

TSH

(Standardization Challenges)

IQC13, Friday, April 24, 2015

Mohammad Reza Bakhtiari, DCLS, PhD

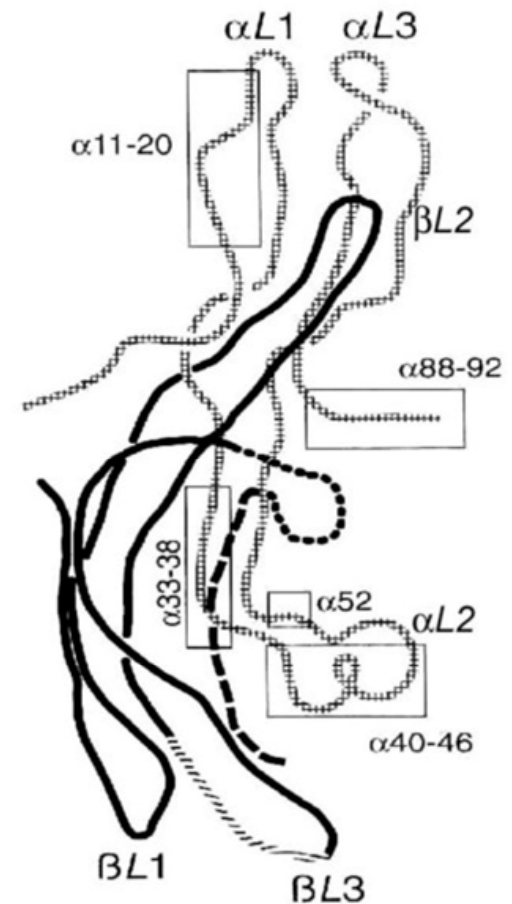
Iranian Research Organization for Science & Technology (IROST)

Tehran, Iran

Thyroid Stimulating Hormone

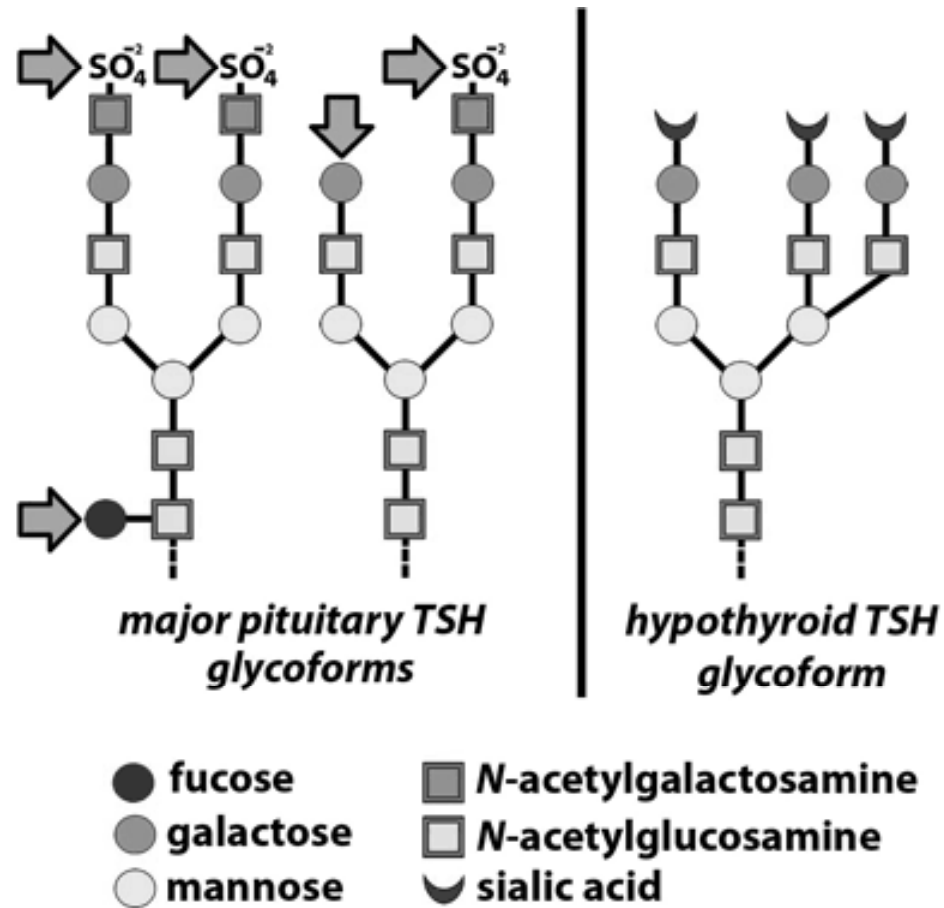
(Definition)

- ✓ A heterodimeric glycosylated peptide (92+118)
- ✓ 28- to 30- kDa
- ✓ Synthesized & secreted from thyrotrophs of the anterior pituitary
- ✓ Turnover: 40-150 mU/day
- ✓ Half Life: 1 hour
- ✓ Major role: Regulates the growth and function of thyroid gland



Grossmann, M., Weintraub, B.D. & Szkudlinski, M.W.. Novel insights into the molecular mechanisms of human thyrotropin action: structural, physiological, and therapeutic implications for the glycoprotein hormone family. *Endocr Rev* , 18 , 476-501. (1997)

Thyroid Stimulating Hormone (Glycobiology)



Thyroid Stimulating Hormone

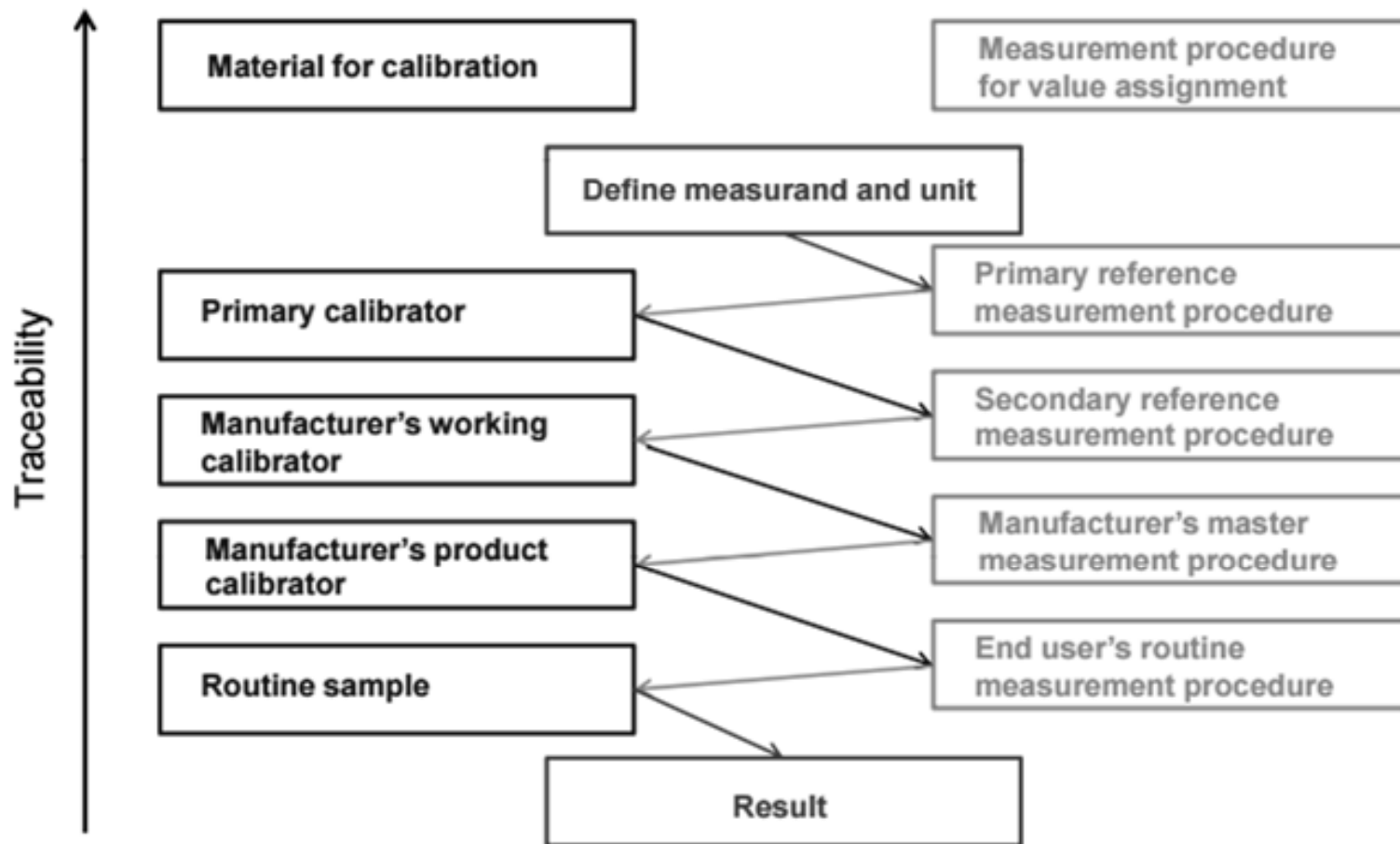
(Assay Generations)

Generation	Functional Sensitivity*
First	1 – 2 μ IU/mL
Second	0.1 – 0.2 μ IU/mL
Third	0.01 – 0.02 μ IU/mL

*<20% interassay precision within these ranges.

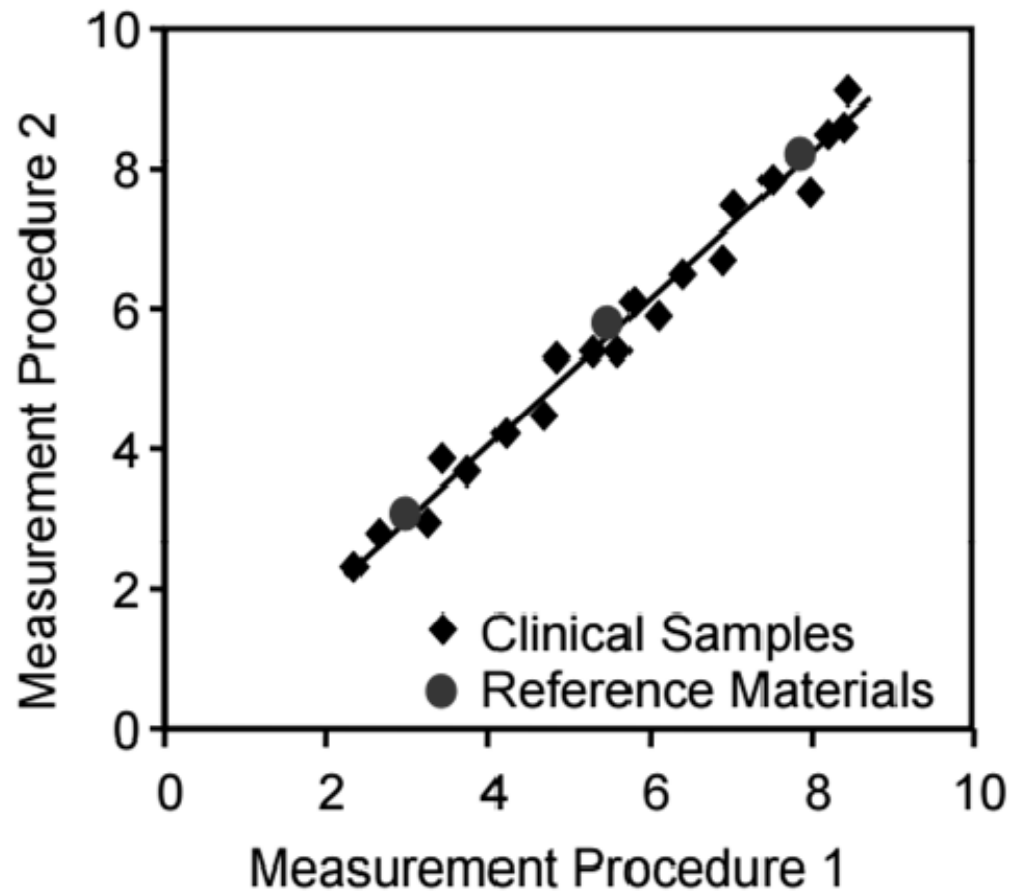
Assay Standardization

(Full Metrological Traceability)



Adapted from EN ISO 17511

Assay Standardization (Commutability)



Thyroid Stimulating Hormone

(Assay Standardization)

- **Goal:** Measurement results be comparable between laboratories and methods, over time, with common reference ranges.
- **Definition:** Calibration traceable to International System of Units using a RMP
(to cause to conform with a standard)
- **Requirements:**
 - ✓ Reference Measurement Procedure (RMP)
Not Available for TSH
 - ✓ Certified Standard Reference Material (CRM)
WHO Standard: NIBSC code: 81/565 ???
 - ✓ Traceability
No
 - ✓ Commutability
No
 - ✓ Broad Range Coverage
?

TSH Standardization

(Not Available: How about Harmonization?)

- **Goal:** Measurement results be comparable between laboratories and methods, over time, with common reference ranges.
- **Definition:** To bring into an agreement, (to reach to a consensus)
- **Requirements:**
 - ✓ Applying Statistical Methods
 - ✓ Recalibration of Methods / Kits against consensus values
 - ✓ Manufactures contribution

TSH Harmonization

(A Progress Report of the IFCC Committee for Standardization of Thyroid Function Tests)

Table 1. Characteristics of the FT4 and TSH serum panel

	FT4 panel	TSH panel						
Number of samples	74	94						
Target setting	ED ID-LC/tandem MS	APTM						
Concentration range	3–77 pmol/l	0.04–80 mIU/l						
Inclusion criteria	<p>Individuals were at least 18 years old and competent to give informed consent, as considered by the physician, study nurse or other health care professional interviewing the patient Individuals being evaluated for a thyroid disorder and classified into one of the following groups (if possible evenly distributed):</p> <table border="0"> <tr> <td style="vertical-align: top;"> <p>D: hyperthyroid (n = 30) Patients with FT4 values >28 pmol/l up to 40 pmol/l*</p> </td> <td style="vertical-align: top;"> <p>A: hyperthyroid (n = 30) A1: 10 patients with suppressed TSH, around 0.01 mIU/l A2: 10 patients with TSH values between 0.01 and 0.1 mIU/l A3: 10 patients with TSH values between 0.1 and 0.3 mIU/l*</p> </td> </tr> <tr> <td style="vertical-align: top;"> <p>E: euthyroid (n = 120) Patients with FT4 values between 10 and 28 pmol/l*</p> </td> <td style="vertical-align: top;"> <p>B: euthyroid (n = 30) Patients with TSH values between 0.3 and 3.0 mIU/l*</p> </td> </tr> <tr> <td style="vertical-align: top;"> <p>F: hypothyroid (n = 30) Patients with FT4 values between 3 and 10 pmol/l*</p> </td> <td style="vertical-align: top;"> <p>C: hypothyroid (n = 40) C1: 20 patients with TSH values between 3.0 and 50 mIU/l* C2: 20 patients with TSH values >50 mIU/l up to 100 mIU/l*</p> </td> </tr> </table> <p>Donors treated for thyroid dysfunction were included, provided information on the type of treatment and start of the treatment was available Note: samples were measured for their endogenous analyte concentration, hence subjects treated with L-thyroxine were only included in the TSH panel and vice versa for patients treated with recombinant TSH</p>		<p>D: hyperthyroid (n = 30) Patients with FT4 values >28 pmol/l up to 40 pmol/l*</p>	<p>A: hyperthyroid (n = 30) A1: 10 patients with suppressed TSH, around 0.01 mIU/l A2: 10 patients with TSH values between 0.01 and 0.1 mIU/l A3: 10 patients with TSH values between 0.1 and 0.3 mIU/l*</p>	<p>E: euthyroid (n = 120) Patients with FT4 values between 10 and 28 pmol/l*</p>	<p>B: euthyroid (n = 30) Patients with TSH values between 0.3 and 3.0 mIU/l*</p>	<p>F: hypothyroid (n = 30) Patients with FT4 values between 3 and 10 pmol/l*</p>	<p>C: hypothyroid (n = 40) C1: 20 patients with TSH values between 3.0 and 50 mIU/l* C2: 20 patients with TSH values >50 mIU/l up to 100 mIU/l*</p>
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Exclusion criteria	<p>Individuals previously enrolled into this clinical study Individuals diagnosed with a severe NTL, defined as a state of dysregulation where levels of T3, T4, FT3, and/or FT4 are abnormal although the thyroid gland does not appear to be dysfunctional Individuals with known pregnancy</p>							

TSH Harmonization

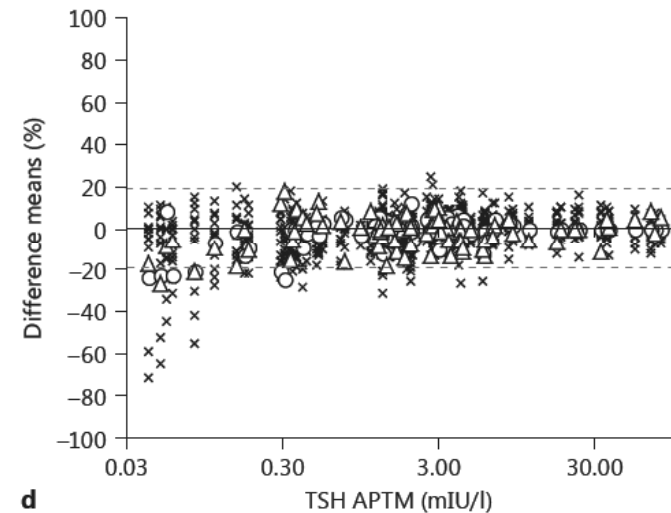
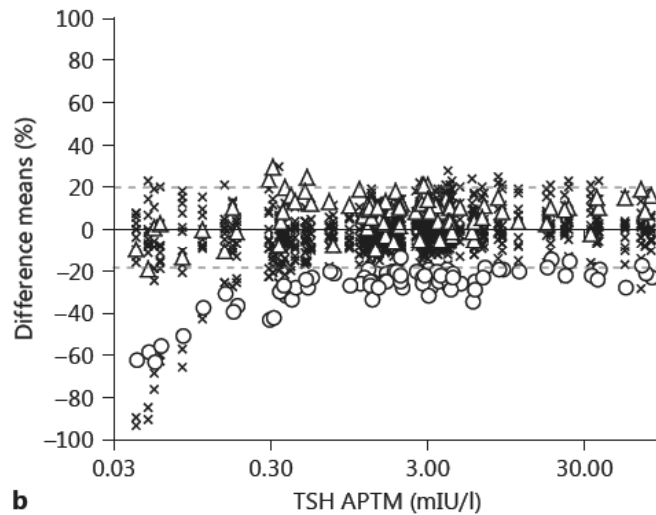
(A Progress Report of the IFCC Committee for Standardization of
Thyroid Function Tests)

Table 2. Study participants and assays

Assay manufacturer	Assay	Analyte
Abbott Diagnostics (Abbott Park, Ill., USA)	Architect i2000SR	FT4 and TSH
Beckman Coulter, Inc. (Brea, Calif., USA)	Access 2	FT4 and TSH
bioMérieux s.a. (Marcy-l'Etoile, France)	VIDAS FT4	FT4
	VIDAS TSH & TSH3	TSH
DiaSorin S.p.A. (Saluggia, Italy)	Liaison	FT4 and TSH
Ortho-Clinical Diagnostics (Buckinghamshire, UK)	VITROS Immunodiagnostic Systems (ECiQ and 3600)	FT4 and TSH
Roche Diagnostics GmbH (Mannheim, Germany)	Elecsys	FT4 and TSH
Siemens Healthcare Diagnostics Inc. (Deerfield, Ill., USA)	ADVIA Centaur	FT4
	ADVIA Centaur TSH3-UL	TSH
	Dimension RxL	FT4 and TSH
	Dimension EXL with LOCI module	FT4
	Dimension EXL with LOCI module (3rd generation)	TSH
	Dimension Vista 1500	FT4 and TSH
	IMMULITE 2000	FT4
	IMMULITE 2000 (Third Generation TSH)	TSH
Tosoh Corporation (Tokyo, Japan)	AIA-2000 (ST AIA-PACK)	FT4 and TSH

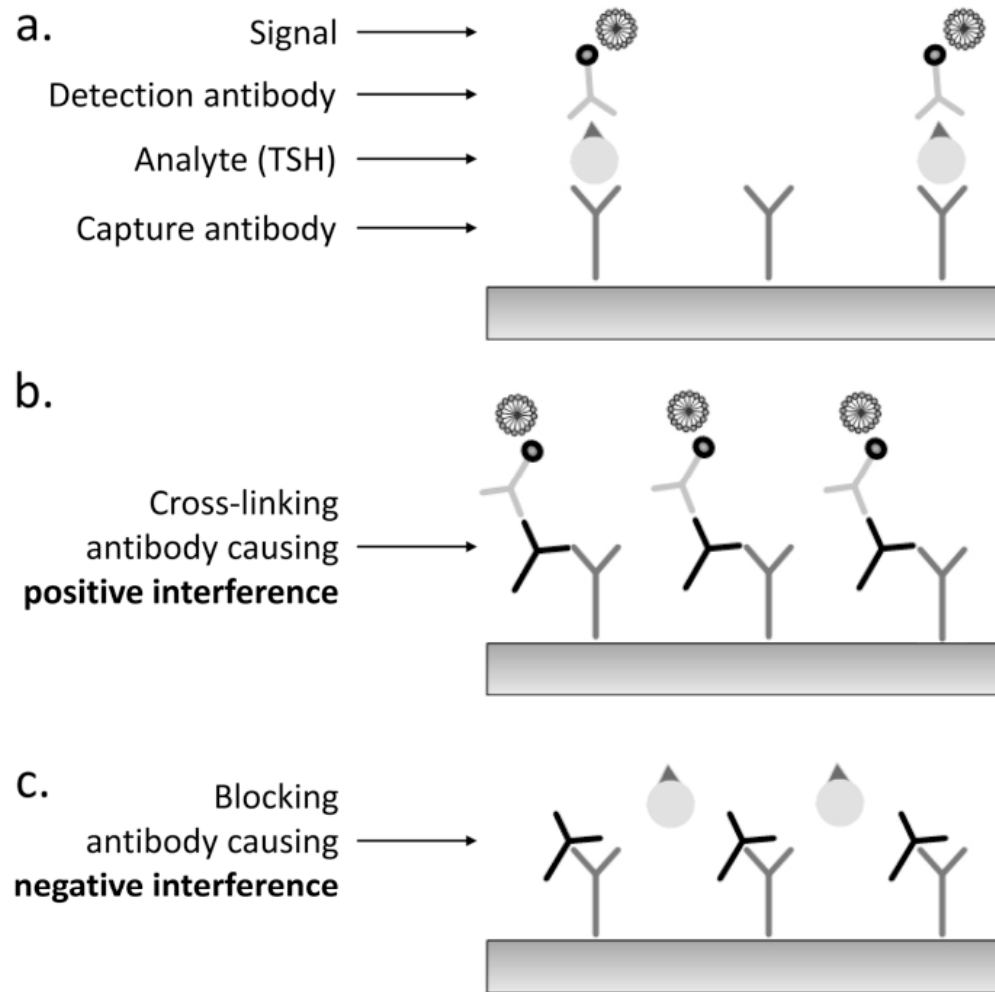
TSH Harmonization

(A Progress Report of the IFCC Committee for Standardization of Thyroid Function Tests)

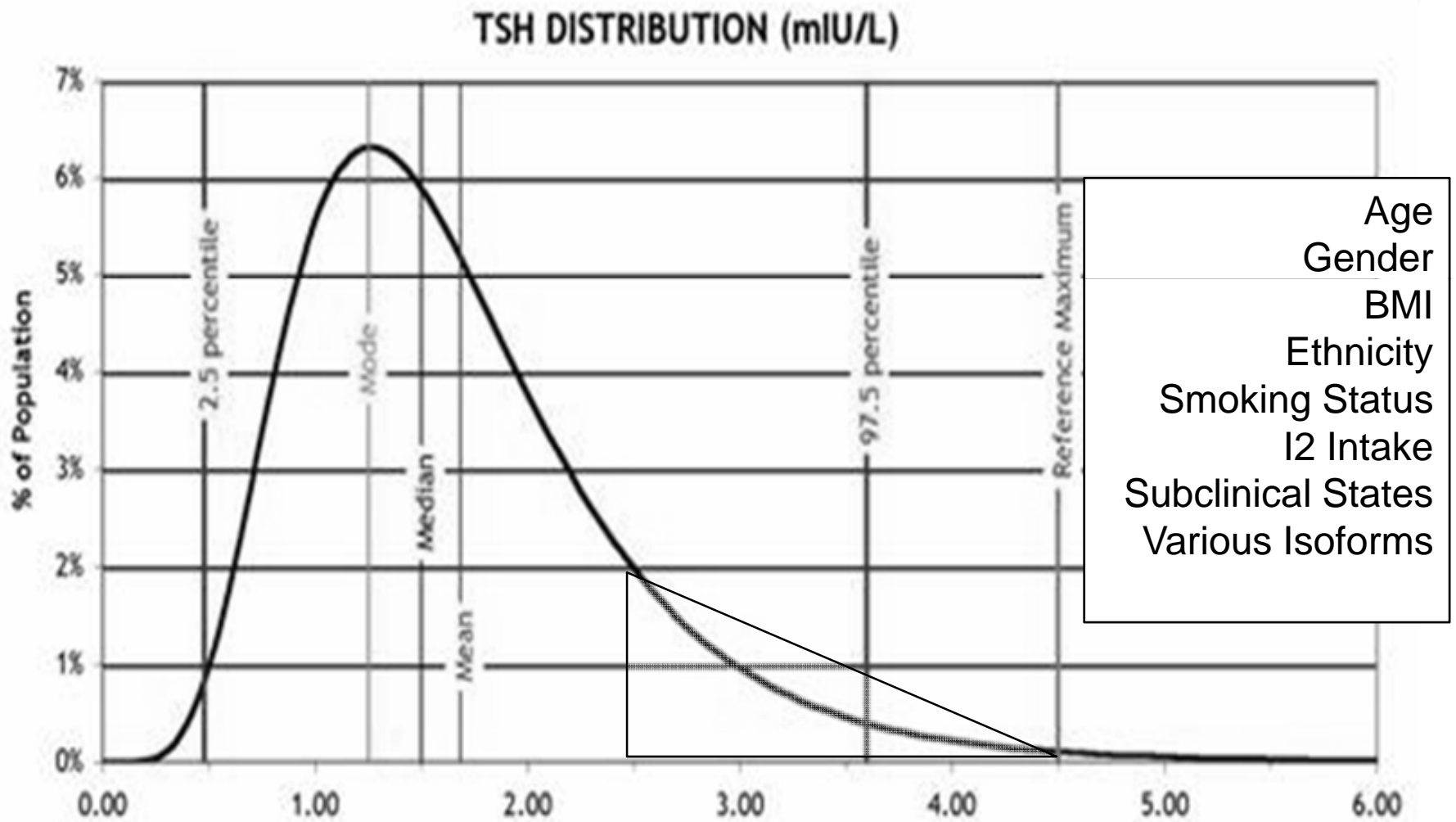


TSH assay	Before recalibration			After recalibration		
	0.03–0.5 mIU/l	0.5–5 mIU/l	>5 mIU/l	0.03–0.5 mIU/l	0.5–5 mIU/l	>5 mIU/l
I	-33	-23	-21	-10	0.8	-1.1
A	-7.7	-8.4	-17	-5.9	5.0	5.2
J	-10	-6.2	-2.3	4.3	1.4	-0.4
M	-8.7	-5.4	-0.3	-8.3	-6.7	-3.3
L	-3.6	-3.8	-6.8	-2.0	-0.7	-0.5
F	-19	-1.9	-0.3	-19	-2.7	1.8
H	-7.4	-1.9	7.4	-2.8	0.0	-0.3
N	-3.7	-1.4	3.5	-0.8	-3.0	-0.3
D	4.4	0.7	-1.2	5.6	1.4	-0.2
G	-19	1.2	4.6	-21	-0.3	3.8
E	7.6	7.7	7.6	-2.0	-0.9	-1.9
K	12	8.3	12	-3.6	-1.5	-1.4
C	-2.1	9.4	8.4	-10	1.5	-1.2
B	4.4	11	-17	-15	1.4	6.0

Thyroid Stimulating Hormone (Assay Interference)



TSH Reference Interval



Pregnancy TFTs Reference Intervals

(ATA recommendations)

TSH:

1st T: 0.1 – 2.5

2nd T: 0.2 – 3.0

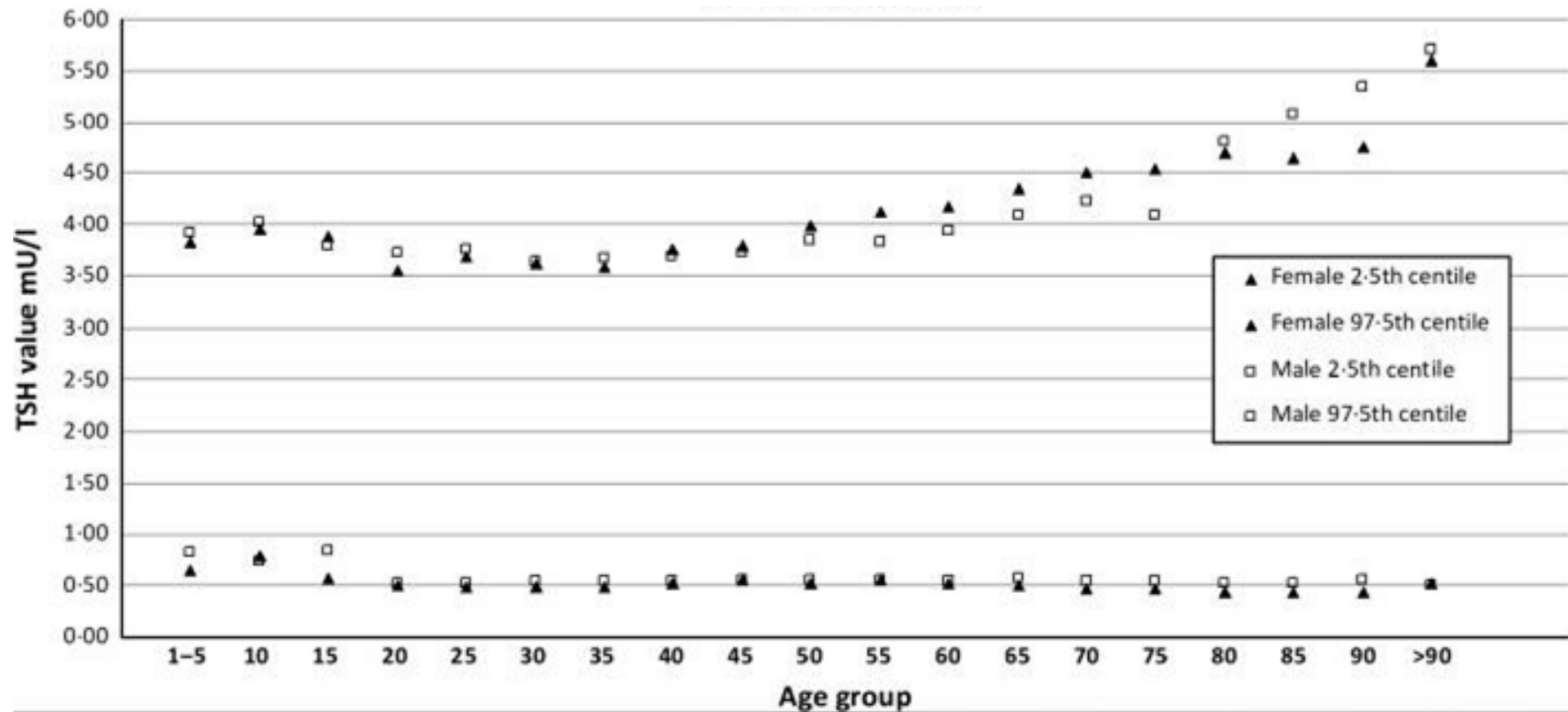
3rd T: 0.3 – 3.0

TT4:

Adult RI * 1.5

Aging and TSH Reference Interval

Age Specific RI: for >70 years up to 6.0



Thank you for your Attention!

Questions?

Mohammad Reza Bakhtiari, DCLS, PhD

• Iranian Research Organization for Science & Technology (IROST)

• Tehran, Iran