

2014 ABTH-A PARTICIPANT SUMMARY

Discussion

This exercise represents the first mailing of the CAP Accuracy-Based Thyroid Survey, and we are pleased to report that it provided several interesting findings. To start, though, we should review the nature of the samples, and the way we chose to evaluate the results.

Each sample in this Survey comes from a pool of roughly 6 healthy subjects. In an attempt to achieve a range of concentrations of the analytes, we pooled samples based on the individual TSH results. We wanted to be able to make pools with TSH values representing low normal, mid-normal, and high-normal values; although the values in this set of samples range from roughly 1.0 mIU/L to 3.5 mIU/L, we would have preferred a slightly larger range, especially on the low end.

As has been the case with all of our other Accuracy-Based Surveys, because of the fact that these samples were prepared from fresh frozen off-the-clot human serum with minimal processing, they are largely, if not entirely, free of so-called “matrix effects” of typical proficiency testing materials and QC materials. In short, these samples are **commutable**, and they can be used to determine whether values from different methods are **harmonized** (that is, the extent to which these methods agree with other on typical samples from patients.)

In addition, we can establish the true value for any measurand (eg, Free T4) if a reference measurement procedure (RMP) is performed on such commutable samples. In these cases, we can determine whether an individual laboratory's results are **accurate** (that is, the extent to which the results agree with the true value.)

TSH Values

As noted above, in the absence of a reference method procedure for TSH, we are unable to assign target values for these three samples. However, because the samples are commutable, we can still assess the degree of harmonization among methods. The range of median values among methods for each sample were as follows: 3.02 mIU/L – 3.85 mIU/L for ABTH- 01, 1.04 mIU/L – 1.24 mIU/L for ABTH-02, and 1.69 mIU/L – 2.05 mIU/L for ABTH-03. It would be interesting to know whether the reference intervals among methods reflect these (relatively small) differences. In other words, how much higher is the upper limit of the reference interval for the method whose median on ABTH-01 was 3.85 versus the method whose median was 3.02? Unfortunately, that is a matter beyond the scope of this discussion.

Total T4 and Free T4

Among the interesting findings with the Total T4 and Free T4 values is that they were the same by the NIH method on all three samples. (Strictly speaking, the Total T4 on ABTH-03 was slightly lower than the others (7.7 $\mu\text{g/dL}$ versus 8.2 $\mu\text{g/dL}$), but that is not much of a difference.) This is a little surprising in that the TSH values on the three samples were, as noted above, reasonably different. It is true that all three values were within the reference interval, but still one might expect the Free T4, if not the Total T4, to show inverse variation (such as is the case for PTH and serum calcium).

For additional insight into these measurands, we prepared the following graphs in which we have plotted the median values (circles) and high and low values (the line) for each method for ABTH-01. The findings are comparable for ABTH-02 and ABTH-03. (The target value has only a circle because it represents the mean value of three replicates by the NIH method.)

In the current Survey, we arranged to have the National Institute of Health (NIH) Laboratory determine values for Total T4, Free T4, Total T3, and Free T3 on each of these samples. We learned later that it is not clear whether these determinations represent true RMPs; more on that topic later. In any case, for the purpose of this exercise, those values are used as “reference targets” in the accompanying tables. Since there is no reference method procedure for TSH, there is no genuine “true” value to which we can compare results, so we can only discuss the degree of harmonization for TSH.

Because this is the first exercise for Accuracy-Based Thyroid, we decided not to formally grade the results. Instead, we offer the following analysis and comments in an effort to encourage participants to review, and think critically about, their own results.

For Total T4, it is apparent that all the peer groups, except Abbott, have median values reasonably close to the target value. The Abbott Architect method has a distinctly different median value. Again, one wonders whether the reference interval for this method differs from that for the other methods (and, for that matter, how closely the reference intervals for the other methods match each other).

In contrast, for Free T4, all the peer groups have median values reasonably close to each other (1.1 ng/dL), but that value is strikingly different from the target value (1.6 ng/dL). In other words, the Free T4 values are **well harmonized**, but they appear to be **inaccurate**. We found this finding so striking that we were forced to delve deeper into the procedures used by reference laboratories for Free T4.

T4 is a simple, well-defined molecule, so one can determine a true value by mass spectrometry. However, what we did not realize is that there are several methods for separating free from bound T4 and that they are not well standardized; different, well-recognized, high quality laboratories use different procedures. Because of the differences between the immunoassay values for Free T4 and the NIH laboratory, we arranged to have a second reference laboratory, using a totally different separation technique, perform analyses of Free T4 (and Free T3). We were encouraged by the fact that, despite differences in technique, these laboratories agreed on all Free T4 measurements.

Again, this begs the question as to whether the reference intervals are similarly “biased”. For at least one of the immunoassay methods and the second laboratory’s reference method, that is the case: the reference interval for the immunoassay is roughly 0.5 ng/dL lower.

Total T3 and Free T3

A comparable analysis for Total T3 and Free T3 was performed. In this case, the Total T3 methods agreed with each other and with the target values (harmonized and accurate), and the Free T3 values agreed reasonably well with each other (harmonized) and with the target values for ABTH-01 and ABTH-02 (accurate). (Because the two reference laboratories obtained strikingly different values for Free T3 on ABTH-03, we decided not to include a target value for that sample.)

Figure 1. Thyroxine (T4), total for ABTH-01

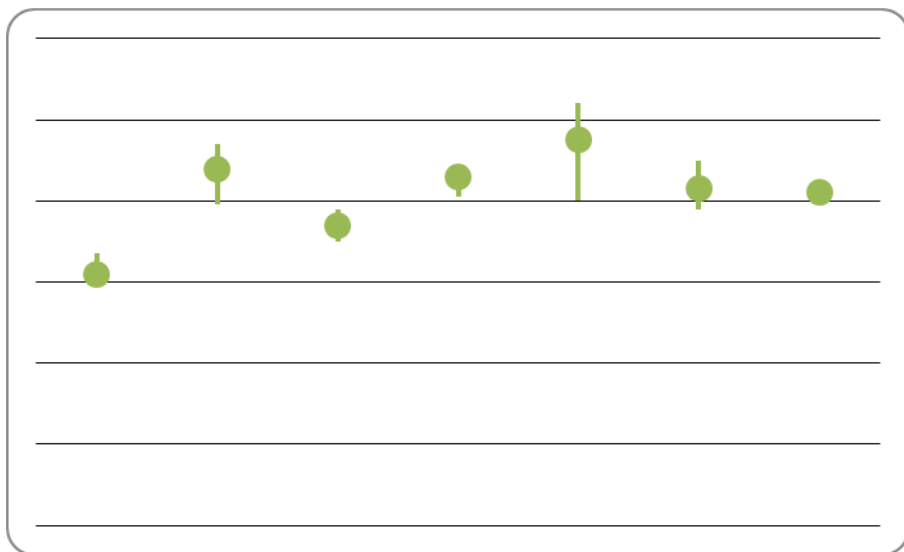


Figure 2. Thyroxine (T4), free for ABTH-01

