Newborn screening for congenital adrenal hyperplasia. Systematic Review
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Record Status
This is a bibliographic record of a published health technology assessment from a member of INAHTA. No evaluation of the quality of this assessment has been made for the HTA database.

Citation

Authors' objectives
The main objective was to assess both the efficacy/effectiveness and safety of neonatal screening of the classic form of congenital adrenal hyperplasia (CAH) and the analytical validity of the screening test sensitivity, specificity and predictive values. As a secondary objective, the disease's incidence/prevalence, natural history, prognosis, morbidity-mortality and early treatment were also analysed. The end purpose was to address the screening principles contained in the "Population Screening Framework Document", which was drawn up by the Population Screening Board on behalf of all of Spain's Autonomous Regions (Comunidades Autónomas) and was approved by the Public Health Committee of the National Health System Interterritorial Council.

Authors' conclusions
Classic CAH is an important health problem whose incidence in Europe ranges from 1:975 to 1:16,964 newborns, with the ratio for Spain estimated to be 1:16,441. Salt-wasting forms register a high morbidity-mortality if not treated in time. This form of the disease is potentially lethal, with the studies located reporting a mortality rate due to adrenal crises in unscreened newborns of 4% to 11.9%. Early diagnosis and treatment is crucial to prevent these crises, which can prove life-threatening and have irreversible sequelae, such as intellectual impairment due to brain damage. Hence, the screening priority is to detect such cases before the appearance of clinical symptoms. Clinical diagnosis is more complicated in the case of males, since they do not present with ambiguous genitalia. Although 17-OHP analysis may be an effective tool for early detection of CAH, it is nevertheless a test with a high FP rate and with values that are difficult to interpret. The cut points used for this test by the various screening programmes varied widely and depended on different factors, such as method of analytical determination, antibodies used, gestational age, birth weight or sample date (postnatal age). Among other criteria, justification for CAH screening is based on the fact that early detection of the classic salt-wasting form (before clinical symptoms), followed by immediate treatment, can prevent adrenal crises and, by extension, the related mortality and morbidity. The studies retrieved were of moderate-low quality. Although screening is reported to be able to prevent mortality from salt-wasting forms, most of the studies furnish no data on this outcome variable or are based on hypothetical data which suggest that screening could prevent 74%-86% of the mortality due to this disease. Arguments in favour of screening are mainly based on: -- preventing adrenal crises marked by potentially lethal saline loss and major irreversible sequelae; -- there are fewer instances of hyponatraemia in newborns detected by screening versus those detected by clinical diagnosis; -- preventing erroneous assignment of sex in girls with the simple virilising form; -- preventing hyperandrogenisation through early diagnosis of the simple virilising forms; and, -- reducing stress in the families of the children detected and time of hospitalisation thanks to early diagnosis. Arguments against screening point to a number of drawbacks: -- there is poor evidence to indicate a reduction in morbidity-mortality and, moreover, it is of moderate-low quality; -- the latency period of the salt-wasting forms is short, so that early clinical onset could occur in cases where screening results are delayed; -- there is neither a standard protocol nor consensus as to the cutoffs for interpretation of the analytical test; -- difficult interpretation of results due to cross-reactions, particularly among premature newborns; low PPV of the DELFIA® analytical method, which entails unnecessary follow-up of a high number of FPs; -- identification of asymptomatic patients, among whom the possible adverse effects of the treatment are unknown; and, -- it does not identify all patients with moderate forms of classic CAH. Before any new metabolic disorder is implemented within the context of an already established neonatal screening programme, its feasibility in the light of available resources must be ensured in order to guarantee a quality programme that will afford coverage at all stages, including treatment. In the case of classic salt-wasting CAH,
there must be no delay in early diagnosis before the possible onset of clinical signs and symptoms, to ensure that the neonate obtains the full benefit of screening in terms of a reduction in mortality and the irreversible sequelae of adrenal crises.

**Final publication URL**
https://catalogobibliosaude.sergas.es/ASSCC711S_Linked_Documents/avalia-t201305CribadoHiperplasia.pdf

**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
Humans; Infant, Newborn; Adrenal Hyperplasia, Congenital; Neonatal Screening

**Language Published**
Spanish

**Country of organisation**
Spain

**English summary**
An English language summary is available.

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**AccessionNumber**
32014000950

**Date abstract record published**
01/08/2014