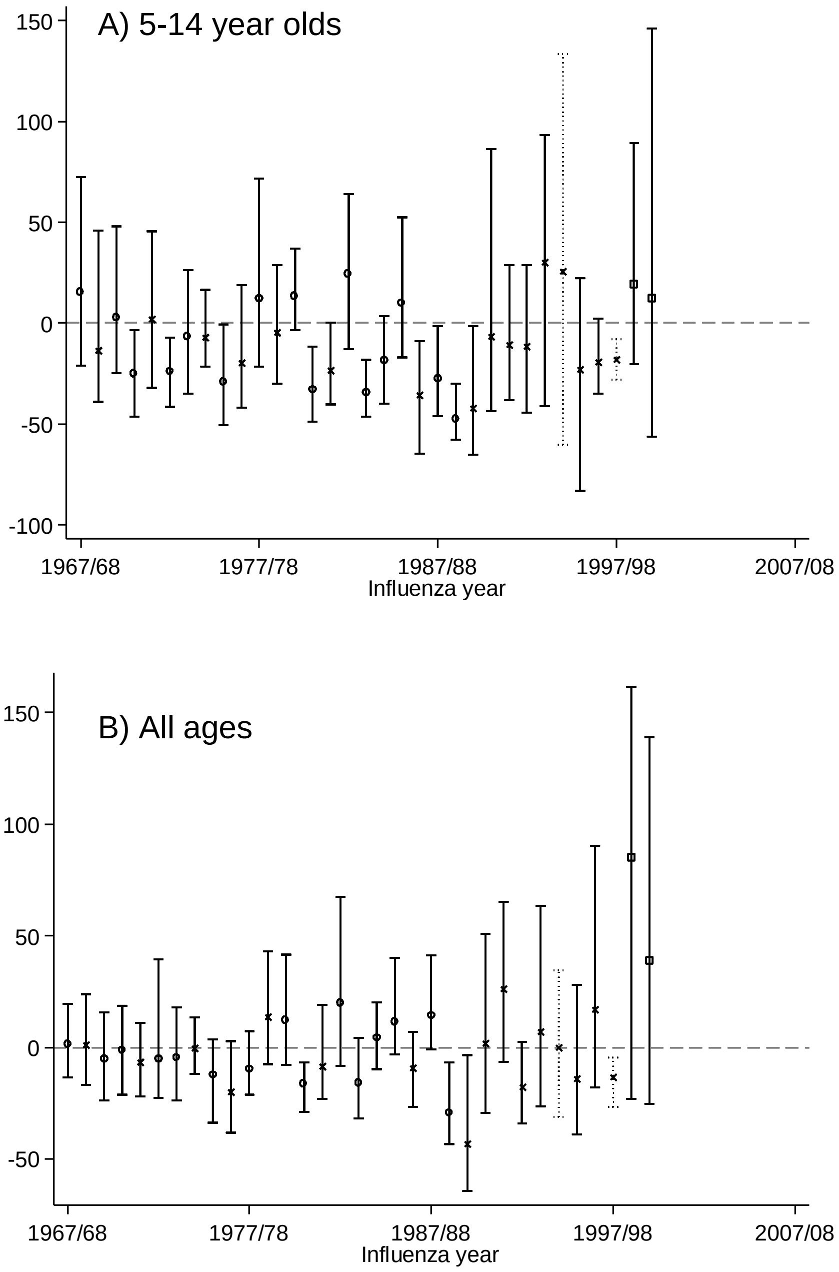
Web Figure 5.8: Estimated weekly values of the contact parameter from the simple mass action model, based on ILI consultation rates for all ages, 1967/68 to 2007/08 influenza years. The reporting fraction was assumed to be 30% in all years; the proportion susceptible at the start of each year was based on season-specific serological data where possible. Grey rectangles show the approximate timing of school holidays.



Alternative assumptions about the reporting fraction in the simple mass action model

Assuming that the reporting fraction was 70% led to slight reductions in the estimates of the contact parameter but had very little effect on the estimates of the changes in the contact parameter associated with school holidays in each influenza year (Web Figure 5.9). Based on the consultation data, the estimated percentage difference between the contact parameters for termtime and holiday were changed by <8 percentage points in each year by assuming the reporting fraction was 70% rather than 30% (or 50% for 5-14 year olds). For 5-14 year olds only, increasing the reporting fraction to 70% reduced the number of influenza years which showed evidence that the contact parameter was lower during school holidays than during termtime: the CIs for the percentage change in 1981/82 and 2000/01 included zero when the reporting fraction was assumed to be 70% but just excluded zero when it was assumed to be 50%.

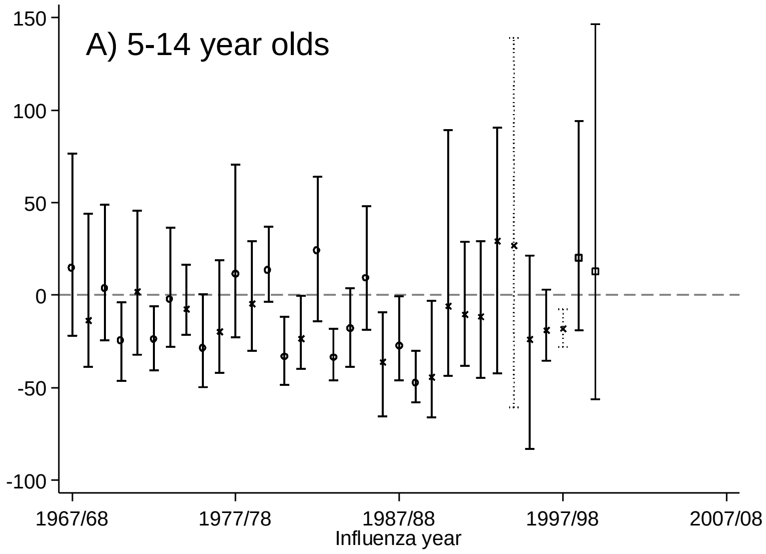
Web Figure 5.9: Estimated percentage changes in the value of the contact parameter for influenza during school holidays based on ILI consultation data and the simple mass action model for A) 5-14 year olds and B) all ages combined. The reporting fraction was assumed to be 70%. Crosses: single dominant subtype; Circles: more than one subtype circulating; Squares: unknown number of subtypes circulating. Error bars show 95% confidence intervals; dotted lines indicate years in which there were ≤2 estimates of the contact parameter during termtime and / or holidays.

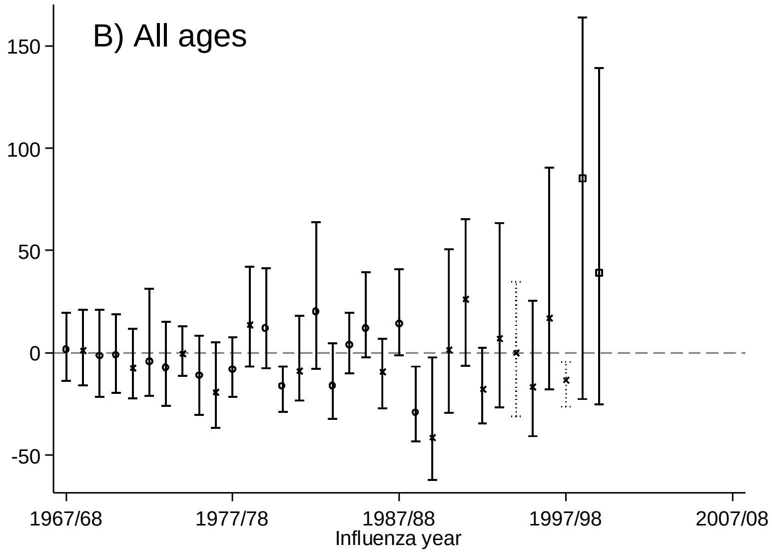


Alternative assumptions about the proportion of individuals who were susceptible at the start of each influenza year in the simple mass action model

Assuming that 70% of individuals were susceptible at the start of each influenza year had no effect on the season-specific estimates of the percentage difference between the contact parameter during school holidays compared to termtime (Web Figure 5.10).

Web Figure 5.10: Estimated percentage changes in the value of the contact parameter for influenza during school holidays based on the simple mass action model and ILI consultation data for A) 5-14 year olds and B) all ages combined, assuming that 70% of individuals were susceptible at the start of each outbreak. The reporting fraction was assumed to be 50% for 5-14 year olds and 30% for all ages combined. Crosses: single dominant subtype; Circles: more than one subtype circulating; Squares: unknown number of subtypes circulating. Error bars show 95% confidence intervals; dotted lines indicate years in which there were ≤2 estimates of the contact parameter during termtime and / or holidays.

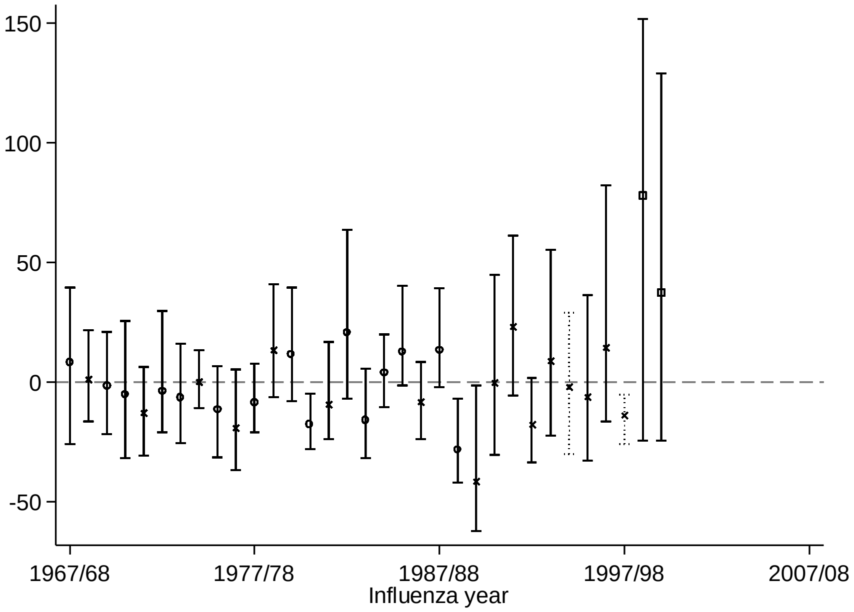




Estimates from the simple mass action model for all ages combined

The contact parameter as calculated for all ages combined was lower during school holidays than during termtime in 25 influenza years (Web Figure 5.11). In 6 years, the point estimate of the percentage difference was negative and the 95% CI excluded zero; in these years, the contact parameter was estimated to be 14% (95% CI: 5, 26%) to 49% (95% CI: 38, 55%) lower during school holidays compared to termtime.

Web Figure 5.11. Estimated percentage changes in the value of the contact parameter for influenza during school holidays based on the simple mass action model applied to ILI consultation data for all ages combined (reporting fraction assumed to be 30%). Crosses: single dominant subtype; Circles: more than one subtype circulating; Squares: unknown number of subtypes circulating. Error bars show 95% confidence intervals; dotted lines indicate years in which there were ≤2 estimates of the contact parameter during termtime and / or holidays.



Restricting the meta-analysis to influenza seasons for which serological data were available regarding the proportion of individuals who were susceptible at the start of the season

The meta-analysis of the estimated difference in the contact parameter for 5-14 year-olds, based on the simple mass action model and data for influenza seasons for which serological data were available, produced a pooled estimate for the change in the contact parameter of 14% (95% CI 5, 24%), but with marked heterogeneity (I^2 = 51%, Web Table 5.7). The estimated reduction was similar when the analysis was restricted to years in which a single influenza strain circulated, but the heterogeneity was removed.

For all ages combined, there was weak evidence of a small change in the contact parameter during school holidays: the pooled estimate using results for all years with serological data available suggested a reduction in the contact parameter of 6% (95% CI 1, 11%) during holidays.

Web Table 5.7: Estimates of the percentage difference in the contact parameter based on consultation data and the simple mass action model, comparing school holidays to termtime, by age group and number of circulating influenza strain. Analysis was restricted to influenza years for which serological data were available on the proportion of the population that was susceptible at the start of the year.

	Change in contact parameter during holidays (%)	95% CI	Number of years included in estimate	I^2 (%)
5-14 year olds				
All years	-14	-24, -5	17	51
Years with a single circulating subtype	-16	-26, -6	7	0
Years with >1 circulating subtype	-12	-27, 3	10	69
All ages				
All years	-6	-11, -1	20	27
Years with a single circulating subtype	-7	-15, 0.6	9	30
Years with >1 circulating subtype	-5	-11, 2	11	31

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