# Intravenous immunoglobulin treatment for encephalitis in children aged 6 months to 16 years: the IgNiTE RCT

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## **Disclosure of interests**

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Primary conflicts of interest: Mildred A Iro was a trainee member of the NIHR Efficacy and Mechanism Evaluation Funding Committee from October 2020 to October 2021. Michael Absoud has received a grant from the NIHR in the last 36 months, for research unrelated to the submitted work. Manish Sadarangani has been an investigator on projects funded by GlaxoSmithKline, Merck, Moderna, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo and VBI Vaccines; all funds have been paid to his institute. Ava Easton is Chief Executive of the Encephalitis Society, which has previously received grants from CSL Behring (UK). Ming Lim has received grants from the GOSH charity, Boston Children's Hospital Research Fund and Action Medical Research in the last 36 months, all for research unrelated to the submitted work. Ming Lim is co-chair of the European Paediatric Neurology Education and Training Board and works for an institution which holds research accounts with Roche (Switzerland), Octapharma (Switzerland) and Novartis (Switzerland). Tom Solomon is supported by the NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, NIHR Programme Grant for Applied Research, NIHR Global Health Research on Brain Infections and the European Union's Horizon 2020 research and innovation program ZikaPLAN. Tom Solomon is a consultant for the Medicines and Healthcare products Regulatory Agency (MHRA) Vaccine Benefit Risk Expert Working Group. Angela Vincent is a consultant for Aspen NewCo Inc and has received honoraria from UCB and Alexion. Ly-Mee Yu had membership with NIHR HTA Efficient Study Designs from November 2015 to July 2016. Andrew J Pollard is chair of the Department of Health and Social Care's Joint committee on Vaccines and Immunisation (JCVI) and was a member of WHO's SAGE until 1 January 2022. Oxford University has entered a partnership with AstraZenenca on COVID-19 vaccines, but Andrew J Pollard does not participate in the JCVI COVID-19 committee.

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## Plain language summary

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# Plain language summary

Encephalitis (inflammation of the brain) is a serious but rare condition affecting approximately 5 in 100,000 children in England. Encephalitis can have a big impact on affected children and their families. Approximately 12 out of 100 affected children will die and half of those that survive experience varying difficulties in the long term; these might include problems with memory, physical disabilities, seizures and changes in how they think and behave.

There is some evidence that a treatment called intravenous immunoglobulin may benefit people affected by encephalitis. Intravenous immunoglobulin contains antibodies obtained from blood donations by different people, which is used to treat some types of inflammation. However, there have been no research studies investigating the effect of intravenous immunoglobulin when used in large numbers of children with all types of encephalitis. Furthermore, although intravenous immunoglobulin is sometimes used to treat children with encephalitis, it is often given after other treatments have been unsuccessful. Outcomes from encephalitis are determined largely by the amount of brain inflammation; it would therefore seem logical that giving a treatment early in the illness to limit the inflammation would be beneficial.

In the ImmunoglobuliN in the Treatment of Encephalitis study, we aimed to find out whether giving intravenous immunoglobulin to children with encephalitis early in the illness can help them get better more quickly and reduce the difficulties they experience later on. Half of the children in the trial received intravenous immunoglobulin and the other half received an inactive medicine, known as placebo, in addition to the normal care they would receive in a hospital. We aimed to compare the recovery and outcomes between children in these two groups.

This trial was stopped early due to withdrawal of funding, as fewer children than expected were enrolled into the study. Too few children were enrolled for us to be sure whether intravenous immunoglobulin benefits children with encephalitis. However, the trial findings highlight the impact of encephalitis on affected children, with around half of children demonstrating ongoing difficulties 1 year after the illness.

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