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# Decreasing stochasticity through enhanced seasonality in measles epidemics

**N. B. Mantilla-Beniers[1,2,3,*], O. N. Bjørnstad[4,5,8], B. T. Grenfell[4,5,8] and P. Rohani[6,7]**

[1]*Centro de Ciencias de la Complejidad (C3),* [2]*Instituto de Física, and* [3]*Facultad de Ciencias, Universidad Nacional Autónoma de México, CP 04510, México, D.F. México*
[4]*Department of Biology, and* [5]*Center for Infectious Disease Dynamics, Penn State University, University Park, PA 16802, USA*
[6]*Department of Ecology and Evolutionary Biology, and* [7]*Center for the Study of Complex Systems, University of Michigan, Ann Arbor, MI 48109, USA*
[8]*Fogarty International Center, National Institutes of Health, Bethesda, MD 20892, USA*

Seasonal changes in the environment are known to be important drivers of population dynamics, giving rise to sustained population cycles. However, it is often difficult to measure the strength and shape of seasonal forces affecting populations. In recent years, statistical time-series methods have been applied to the incidence records of childhood infectious diseases in an attempt to estimate seasonal variation in transmission rates, as driven by the pattern of school terms. In turn, school-term forcing was used to show how susceptible influx rates affect the interepidemic period. In this paper, we document the response of measles dynamics to distinct shifts in the parameter regime using previously unexplored records of measles mortality from the early decades of the twentieth century. We describe temporal patterns of measles epidemics using spectral analysis techniques, and point out a marked decrease in birth rates over time. Changes in host demography alone do not, however, suffice to explain epidemiological transitions. By fitting the time-series susceptible–infected–recovered model to measles mortality data, we obtain estimates of seasonal transmission in different eras, and find that seasonality increased over time. This analysis supports theoretical work linking complex population dynamics and the balance between stochastic and deterministic forces as determined by the strength of seasonality.

**Keywords: disease ecology; measles; seasonality; stochasticity; epidemiology; resonance**

## 1. INTRODUCTION

Analyses of ecological time-series data have documented the ubiquity of oscillations in population abundance across taxonomic orders (Anderson *et al.* 1982; Kendall *et al.* 1999). Understanding the underlying mechanisms that generate these cycles, especially the role played by seasonal variation, has been a long-term endeavour (Elton 1924; Lotka 1925; Dietz 1976; Earn *et al.* 1998; Altizer *et al.* 2006; Grassly & Fraser 2006; Keeling & Rohani 2007). Theoretical work has demonstrated how nonlinearities and delayed feedbacks inherent to ecological systems can interact with periodic forcing to produce a range of dynamics, including simple harmonic oscillations (where dynamics have the same period as the forcing) and subharmonic resonance, resulting in longer periodic oscillations that are integer-multiples of the forcing (May 1974; Dietz 1976; Grossman 1980; Nisbet & Gurney 1982; Schwartz & Smith 1983; Greenman & Benton 2005; Choisy *et al.* 2006).

The study of records of childhood disease incidence has arguably provided some of the best empirical demonstrations of the relationship between seasonality and population dynamics. The classic work of Soper (1929) was among the first to attribute a significant dynamical role to seasonality. Soper was intrigued by the stark contrast between the equilibrium dynamics predicted from simple mathematical models and the observed large amplitude and regular biennial measles epidemics in Glasgow. He used straightforward statistical methods to estimate a parameter, $\theta$, which illustrated the 'influence of the season'. He showed that $\theta$ was highest in the autumn months and declined during the summer. Soper attributed this to the aggregation and disaggregation of children in schools during term time and holidays (Soper 1929; Fine & Clarkson 1982). Since then, the work of London & Yorke (1973), Fine & Clarkson (1982), Finkenstadt & Grenfell (2000) and Cauchemez & Ferguson (2008) has

* Author for correspondence (nmantilla@cantab.net).

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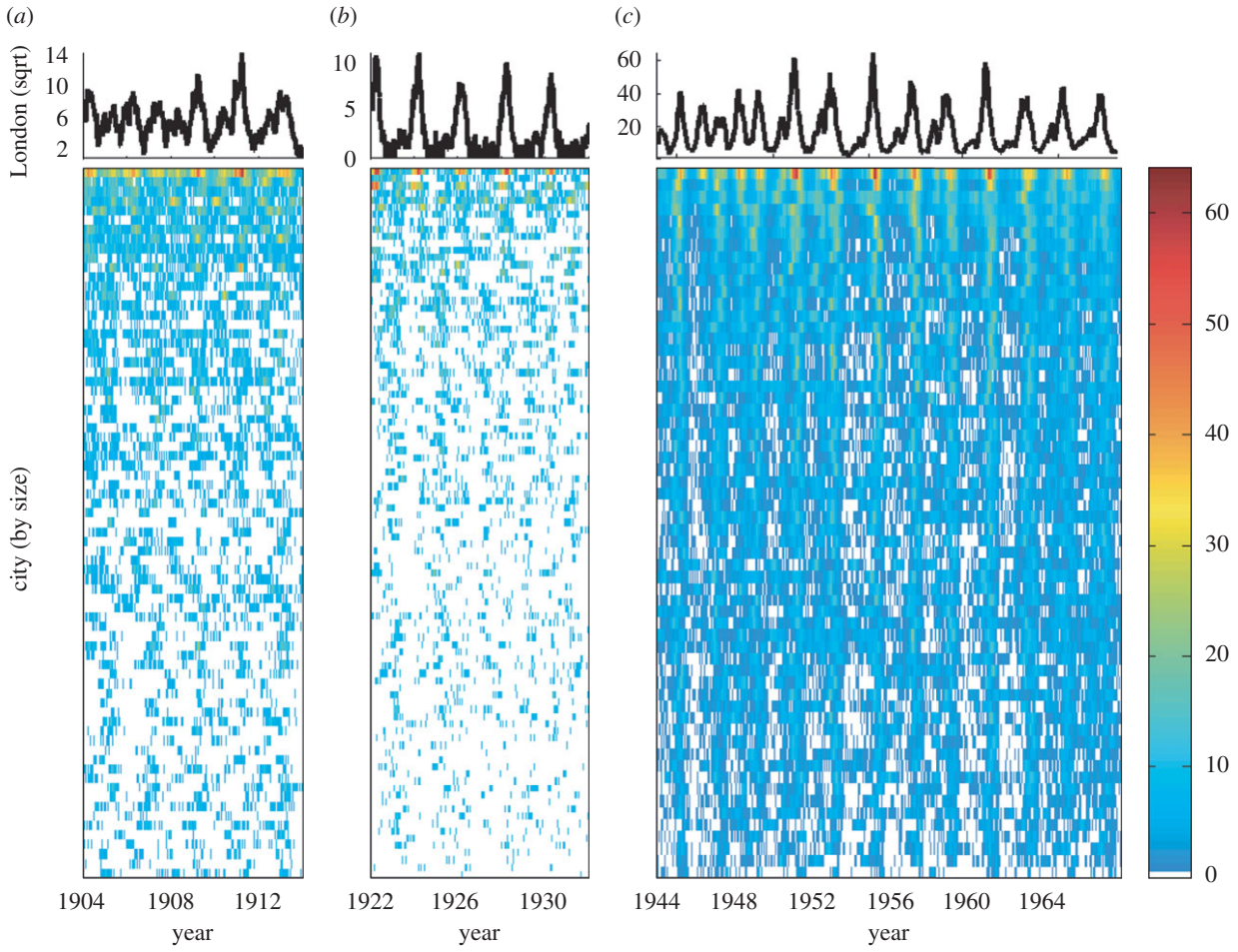


Figure 1. Measles records for three different eras. The graph at the top of each panel shows the square root of measles records in London. This time series is repeated in the first row of the bottom part of the panel, colour-coded. Time series for all other cities in the records are coded with the same scheme and displayed in the following rows, ordered by population size. The colour bar to the right of the figure gives the key to the coding—but note that the particular values associated with the colouring (on a square root scale) correspond to the figure on the right only. The maximum mortality recorded in any week in (*a*) 1904–1914 occurred in London (197 deaths) and went down to 121 deaths in (*b*) 1922–1932. (*c*) The largest number of cases in a week (4100) was observed also in London in 1944–1968. The data from the earlier decade (1904–1914) contain notifications from Berlin, Paris, Amsterdam, Copenhagen, Stockholm and Brussels in the continent, and a number of populations in the United Kingdom. Fewer continental capitals (only Berlin, Amsterdam, Copenhagen and Stockholm) yet more British towns returned records to the Registrar General after 1922 (OPCS, 1904). After 1932, data for continental Europe no longer appear in the weekly returns to the Registrar.

employed increasingly sophisticated statistical methods to establish the time-dependent transmission dynamics of childhood infections.

In this paper, we return to this issue by presenting and analysing previously unexplored records of measles mortality in Europe from the turn of the twentieth century. These data, which span 1904–1914 and 1922–1932, are taken together with the well-studied pre-vaccination records since the Second World War, and thus extend over half a century, providing an excellent opportunity for documenting the dynamical consequences of bifurcations observed in a natural system as a result of changing population demography and contact patterns. We first present the results of spectral analyses (Torrence & Compo 1998*a*; Chatfield 2004) of these data and discuss how our findings relate to changes in birth rates over time. Our analyses document the changing inter-epidemic periods of measles, with epidemics becoming increasingly more predictable and regular through time. This finding is surprising because the *per capita* crude birth rates were significantly higher during the period 1900–1920, which was predicted to result in more regular measles epidemics (Earn *et al.* 2000). We then estimate the strength of seasonality in measles transmission using the time-series susceptible–infected–recovered (TSIR) methodology of Finkenstadt & Grenfell (2000) and explain these contrasting patterns in terms of the dynamical consequences of reduced seasonal forcing in these earlier times.

## 2. THE DATA

Our dataset comprised weekly notifications of measles mortality published by the Office of Population, Censuses and Surveys (OPCS, 1904–1913 and 1922–1932) from European cities during 1904–1914 and 1922–1932, together with weekly records of measles incidence from the largest 60 towns and cities in England and Wales in the pre-vaccine era (1944–1968). A visual comparison of the data in the different eras (plotted in figure 1) reveals that the mortality data (figure 1*a*,*b*) contain

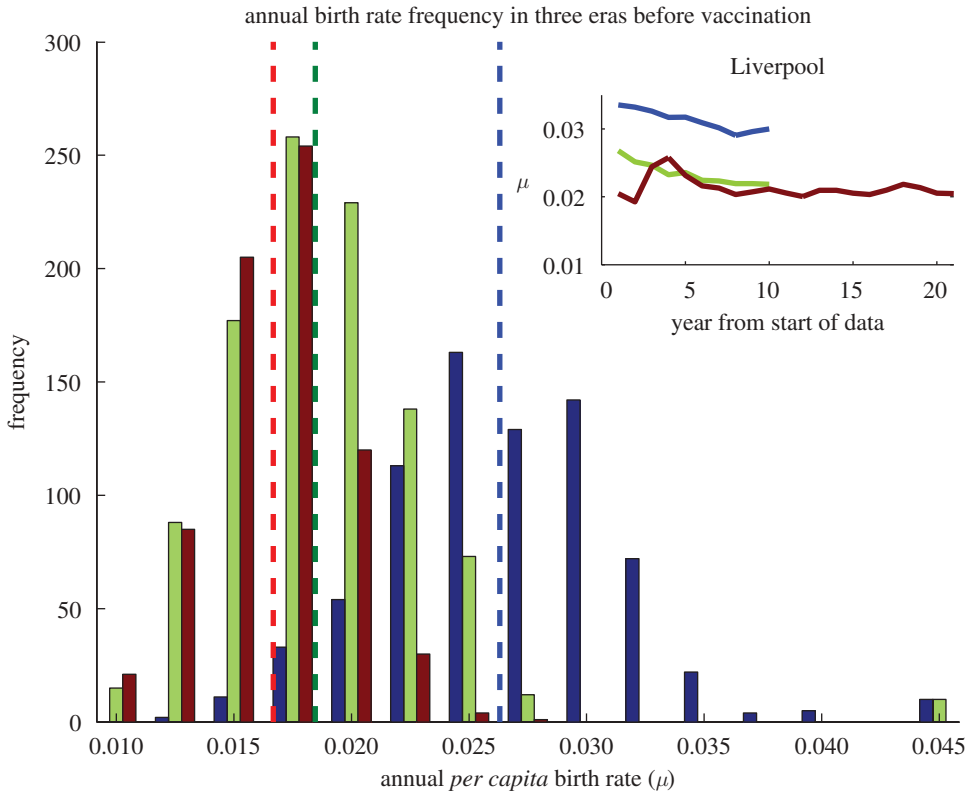


Figure 2. Frequency distribution of annual *per capita* birth rate ($\mu$) in all population centres in the data for each era. Birth rates for 1904–1914 appear in blue; green marks the era between the Wars (1922–1932); and red corresponds to birth rates between 1944 and 1968. Dashed, vertical lines mark mean values for each era. In the inset, example time series of births in Liverpool for the three eras are plotted alongside to illustrate their different temporal patterns which resemble those of other populations in each era.

many more weeks with zero notifications (white regions) than the incidence data (figure 1*c*). This is because only a fraction of cases result in death. In addition, the reduced notifications in 1922–1932 reflect the decline in measles mortality risk that characterized the first half of the twentieth century, and has been noted for other infectious diseases (see Brincker 1938; Woods *et al.* 1988, 1989; Hardy 1993; Cliff *et al.* 1998). While there is no consensus on the causes of this decline among demographers and medical historians, it is usually attributed to improvements in sanitation, access to clean water, housing, nutrition and healthcare practices (Hull 1988; Hardy 1993; Cliff *et al.* 1998).

We estimate that the case fatality rate (the *per capita* probability of dying as a result of infection) was approximately 2–20% during 1904–1914, and 0.5–15% in the 1920s. These estimates are based on two distinct empirical sources. The first is statistics from populations of comparable socioeconomic and demographic characteristics, yet different geographical location or epoch and including some hospital data (values and characteristics of the populations summarized in table S2 of the electronic supplementary material; data in Panum 1847; Hirsch 1883; Drinkwater 1885; Holt 1902; Wilson 1905; Butler 1913, 1947; Chalmers 1930; Morley *et al.* 1963; Editorial 1968; Aaby 1988; Pison & Bonneuil 1988; Preziosi *et al.* 2002; Grais *et al.* 2007). The second, and perhaps more compelling, is a handful of parallel time series of measles morbidity and mortality from European and North American populations at the turn of the twentieth century (Laing & Hay 1902; Butler 1913; Chapin 1926; Linnert 1954). These parallel data demonstrate a significant and meaningful linear association between measles mortality and incidence records, with slopes in the ranges mentioned above (table S1 in the electronic supplementary material). Additionally, examination of these parallel records leads us to conclude that mortality records faithfully trace patterns of incidence, though with reduced amplitude and typically a small delay (of two weeks or less).

Table 1. Mean, minimum and maximum annual *per capita* per cent population birth rates in all cities for the three prevaccination eras. The beginning of the century had significantly higher numbers of births than later years. Average birth rates from 1922 to 1932 and from 1944 to 1968 are not significantly different despite originating from contrasting demographic dynamics (see inset in figure 2).

| era | mean *per capita* birth rate % (min, max) |
|---|---|
| 1904–1914 | 2.6 (1.3, 4.1) |
| 1922–1932 | 1.8 (0.8, 2.8) |
| 1944–1968 | 1.7 (1.0, 3.2) |

In addition to reductions in case fatality probability, European populations experienced other changes during the first half of the twentieth century. These changes include a decline in *per capita* birth rates (figure 2 and table 1), which resulted in smaller

family sizes and consequently less crowded living conditions (Anderson 1993; Hicks & Allen 1999). The different histograms in figure 2 illustrate the considerable decline in both the mean and the range of the annual *per capita* birth rates from 1904 onwards. Note that mean *per capita* birth rates show no significant change from 1922–1932 to 1944–1968 (see table 1), though, as exemplified using data from Liverpool (inset, figure 2), the latter era experienced a pronounced baby boom after the Second World War, which is not observed in 1922–1932.

## 3. HISTORICAL INTEREPIDEMIC PERIODS OF MEASLES

The periodicity of oscillations in measles records was explored with standard spectral analysis techniques (Priestley 1981; Anderson *et al.* 1984; Torrence & Compo 1998*a*; Grenfell *et al.* 2001), using Matlab software provided by Torrence & Compo (1998*b*). Our findings are presented in figure 3, with large circles representing dominant periods and smaller circles portraying other significant periodicities. The results are presented in two different ways. In the upper row, cities are ordered by decreasing population size along the $y$-axis, whereas, in the bottom row, they are ordered using the mean *per capita* birth rate. Interepidemic periods are plotted on the $x$-axis. Figure 3 provides a historical progression of measles dynamics. It reveals, for example, that in contrast with patterns after 1944, when epidemics were predictably biennial in most cities, noisy interepidemic periods that are not multiples of a year were common in the earlier eras. Furthermore, it appears that neither population size nor *per capita* birth rates can predict the periodicities observed in the pre-Second World War data.

Previous analyses of measles epidemics in 1944–1968 have demonstrated that annual epidemics are expected when birth rates are high or low, while intermediate values tend to generate biennial cycles (Keeling & Grenfell 1999; Earn *et al.* 2000; Bauch & Earn 2003). These predicted dynamics are, however, also known to be influenced by the strength of seasonality in transmission (Bauch & Earn 2003; Conlan & Grenfell 2007; Keeling & Rohani 2007). Specifically, the range of parameter values leading to annual behaviour is predicted to expand as the seasonal amplitude decreases from the value estimated for the 1944–1968 data (Grenfell *et al.* 2002; Conlan & Grenfell 2007; see also Rohani *et al.* 2003). Simultaneously, lower seasonality makes the measles attractor less dissipative, lengthening the duration of dynamic transients and increasing the potential importance of stochasticity (Bauch & Earn 2003). To explore whether changes in the pattern of seasonality provide a parsimonious explanation for the observed shifts in dynamics, we next estimate seasonal transmission rates over the different time periods.

## 4. SEASONAL TRANSMISSION PATTERNS OVER TIME

Seasonal changes in transmission were estimated using the standard methodology for a TSIR model (Finkenstadt & Grenfell 2000; Bjornstad *et al.* 2002), applied to data from London, Liverpool, Manchester, Birmingham, Leeds and Sheffield (figures 4 and 5). For an overview of the TSIR methodology, see the electronic supplementary material. This approach yields 26 biweekly transmission coefficients ($\beta_i$, $i = 1, \ldots, 26$), from which we estimate the amplitude of seasonal forcing, defined as the total amount of seasonal variation around the mean,

$$\omega = \sum_{i=1}^{26} |r_i - \bar{r}|, \tag{4.1}$$

where $r_i = \log(\beta_i)$ and $\bar{r}$ is the average. We use transformed values that naturally result from fitting the transformed (linear) model to facilitate contrast with earlier estimates (Bjornstad *et al.* 2002).

A byproduct of the fitting procedure are estimates (denoted by $\chi_t$) of the proportion of actual cases represented in measles mortality or morbidity records (see table 2). These are measured as the derivative of the splines fitted to the cumulative count of disease against the cumulative number of births over a lapse of equal length (spline fitting routines from the statistical package R) and have been previously used as an indicator of reporting fidelity (Finkenstadt & Grenfell 2000). The average fractions of observed cases represented in disease records of different populations are fairly homogeneous in each era, but as would be expected differ considerably between morbidity and mortality reports (see table 2).

Figure 6 illustrates how transmission parameters estimated from measles incidence and case fatality time series from Manchester (1922–1932) differ in magnitude. For low $\chi$ (e.g. measles mortality records), transmission estimates have a lower mean, a considerable degree of short-term variation and greater amplitude. Estimates from death records, therefore, tend to obscure the pattern of seasonal transmission, overestimate the degree of seasonal variability and underestimate the basic reproduction ratio, $R_0$. As a result, it is not possible to assess directly changes in the seasonality of transmission over time using parameters obtained from the available time series as they stand. However, incidence records can be sampled at an adequate rate $\eta$ to create surrogate time series of measles mortality with characteristically lower $\chi$. To keep all things equal in our historical contrast, we also matched the length of time series from the early twentieth century and used 10 years worth of prevaccination incidence records (1950–1960) from the six largest cities that reported measles in all three eras (shown in figures 4 and 5).

Surrogate mortality data were generated by sampling the incidence time series at rates $\eta_{04-50} = 2.87$ per cent and $\eta_{22-50} = 1.47$ per cent. These rates approximate the observed relation

$$\eta \sim \frac{\hat{\chi}_{\mathrm{c}}}{\hat{\chi}_{\mathrm{d}}}$$

between the time- and city-averaged rates for **c**ase ($\hat{\chi}_{\mathrm{c}}$) and death ($\hat{\chi}_{\mathrm{d}}$) reports in each era.

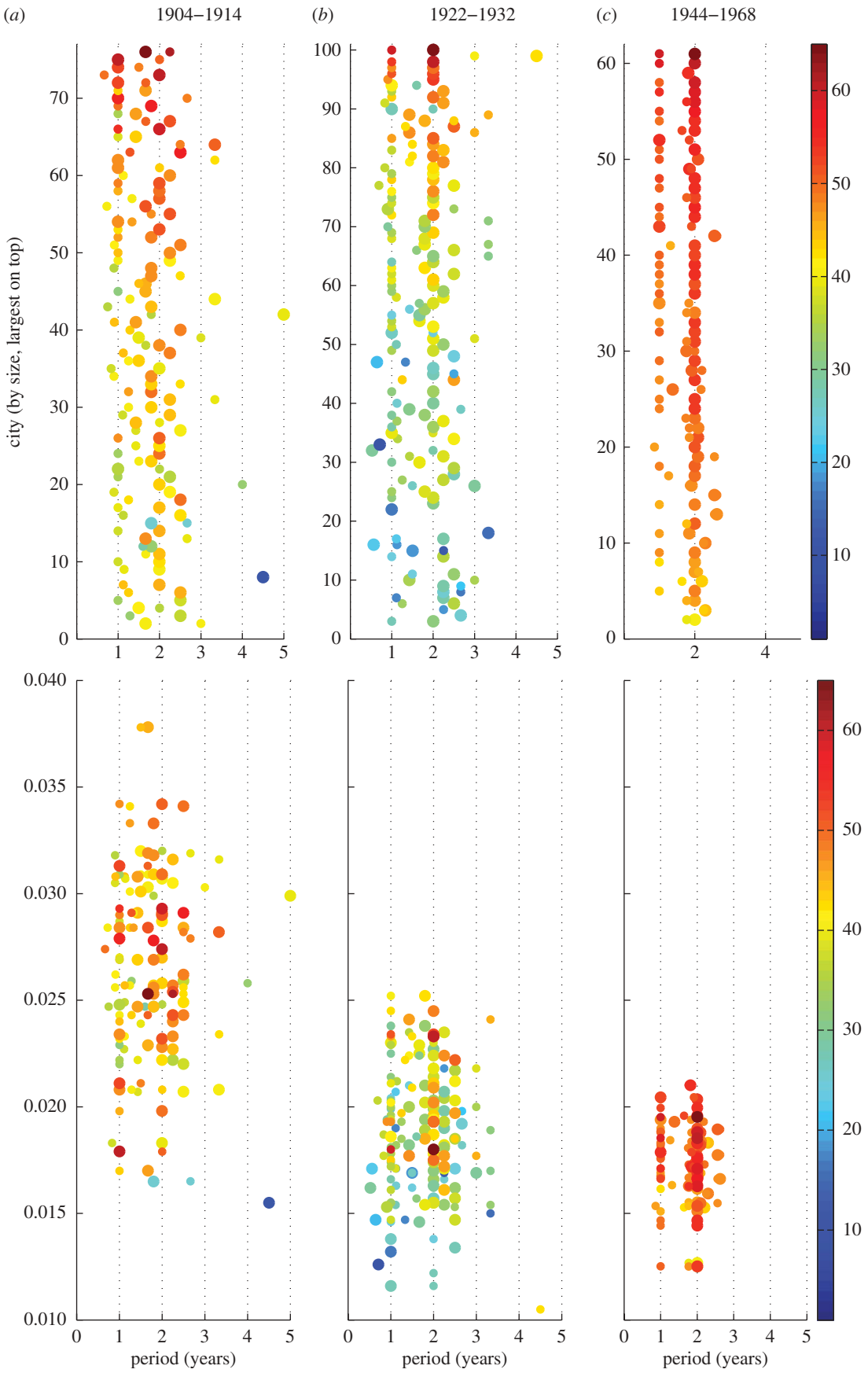


Figure 3. Measles interepidemic periods (on the *x*-axis) for three different eras prior to the start of vaccination. Figures are ordered in time, as (*a*) 1904–1914, (*b*) 1922–1932, (*c*) 1944–1968. In the upper row, cities are ordered by decreasing population size along the *y*-axis. Average *per capita* birth rates in each era are shown on the *y*-axis of the lower row graphs. Large circles mark the period with the greatest significant contribution to the power of the signal. The smaller dots correspond to the period that followed in importance. The scale for the colours appears to the right; ranks were assigned depending on the power of the signal at that frequency relative to its overall power and represent the fraction of the total power that contained in each period.

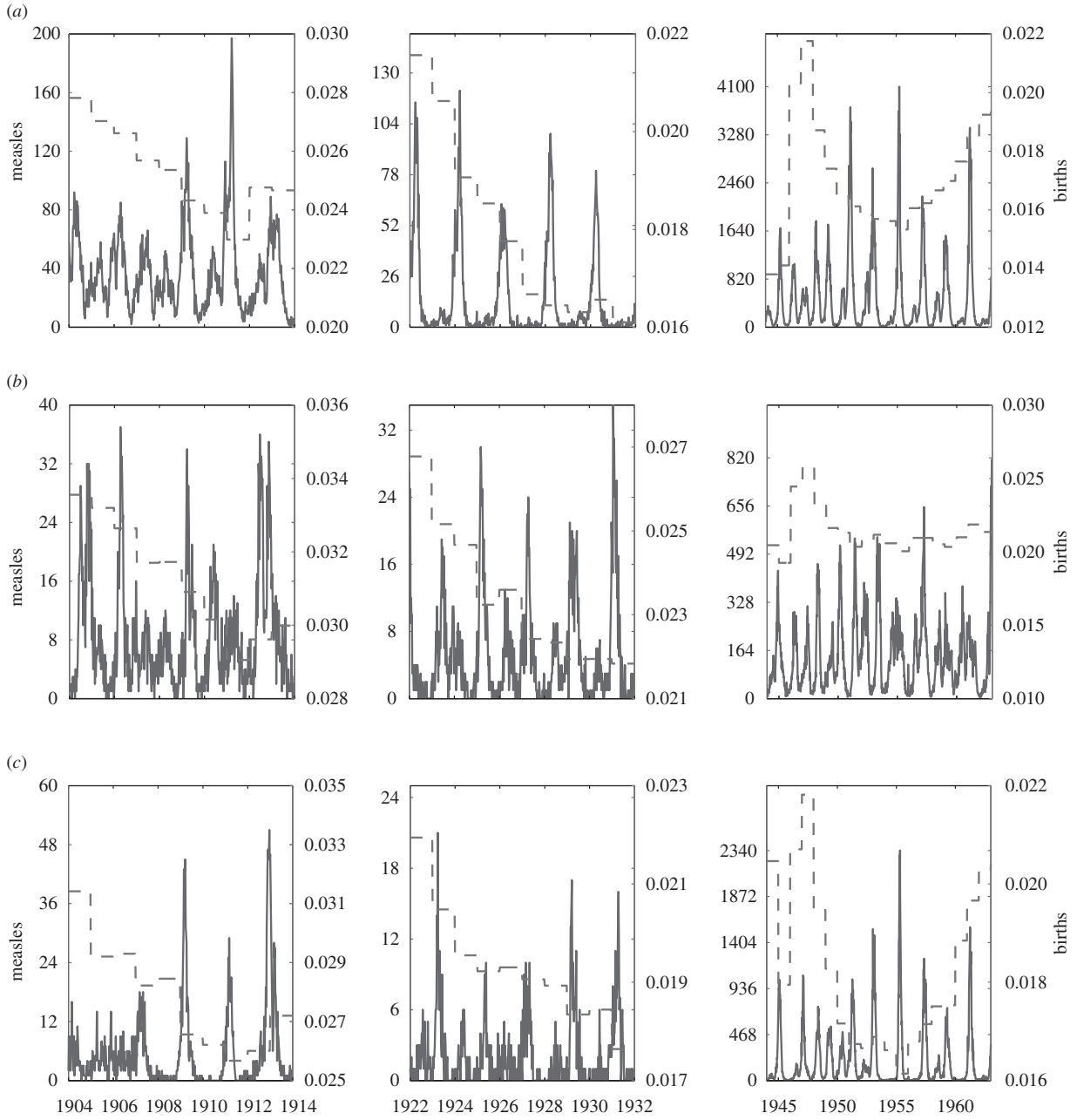


Figure 4. Weekly measles records (solid lines) and birth numbers (dashed lines, scale on the right) in the six largest populations that appear in all three eras (part 1). Birth rate and reports of measles in (*a*) London, (*b*) Liverpool, (*c*) Birmingham through time.

One hundred surrogate mortality time series were fitted and the resulting parameters used to assess the existence of changes over time in mean annual transmission (measured by the arithmetic average $\bar{r}$), and in the amplitude of seasonality $\omega$ as defined in equation (4.1).

Estimates of the rates of disease transmission for each biweek of the year ($\{r_i\}_{i=1}^{26}$) from the selected time series in each era are plotted in figure 7*a–c*. For each era, transmission estimates are centered by the mean value in each population ($\bar{r}$) for ease of comparison. The results shown for 1950–1960 were those obtained from surrogate time series sampled at a rate $\eta_{04-50} = 2.87$ per cent. In all eras, low parameter values (in shades of pink) are commonly observed between biweeks 16 and 19, which span from July to September, coinciding with school summer holidays.

Contrast of summary statistics for parameter values estimated from 1904–1914 measles mortality records against those obtained from surrogate mortality data for 1950–1960 (see figure 8*a*,*b*) shows that there was a significant increase over time in average transmission in Manchester and Birmingham, while a significant decrease was observed in Liverpool and Sheffield, and London and Leeds presented smaller changes. All cities, with the exception of Manchester, experienced an increase in the amplitude of seasonal forcing, which was associated with an increase in predictability (measured through $R^2$). The exception to this association was Liverpool, where $R^2$ was higher in 1904–1914. Manchester had greater $R^2$ in 1950–1960 while experiencing a significant decrease in seasonal amplitude over time.

It is possible that the increase in forcing amplitude seen in Liverpool was associated with a decrease in $R^2$ owing to

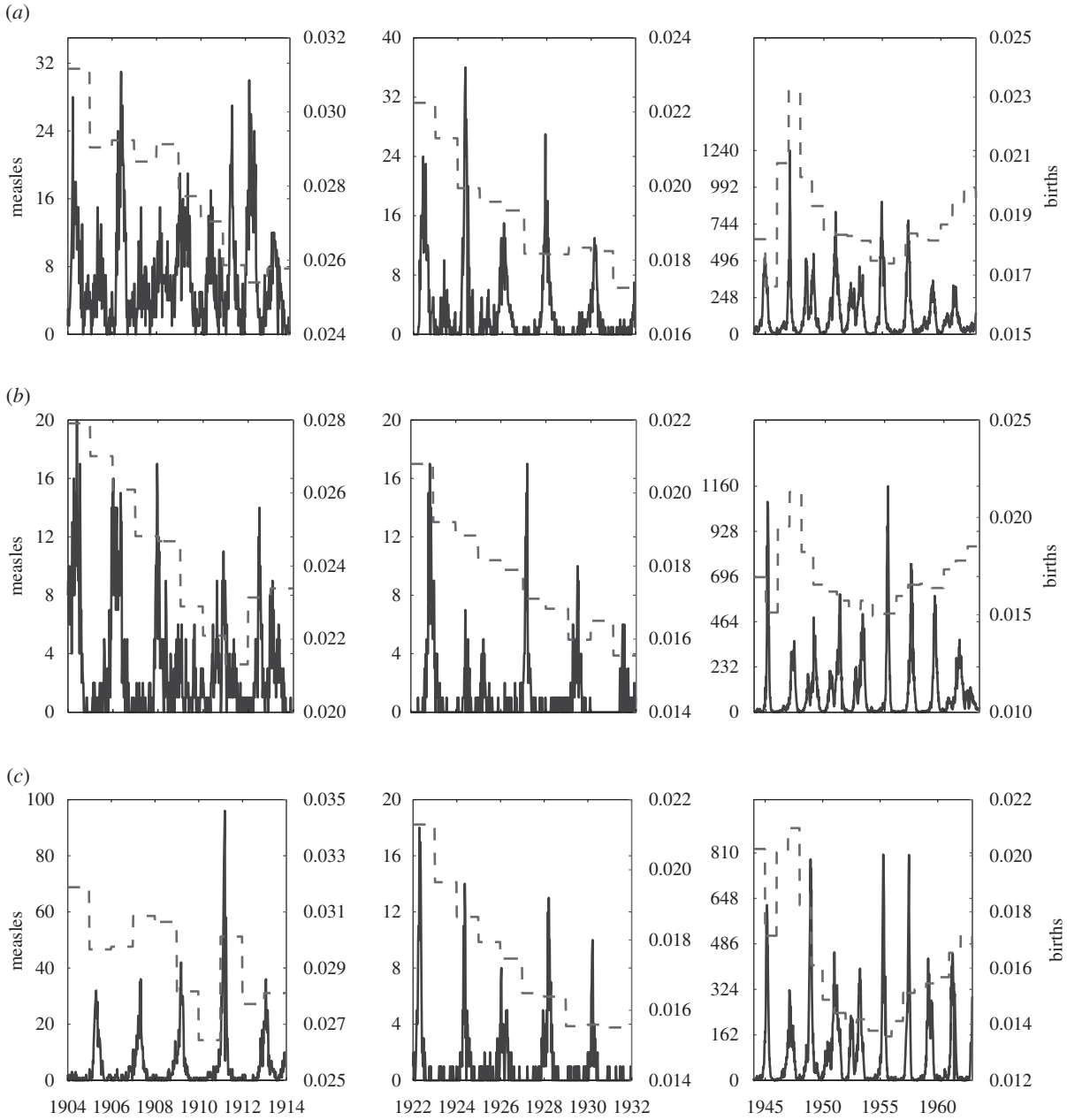


Figure 5. Weekly measles records (solid lines) and birth numbers (dashed lines, scale on the right) in the six largest populations that appear in all three eras (part 2). Birth rate and reports of measles in (*a*) Manchester, (*b*) Leeds, (*c*) Sheffield through time.

Table 2. Average percentage over time of the number of cases represented in measles records ($\hat{\chi}$) in each of the three prevaccination eras. Early twentieth century data record mortality caused by measles, and therefore capture a much smaller proportion of the true cases than what appears in incidence notifications. The ranges in parentheses correspond to the 95 per cent confidence intervals in each dataset.

| era | $\hat{\chi}$ |
|---|---|
| 1904–1914 | 1.4 (0.4,2.3) |
| 1922–1936 | 0.6 (0,1.3) |
| 1944–1968 | 55 (38.7,77.2) |

the concomitant increase in transmission (figure 8*a*). This parameter combination may enhance the role of stochastic forces owing to the presence of coexisting attractors with intermixed basins (Glass *et al.* 2003).

Figure 8*c* shows the contrast between mixing exponents ($\alpha$) in the two eras. This exponent is meant to capture departures from the assumption of homogeneity in mixing (Fine & Clarkson 1982), but may also be seen as a correction of biases arising from the discretization of the time-continuous process of disease spread (Glass *et al.* 2003).

Figure 8*c*,*d* shows the comparison of model parameters from 1922 to 1932 and from 1950 to 1960, along with those obtained from published and surrogate mortality time series of Manchester in 1922–1932 (last column in figure 8*c*,*d*). The latter serve to validate our methodology. The former show that the amplitude of forcing did not significantly change in all cities but Leeds, where it increased over time. Average transmission generally decreased, while $R^2$ was significantly different in Liverpool (lower) and Birmingham (higher) and experienced smaller changes elsewhere.

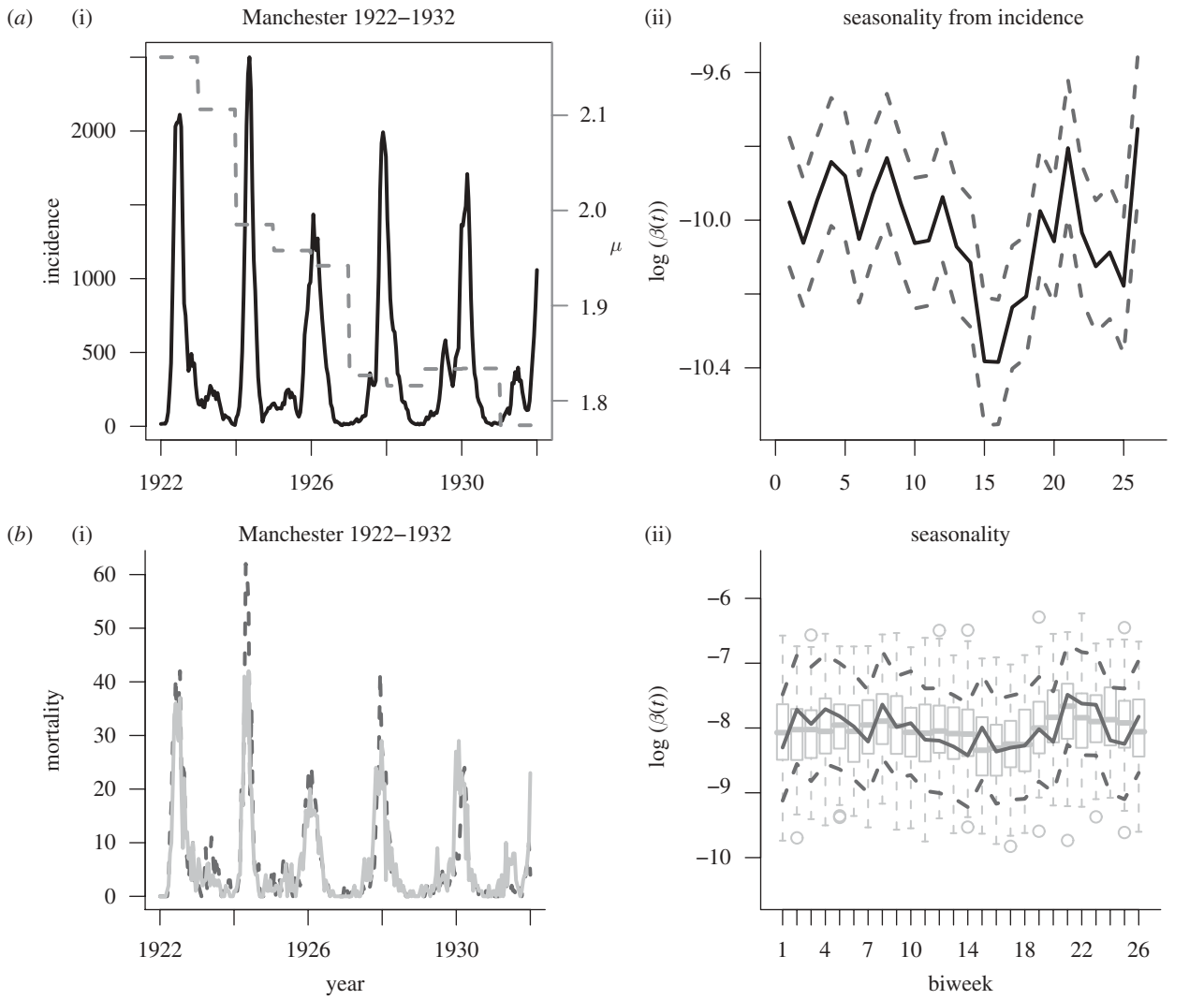


Figure 6. Effect of 'sampling' on seasonal transmission estimates. (*a*) An uncommon time series of measles incidence in (i) Manchester between 1922 and 1932, in parallel with the time series of annual *per capita* birth rates (dashed line). The time series of measles case fatalities in Manchester in the same era appears in (*b*)(i) (continuous, grey line). In the same graph, a dashed line illustrates a surrogate mortality time series obtained by sampling incidence data of measles in Manchester (1922–1932) binomially at rate $\eta_{22-50} = 1.47\%$. Estimates of transmission parameters $r_i$ appear on the right-hand side, with dashed lines marking 1 s.e. around the mean. (*a*)(ii) Seasonal transmission estimates obtained from incidence records. (*b*)(ii) The values estimated from published mortality time series appear in dashed lines and, in grey, the summarized results for 100 mortality surrogates obtained from incidence records from the same era and population. For the latter, the notches mark the 95 per cent confidence interval, while horizontal lines inside each box correspond to the median parameter values of transmission estimates from all surrogate mortality time series.

## 5. DISCUSSION

Epidemiological records have been and remain an invaluable source for the study of population dynamics, where comparison of model predictions with disease records has served to highlight the determinants of various dynamical motifs. One of the ongoing issues of interest in both ecology and epidemiology is disentangling and apportioning the relative roles of stochasticity, nonlinearity and seasonality in generating sustained oscillations (Bartlett 1956; Costantino *et al.* 1997; Bjornstad & Grenfell 2001; Coulson *et al.* 2001, 2004; Keeling *et al.* 2001; Rohani *et al.* 2002).

In recent decades, studies of childhood diseases have highlighted the importance of three mechanisms in generating the observed dynamics. (i) Permanent acquired immunity means that birth of naive individuals is the main source of new recruits to the susceptible pool (Grenfell *et al.* 1995; Finkenstadt *et al.* 1998; Earn *et al.* 2000). Together with a short infectious period relative to host lifespan, acquired immunity also explains the decline in incidence characteristic of the typical epidemic curve (Hamer 1906) and may lead to pathogen extinction from the host population (Bartlett 1957). (ii) Transmission through direct contact between susceptible and infected individuals is a nonlinear process that can generate damped oscillations in disease prevalence (Soper 1929) and give rise to more complex dynamics when contagion is not bilinear (Dietz 1976). Environmental and demographic stochasticity have the potential to excite sustained cycles (Bartlett 1960). However, they often act together with (iii)

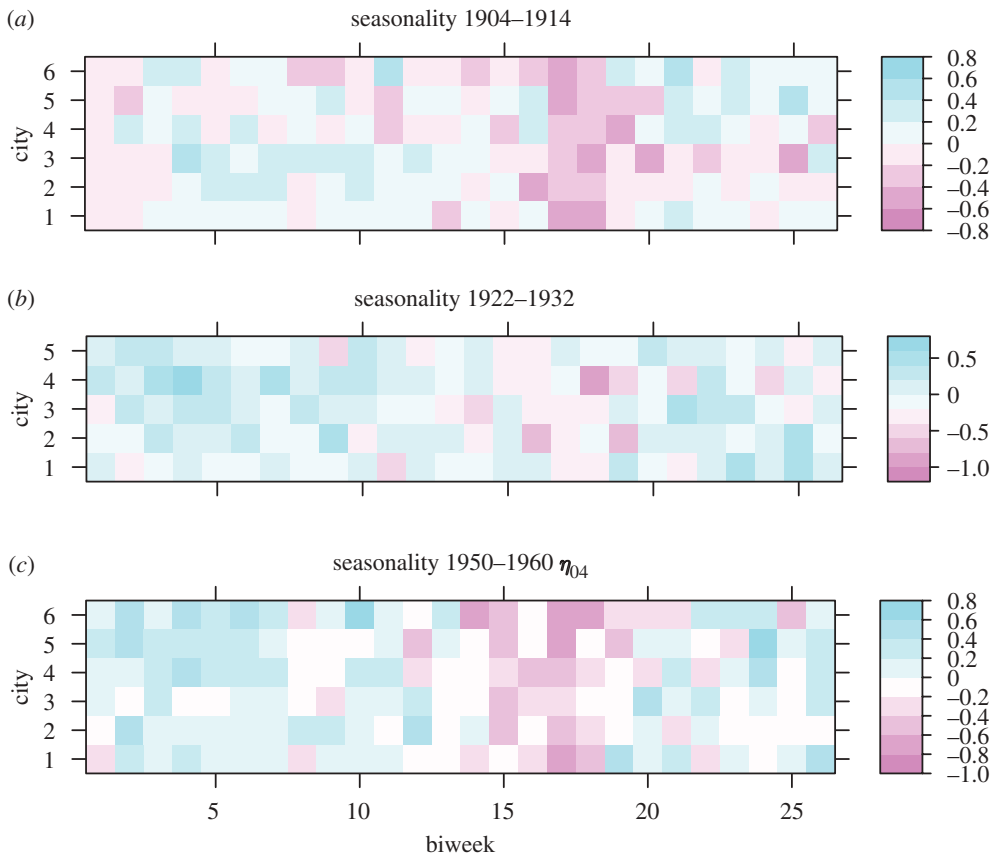


Figure 7. Variation around the annual mean of the (log-transformed) biweekly transmission rates ($r_t = \log(\beta_t)$) is shown along the $x$-axis in ($a$–$c$), colour-coded according to the scheme on the right-hand side of each graph. The $y$-axis displays the results for different populations, and these are split into ($a$,$b$,$c$), for each of the three eras. These estimates were obtained based on published mortality records ($a$) 1904–1914 and ($b$) 1922–1932, and for an example surrogate time series of measles mortality per city taken from ($c$) 1950–1960 incidence records sampled at a rate $\eta_{04-50} = 2.87\%$. As mentioned in the text, transmission estimates that use mortality data have a considerable amount of short-term variation, owing to the loss of detail that results from low sampling (case fatality) rates, which hinders detection of small outbreaks. For this same reason, the time series for Sheffield 1922–1932 could not be fitted.

seasonal changes in transmission, dictated by school terms (London & Yorke 1973; Fine & Clarkson 1982). Seasonality can produce epidemic cycles at frequencies resonant with the forcing period (Greenman *et al.* 2004; Choisy *et al.* 2006). Furthermore, forcing amplitude is among the determinants of the interepidemic period, and the particular shape of seasonality modifies epidemic timing (Schenzle 1984). Stochastic influences may then induce transient dynamics deviating from an underlying deterministic pattern (Rohani *et al.* 1999; Keeling *et al.* 2001; Bauch & Earn 2003), or even dictate the frequency of resonance when transmission rate is sufficiently low (Alonso *et al.* 2007).

Comparisons of epidemic patterns originating in different regions of parameter space have highlighted how nonlinearities in the system can generate contrasting dynamics even when the underlying basic mechanism is the same (Rohani *et al.* 1999; Reuman *et al.* 2006; Alonso *et al.* 2007). In fact, the fine-tuning of disease parameters can be fundamental even to qualitative matches between models and data (Keeling *et al.* 2001; Greenman *et al.* 2004). Recent studies have illustrated how the shape of seasonal forcing provides the key to understanding the spatiotemporal dynamics and persistence of measles in Niger (Conlan & Grenfell 2007; Ferrari *et al.* 2008).

Here, we have presented analyses of previously unexplored data that span an extraordinarily long period, and capture changing measles epidemiology in populations undergoing shifts in demographic, social and economic conditions. Our characterization of the epidemic patterns found in the data and comparison with population size and birth rates suggests that the evolution of measles epidemiology is not satisfactorily explained by trends in local demography. For example, we might have predicted similar periodicity in data from populations in different eras with similar birth rates, which is at odds with our findings (see §3). We attribute this disagreement to differences in seasonally varying transmission rates. Empirical evidence for this was provided via our estimation of transmission parameters directly from disease mortality and incidence records. These estimates provided evidence of an increase in the amplitude of seasonality over time that, we argue, serves to explain why measles epidemic cycles become increasingly predictable as the twentieth century progresses (up to the start of vaccination).

Intuitively, the extent of seasonally varying contact rates might be expected to rise as a result of

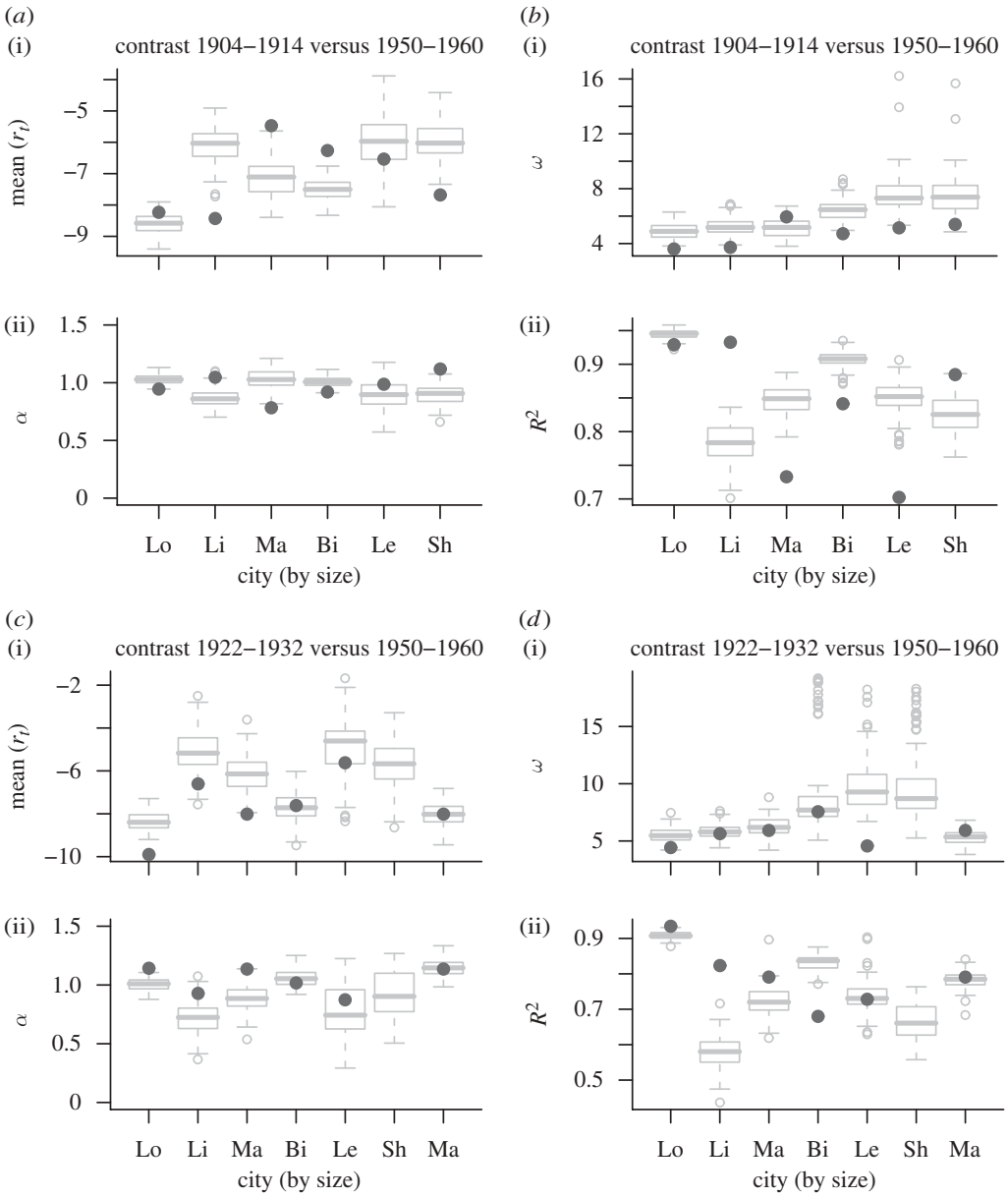


Figure 8. Model parameters and quality of fit for published mortality records (1904–1914 and 1922–1932 in filled circles) and 100 surrogate time series of measles mortality (grey box plots). Surrogates are based on 1950–1960 incidence records, sampled at rates $\eta_{04-50} = 2.87\%$ and $\eta_{22-50} = 1.47\%$. (*a*)(i) and (*c*)(i) show a contrast of the means in the log-transformed biweekly transmission rates; in (*b*)(i) and (*d*)(i), the contrast is in the amplitude of the variation in transmission ($\omega$) as defined in the main text. (*a*)(ii) and (*c*)(ii) show a similar comparison of mixing exponents ($\alpha$) between early data (1904–1914 or 1922–1932) and surrogate mortality data for 1950–1960. (*b*)(ii) and (*d*)(ii) exhibit the graphs that contrast the degree of similarity between predicted and observed time series in different eras, measured using $R^2$. In all graphs, labels for the *x*-axes refer to the names of the populations where the data originate. From left to right, these are: London, Liverpool, Manchester, Brimingham, Leeds and Sheffield. Results for Manchester incidence data for 1922–1932 appear only in (*c*,*d*), last of all.

an increase in the number of children attending schools. However, it is hard to corroborate changes in school attendance directly owing to the lack of quantitative school attendance data from the early twentieth century. Furthermore, some indirect indicators, such as Education Acts that targeted attendance of students in the age group at greatest risk of contracting measles, predate the start of attendance records (Anderson 1993; Sutherland 1993). And yet, the impact of the Act that increased the school leaving age from 10 to 13 in 1890 could have been delayed by the economic conditions of poor British families of the turn of the century, which slowly improved in the following decades. We speculate that such improvements freed children from work, thus increasing the numbers attending school and with that seasonal forcing amplitude.

Another, perhaps more significant, factor that can increase the amplitude of seasonality, is a rise in the mean age at infection. While specific age at infection data from the early part of the twentieth century are rare, records for Aberdeen 1880–1900 (Wilson 1905) and Copenhagen hospitals 1915–1925 (Aaby 1988) document that mean age at infection was 4.7 and 3 years, respectively. This suggests that at the turn of the twentieth century children in these cities often

acquired measles before entering school, thus reducing the impact of the school calendar on measles transmission patterns. We hypothesize that higher birth rates characteristic of the early 1900s were a key factor in measles transmission among the youngest age groups and decreased the dynamical impact of school terms.

One technical and as yet unresolved issue highlighted in this work is contrasting parameter estimates obtained using the TSIR methodology when measurement error is large. We found considerable discrepancy in the transmission rates estimated from case fatality and incidence records (see figure 6*a*(ii),*b*(ii)), which is indicative of a bias introduced by the methodology at low sampling rates. Future work needs to examine whether alternative estimation methods (see Ionides *et al.* 2006; Cauchemez & Ferguson 2008; He *et al.* 2009) are similarly sensitive to the measurement process and reporting fidelity.

In addition to seasonality, the increase in frequency and range of travel observed during the first half of the twentieth century (in the prevaccination era) may have contributed to synchronize epidemics in different populations. As a result of increased coupling between populations, larger towns with regular dynamics could have driven epidemic cycles with similar timing in smaller populations. However, coupling alone has limited influence over epidemic phase, which in fact shows drastic changes over time (Mantilla-Beniers 2004).

On the other hand, seasonal changes in transmission can prevent outbreaks from occurring during the low season, thus helping to define epidemic phase (Stone *et al.* 2007). Disease cycles under the influence of seasonal forcing are therefore more likely to either have similar phase in different populations (i.e. $\phi_1 \sim \phi_2$) when epidemics are annual or multi-annual and synchronized, or to appear syncopated, with $\phi_1 \sim \phi_2 + \pi$, if 2 year cycles (common in measles) are out of phase. Detailed analyses of measles spatial dynamics from 1904 to 1968 have shown that the phase of biennial outbreaks of measles has a better defined bimodal distribution in 1922–1932 than in 1904–1914, and is essentially unimodal in 1944–1968 (Grenfell *et al.* 2001; Mantilla-Beniers 2004). In consequence, we believe that seasonality in transmission is a key factor determining the patterns described in this paper.

Our study documents unique shifts in parameter space and illustrates changes in the relative weight of nonlinear, deterministic mechanisms and stochastic forces in populations over time. Declining birth rates, together with increasing seasonal forcing, led to measles dynamics that became ever more regular and predictable in European populations over the course of the first half of the twentieth century (up to the start of measles vaccination). The observed transitions constitute a rare example of changes in the balance of determinism and stochasticity documented in nature.

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