Is socioeconomic position associated with bronchiolitis seasonality? A cohort study

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ABSTRACT

Background Understanding differences in the seasonality of bronchiolitis can help to plan the timing of interventions. We quantified the extent to which seasonality in hospital admissions for bronchiolitis is modified by socioeconomic position.

Methods Using Hospital Episode Statistics, we followed 3,717,329 infants born in English NHS hospitals between 2011 and 2016 for one year. We calculated the proportion of all infant admissions due to bronchiolitis and the incidence rate of bronchiolitis admissions per 1000 infant-years, according to year, month, age, socioeconomic position and region. We used harmonic Poisson regression analysis to assess whether socioeconomic position modified bronchiolitis seasonality.

Results The admission rate for bronchiolitis in England increased from 47.4 (95% CI 46.8 to 47.9) to 58.9 per 1000 infant-years (95% CI 58.3 to 59.5) between 2012 and 2016. We identified some variation in the seasonality of admissions by socioeconomic position: increased deprivation was associated with less seasonal variation and a slightly delayed epidemic peak. At week 50, the risk of admission was 38% greater (IRR 1.38; 95% CI 1.35 to 1.41) for infants in the most deprived socioeconomic group compared to the least deprived group.

Conclusion These results do not support the need for differential timing of prophylaxis or vaccination by socioeconomic group, but suggest that infants born into socioeconomic deprivation should be considered a priority group for future interventions. Further research is needed to establish if the viral aetiology of bronchiolitis varies by season and socioeconomic group, and to quantify risk factors mediating socioeconomic deprivation and bronchiolitis rates.

INTRODUCTION

Bronchiolitis is an acute lower respiratory tract infection that commonly affects children under one year.[1] Mild cases of bronchiolitis can be managed at home, but a significant number of infants require supportive hospital care to aid feeding and respiration.[2] In 2011, 3.8% of infants less than one year old required admission to hospital for bronchiolitis in England.[3 4] Respiratory syncytial virus (RSV) —a virus for which there is currently no vaccine available —causes an estimated 80% of bronchiolitis cases that require hospitalisation.[1 5] A monoclonal antibody called Palivizumab (Synagis) can reduce the risk of severe infection during periods of RSV circulation; however, it is costly and therefore only recommended for infants at high risk of serious complications.[6 7] Notably, severe symptoms of RSV infection is associated with an increased risk of wheeze and asthma in later childhood

In temperate climates in the Northern Hemisphere, such as the UK, RSV circulation peaks between December and February,[8] leading to an increased burden on both primary and secondary care services during winter months.[3 9] Previous research shows that children from lower socioeconomic groups are at particular risk of admission to hospital and paediatric intensive care for bronchiolitis,[3 10] but it is not known whether differences also exist in the seasonality of bronchiolitis admissions. RSV transmission may differ because of socially patterned risk factors, such as residential overcrowding and family size, thereby leading to different seasonal patterns of admissions.[7 11] Understanding these patterns could help to inform preventive interventions to reduce bronchiolitis admissions, including optimal timing of palivizumab prescribing in different population groups, or targeting of maternal RSV vaccination, when this becomes available in the future.[12]

The aim of this study was to determine how socioeconomic position is associated with the seasonality of hospital admissions for bronchiolitis amongst infants in England. Our objectives were twofold: to describe seasonality of infant bronchiolitis hospital admissions in England from 2012 to 2016; and quantify the extent to which this seasonality is modified by socioeconomic position.

METHODS

Data source

We used Hospital Episodes Statistics Admitted Patient Care (HES APC) data to identify bronchiolitis admissions and the infant population at risk. HES APC is a database of all hospital inpatient admissions funded by the English NHS and captures approximately 97% of all births in England.[13][14] NHS Digital, the body that houses and supplies access to HES, links patient records over time and provides each database extract with a pseudo-anonymised identifier (HESID) unique to each individual, enabling researchers to create longitudinal patient cohorts. HES APC was linked to the Office for National Statistics (ONS) mortality records.[15]

Cohort population and follow-up

A birth cohort of all live singleton births recorded in HES APC between 1st January 2011 and 31st December 2016 was created from HES APC. To enhance data completeness, we linked infant birth records to mothers' delivery records following methods described in Harron et al.[16] Using these methods, 43.5% of birth and delivery records were deterministically linked, 51.5% were probabilistically linked and 5.0% were unlinked. Using the infant's HESID, data on admissions to hospital within the first year of life were added to birth data; figures from other sources show that 90% of bronchiolitis admissions occur in the first year of life and two thirds of admissions are in children less than 6 months old.[5][17]

Infants were followed from birth or the 1st January 2012, whichever occurred last, until their first birthday, date of out-migration, 31st December 2016 or date of death, whichever occurred first. This study period ensured that we had follow-up for children aged up to 12 months in all study years, including the first. Infants were excluded from cohort analyses if they had missing information, were from a multiple birth or were stillborn.[18] Infants with a non-English address recorded at birth were excluded to prevent potential loss to follow up. Where a non-English address was recorded in a subsequent infant admission, a censoring date was placed half way between the date of the infant's last known resident admission and the non-resident admission.

Outcome

We identified hospital admissions with a diagnosis of bronchiolitis in HES APC using the International Classification of Diseases version 10 code J21 for acute bronchiolitis. All J21 subcategories were included in our definition (J21.0 acute bronchiolitis due to RSV, J21.1 acute bronchiolitis due to human metapneumovirus, J21.8 acute bronchiolitis due to other specified organisms and J21.9 acute bronchiolitis, unspecified) because of the low sensitivity of RSV-specific ICD-10 codes.[19] To calculate the total burden of infant admissions attributable to bronchiolitis, we extracted all hospital admissions (excluding birth admissions) between 1st January 2012 and 31st December 2016 where the patient was ≤365 days old. All admissions with bronchiolitis recorded as either the primary or secondary diagnosis for an infant during their first year of life were included in the analyses. To calculate admission rates, any admission for RSV bronchiolitis within 14 days of discharge from another RSV bronchiolitis admission was assumed to be associated with the same infection, and therefore only the first of these admissions was included in the analyses.

We used the Index of Multiple Deprivation (IMD) 2010 to capture socioeconomic position for each cohort member. IMD is constructed by assigning to each lower super output area (approximately 650 households and 1500 residents) across England a composite score summed from seven domains of deprivation: income, employment, health and disability, education skills and training, barriers to housing and services, living environment and crime.[20] IMD was derived from mother's postcode at delivery or the earliest mention of postcode in infant's hospital admission. IMD was split into fifths for analyses; highest ranked IMD means the most deprived category.

Infant sex (male or female), month and year of birth were extracted from infant's birth record. Infant's age at admission for bronchiolitis was calculated by subtracting the bronchiolitis admission date from the infant's admission date in their birth episode. Age was split into three groups: <3 months, 3 to <6 months and 6 to <12 months. Government office region of residence was used to indicate the area of England within which the infant lived at time of birth.[21] HES APC includes information on additional risk factors such as gestational age, mode of delivery and congenital anomalies; however, as these variables are likely on the causal pathway between socioeconomic position and admission for bronchiolitis,[22-24] they were not included in our analyses. Inclusion of mediators in associational analyses introduces overadjustment bias into the model.[25]

Statistical analysis

To calculate the proportion of all infant admissions attributed to bronchiolitis, we divided the number of bronchiolitis admissions (including those within 14 days of one another) by the total number of hospital admissions among infants. Bronchiolitis admission rates were calculated by dividing the number of new admissions for bronchiolitis by person-time at risk for all infants at risk in the birth cohort, and are expressed as annual admission-based rates per 1000 infant-years. We also calculated person-based rates where, for infants with multiple admissions, only the first admission was counted. Stata 15.0[26] was used for data analysis and Microsoft Excel 2013 to create graphs.

Event rates were modelled using a Poisson regression model with robust standard errors to account for multiple admissions for the same child. Negative binomial models were also considered but there was no evidence of overdispersion in event rates. The impact of seasonality on rates of admission was modelled using a harmonic function of time in weeks (t) expressed as: $\beta_1(\sin(2\pi t/T))+\beta_2(\cos(2\pi t/T))$, where T = number of periods within one cycle (i.e. 1 year = 52.14 weeks).[27 28] The model included interaction terms of IMD group with the sine and cosine regression coefficients (denoted δ_{1j} and δ_{2j}) to assess evidence of effect modification of IMD group by seasonality, formally tested using a Wald χ^2 test. Year of admission, region, sex, month of birth, age group and interaction terms of age group with the sine and cosine regression coefficients were selected a priori as covariates in the model to increase precision given their known associations with the outcome as identified in the literature.[3 7 29] See online supplementary Box S1 for full model parameterisation.

Using the estimated model coefficients, we calculated the following quantities for the epidemic curve of each IMD group j=1,…,5 at reference values of the other covariates (where betas, gammas and deltas are replaced by their estimates):[30] the amplitude (log) = $\sqrt{(\beta_1+\delta_{1j})^2+(\beta_2+\delta_{2j})^2}$; the phase (in radians) = $\arctan(\beta_1+\delta_{1j})/(\beta_2+\delta_{2j})$; the peak week = $52.14*(\text{phase}_j/2\pi)+1$; and incidence rate ratios (IRR) of admissions at the average peak week of the top four IMD groups relative to the lowest IMD group. The delta method, as implemented by the Stata command *lincom*, was used to calculate 95% confidence intervals for each parameter. Epidemic duration for each IMD group was calculated as the time in weeks from the first of three consecutive weeks with increasing predicted rates to the first of three consecutive weeks with decreasing predicted rates.

RESULTS

Our cohort comprised 3,717,329 singleton infants, of which 48.7% were female and 19.0% were born to mothers residing in London (Table 1). Missing information about IMD, region or sex was present for 67,422 (1.8%) infants, who were excluded from further analyses (see online supplementary Figure S1). The average annual proportion of all infant hospital admissions in England attributed to bronchiolitis was 15.0% over the five study years. The burden of bronchiolitis was concentrated in the winter months. In December, 2012 to 2016 combined, 39.8% of the total admissions for infants included a diagnosis of bronchiolitis compared to 2.3% of August admissions over the same period (online supplementary Table S1).

There were 155,479 admissions for bronchiolitis by cohort members over the study period; an average annual admission-based rate of 50.3 admissions per 1000 infant-years (95% CI 50.0 to 50.5). The average follow-up time per infant was 304.5 days (indicating that most infants were followed-up until their first birthday) and 12,279 (7.9%) of events were readmissions. The overall infant-based admission rate was 46.3 per 1000 infant-years (95% CI 46.1 to 46.6). Rates of admissions were highest in the most socioeconomically deprived groups, males, younger infants and those residing in the North West or North East of England. The average admission rate was 79.3 per 1000 infant-years (95% CI 78.3 to 80.4) for infants born in October compared to 33.7 (95% CI 33.0 to 34.4) for March births. Bronchiolitis admission rates increased from 47.4 per 1000 infant-years (95% CI 46.8 to 47.9) in 2012 to 58.9 per 1000 (95% CI 58.3 to 59.5) in 2016.

Figure 1 displays weekly crude rates of admissions by IMD, illustrating differential rates of admissions by level of socioeconomic position across the year and a clear annual peak in December. The multivariable model that included interaction terms between IMD and the two harmonic functions fitted the data better than the model without interactions, Wald test, $\chi^2(8) = 238.07$, $p<0.001$ (Table 2). Fitted values and seasonal estimates from the model are presented in Figure 2 and Table 3. The amplitude of the epidemic curve ranged from 3.33 (95% CI 3.25 to 3.41) in the most deprived to 4.05 (95% CI 3.89 to 4.21) in the least deprived group, pointing to less seasonal variation in the rates of admissions in the more disadvantaged groups. The phase shift is greatest in the most deprived, corresponding to the slightly delayed peak timing. The average peak timing of the annual epidemic varied marginally across the groups, from week 49.5 (95% CI 49.3 to 49.6) in the least deprived to week 50.2 (95% CI

50.1 to 50.4) in the most deprived group. The estimated epidemic duration was 26 weeks across all groups. After adjustment for covariates, infants in the most deprived group had a 1.38 (95% CI 1.35 to 1.41) greater risk of admission to hospital for bronchiolitis at week 50 compared to infants in the least deprived group.

DISCUSSION

This study presents a continuation of previous findings that show ever increasing rates of bronchiolitis admissions to hospitals in England,[3] with admission rates reaching 58.9 per 1000 infant-years in 2016. The data present a single annual peak in bronchiolitis admissions across England in mid-December, when 40% of all infant admissions included a bronchiolitis diagnosis. There is a clear socioeconomic gradient to these admissions, and at week 50 (peak admission week) infants born into the highest level of socioeconomic deprivation had a risk of admission 38% greater than the lowest group. Our results suggest that the association between seasonality and bronchiolitis admission rates is marginally moderated by level of socioeconomic position, with increasing socioeconomic deprivation associated with less seasonal variation and a slightly delayed epidemic peak.

Our study data were derived from a national hospital administrative dataset, which enabled us to create a representative birth cohort with minimum selection bias and apply linkage methodology, which was crucial for acquiring socioeconomic data as this information was missing for infant records before 2014 (but available in maternal records). However, the probabilistic method used is likely to have included erroneous links, introducing some bias into the dataset.[31] Using IMD as a proxy for individual socio-economic position may have led to a weakened association between socioeconomic position on rates of bronchiolitis admissions.[32] Defining RSV bronchiolitis without laboratory testing meant that we could not attribute the bronchiolitis admissions to particular pathogens, although previous work from England shows that 80% of bronchiolitis admissions in infants (defined using ICD-10 code J21) are due to RSV.[3][5] More broadly, this study is a measure of hospital use and therefore does not measure community, or primary care burden of bronchiolitis.

We added harmonic functions to our regression model to account for sinusoidal patterns in a highly seasonal infection;[33] however, our model underestimates the size of the amplitude across socioeconomic groups. Improved estimation could have been achieved with the addition of more

harmonic pairs or by using splines; however, these methods would have added undue complexity to the estimation of seasonal parameters required by our research aim.[29] [30] The likeness in the relative difference between amplitudes by IMD across observed and fitted rates (Figures 1 and 2) gives us confidence in our results.

This is the first study investigating seasonality and socioeconomic position in relation to bronchiolitis admissions in the English population. Our work presents a small, but not consequential, difference in epidemic timing—the two most extreme IMD groups had a 0.7 week difference in predicted peak—and no difference in the relative duration of the epidemic. Less seasonal variation in lower socioeconomic groups may reflect continued (but low level) admissions for bronchiolitis during warmer months of the year amongst these infants. Understanding precise viral aetiology of bronchiolitis by time of the year and socioeconomic group may help to delineate seasonal differences further. Future work would benefit from linkage to surveillance datasets, such as Public Health England's Second Generation Surveillance or Respiratory Datamart Systems, to assess these factors.[34] [35]

Research from Western Australia found no difference in the seasonality of RSV positive specimens among aboriginal children (a population that experience high levels of socioeconomic deprivation) compared to non-aboriginal children.[29] USA-based research, on the other hand, found a negative association between the proportion of the population from a black ethnic group (correlated with socioeconomic position of the population) and seasonal peak timing at the ZIP-code level.[36] We have previously investigated the relationship between socioeconomic deprivation and seasonality by geographical area, finding a 3-week difference in peak timing across Clinical Commissioning Groups (CCGs) in England.[37] In this study, CCGs with both low and high IMD scores were associated with earlier peak timing of bronchiolitis, after adjustment for population density. However, these two factors explained less than 40% of the variation in the timing of epidemic peak, highlighting the potential role of other unmeasured factors such as living in areas with major transport connections.

In the context of current UK guidelines for administering Palivizumab, our results present little evidence to support differential timing of interventions for RSV bronchiolitis amongst socioeconomic groups in England at the current time. Our work does, however, present substantial difference in admission rates across population subgroups irrespective of season. This study highlights that, at the very least, infants from poorer backgrounds should be considered a priority group for future interventions. Based on

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previous research, we hypothesise that a combination of individual risk factors, such as prematurity and presence of congenital anomalies, and environmental factors, such as exposure to tobacco smoke and housing conditions, contribute to inequities.[3 11 38 39] Further work using formal methods to establish pathways through which these factors affect the risk of bronchiolitis is needed to guide the most appropriate interventions. We also demonstrate that the previously observed increase in bronchiolitis admissions in England is continuing through to 2016,[3] highlighting the need to stem the flow of bronchiolitis admissions and the urgent need for a vaccine against RSV. Further, other research has shown that hospital and healthcare policies such as changes in admission thresholds, accessibility of primary care services and hospital bed availability are an important driver of this increase, rather than changes in the transmissibility or severity of RSV. [3 38] Evaluations of alternative models of care for acutely ill infants which reduce the need for hospital admission could therefore also contribute to the reduction in bronchiolitis admissions.[40]

CONCLUSION

Our study used a population-based cohort, created from administrative data, to investigate the association between seasonality and socioeconomic position on bronchiolitis admissions. We have updated current knowledge on the burden of this infection and have presented results using harmonic analysis, which allowed us to model seasonality—an essential component of RSV bronchiolitis. Our results suggest that differential timing of interventions may not be necessary for the groups studied, but highlight the continued gap in admissions rates between socioeconomic groups. Moving forward, investigating the precise viral aetiology of bronchiolitis by season and socioeconomic group, as well as the risk factors mediating the link between socioeconomic deprivation and bronchiolitis rates, will aid understanding further of this complex condition.

What is already known on this topic?

- Bronchiolitis causes a substantial burden on the English health system during winter.

- In addition to seasonality, socioeconomic position is associated with the risk of hospital admission for bronchiolitis.

What this study adds?

- Almost 4 in every 10 infant admissions to hospitals in England during December include a diagnosis of bronchiolitis.

- The seasonality of admissions varied marginally by socioeconomic group; the predicted peak epidemic week was 49.5 among the least deprived and 50.2 among the most deprived infants.

- Socioeconomic disparities in admissions to hospital for bronchiolitis persist after taking seasonality into account.

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Table 1. Distribution of births and bronchiolitis admissions in the cohort, with bronchiolitis admission rates per 1000 infant-years

Variable	Infants		Bronchiolitis admissions			
			Admission-based		Person-based	
	N	%	N	Rate (95% CI)	N	Rate (95% CI)
Total	3,717,329	100.0	155,479	50.3 (50.0–50.5)	143,200	46.3 (46.1–46.6)
IMD groups*						
1 - Least deprived	1,049,820	28.2	18,101	41.0 (40.4–41.6)	47,537	54.5 (54.0–55.0)
2	842,218	22.7	22,063	44.4 (43.9–60.3)	32,941	47.0 (46.5–47.5)
3	700,520	18.8	27,357	47.0 (46.5–51.7)	25,404	43.6 (43.0–44.1)
4	595,024	16.0	35,890	51.1 (50.6–47.6)	20,487	41.4 (40.8–41.9)
5 - Most deprived	529,747	14.3	52,072	59.8 (59.3–45.0)	16,831	38.2 (37.7–38.8)
Sex**						
Female	1,808,544	48.7	61,349	40.8 (40.4–41.1)	85,830	54.1 (53.7–54.5)
Male	1,908,785	51.4	94,134	59.3 (59.0–59.7)	57,370	38.1 (37.8–38.4)
Region†						
North East	167,386	4.5	8,862	63.8 (62.5–65.1)	8,219	59.1 (57.9–60.4)
North West	487,973	13.1	27,968	69.0 (68.2–69.8)	25,583	63.1 (62.4–63.9)
Yorkshire and the Humber	361,359	9.7	17,282	57.6 (56.8–58.5)	15,960	53.2 (52.4–54.0)
East Midlands	291,324	7.8	12,090	50.0 (49.1–50.9)	11,286	46.6 (45.8–47.5)
West Midlands	400,847	10.8	19,302	58.1(57.3–58.9)	17,600	53.0 (52.2–53.8)
East of England	400,457	10.8	14,865	44.6 (43.9–45.3)	13,807	41.4 (40.7–42.1)
London	707,389	19.0	18,375	31.2 (30.7–31.6)	16,840	28.6 (28.1–29.0)
South East	573,920	15.4	22,483	47.1 (46.5–47.7)	20,707	43.4 (42.8–44.0)
South West	326,674	8.8	14,256	52.2 (51.4–53.1)	13,198	48.3 (47.5–49.2)
Month of birth						
January	309,933	8.3	9,362	36.4 (35.7–37.1)	8,492	33.0 (32.3–33.7)
February	284,297	7.7	8,022	33.9 (33.2–34.7)	7,172	30.3 (29.6–31.1)
March	304,850	8.2	8,535	33.7 (33.0–34.4)	7,561	29.9 (29.2–30.5)
April	297,113	8.0	8,847	35.9 (35.1–36.6)	7,883	32.0 (31.3–32.7)
May	315,676	8.5	10,282	39.2 (38.4–39.9)	9,336	35.5 (34.8–36.3)
June	308,913	8.3	11,140	43.5 (42.7–44.3)	10,187	39.8 (39.0–40.6)
July	324,817	8.7	13,636	50.6 (49.7–51.4)	12,507	46.4 (45.6–47.2)
August	318,620	8.6	15,767	59.5 (58.6–60.5)	14,552	54.9 (54.0–55.8)
September	321,956	8.7	18,979	70.8 (69.8–71.9)	17,723	66.1 (65.2–67.1)
October	321,806	8.7	21,306	79.3 (78.3–80.4)	20,004	74.5 (73.4–75.5)
November	303,744	8.2	17,567	69.4 (68.3–70.4)	16,584	65.5 (64.5–66.5)
December	305,604	8.2	12,036	47.2 (46.3–48.0)	11,199	43.9 (43.1–44.7)
Age at event						
< 3 months			61,924	80.3 (79.7–80.9)	60,498	78.5 (77.8–79.1)
3 to < 6 months			45,906	59.4 (58.9–60.0)	41,784	54.1 (53.6–54.6)
6 to < 12 months			47,649	30.8 (30.5–31.1)	40,918	26.4 (26.2–26.7)
Year of event						
2012			29,847	47.4 (46.8–47.9)	28,556	45.3 (44.8–45.8)
2013			27,592	44.1 (43.5–44.6)	25,558	40.8 (40.3–41.3)
2014			28,726	46.6 (46.1–47.2)	26,467	43.0 (42.4–43.5)
2015			33,286	54.9 (54.3–55.5)	30,160	49.7 (49.2–50.3)
2016			36,028	58.9 (58.3–59.5)	32,459	53.0 (52.4–53.6)

Month of event

January	19,151	73.0 (71.9–74.0)	17,328	66.0 (65.0–67.0)
February	10,968	45.6 (44.7–46.4)	9,249	38.4 (37.7–39.2)
March	9,301	35.5 (34.7–36.2)	7,597	28.9 (28.3–29.6)
April	6,536	25.7 (25.1–26.3)	6,497	25.6 (24.9–26.2)
May	5,094	19.4 (18.8–19.9)	4,774	18.2 (17.6–18.7)
June	3,246	12.8 (12.3–13.2)	2,910	11.5 (11.0–11.9)
July	2,800	10.7 (10.3–11.1)	2,469	9.4 (9.0–9.8)
August	1,575	6.0 (5.7–6.3)	1,401	5.3 (5.1–5.6)
September	4,419	17.4 (16.9–17.9)	3,938	15.5 (15.0–16.0)
October	11,593	44.2 (43.4–45.0)	10,761	41.0 (40.2–41.8)
November	33,838	133.9 (132.4–135.3)	32,123	127.1 (125.7–128.5)
December	46,958	180.6 (178.9–182.2)	44,153	169.7 (168.1–171.3)

*61,627 (1.6%) infants had missing information for IMD; **776 (<0.0%) infants had missing information for sex; †18,085 (0.5%) infants had missing information for region

Table 2. IRRs from multivariable harmonic Poisson regression model with 95% confidence intervals

Variable	IRR (95% CI)
IMD group	
1 - Least deprived	Ref.
2	1.11 (1.07–1.15)
3	1.22 (1.18–1.26)
4	1.41 (1.37–1.46)
5 - Most deprived	1.68 (1.62–1.73)
Sine	0.55 (0.53–0.57)
Cosine	3.54 (3.42–3.67)
Age group	
< 3 months	1.85 (1.81–1.89)
3 to < 6 months	1.68 (1.65–1.71)
6 to < 12 months	Ref.
Sex	
Male	1.46 (1.44–1.47)
Year of event	
2012	1.07 (1.05–1.08)
2013	Ref.
2014	1.06 (1.04–1.08)
2015	1.24 (1.22–1.26)
2016	1.33 (1.31–1.35)
Region	
North East	2.06 (2.00–2.12)
North West	2.25 (2.21–2.30)
Yorkshire and the Humber	1.91 (1.86, 1.95)
East Midlands	1.72 (1.68–1.77)
West Midlands	1.89 (1.85–1.93)
East of England	1.57 (1.53–1.61)
London	Ref.
South East	1.70 (1.67–1.74)
South West	1.85 (1.80–1.89)

Month of birth	
January	Ref.
February	1.12 (1.08–1.16)
March	1.22 (1.18–1.26)
April	1.31 (1.26–1.35)
May	1.35 (1.31–1.40)
June	1.37 (1.33–1.42)
July	1.42 (1.38–1.47)
August	1.48 (1.43–1.53)
September	1.53 (1.48–1.58)
October	1.54 (1.50–1.59)
November	1.35 (1.31–1.39)
December	1.04 (1.01–1.07)
Interaction between sine and age	
< 3 months	1.15 (1.12–1.18)
3 to < 6 months	1.12 (1.09–1.15)
6 to < 12 months	Ref.
Interaction between cosine and age	
< 3 months	1.66 (1.61–1.71)
3 to < 6 months	1.04 (1.01–1.07)
6 to < 12 months	Ref.
Interaction between sine and IMD groups	
1 - Least deprived	Ref.
2	1.06 (1.02–1.10)
3	1.13 (1.09–1.17)
4	1.17 (1.14–1.21)
5 - Most deprived	1.20 (1.17–1.24)
Interaction between cosine and IMD groups	
1 - Least deprived	Ref.
2	0.98 (0.94–1.02)
3	0.98 (0.94–1.02)
4	0.93 (0.90–0.97)
5 - Most deprived	0.87 (0.84–0.91)

Table 3. Derived average annual seasonal estimates following Poisson regression*, by IMD group

IMD groups	Amplitude** (95% CI)	Phase shift (95% CI)	Peak week (95% CI)	IRR at week 50 (95% CI)
1 - Least deprived	4.05 (3.89–4.12)	-0.44 (-0.46– -0.42)	49.5 (51.2–51.5)	Ref.
2	3.89 (3.75–4.03)	-0.41 (-0.43– -0.39)	49.8 (49.6–49.9)	1.07 (1.04–1.10)
3	3.77 (3.65–3.90)	-0.36 (-0.38– -0.35)	50.1 (50.0–50.3)	1.14 (1.11–1.17)
4	3.57 (3.47–3.67)	-0.35 (-0.37– -0.33)	50.2 (50.1–50.4)	1.25 (1.22–1.28)
5 - Most deprived	3.33 (3.25–3.41)	-0.35 (-0.37– -0.34)	50.2 (50.1–50.4)	1.38 (1.35–1.41)

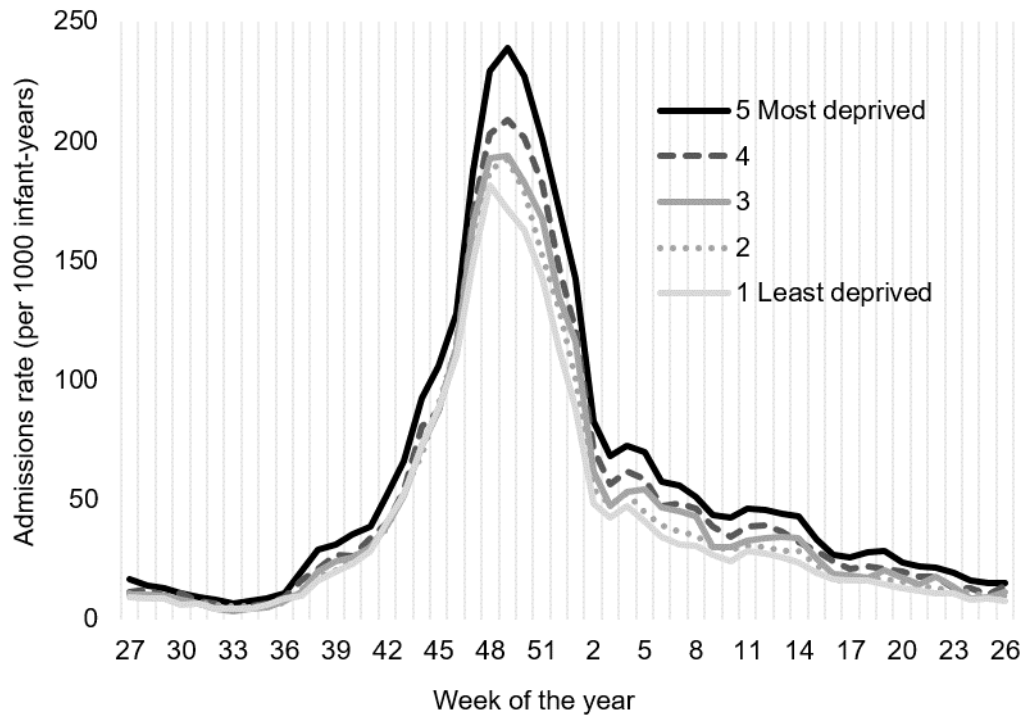*Adjusted for year of admission, **amplitude exponentiated

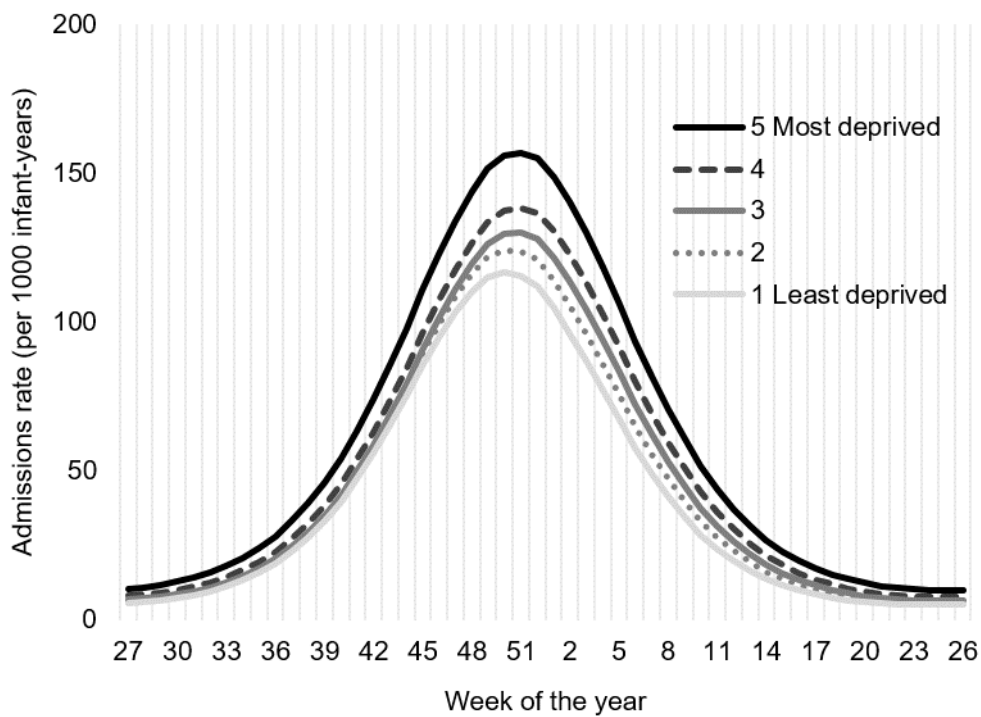**Fig1.** Observed weekly rates of hospital admission for bronchiolitis, by IMD: England 2012-2016

Fig2. Predicted weekly rates of hospital admission for bronchiolitis, by IMD: England 2012-2016

Date availability: Data may be obtained from a third party and are not publicly available. This study uses NHS hospital episode statistics data and was provided within the terms of a data sharing agreement (NIC-393510-D6H1D-v3.2) to the researchers by the Health and Social Care Information Centre ('NHS Digital'). The data do not belong to the authors and may not be shared by the authors, except in aggregate form for publication. Data can be obtained by submitting a data request through the NHS Digital Data Access Request Service.

Contributors: All authors designed the study and revised the paper. KML cleaned and analysed the data, and drafted the paper. PH supervised the study.

Competing interest: None declared.

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Box S1. Model parametrisation [27] [28]

Let $n_{jk}(t)$, the number of bronchiolitis admissions in IMD group j and year k observed at time t (measured in weeks), follow a Poisson distribution with rate $\lambda_{jk}(t) = E(n_{jk}(t))/N_{jk}(t)$ where $N_{jk}(t)$ denote the person-time at risk in IMD group j and year k at time t. We modelled this rate, after log-transformation, as a function of year and time of admission as follows:

$$log(\lambda_{jk}(t)) = \beta_0 + \beta_1(sin(2\pi t/T)) + \beta_2(cos(2\pi t/T)) + \sum_{j=1}^{5} \alpha_j\, I_{\text{IMD}=j} + \sum_{j=1}^{5} \delta_{1j}\, sin(2\pi t/T)I_{\text{IMD}=j}$$

$$+ \sum_{j=1}^{5} \delta_{2j}\, cos(2\pi t/T)I_{\text{IMD}=j} + \sum_{k=1}^{3} \theta_k\, I_{\text{age}=k} + \sum_{k=1}^{3} \theta_k\, sin(2\pi t/T)I_{\text{age}=k}$$

$$+ \sum_{k=1}^{3} \theta_k\, cos(2\pi t/T)I_{\text{age}=k} + \sum_{k=1}^{K} \theta_k\, I_{x=k}$$

Where: T is the length of period within one harmonic cycle (i.e. 1 year = 52.14 weeks); and $I_{X=x}$ is the binary indicator of the covariates X taking value x; K indicates the number of covariates included in the model (e.g. sex and year categories). The parameter β_0 is the intercept, β_1 and β_2 are harmonic function coefficients, δ_{1j} and δ_{2j} are IMD group-specific harmonic function coefficients, and the parameters $\alpha_1, \delta_{11}, \delta_{21}$ and θ_1 are all constrained to be zero to deal with the collinearity of the binary indicators.

Figure S1. Flow diagram to show study participant and hospital admission selection
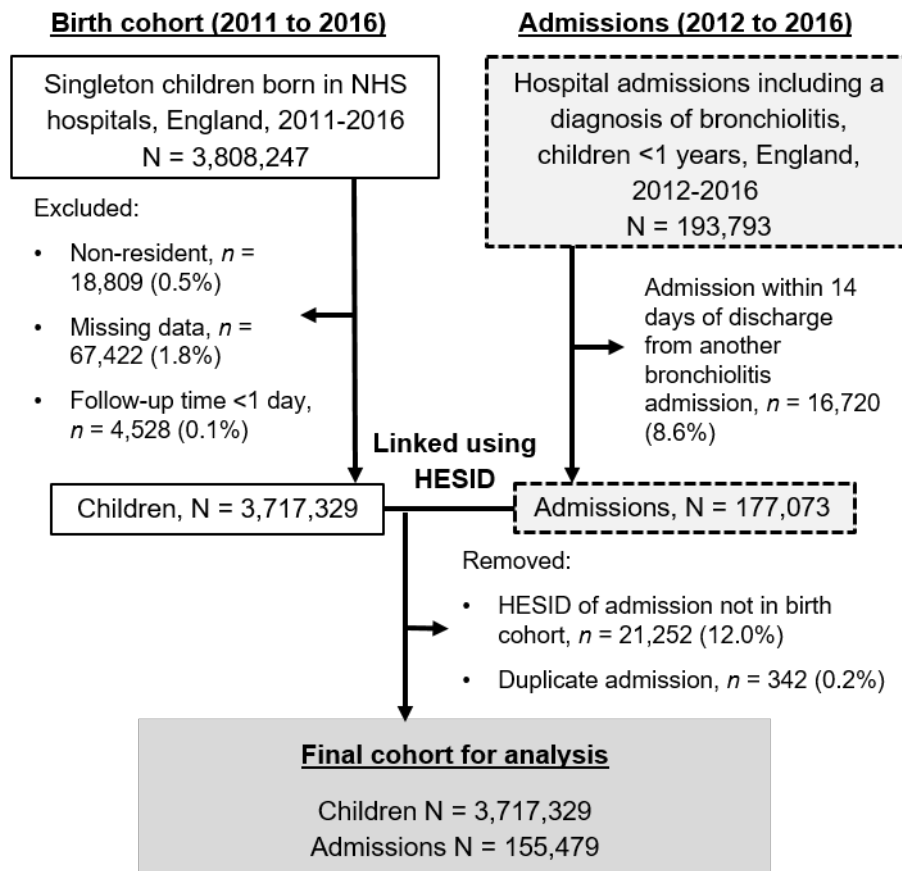
Table S1. Hospital admissions in children <1 year olds, total and due to bronchiolitis, by year and month:

England, 2012-2016

		Any condition (N)	Bronchiolitis (N)	Proportion of all (%)
Year	**2012**	262,411	37,136	14.2
	2013	252,053	34,264	13.6
	2014	250,454	35,982	14.4
	2015	255,866	41,408	16.2
	2016	271,865	45,003	16.6
Month	**January**	112,008	24,116	21.5
	February	104,485	13,787	13.2
	March	113,802	11,647	10.2
	April	101,518	8,077	8.0
	May	100,649	6,238	6.3
	June	93,729	4,004	4.3
	July	96,421	3,432	3.6
	August	85,770	1,990	2.3
	September	90,995	5,358	5.9
	October	109,270	14,181	13.0
	November	135,434	41,794	30.9
	December	148,568	59,079	39.8

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