

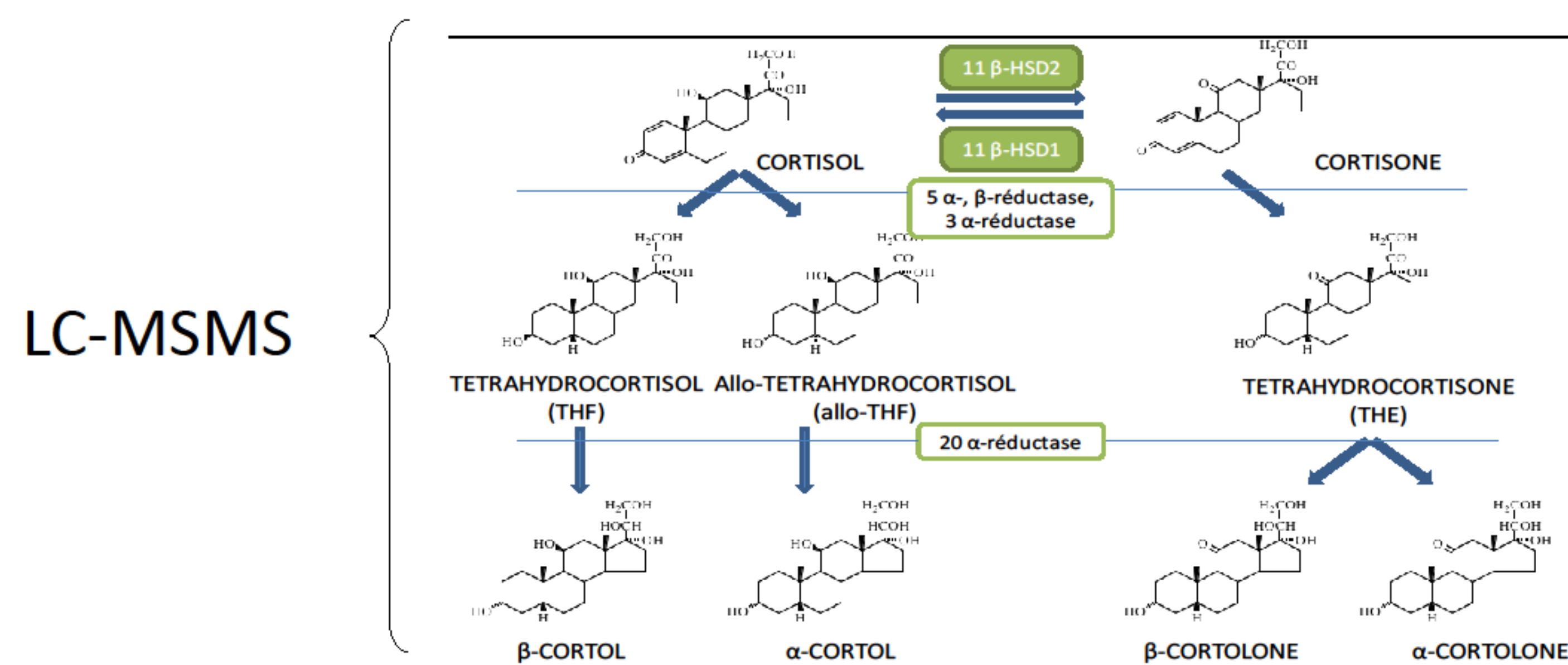
# Urinary glucocorticoid metabolites: biomarkers to classify adrenal incidentalomas?

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**Objectives:** Total urinary cortisol metabolites represent cortisol production and metabolism. We hypothesized that to assay metabolites could add some information to the one provided by a sole cortisol assay.

**Design and patients:** We set up an multiplex mass spectrometry assay to quantify cortisol metabolites. We investigated 43 patients with benign secreting (AT+) or silent (AT-) adrenal tumours (1) compared to 48 lean (NI) or 143 obese (Ob) subjects. The initial investigation assayed immunoreactive urinary free cortisol (UFC).



	Ctl		AT	
	N	Ob	AT-	AT+
age (yrs)	45 [25-72]	46 [19-74]	58 [39-72] ***	56 [26-71]
sex ratio	0.3 [37/11]	0.28 [112/31]	0.35 [20/7]	0.33 [12/4]
BMI (kg/m <sup>2</sup> )	23 [18-30]	39 [31-55] ***	27 [21-40]	25 [18-38]
Cortisol 8h (nmol/L)	544 [186-767]	485 [264-784]	477 [264-852]	477 [295-864]
ACTH 8h (pmol/L)	8 [1.7-12.1]	5.3 [1.2-18.0]	4.3 [1.4-11.2]	1.8 [1.2-3.5] ***
irUFC (µg/24h)	34 [19-79]	28 [9-91]	41 [15-78]	93 [18-530] ***
Cortisol post-DST (nmol/l)	43 [27-63]	42 [27-119]	51 [27-117]	108 [63-847] ***
Cortisol 0h (nmol/L)	145 [62-281]	137 [44-290]	155 [40-419]	224 [136-820] *
ACTH 0h (pmol/L)	2.5 [1.3-5.9]	2.4 [1.2-9.2]	1.5 [1.2-7.9] *	1.2 [1.2-2.4] ***

**Criteria of AT+/AT- classification:**

Cortisol post-DST (nmol/l) > 83 nmol/L  
 irUFC (µg/24 h) > 90µg/24h  
 ACTH 8 h (pmol/l) < 10pg/mL

AT+ = 2 or 3 criteria  
 AT- = 1 criterium

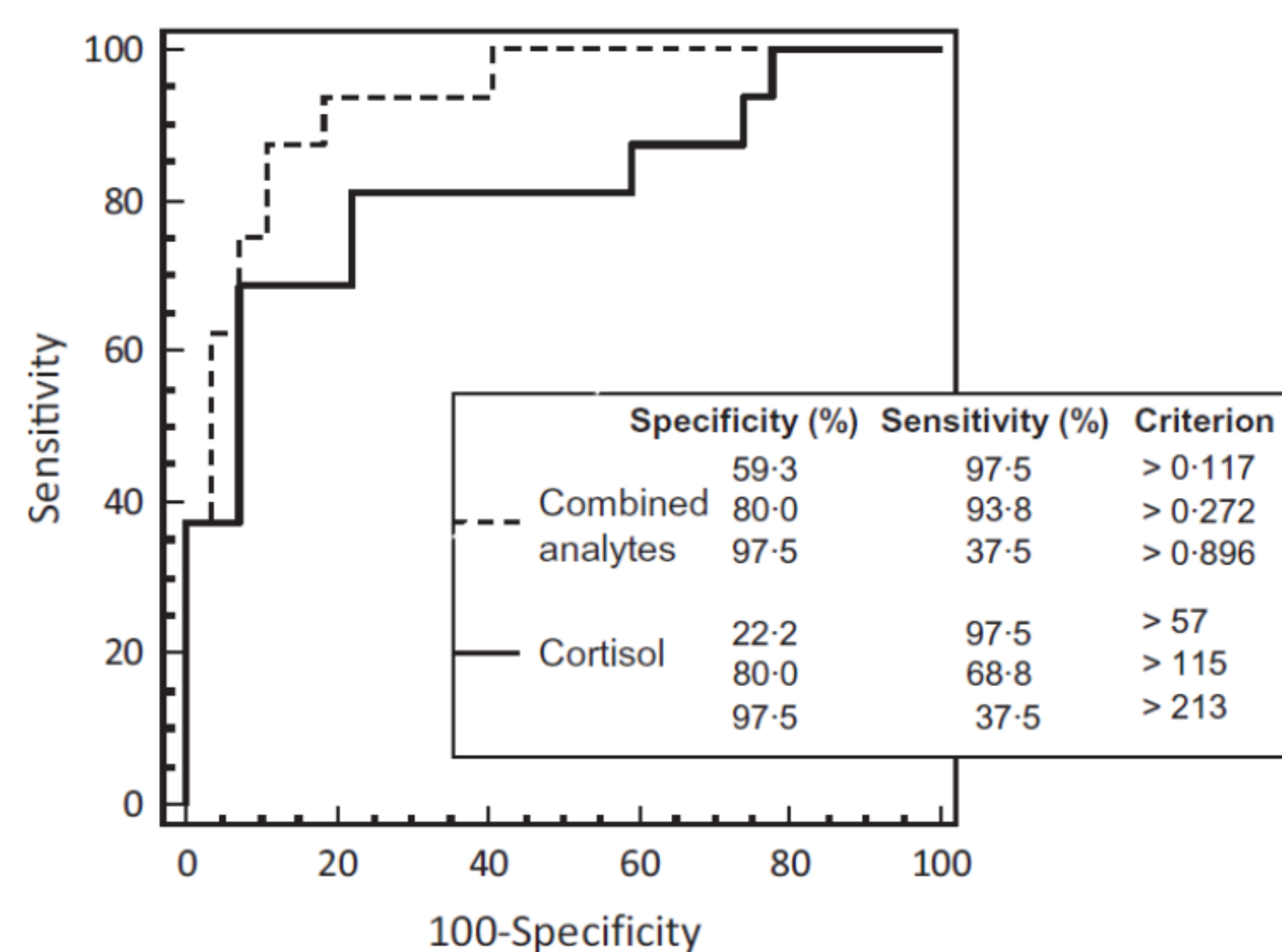
## Results: Comparison sole cortisol immunoassay and metabolite cortisol spectrometric assay

### Significant difference between cortisol and α-cortol concentration for AT+ and AT-

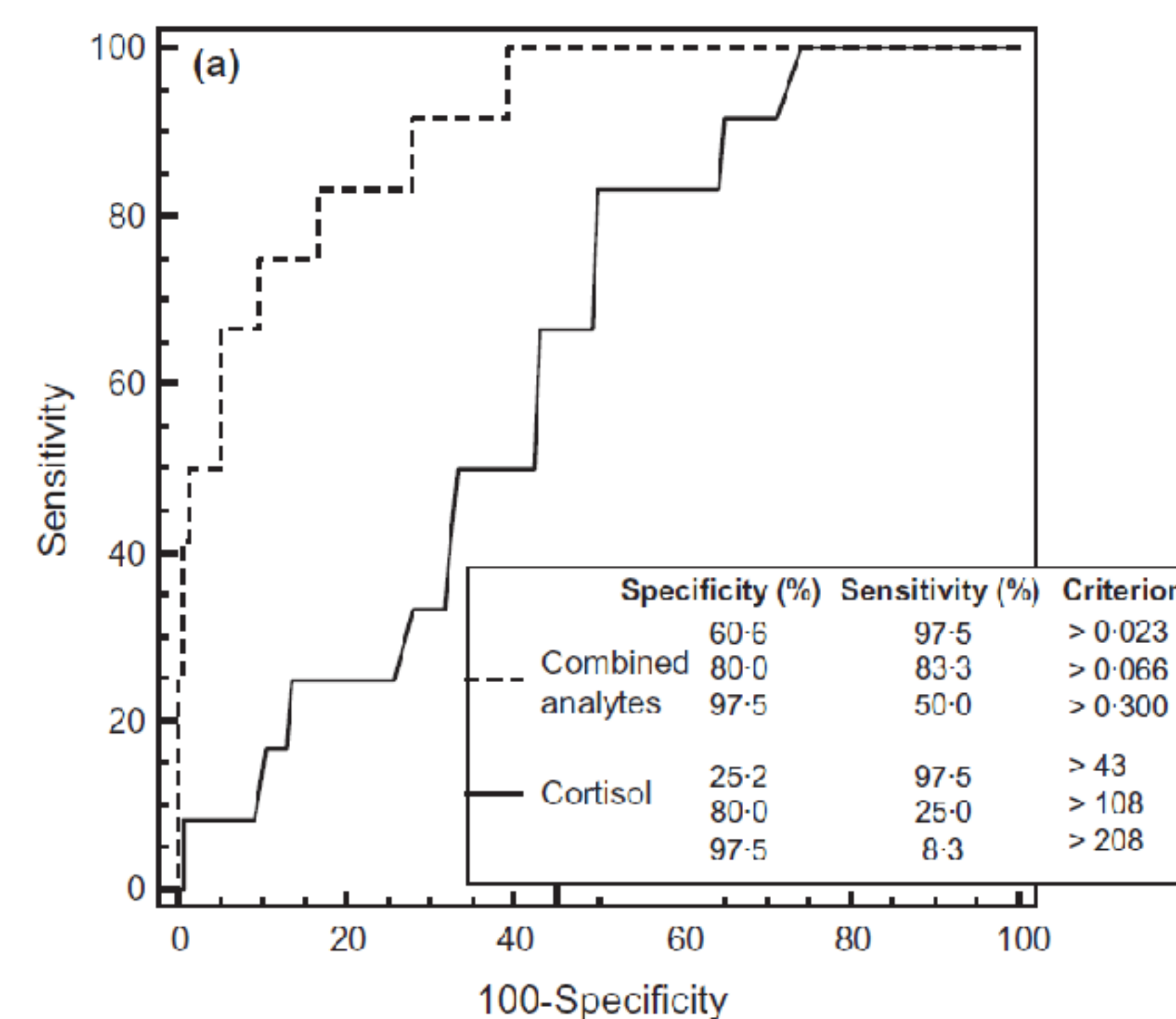
	irUFC	Cortisol	cortisone	THF	alloTHF	THE	α-cortol	β-cortol	α-cortolone	β-cortolone
<b>Ctl</b>										
median (µg/24h)	29	68	100	2400	245	3261	163	239	909	202
[2,5th-97,5th percentile]	[10-89]	[17-208]	[19-256]	[727-8048]	[70-1208]	[823-8938]	[41-462]	[48-692]	[176-1974]	[39-553]
<b>AT-</b>										
median (µg/24h)	41	82	106	2752	315	3568	147	258	645	296
[2,5th-97,5th percentile]	[15-78]	[43-213]	[39-311]	[1440-6871]	[129-629]	[1226-7741]	[61-408]	[128-635]	[281-1101]	[96-747]
<b>AT+</b>										
median (µg/24h)	93 ***	185 ***	156 **	4054 **	200	4601 **	252	471 *	1079	512 **
[2,5th-97,5th percentile]	[18-530]	[63-720]	[39-405]	[1129-12066]	[114-477]	[1521-11269]	[80-829]	[124-1114]	[269-2199]	[153-1288]

irUFC, immunoreactive free cortisol; THF, tetrahydrocortisol; THE, tetrahydrocortisone. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001 compared to normal subjects; \*\*\*\*P < 0.05 compared to AT subjects. Ctl control subjects.

Cortisol + allo-THF + THE in combinaison better distinguish AT- vs. AT+



Cortisol + α-cortolone + β-cortolone in combinaison better distinguish AT- vs control



**Discussion:** Cortisol metabolite excretion is modified in AT, including AT-, patients even without modification of UFC. Clinical usefulness of these biomarkers has to be investigated in prospective studies following up patients with AT

**References:** 1- Arlt, W., Biehl, M., Taylor, A.E. et al. Urine steroid metabolomics as a biomarker tool for detecting malignancy in adrenal tumors. JCEM (2011).  
 2-Chiodini, I. Clinical review: diagnosis and treatment of subclinical hypercortisolism. JCEM. (2011)