

## Beoordeling SKML QC voor steroiden

Jacquelien Hillebrand  
Laboratorium Endocrinologie  
AMC Amsterdam

09-12-2015



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## Externe QC laboratorium bepalingen

- Inzicht of de meetresultaten overeenkomen met laboratoria die dezelfde of een vergelijkbare meetmethode gebruiken (juistheid)
- Inzicht over de consistentie van de meetmethode over een langere periode
- Een benchmark voor de prestaties van het laboratorium ten opzichte van anderen (score systeem)



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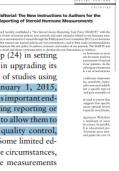
### 5.6.3 Interlaboratoriumvergelijkingen

#### 5.6.3.1 Deelname

Het laboratorium moet deelnemen aan (een) interlaboratoriumvergelijking(s) per periode, en interpreteren van onderzoeksresultaten. Het laboratorium moet de resultaten van interlaboratoriumvergelijking(s)programma(s) monitoren en deelnemen aan hieraangevoerde programma's om de juistheid van de resultaten te verifiëren. Deelname moet worden voldaan aan de voorwaarden van de betreffende interlaboratoriumvergelijking(s)programma(s).

OPMERKING - Het laboratorium behoort niet te namen aan interlaboratoriumvergelijkingen volgens de relevante eisen van ISO/IEC 17043.

uring  
ance-  
cific  
score), the *Journal* is taking the next step (24) in setting acceptable assay standards for the field in upgrading its submission requirements for publication of studies using sex steroid measurements. Effective January 1, 2015, manuscripts describing steroid assays must include a statement that indicates the methods used to allow them to be reproduced together with standard quality control, specificity, and reproducibility metrics. Some limited editorial discretion may be exercised for rare circumstances, such as where a study reports hormone measurements



## Externe QC laboratorium bepalingen

### Ronde samenvattingssrapport, histogrammen, jaaroverzicht:

- Welke methode worden gebruikt (in NL)
- Prestaties van verschillende methode groepen



## Externe QC laboratorium bepalingen

### Ronde samenvattingssrapport, histogrammen, jaaroverzicht:

- Welke methode worden gebruikt (in NL)
- Prestaties van verschillende methode groepen

- Hormonen in serum: ± 123 deelnemers
  - o.a. steroiden
- Hormonen in urine: ± 37 deelnemers
  - cortisol, cortison
- Hormonen in speeksel: ± 18 deelnemers
  - cortisol, cortison

ACTH	Aldosteron
Androsteendion	C-peptide
Cortisol	DHEAS
Digoxine	Ferritine
Folaat	FSH
Groeihormoon	IGF-1
Insuline	LH
Oestradiol	Progesteron
Progesteron,17OH	Prolactine
PTH	SHBG
T3	T3, vri
T4	T4, vri
TBG	Testosteron
TSH	Vit. D 1,25 (OH)-
Vitamine B12	Vitamine D, 25OH



## Externe QC laboratorium bepalingen

Welke kwaliteit heb je nodig voor diagnose en behandeling van:

- glucocorticoid excess
- pubertas praecox
- androgeen excess

Is huidige kwaliteit voldoende?

- jaaroverzicht bindingsanalyse 2014 (de "Lentjes"plots)
- ronde overzichten hormonen in serum/urine/speeksel 2015



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ZO  
DAT WAREN  
DE REGELS  
DAN GAAN WE  
NU OVER NAAR  
DE REALITEIT

Loesje

Postbus 1045 6801 BA Arnhem www.loesje.nl



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## Glucocorticoid excess

Diagnose + follow-up behandeling:

- Cortisol plasma na dexamethason
- Cortisol urine
- Cortisol speeksel middernacht

gebruikelijk: cortisol <50 nmol/L  
sterk afh van methode  
gebruikelijk: cortisol <4 nmol/L

Is de kwaliteit voldoende?

**Referentie:**  
Hollenman F et al. Evaluation of endocrine tests. B: screening for hypercortisolism. Neth J Med, 2005; 63: 348-353  
Bons J et al. Cortisol en het syndroom van Cushing. NTVG 2012;156:A3556Q



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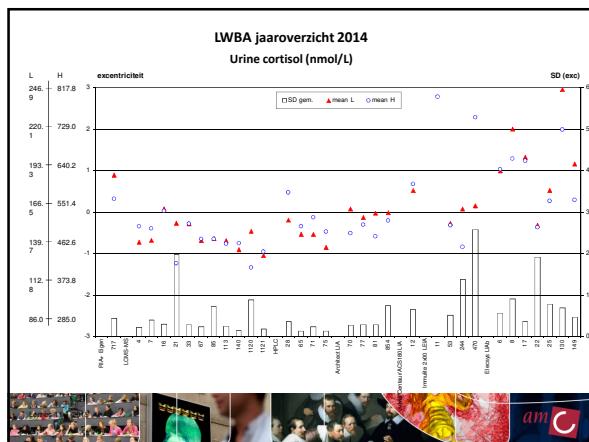
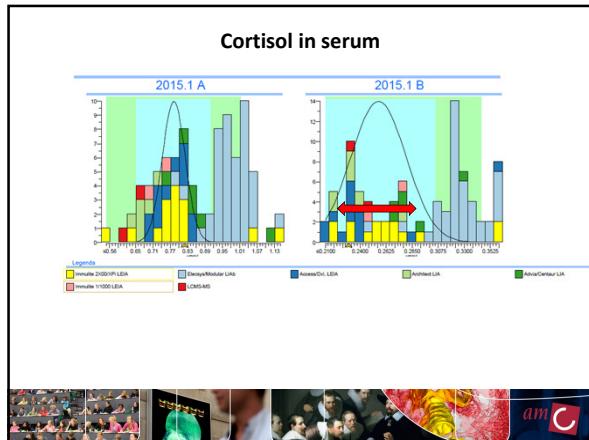
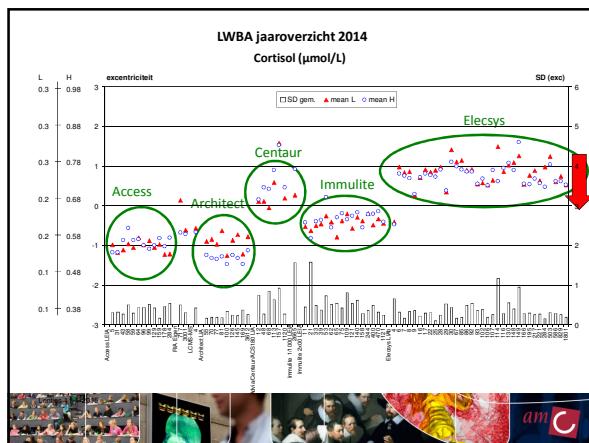
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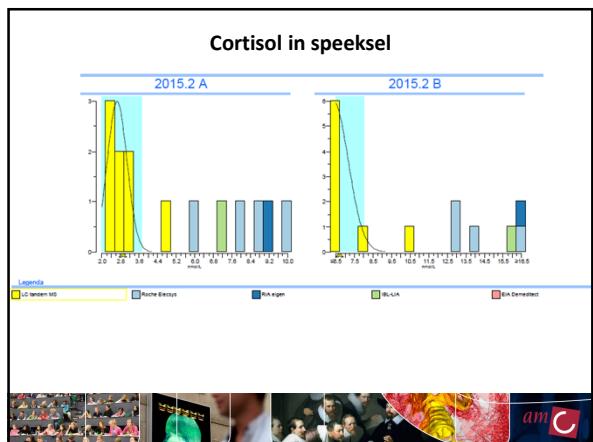
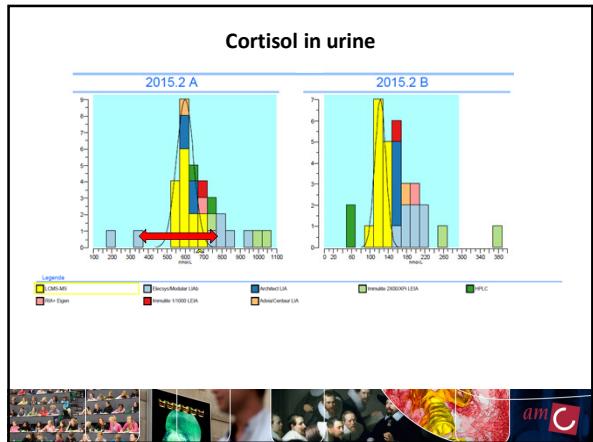
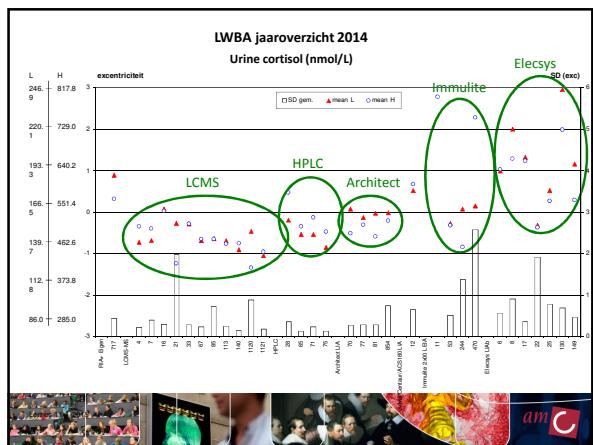
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## Glucocorticoid excess

### Conclusies:

- Variatie tussen platforms
- Noodzaak tot standaardiseren/harmoniseren
- Tot die tijd: eigen referentiewaarden / cut-off vaststellen

### Diagnose + follow-up behandeling:

• Cortisol plasma na dexamethason	AMC <95 nmol/L
• Cortisol urine	AMC <180 nmol/L
• Cortisol speeksel	AMC <4.8 nmol/L

### Referentie:

Hollenstein P et al. Evaluation of endocrine tests. B: screening for hypercortisolism. Neth J Med, 2005; 63: 348-353

Bons J et al. Cortisol en het syndroom van Cushing. NTvG 2012;156:A3556Q



## Pubertas Praecox



## Pubertas Praecox

Oestradiol,  
Testosteron

### Diagnose:

- GnRH stimulatietest: LH > 6 U/L, LH/FSH >1
- Basaal LH > 0,6 U/L LH/FSH >1

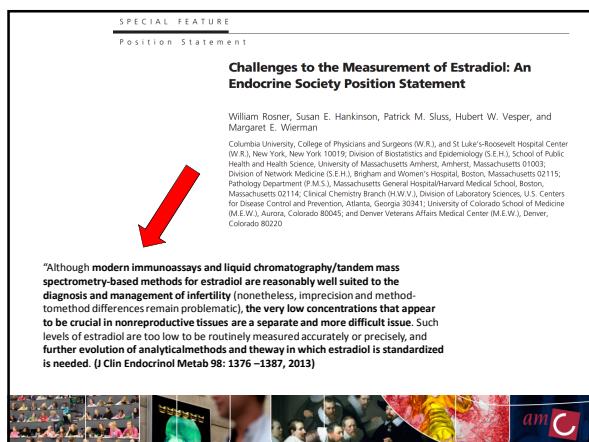
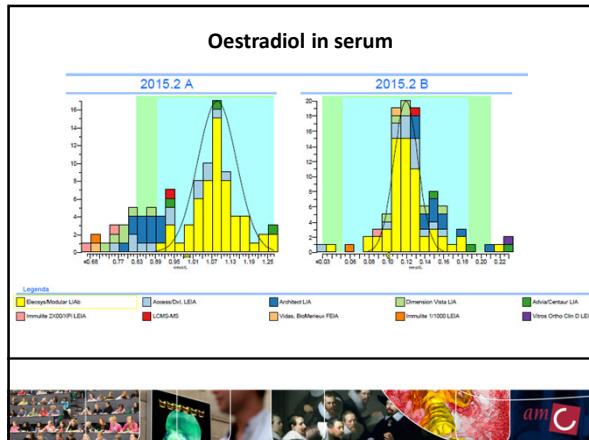
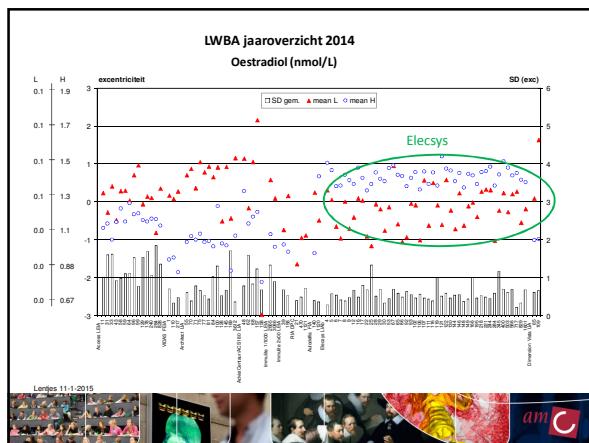
### Is de kwaliteit voldoende?

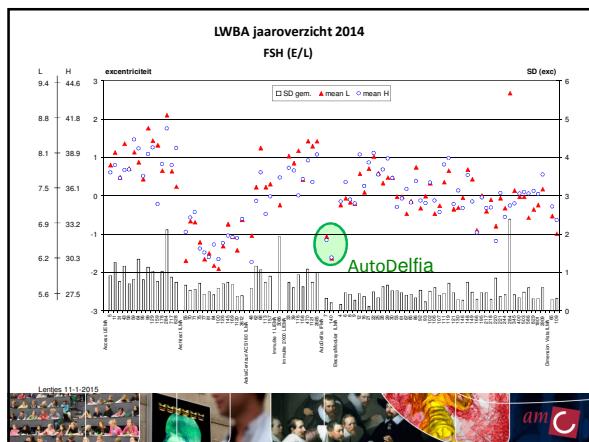
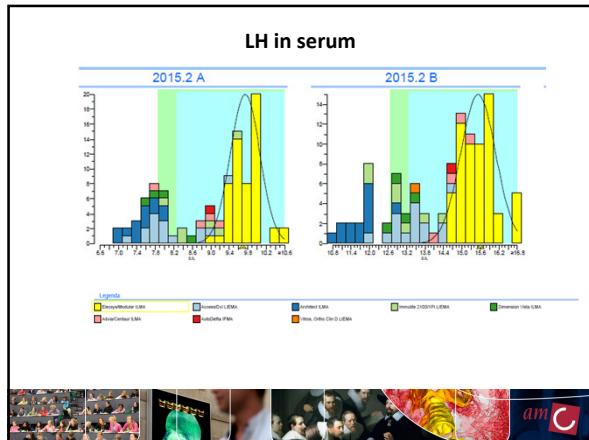
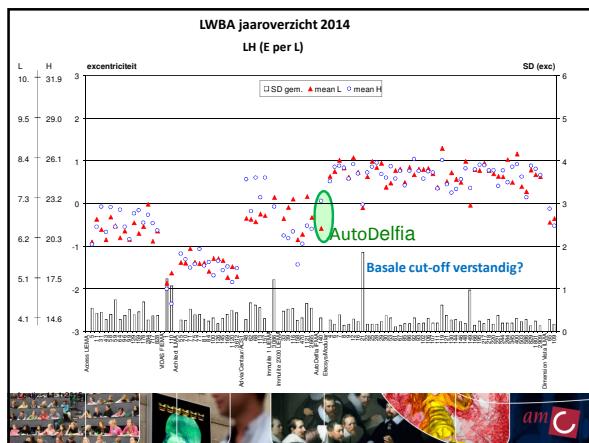
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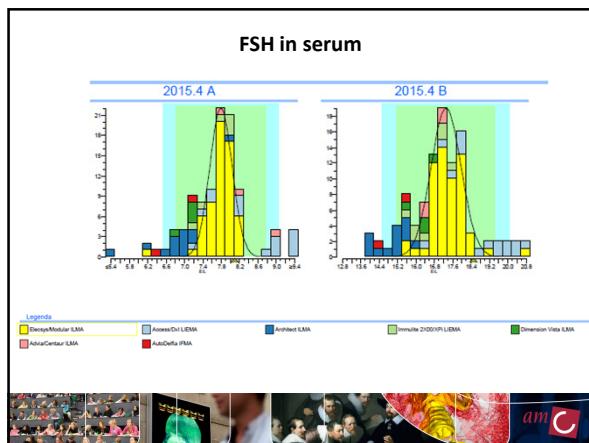
Werkboek kinderendocrinologie

Brito VN et al. Diagnostic value of fluorimetric assays in the evaluation of precocious puberty. JCEM 1999 Oct;84(10):3539-44.










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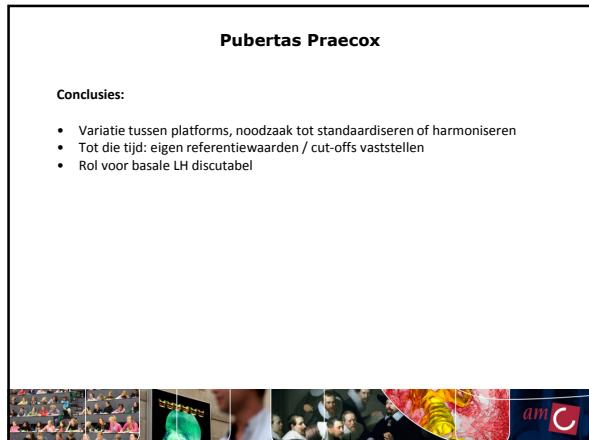
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## Androgeen excess

### Diagnose en behandeling:

- 17OHP
- Androsteendion
- Testosteron

Is de kwaliteit voldoende?



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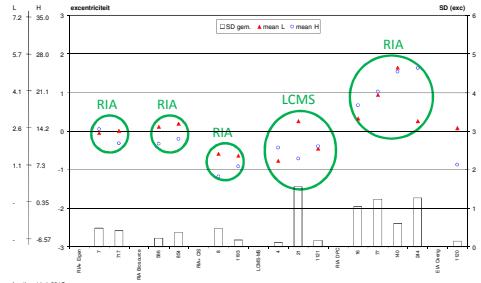
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## LWBA jaaroverzicht 2014 17-hydroxy-Progesteron (nmol/L)



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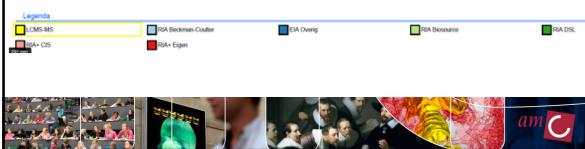
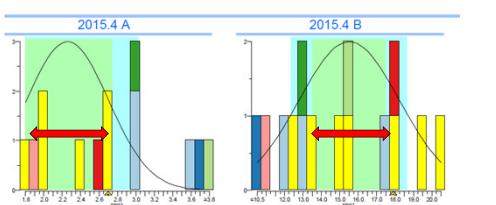
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## 17OHP in serum



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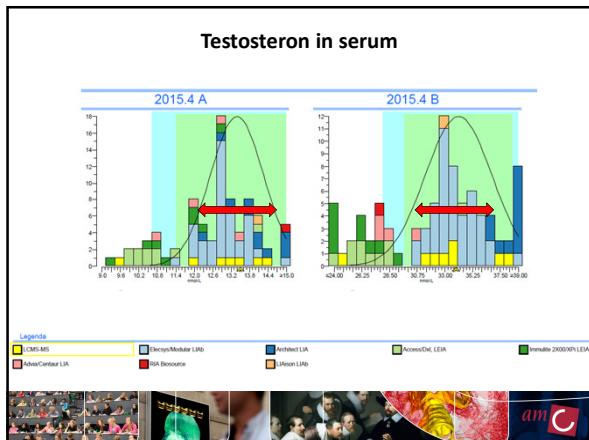
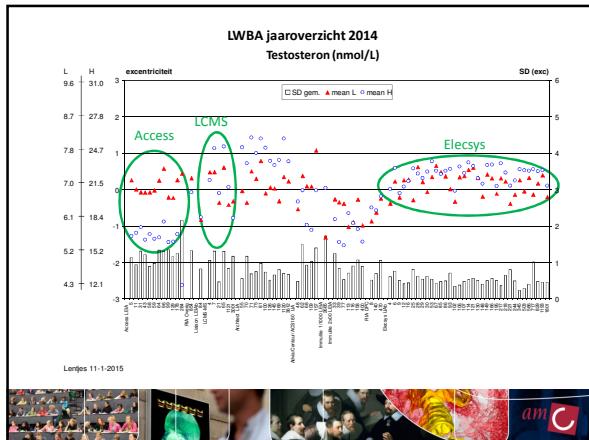
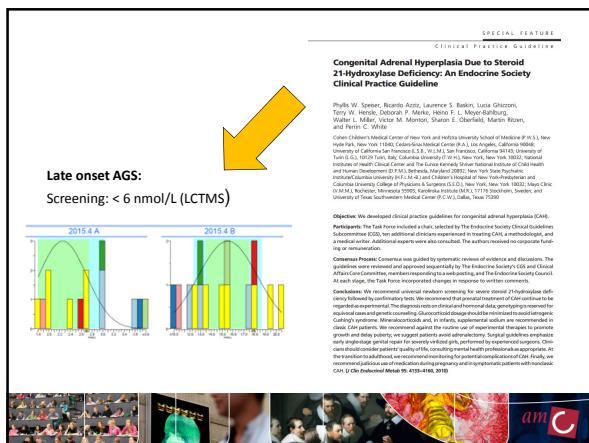
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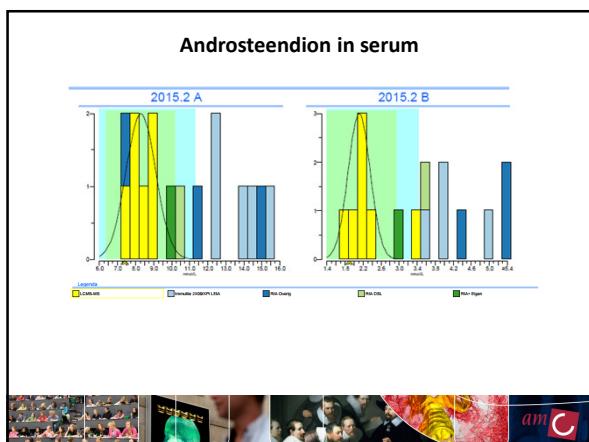
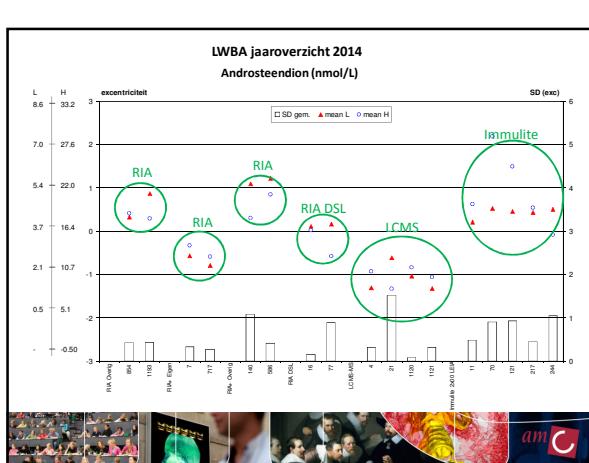
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## Androgeen excess

**Conclusies:**

- Vaker gemeten met LC-MS, waardoor minder problemen van kruisreactiviteit
- Verwachting van verminderde spreiding bij LC-MS komt nog niet geheel uit




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Clinical Chemistry 61:12  
DOI 10.1209/clinchem.2015.27307

Endocrinology and Metabolism

**Comparison of 7 Published LC-MS/MS Methods for the Simultaneous Measurement of Testosterone, Androstenedione, and Dehydroepiandrosterone in Serum**

Rahel M. Buttler,<sup>1</sup>\* Frans Martens,<sup>2</sup> Flavia Fausti,<sup>2</sup> Hail T. Pham,<sup>2</sup> Max M. Kushner,<sup>2,3</sup>\*\* Marcel J.W. Jonkman,<sup>2</sup> Laura Over,<sup>2</sup> Angelica Taylor,<sup>2</sup> Tos Sedoroff,<sup>2</sup> Mariana A. Blaquier,<sup>2</sup> and Alvernaeke C. Heijboer,<sup>2</sup>†

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Correspondence: Received: March 1, 2015; revised: June 1, 2015; accepted: July 1, 2015; published online: August 24, 2015. © 2015 American Association for Clinical Chemistry

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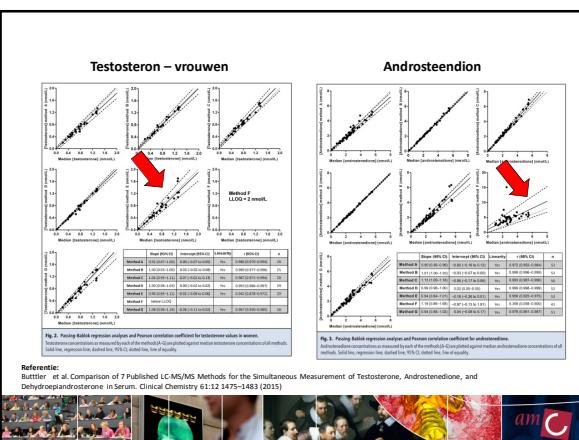
## Testosteron – vrouwen

## Androsteendion

Fig. 2. Peeling-Babitt regression analysis and Pearson correlation coefficient for testosterone values in women.

Fig. 3. Peeling-Babitt regression analysis and Pearson correlation coefficient for androsteendion.

References:  
Buttler et al. Comparison of 7 Published LC-MS/MS Methods for the Simultaneous Measurement of Testosterone, Androstenedione, and Dehydroepiandrosterone in Serum. *Clinical Chemistry* 61:12 1475–1483 (2015)




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### Concluderend: Externe QC laboratorium bepalingen

- Belangrijk: inzicht in juistheid methode, ISO15189
- Variatie tussen methoden blijft bestaan
- LC-MS niet altijd beter; tussen LC-MS labs nog aanzienlijke variatie:
  - Calibratie?, methode optimalisatie?, matrix?, ionisatie suppressie?,
- Noodzaak tot standaardisatie/harmonisatie
- Noodzaak tot methode-specifieke referentiewaarden/cut-offs



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### Vragen?



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