

**BRITISH PAEDIATRIC SURVEILLANCE UNIT**

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## **UK Surveillance of Primary Congenital Hypothyroidism in Children Aged Five Years and Under (UKCHT)**

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<b>Abstract</b>	This UK study aims to determine how many babies and children up to and including five years of age are found each year to have primary congenital hypothyroidism (CHT), diagnosed subsequent to a presumed positive newborn screening test or because of clinical manifestations. We will describe their characteristics, diagnostic tests and initial treatment. We will collect additional information about each child's health after one and two years, particularly to define transient cases. In a population covered by newborn screening, this study will enable us to determine the incidence and characteristics of children diagnosed with primary congenital hypothyroidism, the proportion and outcomes of those detected by screening as well as to describe variations in clinical management and care.
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<b>Website</b>	<a href="http://www.rcpch.ac.uk/what-we-do/bpsu/current-studies/CHT">www.rcpch.ac.uk/what-we-do/bpsu/current-studies/CHT</a>
<b>Background</b>	Primary congenital hypothyroidism (CHT) is a disorder involving reduced thyroxine production by the thyroid gland. This may be due to an abnormally sited or absent thyroid gland or a failure of hormone production within the gland. Babies with CHT may have feeding difficulties, sleepiness, constipation and jaundice. Infants, who do not start treatment with replacement oral thyroxine therapy soon after birth, may have problems with their mental development and growth. Around 200 babies with CHT are born in the UK each year and most are detected by newborn bloodspot (heel-prick) screening. Although newborn screening for CHT started in 1981, we do not know how successful it is in identifying babies who require lifelong therapy.
<b>Coverage</b>	United Kingdom
<b>Duration</b>	June 2011 – June 2012 (13 months of surveillance). Follow-up until June 2014.
<b>Research Questions</b>	Specific aims of the study are to: <ol style="list-style-type: none"><li>1. Determine the incidence in the UK of confirmed diagnoses of primary CHT in children up to and including age five years and report the distribution by age, sex and ethnic group.</li><li>2. Report the clinical features at presentation and describe variations in referral and clinical management including initiation of replacement therapy.</li><li>3. Describe clinical outcomes at one and two years post-diagnosis, including the proportion of infants who are recognised to have transient hypothyroidism.</li><li>4. Evaluate performance of the newborn screening test for CHT, including estimation of confirmed cases as a proportion of referrals for confirmatory tests following screening results suggestive of CHT and of late diagnoses up to five years of age.</li></ol>
<b>Case definition</b>	Any child up to and including five years of age who, during the past month, has been referred EITHER for diagnostic confirmation following a newborn screening test result suggestive of primary CHT, OR has been confirmed with a diagnosis of primary CHT (known or considered likely to be present from birth), based on a serum TSH $\geq 10\text{mU/l}$ .

## Reporting instructions

Please report any child up to and including 5 years of age who, during the past month, has

- a. been referred for diagnostic confirmation following a newborn screening test result suggestive of primary CHT,
- OR
- b. been confirmed with a diagnosis of primary CHT (known or considered likely to be present from birth), based on a serum TSH  $\geq 10$ mU/l.

*Please do not report children in whom it is confirmed that they have:*

- Secondary CHT due to pituitary under-production of TSH;
- Acquired hypothyroidism.

**If in doubt, or awaiting further tests, please report the child.**

## Methods

### *Surveillance*

Active national surveillance of all children who fulfil the case definition will be undertaken through the BPSU and UK Newborn Screening Laboratory Network. We aim to identify all babies with a positive screening test result including those who are negative for CHT on further diagnostic testing, as well as children who present clinically with CHT (and therefore possibly 'missed' by screening). This will allow us to evaluate the performance of the current newborn screening programme and also to examine the relationship between a positive screening test result, confirmation of diagnosis and the impact of variations in local screening laboratory TSH thresholds.

Children with a confirmed diagnosis of primary CHT or who commence replacement therapy, will be followed up at one and two years after diagnosis to determine whether treatment is still required, as well as to appraise longer-term outcomes and variations in clinical management.

### *Questionnaires*

We will send questionnaires to collect demographic and clinical data, including sex, date of birth, screening test results, results of diagnostic testing, gestation and weight at birth and clinical features at the time of presentation. Clinicians who notify children with a confirmed diagnosis of primary CHT (or taking regular thyroxine replacement therapy), will be sent further questionnaires at one and two years after diagnosis, to assess whether CHT is permanent and to appraise longer-term clinical outcomes.

We propose to use an online, electronic questionnaire to simplify data entry and collection. Data will be entered directly through this system and sent to the study team via an encrypted link. This methodology has been approved as secure by the NIGB.

### *Long-term follow-up*

We have been granted NIGB approval to collect and store NHS numbers, sex and date of birth beyond the surveillance period so that these are available for future analysis of outcomes using record linkage, for example using routinely collected hospital episodes statistics (HES) data. However, any future record linkage would constitute an independent study for which appropriate research ethics and NIGB approvals would be sought.

## Ethics approval

This study has been approved by Cambridge South REC (Ref: 11/EE/0152) and has been granted Section 251 NIGB permission under reference: ECC 3-04(k)/2011.

## Funding

UK NHS Newborn Screening Programme Centre (Department of Health)

## Collaborators

UK NHS Newborn Screening Programme, British Society of Paediatric Endocrinology and Diabetes (BSPED), UK Newborn Screening Laboratory Network (UKNSLN), British Thyroid Foundation (BTF)

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