Evidence Synthesis Ireland Fellowship Scheme
Review Identification Form

Review Centre/Group Mentors

Review Centre: West Midlands Evidence Synthesis Group (WM-ESG), across Universities of Warwick & Birmingham **Mentors:** Jacqueline Dinnes, Katie Scandrett

Review title

A methodological review of methods and mechanisms for measuring and monitoring outcomes from newborn screening

Review type and methods

Methodological review. This methods review will build on the findings from a currently ongoing NIHR-funded scoping review (phase 1) to identify the breadth and scope of available evidence evaluating newborn screening, including newborn bloodspot screening and genetic screening. The scoping review will identify and describe the different types of approaches that have been used to evaluate the range of outcomes relevant to newborn screening. The results of the review will be used to select the most useful studies for detailed evaluation in the methodological review (phase 2). ESI Fellows reviewer will be expected to conduct title and abstract screening and full text assessment of any additional searches that are carried out for phase 2, to contribute to critical appraisal, data extraction and synthesis.

Review information

This review is through the West Midlands Evidence Synthesis Group (WM-ESG), funded by NIHR Evidence Synthesis Programme (NIHR ESP), and commissioned by the UK National Screening Committee (NSC).

Review details

Background: Newborn screening programmes across the world screen for various rare diseases in newborns, often using a newborn blood spot (NBS) test. Current research is considering use of

genomic testing as a screening strategy. In the United Kingdom (UK), newborns are screened for nine rare genetic conditions using a NBS test. Whilst data on process measures (number screened, timeliness of screening, yield, etc.) confirms that the UK NBS programme is operating efficiently, the net benefit on patients and their families is less clear. There is also a lack of evidence to inform decisions regarding candidates for additions to current screening programmes. Outcomes associated with screening programmes that could be measured range from epidemiological outcomes such as incidence and prevalence, to natural history outcomes tracking the course of disease, test accuracy, and clinical and educational outcomes following treatment or surveillance. Due to difficulties in conducting randomised controlled trials (RCTs) for rare diseases, most studies evaluating relevant outcomes are likely to be observational, so it is important to identify appropriate methods and mechanisms that could be used to collect outcome data. To understand which methods may be most appropriate, we must first understand which methods are currently being used.

Aim: To conduct an in-depth methodological review of studies reporting different methods and mechanisms to measure and monitor outcomes from existing or candidate newborn screening programmes. This review will follow on from a scoping review to identify the breadth of available evidence. Our review objectives are to summarise and critically appraise evidence on the following:

- the study designs, their respective objectives and data sources used
- the populations in which the outcomes (short-term and long-term) have been assessed
- the outcomes included in the relevant studies, including outcomes evaluated in older children, adolescents and adults
- identify evaluation approaches which provide the information required to inform UK NSC decision making

Methods: This methodological review will be structured in accordance with PRISMA reporting guidelines. Primary electronic searches have been developed and conducted by an experienced information specialist. Search results were screened for phase 1 of the project according to eligibility criteria following a SPIDER framework (Sample, Phenomenon of Interest, Design, Evaluation, Research type) as specified by the UK National Screening Committee (NSC). Follow-on searches using citation searching or snowball searches may be needed for phase 2. Any title and abstract or full text screening will be performed by one review author and a random sample of 20% will be independently screened in duplicate by a second review author. A data extraction form will be piloted on five studies. Data extraction will be conducted by one author, and a random sample of 20% of data extractions will be done independently in duplicate. All results will be described narratively. Methods and mechanisms will be grouped into categories, and we will synthesise evidence based on these categories. Outcomes will be grouped thematically (epidemiological, natural history, test accuracy, clinical, educational) within each methods/mechanism category.

Review current status

The scoping review (phase 1) is ongoing and due for completion by end March 2025. The phase two methodological review will follow directly after. The protocol for the scoping review has been uploaded to OSF (https://doi.org/10.17605/OSF.IO/U2JCZ).

Any specific/desirable requirements for fellow (e.g. clinical expertise, methodological expertise)

A basic understanding of research methods and study designs is required. An interest in screening would be desirable.

Estimated start and completion dates

Fellows could start in March or April 2025