Diagnostic uncertainty in children with fever impacts NHS resources

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The management of febrile illness (fever) in children has a substantial impact on National Health Services resources, predominantly due to diagnostic uncertainty resulting from a lack of accurate tests to distinguish between viral and bacterial illness, a new study reports.

Uncertainty over the causes of fever, and associated added cautiousness by clinicians, results in increased observation times, inpatient admissions, and precautionary use of antibiotics, say researchers at the University of Liverpool and Liverpool School of Tropical Medicine.

Published in *BMC Medicine*, the researchers suggest that the development of rapid diagnostic tests to quickly identify life-threatening bacterial infections could significantly reduce the financial burden on the NHS and help avoid unnecessary inconvenience and distress to children and parents.

Precautionary prescription of antibiotics has been associated with increased health service use, predominantly because of increases in patient admission, according to the study, which examined data on 6,518 febrile children presenting to Liverpool's Alder Hey Children's Hospital Emergency Department from 2012 to 2013. The study found that approximately 32.4% of febrile children were prescribed antibiotics, but only 7% were retrospectively diagnosed with bacterial illness that required antibiotic treatment.

The researchers also found that resource use was highest in infants aged 0-3 months, with a mean treatment cost of £1000.28 per patient, which was over 6-fold higher than the group with the least resource use; children aged 3-6 years (£159 per patient).

Other factors associated with increased resource use were patients being identified as needing urgent or immediate attention (high risk), and patients being managed by less experienced doctors.

Professor Enitan Carrol, Chair in Paediatric Infection at the University's Institute of Infection and Global Health, who led the study said: "Fever is a common cause of presentation to paediatric emergency departments, accounting for approximately 20% of all visits. Most children with fever

have self-limiting viral illnesses, however, severe bacterial infections can result in almost identical clinical presentations, making an early clinical diagnosis extremely challenging.

"Because of the catastrophic consequences of missing a potentially life-threatening bacterial infection, a cautious stepped approach to the management of the febrile child is often taken, which involves extended periods of observation, investigations, and the precautionary use of antibiotics, often without definitive evidence of bacterial infections.

"If we can come up with a solution to this diagnostic uncertainty, it will have a positive impact on patient outcomes, on NHS resource use and on antimicrobial resistance."

Health economist Simon Leigh, a Ph.D. student at the Institute of Infection and Global Health and first author on the study said: "Our study highlights the role that new diagnostic tests could play in emergency departments, not only in reducing clinically unnecessary antibiotic use but also in improving the efficiency and appropriateness of the NHS services."

Professor Louis Niessen, Chair of Health Economics at the Liverpool School of Tropical Medicine and the other leading senior author of the paper adds that diagnostic uncertainty in the case of acute fever is universal, including both very young children and also adults. "This is an overlooked global problem and our study indicates that there are major societal resources involved to avoid fatal outcomes. New and better diagnostics, potentially, will have huge benefits for our health services world-wide and all those involved, especially in resource-poor settings."

The work was supported in part by the Personalised Risk assessment in Febrile illness to Optimise Real-life Management across the European Unions (PERFORM) consortium, which seeks to identify and validate

promising new signatures of bacterial and viral infection including transcriptomic, proteomic and clinical phenotype markers, which will help to reduce the diagnostic uncertainty in the assessment of febrile children.

More information: Simon Leigh et al. The cost of diagnostic uncertainty: a prospective economic analysis of febrile children attending an NHS emergency department, *BMC Medicine* (2019). DOI: 10.1186/s12916-019-1275-z

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