Hospital admission rates for viral meningitis in children in England over five decades: a population based observational study

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Summary

Background: Since the substantial reduction in bacterial meningitis following successful implementation of immunisation programmes, most childhood meningitis in developed countries is now caused by viruses. Long term trends in paediatric viral meningitis in England have not previously been reported. The objective of this study is to report on epidemiological trends, over time, in childhood viral meningitis in England.

Methods: Annual age-specific admission rates for viral meningitis, including specific viral aetiologies, in children <15 years were analysed using routinely-collected hospital discharge records from English National Health Service hospitals from 1968-2011.

Findings: Viral meningitis admission rates from 1968-1985 varied annually, but averaged 13.5 per 100 000 children aged <15 per year (95% confidence interval 13.0-14.0). Rates declined during the late 1980s and from 1989-2011 rates averaged 5.2 per 100 000 (5.1-5.3). The decline was wholly in children aged 1-14 years. Rates in infants fluctuated from 1968-2004, and increased in recent years, to 70.0/100 000 (63.7-76.2) in 2011, caused by increased rates in infants aged ≤90 days. In 1968-1985 the majority of cases in children were in those aged 1-14 years (89%, 22150/24920). By 2007-2011 most cases (72%, 1716/2382) were in infants. Admissions for mumps meningitis almost disappeared following introduction of the measles-mumps-rubella (MMR) vaccine in 1988. Admissions with a specified viral aetiology have increased since 2000.

Interpretation: Trends in viral meningitis admission rates have changed substantially over the past five decades, and likely reflect the impact of the MMR vaccine programme, and the use of more sensitive diagnostic techniques.

Funding: none

Introduction

A striking decline in bacterial meningitis caused by *Neisseria meningitidis, Haemophilus influenzae* type b, and *Streptococcus pneumoniae* has occurred in the UK following the implementation of highly effective conjugate vaccines.[1] The majority of childhood meningitis in highly immunised populations is now aseptic, and most cases are caused by viruses when a cause is identified.[2,3] Before routine measles-mumps-rubella (MMR) vaccination, mumps was reported to be the commonest cause of viral meningitis in England and Wales, with epidemics occurring every 2-3 years.[4-6] Enteroviruses (EV) are now responsible for >75% of viral meningitis cases where a pathogen is identified.[7,8] However, for many cases of meningitis no cause is identified.[7,8]

Viral meningitis is usually a self-limiting disease and the majority of children require supportive management only. However, most children with cerebrospinal fluid (CSF) pleocytosis are admitted to hospital and receive intravenous antibiotics while a bacterial aetiology is excluded.[8,9] If a pathogen is not found, children often complete 10-14 days of treatment to cover the possibility of bacterial meningitis.[9,10]

During the past 40 years, introduction of vaccines, improvements in diagnostics, and the availability of antiviral therapy for herpes simplex virus infection are likely to have impacted hospital admissions due to viral meningitis. MMR vaccination was introduced in the UK in 1988, and mumps disease almost disappeared.[4-6] The development of polymerase chain reaction (PCR) has significantly improved clinical diagnostics since the 1990s and is now widely applied to CSF samples.[11,12] Results from EV-PCR testing can be available rapidly where resources allow,[11,12] and it results in reduced length of hospital admission.[13-15]

Long term trends in hospital admission rates for viral meningitis in children in England have not previously been reported. Improved knowledge of the epidemiology and true burden of hospital admissions is important to inform future research into prevention through vaccination, improved rapid diagnostic techniques, clinical management guidelines, and as the basis for healthcare cost-effectiveness analyses. The objective of this study was to analyse trends, over 44 years, in hospital admission rates for viral meningitis in children.

Methods

Datasets

Datasets were analysed that included routinely collected administrative statistics on hospital care. From 1968-1985, hospital admission statistics in England were collected in the Hospital In-Patient Enquiry (HIPE). HIPE was a 10% sample of every hospital admission in the English National Health Service (NHS). From 1989, English national data have been collected in the Hospital Episode Statistics (HES) dataset on a 100% basis covering all NHS inpatients. The 10% sample in HIPE was scaled by multiplying by ten. For most of the years covered, the English data were based on numbers of episodes of care. The data were linkable from 1999, allowing the same patient to be counted only once through multiple admissions or inter-hospital transfers and, from then, both episode-based (numbers of admissions) and person-based (numbers of people receiving care) rates are reported. The HES data were provided, as individual-level records for each episode of care, by the Health and Social Care Information Centre (HSCIC), and were linked by the Oxford Record Linkage Study (ORLS) team. Data were linked by exact matching on encrypted unique identifiers (NHS and HES patient ID numbers). Match rates are considered to be very high; missing values, for data items relevant to this study, are very low. English national hospital statistics were not collected from 1986-1988; and the HSCIC was unable to provide HES data for 2012-2015.

Data were also analysed from the ORLS, which includes data on all NHS hospital admissions in the former Oxford NHS Regional Health Authority area from 1963-2011. Successive admissions for the same individuals were always linked in ORLS (by encrypted full names, addresses and dates of birth). The ORLS and national HIPE datasets were

collected independently of each other. From 1999, the ORLS was the regional subset of English national HES. For simplicity, unless otherwise stated, the data given are those for all England.

Ethical approval was obtained from the Central and South Bristol Multi-Centre Research Ethics Committee (04/Q2006/176).

Analysis

Annual age-specific and age-standardised admission rates were analysed for viral meningitis defined by any relevant International Classification of Disease (ICD) code in children aged <15 years (Appendix, page 1, table 1). Age-specific rates in infants, in days, were available within the HES dataset from 1989. The terminology and ICD codes for viral meningitis are complicated, because of changes and some inconsistencies in terminology and coding between ICD revisions. Admission rates for viral meningitis caused by mumps virus, measles virus, enteroviruses, varicella zoster virus (VZV), and herpes simplex virus (HSV) were also analysed separately. Cases coded as encephalitis were not included. Cases were included if the diagnosis was recorded in any diagnostic position. Population denominators from the Office for National Statistics were used.[16] Admission rates and their 95% confidence intervals were calculated using the direct method of standardisation, confined to people aged under 15 years, and the European standard population. Joinpoint regression analysis was used to identify the best-fitting points where a statistically significant change in the log-linear slope of trend occurred (Appendix, page 2). An annual percentage change (APC) with confidence intervals is calculated for each line segment.

The median length of hospital admission was calculated for all viral meningitis, and the subset of children with enteroviral meningitis, in five-calendar-year groups from 1968-2011, for infants, and children aged 1-14 years. A hospital admission was defined as a day case (with admission), or overnight inpatient, but does not include emergency department visits without admission. Hospital admission rates for viral meningitis were also analysed by Government Office Region using the English HES national data (Appendix page 3, table 2).

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

All cause viral meningitis

There were 25 980 cases of childhood viral meningitis from 1968-1985 (mean 1443 per year) and 2584 in 2007-2011 (mean 517 per year). Overall admission rates from 1968-1985 varied annually, with peaks and troughs, but averaged 13.5 episodes per 100 000 children per year (95% confidence interval 13.0-14.0) (figure 1a). Rates decreased in the mid to late 1980s, shown in the ORLS for years in which national data were missing (figure 1a). Rates in England fell from 13.7 per 100 000 (11.3-16.2) in 1985 to 7.5 per 100 000 (7.0-8.1) in 1989. Thereafter rates remained relatively low, averaging 5.2 episodes per 100 000 children per year (5.1-5.3) in England from 1989-2011 (range 2·5 per 100 000 (2·2-2·8) to 9·4 per 100 000 (8·8-10·1). There was a significant peak in 2000-01; the rate increased from 3.4 per 100 000 (3.0-3.8) in 1999, to 9.4 per 100 000 (8.8-10.0) in 2000, and fell to 2.9 per 100 000 (2.5-3.3) in 2002. The overall difference between 1968-1985 and 1989-2011 was statistically significant (see CIs).

The decline was wholly in children aged 1-14 years (figure 1c); there was no decline in infants during the same period (figure 1b). The rates in children aged 1-4, 5-9 and 10-14 years were similar (figure 1c). In children aged 1-14 years, the rates from 1968-1985 averaged 12.8 per 100 000 children (12.3-13.3); from 1989-2011 they averaged

3.0 per 100 000 (2.9 to 3.1). There were small peaks in 2000 and 2001 (Appendix, page 4, table 3a). Joinpoint analysis showed a -14.1 annual percent change (CI -18.7 to -9.1) in admission rates for children aged 1-14 years between 1984-1998 (figure 2a). The rates in infants fluctuated considerably from year to year. However, notably, the highest rates occurred in three of the last four years of the study: 59.9 per 100 000 infants (54.1-65.8) in 2008, 67 (60.9-73.3) in 2010, 70.0 (63.7-76.2) in 2011, caused by increased admission rates in infants aged ≤90 days (figure 1d). Joinpoint analysis showed a +13.0 annual percent change (95% CI 4.0-22.8) in admission rates for infants between 2005-2011 (figure 2b).

The fall in rates in children aged 1-14 years has substantially changed the age profile of hospitalised children with viral meningitis. In 1968-1985 the great majority of cases (89%, 23060/25980) were in children aged 1-14. The corresponding figures were 64% (3000/4669) in the 1990s, and 55% (1723/3144) in 2000-2006. By 2007-2011 the majority (73%, 1877/2584) were in infants. Male rates were higher than female rates, especially for children aged 1-14 years in the pre-1985 data (Appendix page 6, figure 1a), and for infants after 1989 (Appendix page 6, figure 1b)). The all-England data and the ORLS data, and the episode-based and person-based data, generally showed very similar rates (figures 1a–1b).

The great majority of viral meningitis cases were for aseptic meningitis without specification of virus type (figure 3). In recent years, however, an increasing percentage of cases have a specified virus, particularly in infants. From 1968-1985, 92% (2550/2770) of cases in infants and 89% (19820/22150) of cases in children aged 1-14 years were unspecified viral meningitis. By the last five years of the study, the corresponding figures were 50% (860/1716) in infants and 82% (544/666) in children aged 1-14 years.

The median LOS for viral meningitis was longest from 1968-79. For infants, median LOS was five days from 1980-2004, and four days from 2005-2011. For children aged 1-14 years, median LOS was three days across the past three decades (table 1).

Geographical analysis showed some variation in hospital admission rates between Government Office Regions (Appendix page 3, table 2).

Enteroviral meningitis

Hospital admission rates for enteroviral meningitis, including only the correct ICD codes (see below) for specific enteroviruses, remained low prior to 2000 at 0-0·9 episodes per 100 000 children (figure 4). There was an increase in admission rates from 2000, peaking at 2·9 episodes per 100 000 (2·5-3·2) for all children aged <15 years and 36·8 episodes per 100 000 (32.4-41.7) for infants in 2011 (Appendix page 5, table 3b). In 1968-1985 enteroviral meningitis was specified in 3% (90/2770) of viral meningitis cases in infants and 2% (340/22150) in children aged 1-14. By 2007-2011 enteroviral cases were specified in 47% (811/1716) of cases in infants and in 12% (77/666) of cases in children aged 1-14. Consistent with viral meningitis trends overall, a peak in admission rates was seen in 2000-2001.

During the years covered by ICD versions 8 and 9, any unspecified viral or aseptic meningitis was classified within the three-digit code for ‘meningitis due to enterovirus’. This is an error in the ICD. For completeness, and so that there is a record of the trends, we have included a separate analysis of these data including the codes wrongly classified as enteroviral meningitis, ICD-8 045·9 and ICD-9 047·9 (Appendix page 7, figure 2); but the data for the early years are artefactual.

The median LOS for enteroviral meningitis (specific ICD codes) was 5 days for infants and 3 days for children 1-14 years (table 2). In recent years, there was a reduction in LOS in infants from 6 days 2000-04 to 4 days 2010-11.

Mumps and measles meningitis

The hospital admission rate for mumps meningitis from 1979-1985 was between 0·6 (0·1-1·1) and 2·1 (1·2-3·1) episodes per 100 000 children (figure 5a). Admissions for mumps meningitis almost disappeared from 1990 following the 1988 introduction of the MMR vaccination. A small peak in admissions occurred in 2005 at 0·05 episodes per 100 000(0·01-0·10). Measles meningitis did not have a separate ICD code prior to 1995, and from 1995-2011, only one hospital admission was recorded.

VZV and HSV meningitis

Hospital admissions for meningitis caused by VZV were low from 1979-2002 with the exception of a peak in 1981 (figure 5b). An increase in admission rates occurred from 2003-2011, coinciding with increased use of CSF PCR. There were similar low rates of hospital admissions for meningitis caused by HSV from 1979-2007 with a peak seen in 1983. HSV meningitis admission rates increased in the late 2000s, but remained low.

Discussion

Overall, admission rates for viral meningitis in children fell by almost two-thirds in the period covered by this study. The decline was wholly in the age group 1-14 years. Viral meningitis admission rates in infancy, conversely, increased in the last few years of the study. The contrasting changes over time in the two age groups have substantially altered the age-related epidemiological profile of viral meningitis in childhood. Mumps meningitis has almost disappeared.

The reduction in admissions due to childhood viral meningitis was abrupt, and occurred during the late-1980s. The great majority of cases of viral meningitis in hospital statistics, both historically and in recent years, are recorded without a specific virus type. It is therefore difficult to be precise about the aetiological components of the decline. One factor known to have changed is the 1988 widespread introduction of immunisation against mumps,[4,17] probably the commonest cause of childhood viral meningitis pre-1988.[4-6]Other viruses, notably enteroviruses, also caused quite a high proportion of unspecified viral meningitis cases then.[7,8,15] It seems likely, however, that much of the large decline in rates of 'unspecified' viral meningitis, between 1985 and 1989, was an unrecognised decline in mumps meningitis.

Age-related differences in clinical practice may also have contributed to differences in admission rates observed for children and infants. Lumbar punctures (LP) have probably been performed less frequently recently.[18] Most LPs are performed in young infants as part of a sepsis screening protocol for febrile children, whereas older children will only have an LP if there is clinical suspicion of meningitis.[8,9] This may mean that diagnoses of viral meningitis are missed more often in children than infants. Furthermore, enteroviral meningitis in the absence of CSF pleocytosis has been increasingly described, specifically in young infants.[19,20] Although practices probably differ between hospitals for performing CSF PCR in acellular samples,[20] these cases are unlikely to have been detected prior to widespread use of PCR, and may have contributed to increased admission rates in young infants compared with older children.

Improved aetiological attribution has resulted from availability of PCR testing of CSF samples and this is reflected also in the arrival of specific coding for enteroviral meningitis. However, there does also seem to have been a recent absolute increase in total viral meningitis admission rates for young infants, indicating either a change in medical practice, or a true underlying increase in disease incidence. Stochastic changes in the biological properties of enteroviruses and changes in host immunity could contribute to an increase in incidence.[21] PCR testing is also likely to have significantly contributed to the decrease in proportion of viral meningitis coded without specification of type. Improving microbiological diagnostics means that clinicians can diagnose viral meningitis more accurately. Prior to the widespread availability of viral PCR, CSF pleocytosis was usually treated as bacterial meningitis.[8-10,13,15]

Several studies have shown reduction in LOS and antibiotic use for children who are CSF EV PCR positive, compared with children who are tested and are EV PCR negative.[13-15] The median LOS of 3-5 days for viral and enteroviral meningitis observed in these present data is longer than has been previously reported in studies from other countries, which typically report LOS of 2-3 days,[8-10,12-15,22,23] suggesting room for improvement in availability of rapid PCR results in the UK.

These hospital datasets are the most complete data available in England to report historic population-based incidence of cases termed as viral meningitis. Other sources of data are statutory infectious disease notifications, which are frequently incomplete;[24] mortality statistics from death registrations, which do not provide disease burden estimates; and microbiologically confirmed cases reported to Public Health England, which have incomplete ascertainment. Microbiologically confirmed datasets are limited, because they do not include cases of with no pathogen identified, which are the majority in these data. The peak in admissions for viral meningitis noted in our data in 2000-2001 was also seen in laboratory notification data in the UK.[25,26] Although the peak in enteroviral meningitis hospital admissions during this period is smaller than the peak in overall viral meningitis, the increase in hospitalisations is likely to have been caused by reported outbreaks of laboratory confirmed cases of meningitis caused by echovirus 13 in 2000 and echovirus 30 in 2001 in England and Wales.[27,28] The increase in viral meningitis hospitalisations observed from 2002 to 2011 is consistent with a recent study that reported an increase in meningo-encephalitis laboratory confirmed cases from 0·6/100 000 in 2004 to 3·9/100 000 in 2013 at all ages in England and Wales.[29] One third of these cases occurred in children, with incidence peaking at 329/100 000 in infants <3 months in 2013.[29]

Although the proportion of viral meningitis admissions attributed to enteroviruses increased in 2007-11 to 47% in infants and 12% in children aged 1-14 years, as expected, these proportions are lower than were reported by a recent UK laboratory study,[29] which identified enteroviruses in 92% of cases with a pathogen found among infants <3 months, and 52% at all ages.[29] Microbiological surveillance from 1975 to 1994 identified CSF enteroviral isolates in 2/100 000 infants which is higher than our reported rates for specific enteroviral meningitis codes.[30]

Human parechovirus 3 causes central nervous system infection and sepsis-like illness in young infants.[31,32] Parechoviruses were only reclassified as a distinct genus from enteroviruses in 1999,[33] and therefore have not yet been coded separately within the ICD. Notably, peaks of viral meningitis hospital admissions in young infants in these present data appear to match reported peaks of parechoviral disease incidence occurring biannually in even years in studies from the UK and Europe since the mid-2000s.[31,32,34]

The small increase in mumps meningitis admissions seen in 2005 is consistent with a mumps outbreak in England which occurred in 2004-05. This was partly caused by the presence of an unimmunised cohort in the population, and incomplete immunisation coverage, demonstrating the importance of maintaining high two dose vaccine coverage even when rates of background disease are low.[17]

Although there are few comparable studies, hospital admission rates for viral meningitis in the UK are lower than are reported by studies from the USA, but appear consistent with data from other countries in Western Europe. Hospitalization rates for viral meningitis in one USA study from 1988-99 were 213/100 000 for infants, and 14/100 000 for children aged 1-4 and 5-19 years.[35] Another USA study of emergency department admissions for all-cause meningitis from 1993-2008 identified 31 visits per 100 000 children <18 years, with 91% of visits for viral or unspecified meningitis in adults and children.[36] A birth cohort study of 12000 children in Finland from 1966 reported a viral meningitis incidence from hospital data of 28/100 000 per year in children <14 years and 219/100 000 in infants.[5] A Danish study based on ICD coding, from 1977-2001, observed 39/100 000 per year viral meningitis hospitalisations in the first 6 months of life, and between approximately 4-16/100 000 hospitalisations at ages 1-14.[37] Although the admission rates are higher in the Finnish study,[5] the rates reported in the Danish study[37] and a Greek study[38] are comparable with these present data, particularly before the reduction observed in the UK

during the 1980s. The higher admission rates reported in the USA may be caused by differences in coding, healthcare behaviour or diagnostic practices.

Limitations

The quality and consistency of HES data are largely unknown. Findings from a systematic review in the UK suggest that the accuracy of reporting might be improving.[39] Data precision is likely to have been affected by changes in clinical practice, for example changes in numbers of LPs performed for febrile children, in addition to advancements in microbiological diagnostic techniques. Changes in codes and terminology for viral meningitis across the relevant three editions of the ICD and changes in hospital coding practice could also have affected our findings. Geographical variation in rates may also reflect differences in diagnostic tests and coding practices between hospitals. ICD coding for specific viral aetiologies are not always available, for example parechoviruses. Nonetheless, the trends shown are consistent with available microbiological surveillance data; rates reported by the ORLS and HIPE corroborate each other suggesting both datasets are probably reliable; and these are the only long term population datasets of their kind.[25,27,29]

Conclusions

Viral meningitis hospital admission rates reduced significantly from 1968-85 to 1989-2011 in children aged 1-14 years. In contrast, viral meningitis admission rates in infants have increased in recent years. The impact of mumps vaccination, the widespread use of PCR allowing detection of specific viruses, and differences in clinical management of children related to their age likely contributed to these findings. The reasons behind the changing trends, especially the cause of the increase in infant viral meningitis admissions, warrants further investigation including prospective cohort studies, to direct strategies to improve infant health.

Research in Context

Evidence before this study

We searched PubMed up to Jan 23, 2016 for papers reporting paediatric meningitis disease trends, and length of hospital admission for viral or aseptic meningitis. We used the search terms “meningitis”, “viral meningitis”, “aseptic meningitis”, “enteroviral meningitis”, “hospital admissions”, “hospital episode statistics”, “epidemiology”, “length of stay” and “length of admission”. We also reviewed references from relevant articles that were not identified in the original search. We reviewed studies reporting disease incidence from microbiological surveillance data or hospital admission statistics in the UK and other countries with similar disease burden and vaccine programmes. One recent UK study showed an increase in laboratory confirmed cases of viral meningo-encephalitis from 2004 to 2013 at all ages, however, because many cases of viral meningitis are not microbiologically confirmed, this study would have under-estimated the actual number of cases.[29] A few studies reporting viral meningitis hospitalisation rates from other European countries and the USA were identified, limited to shorter periods of surveillance.[5,35-38] These studies showed higher admission rates in infants compared with older children, although overall rates varied between studies.

Added value of this study

Our findings show radical changes in the age-related demography and epidemiological profile of viral meningitis, likely to be caused by widespread MMR vaccination, advancements in microbiological diagnostics and changes in clinical and coding practises during the long period of surveillance. Length of hospital admission for viral meningitis in England is higher than is reported in other countries suggesting there is still room for improvement with rapid diagnostic testing.

Implications of all available evidence

To the best of our knowledge, our study reports the most complete population based dataset in the UK of disease incidence for viral and aseptic meningitis between the 1960s and 2011. Ongoing disease surveillance to inform clinical guidelines, further advances in rapid diagnostic techniques, and research into prevention of viral meningitis including development of vaccines for enteroviruses remains important.

Declaration of Interests

NGM - Nothing to declare

MAI - Nothing to declare

MS - Co-investigator on investigator-initiated research grants from Pfizer, outside the submitted work.

RG - Nothing to declare

AJP - Nothing to declare

MJG - Nothing to declare

Sources of Funding: This study has no specific funding. The Unit of Health-Care Epidemiology was funded by the English National Institute for Health Research to build the record linkage datasets (grant number RNC/035/002). The work of the Oxford Vaccine Group was also supported with funding from the National Institute of Health and Research Oxford Biomedical Research Centre. The funders had no role in the design or analysis of the data and the views expressed in this paper do not necessarily reflect those of the funders.

Authors' Contributions

All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. NGM, MJG, AJP, MAI, RG and MS had the idea for and designed the study. MJG collected the data and designed the analysis. RG conducted the analyses. MJG, NGM, AJP, MAI, RG and MS contributed to data interpretation. NGM performed the literature search and wrote the first draft of the paper. MJG, NGM, AJP, MAI, RG and MS contributed to the review and final approval of the report.

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Table 1: Median length of hospital admission (LOS) in days for viral meningitis and enteroviral meningitis in children aged less than 14 years in England

Viral meningitis				
Year	**0-1 year median LOS in days (interquartile range)**	**n**	**1-14 years median LOS in days (interquartile range)**	**n**
1968-74	9 (5-14)	141	6 (4-10)	868
1975-79	7 (4-10)	81	4 (2-7)	722
1980-85	5 (3-7)	109	3 (2-5)	716
1989-94	5 (3-7)	1021	3 (2-4)	2511
1995-99	5 (3-7)	849	3 (2-5)	961
2000-04	5 (3-7)	964	3 (2-4)	1412
2005-09	4 (3-6)	1406	3 (2-5)	730
2010-11	4 (3-6)	928	3 (2-5)	288
all years	5 (3-7)	5460	3 (2-5)	8208
Enteroviral meningitis				
Year	**0-1 year median LOS in days (interquartile range)**	**n**	**1-14 years median LOS in days (interquartile range)**	**n**
1968-74	15·5 (14-17)	2	11 (8·5-15·5)	12
1975-79	8 (5-27)	3	3.5 (2-8)	14
1980-85	10.5 (6·5-12·5)	4	3.5 (2-4·5)	8
1989-94	8 (5-10)	29	2 (1-3·5)	24
1995-99	7 (6-10)	59	5 (2-6)	21
2000-04	6 (4-8)	132	3 (2-5)	51
2005-09	5 (3-7)	505	3 (2-5)	57
2010-11	4 (3-6)	452	3 (2-5)	40
all years	5 (3-7)	1186	3 (2-6)	227

Note: no data 1986-88

Figure 1a. Hospital admission rates for viral meningitis in children younger than 15 years

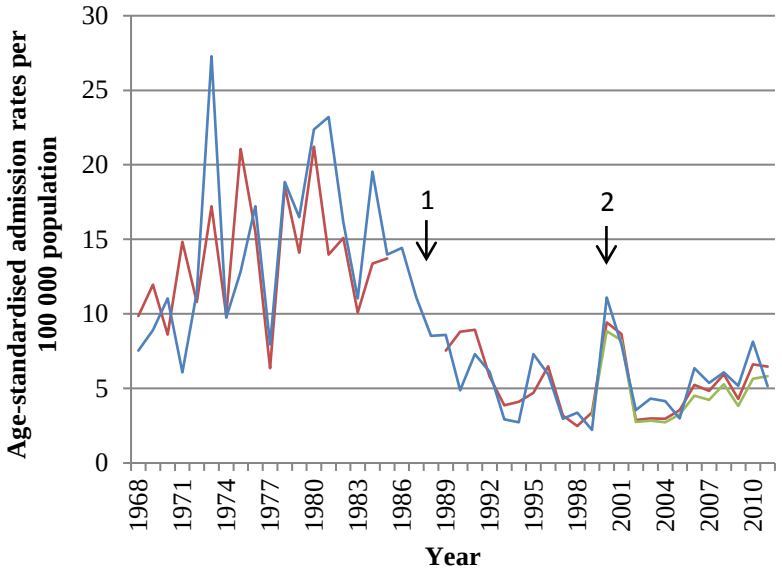


Figure 1b. Hospital admission rates for viral meningitis in children younger than 1 year

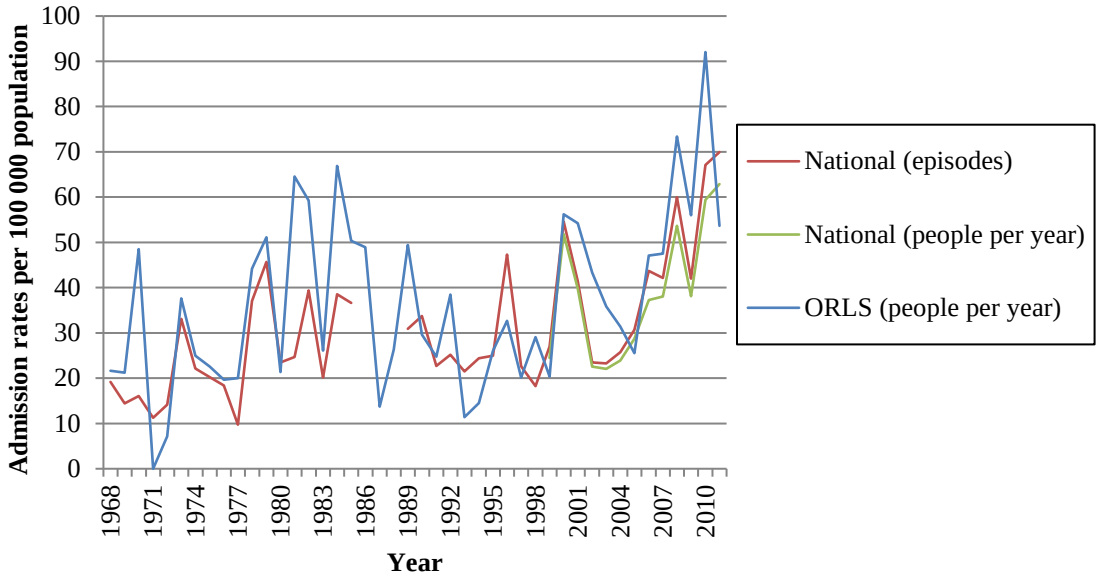


Figure 1c. Age-specific hospital admission rates for viral meningitis in age groups 1-4, 5-9 and 10-14 years, England 1968-2011

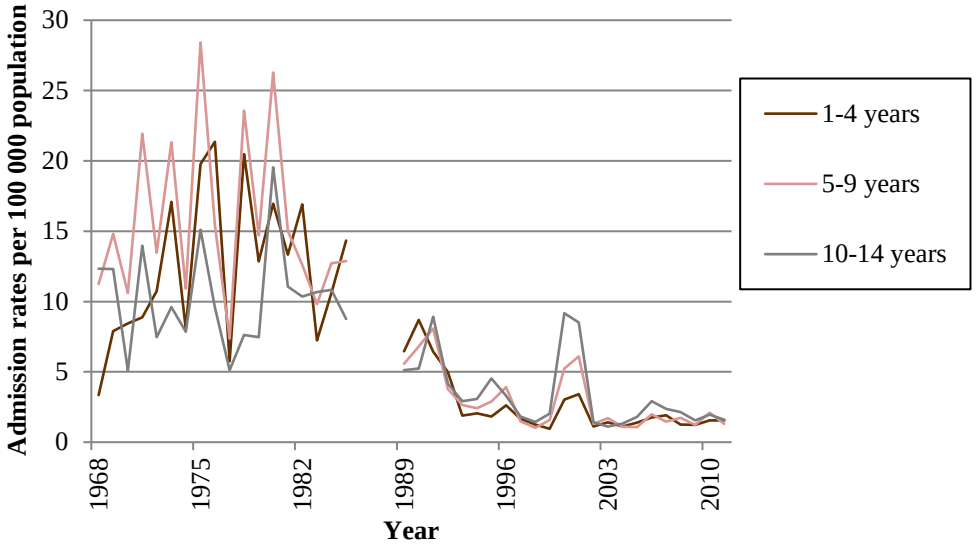
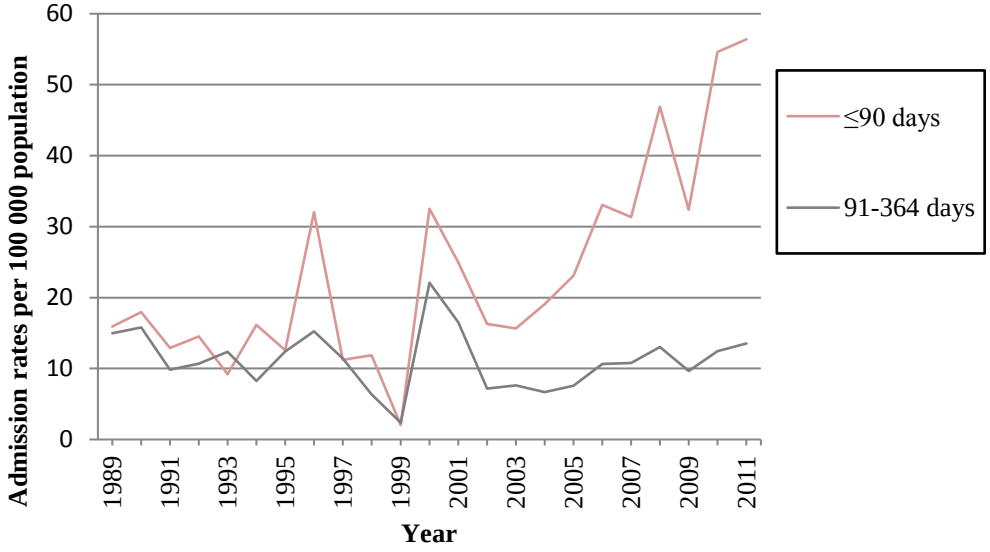


Figure 1d. Age-specific hospital admission rates for viral meningitis in infants in age groups ≤90 days and 91-364 days from 1989 to 2011



Note: Arrow 1 shows the time of widespread introduction of MMR. Arrow 2 is the time of known outbreaks of Echovirus 13 and 30 in 2000 and 2001. Figure 1c and 1d are episodes of care.

Figure 2a. Joinpoint regression analysis of hospital admission rates for viral meningitis in children aged 1-14 years, annual percentage change (APC) for each line segment, and 95% confidence intervals

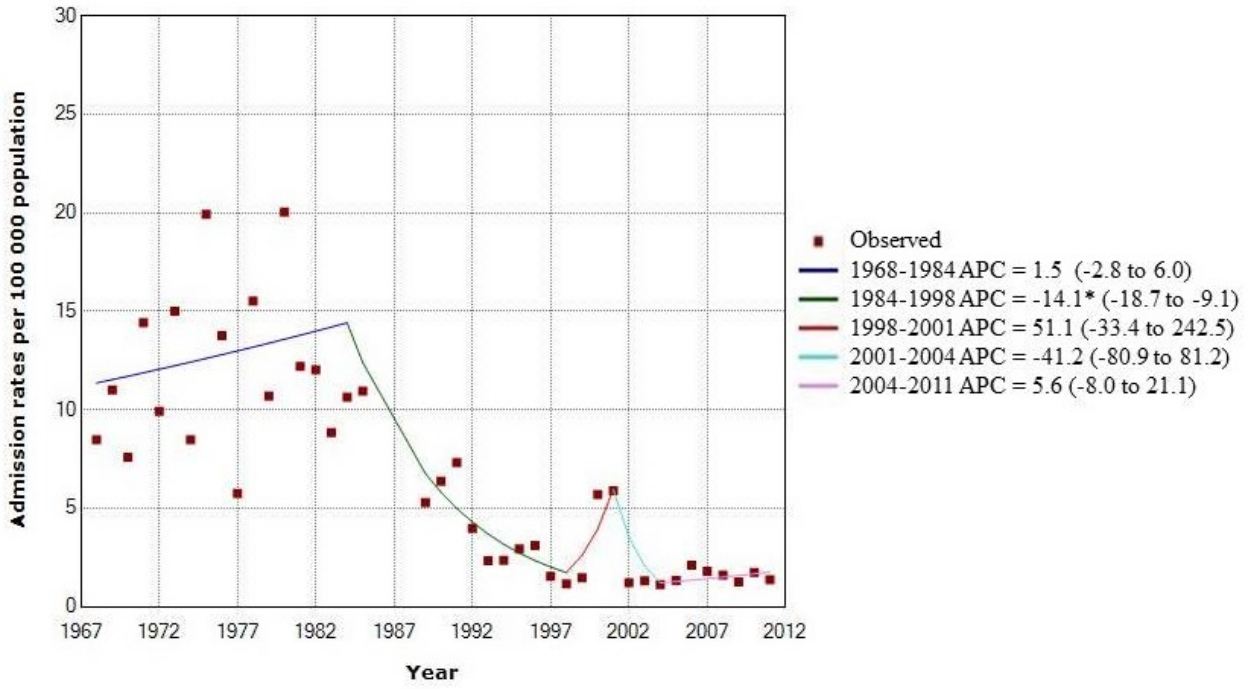
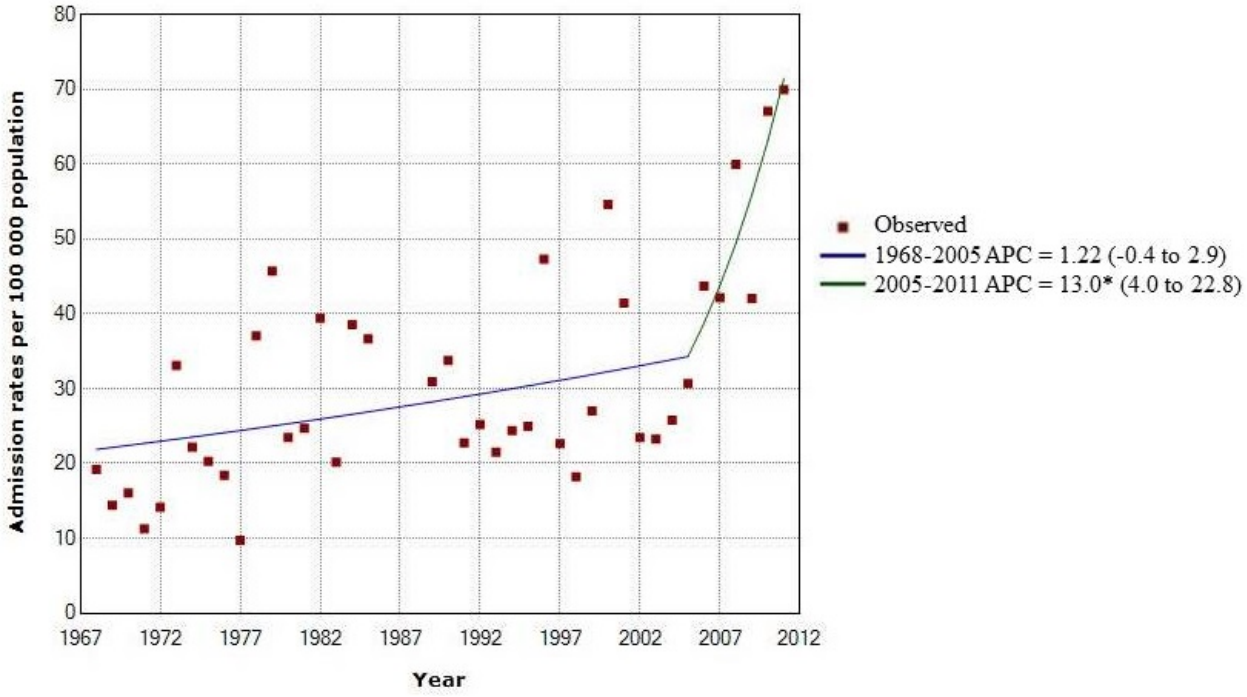


Figure 2b. Joinpoint regression analysis of hospital admission rates for viral meningitis in children younger than 1 year, annual percentage change (APC) for each line segment, and 95% confidence intervals



Notes: 1. APC=Annual Percentage Change, 2. *p=<0.05

Figure 3a. National hospital admission rates for all viral meningitis and for the subset of viral meningitis without specification of organism, children aged 1-14 years

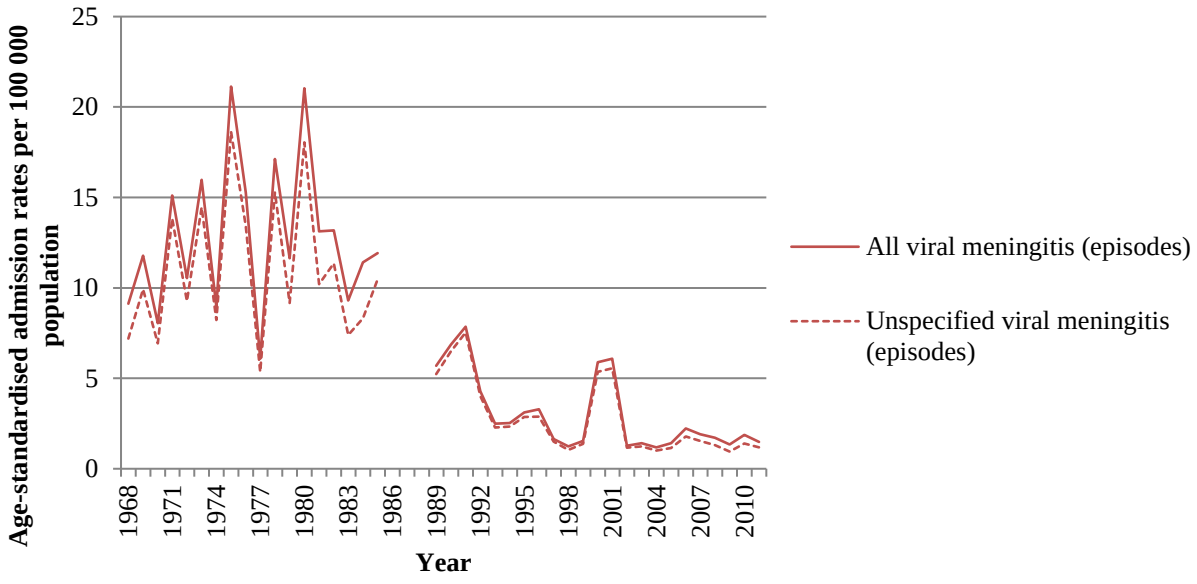


Figure 3b. National hospital admission rates for all viral meningitis and for the subset of viral meningitis without specification of organism, children aged <1 year

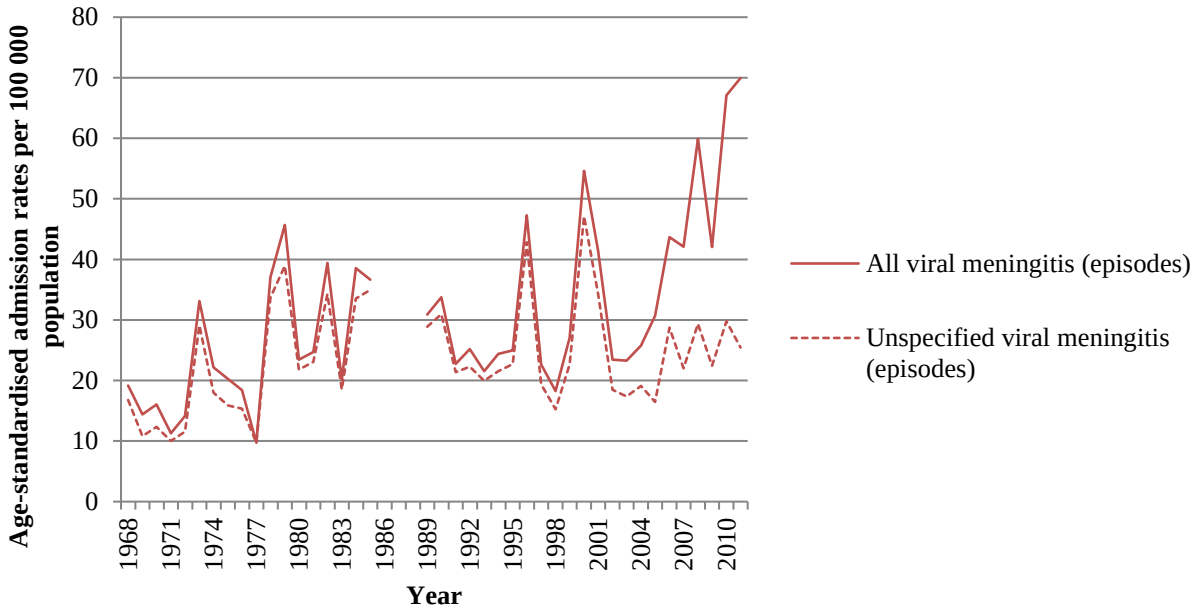


Figure 4a. Hospital admission rates for enteroviral meningitis in children younger than 15 years in England

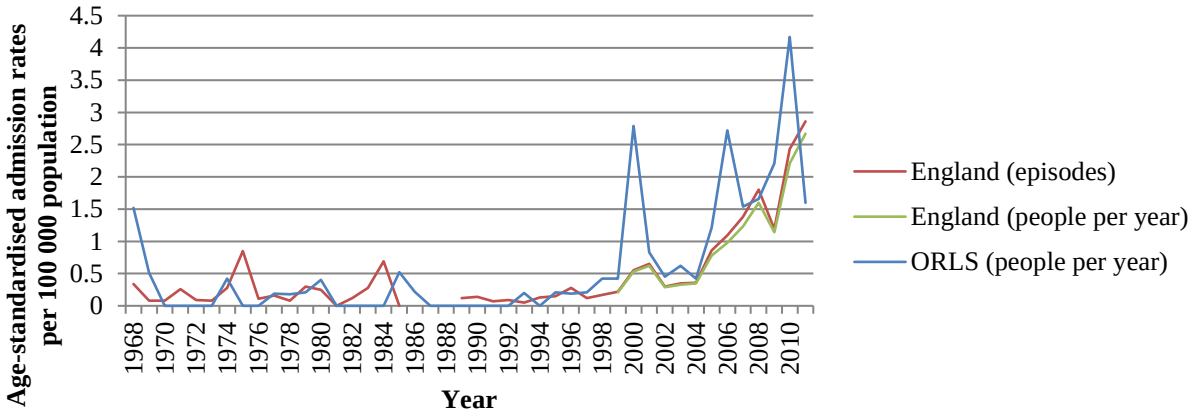
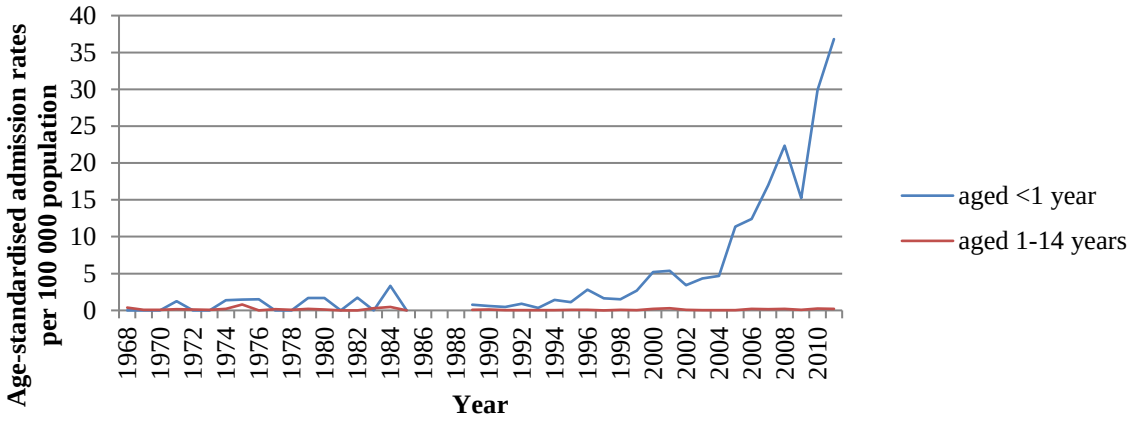
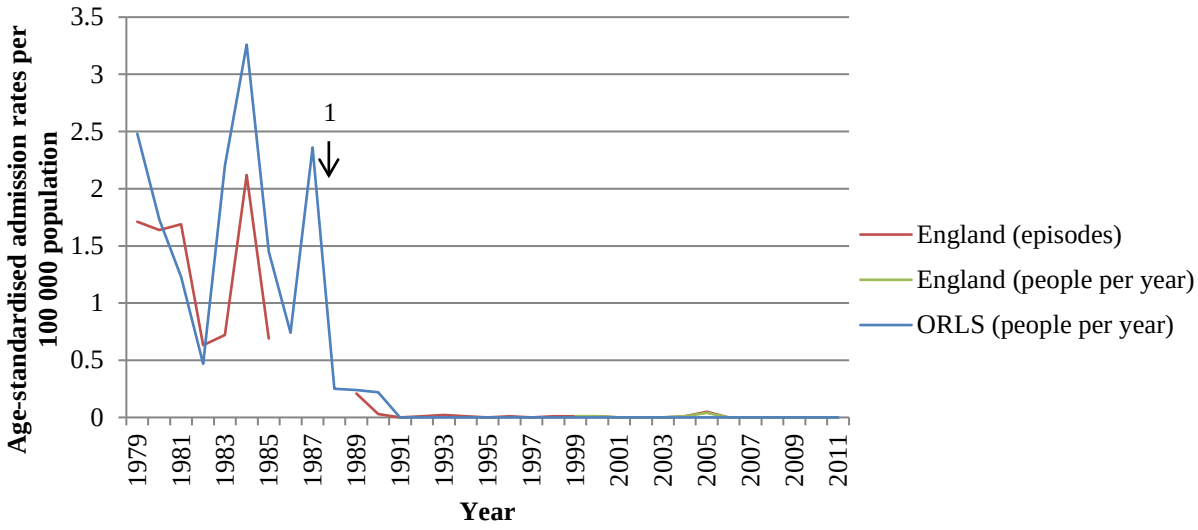


Figure 4b. Hospital admission rates for enteroviral meningitis in children aged <1 and 1-14 years in England



Note: These data exclude "unspecified" codes ICD9 047.9 and ICD8 045.9 (see Appendix Page 7, figure 2)

Figure 5a. Hospital admission rates for mumps meningitis in children younger than 15 years in England



Arrow 1: the 1988 introduction of MMR vaccination.

Figure 5b. Hospital admission rates for meningitis caused by varicella zoster virus and herpes simplex virus in children younger than 15 years in England