CHANGING TRENDS IN AGE AT GUTHRIE SAMPLING, LABORATORY TESTING AND NOTIFICATION WITH TSH ELEVATION ON NEWBORN SCREENING FOR CONGENITAL HYPOTHYROIDISM

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INTRODUCTION

Effective newborn screening service depends on: timely sampling

- An adequate sample transport system
- Prompt laboratory testing
- Efficient communication of results to the clinician
- Early clinical review and (if necessary) treatment.
- Previous audits of the Scottish programme have highlighted problems with late initial capillary TSH sampling, particularly in sick infants[1] and delay between initial and recall sampling[2]
- This analysis of the thyroid screening programme in Scotland focuses on trends in age at initial screening, interval between initial sample and laboratory processing, and age of notification after single screening and second screening.

PATIENTS AND METHODS

- The Scottish Congenital Hypothyroid database (held since 1979) was interrogated for age (days) at first newborn "Guthrie" screening test (G1), age at laboratory receipt/testing, notification and start of treatment; and age at second "Guthrie" test (G2).
- Trends were analysed by comparing **SEVEN** time periods: 1980-4, 1985-9, 1990-4, 1995-1999, 2000-2004; 2005-2009; and 2010-13.
- Patients were grouped into 4 categories: definite congenital hypothyroidism; probable congenital hypothyroidism; status uncertain; and transient TSH elevation as previously described1,2,3.
- Data are expressed as median, mean ± standard error of the mean (SEM), lower quartile (Q1) and upper quartile (Q3).
- The following standards were set:

- Age at first "Guthrie" (G1) 4-7 days
- Interval between G1 and testing by laboratory 4 days
- Interval between G1 and notification 7 days
- Age of notification after single sampling 14 days
- Age at notification for infants requiring 2nd sampling 26 days

RESULTS 1

Between 1980 and 2013 2,071,759 newborns were screened and 903 infants were referred with capillary TSH elevation: 609 with definite congenital hypothyroidism, 15 with probable congenital hypothyroidism, 45 with status uncertain, 200 with transient TSH elevation, and 34 with insufficient data.

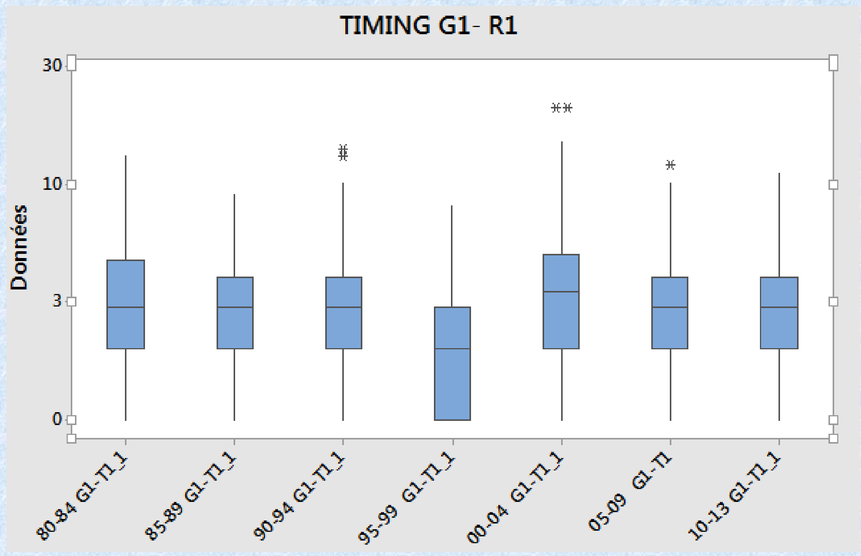
TABLE 1: AGE AT INITIAL SAMPLING (G1) FOR ALL PATIENTS (STANDARD 4-7 DAYS)

PERIOD	Patients (n)	G1 4-7 days number and percentage		G1 8-10 days number and percentage		Patients G1 ≥ 7 days	
						Day	number
1980-1984	95	68	71,5%	27	28,4 %	7D	13
						8D	13
						9D	8
						10 D	6
1985-1989	147	120	81,6%	27	18,4 %	7D	31
						8D	9
						9D	13
						10 D	5
1990-1994	119	95	79,8%	24	20,2 %	7D	25
						8D	10
						9D	11
						10 D	3
1995-1999	112	98	87,5%	14	12,5 %	7D	16
						8D	6
						9D	7
						10 D	1
2000-2004	150	136	90,6%	14	9,4 %	7D	22
						8D	9
						9D	5
						10 D	0
2005-2009	156	149	95,5%	7	4,5 %	7D	8
						8D	3
						9D	3
						10 D	1
2010-2013	118	115	97,4%	3	2,6 %	7D	3
						8D	0
						9D	1
						10 D	2

Age at initial sampling shows a marked drop in infants sampled late (>7 days), with 22, 8 and 3 between 2000-2004, 2005-2009 and 2010-2013 respectively.

RESULTS 2

FIGURE 1 – INTERVAL BETWEEN INITIAL SAMPLE (G1) AND RECEIPT (ALL PATIENTS)



Box and whisker plot showing that interquartile intervals between initial samping (G1) and receipt/testing by the laboratory are within the standard. However interval is still > 4 days in some patients, eg. 19/150 (12.6%) infants between 2000-2004, 15/156 (9.6%) between 2005-2009 and 13/118 (11%) between 2010-13.

TABLE 2: NOTIFICATION AFTER SINGLE SAMPLING (ALL PATIENTS). REQUIRED STANDARD = 14 DAYS

PERIOD	All Patients (n)	Patients with single sampling (n)	Median (Min-Max) age notified in days	Notification Mean +/-SEM (Q1-Q3)	Patients ≤ 14 Day (n)	Patients 14 Day (n)	Patients >14 Day (n)
1980-1984	95	84	13 (7- 59)	14,15 ± 0,68 (11- 16)	53 (63%)	6 (7,1%)	31 (37%)
1985-1989	147	116	12 (6 -52)	13,38 ± 0,65 (10 -14)	91 (78,4%)	11 (9,4%)	23 (19,8%)
1990-1994	119	98	11 (5- 54)	12,56 ± 0,7 (10- 13)	82 (83,6%)	6 (6,1%)	15 (15,3%)
1995-1999	112	82	9 (3 - 34)	10,3 ± 0,51 (8 -11)	76 (92,6%)	3 (3,6%)	4 (4,8%)
2000-2004	150	100	11 (6 -78)	13,66 ± 0,92 (10- 14)	75 (75%)	4 (4%)	24 (24%)
2005-2009	156	110	11 (7 - 52)	11,8 ± 0,5 (9- 13)	101 (91,8%)	9 (8,1%)	8 (7,2%)
2010-2013	118	81	10 (7 -32)	10,8 ± 0,4 (9- 12)	73 (90,1%)	3 (3,7%)	5 (6,1%)

Median and mean ages at notification are well within the standard of 14 days. During 2000-2004, 2005-2009, and 2010-2013 24 (24%), 8 (7.2%) and 5 (6.1%) infants were notified later than 14 days

TABLE 3: AGE AT NOTIFICATION FOR INFANTS REQUIRING SECOND SAMPLING. REQUIRED STANDARD 26 DAYS

PERIOD	All Patients (n)	Patients requiring second sampling (n)	Median (Min-Max) age notified in days	Notification Mean ± SEM (Q1-Q3)	Patients ≤ 26 Day (n)	Patients 26 Day (n)	Patients >26 Day (n)
1980-1984	95	11	18 (11-41)	20,2 ± 2,95 (13,25- 26)	6 (54,5%)	3 (27,2%)	2 (18,1%)
1985-1989	147	32	20 (9-38)	19,81 ± 1,5 (11,25-25)	22 (68,7%)	3 (9,3%)	7 (21,8%)
1990-1994	119	21	23 (10-52)	25 ± 2,97 (16,5-29,5)	15 (71,4%)	1 (4,7%)	6 (28,5%)
1995-1999	112	30	22 (15-38)	20,90 ± 1,46 (15,5 -24,5)	23 (76,6%)	0 (0%)	6 (20%)
2000-2004	150	51	15 (11-60)	18,31 ± 1,66 (10 -22)	44 (86,2%)	1 (2%)	7 (13,7%)
2005-2009	156	46	21 (10-70)	23,3 ± 1,85 (16 -26)	36 (78,2%)	2 (4,3%)	10 (21,7%)
2010-2013	118	37	19 (16-131)	23,16 ± 3,17 (16 - 24)	31 (83,7%)	1 (2,7%)	6 (16,2%)

The trend is less satisfactory for the smaller number of infants requiring second sampling - 7/51 (13.7%), 10/46 (21.7%) and 6/37 (16.2%) of infants were notified beyond the standard age of 26 days between 2000-2004, 2005-2009 and 2010-2013.

RESULTS 3

TABLE 4: PATIENTS WITH TRUE CH (DEFINITE AND PROBABLE)

PERIOD	Patients (n)	Median (range) age at G1 in days	Median (range) age at receipt in days	Median (range) age at notification in days	Median age (range) at start of thyroxine in days	Patients starting thyroxine (n)
1980-1984	81	7 (4-56)	10 (6-62)	13 (7-59)	16 (8-313)	74
1985-1989	91	6 (4-35)	9,5 (6-42)	12 (8-43)	13 (8-212)	82
1990-1994	85	6 (4-49)	9 (5-51)	10 (5-54)	12 (2-195)	79
1995-1999	88	6 (1-13)	8 (4-21)	10 (5-38)	11 (1-177)	82
2000-2004	90	6 (4-17)	10 (5-24)	11 (7-31)	12 (7-200)	85
2005-2009	104	5 (1-12)	8 (4-13)	11 (5-56)	12 (1-94)	96
2010-2013	82	5 (4-15)	8 (5-17)	10,5 (7-32)	11 (1-48)	70

Infants with definite and probable hypothyroidism (in whom TSH elevation is greater) show encouraging trends in sample receipt, notification and start of L-T4 treatment. E.g. from 2010-2013 median and range ages at notification and start of treatment have reduced to 10.5 (7-32) and 11 (1-48) days compared with 11 (5-56) and 12 (1-94) between 2004-2009.

DISCUSSION

- Virtually all infants referred with TSH elevation in Scotland now undergo initial testing within 4-7 days.
- Although the laboratory is able to start processing samples within 4 days in most cases, about 10% of infants are processed later than this.
- Sending samples by express mail rather than first class post in all Scottish newborns would be too costly but reducing the age at testing to 3-4 days should be considered.
- Recent Scottish quality indicators have stated that a baby should be seen by the clinician on day 14 of life after single sample, and by day 21 for infants referred after a second sample. Scrutiny of our time lines for transport of samples to the laboratory and notification of results led us to select a target age of 26 rather than 21 days for these infants
- Age at notification is usually well within the 14 day standard for first sample referrals, particularly in true congenital hypothyroidism.
- However, for second sampling 13-21% of infants have failed to meet the extended target of 26 days during the past 13 years
- Strategies are needed to reduce the interval between first and second sampling. These include the compulsory use of either email or telephone when second samples are required.

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