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Title **Clinical Effectiveness of Newborn Screening for Inborn Errors of Metabolism using Mass Spectrometry. Part IV: 3-hydroxy-3-methyl glutaric aciduria (HMG) and β-Kethiolase deficiency (BKT).**

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Reference Cantero Muñoz P, Paz Valiñas L, Atienza Merino G. Clinical Effectiveness of Newborn Screening for Inborn Errors of Metabolism using Mass Spectrometry. Part IV: 3-hydroxy-3-methyl glutaric aciduria (HMG) and β-Kethiolase deficiency (BKT). Santiago de Compostela: Agencia de Evaluación de Tecnologías Sanitarias de Galicia, avalia-t; 2015. Report No.: avalia-t 2015/04. Available from: http://avalia-t.sergas.es/DXerais/564/avalia-t201504CribadoNeonatalParteIV.pdf

Aim

To assess the clinical effectiveness of newborn screening of the following diseases: 3-hydroxy-3-methyl glutaric aciduria (HMG) and β-Kethiolase deficiency (BKT).

Conclusions and results

- Evidence of the effectiveness of HMG- and BKT-deficiency screening programmes was of low quality, and was based on observational-type studies without a control group, basically case series.
- 3-hydroxy-3-methylglutaric aciduria has a long enough latency period to ensure that implementation of the complete screening process would be feasible. However, the disease's natural history is not properly known because there is no clear genotype-phenotype relationship, thus rendering it extremely difficult to predict precisely what percentage of patients will really develop the disease. Similarly, there is insufficient evidence to show the effectiveness of screening in terms of reducing mortality or morbidity, or that administration of the treatment in the latency or asymptomatic stage would be more beneficial.
- While beta-ketothiolase deficiency also has an adequate latency period, inasmuch as onset in the neonatal stage is extremely infrequent, it does not fulfil some of the principal requirements for implementation, i.e., severe disease or important health problem (incidence/prevalence <1:1 000 000 RN) or clear knowledge of the natural history of the disease. Furthermore, evidence of the screening test's usefulness is not only insufficient, but also exhibits certain limitations.
- Lastly, it is essential that all screening programmes, national and regional alike, comply with the goals, quality standards and information system established by the Public Health Committee Work Group for development of the Newborn Screening Information System: this would ensure proper follow-up and assessment of results.

Methods

Systematic literature review of the principal biomedical databases: Medline, Embase, Cochrane Library Plus, HTA, DARE, NHSEED, ISI Web of Science and Scopus, among others. Two search strategies were used, one centred on epidemiology, natural history, morbidity, mortality, diagnosis and treatment, and the other centred on the screening of each disease. To retrieve all existing systematic reviews and assessment reports on screening programmes, we updated the bibliographic searches of the *avalia-t* reports until Febrary 2015. Studies were selected on the basis of a series of inclusion/exclusion criteria. This procedure was completed by a manual review of the bibliographic references cited in the papers selected. As final conclusions, the 18 national screening criteria set out in the "Framework Document" were answered. These criteria provide guidance for strategic decision to implement screening population programs.

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