Establishing population and gestational age specific TSH reference intervals for common methods in Australia using the transference technique

Zhong X Lu[1,2,3], Christine A Houlihan[4,5], Elif I Ekinci[4,6], Wei-Ling Chiu[4], Que Lam[7], Alan R McNeil[8], James CG Doery[2,3], and Ken A Sikaris[1,9]
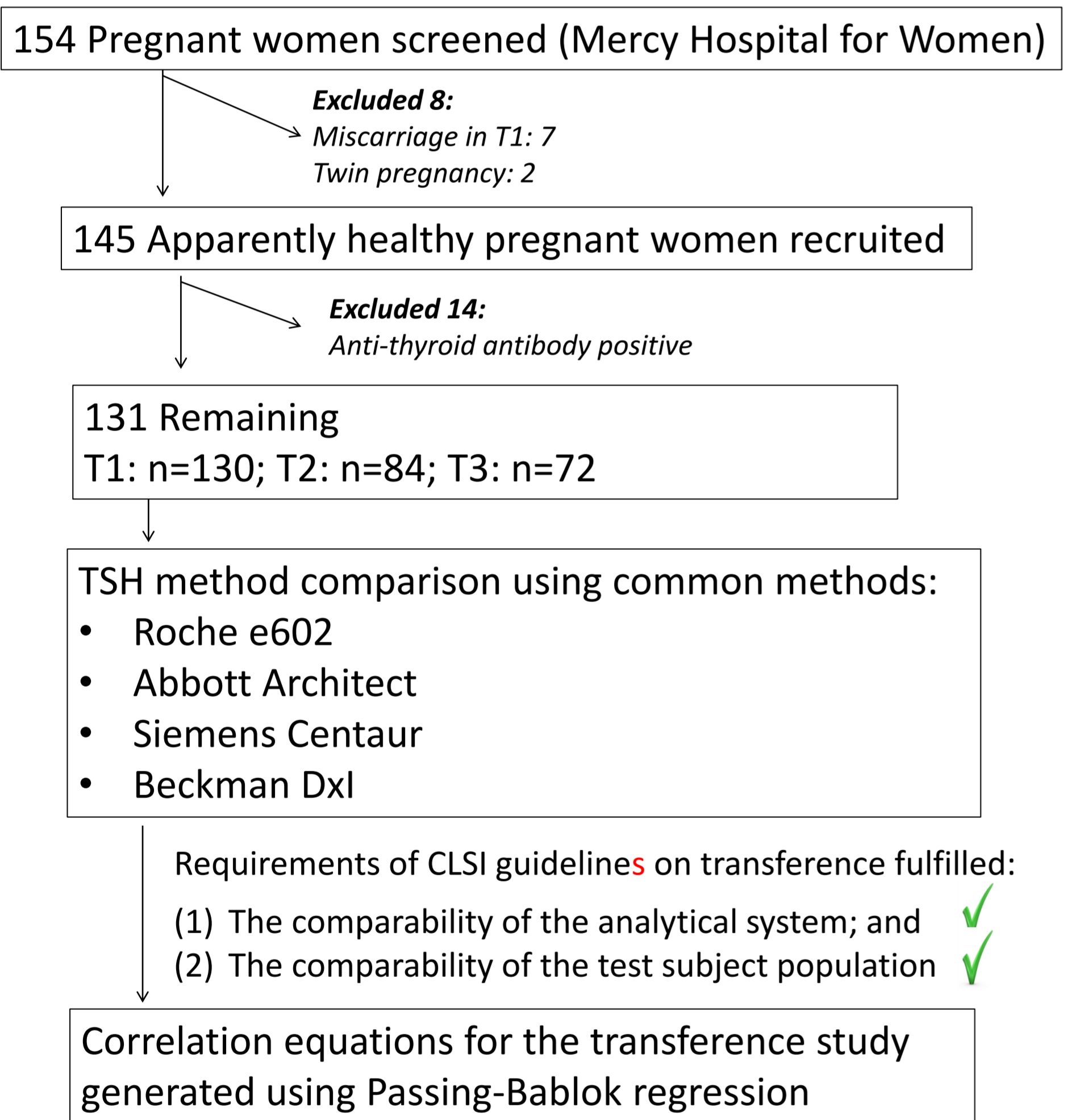
[1]Department of Chemical Pathology, Melbourne Pathology, Collingwood, Victoria; [2]Biochemistry, Monash Pathology and [3]Department of Medicine, Monash University, Clayton, Victoria; [4]Department of Endocrinology and [7]Biochemistry, Austin health, Victoria; [5]Mercy Hospital for Women, Heidelberg, Victoria; [8]Biochemistry, Dorevitch Pathology, Heidelberg, Victoria. [6]Department of Medicine and [9]Department of Pathology, Melbourne University, Parkville, Victoria, Australia.

2017 ATA guidelines recommend using trimester- and method-specific TSH reference intervals defined in local populations. We used the transference technique to convert Roche TSH intervals to other common methods.

Methods

Population and gestational age-specific intervals for TSH by the Roche e602 method were established by mining data using local data from the Melbourne Pathology database[1] (see poster number 101).

An equation for the transference method was obtained using specimens collected from healthy pregnant women who participated in a longitudinal study of thyroid function in pregnancy[2]. Details of subject recruitment and method comparison are shown below:

154 Pregnant women screened (Mercy Hospital for Women)

> **Excluded 8:**
> Miscarriage in T1: 7
> Twin pregnancy: 2

145 Apparently healthy pregnant women recruited

> **Excluded 14:**
> Anti-thyroid antibody positive

131 Remaining
T1: n=130; T2: n=84; T3: n=72

TSH method comparison using common methods:
- Roche e602
- Abbott Architect
- Siemens Centaur
- Beckman DxI

Requirements of CLSI guidelines on transference fulfilled:
(1) The comparability of the analytical system; and ✓
(2) The comparability of the test subject population ✓

Correlation equations for the transference study generated using Passing-Bablok regression

The correlation equations were then applied to Roche TSH reference intervals (obtained by data mining[1]) to generate reference intervals for the other methods according the CLSI guidelines on transference[3].

Gestational age partitioning (weeks of gestation):
1st Trimester (T1): ≤ 13; (Early T1: 4-6; Late T1: 7-13);
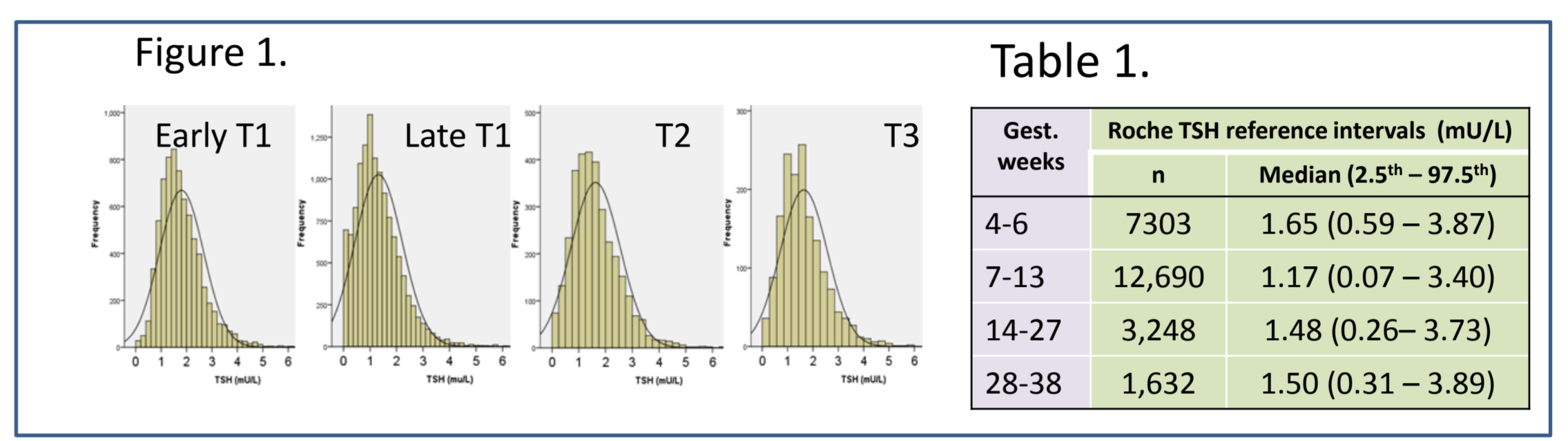2nd trimester (T2): 14-27; 3rd trimester (T3): ≥28.

Results

Establishing TSH reference intervals for the Roche method:
Of 70,983 episodes, after removing those with history of thyroid disease and/or other medical conditions, positive thyroid auto-antibody, repeat thyroid testing, or markedly abnormal TSH, 24,874 were used in the final analysis.

The data distribution of TSH (Figure 1) and the intervals (Table 1) in different gestational age groups for the Roche method using data mining are shown below:

Figure 1.

Table 1.

Gest. weeks	Roche TSH reference intervals (mU/L)	
	n	Median (2.5th – 97.5th)
4-6	7303	1.65 (0.59 – 3.87)
7-13	12,690	1.17 (0.07 – 3.40)
14-27	3,248	1.48 (0.26– 3.73)
28-38	1,632	1.50 (0.31 – 3.89)

Correlation equations by method comparison
TSH results were available for all of the methods from 266 specimens. The correlation of each method compared with the Roche TSH are shown in Figure 2 and the equations in Table 2.
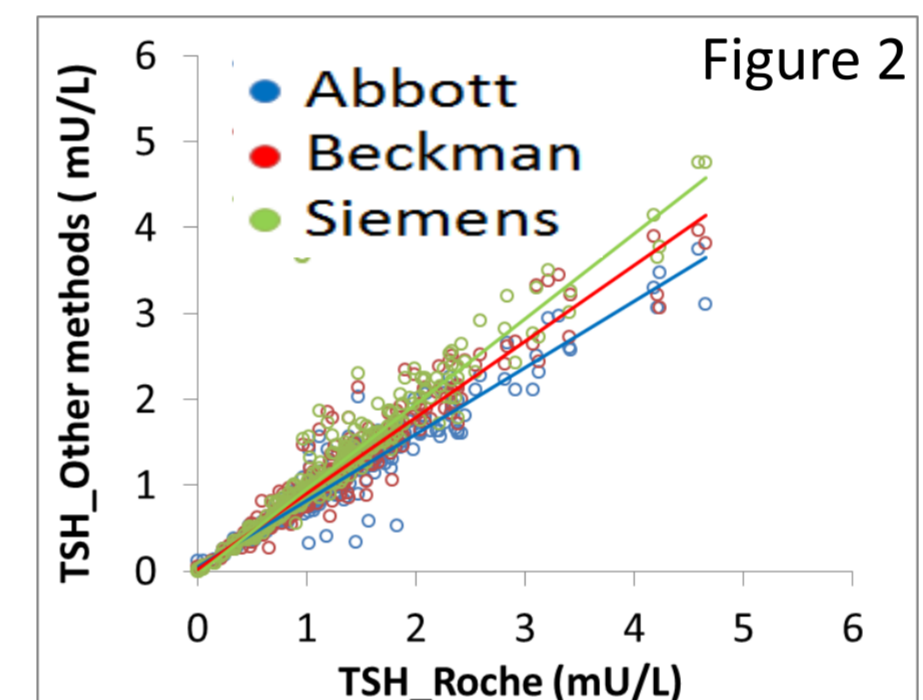

Figure 2

Table 2. Equations for different TSH methods against the Roche method by the Passing-Bablok regression.

Method	Slope	Intercept	R^2
Abbott	0.802	0.006	0.95
Siemens	1.0	-0.064	0.97
Beckman	0.913	-0.025	0.96

Table 3. TSH reference intervals in different gestational age groups for the Abbott Architect, Siemens Centaur and Beckman DxI methods by transference. Values were obtained by applying the equations in Table 2 to the Roche TSH reference intervals obtained by data mining in Table 1.

Gestational weeks	Roche TSH Median (2.5th – 97.5th)	Abbott Median (2.5th – 97.5th)	Siemens Median (2.5th – 97.5th)	Beckman Median (2.5th – 97.5th)
4-6 (early T1)	1.65 (0.59 – 3.87)	1.33 (0.48-3.11)	1.59 (0.53-3.81)	1.48 (0.51-3.51)
7-13 (late T1)	1.17 (0.07 – 3.40)	0.94 (0.06-2.73)	1.11 (0.01-3.34)	1.04 (0.04-3.08)
14-27 (T2)	1.48 (0.26– 3.73)	1.19 (0.21-3.00)	1.42 (0.20-3.66)	1.33 (0.21-3.38)
28-38 (T3)	1.50 (0.31 – 3.89)	1.21 (0.25-3.13)	1.44 (0.25-3.83)	1.34 (0.26-3.53)

Discussion

The gestational age-specific intervals derived by the transference technique for the Abbott TSH were very close to the intervals obtained in another study by data mining[4]; all (except one value) were within 0.08 mU/L absolute differences. The interval for Beckman TSH by transference in late T1 was almost identical to that obtained in the direct reference interval study[2].

Whilst there were different among methods, the reference limits obtained in this study were all lower than the 2017 ATA 4.0 mU/L cut-off recommended when the trimester- and method-specific intervals are not available, but higher than the widely used 2.5 mU/L cut-off from the 2012 ATA guidelines.

References:

1. Lu ZX et al. Establishing population and gestational age specific TFT reference intervals for the Roche method using local data by data mining. 2018 Pathology Update Poster number 101.
2. Ekinci EI, Lu ZX, Sikaris K, Churilov L, Bittar I, Lam Q, Crinis N, Houlihan CA. Longitudinal Assessment of Thyroid Function in Pregnancy. Annals of Clinical Biochem 2013;50:595-602.
3. CLSI. Defining, establishing, and verifying reference intervals in the clinical laboratory; Approved guideline – Third Edition. CLSI document EP28-A3c. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
4. Lu ZX et al. Establishing population and gestational age specific TFT reference intervals for the Abbott method using local data mining. 2018 Pathology Update Poster number 102.