Supplementary Table S1: Characteristics of 21 children who were clinically detected

Sex	Gestation (weeks)	Clinical presentation	Bloodspot TSH (mU/L)	Serum TSH (mU/L)	Began treatment	Outcome at 3 years
F	≥37	Jaundice	3	9	yes	Confirmed permanent CH (trial off therapy)
F	≥37	Congenital anomaly	1	-	yes	Confirmed permanent CH (trial off therapy)
F	≥37	Suspected before screen; Family history	7	15	yes	Confirmed permanent CH (high dose thyroxine)
M	<32	Sick neonate	1	-	yes	Confirmed permanent CH (trial off therapy)
F	32-37	Jaundice; Family history	3	13	yes	Probably permanent CH
M	<32	Jaundice	1	13	yes	Probably permanent CH
M	≥37	Jaundice	5	15	yes	Probably permanent CH
F	≥37	Jaundice	5	14	yes	Probably permanent CH
M	32-37	Congenital anomaly	4	9	yes	Probably permanent CH
M	<32	Sick neonate	1	29	yes	Probably permanent CH
F	<32	Congenital anomaly	4	47	yes	Probably permanent CH
M	32-37	Suspected before screen; Sick neonate	8	16	yes	Probably permanent CH
F	≥37	Suspected before screen; Congenital anomaly	40	100	yes	Probably permanent CH
M	≥37	Suspected before screen; Family history	20	98	yes	Probably permanent CH
M	<32	Congenital anomaly	2	4	yes	Not CH (trial off therapy)
M	32-37	Congenital anomaly	-	14	yes	Not CH (trial off therapy)
F	≥37	Jaundice	4	34	yes	Not CH (trial off therapy)
F	≥37	Congenital anomaly	-	16	yes	Not CH (clinical evaluation)
M	≥37	Poor growth	-	55	yes	Not CH (clinical evaluation)
F	32-37	Congenital anomaly	-	16	yes	Not CH (clinical evaluation)
F	<32	Sick neonate	14	21	no	Not CH (clinical evaluation)

Abbreviations TSH thyroid stimulating hormone; **M** male; **F** female; **CH** congenital hypothyroidism

Supplementary Table S2: Screening programme performance at different test cut-offs for a hypothetical population of 100,000 infants

	Screening performance – comparing cut-offs*								
	Group 1** Actual population screened n=315944				Group 2** Actual population screened n=125886			Group 3** Actual population screened n=252028	
TSH (mU/L)	≥6	≥8	≥10	>20	≥8	≥10	>20	≥10	>20
Standardised population of screened infants (n)	**100,000†**				**100,000†**			**100,000†**	
Expected cases (n)	57				57#			57##	
Positive screen result (n)	**90**	**63**	**55**	**44**	**75**	**61**	**51**	**67**	**54**
True positives (n)	56	49	45	38	55	48	41	48	43
False positives (n)	34	14	10	6	20	13	10	19	11
Negative screen result (n)	**99910**	**99937**	**99945**	**99956**	**99925**	**99939**	**99949**	**99933**	**99946**
False negatives (n)	1	8	12	19	2	9	16	9	14
True negatives (n)	99909	99929	99933	99937	99923	99930	99933	99924	99932
Detection rate (%)	**98.2%**	**86.0%**	**79.0%**	**66.7%**	**96.5%**	**84.2%**	**71.9%**	**84.2%**	**75.4%**
PPV (%)	**62.2%**	**77.8%**	**81.8%**	**86.4%**	**73.3%**	**78.7%**	**80.4%**	**71.6%**	**79.3%**
False positive rate (%)	**0.03%**	**0.01%**	**0.01%**	**0.01%**	**0.02%**	**0.01%**	**0.01%**	**0.02%**	**0.01%**

Notes *based on 13 newborn screening laboratories in England; screening programme coverage for 2011-2012 was 86%; PPV=positive predictive value;

Group 1 included 6 laboratories of which 1 used a threshold of ≥5mU/L and 5 used a threshold of ≥6mU/L; Group 2 included 3 laboratories, all using a threshold of ≥8mU/L; Group 3 included 4 laboratories, all using a threshold of ≥10mU/L. As exact values for TSH are not provided for negative screen results, these were reported only as 'negative', therefore estimates can only be made of screening performance at a cut-off TSH ≥6mU/L for Group 1 (and not for Groups 2 and 3).

** The percentage who were of white ethnicity were 68% in Group 1, 79% in Group 2 and 70% in Group 3

† 100,000 live births **directly standardised**[15] using the actual English population profile (by sex, ethnicity and gestation) for 2011-2012

1 additional false negative to account for case detected at cut-off of 6 in Group 1

2 additional false negatives to account for cases detected at cut-off of 6 in Group 1

Total number of babies screened (Tables S1 and S2) is greater (n=110 [0.01% of 800,000) than the total English live births reported in Table 3 as the data sources varied. This is because the denominator in Table 3 was from monthly figures provided by the Office for National Statistics for *live births* occurring in England, while the 'screened population' denominator in Tables S1 and S2 was provided by the screening programme from annual reporting of babies *screened* in England. The minor discrepancy may be due to several reasons, including some births occurring outside England but being screened in England in border areas, or inaccuracies in national reporting systems. The relevant denominator was therefore used for each table.

Supplementary Table S3: Children who would have been missed at the national screening cut-off TSH≥10mU/L

	Gestation	Bloodspot TSH (mU/L)	Serum TSH (mU/L)	SerumT4 (pmol/L)	Confounding factors	Scan	CH confirmation
Children who would be detected at TSH≥6mU/L but not at TSH≥8mU/L							
A	≥37 weeks	6.3	50.5	13.7	Congenital syndrome	Abnormal	Agenesis (scan)
B	≥37 weeks	6.8	16.4	17.0	None	Normal	Trial-off therapy
C	≥37 weeks	7.8	22.0	NK	None	Abnormal	Trial-off therapy
D	≥37 weeks	7.0	64.2	14.4	None	Abnormal	Trial-off therapy
Children who would be detected at TSH≥8mU/L but not at TSH≥10mU/L							
E	<32 weeks	8.0	NK	NK	None	Normal	Trial-off therapy
F	≥37 weeks	8.0	51.8	19.0	None	Abnormal	High dose thyroxine
G	<32 weeks	9.3	NK	3.6	None	Normal	Trial-off therapy
H	≥37 weeks	9.3	20.3	12.4	None	Abnormal	Trial-off therapy
J	32-37 weeks	9.9	17.6	NK	None	No scan	High dose thyroxine
K	≥37 weeks	9.9	16.0	13.0	None	Abnormal	High dose thyroxine

Notes Total screened population (Groups 1 and 2) of 441830 newborns. TSH and T4 levels were those recorded at initial clinical referral after a positive screening result. Abnormal scans showed avid or poor uptake and were suggestive of dyshormonogenesis, except for the scan confirming agenesis.
Abbreviations TSH thyroid stimulating hormone; **CH** congenital hypothyroidism; **NK** not known (information not found in medical records)