

Implementation of Percentiler and Flagger in the C-STFT project

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EMPOWER *IVD* ● **GLOBE**

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IFCC Committee for Standardization of Thyroid Function Tests (C-STFT)

Chair: Prof. Dr. L. Thienpont



Terms of reference

- **Develop reference measurement systems for free thyroid hormones and TSH**
- **Establish a network of competent reference laboratories**
- **Liaise with key stakeholders to implement traceable methods in routine clinical practice**

<http://www.ifcc.org/ifcc-scientific-division/sd-committees/c-stft/>

C-STFT Phase I - III

3 method comparison studies for FT4 and TSH

- **Good quality of performance, however, with room for improvement**
- **Confirmed the need for standardization (FT4) and/or harmonization (TSH)**
- **Demonstrated the feasibility by recalibration using a “targeted” panel (clinically relevant concentration range)**
- **Targets set by:**
 - **FT4 conventional RMP (ED ID-MS) (LoQ: 1.3 pmol/L)**
 - **Statistically derived “All-Procedure Trimmed Mean” (APTMM)**

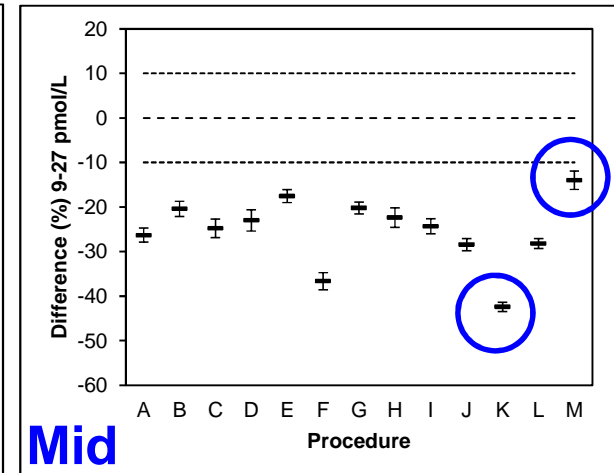
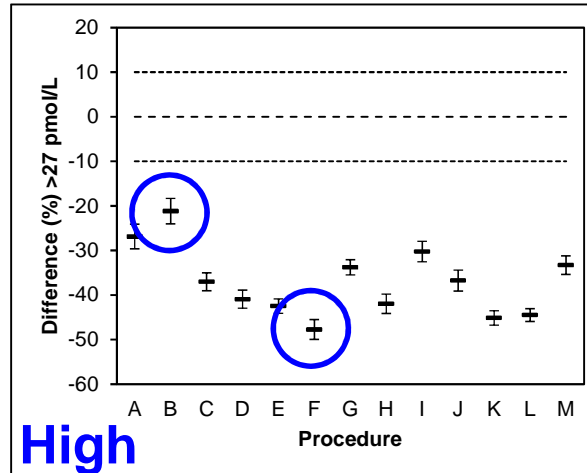
References

- Thienpont LM, Van Uytfanghe K, Beastall G, Faix JD, Ieri T, Miller WG et al. Report of the IFCC working group for standardization of thyroid function tests
 - part 1: Thyroid-stimulating hormone. [Clin Chem 2010;56:902-11.](#)
 - part 2: Free thyroxine and free triiodothyronine. [Clin Chem 2010;56:912-20.](#)
 - part 3: Total thyroxine and total triiodothyronine. [Clin Chem 2010;56:921-9.](#)
- Thienpont LM, Van Uytfanghe K, Van Houcke S; IFCC Working Group for Standardization of Thyroid Function Tests (WG-STFT). Standardization activities in the field of thyroid function tests: a status report. [Clin Chem Lab Med 2010;48:1577-83.](#)
- Thienpont LM, Van Uytfanghe K, Van Houcke S, Das B, Faix JD, MacKenzie F et al. A Progress report of the IFCC Committee for Standardization of Thyroid Function Tests. [Eur Thyroid J 2014;3:109-16.](#)

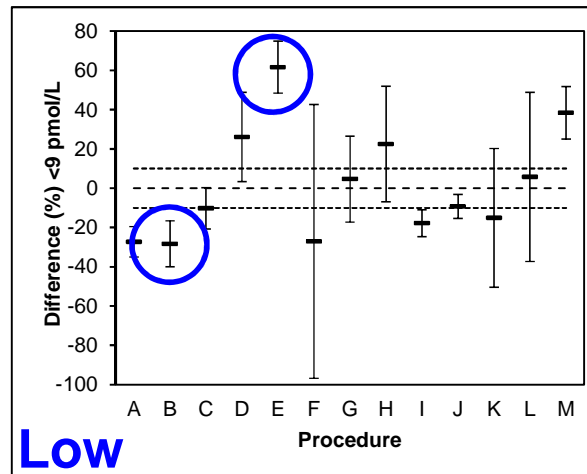
Standardization status – FT4

Phase III – Bias to ED ID-MS#

>27 pmol/L:
-37% (mean)
 Range: -21% to -48%



9–27 pmol/L:
-25% (mean)
 Range: -14% to -42%



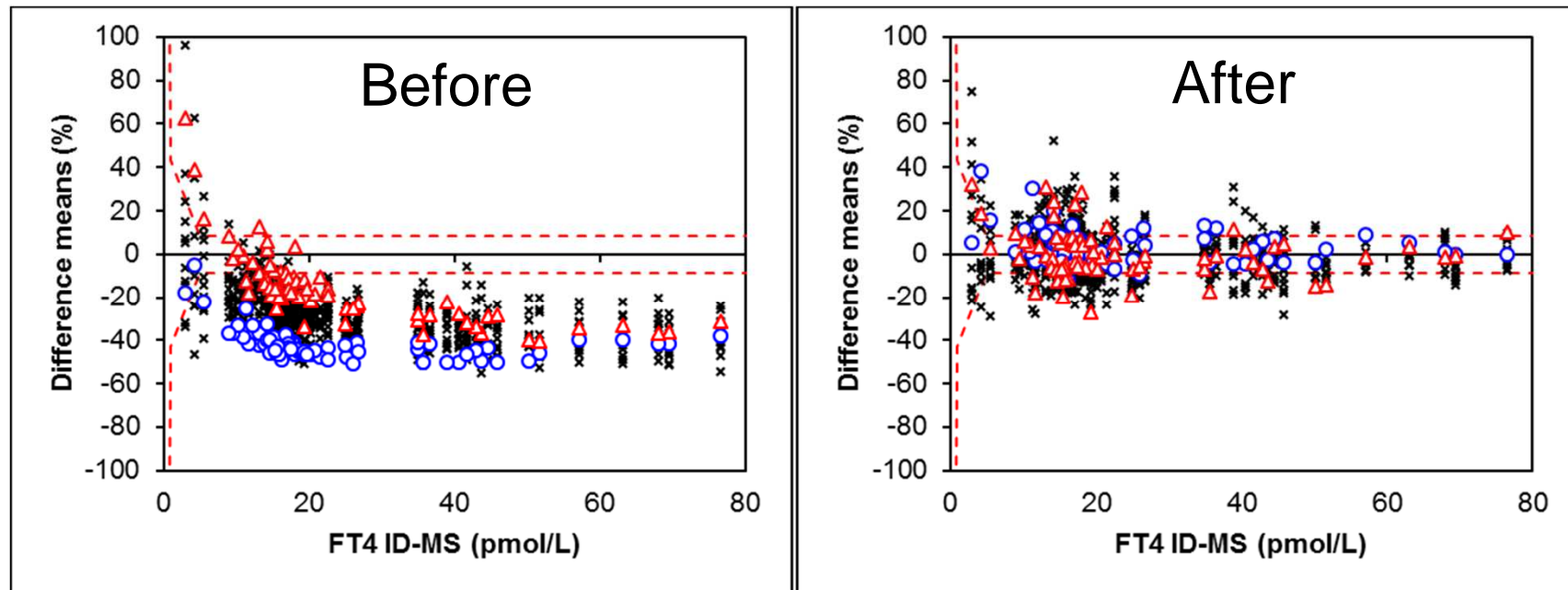
**FT4 concentration
 range of the panel:
 3 to 77 pmol/L**

All assays strongly negatively biased

#Thienpont et al. Eur Thyroid J 2014;3:109-16.

Feasibility of standardization/recalibration

FT4 – Phase III#



- Bias to ED ID-LC/tandem MS removed
- Residual dispersion nearly entirely due to within-assay effects

#Thienpont et al. [Eur Thyroid J 2014;3:109-16.](#)

C-STFT Phase IV

Technical recalibration

- **Measurements done**
- **Final data treatment on-going**
- **Recalibration by manufacturers to follow**

Prior to implementation

- **Liaise with regulatory authorities and key stakeholders**
- **Do risk-benefit analysis at all levels of stakeholders**
- **Educate stakeholders about impact/changes**
- **Coordinate implementation of standardized/harmonized assays by all manufacturers at the same point in time and worldwide**
- **Monitor sustainability of standardization status**

Percentiler and Flagger

Objective for use in the C-STFT project

- **Start in the “pre”-standardization/harmonization phase**
 - **Recruit sufficient participants**
 - **Get experienced with interpretation**
- **Fully exploit in “post”-standardization/harmonization phase**
 - **Sustainability of new calibration status**
 - **Impact of analytical quality/instability on daily surrogate medical decision making**

Overview current participants

	Percentiler		Flagger	
	Participants	Instruments	Participants	Instruments
Abbott Architect	9	18	1	1
Beckman Synchron	11	14	6	7
OCD Vitros	4	9	1	1
Roche Cobas Elecsys	33	64	12	13
Siemens Centaur	7	19	2	2
Siemens Immulite	2	4	0	0
Siemens Vista	3	5	1	3

Percentiler: 69 participants with 133 instruments

Flagger: 23 participants with 27 instruments

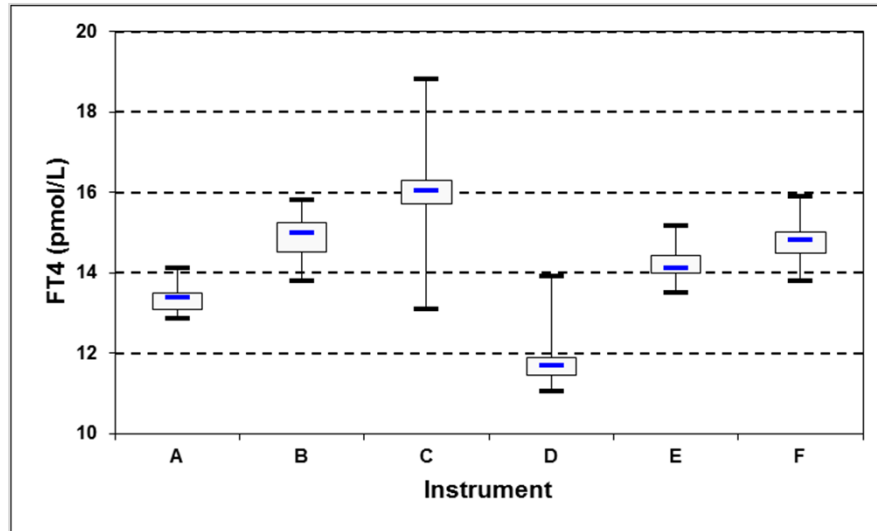
Bias specifications for interpretation

	Bias Biology (%)	Bias Empower (%)	Bias Biology (unit)	Bias Empower (unit)	Median "SI"	Limit (relative %)	Minimum limit (absolute %)	Unit
FT4	3.3	3.4	0.5	0.5	14.9	30	1	pmol/L
TSH	7.8	7.3	0.13	0.12	1.65	30	1	mIU/L

- **Starting point: bias limits inferred from the biological variation model[#]**
- **Currently set limits seem achievable by several participants/assays**
- **If necessary, the current performance of IVD assays will be taken into account**

[#https://www.westgard.com/biodatabase1.htm](https://www.westgard.com/biodatabase1.htm)

Percentiler vs C-STFT Phase I

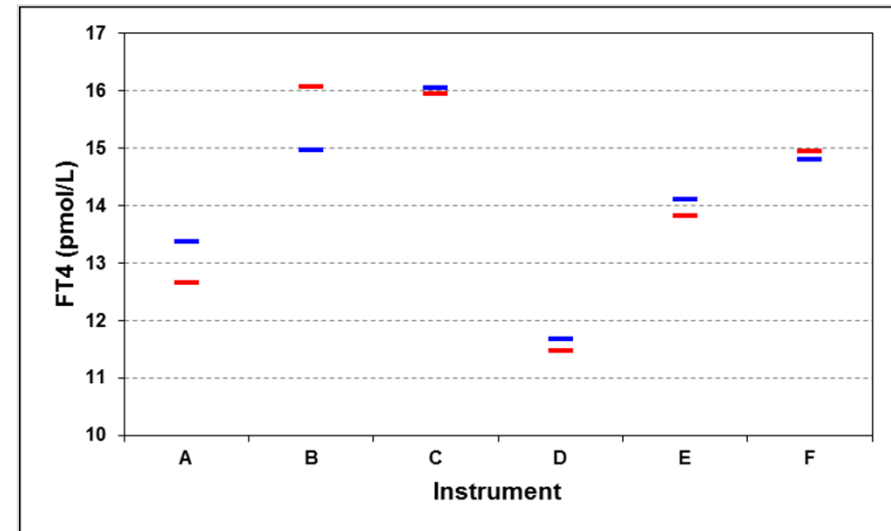


Peer group medians

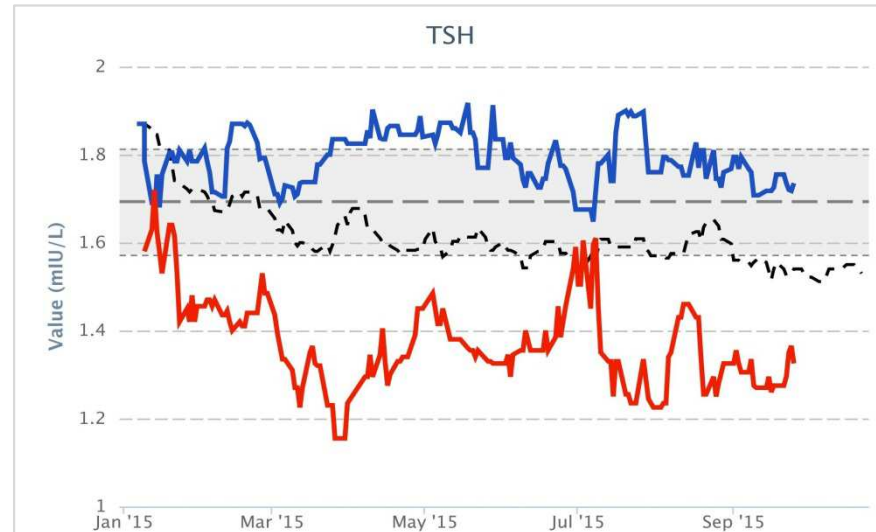
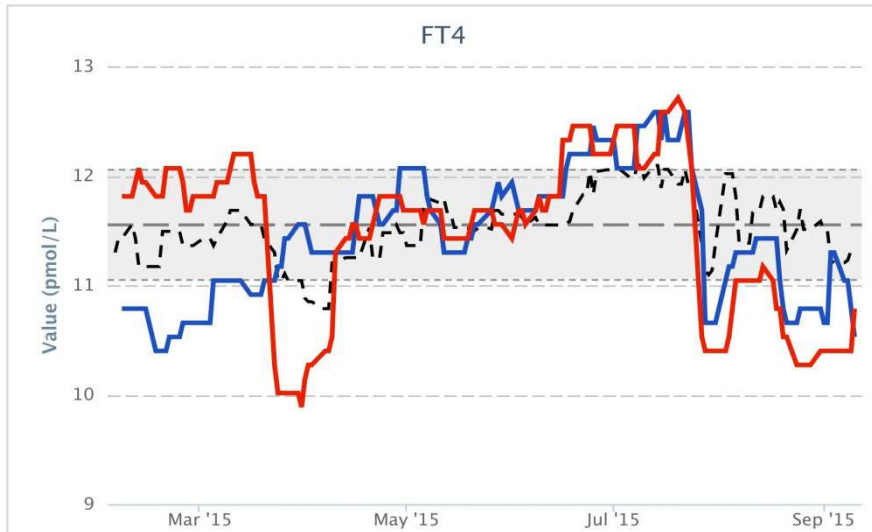
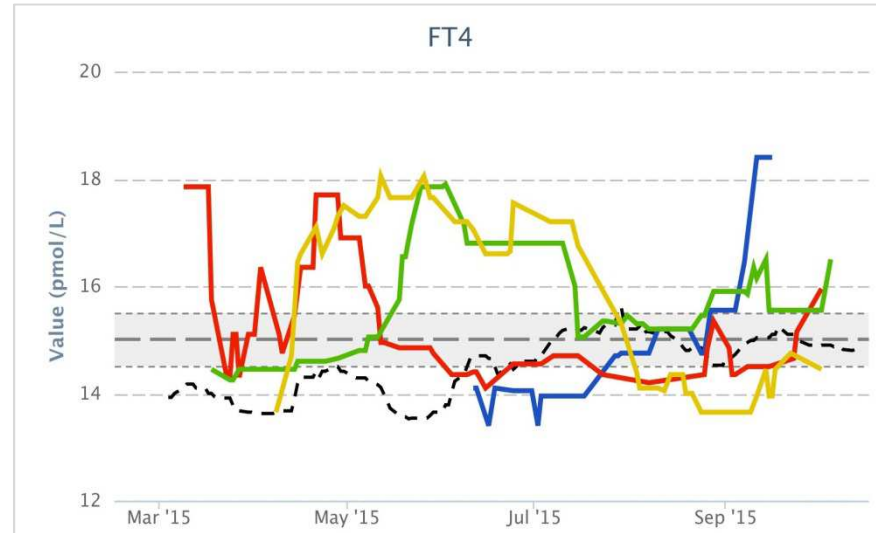
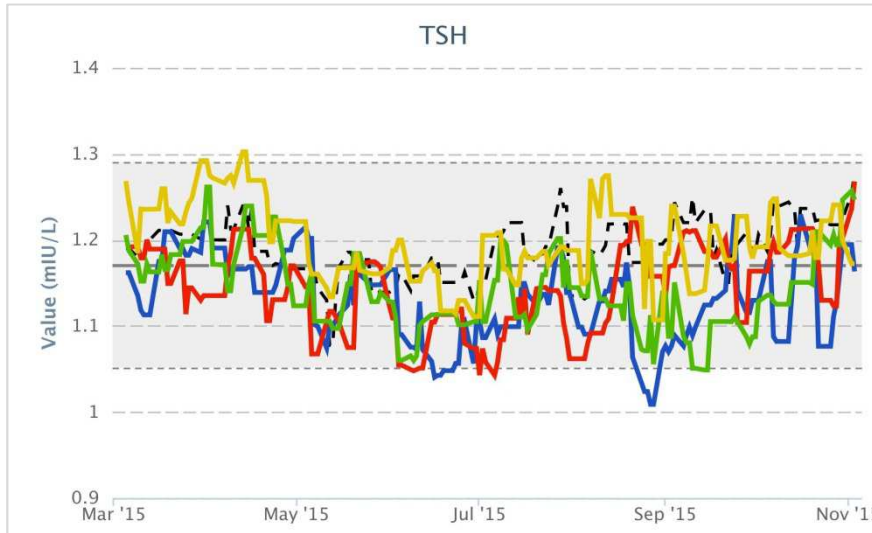
- Median from 11.7 – 16 pmol/L

Median values

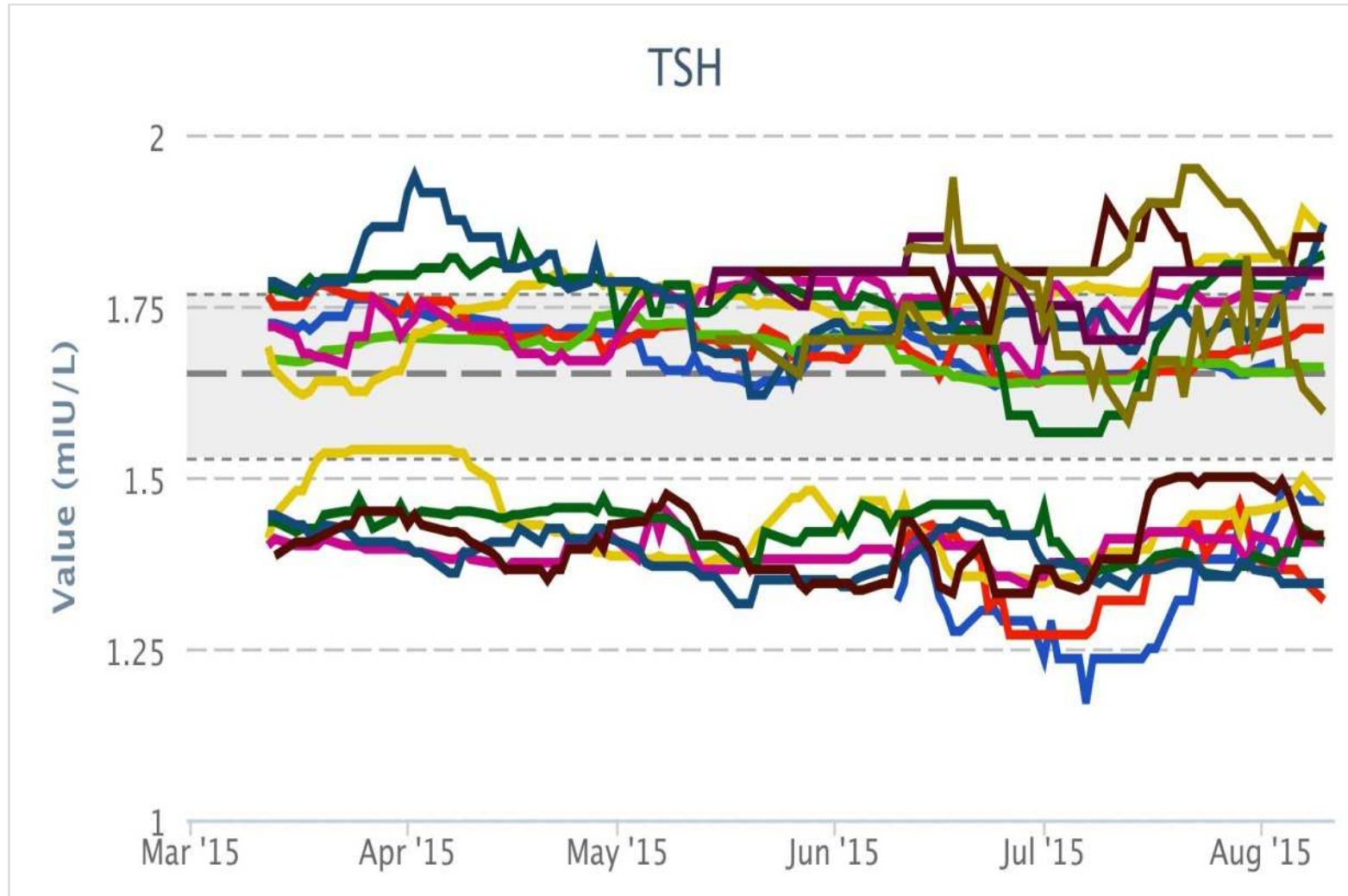
- Blue: Percentiler: outpatients
- Red: Phase I: euthyroid panel



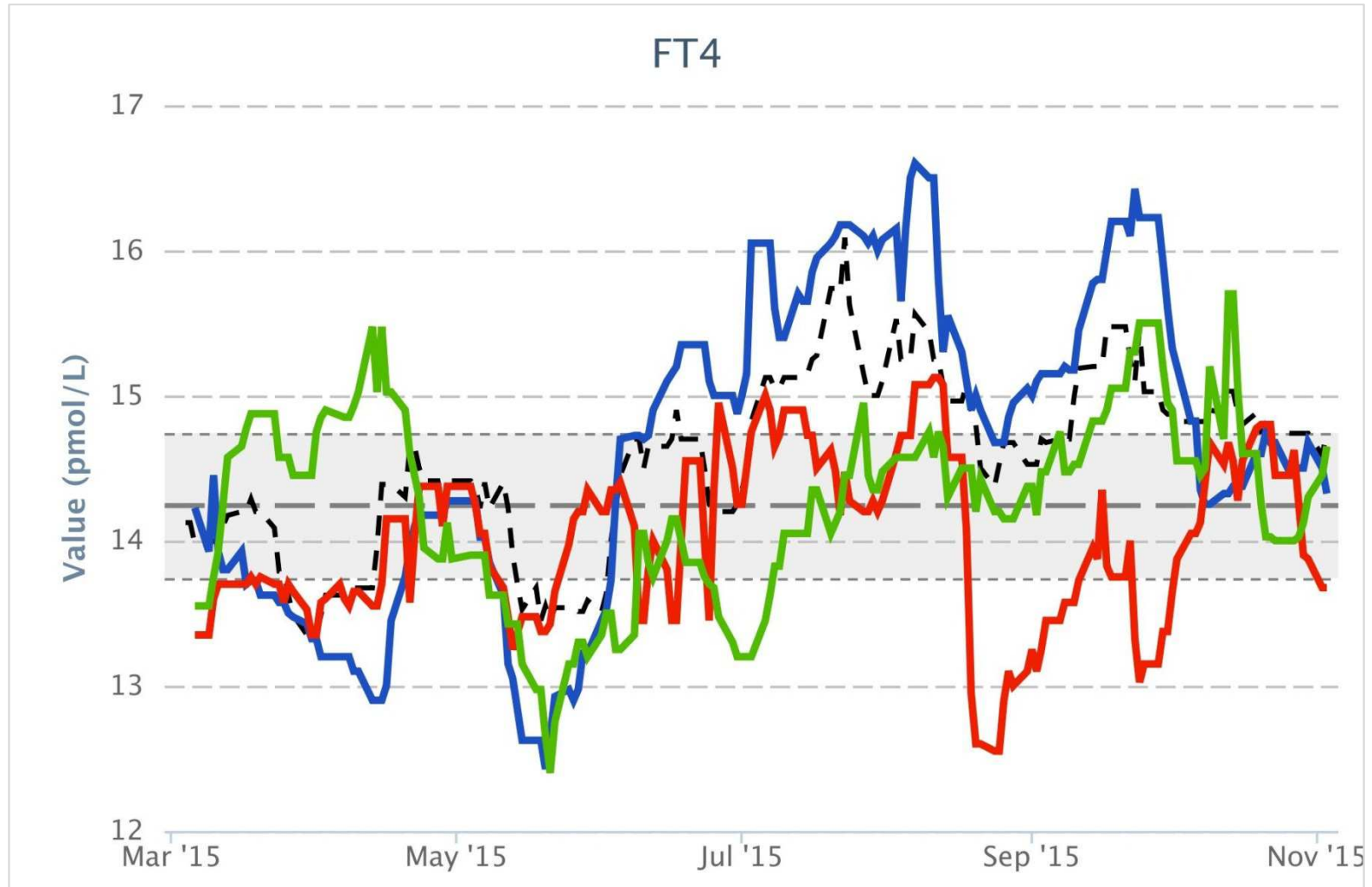
Examples Percentiler



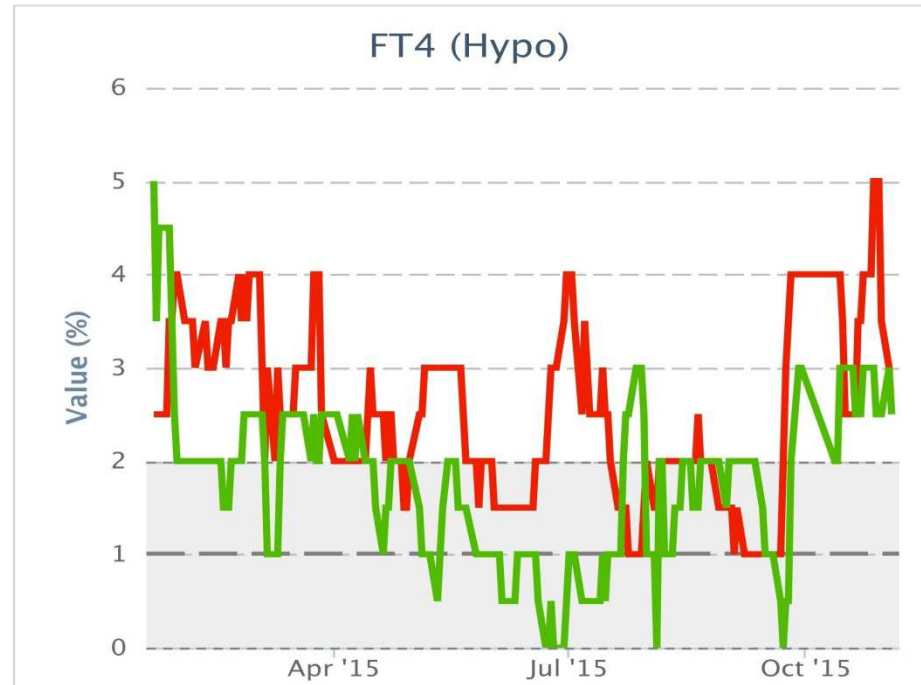
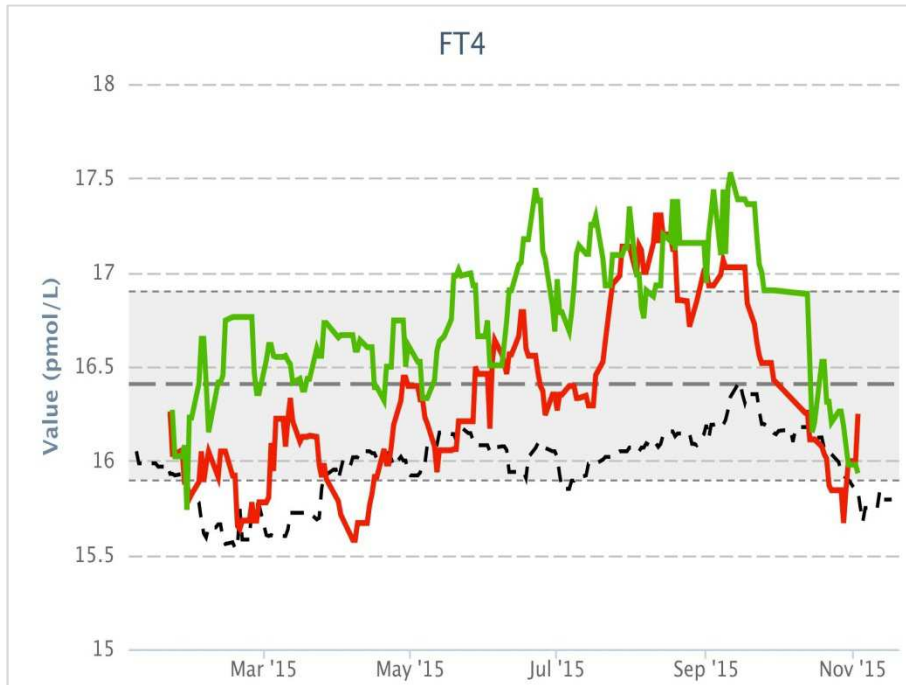
Example 2 subgroups for TSH



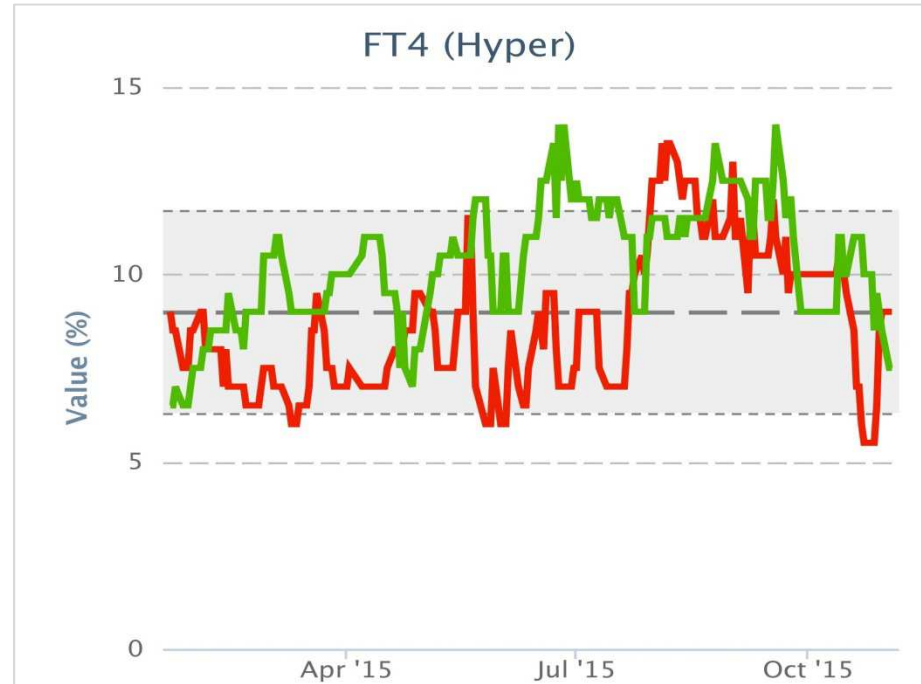
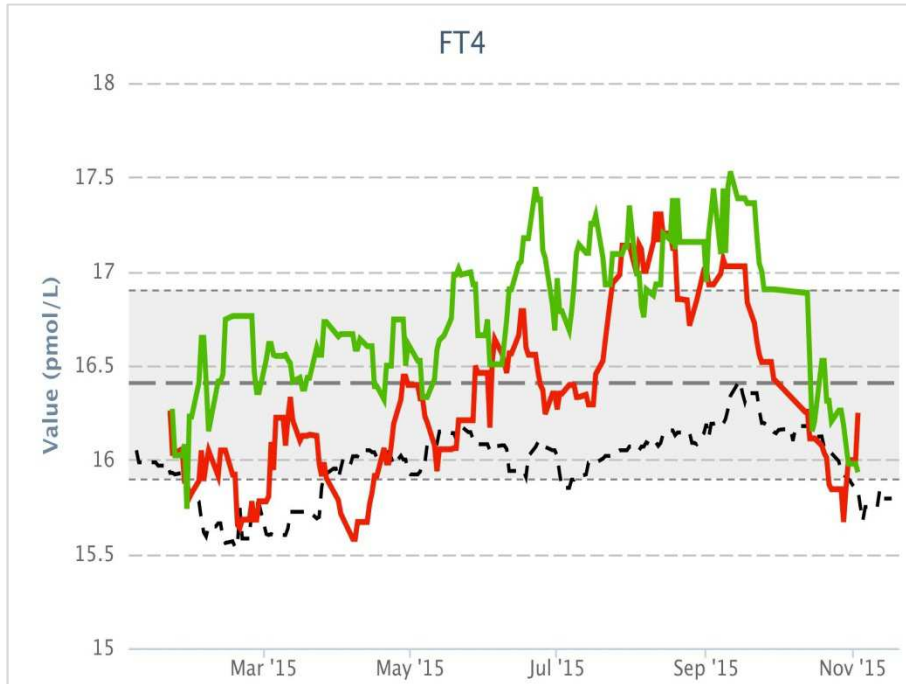
Instability FT4 assays



Percentiler vs Flagger



Percentiler vs Flagger



In conclusion

Percentiler and Flagger for C-STFT

- **Utility is shown in pre-standardization phase**
- **Monitor sustainability of recalibration status**

Limitations to be resolved

- **More participants**
- **Representation of all manufacturers involved in the project**
- **Better definition of outpatient results**

Invitation

Percentiler

- Include FT4 and TSH to the clinical chemistry analytes

Flagger

- Join the Flagger with FT4 and TSH

