Establishing population and gestational age specific TSH reference intervals for common methods in Australia using the transference technique
Zhong X Lu1,2,3, Christine A Houlihan4,5, Elif I Ekinci4,6, Wei-Ling Chiu4, Que Lam7, Alan R McNeil8, James CG Doery3, and Ken A Sikaris1,9

1Department of Chemical Pathology, Melbourne Pathology, Collingwood, Victoria; 2Biochemistry, Monash Pathology and 3Department of Medicine, Monash University, Clayton, Victoria; 4Department of Endocrinology and 5Biochemistry, Austin Health; Victoria; 5Mercy Hospital for Women, Heidelberg, Victoria; 6Biochemistry, Dorevitch Pathology, Heidelberg, Victoria. 6Department of Medicine and 7Department 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 database1 (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 pregnancy2. Details of subject recruitment and method comparison are shown below:

1.54 Pregnant women screened (Mercy Hospital for Women)
1.45 Apparently healthy pregnant women recruited
1.31 Remaining
T1: n=130; T2: n=84; T3: n=72

TSH method comparison using common methods:
• Roche e602
• Abbott Architect
• Siemens Centaur
• Beckman Dxl

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:

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

Gestational age partitioning (weeks of gestation):
1st Trimester (T1): ≤ 13; (Early T1: 4-6; Late T1: 7-13);

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.

Table 1. 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:

<table>
<thead>
<tr>
<th>Gest. weeks</th>
<th>Roche TSH reference intervals [mIU/L]</th>
<th>Abbott TSH reference intervals [mIU/L]</th>
<th>Siemens TSH reference intervals [mIU/L]</th>
<th>Beckman TSH reference intervals [mIU/L]</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-6 (early T1)</td>
<td>1.65 (0.59–3.87)</td>
<td>1.33 (0.48–3.11)</td>
<td>1.59 (0.53–3.81)</td>
<td>1.48 (0.51–3.51)</td>
</tr>
<tr>
<td>11-13 (late T1)</td>
<td>1.17 (0.07–3.40)</td>
<td>0.94 (0.06–2.73)</td>
<td>1.1 (0.01–3.34)</td>
<td>1.04 (0.04–3.08)</td>
</tr>
<tr>
<td>14-27 (T2)</td>
<td>1.48 (0.26–3.73)</td>
<td>1.19 (0.21–3.00)</td>
<td>1.42 (0.20–3.66)</td>
<td>1.33 (0.21–3.38)</td>
</tr>
<tr>
<td>28-38 (T3)</td>
<td>1.50 (0.31–3.89)</td>
<td>1.21 (0.25–3.13)</td>
<td>1.44 (0.25–3.83)</td>
<td>1.34 (0.26–3.53)</td>
</tr>
</tbody>
</table>

Discussion
The gestational age-specific intervals derived by the transference technique for the Abbott Architect were very close to the intervals obtained in another study by data mining2; all (except one value) were within 0.08 mIU/L absolute differences. The interval for Beckman TSH by transference in late T1 was almost identical to that obtained in the direct reference interval study2.

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

References: