

Incidence and healthcare costs of viral meningitis in adults - a multicentre prospective observational study in England.

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Abstract

Background: As bacterial meningitis decreases in incidence, viruses are becoming relatively more important. The incidence, aetiology and costs of viral meningitis in UK adults are unknown. Knowing the burden of viral meningitis can help guide clinical care, direct research policy and identify areas where savings can be made.

Material/methods: An epidemiological study of adults with suspected meningitis in the Northwest of England, nested within a national multicentre prospective cohort study, was carried out between 2011 and 2014. We estimated incidence and healthcare costs using patient level data from the Northwest of England, and extrapolated to estimate resource use throughout the UK.

Results: Among 1117 patients enrolled, 638 (57%) had meningitis. 231/638 (36%) had viral meningitis, 99/638 (16%) bacterial and 267/638 (42%) unknown aetiology. Estimated annual incidences of viral and bacterial meningitis were 2.73 and 1.24 per 100,000 respectively. The yearly healthcare cost of viral and bacterial meningitis were similar: £3,220,343 (95% CI £1,206,963 – £4,418,424) and £4,860,218 (95% CI £3,728,598 – £6,358,419) respectively, $p=0.57$. The median length of stay for patients with viral meningitis was 4 days, increasing to 8 days in those treated with antivirals, which are of no proven benefit. Hospitalisation accounted for 79% of the healthcare cost representing the largest potential area for cost-cutting.

Conclusions: Viral meningitis is the predominant cause of meningitis in adults in the UK. The total annual healthcare costs could be reduced by earlier discharge. This might be achieved through speedier diagnostics and avoiding unnecessary treatments.

Methods

Patients were recruited from 41 UK hospitals between September 2011 and September 2014 (figure 1). Eligibility criteria: aged ≥ 16 , suspected community acquired meningitis, and having an LP (if LP was contraindicated a positive blood culture or polymerase chain reaction (PCR) in the blood for a significant pathogen +/- radiological features consistent with meningitis).

To estimate the national incidence we estimated the number of patients with meningitis in the Northwest of England using census data as the denominator. We then performed a proportional uplift to account for any missing cases (based on a known number of missed cases in sentinel sites). Finally we extrapolated that figure to the rest of the UK.

To estimate the economic burden we focused purely on direct costs. We investigated the consumption of resources contributing most to the cost of meningitis: hospitalisation, investigations, and antimicrobials.¹² Unit costs were sourced from NHS reference costs,¹³ the British National Formulary¹⁴ and diagnostic laboratories.

Results

1117 patients with suspected meningitis were analysed. 638/1117 (57%) had confirmed meningitis (defined by a corrected CSF leukocyte count $> 4 \times 10^6$ cells/L). The aetiologies are shown in figure 2. 42% of patients with meningitis had no cause found.

The incidence of viral meningitis and bacterial meningitis was estimated to be 2.73 and 1.24 per 100,000 adults per year respectively (table 1). When all cases of meningitis were considered, including those where no specific aetiology was established, the annual incidence was 13.47 per 100,000 population.

The median length of stay for patients with viral meningitis was four days. Patients with herpes meningitis (HSV and VZV) stayed in hospital longer than patients with enteroviral meningitis (6 days vs. 3.5 days, $p<0.001$) and those with VZV meningitis stayed longer than those with HSV (8 days vs 5 days, $p=0.02$). Those who received antivirals were in hospital longer than those who didn't (8 days vs. 3 days, $p<0.001$). Most patients who had antivirals had intravenous treatment. Only four patients (4%) had solely oral treatment.

The mean cost per patient with viral meningitis was £2149 (95% CI £805-2948), significantly less than that for bacterial meningitis at £7139 ((95% CI £5477-9340) ($p<0.001$). However, the total annual costs for all patients with viral meningitis in the UK, based on our estimated incidence, is similar to that of bacterial meningitis £3,220,343 (95%CI £1,206,963 – £4,418,424) and £4,860,218 (95%CI £3,728,598– £6,358,419) respectively, $p=0.57$. Many patients did not have a pathogen identified and the total resource burden imposed on the NHS, by all patients with meningitis, was estimated to be £30,675,497 per year (95% CI £24,820,493- £37,940,889).

Figure 2: Aetiology of meningitis (number of patients)

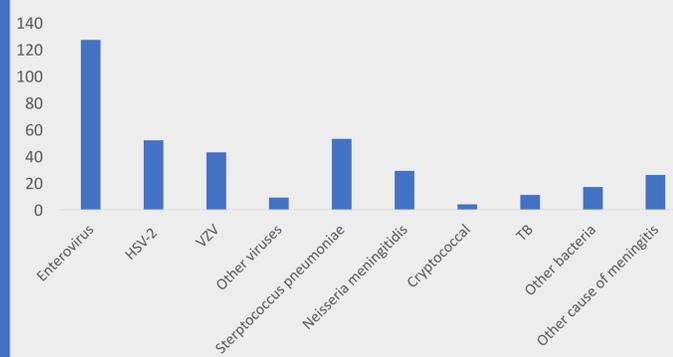


Table 1. Incidence and direct health care cost of different aetiologies of meningitis in UK adults.

Aetiology	Incidence per 100,000 (95%CI)	Total annual direct health care costs (£) (95%CI)
Enterovirus	1.57 (1.11-2.14)	
Herpes Simplex	0.78 (0.48-1.27)	
Varicella zoster	0.36 (0.19-0.59)	
Confirmed viral meningitis	2.73 (2.13-3.44)	3,220,343 (1,206,963-4,418,424)
<i>S. pneumoniae</i>	1.04 (0.53-1.73)	
<i>N. meningitidis</i>	0.12 (0.04-0.25)	
Confirmed bacterial meningitis	1.24 (0.76-1.87)	4,860,218 (3,728,598-6,358,419)
Unknown aetiology	10.58 (8.4-13.14)	
All meningitis	13.47 (11.55-15.59)	30,675,497 (24,820,493-37,940,889)

Introduction and Purpose

Bacterial meningitis is decreasing in incidence and molecular diagnostics are increasing in popularity. As a result viruses are becoming relatively more important in adult onset meningitis. Recent trends in bacterial, fungal, and mycobacterial meningitis in the UK have been published but there have been no attempts to determine the clinical or economic burden of viral meningitis in UK adults. Identifying the prevalent causes allows for improved clinical care. Knowing the cost of illness helps target resource.

We, therefore, performed a national prospective observational study with the primary aim of determining the incidence and aetiology of viral meningitis in UK adults. As a secondary objective we estimated the direct healthcare costs imposed by meningitis using a detailed patient level resource analysis.



Figure 1: Sites in the UK Meningitis Study

Conclusions

This study provides an estimate of the incidence and cost of viral meningitis in UK adults in the era of declining bacterial meningitis. Recent studies of meningitis in the UK are based on laboratory reports only, missing patients with meningitis who do not have a proven microbiological cause, or those that are not reported^{1,2}. We found that viral meningitis is the most frequent form of meningitis in adults, where a cause is found, with enteroviruses the most common aetiology. Herpes viruses also accounted for a significant amount of disease - twice that of the commonest bacterial cause, *S. pneumoniae*. We estimate the annual incidence of confirmed viral meningitis in UK adults to be almost 3 per 100,000 giving approximately 1400 cases in the UK every year. The incidence of all meningitis, including those with no proven aetiological agent, is 13.5 cases per 100,000 population. Other data sources such as the notification of infectious diseases and hospital episodes statistics underestimate this; reporting 127 and 612 cases respectively for the year 2012^{3,4}.

The detailed resource analysis undertaken in this study allows us to show that although individual patients with bacterial meningitis cost more than those with viral meningitis, the total annualised costs are similar due to the larger numbers of patients with viral meningitis. The resource use was dominated by hospitalisation, accounting for 79% of the total costs. Any intervention that reduces the length of hospital stay offers the potential to significantly decrease the burden imposed on both patients and the health service.

In summary viral meningitis is the major cause of meningitis in UK adults and it imposes a significant economic burden to the NHS much of which could be reduced by decreasing the length of hospitalisation. Given the problems that viral meningitis places on the patients and the health service there is a pressing need to improve and implement rapid diagnostic techniques, deliver viral diagnostics locally, and to develop and evaluate treatments that may allow quicker recovery and more rapid discharge from hospital.

1. Kadambari S, Okike I, Ribeiro S, et al. Seven-fold increase in viral meningo-encephalitis reports in England and Wales during 2004-2013. *J Infect* 2014; **69**(4): 326-32. Okike IO, Ribeiro S, Ramsay M, Heath PT, Sharland M, Ladhani SN. Trends in bacterial, mycobacterial and fungal meningitis in England and Wales 2004-11: an observational study. *Lancet Infect Dis* 2014; **14**: 301-7. 3. Public Health England. Notifiable diseases: historic annual totals. 2016. <https://www.gov.uk/government/publications/notifiable-diseases-historic-annual-totals> (accessed 20th June 2016). 4. Health and Social Care Information Centre. Hospital Episodes Statistics. <http://www.hscic.gov.uk/hes> (accessed June 20th 2016).