Thyroid Function Tests: reference ranges, testing strategy and clinical interpretation ~ a National Audit

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Introduction and Method

The aim was to collate and feedback data on the national picture and to highlight extremes of variation and to encourage Laboratories to re-evaluate their local practice. Free Hormone and TSH assay formulations and analytical characteristics change over time as does the relative proportions of users of assays from the major global diagnostics providers. For this reason, it is important to keep up to date with the evolving practice in the UK, as it cannot be assumed older literature findings remain valid. Ranges set by one method are not necessarily easily converted to a second method.

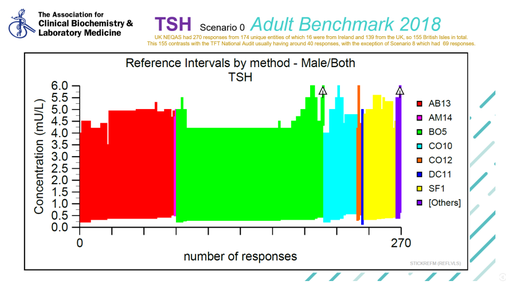
Standards / Guidelines / Audit Method

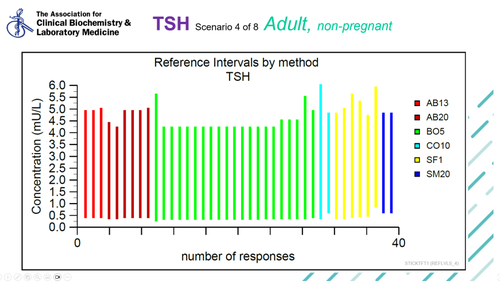
The Audit was not directly comparing against any single existing guideline but was more than a simple data gathering exercise. It did use an earlier UK NEQAS for Thyroid Hormones Adult Reference Range data as a starting point and anchor to further questions. It could be considered as a re-benchmarking exercise. In August 2022, a Survey Monkey audit was constructed with input from local and national audit leads to ascertain what the current practice across a range of patient types and demographics. This included adults, different pregnancy trimesters, paediatric and neonates. In addition, the raw Reference Ranges themselves were collected.

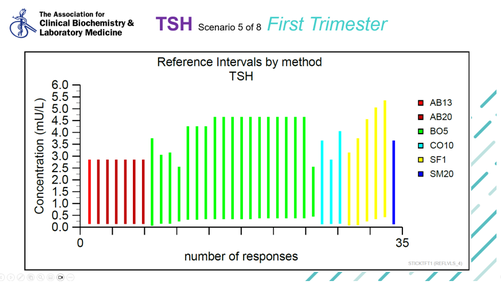
Results

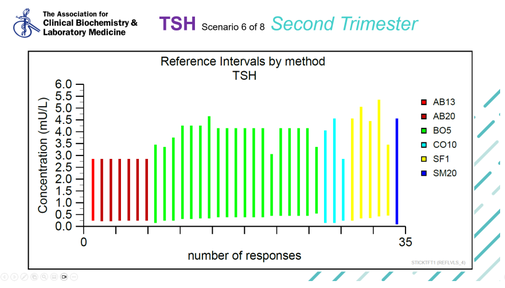
The number of responses varied from approximately 30 to 80, with fewest for the Paediatric and Free T3 responses. The results confirmed our expectation about the variety of approaches in use for Paediatrics and Neonates, but there was much closer agreement for the adult and trimester-specific data.

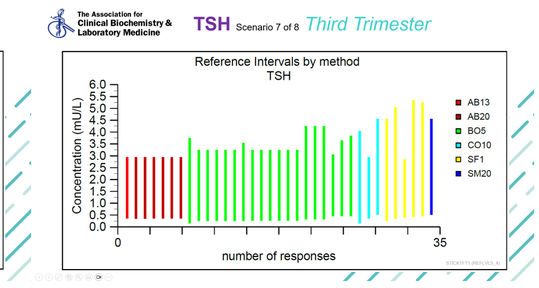
Reference Ranges quoted for TSH and for Free T4 across a range of adult scenarios

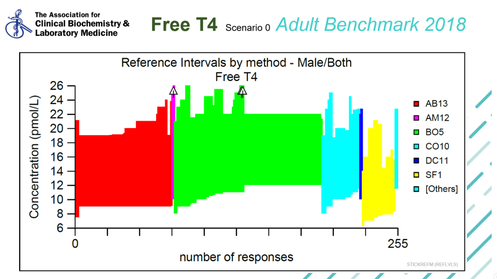


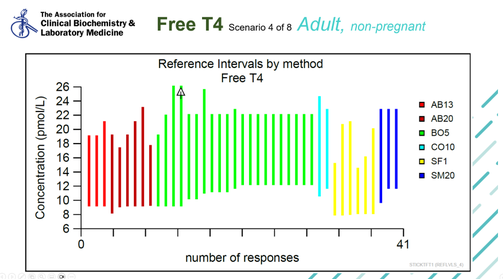


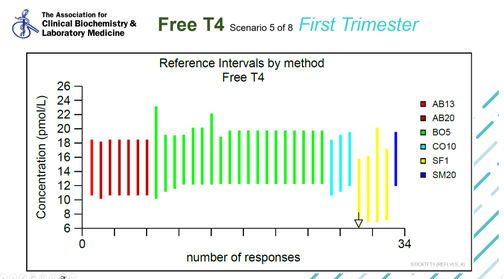


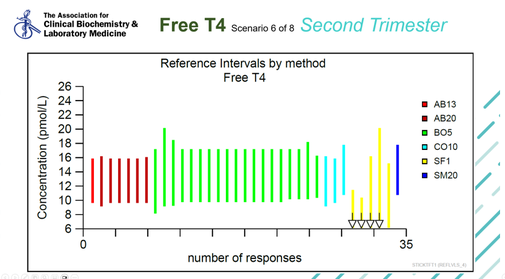


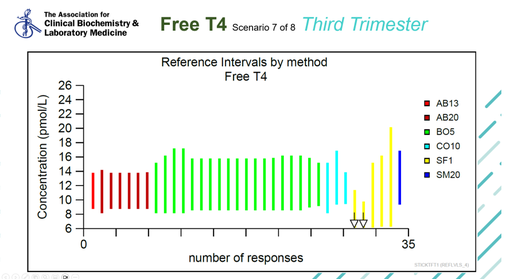




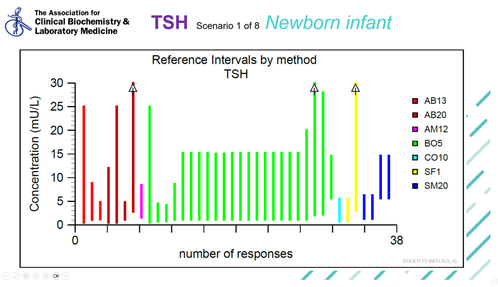


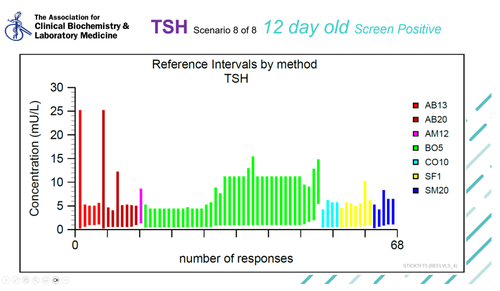


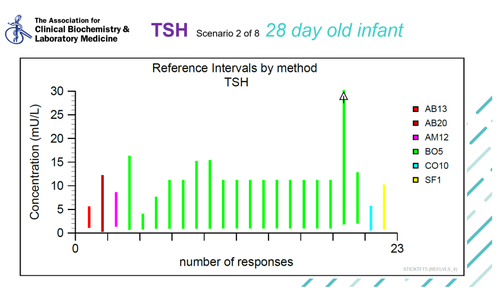


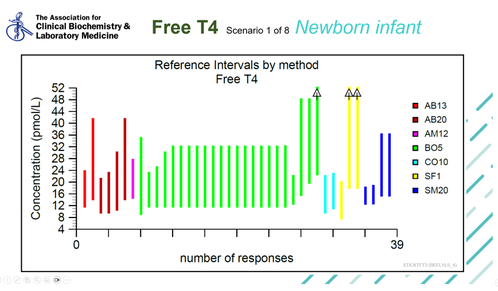


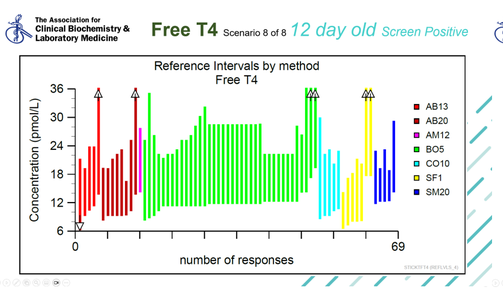
Reference Ranges quoted for TSH and for Free T4 for Paediatrics

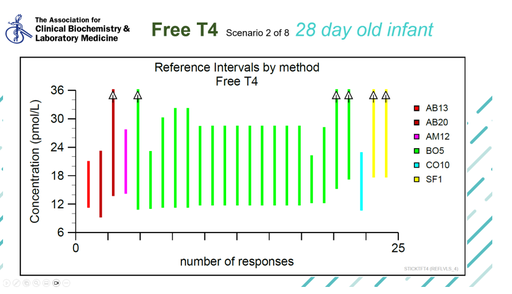








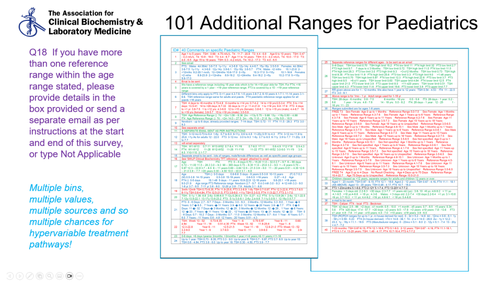




The data collected for the adult ranges is in keeping with the data from the larger data-set that Birmingham Quality /UK NEQAS achieved.

The Trimester-specific TSHs have a marked method-specific pattern which is different to that seen for the non-pregnant adult.

Given the marked within-method difference reported for Roche Free T4 at the lower end of the range, it is difficult to extrapolate to the Pregnancy ranges.



There is an incredibly high number of ranges for Paediatrics in use across the UK. This is not only in the ranges quoted but also in terms of age bins used. This makes comparisons almost impossible to make.

For Paediatrics, the findings would suggest that a more targeted approach is required from Laboratories to data-mine their own Laboratory Information Systems and share data across as many sites as possible. There doesn't seem to be any possibility of collecting data in any other way. Analyses on real samples across methods in the numbers required would seem to be an impossible ask.

Conclusions

Birmingham Quality will continue to periodically survey all its Participants for Adult Reference Ranges for all endocrine tests including TFTs. This is important as assay architecture from manufacturers does change, and not always in a good way. For example, 2-step Free T4 assays can be replaced by 1-step which can be less immune from interferences. Similarly, there are numerous examples of assays changing over time - and not by design - and so stability has to be proven, not just taken for granted. There remain very large between-method differences between the numerical values that assays produce, and these are not reflected in the ranges in use. The number of free T4 and TSH values on clinical samples that do not 'match' is always a talking point from the Laboratories community and the whole Reference Range approach has its detractors. While Laboratories continue to measure TFTs there remains a imperative to have a variety of measures to support, challenge and oversee the process. The Patients deserve this.

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