Adrenal Incidentalomas

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Outline

- Review the epidemiology of adrenal incidentalomas and their various subtypes
- Highlight the diagnostic approach to adrenal incidentalomas
  - Radiographic features
  - Biochemical evaluation
- Highlight the clinical implications of untreated hormone excess

Epidemiology

- Adrenal incidentalomas
  - Adrenal mass >1cm serendipitously discovered on radiologic examination
    - CT, MRI
  - Prevalence
    - **Increased with more frequent utility of cross-sectional imaging**
      - 0.4% before 2000 → 7.3% by 2020
    - **Increases with age**
      - <1% if <30 yo; 3% if >50 yo; 10% if >80 yo

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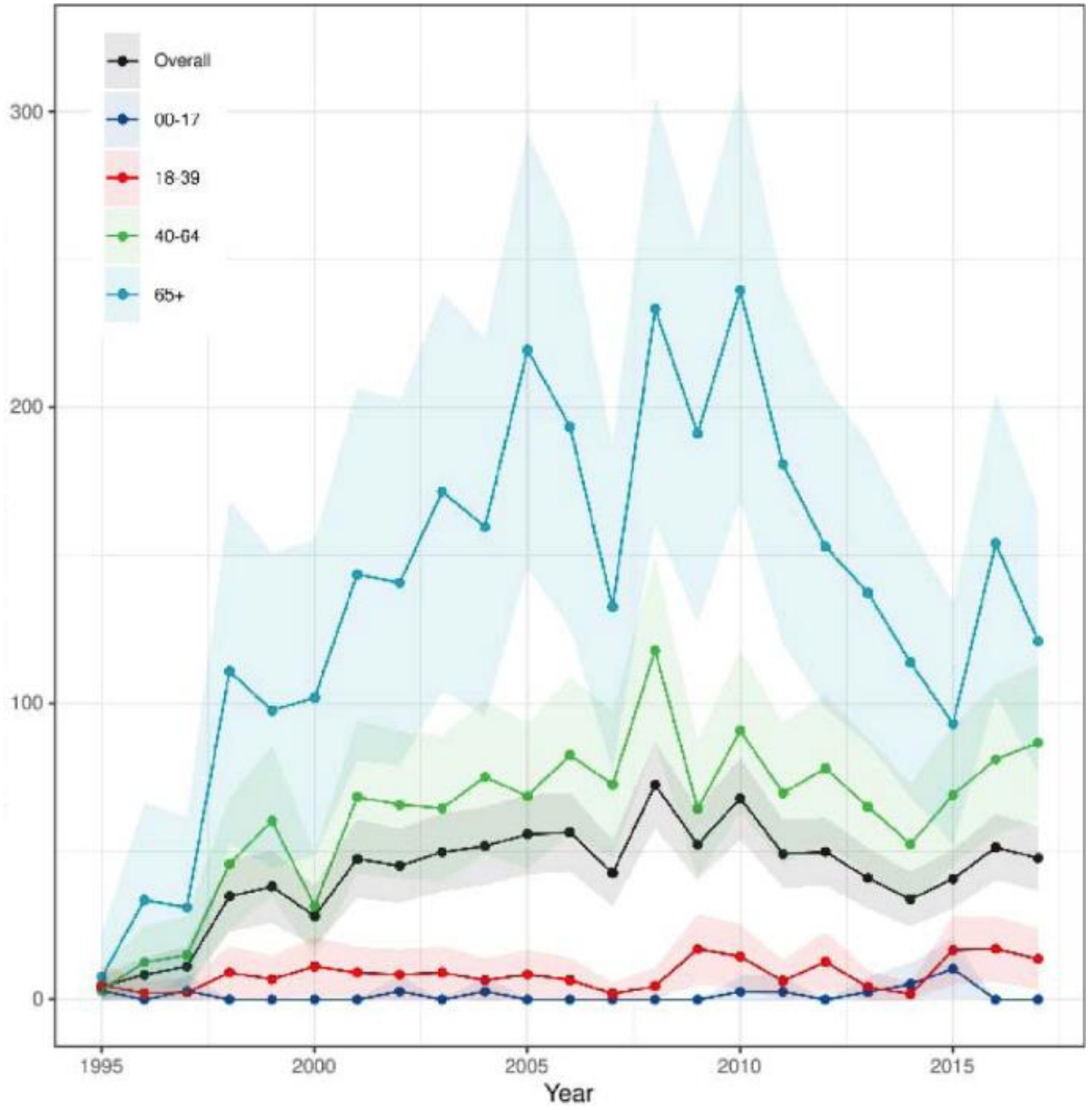
Increased Prevalence of Adrenal Incidentalomas in CT Series Over Time

Study	Study Period	Patients, No.	Age at Diagnosis, y	Female Sex, %	Type of CT	Frequency of Adrenal Incidentalomas, %	Mass size, mm	Bilateral mass, %
Glazer, 1982 (1)	NA	2200	NA	NA	NA	0.6	NA	NA
Prinz, 1982 (2)	1981	1423	41-73	44.4	Abdominal	0.6	10-40	0
Abecassis, 1985 (3)	1983-1985	1459	NA	NA	NA	1.3	NA	NA
Belldegrun, 1986 (4)	1976-1983	12 000	NA	NA	Abdominal	0.7	NA	NA
Herrera, 1991 (5)	1985-1989	61 054	62	60.2	NA	0.4	25, (10-110)	NA
Caplan, 1994 (6)	NA	1779	NA	NA	NA	1.90		NA
Song, 2008 (8)	Jan 2000-Dec 2003	65 231	64, (19-100)	NA	Abdominal and thoracic	1.5	20, (4-82)	7.8
Hammarstedt, 2010 (23)	Oct 2002-Apr 2004	34 044	69, (30-94)	56.9	Abdominal and thoracic	4.5	25.8, (8-94)	25.1
Bovio, 2006 (7)	Apr 2001-Dec 2001	520	58, (50-79)	26.1	Chest scan	4.4	12-38	13.2
Davenport, 2011 (25)	Jan 2006-Dec 2007	3099	68, (45-92)	46	Abdominal and thoracic	0.98 abdomen 0.81 thorax	26 ± 12	2.7
Grossman, 2016 (24)	NA	673	50.93 ± 11.1	NA	Abdominal CT	4.2	NA	11
Present study	Jan 2017-Jun 2018	601	65.6 ± 10.3	27.3	Abdominal CT	7.3	21, (10-50)	29.5

Reimondo G, Castellano E, Grosso M, et al. Adrenal Incidentalomas are Tied to Increased Risk of Diabetes: Findings from a Prospective Study. *J Clin Endocrinol Metab.* 2020;105(4).

Image Modifications Adapted from Ricardo Correa, MD

Sex-Standardized Incidence Rate of Adrenal Tumor Patients Diagnosed per 100,000 Person-years by Age at Diagnosis



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Adrenal Incidentaloma Subtypes by Prevalence

Etiology	Prevalence of the different entities among adrenal incidentalomas
Adrenocortical adenoma or macronodular bilateral adrenal hyperplasia	80%-85%
• Nonfunctioning	40%-70%
• Mild autonomous cortisol secretion	20%-50%
• Primary aldosteronism	2%-5%
• Overt Cushing's syndrome	1%-4%
Other benign mass	
• Myelolipoma	3%-6%
• Cyst and pseudocyst	1%
• Ganglioneuroma	1%
• Schwannoma	<1%
• Hemorrhage	<1%
Pheochromocytoma	1%-5%
Adrenocortical carcinoma	0.4%-4%
Other malignant mass (mostly adrenal metastases)	3%-7%

1. Reimondo G, Castellano E, Grosso M, et al. Adrenal Incidentalomas are Tied to Increased Risk of Diabetes: Findings from a Prospective Study. *J Clin Endocrinol Metab.* 2020;105(4).
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European Journal of Endocrinology, 2023, 189, G1–G42
https://doi.org/10.1093/ejendo/lvad066
Advance access publication 15 June 2023
Clinical Practice Guideline

European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors

Martin Fassnacht,[1,2,*] Stylianos Tsagarakis,[3] Massimo Terzolo,[4] Antoine Tabarin,[5] Anju Sahdev,[6] John Newell-Price,[7,8] Iris Pelsma,[9] Ljiljana Marina,[10] Kerstin Lorenz,[11] Irina Bancos,[12] Wiebke Arlt,[13,14] and Olaf M. Dekkers[9,15]

Diagnostic Approach

- Is it **malignant**?
  - Radiographic features
    - Collaborate with radiology
  - History
- Is it **hormonally active**?
  - Biochemical evaluation
    - **Cortisol**
    - **Aldosterone**
    - **Catecholamines**
    - Sex hormones, steroid precursors

Malignant Potential on Imaging

- The **single best test** to assess for **malignant potential** is the **unenhanced HU** measurement of **homogeneous** adrenal masses, so look for this in the report
- Always be in collaboration with your radiologist

- 6 total studies
  - Unenhanced CT density HU >10 with a 100% sensitivity for detection of adrenal malignancy
  - **Adrenal masses with a density of ≤10 HU are virtually never malignant**
  - Specificity was lower at 58% → significant number of benign lesions with HU >10
- 5 studies also provided data for HU cutoff >20
  - Sensitivity was high at 97% in detecting

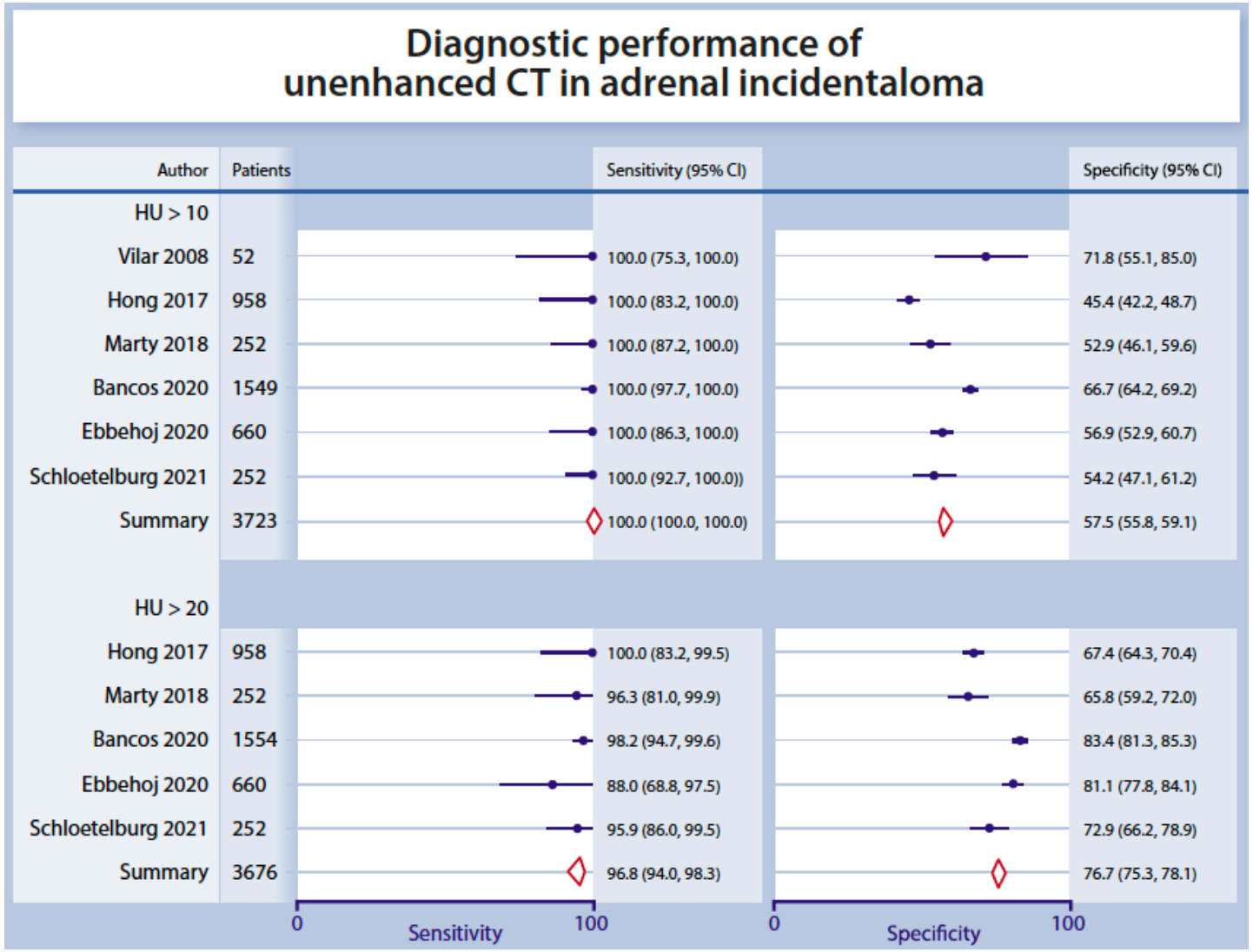

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Table 4. Imaging criteria to discriminate benign from malignant adrenal masses.[a]

Method	Criteria favoring a benign mass	Strength of evidence[b]
Noncontrast CT	≤ 10 HU[c]	⊕⊕⊕◯
FDG-PET/CT	Absence of FDG uptake or uptake less than the liver[d]	⊕◯◯◯
MRI—chemical shift	Loss of signal intensity on out-phase imaging consistent with lipid-rich adenoma	⊕◯◯◯
CT with delayed contrast media washout[e]	Relative washout > 58%[f]	⊕◯◯◯

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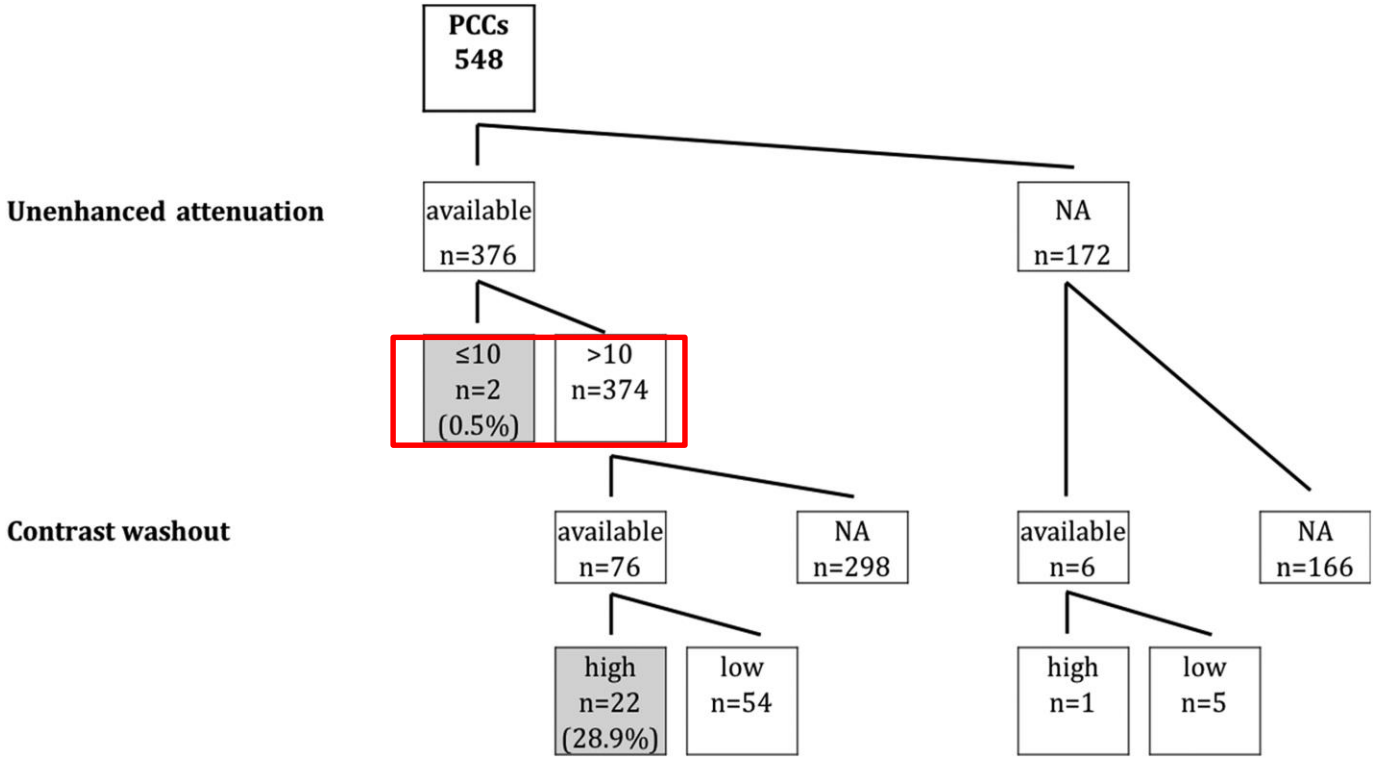
What about PHEO?

- The **single best test** to assess for possibility for **PHEO** is the **unenhanced HU** measurement of **homogeneous** adrenal masses, so look for this in the report

CT Characteristics of Pheochromocytoma: Relevance for the Evaluation of Adrenal Incidentaloma

Letizia Canu,[1,2] Janna A. W. Van Hemert,[1] Michiel N. Kerstens,[3] Robert P. Hartman,[4] Aakanksha Khanna,[5] Ivana Kraljevic,[6] Darko Kastelan,[6] Corin Badiu,[7] Urszula Ambroziak,[8] Antoine Tabarin,[9] Magalie Haissaguerre,[9] Edward Buitenwerf,[3] Anneke Visser,[10] Massimo Mannelli,[2] Wiebke Arlt,[11] Vasileios Chortis,[11] Isabelle Bourdeau,[12] Nadia Gagnon,[12] Marie Buchy,[13] Francoise Borson-Chazot,[13] Timo Deutschbein,[14] Martin Fassnacht,[14,15] Alicja Hubalewska-Dydejczyk,[16] Marcin Motyka,[16] Ewelina Rzepka,[16] Ruth T. Casey,[17] Benjamin G. Challis,[17] Marcus Quinkler,[18] Laurent Vroonen,[19] Ariadni Spyroglou,[20,21] Felix Beuschlein,[20,21] Cristina Lamas,[22] William F. Young,[5] Irina Bancos,[5] and Henri J. L. M. Timmers[1]

- Multicenter retrospective study of 533 patients with 548 histologically confirmed PHEOs
- **Among the 376 PHEOs for which unenhanced CT attenuation data were available, 374 had an attenuation of >10 HU (99.5%)**
- In the **2 exceptions** (0.5%), the **unenhanced CT attenuation was exactly 10 HU**
- Washout unreliable



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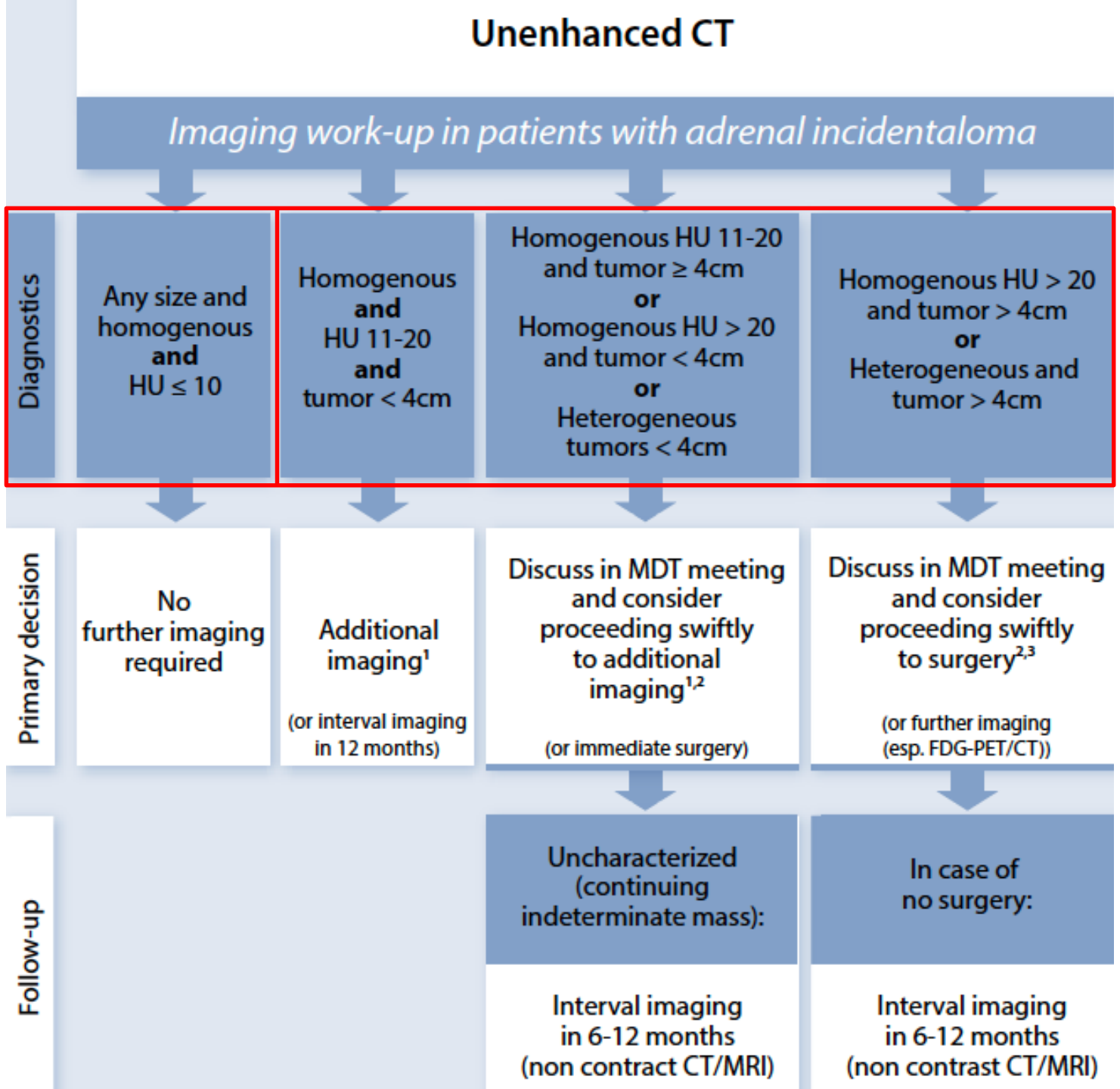
Imaging Phenotype Summary

- The **single best test** to assess for **malignant potential or possibility of PHEO** is the **unenhanced HU** measurement of **homogeneous** adrenal masses
  - HU <10 rules out malignancy or PHEO
  - HU ≥10 warrants biochemical work-up for PHEO and/or at least surveillance imaging for possible malignancy, depending on other factors
- Always be in collaboration with radiology



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  - For all adrenal masses
  - 1mg dexamethasone suppression test (DST)
- **Aldosterone Excess**
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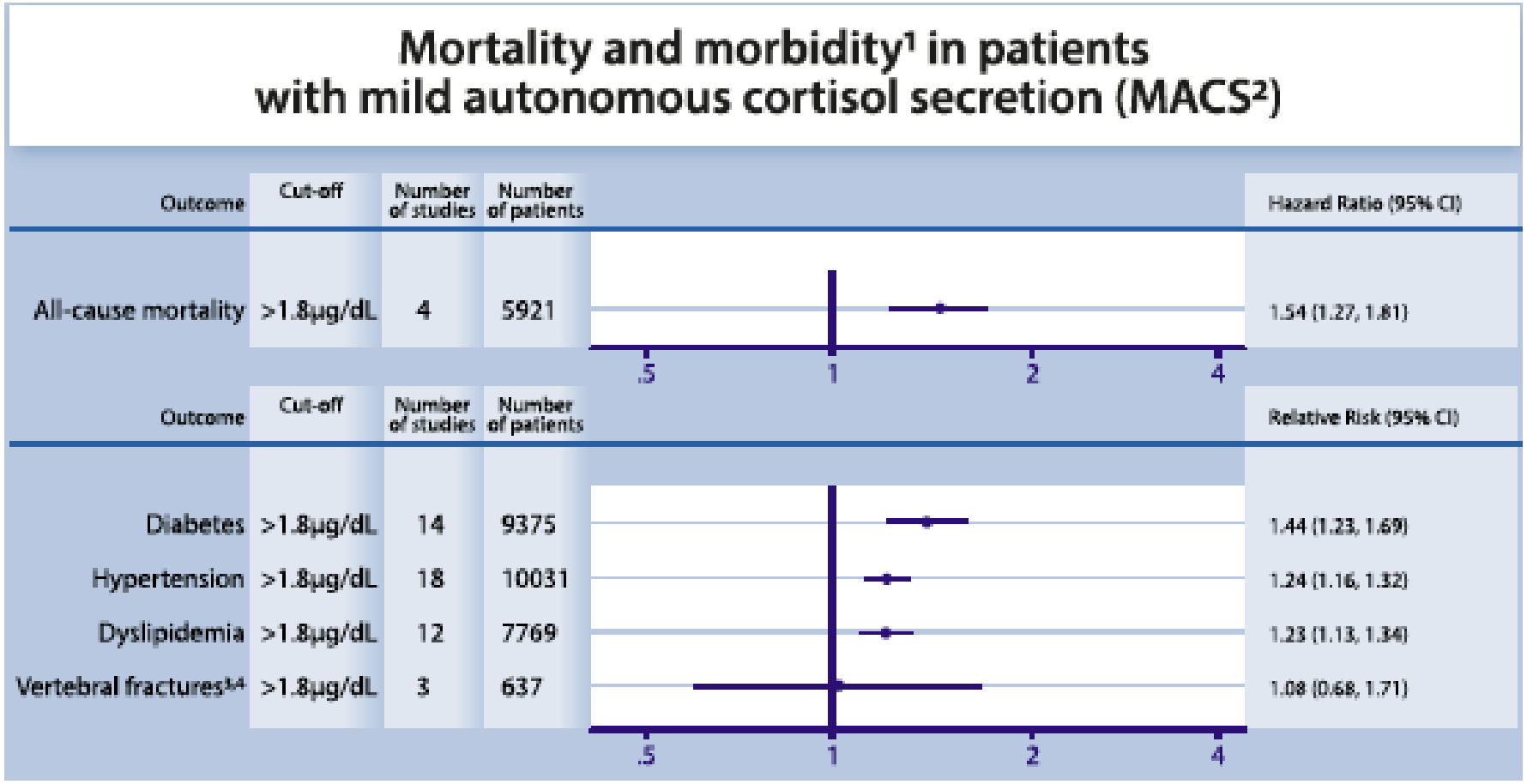
  - AM fasting upright renin, aldosterone, BMP
- **Catecholamine Excess**
  - For all adrenal masses with HU ≥10 on unenhanced CT
  - Plasma fractionated metanephrines
- Sex hormones, steroid precursors
  - For patients with clinical or radiographic features of adrenocortical carcinoma, androgen excess, etc.

Importance of Biochemical Assessment

- **Aldosterone** and **cortisol** excess often seen in benign adenomas
- **Cardiovascular, renal, and cerebrovascular outcomes worse in patients with primary aldosteronism** compared to those with essential HTN
  - Treatment to raise renin reduces morbidity and mortality
- **Mortality and cardiometabolic + fracture outcomes are worse in patients with mild autonomous cortisol secretion (MACS)** compared to those with non-functioning adrenal incidentalomas
  - **MACS can account for up to 50% of benign-appearing**

MACS vs. Nonfunctioning adrenal tumors



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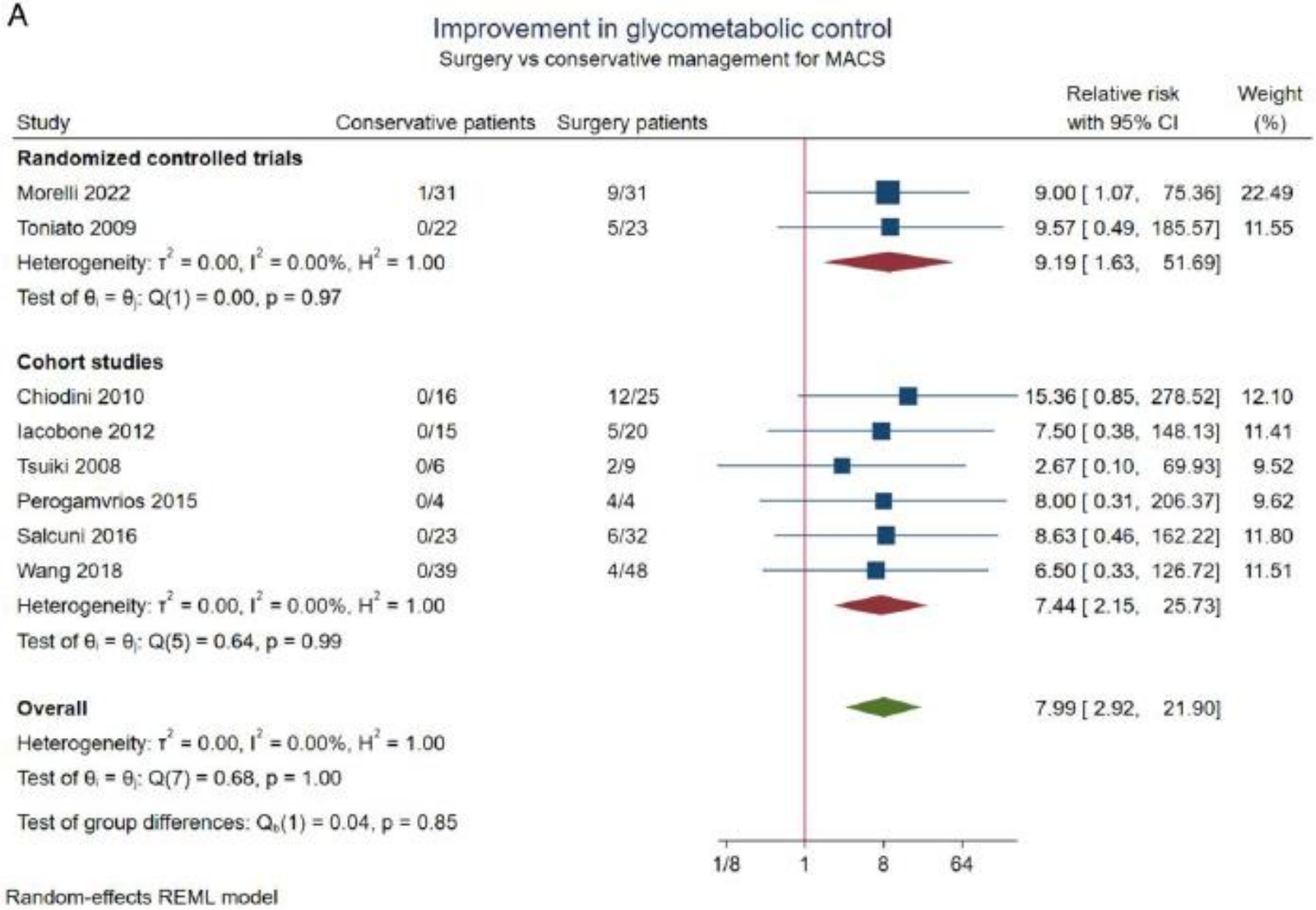

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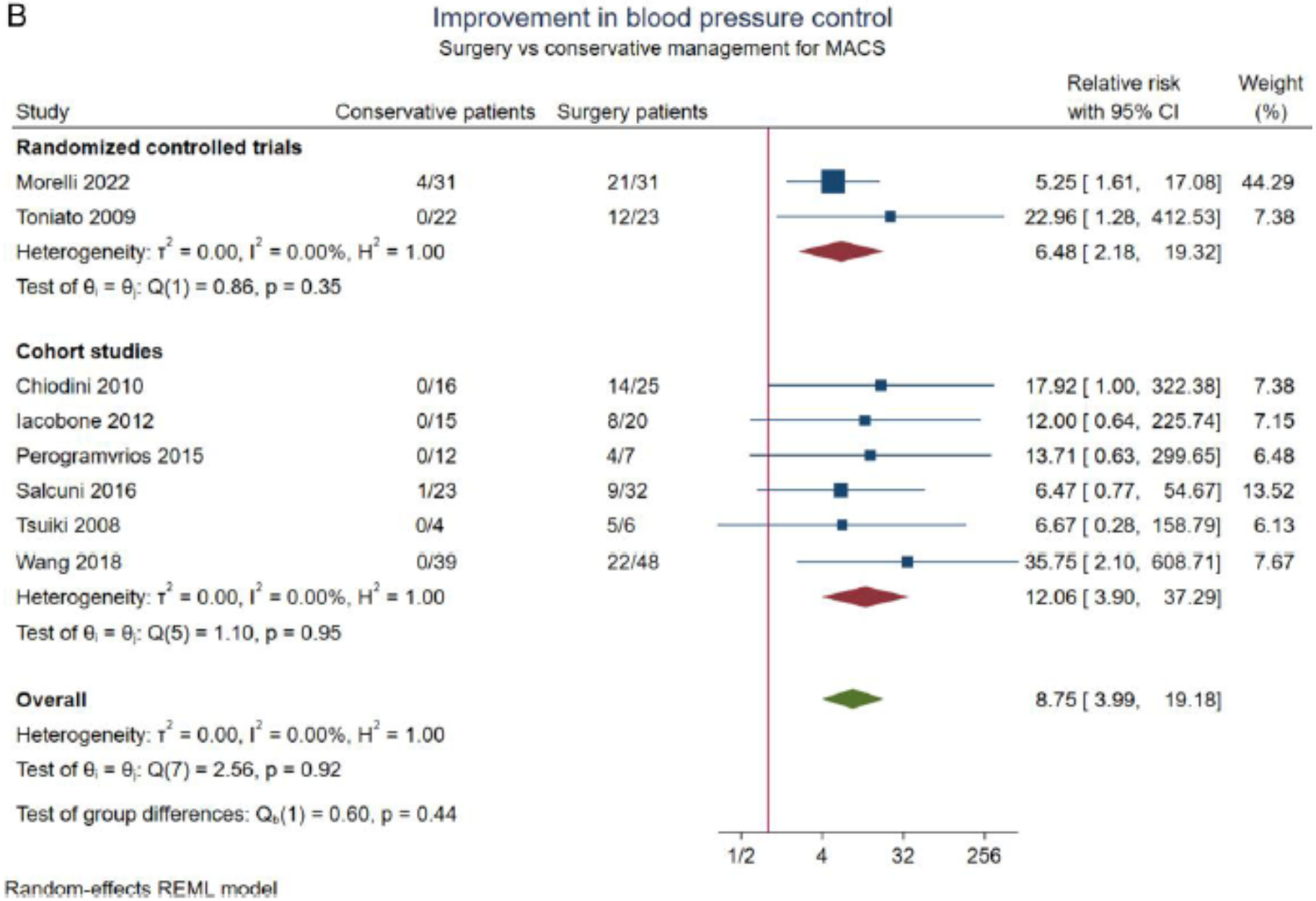

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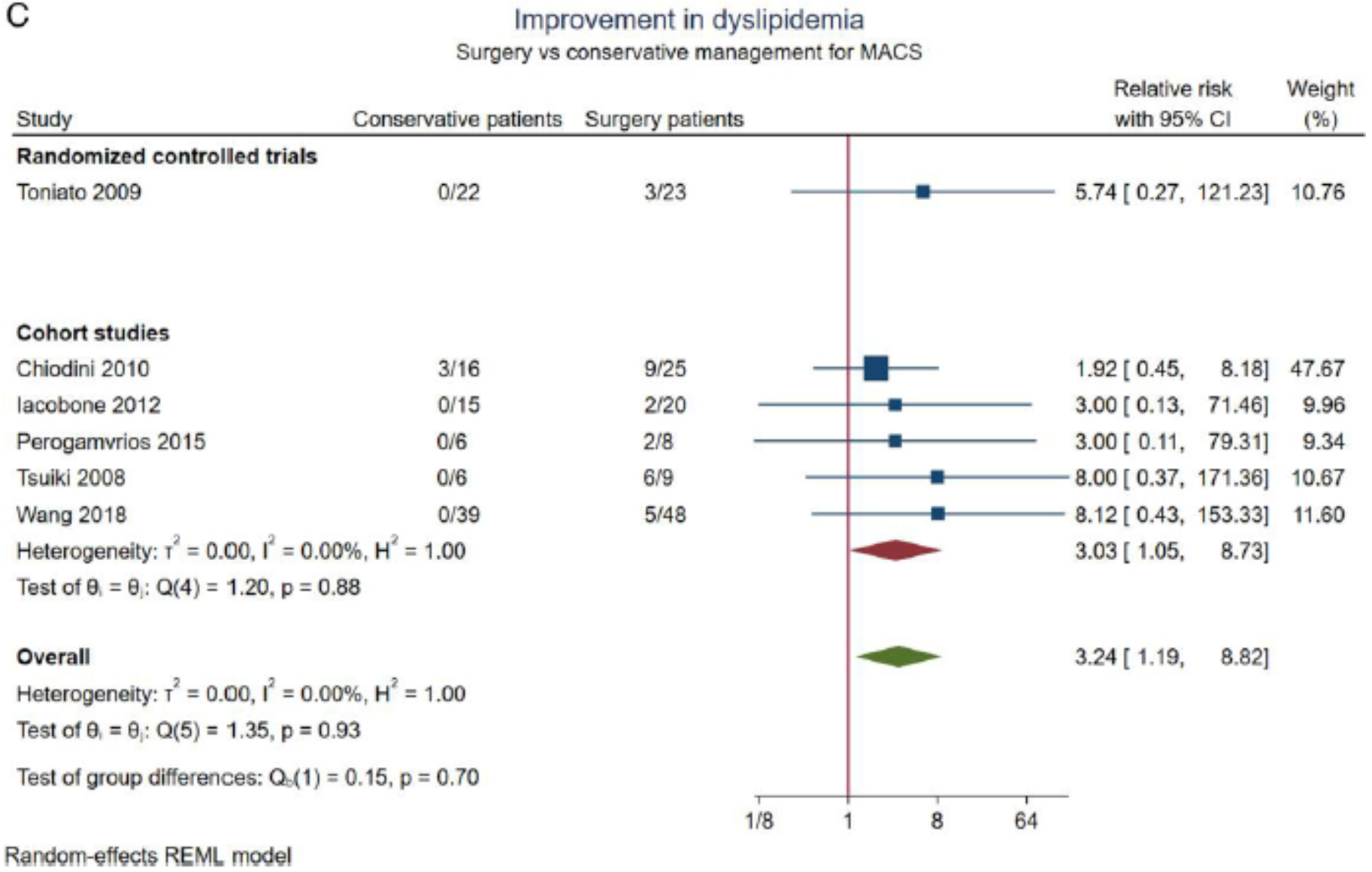

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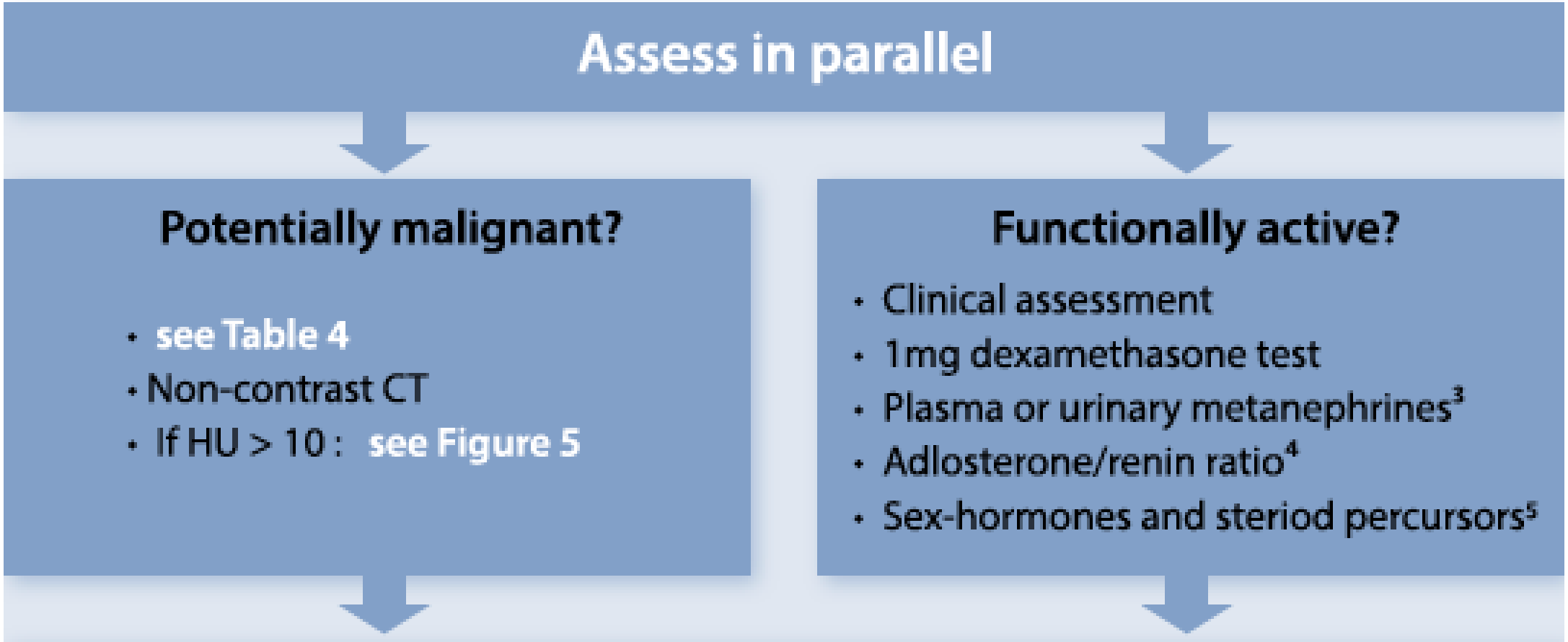
Adrenal incidentaloma[1,2]



Aim at the establishment of a definitive diagnosis

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Hormonal/Biochemical Assessment

- **Minority (3-20%)** of patients with adrenal incidentalomas undergo biochemical testing
  - **Sweden:** 17726 patients with adrenal masses; 2.8% underwent at least 1 biochemical test on adrenal function, and only 0.4% underwent evaluation of all 3 adrenal axes (JAMA 2023)
  - **Nova Scotia Health:** 124 patients with adrenal masses; complete biochemical work-up completed in 4% of cases, and 11% were referred to Endocrinology (JES 2021)
  - **University of Colorado:** 305 patients with adrenal masses; 21% were tested for hypercortisolism (JES 2021)
    Kaiser (Georgia, Southern CA): 24259 patients with adrenal masses; 7% underwent DST (Biomedicines 2021)

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  - For all adrenal masses
  - 1mg dexamethasone suppression test (DST)
- **Aldosterone Excess**
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  - For all adrenal masses with HU ≥10 on unenhanced CT
  - Plasma fractionated metanephrines
- Sex hormones, steroid precursors
  - For patients with clinical or radiographic features of adrenocortical carcinoma, androgen excess, etc.

When to Consult Endo?

- If there is any **abnormal biochemical** screening result
  - **1 mg DST** (do this on a **separate** day from the other tests)
    - Take 1 mg dexamethasone at 11pm, then obtain 8am fasting serum cortisol the next day
    - Serum cortisol >1.8 mcg/dL
  - **AM fasting upright renin, aldosterone, BMP**
    - Plasma aldosterone concentration (PAC) >10 ng/dL AND plasma renin activity (PRA) <1 ng/mL/hr
    - PAC/PRA >20 ng/dL per ng/mL/hr
  - **Plasma fractionated metanephrines**
    - Values above the reference range
- If there are concerns that the adrenal mass **may not be benign** (unenhanced HU ≥ 10)
- If **any** questions on diagnostic work-up, place an eConsult

Questions?

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