The Impact of Preterm Birth on Hospital Admissions and Costs: Evidence from the Oxford Record Linkage Study

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Abstract

Background: Although the health sequelae of preterm birth are well documented, relatively little is known about the condition's long-term economic implications. This study estimated the long-term hospital inpatient service utilisation and costs of a large, geographically defined cohort of infants in part of southern England.

Methods: Data from the Oxford Record Linkage Study, a collection of birth registrations, death certificates and statistical abstracts of hospital inpatient and day case admissions, formed the basis of the investigation. The study population comprised all infants born to women who both lived and delivered in Oxfordshire or West Berkshire during the period 1st January 1970–31st December 1993 (n=239,694). The total duration of hospital admissions, including the initial birth admission, during the first 5 years of life was compared between gestational age subgroups and time periods of birth using a multivariate negative binomial regression. The effect of gestational age on total five-year costs was analysed, first in a simple linear regression and then in multiple regression, taking account of a range of confounding clinical and sociodemographic factors.

Results: The total duration of hospital admissions for infants born at < 28 and at 28-31 gestational weeks was, respectively, 85 and 16 times that for term infants, once duration of life had been taken into account. Hospital inpatient service costs were significantly higher for preterm infants than for term infants, with the cost differences persisting throughout infancy and early and mid childhood. Over the first 5 years of life, the adjusted mean cost difference was estimated at £14614 (95%CI: £14268-£14960) when infants born at less than 28 weeks gestational age were compared to term infants, and £11958 (95%CI: £11756-£12160) when infants born at 28-31 weeks gestational age were compared to term infants (P<0.0001). Independent contributions to total cost came from being born: small for gestational age, a multiple, during the 1970s and early 1980s, to a woman of extreme maternal age or who was hospitalised antenatally, and from experiencing extended survival or childhood disease. However, preterm birth remained the strongest predictor of high cost.

Conclusions: Interventions, which are effective at preventing preterm birth, or alleviating its effects, are likely to result in large cost savings. Our data should be of interest and use to researchers planning to evaluate new or existing interventions from an economic perspective, particularly those wishing to incorporate within a decision-analytic framework the long-term economic impact of preterm birth and the cost-effectiveness of prevention and treatment strategies.

Introduction

The high rates of morbidity and mortality arising from preterm birth impose a considerable burden on finite health care resources. Preterm infants are at increased risk of a range of adverse neonatal outcomes including chronic lung disease,[1] severe brain injury,[2] retinopathy of prematurity,[3] necrotising enterocolitis[4] and neonatal sepsis.[5] In later life, preterm infants are at increased risk of motor and sensory impairment,[6,7] learning difficulties[8-12] and behavioural problems.[13-16]

Although the health sequelae of preterm birth are well documented, relatively little is known about its economic consequences. The Organisation for Economic Co-operation and Development (OECD) has provided estimates of the cost of a range of conditions originating in the perinatal period, including preterm birth, to the acute health services of several industrialised countries.[17] However, these cost estimates were derived from widely differing national data systems with a varying degree of methodological rigour. In addition, a number of studies have been conducted with the specific aim of estimating the costs of preterm birth during the neonatal period.[18,19] Although informative, these studies have tended to overlook the condition's economic impact over the longer term.

Assessments of the economic consequences of preterm birth throughout childhood could provide a framework for identifying priorities for research and development, inform future economic evaluations of prevention and treatment strategies, and act as an invaluable resource to clinical decision-makers and budgetary and service planners. The study reported in this paper set out to overcome the limitations of earlier studies by conducting a comprehensive economic assessment of the long-term hospital inpatient service utilisation and costs of a large, geographically defined cohort of infants. The study also set out to identify clinical and sociodemographic predictors of long-term hospital inpatient costs in childhood. The specific hypothesis tested was that preterm birth is associated with significantly increased hospital inpatient service utilisation and costs throughout infancy and early and mid-childhood.

Methods

Oxford Record Linkage Study

Data from the Oxford Record Linkage Study (ORLS) formed the basis of the investigation. The ORLS is a collection of linked, anonymised birth registrations, death certificates and statistical abstracts of National Health Service (NHS) hospital inpatient and day case admissions for part of southern England.[20] The dataset is derived from linked Hospital Activity Analysis (HAA), Hospital Inpatient Enquiry (HIPE) and Hospital Episodes Statistics (HES) records.[21] Data collection in the ORLS covered part of Oxfordshire from 1963-5, and increased its population coverage to include all of Oxfordshire and West Berkshire from 1966, six of the eight districts of the former Oxford Region from 1975 and the whole of the former Oxford Region from 1984.[20] The ORLS maternity and perinatal data were derived from the ORLS's own data collection systems, which covered Oxfordshire and West Berkshire only, until 1989; and from maternity HES thereafter.

Study population

The study population comprised all infants born to women who both lived and delivered in Oxfordshire or West Berkshire during the period 1st January 1970–31st December 1993. These time limits arose because prior to 1970, much of the relevant perinatal information had not been routinely extracted from the patient records, whilst a delivery cut-off point of 31st December 1993 was required for follow-up to cover the first five years of life. For the purpose of analysis, the data were stratified into four subgroups according to the infants' gestational age at birth: less than 28 weeks; 28 weeks to 31 completed weeks inclusive; 32 weeks to 36 completed weeks inclusive; and 37 weeks and greater. The data were also stratified into four six-year time periods according to their date of birth (1970-75, 1976-81, 1982-87, 1988-93) in order to capture the impact of alterations in health care practices during the study period. Over the study period, approximately 6% of births to residents of Oxfordshire and West Berkshire took place outside of these two areas. These were not included in the analyses. In addition, it was not possible to trace the admissions of the study population to hospitals outside the areas covered at the relevant times by the ORLS.

Hospital service utilisation

A record of hospital inpatient service utilisation between birth and 5 years of age was compiled for all study infants. The data extracted from the ORLS included the date of each hospital admission, the duration of hospital stay, specialty on admission, operative procedures performed, and diagnoses recorded on discharge from hospital, based on codes from the eighth and ninth revisions of the *International Classification of Diseases (ICD).*[22,23] Each day case admission was counted as a full 24 hour period for the purposes of this study. We calculated the total time spent in hospital by each individual by summing the lengths of stay of each individual's successive admissions. In addition, estimates of service utilisation were calculated for all infants who were alive at the start of the period of life of interest (initial birth admission, consecutive years of life, first 5 years), with censoring for deaths.

Hospital service costs

Hospital inpatient service costs were calculated for each hospital admission, regardless of the diagnoses recorded on discharge. The cost of each hospital admission was estimated by multiplying the length of stay by the *per diem* cost of the respective specialty. The specialty-based *per diem* costs were based on the English Department of Health's NHS Trust Financial Returns (TFR2) for 1997-98 and 1998-99, which had been averaged over these two financial years to eliminate any random fluctuation in the data. For the hospital records with an unknown or incorrect specialty code, the *per diem* medical or surgical cost was applied, depending on the approximate ORLS code range. No subspecialty coding was available for psychiatric hospitalisations, so *per diem* psychiatric costs were applied to each day of a psychiatric admission. All costs are expressed in constant £ 1998-99 sterling using the NHS Hospital and Community Health Services pay and price deflators provided by the English Department of Health.

Statistical analysis

A detailed statistical analysis plan was followed. The number of deaths over the first five years of life, amongst live births, was examined using survival analysis. A multivariate Cox regression model was used to compare the number of deaths in the four gestational age subgroups and over the four time periods. Hazard ratios (HR) and 95% confidence intervals

(CIs) for the independent effects of gestational age and time period were calculated. The probabilities of early neonatal deaths (0-7 days), late neonatal deaths (8-28 days), postneonatal deaths (29-365 days) and deaths during years 1-5, conditional on being alive at the start of the period, were estimated using the life-table method.

The total duration of hospital admissions, including the initial birth admission, during the first 5 years of life was compared between gestational age subgroups and time periods of birth using a multivariate negative binomial regression.[24] Data on all study infants were incorporated into this analysis. Relative rates and 95% CIs for the number of days of hospitalisation are reported for the multivariate negative binomial regression, accounting for and not accounting for duration of life.

Cost differences between the four gestational age subgroups that occurred during the initial birth admission and during each of the first 5 years of life were tested using simple linear regression, with only children alive at the start of each period included within cost estimates. In addition, the effect of gestational age on the total five year costs of all study infants was analysed, first in a simple linear regression and then in a multiple regression, taking account of clinical and sociodemographic factors that were considered to influence costs.[19] Confounding factors considered in the regression analyses included whether or not the infant was small for gestational age (< 10^{th} centile of birth weight),[25] year of birth (1970-75, 1976-81, 1982-87, 1988-93), sex, survival period (< 8 days, 8-28 days, 29 days-1 year, 1-5 years, > 5 years), maternal age at time of delivery (< 20 years, 20-35 years, >35 years), multiplicity of birth (singleton, multiple), social class based on the male partner's occupation (I, II, III, IV V),[26] maternal hospitalised days during the antenatal period (none, 1-10, 11-20, ≥21) and the presence at any time point during the study period of childhood diseases included in the ICD classifications.[22,23] The size of the study sample (n=233,082 in the multiple regression) was sufficiently large to expect robust parameter estimates and, therefore, alternative methods such as bootstrapping techniques were not applied.[27]

For all statistical analyses, differences were considered significant if *P* values were 0.001 or less. All analyses were performed with a microcomputer using SAS software (version 8.0; SAS Institute Inc., Cary, North Carolina, USA).

Results

Study population

A total of 281,212 infants were born to women who both lived and delivered in Oxfordshire or West Berkshire during the study period, 278,683 of whom were born alive. Information on gestational age at birth was available for 239,694 (86.0%) infants, who closely resembled the total population of live births in terms of clinical and sociodemographic characteristics (data available upon request). The number of births, deaths and mortality rates among infants for whom information on gestational age at birth was available is shown in table 1. When compared to term infants (born at ≥ 37 gestational weeks), the number of deaths over the first five years of life was 146 times higher (HR=145.7, 95%CI: 127.1-166.9) among infants born at less than 28 gestational weeks, 33 times higher (HR=33.3, 95%CI: 28.9-38.2) among infants born at 28-31 gestational weeks and 5 times higher (HR=5.2, 95%CI: 4.6-5.8) among infants born at 32-36 gestational weeks. Mortality differences between the gestational age groups were greatest during the early neonatal period. When compared to term infants, the numbers of early neonatal deaths were 368 (HR=368.5, 95%CI: 310.7-437.0), 85 (HR=84.6, 95%CI: 70.8-101.0) and 11 times higher (HR=10.6, 95%CI: 8.9-12.4) among infants born at less than 28, 28-31 and 32-36 gestational weeks, respectively. The number of deaths during the first five years of life declined over the four time periods. Compared to the period 1970-1975, the number of deaths decreased by 20% (95%CI: 12-28%), 48% (95%CI: 42-54%) and 68% (95%CI: 64-72%) during 1976-1981, 1982-1987 and 1988-1993, respectively. Probabilities of early, late and post-neonatal deaths and deaths during years 1-5 of life are shown in Table 1, by gestational age and time period.

Hospital service utilisation

The median number (and interquartile range) of admissions during the first 5 years of life, for infants born at less than 28 gestational weeks, at 28-31 gestational weeks, at 32-36 gestational weeks and at term were 2 (1,2), 2 (1,3), 1 (1,2) and 1 (1,2) respectively. The total duration of hospital admissions during the first 5 years of life for infants born at less than 28 gestational weeks and for infants born at 28-31 gestational weeks was almost 8 times that for term infants (Table 2). Taking into account duration of life, the total duration of admissions for infants born at less than 28 gestational weeks and for infants born at 28-31 gestational weeks increased to 85 and 16 times that for term infants respectively. The total duration of admissions for infants born at 32-36 gestational weeks was 2.6 times that for term infants, without accounting for duration of life, and 3 times that for term infants, once duration of life had been accounted for.

The median number (and interquartile range) of admissions during the first 5 years of life for infants born between 1970-75, between 1976-81, between 1982-87 and between 1988-93 were 1 (1,1), 1 (1,2), 1 (1,2) and 1 (1,1) respectively. The total duration of admissions for infants born during the first three time periods was between 1.17 and 1.30 times that for infants born during 1988-93, without accounting for duration of life, and between 1.21 and 1.33 times, once duration of life had been accounted for (Table 2).

Cost differences between gestational age subgroups

For each gestational age subgroup, the largest component of cost was incurred during the infant's first year of life (Table 3). Relative to term infants, initial birth admission costs were significantly higher for all preterm subgroups (P<0.0001); £5818 (95%CI: £5730-£5905) higher among infants born at less than 28 gestational weeks, £5948 (95%CI: £5895-£6002) higher among infants born at 28-31 gestational weeks, and £1170 (95%CI: £1151-£1188) higher among infants born at 32-36 gestational weeks. Among infants who survived the initial birth admission, the cost of first year readmissions was £10333 (95%CI: £9991-£10675) higher for infants born at less than 28 gestational weeks compared to term infants, £6976 (95%CI: £6802-£7149) higher for infants born at 28-31 gestational weeks, and £1720 (95%CI: £1663-£1776) higher for infants born at 32-36 gestational weeks. The cost differences between the preterm subgroups and the term reference group persisted through the subsequent four years of life (P<0.0001), with the exception of the £44 cost difference in 5th year readmission costs between infants born at less than 28 gestational weeks and those born at term (P=0.32).

Clinical and sociodemographic characteristics in relation to total cost

Relationships between the clinical and sociodemographic characteristics of the study population and total hospital inpatient service costs during the first 5 years of life are shown in table 4. The simple linear regression revealed gestational age at birth to be the strongest predictor of total costs during the first 5 years of life (R^2=0.093). Other factors significantly associated with total costs during the first 5 years of life included: small for gestational age (R^2=0.007); year of birth (R^2=0.003); sex (R^2=0.001); survival period (R^2=0.020); multiplicity of birth (R^2=0.008); maternal age at time of delivery (R^2=0.001); maternal hospitalised days prior to birth (R^2=0.007); and the presence of all categories of childhood disease (R^2 between 0.002 and 0.033). Although social class was also significantly associated with total costs, it was excluded from further analyses, partly as a consequence of its low explanatory value (R^2=0.0004), and partly because social class data were not collected in the hospital systems after 1990.

Clinical and sociodemographic predictors of total cost

The results of the multiple regression analysis are shown in table 5. Preterm birth was significantly associated with increased hospital inpatient service costs during the first 5 years of life (P<0.0001). The adjusted mean cost difference was estimated at £14614 (95%CI: £14268-£14960) when infants born at less than 28 weeks gestational age were compared to term infants, and £11958 (95%CI: £11756-£12160) when infants born at 28-31 weeks gestational age were compared to term infants. All other clinical and sociodemographic factors incorporated within the multiple regression were independently associated with total hospital inpatient service costs during the first 5 years of life, with the exception of the sex of the infant (P=0.032). On average, costs were greater for infants who were born small for gestational age (P<0.0001), during the 1970s and early 1980s (P<0.0001) and survived for greater than 28 days (P<0.0001). In addition, being born a multiple (P<0.0001), to mothers aged less than 20 years or greater than 35 years (P=0.0009) or to mothers who were hospitalised antenatally (P<0.0001) was associated with significantly increased costs. The presence of all categories of childhood disease at any time point during the study period was also associated with significantly increased costs (P<0.0001).

Discussion

A search of the published and unpublished medical and health economics literature by the authors revealed that relatively few studies have estimated the long-term economic impact of preterm birth.[18,19,28] Moreover, the studies that have been conducted were based on relatively small samples of infants and frequently violated current methodological requirements of health economic evaluation.[19] The major strengths of this study are that it was based on a large cohort of infants in a geographically defined area, and include a comprehensive and validated record of hospital inpatient service data.[29,30] The availability of linked data enabled us to relate gestational age at birth to subsequent admissions; and to sum lengths of stay of individuals' successive admissions in order to calculate their total time spent in hospital. This provided a reliable basis for estimating the economic implications of preterm birth. The study cost accounting was comprehensive and included all significant hospital inpatient cost items, whose values were calculated according to established principles in economic theory. Furthermore, the study sample size was large enough to detect statistically significant differences in the cost of hospital inpatient care between infants of varying gestational age at birth. Therefore, we would argue that the study was sufficiently sized to arrive at conclusions that are both meaningful and relevant to decision-makers.

The study does have limitations, which should be borne in mind. By focusing on the cost of hospital inpatient services provided to infants, this study has adopted a narrow health service perspective. A small number of studies have shown that survivors of low gestational age and birth weight consume significantly greater family practitioner services,[31] education services[32] and social services[33] than infants born at term or at normal birth weight. Moreover, it is likely that preterm birth has other long-term consequences that require evaluation from an economic perspective. These include the support provided by local authorities and voluntary organisations, such as adaptations that have to be made to the infant's home as a result of their impaired state of health, and additional costs borne by families as a result of modifications to their everyday activities. Other costs excluded from the analysis include direct non-medical costs (e.g. travel and child care costs), indirect costs (e.g. lost productivity) and intangible costs (e.g. costs of pain and suffering) attributable to preterm birth.

A second limitation is the 5-year time frame upon which the economic study is based. Although the effects of preterm birth are acutely felt during the first 5 years postpartum,[1-7] it is likely that the condition has longer term consequences in terms of health status and health service utilisation over the child's lifetime[6] and in terms of the child's educational[8-12] and social[13-16] requirements. If this is the case, then longer-term research is required to provide a complete assessment of the condition's economic implications.

A third limitation of the study is that the specialty-based *per diem* costs applied to each hospital admission may not have captured subtle differences in the care provided to infants with varying diagnoses. The English Department of Health has compiled an alternative data set of NHS Reference Costs,[34] which is based on categories of acute care interventions that are clinically distinct and have similar implications for resources. However, these costs have been criticised for having improbably wide ranges of values for the same healthcare resource groups,[35] and it was therefore decided that the NHS Trust Financial Returns provided the most rigorous values for our calculations.

A fourth limitation of the study is that the dataset did not include admissions of the study population to hospitals outside the former Oxford Region. National statistics indicate that 4.7% of children aged under 15 years migrated out of the local authorities covered by the former Oxford Region during 2000-2001.[36] Although part of this migration would have been to other local authority areas covered by the ORLS, we might have underestimated the *absolute* levels of hospital service utilisation and costs for our study population. Nevertheless, there is no evidence to suggest that the mean *difference* in care costs between the gestational age subgroups and, consequently, the costs that can be attributed to preterm birth, is affected by the level of migration.

Despite the limitations of our study, the results have important implications for clinical decision-makers and budgetary and service planners. The study generated a mean cost difference of £14614 when infants born at less than 28 weeks gestational age were compared to term infants, and £11958 when infants born at 28-31 weeks gestational age were compared to term infants. Moreover, these cost differences had been calculated after a multivariate analysis controlled for a wide range of clinical and sociodemographic confounding factors, including birthweight for gestational age, year of birth, sex, survival period, maternal age and morbidity, multiplicity of birth and a comprehensive profile of childhood diseases. Given recent evidence of an increasing incidence of preterm birth,[37] it is imperative that health service providers recognise the overall economic impact of the condition in their service planning, as well as the potential contribution of clinical and sociodemographic factors to future health care costs.

In addition to informing the planning of services, the broad economic aggregates that we have estimated can provide a basis for assessing competing strategies for research and prevention. However, it should be noted that cost data alone cannot identify the most efficient allocation of finite health care resources. Rather, it is information on incremental costs and incremental health gains attributable to particular health care interventions that can identify the combination of human and material inputs that maximise health benefits. This can be achieved through the general framework of economic evaluation. A number of interventions are effective at ameliorating the morbidity and mortality associated with preterm birth.[38] In contrast, with the exception of treatment of urinary tract infection, cerclage, and treatment of bacterial vaginosis in high-risk women, relatively few interventions have proved effective at preventing or delaying preterm birth.[38] In order for finite resources in this area to be allocated in an efficient manner, it is imperative that economic evaluations of effective interventions are carried out. Our data should be of interest and use to researchers planning to evaluate new or existing interventions from an economic perspective, particularly those wishing to incorporate within a decision-analytic framework the long-term economic impact of preterm birth and the cost-effectiveness of prevention and treatment strategies.

In conclusion, the results of this study should facilitate the effective planning of services and should be used to inform the development of future economic evaluations of interventions aimed at preventing preterm birth or alleviating its effects. Further research is required that identifies, measures and values the broader and longer-term economic impact of the condition in a valid and reliable manner.

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TABLE 1. Changes between time periods in the number of births, deaths and mortality rates among babies born to women living and delivering in Oxfordshire or West Berkshire, by gestational age

	< 28 weeks					28-31 weeks					32-36 weeks					≥ 37 weeks				
	1970-75	**1976-81**	**1982-87**	**1988-93**	**Total**	**1970-75**	**1976-81**	**1982-87**	**1988-93**	**Total**	**1970-75**	**1976-81**	**1982-87**	**1988-93**	**Total**	**1970-75**	**1976-81**	**1982-87**	**1988-93**	**Total**
Total births	110	125	149	144	**528**	378	397	377	455	**1,607**	3,344	2,796	2,912	3,156	**12,208**	60,004	54,507	51,825	60,428	**226,764**
Live births	99	116	144	141	**500**	301	338	332	375	**1,346**	3,127	2,697	2,836	3,068	**11,728**	59,701	54,380	51,724	60,315	**226,120**
Early neonatal deaths:[a] - n	66	51	48	40	**205**	75	66	20	14	**175**	91	74	32	20	**217**	175	124	63	40	**402**
- probability*	0.667	0.440	0.333	0.284	**0.410**	0.249	0.195	0.060	0.037	**0.130**	0.029	0.027	0.011	0.007	**0.019**	0.003	0.002	0.001	0.001	**0.002**
Late neonatal deaths:[b] - n	2	4	4	11	**21**	8	7	2	6	**23**	9	9	12	6	**36**	47	53	29	18	**147**
- probability*	0.061	0.062	0.042	0.109	**0.071**	0.035	0.026	0.006	0.017	**0.020**	0.003	0.003	0.004	0.002	**0.003**	0.001	0.001	0.001	0.000	**0.001**
Postneonatal deaths:[c] - n	3	4	8	7	**22**	10	10	5	4	**29**	38	21	20	20	**99**	199	155	145	78	**577**
- probability*	0.097	0.066	0.087	0.078	**0.080**	0.046	0.038	0.016	0.011	**0.025**	0.013	0.008	0.007	0.007	**0.009**	0.003	0.003	0.003	0.001	**0.003**
Deaths, days 366-1825: - n	0	0	1	0	**1**	1	2	1	1	**5**	6	8	4	2	**20**	117	77	59	42	**295**
- probability*	0.000	0.000	0.012	0.000	**0.004**	0.005	0.008	0.003	0.003	**0.005**	0.002	0.003	0.001	0.001	**0.002**	0.002	0.001	0.001	0.001	**0.001**

[a] Death during days 1-7.
[b] Death during days 8-28.
[c] Death during days 29-365.
* Calculated using the life-table method, conditional on being alive at the start of the specified period.

TABLE 2. Total duration of hospital admissions (days) during the first 5 years of life, by gestational age and time period of birth

		Total duration				**Not allowing for duration of life***			**Allowing for duration of life***		
	n	**Median**	**Interquartile range**	**Mean**	**SD**	***P***	**Relative rate**	**95% CI**	***P***	**Relative rate**	**95% CI**
Gestational age						<0.0001			<0.0001		
< 28 weeks	*500*	8	(2, 86)	49.0	(65.0)		7.97	(7.53, 8.43)		84.89	(77.36, 93.14)
28-31 weeks	*1,346*	39	(13, 71)	48.7	(45.8)		7.81	(7.55, 8.08)		16.03	(15.30, 16.78)
32-36 weeks	*11,728*	9	(6, 21)	16.2	(20.8)		2.58	(2.55, 2.61)		3.00	(2.96, 3.04)
≥ 37 weeks	*226,120*	5	(4, 7)	6.3	(11.1)		1.00			1.00	
Year of birth						<0.0001			<0.0001		
1970-75	*63,228*	4	(4, 6)	6.9	(17.0)		1.17	(1.16, 1.18)		1.21	(1.20, 1.22)
1976-81	*57,531*	5	(3, 8)	7.9	(12.0)		1.30	(1.29, 1.31)		1.33	(1.32, 1.34)
1982-87	*55,036*	5	(3, 8)	7.5	(12.7)		1.20	(1.19, 1.21)		1.22	(1.21, 1.23)
1988-93	*63,899*	4	(3, 6)	6.2	(10.2)		1.00			1.00	

* Calculated using a multivariate negative binomial regression.

TABLE 3. Mean cost of hospital inpatient services (£ UK 1998-99) during infancy and early and mid-childhood, by gestational age*

	< 28 weeks		**28-31 weeks**		**32-36 weeks**		**^{3} 37 weeks**		***P*****
Initial birth admission	6569	*(n=500)*	6700	*(n=1,346)*	1922	*(n=11,728)*	752	*(n=226,120)*	<0.0001
Readmissions commencing in:									
- 1st year of life	10630	*(n=301)*	7272	*(n=1,174)*	2016	*(n=11,578)*	297	*(n=225,849)*	<0.0001
- 2nd year of life	561	*(n=252)*	371	*(n=1,119)*	162	*(n=11,376)*	95	*(n=224,994)*	<0.0001
- 3rd year of life	339	*(n=252)*	316	*(n=1,115)*	123	*(n=11,367)*	68	*(n=224,885)*	<0.0001
- 4th year of life	325	*(n=252)*	217	*(n=1,115)*	96	*(n=11,363)*	63	*(n=224,814)*	<0.0001
- 5th year of life	105	*(n=251)*	321	*(n=1,114)*	100	*(n=11,361)*	61	*(n=224,757)*	<0.0001
Entire study period	13639	*(n=500)*	14059	*(n=1,346)*	4378	*(n=11,728)*	1333	*(n=226,120)*	<0.0001

* Only children alive at the start of the specified period were included within cost estimates.
** Gestational age subgroups were compared using simple linear regression.

TABLE 4. Clinical and sociodemographic factors predicting cumulative hospital inpatient service costs (£ UK 1998-99) by age 5, determined by simple linear regression (n=239,694)

Factor	n	Mean cost	SD	Regression coefficient (95% CI)	*P* value
Gestational age					< 0.0001
< 28 weeks	500	13639	19333	12306 (11957, 12655)	
28-31 weeks	1,346	14059	14429	12727 (12514, 12940)	
32-36 weeks	11,728	4378	6458	3045 (2971, 3119)	
≥ 37 weeks	226,120	1333	3540		
Small for gestational age*					< 0.0001
Yes	19,180	2708	5545	1238 (1178, 1298)	
No	219,805	1470	3939		
Year of birth					< 0.0001
1970-75	63,228	1471	5513	161 (115, 207)	
1976-81	57,531	1820	3686	509 (462, 556)	
1982-87	55,036	1763	3904	452 (404, 499)	
1988-93	63,899	1311	3126		
Sex*					< 0.0001
Male	123,100	1707	4810	264 (230, 297)	
Female	116,548	1444	3372		
Survival period					< 0.0001
< 8 days	999	603	583	-941 (-1198, -684)	
8 – 28 days	227	4056	2819	2512 (1974, 3050)	
29 days - 1 year	727	8241	13874	6697 (6396, 6998)	
1 - 5 years	321	13830	21451	12286 (11834, 12738)	
> 5 years	237,420	1544	4004		
Maternal age at time of delivery*					< 0.0001
< 20 years	14,767	2018	9583	466 (396, 536)	
> 35 years	13,983	1610	3754	58 (-13, 130)	
20-35 years	208,250	1551	3537		
Multiplicity of birth*					< 0.0001
Multiple	5,604	3948	6417	2423 (2313, 2534)	
Singleton	232,414	1525	4098		
Social class*					< 0.0001
Class II	54,796	1575	3860	76 (14, 138)	
Class III	89,523	1691	5135	192 (134, 249)	
Class IV	22,015	1707	3678	208 (131, 285)	
Class V	6,363	1908	4974	408 (289, 527)	
Class I	29,566	1499	2964		
Maternal hospitalised days prior to birth*					< 0.0001
1 - 10 days	112,730	1670	4818	281 (247, 316)	
11 - 20 days	3,899	3281	5910	1893 (1759, 2026)	
≥ 21 days	2,543	3714	6925	2326 (2161, 2490)	
None	114,950	1388	3263		
Infectious and parasitic diseases					< 0.0001
Present	7,741	4548	8236	3068 (2974, 3161)	
Absent	231,953	1480	3930		
Neoplasms					< 0.0001
Present	1,458	5453	11310	3898 (3684, 4112)	
Absent	238,236	1555	4082		

Endocrine, nutritional and metabolic diseases					< 0.0001
Present	1,521	8015	12108	6477 (6268, 6686)	
Absent	238,173	1538	4042		
Diseases of the blood					< 0.0001
Present	832	7382	13133	5824 (5540, 6107)	
Absent	238,862	1559	4095		
Mental and behavioural disorders					< 0.0001
Present	440	17238	53847	15688 (15303, 16073)	
Absent	239,254	1550	3419		
Diseases of the nervous system					< 0.0001
Present	11,663	4792	13048	3377 (3301, 3454)	
Absent	228,031	1415	3010		
Diseases of the circulatory system					< 0.0001
Present	647	10318	14586	8763 (8442, 9083)	
Absent	239,047	1555	4086		
Diseases of the respiratory system					< 0.0001
Present	16,997	4158	7817	2776 (2712, 2840)	
Absent	222,697	1382	3681		
Diseases of the digestive system					< 0.0001
Present	8,483	4669	9694	3203 (3114, 3293)	
Absent	231,211	1466	3776		
Diseases of the genito-urinary system					< 0.0001
Present	6,200	3564	6565	2038 (1933, 2143)	
Absent	233,494	1526	4079		
Diseases of skin and subcutaneous tissue					< 0.0001
Present	3,901	3161	6228	1608 (1476, 1740)	
Absent	235,793	1553	4127		
Diseases of the musculoskeletal system					< 0.0001
Present	1,337	4647	8149	3085 (2861, 3309)	
Absent	238,357	1562	4135		
Congenital anomalies					< 0.0001
Present	22,214	3764	10472	2408 (2351, 2465)	
Absent	217,480	1356	2733		
Conditions of perinatal period					< 0.0001
Present	105,647	2309	5465	1305 (1272, 1338)	
Absent	134,047	1004	2622		
Diseases of symptoms/ill-defined conditions					< 0.0001
Present	12,999	4757	8835	3360 (3288, 3433)	
Absent	226,695	1397	3652		
Accidents, poisoning, violence					< 0.0001
Present	11,945	3469	7099	1989 (1913, 2065)	
Absent	227,749	1480	3937		

* n<239,694 because of an element of missing data for explanatory variable.

TABLE 5. Clinical and sociodemographic factors predicting cumulative hospital inpatient service costs (£ UK 1998-99) by age 5, determined by multiple regression (n=233,082*)

Factor	Regression coefficient (95% CI)	Standardised regression coefficient b	*P* value
Gestational age			<.0001
< 28 weeks	14614 (14268, 14960)	0.15	
28-31 weeks	11958 (11756, 12160)	0.21	
32-36 weeks	2306 (2236, 2375)	0.12	
≥ 37 weeks			
Small for gestational age	658 (605, 712)	0.04	<.0001
Year of birth			<.0001
1970-75	324 (283, 364)	0.03	
1976-81	312 (271, 353)	0.03	
1982-87	206 (164, 247)	0.02	
1988-93			
Male	-32 (-61, -3)	0.00	0.032
Survival period			<.0001
< 8 days	-7106 (-7356, -6856)	-0.10	
8 - 28 days	-1412 (-1892, -933)	-0.01	
29 days - 1 year	4567 (4305, 4830)	0.06	
1 - 5 years	8501 (8107, 8895)	0.08	
> 5 years			
Maternal age at time of delivery			0.0009
< 20 years	82 (23, 142)	0.00	
> 35 years	86 (25, 148)	0.00	
20-35 years			
Multiple	663 (562, 765)	0.02	<.0001
Maternal hospitalised days prior to birth			<.0001
1 - 10 days	91 (61, 120)	0.01	
11 - 20 days	603 (489, 718)	0.02	
≥ 21 days	751 (609, 892)	0.02	
None			
Diagnosis present at any admission			
Infectious and parasitic diseases	1470 (1387, 1553)	0.06	<.0001
Neoplasms	2607 (2422, 2792)	0.05	<.0001
Endocrine, nutritional and metabolic diseases	3834 (3652, 4016)	0.07	<.0001
Diseases of the blood	3007 (2762, 3252)	0.04	<.0001
Mental and behavioural disorders	12113 (11777, 12449)	0.13	<.0001
Diseases of the nervous system	1740 (1671, 1809)	0.09	<.0001
Diseases of the circulatory system	4991 (4711, 5270)	0.06	<.0001
Diseases of the respiratory system	1261 (1203, 1320)	0.08	<.0001
Diseases of the digestive system	1643 (1564, 1722)	0.07	<.0001
Diseases of the genito-urinary system	1104 (1013, 1195)	0.04	<.0001
Diseases of skin and subcutaneous tissue	794 (680, 908)	0.02	<.0001
Diseases of the musculoskeletal system	1930 (1738, 2122)	0.03	<.0001
Congenital anomalies	1697 (1647, 1747)	0.12	<.0001
Conditions of perinatal period	779 (749, 809)	0.09	<.0001
Diseases of symptoms/ill-defined conditions	1547 (1480, 1613)	0.08	<.0001
Accidents, poisoning, violence	1340 (1274, 1406)	0.07	<.0001

$R^2 = 0.27$. * Data on all factors available for 97% of cases.