Neonatal infection: a major burden with minimal funding

Further progress in decreasing child mortality depends on reducing the 2·9 million neonatal deaths each year, around a quarter of which are directly due to infection.[1] However, systemic underfunding is limiting research and threatens further advances. The need is great: an estimated 6·9 million neonates required treatment for possible serious bacterial infection in 2012 in high-burden settings,[2] and the Global Burden of Disease Study estimates suggest that neonatal infections account for around 3% of disability-adjusted life-years (DALYs), with insufficient data to estimate long-term disability after sepsis or pneumonia.[3,4]

Even with the limitations in the available data on DALYs, the funding gap is huge. The Research Investments in Global Health study[5] analysed public and philanthropic infectious disease research awards to UK institutions (1997–2013), and compared them to the burden in DALYs,[3] describing a new metric of "investment per DALY observed". The results are stark: neonatal infectious diseases received the lowest investment of all infections, £0·01 per DALY. By contrast, HIV and malaria had investments of £0·46 and £0·34 per DALY (figure, appendix) and some neglected tropical diseases have strikingly high investments—eg, African trypanosomiasis received £9·06 per DALY.

Attracting additional funding and increasing capacity is essential to meet research needs and must be matched with improved scientific reporting; the forthcoming Strengthening Publications Reporting Infections in Newborns Globally (SPRING) standards are an important step towards this goal. However, well funded research in neonatal infection is essential. In health facilities, high quality surveillance data can provide important information on cause[6] and antimicrobial resistance.[7] But such data require significant resources, including strengthening laboratory quality control and assurance measures, and use and appropriate interpretation of molecular diagnostics to detect pathogens (including viruses). More population-based data are needed; these are difficult to acquire because most neonatal deaths occur in the first few hours after birth when access to care may be limited. Results of the Aetiology of Neonatal Infections in South Asia (ANISA) study are awaited, and forthcoming work includes the Child Health and Mortality Prevention Surveillance Network funded by the Bill & Melinda Gates Foundation in south Asia and sub-Saharan Africa.

Preventing infection depends on improving our understanding of maternal health, including maternal colonisation, as well as vertical transmission (HIV, malaria, other congenital infections, and ascending

For the **Child Health and Mortality Prevention Surveillance Network** see http://www.gatesfoundation.org/Media-Center/Press-see Releases/2015/05/Child-Health-and-Mortality-Prevention-Surveillance-Network

See **Online** for appendix

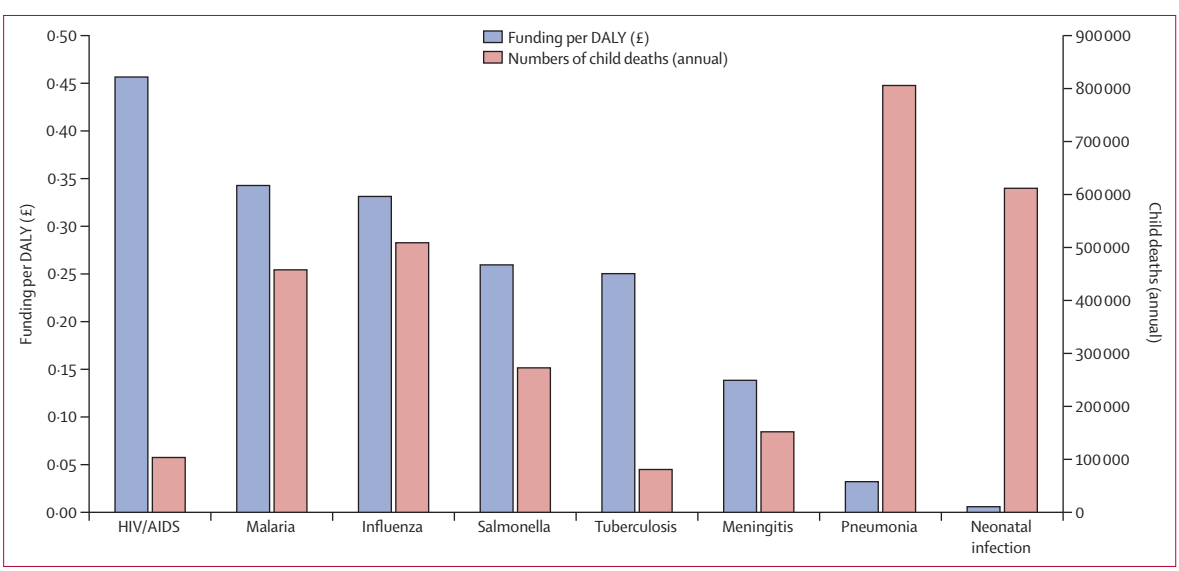

Figure: **UK research investment per DALY per year for infections and number of child deaths in a year for those infections**
The metric illustrates relative levels of investment for each infection and used the following equation (sum investment 1997–2009 / DALYs 2010[3]) / 13 (number of years of investment included). The number of child deaths are given based on Global Burden of Disease estimates for 2013.[11,10]

bacterial infections) and hospital-acquired infections, particularly with multiresistant Gram-negative bacteria. Infection control management is important, and interventions, isolated or as part of care bundles, need detailed, prospective evaluation in outbreak situations, such as those proposed by the International Nosocomial Infection Control Consortium.

For the **International Nosocomial Infection Control Consortium** see http://www.inicc.org/

Improving case management partly depends on improving recognition of danger signs by carers and primary health centres. Clinical algorithms used for diagnosing possible serious bacterial infection could be improved through the use of bedside tests, such as pulse oximetry, as well as point of care tests. Clinical trials have recently examined whether outpatient care can be provided to neonates who are not critically ill and where referral for hospital treatment is not possible.[8] These trials have informed new WHO guidelines.[9] However, further research is needed to determine health-system requirements for implementation, and whether this approach reduces uptake of referral to hospital, which remains the standard of care. There are important bottlenecks in health systems to improving neonatal infection case management,[10] and overcoming these, with appropriate metrics to track neonatal care coverage, are essential. Future trials need to focus on improving mortality outcomes in newborns with sepsis and defining management strategies in settings of varying levels of antimicrobial resistance. The optimum choice of drug, dose, and duration in settings of high resistance to WHO first-line empirical therapy is completely unknown.

A joined-up approach from funders and research institutions is urgently needed to strengthen neonatal infection research. This could be through a formal prioritisation exercise leading to calls for specific research funding to support research on neonatal infection. Developing research capacity worldwide is essential to drive forward measures to reduce deaths[11] and disability from neonatal infection, and to reduce gross inequities in health.

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