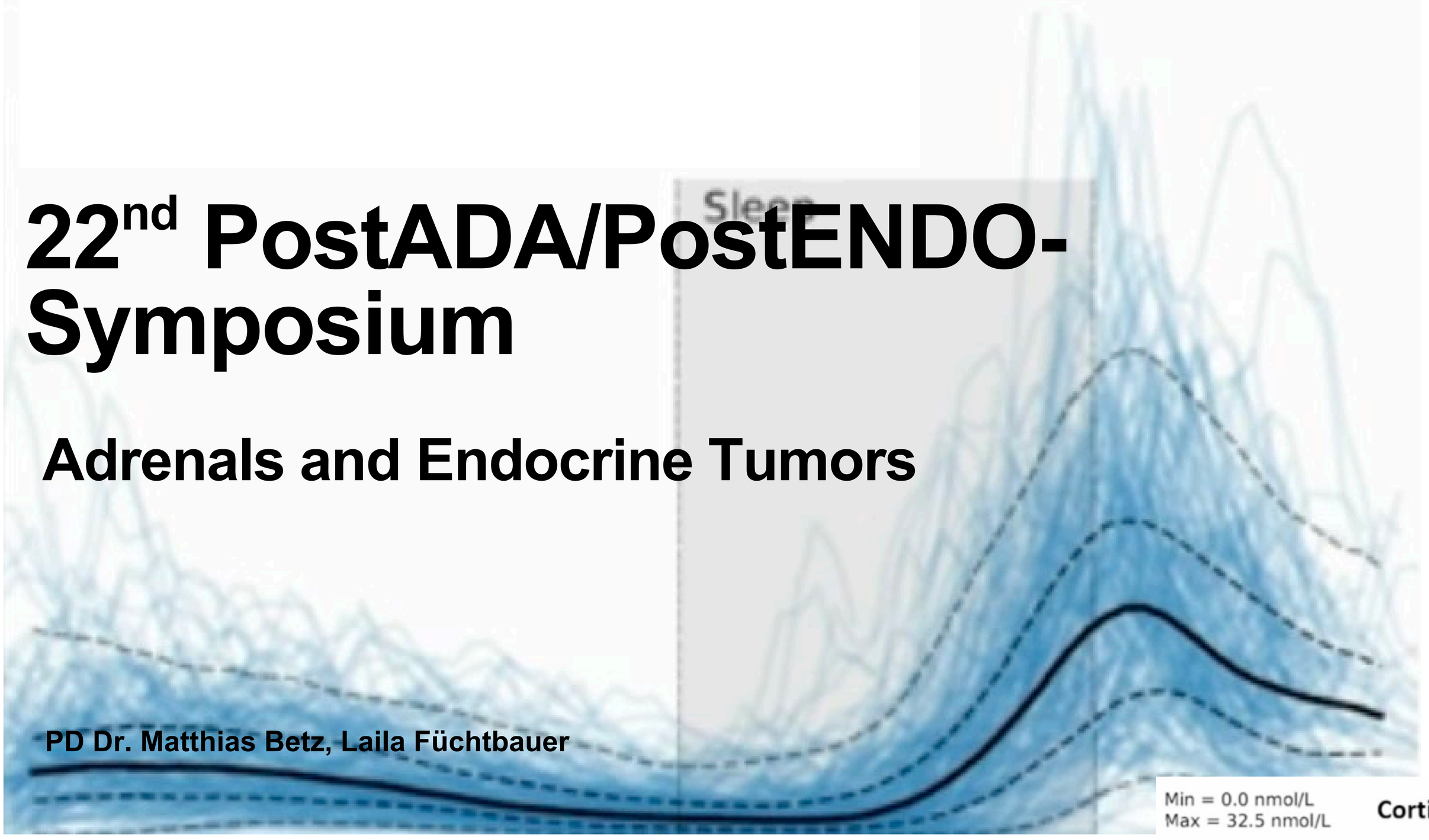
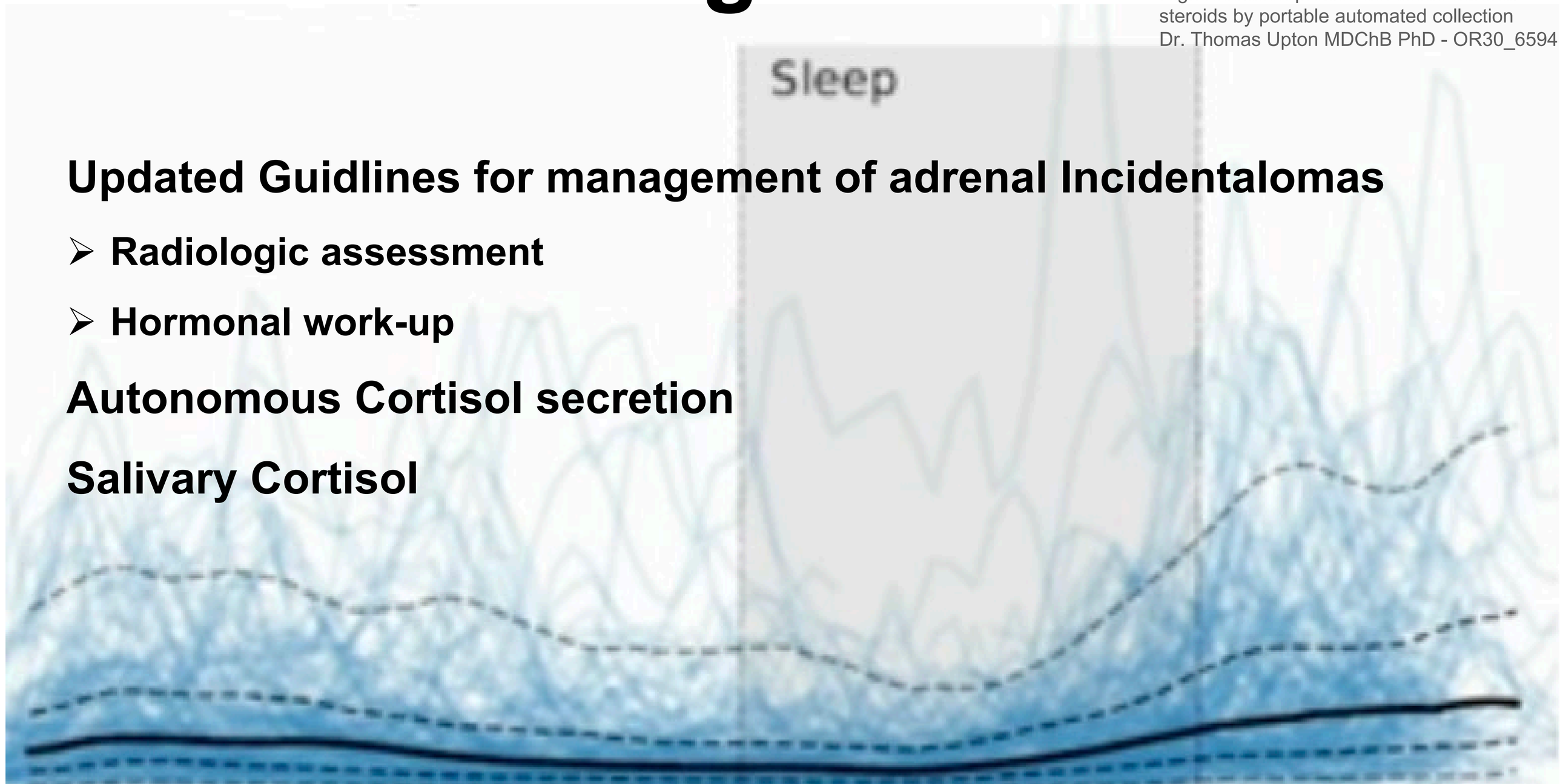
22nd PostADA/PostENDO-Symposium

Adrenals and Endocrine Tumors

PD Dr. Matthias Betz, Laila Füchtbauer



Agenda

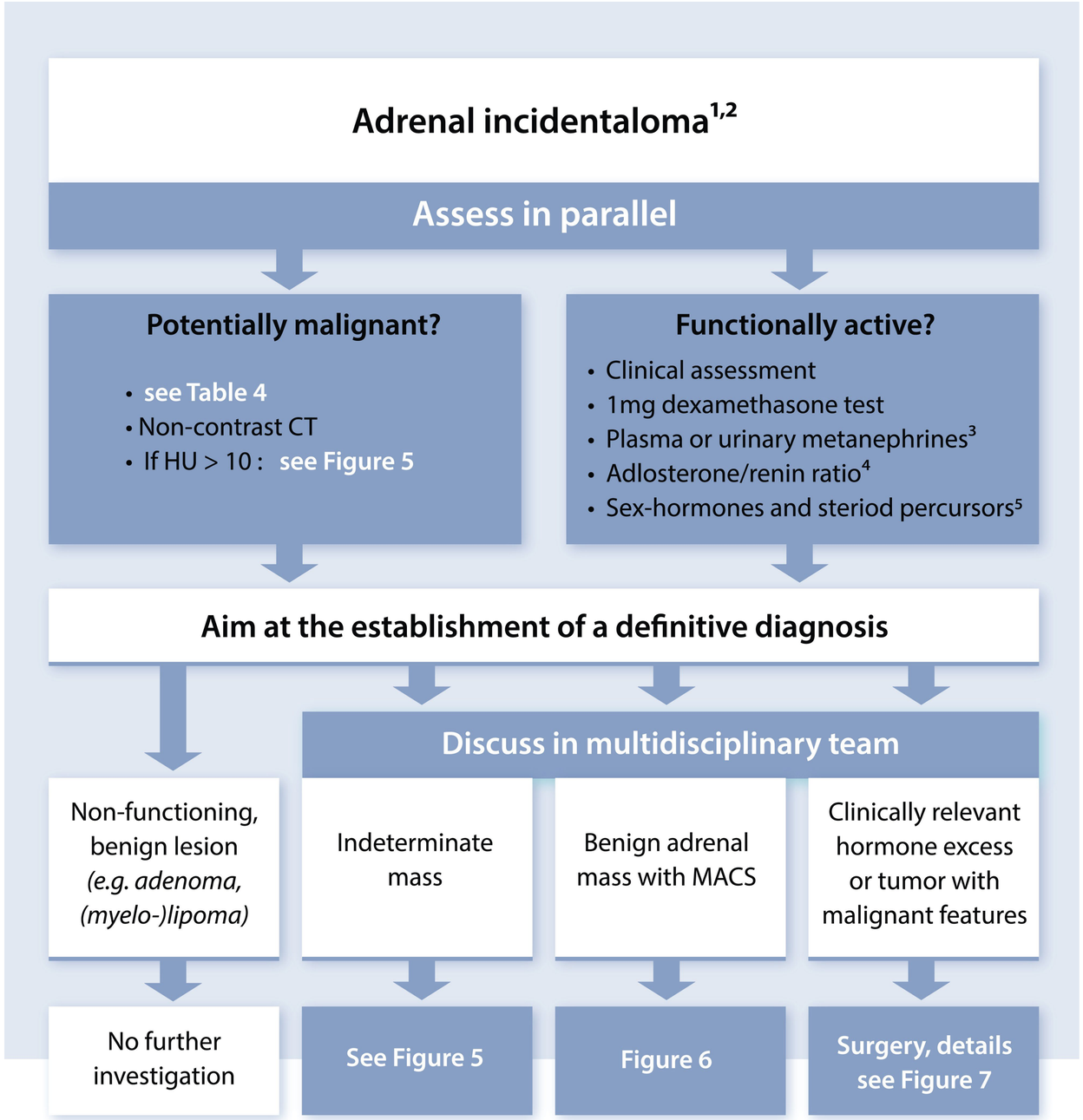


Updated Guidlines for management of adrenal Incidentalomas

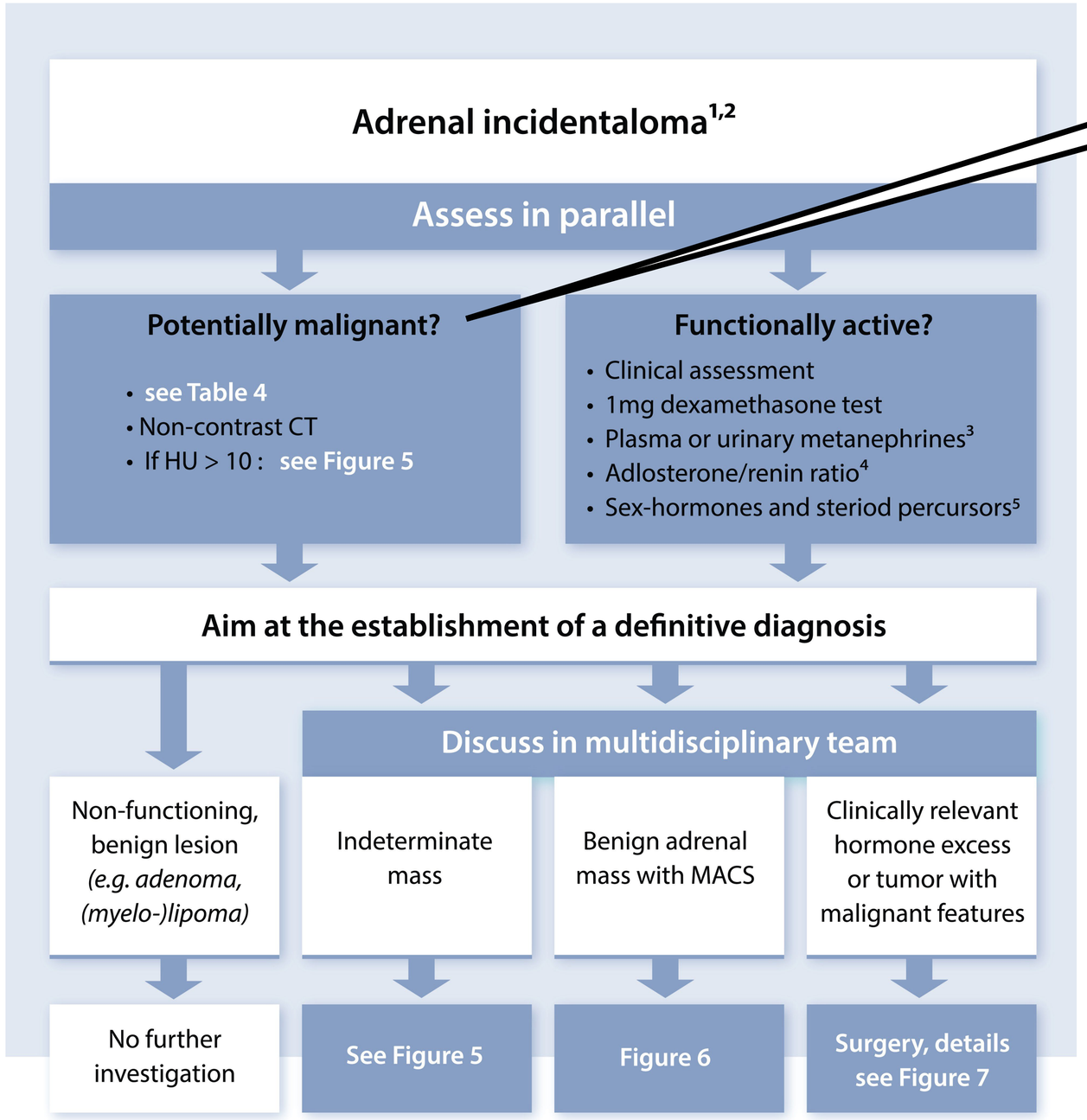
- Radiologic assessment
- Hormonal work-up

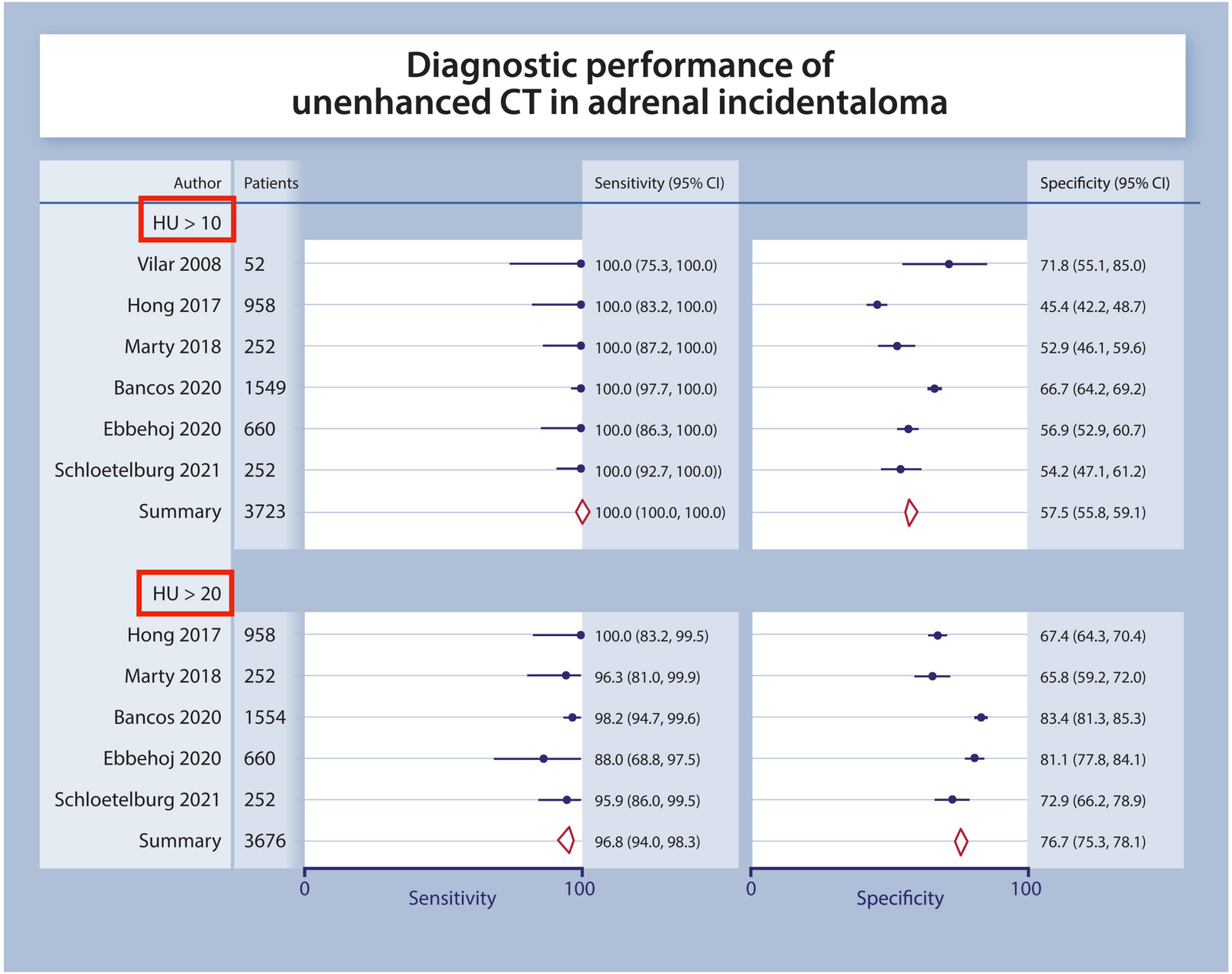
Autonomous Cortisol secretion

Salivary Cortisol

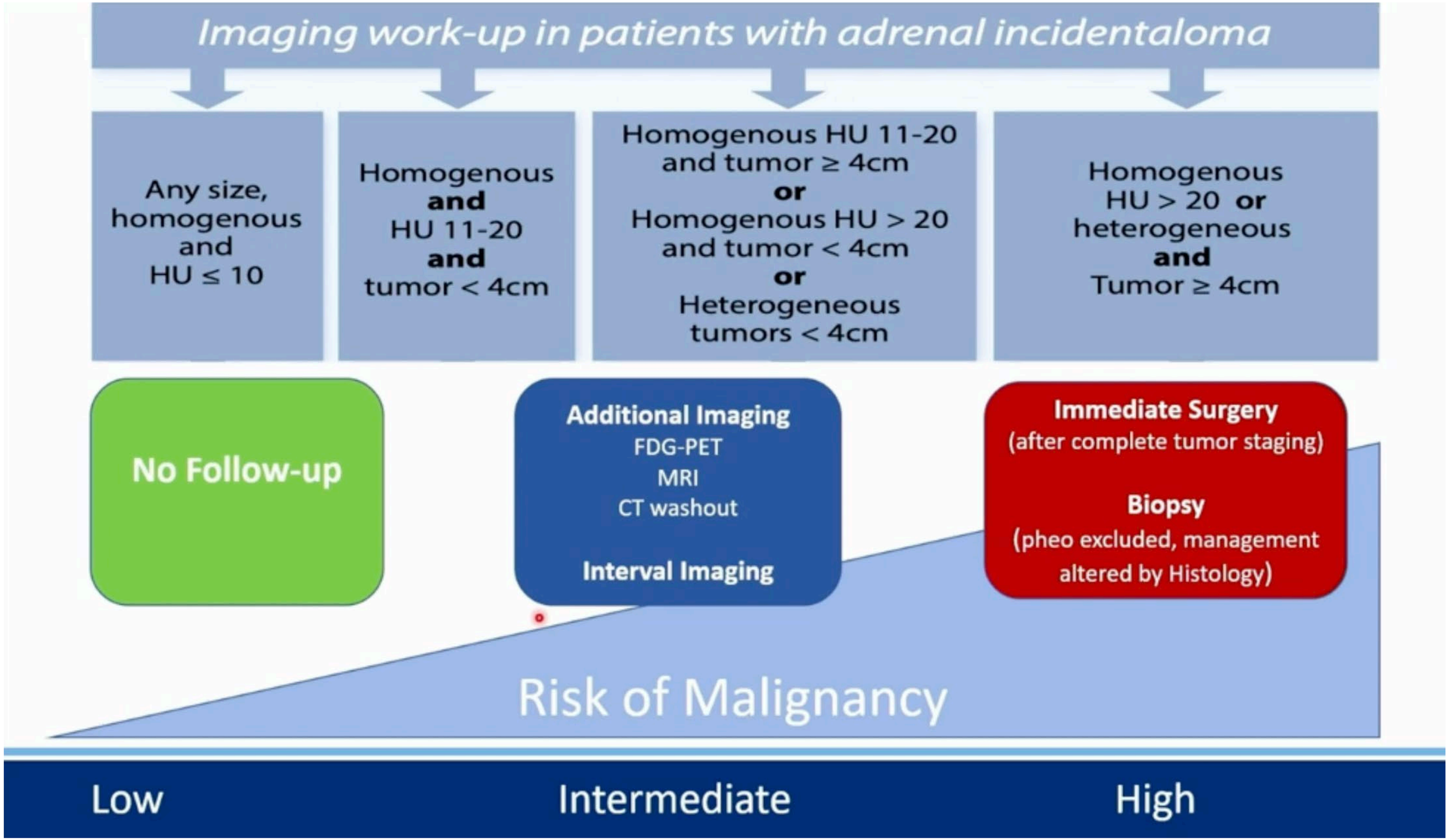

Adrenal incidentaloma[1,2]
Assess in parallel
Potentially malignant?
• see Table 4
• Non-contrast CT
• If HU > 10 : see Figure 5
Functionally active?
• Clinical assessment
• 1mg dexamethasone test
• Plasma or urinary metanephrines[3]
• Adlosterone/renin ratio[4]
• Sex-hormones and steriod percursors[5]
Aim at the establishment of a definitive diagnosis
Discuss in multidisciplinary team
Non-functioning, benign lesion (e.g. adenoma, (myelo-)lipoma)
Indeterminate mass
Benign adrenal mass with MACS
Clinically relevant hormone excess or tumor with malignant features
No further investigation
See Figure 5
Figure 6
Surgery, details see Figure 7

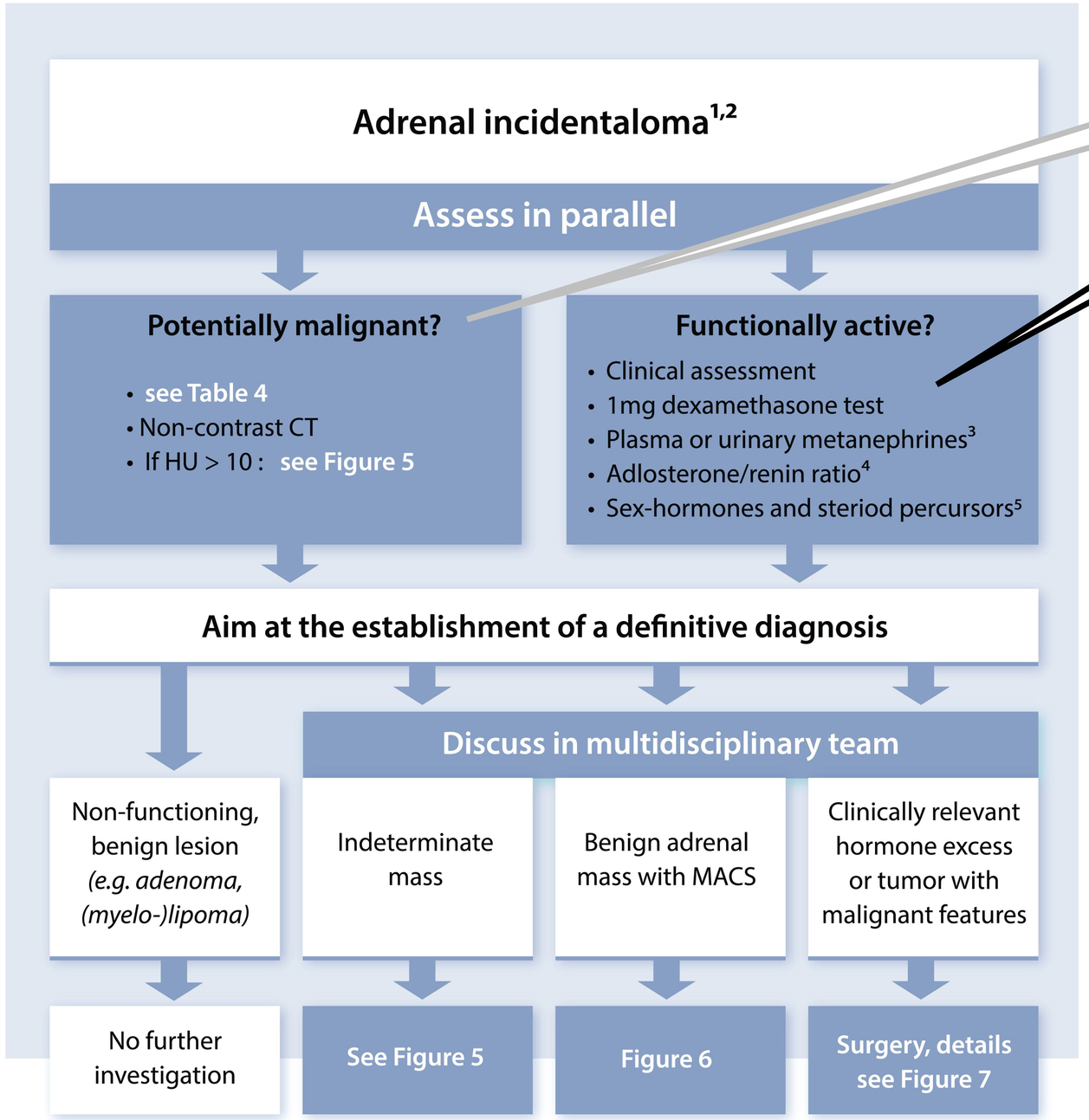
MTP26:Bilateral adrenal masses: Evaluation and Management
Prof. Stylianos Tsagarakis, Athens, Greece





Sensitivity = malignant tumors are correctly identified
Specificity = correct identification of benign lesions


Imaging work-up in patients with adrenal incidentaloma
Any size, homogenous and HU ≤ 10
Homogenous and HU 11-20 and tumor < 4cm
Homogenous HU 11-20 and tumor ≥ 4cm or Homogenous HU > 20 and tumor < 4cm or Heterogeneous tumors < 4cm
Homogenous HU > 20 or heterogeneous and Tumor ≥ 4cm
No Follow-up
Additional Imaging
FDG-PET
MRI
CT washout
Interval Imaging
Immediate Surgery
(after complete tumor staging)
Biopsy
(pheo excluded, management altered by Histology)
Risk of Malignancy
Low
Intermediate
High



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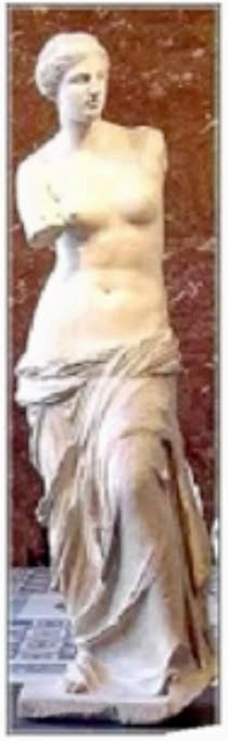
CONTINUUM OF AUTONOMOUS CORTISOL SECRETION



Normal

1.8 µg/dl
(50 nmol/l)

5 µg/dl
(138 nmol/l)

Overt CS

excluded

possible autonomous cortisol secretion

autonomous cortisol secretion

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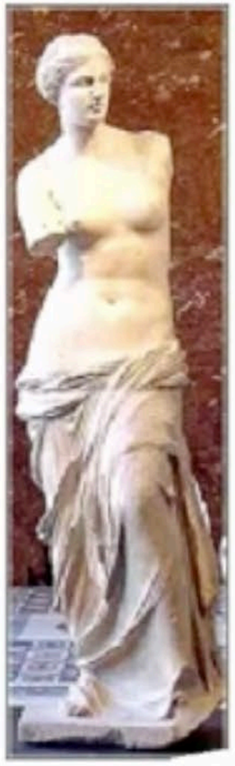
CONTINUUM OF AUTONOMOUS CORTISOL SECRETION



Normal

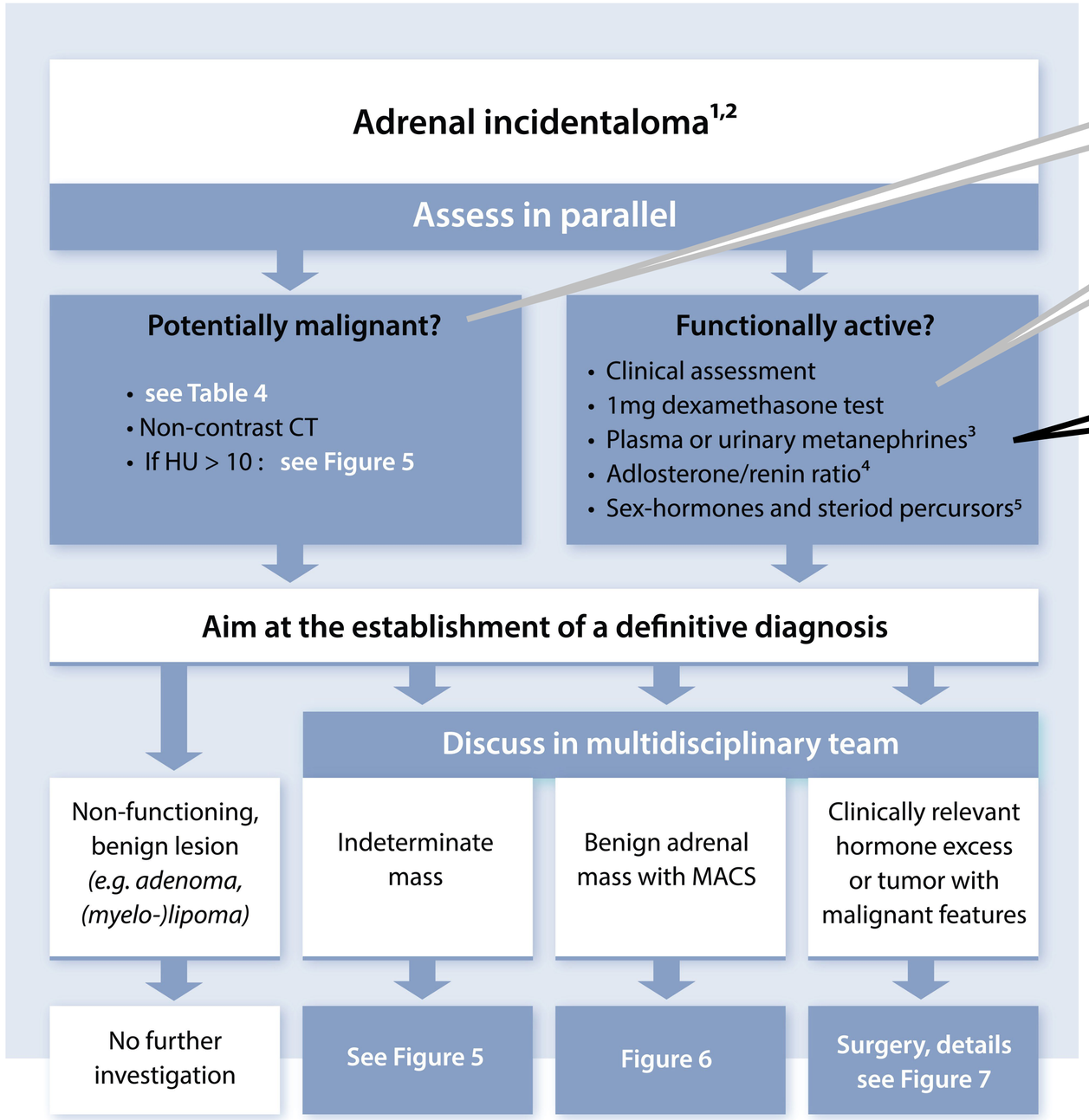
1.8 µg/dl
(50 nmol/l)

excluded

mild autonomous cortisol secretion

MACS

Overt CS



MTP26:Bilateral adrenal masses: Evaluation and Management
Prof. Stylianos Tsagarakis, Athens, Greece

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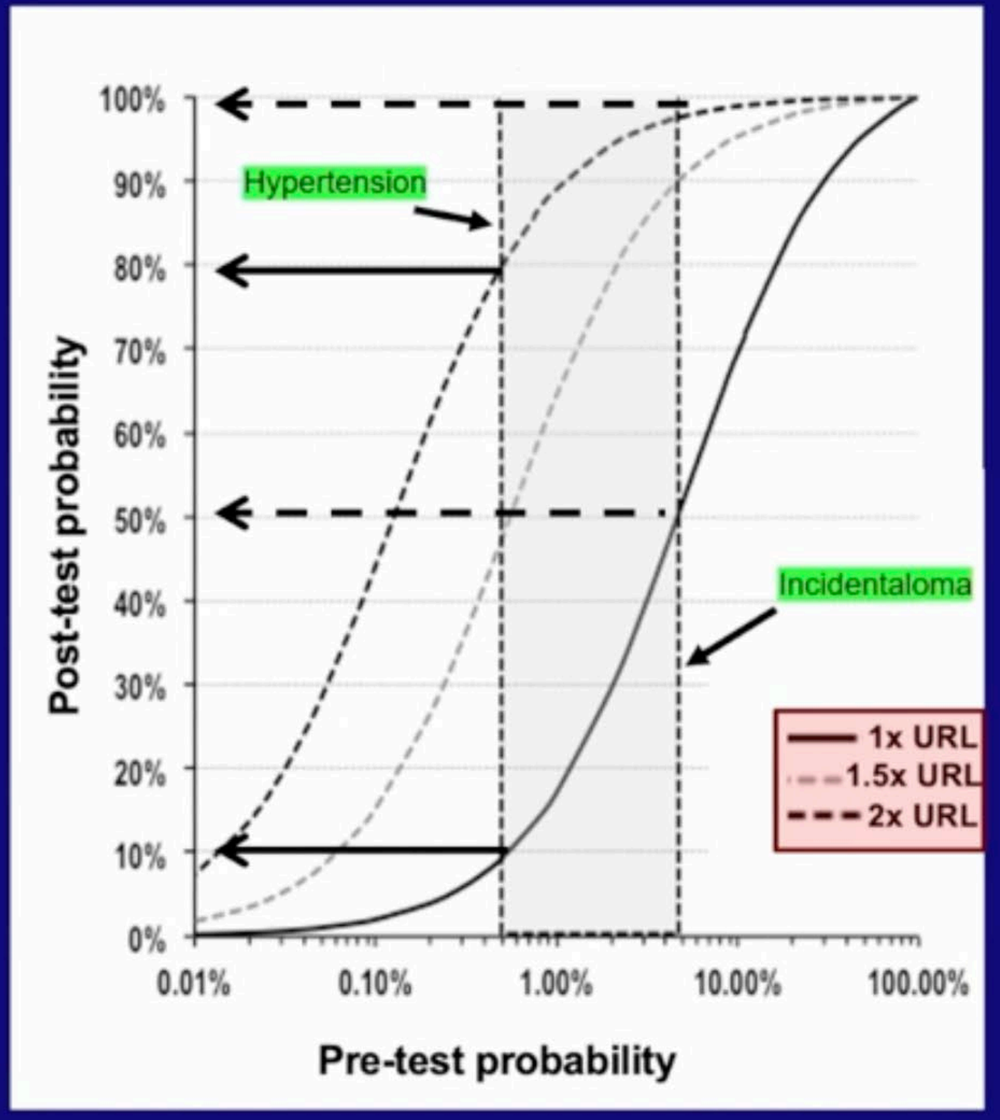
MTP10: Pearls and Myths in the Evaluation and Management of Pheochromocytoma
Prof. Karel Pacak, NIH, Bethesda, MD, USA

Pre- and post-test probability based on elevation of catecholamine metabolites above the URL in PHEO/PGL diagnosis and teaching points (4)

Elevation of plasma free metanephrines or methoxytyramine increases the likelihood of PHEO/PGL



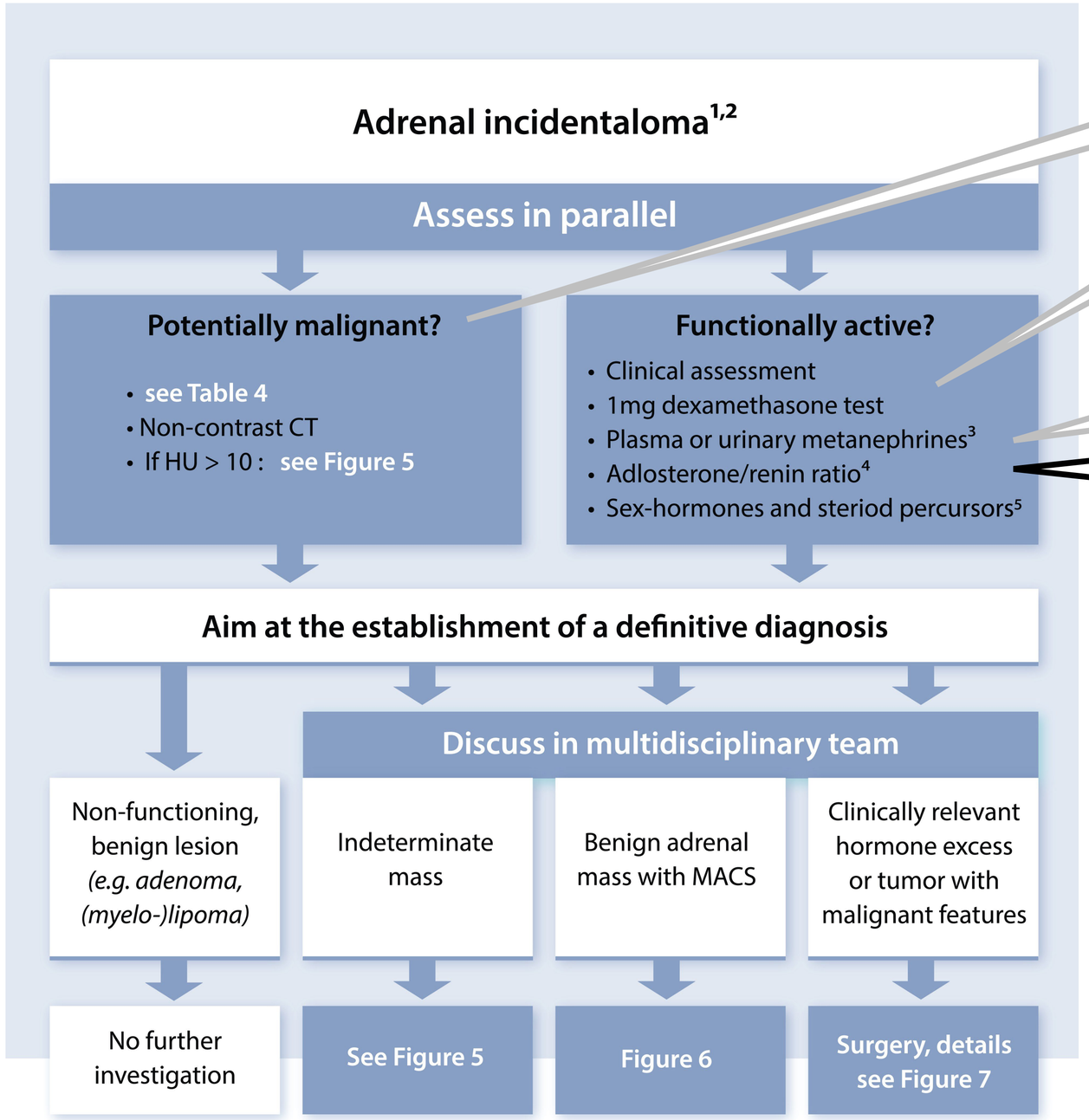
- Patients with hypertension or other symptoms/signs have a low likelihood of PHEO/PGL. In those patients, pre-test probability of having PHEO/PGL is less than 1%.

- Patients with adrenal incidentaloma, previous history of PHEO/PGL, and genetic predisposition have a higher likelihood of PHEO/PGL. In those with an adrenal incidentaloma, pre-test probability of having PHEO/PGL is 5%.

Diagnostic pearl: These and other results strongly support that plasma metanephrines & methoxytyramine offer better diagnostic performance than urine tests for patients who have a high likelihood of having PHEO/PGL.

URL: Upper reference limit

Eisenhofer & Lenders Endcrin. Rev. 2023; in press
Eisenhofer et al. Clin. Chem. 2018; 64:1646



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Prof. Karel Pacak, NIH, Bethesda, MD, USA

SY085_1647 Diagnostic challenges in pheochromocytoma & Paraganglioma in patients with chronic kidney desease
MD, PdD, PD Christina Pamporaki, Dresden, Germany

Biochemical work up of patients with advanced CKD

- Plasma samples should be preferred
- Measure free metanephrines and not deconjugated in plasma
- Do not assess methoxytyramine for patients with advanced CKD
- Blood should be drawn after at least 20 min of supine rest
- Blood should be drawn from the shunt at the end of HD
- Use LC/MS-MS
- Use CKD specific reference intervals

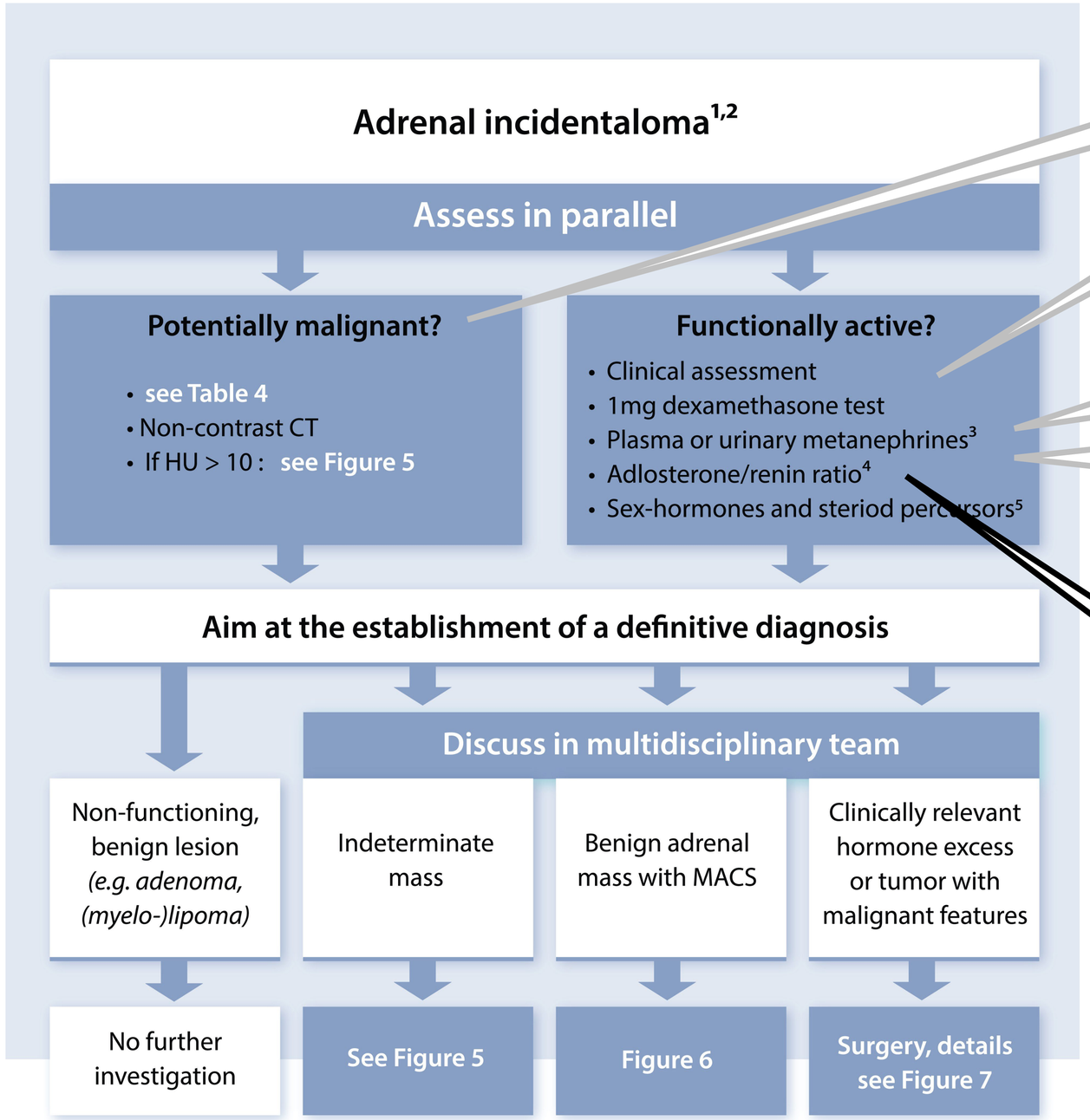
	Stage III	Stage IV/HD	HD
			Shunt
Upper Cut offs (nmol/L)			
Normetanephrine	1.158	1.535	1.055
Metanephrine	0.417	0.413	0.472

Eisenhofer G, Pamporaki C, Lenders JWM. Endocr Rev. 2023;bnad011.

Universitätsklinikum
Carl Gustav Carus
DIE DRESDNER.

Adrenal Research
CRC/TRR 205

ENDO2023



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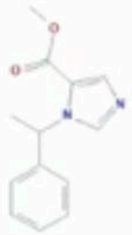
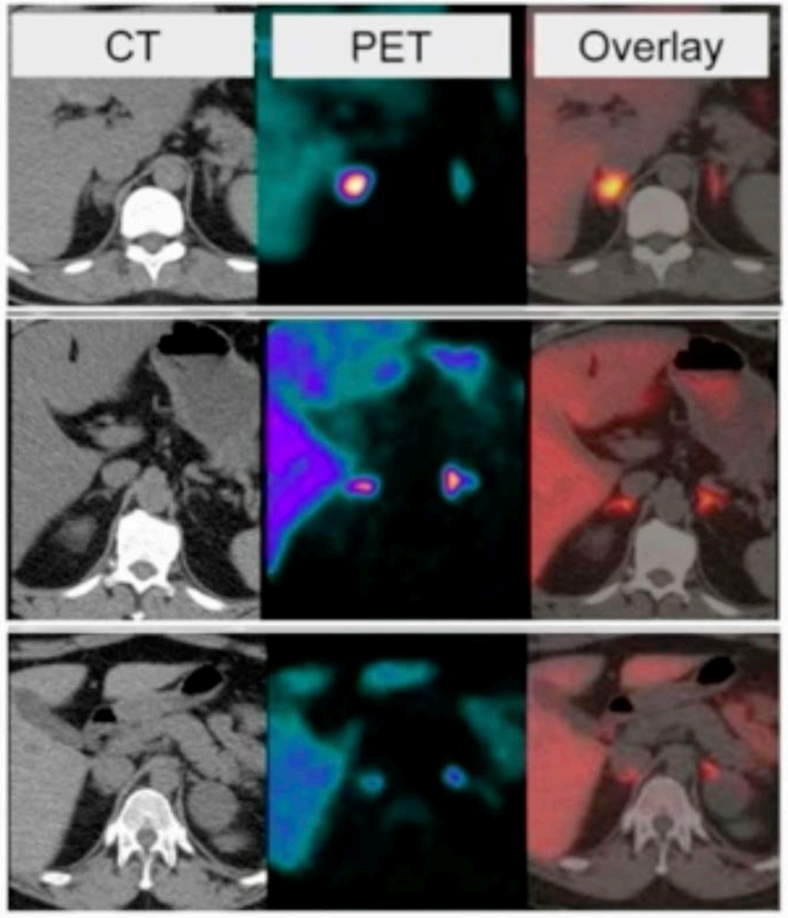
SY085_1647 Diagnostic challenges in pheochromocytoma & Para-ganglioma in patients with chronic kidney desease
MD, PdD, PD Christina Pamporaki, Dresden, Germany

SY85_1648 Diagnostic challenges in primary aldosteronism
Silvia Monticone, University of Torino, Italy



^{11}C-metomidate PET-CT



Right APA

BAH

Non functioning incidentaloma

Burton TJ, JCEM 2012

Functional imaging - MATCH trial

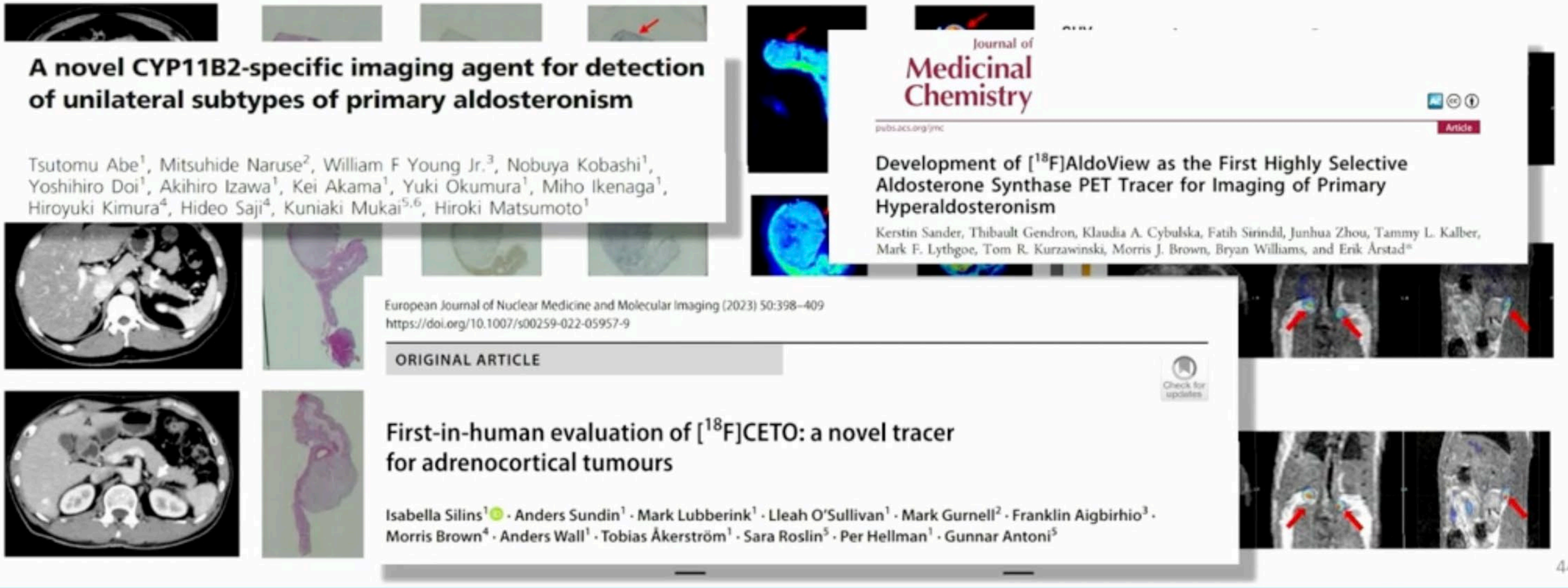
MTO is at least as accurate as AVS in predicting each of the clinical and biochemical outcomes from adrenalectomy

The lower bounds did not cross -17%, that was the pre-specified margin for recognizing non-inferiority

Wu X and Brown MJ, Nat Med 2023

Metomidate is a potent inhibitor of CYP11B1 (11-beta-hydroxylase) and CYP11B2 (Aldosteronsynthase). To improve selectivity and suppress CYP11B1, Patients must be pretreated with 0,5mg Dexamethasone every 6 hours for 3 days prior to scan. Also 11C has a very short half-life, restricting the use to centers with a cyclotron.

New and more specific tracers are currently under development



A novel CYP11B2-specific imaging agent for detection of unilateral subtypes of primary aldosteronism

Tsutomu Abe[1], Mitsuhide Naruse[2], William F Young Jr.[3], Nobuya Kobashi[1], Yoshihiro Doi[1], Akihiro Izawa[1], Kei Akama[1], Yuki Okumura[1], Miho Ikenaga[1], Hiroyuki Kimura[4], Hideo Saji[4], Kuniaki Mukai[5,6], Hiroki Matsumoto[1]

Journal of Medicinal Chemistry

pubs.acs.org/jmc

Article

Development of [^{18}F]AldoView as the First Highly Selective Aldosterone Synthase PET Tracer for Imaging of Primary Hyperaldosteronism

Kerstin Sander, Thibault Gendron, Klaudia A. Cybulska, Fatih Sirindil, Junhua Zhou, Tammy L. Kalber, Mark F. Lythgoe, Tom R. Kurzawinski, Morris J. Brown, Bryan Williams, and Erik Årstad*

European Journal of Nuclear Medicine and Molecular Imaging (2023) 50:398–409
https://doi.org/10.1007/s00259-022-05957-9

ORIGINAL ARTICLE

First-in-human evaluation of [^{18}F]CETO: a novel tracer for adrenocortical tumours

Isabella Silins[1] · Anders Sundin[1] · Mark Lubberink[1] · Lleah O'Sullivan[1] · Mark Gurnell[2] · Franklin Aigbirhio[3] · Morris Brown[4] · Anders Wall[1] · Tobias Åkerström[1] · Sara Roslin[5] · Per Hellman[1] · Gunnar Antoni[5]

Abe T, JCEM 2016; Sander K, Journal of Medicinal Chemistry 2021; Silins I, Eur J Nucl Med Mol Imaging. 2023

Clinical scores & Machine learning algorithms

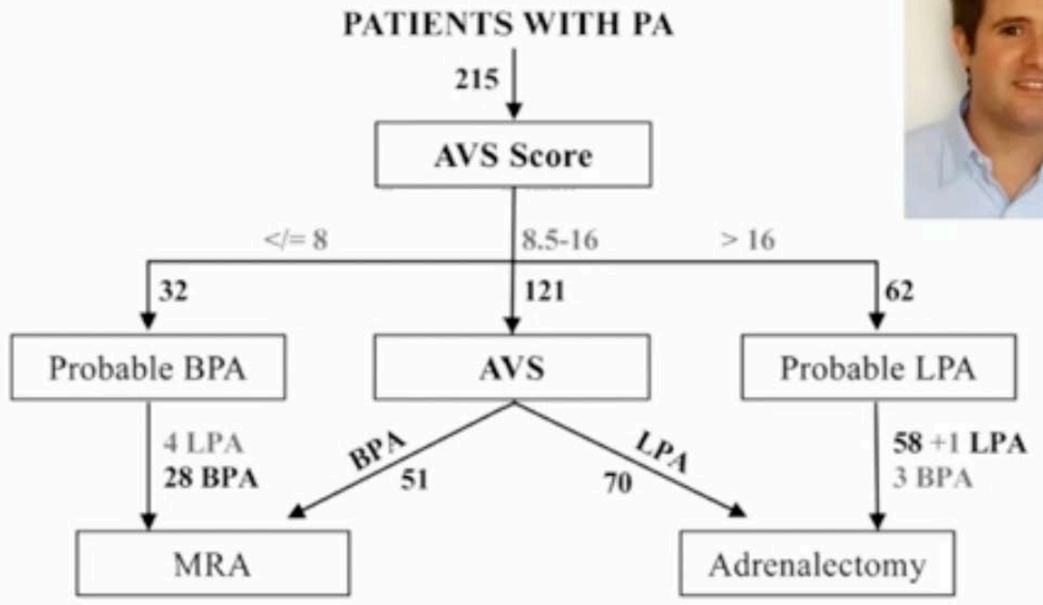
Development and Validation of Prediction Models for Subtype Diagnosis of Patients With Primary Aldosteronism

Jacopo Burrello,[1,*] Alessio Burrello,[2,*] Jacopo Pieroni,[1] Elisa Sconfienza,[1] Vittorio Forestiero,[1] Paola Rabbia,[3] Christian Adolf,[4] Martin Reincke,[4] Franco Veglio,[1] Tracy Ann Williams,[1,4] Silvia Monticone,[1#] and Paolo Mulatero[1,#]

Training cohort (n=150)
internal validation cohort (n=65)

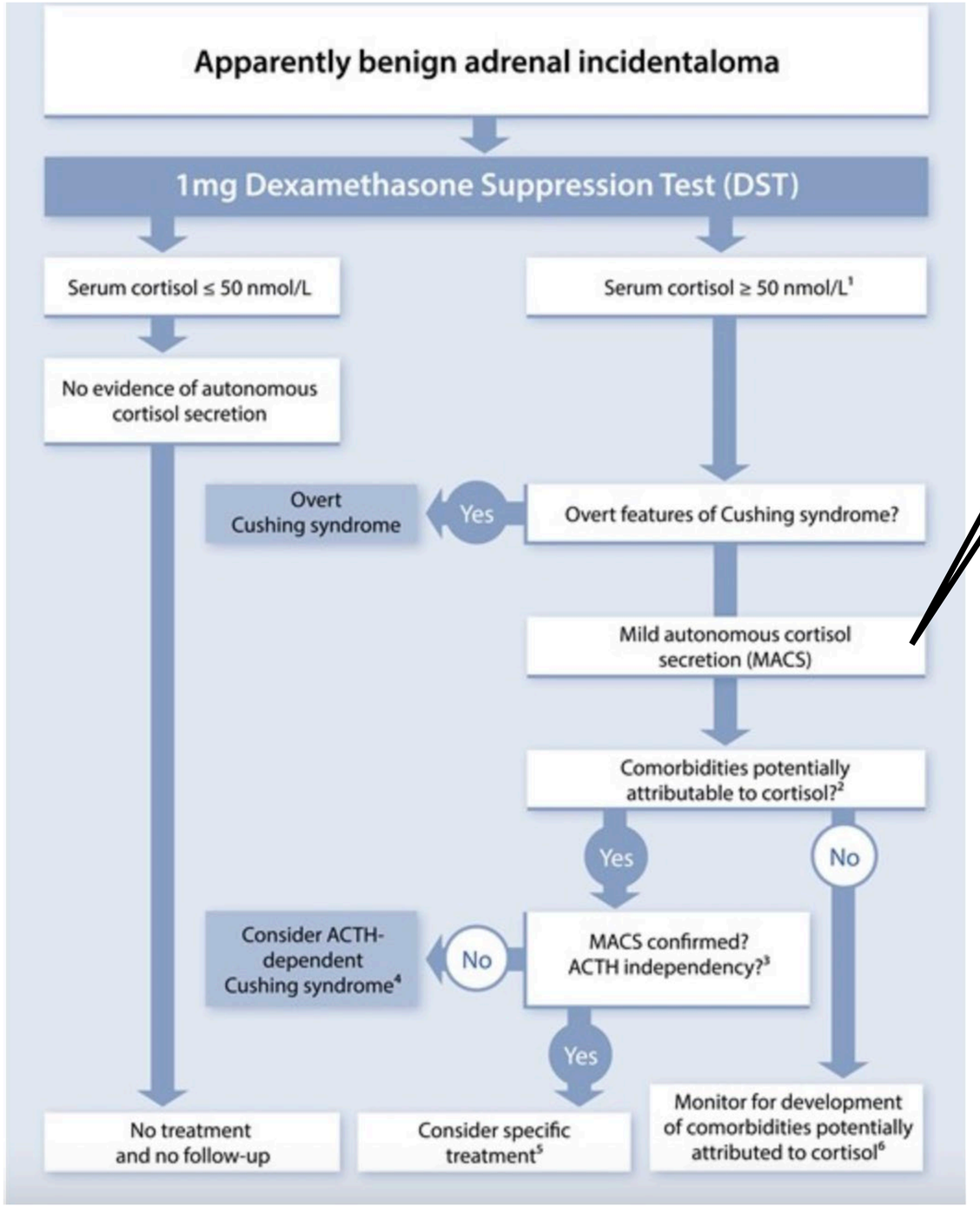
External validation cohort (n=118)

Variable	Label	Points
Aldosterone at screening (ng/dL)	</= 25	0
	> 25	0.5
Lowest Potassium (mEq/L)	< 3.4	5
	3.4 - 3.9	1.5
	>/= 4	0
Aldosterone post-confirmatory test (ng/dL)	</= 15	0
	15.1 – 19.9	1
	>/= 20	2
Nodule at CT scanning	Yes	4
	No	0
Largest nodule at CT scanning (diameter, mm)	</= 10	0
	11-30	1
	> 30	2
CT scanning Findings	Bilaterally Normal	0
	Bilaterally Abnormal	4.5
	Unilateral Abnormality	6.5



Diagnosis		Predicted: LPA	Predicted: BPA		
Real	LPA	128 +1	4	Sensitivity (%)	97.0
	BPA	3	79	Specificity (%)	96.3
				PPV (%)	97.7
				NPV (%)	95.2

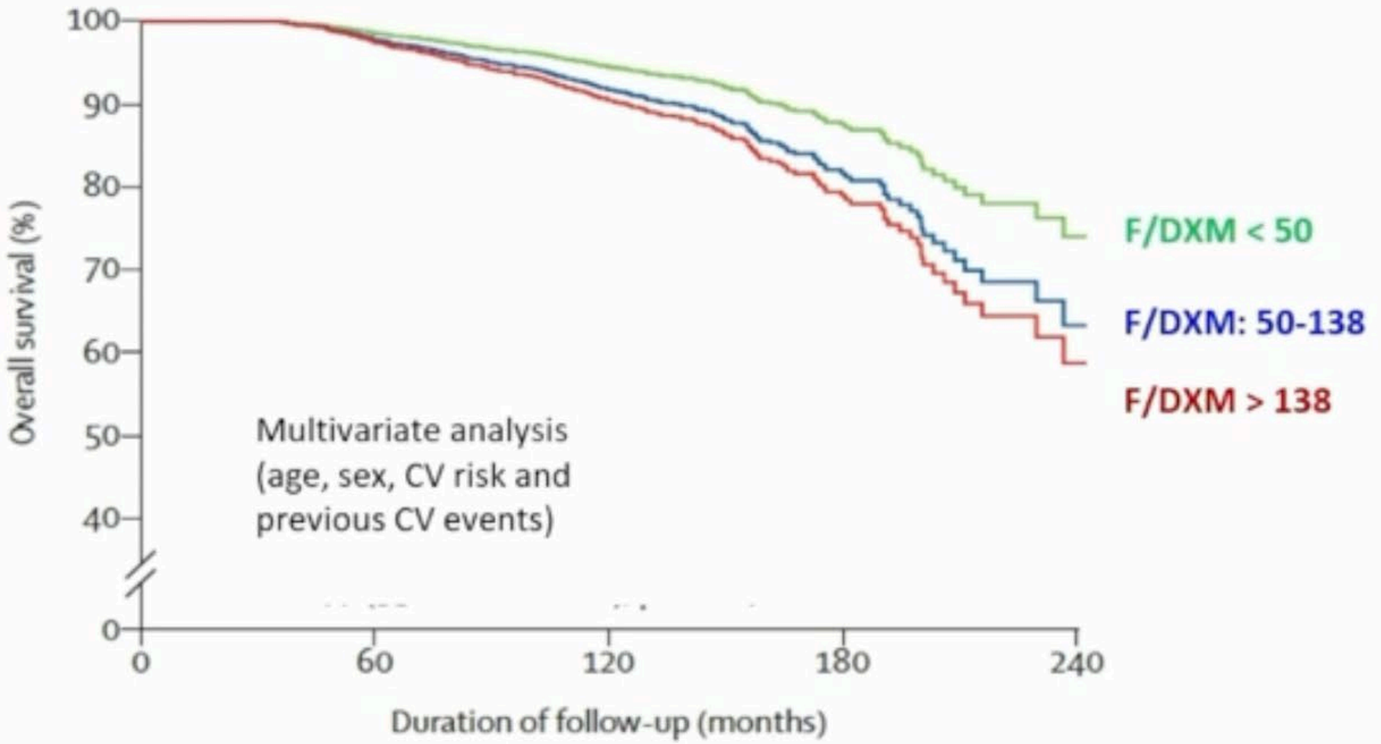
The application of the score in our clinical context would result in the **reduction of 43.7% of AVS**



SP0066:Update on Bilateral Makronodular Adrenocortical Disease (BMAD)
Prof. Jerome Bertherat, Paris Citë University, France

Increased mortality in MACS, especially women < 65 years

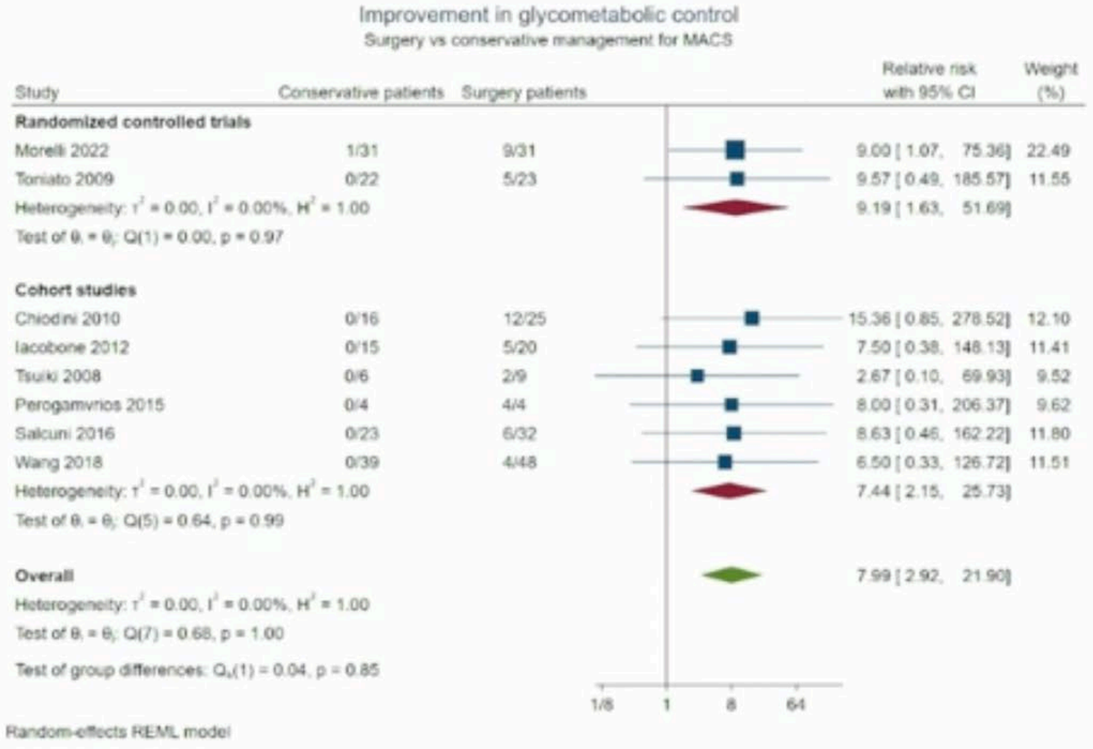
n: 3656



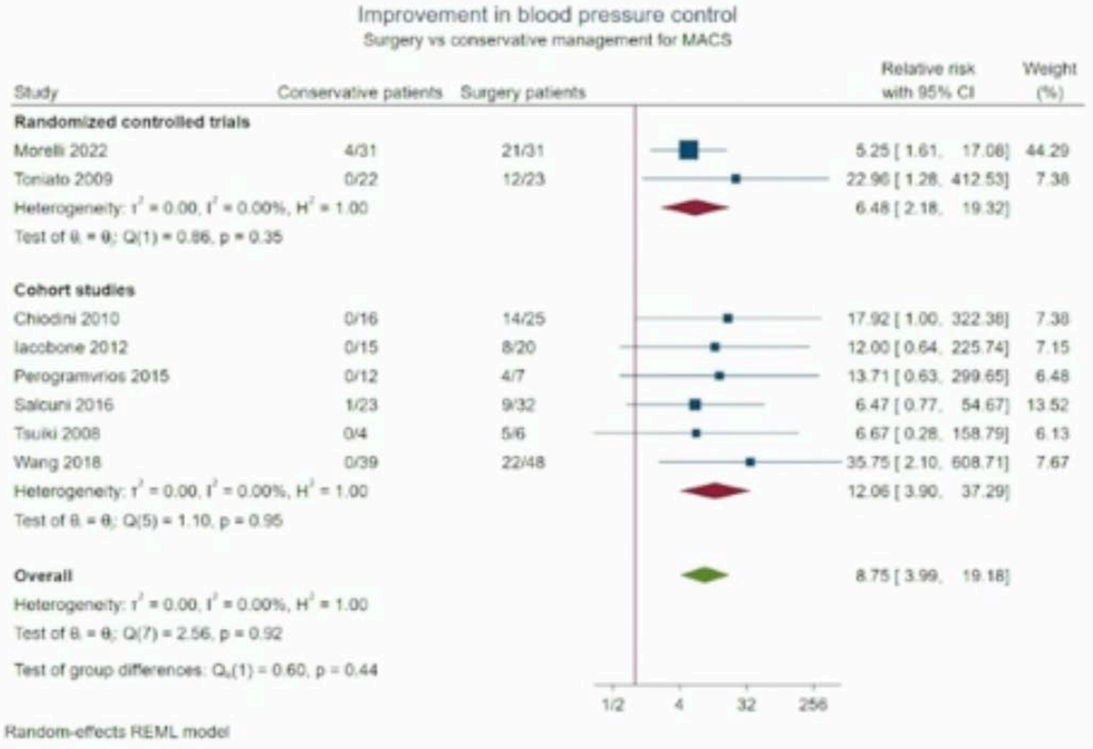
T Detchbein, et al, Lancet D&E 2022

Relative risks for improvement in glycometabolic and cardiovascular parameters in patients with MACS following Surgery

IMPROVEMENT OF GLUCOMETABOLIC CONTROL

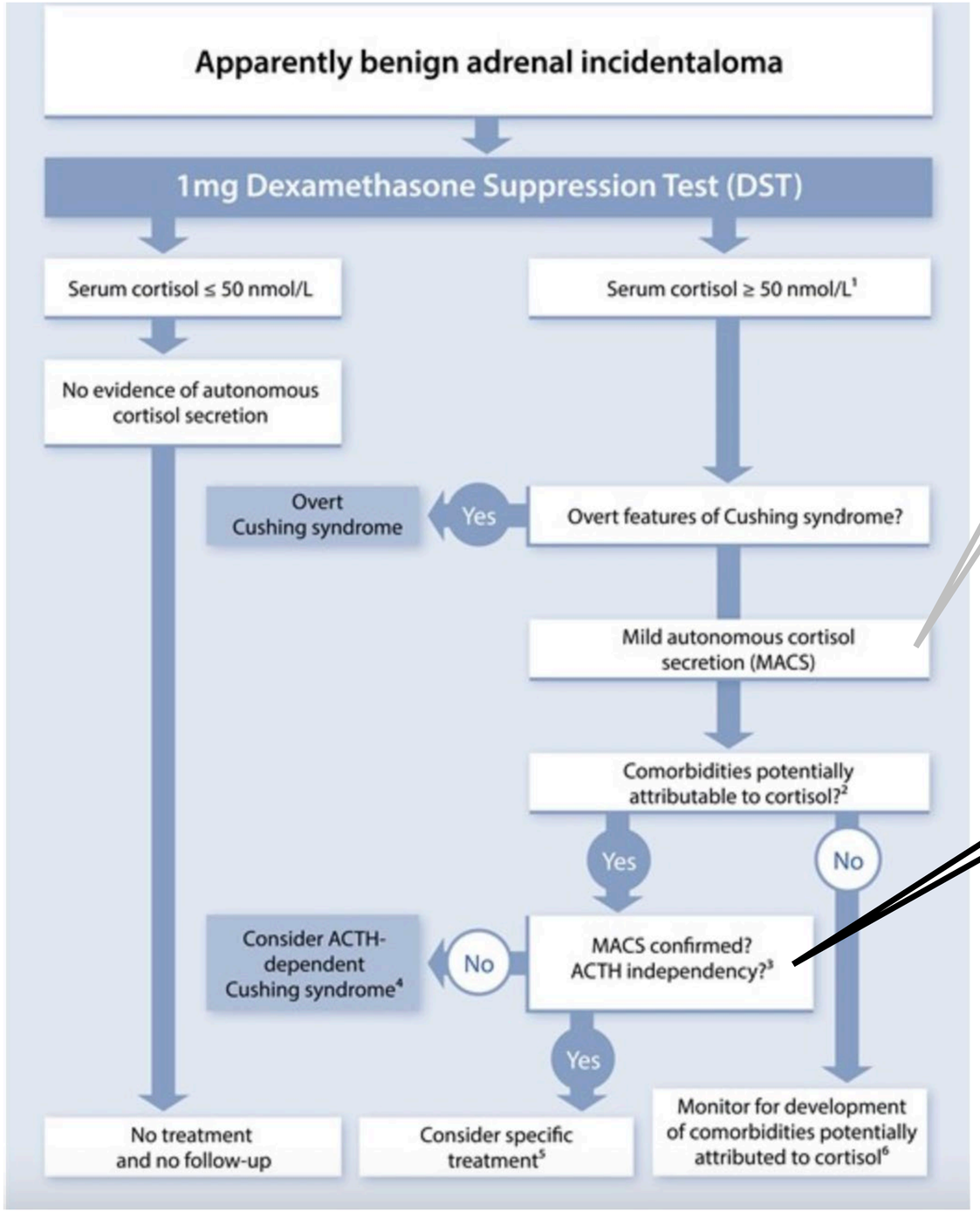


IMPROVEMENT OF HYPERTENSION



Pelsma et al, EJE, (in press)

ENDO2023



SP0066:Update on Bilateral Makronodular Adrenocortical Disease (BMAD)
Prof. Jerome Bertherat, Paris Citë University, France

MTP40: Adrenal Incidentalomas contemporary Evaluation and management
Prof. William F. Young, Mayo Clinic

DHEA-S Shortcut - Background

- ✓ Adrenal DHEA production and secretion is regulated by ACTH
- ✓ DHEA is made by women and men, but reference ranges are different and change with age
- ✓ Sustained suppression of ACTH suppresses DHEA
- ✓ DHEA has a 25 min half-life; but, DHEA-S has a 10-16 hr half-life and is stable thru-out the day and can be used to reflect long term ACTH sup
  "adrenal HbA1C" reflecting chronic
  concentrations

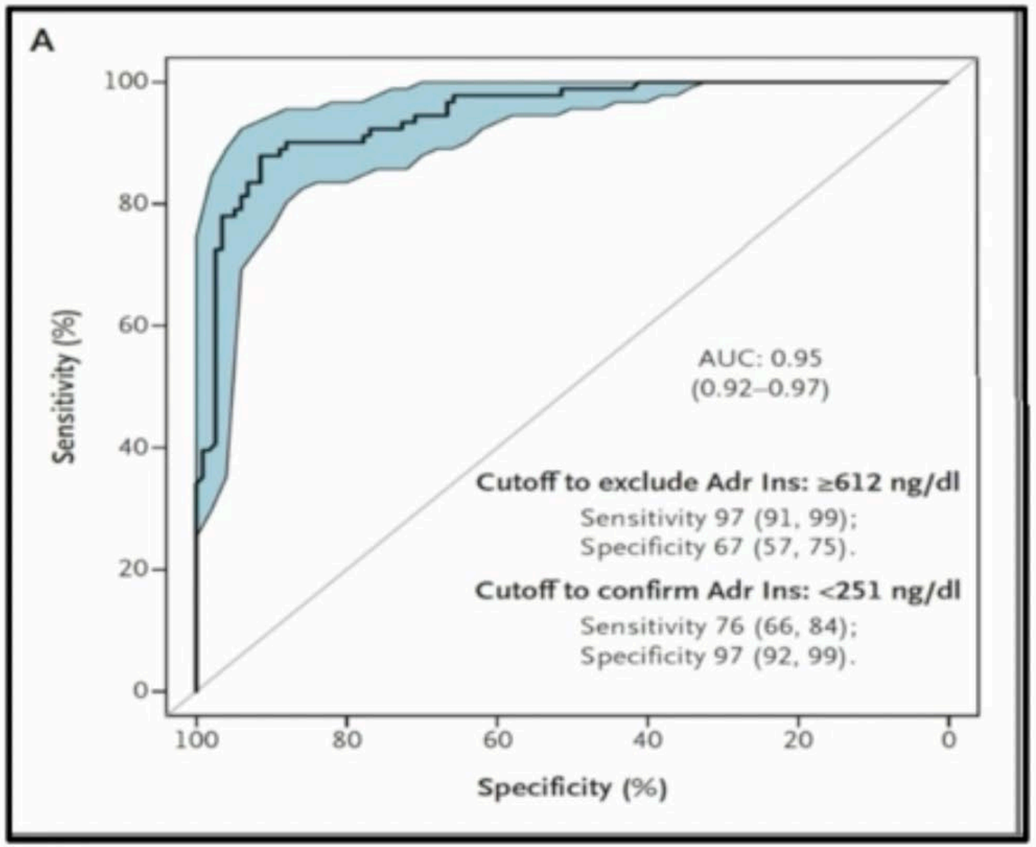
- If DHEA-S **<40 mcg/dL**(<1.1 µmol/L), SCS is likely → confirm SCS with overnight DST
- If DHEA-S **>100 mcg/dL** (>2.7 µmol/L) and ACTH >15 (>3.3 pmol/L) pg/mL, SCS is unlikely, and I skip the overnight DST

So, if DHEA-S is <40 mcg/dL, follow it up with 1 or 2-mg overnight DST and if >1.8 mcg/dL, absolutely confirm the autonomy with 8-mg overnight DST

Liu MS, et al. Performance of DHEAS as a Screening Test for Autonomous Cortisol Secretion in Adrenal Incidentalomas: A Prospective Study. *J Clin Endocrinol Metab*. 2022;107(5):e1789-e1796.

HOME WAKING SALIVARY CORTISONE IS AS ACCURATE AS AN ACTH STIMULATION TEST TO DIAGNOSE ADRENAL INSUFFICIENCY

Waking Salivary Cortisone vs 30min AST



1. Salivary steroids have advantages of stable at room temperature and can be sent by post to central lab
2. Measured by Mass Spec can also measure salivary cortisol; however cortisone more accurate than cortisol (ROC AUC 0.95 vs 0.90).
3. Salivary cortisone reflects serum free cortisol as serum cortisol is converted in salivary gland to cortisone

Debono et al., NEJM Evidence 2023; 2(2)

OR30_6269: Aled Rees

Salivary cortisol response to the high dose ACTH stimulation test provides a reliable alternative to serum cortisol measurement in the evaluation of suspected hypoadrenalism, and is unaffected by cortisol-binding globulin concentration

Nadia El-Farhan, MD, PhD[1], Seren Rees[2], Sarah Tennant, PhD[3], Carol Evans, PhD[3], **Aled Rees, MD,PhD**[4].

CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD
Neuroscience a
Innovation Institute
@neurosciencecu

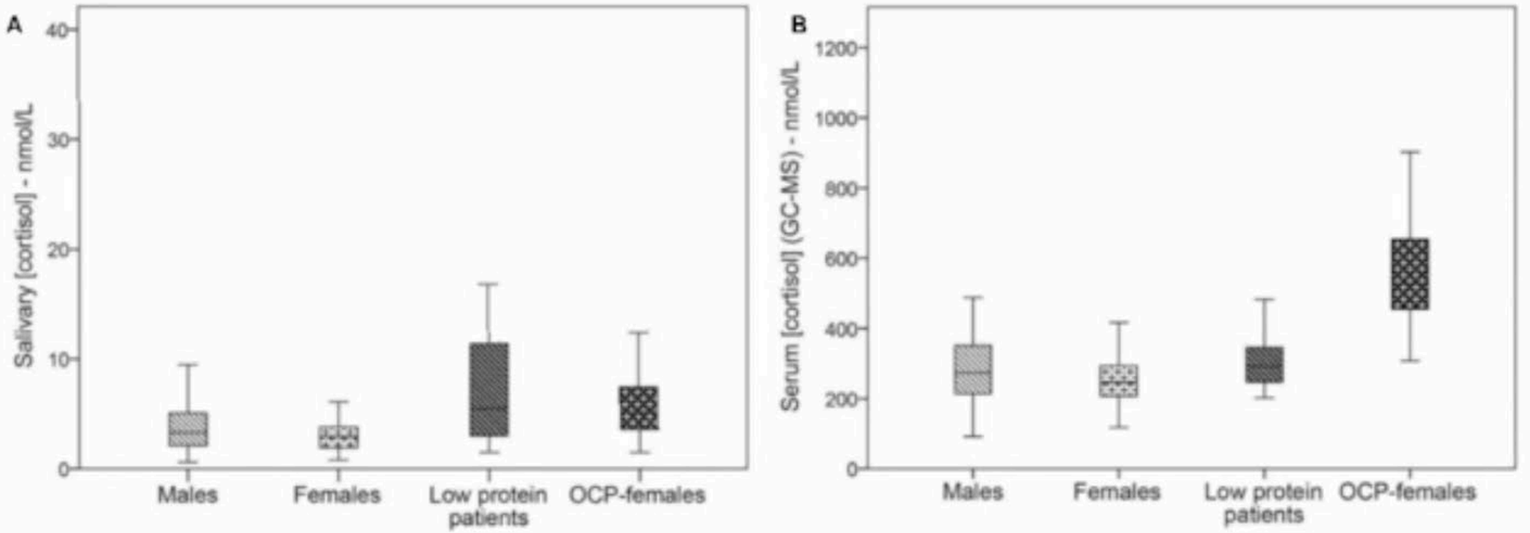
Baseline and post-ACTH serum cortisol concentrations

	Serum cortisol (nmol/L)			
	Males	Females	Low protein patients	OC
Baseline				
GC-MS	274 (131 - 575)	254 (139 - 463)	305 (173 – 537)	537 (
Immunoassay	289 (151 - 556)	247 (134 - 455)*	282 (167 – 476)	465 (301 - 718)†
Post-ACTH				
GC-MS	563 (418 - 757)	555 (421 - 731)	552 (393 – 776)	869 (649 - 1162)†
Immunoassay	577 (430 - 773)	542 (416 - 707)*	514 (384 -688)**	747 (577 - 967)†

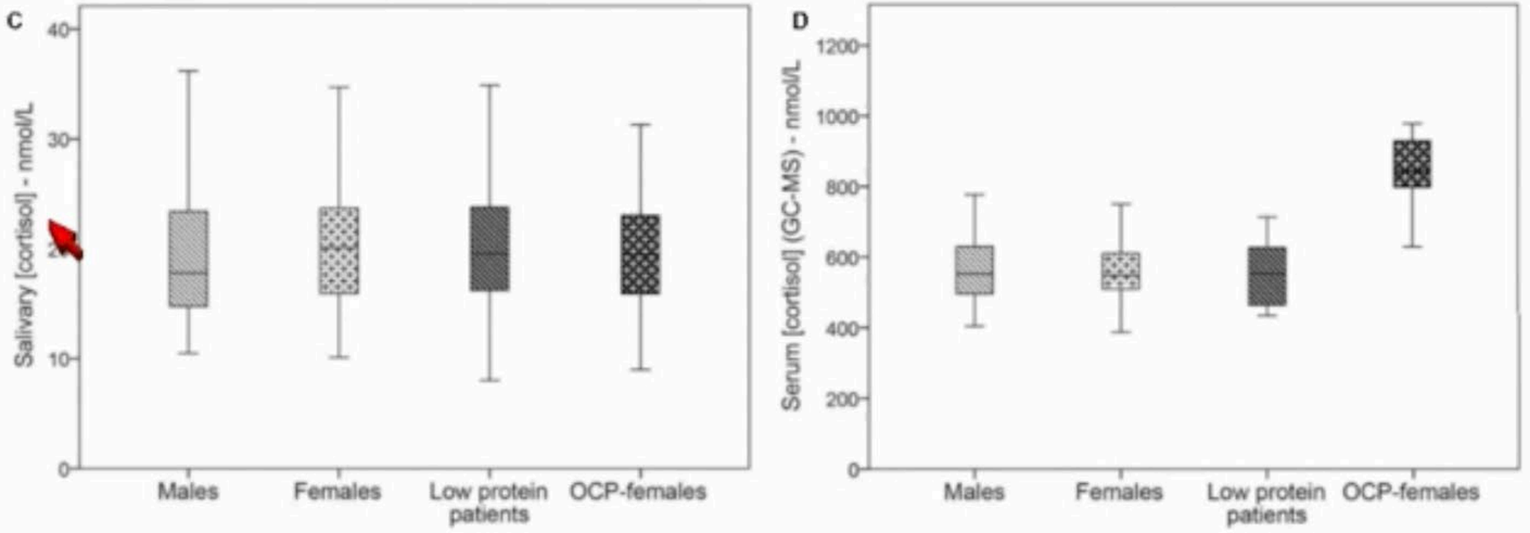
Serum CBG (mg/L)			
Males	Females	Low protein patients	OCP-females
58 (42-81)	64 (43-95)*	41 (28-60)*	116 (84-159)*

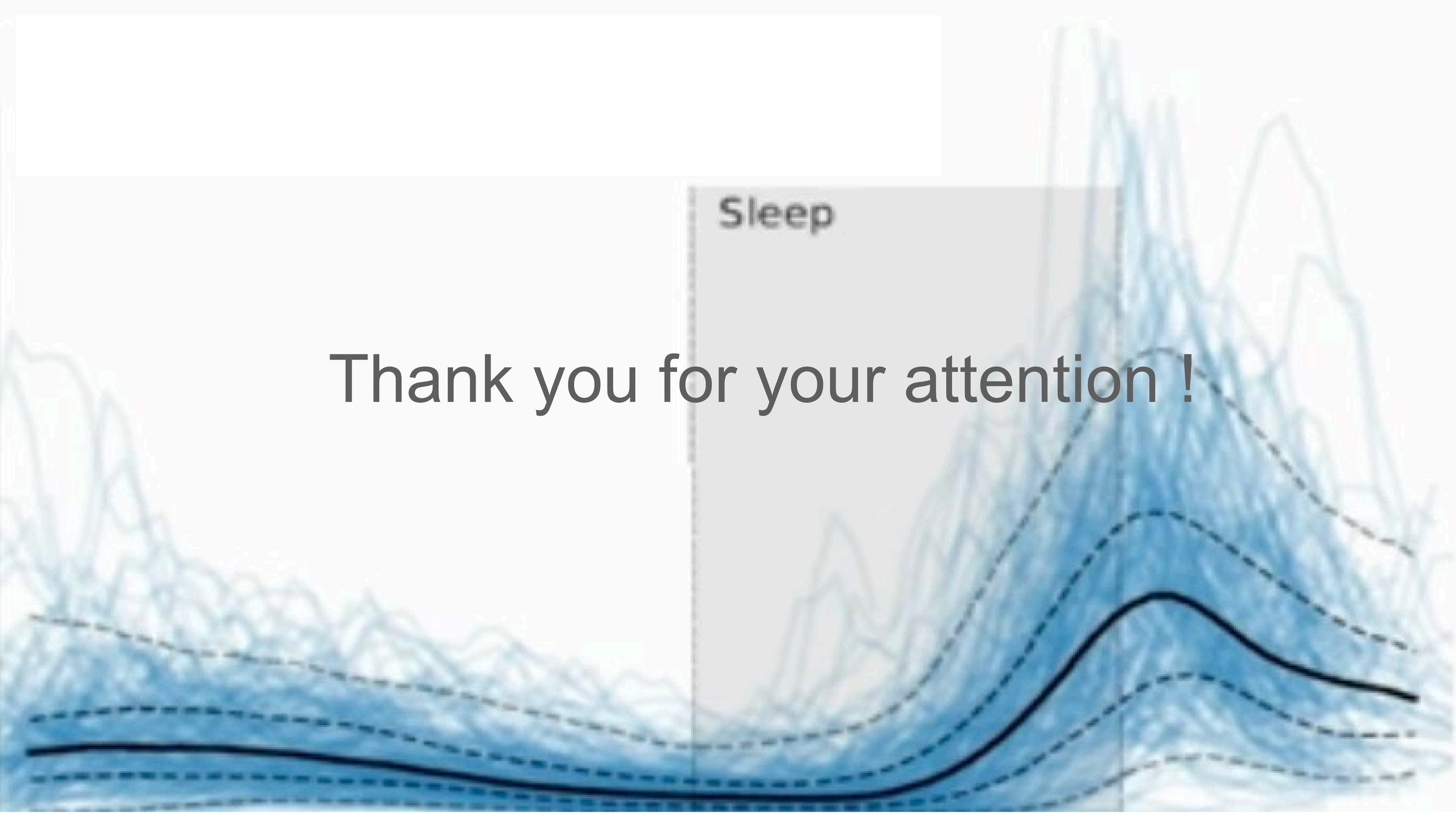
*p<0.01 versus male volunteers

Baseline



Post-ACTH





Thank you for your attention !