**Suppl. Table 1: Search Strategy MEDLINE (Ovid) 1946 to August Week 1 2015**

|  |  |
| --- | --- |
| **1** | exp Adrenal Gland Neoplasms/ (23488) |
| **2** | ACC.mp. (8012) |
| **3** | Pheochromocytoma/ (13666) |
| **4** | ph?eochromocytoma.ti,ab. (13918) |
| **5** | ((adrenal or adrenocortical or adreno-medullary or adrenomedullary) adj2 (mass$ or tumo?r$ or neoplas$ or adenoma$ or carcinoma$ or lesion$ or metasta$ or malignan$ or nodule$)).ti,ab. (11326) |
| **6** | or/1-5 (41886) |
| **7** | (incidental$ or inapparent or silent or unexpected$ or unanticipated or accidental$ or occult$ or anomaly or anomalous or additional$).ti,ab. (783572) |
| **8** | 6 and 7 (3576) |
| **9** | exp Incidental Findings/ or incidentaloma$.mp. (6262) |
| **10** | adrenal.ti,ab. (89229) |
| **11** | 9 and 10 (976) |
| **12** | adrenal adenoma$.mp. or adrenaloma$.ti,ab. (1411) |
| **13** | 8 or 11 or 12 (4848) |
| **14** | (MRI or fMRI or NMRI or CT or PET or CATSCAN).ti,ab. (338948) |
| **15** | exp Tomography, X-ray computed/ (293155) |
| **16** | positron emission tomograph$.ti,ab. (31598) |
| **17** | comput$ tomograph$.ti,ab. (166100) |
| **18** | magnetic resonance imag$.ti,ab. (123627) |
| **19** | (scintigraph$ or scintiscan$).ti,ab. (40165) |
| **20** | exp Magnetic Resonance Imaging/ (298496) |
| **21** | exp positron-emission tomography/ (29703) |
| **22** | exp radiopharmaceuticals/du (43467) |
| **23** | exp radioisotopes/du (67639) |
| **24** | radionuclide imaging/ (24131) |
| **25** | ri.fs. (116027) |
| **26** | or/14-25 (850914) |
| **27** | 13 and 26 (1859) |
| **28** | (benign adj4 (malignancy or malignant or metasta$)).ti,ab. (30050) |
| **29** | (adenoma$ adj4 (non adenoma$ or nonadenoma$ or non-adenoma$)).ti,ab. (212) |
| **30** | ((differentiat$ or characteris$ or characteriz$ or compare or comparison$ or comparing or evaluat$) adj4 (lesion$ or mass$ or nodule$ or neoplas$ or tumo?r$ or adenoma$ or carcinoma$ or metasta$ or malignan$)).ti,ab. (157840) |
| **31** | or/28-30 (179623) |
| **32** | 6 or 12 (41888) |
| **33** | 26 and 31 and 32 (1086) |
| **34** | 27 or 33 (2527) |
| **35** | Limit 34 to yr= “1990 –2015” (2169) |

**Suppl. Table 2: Studies excluded for reasons other than lack of test accuracy data, inadequate reference standards or ineligible populations and details on the reasons for their exclusion (n=28).**

|  |  |  |
| --- | --- | --- |
|  | Study reference | Reason for exclusion |
| 1 | Allan BJ, Thorson CM, Van Haren RM, Parikh P, Lew JI. Risk of concomitant malignancy in hyperfunctioning adrenal incidentalomas. Journal of Surgical Research. 2013;184(1):241-6. | Cannot disaggregate target disorder: >10% medullary in benign group |
| 2 | Bencsik Z, Szabolcs I, Goth M, Voros A, Kaszas I, Gonczi J, et al. Incidentally detected adrenal tumors (incidentalomas): histological heterogeneity and differentiated therapeutic approach. Journal of Internal Medicine. 1995;237(6):585-9. | Ineligible diagnostic threshold; Unenhanced CT (>30mm) |
| 3 | Bernini GP, Miccoli P, Moretti A, Vivaldi MS, Iacconi P, Salvetti A. Sixty adrenal masses of large dimensions: Hormonal and morphologic evaluation. Urology. 1998;51(6):920-5. | Cannot disaggregate target disorder: >10% medullary in benign group |
| 4 | Bhargav PR, Mishra A, Agarwal G, Agarwal A, Verma AK, Mishra SK. Adrenal incidentalomas: experience in a developing country. World Journal of Surgery. 2008;32(8):1802-8. | Ineligible diagnostic threshold; Unenhanced CT or MR (>30mm) |
| 5 | Birsen O, Akyuz M, Dural C, Aksoy E, Aliyev S, Mitchell J, et al. A new risk stratification algorithm for the management of patients with adrenal incidentalomas. Surgery. 2014;156(4):959-66. | Ineligible diagnostic threshold; Unenhanced CT (>10HU plus qualitative features of malignancy (irregular borders, heterogeneity, haemorrhage, central necrosis, calcification or increase in size) |
| 6 | Boland GW, Goldberg MA, Lee MJ, Mayo-Smith WW, Dixon J, McNicholas MM, et al. Indeterminate adrenal mass in patients with cancer: evaluation at PET with 2-[F-18]-fluoro-2-deoxy-D-glucose. Radiology. 1995;194(1):131-4. | Ineligible diagnostic threshold; FDG-PET (qualitative focal uptake plus SUV calculations when present) |
| 7 | Boraschi P, Braccini G, Grassi L, Campatelli A, Di VA, Mosca F, et al. Incidentally discovered adrenal masses: evaluation with gadolinium enhancement and fat-suppressed MR imaging at 0.5 T. European Journal of Radiology. 1997;24(3):245-52. | Ineligible diagnostic threshold; MRI (Qualitative assessment of multiple MR findings; gadolinium enhancement) |
| 8 | Botsikas D, Triponez F, Boudabbous S, Hansen C, Becker CD, Montet X. Incidental adrenal lesions detected on enhanced abdominal dual-energy CT: can the diagnostic workup be shortened by the implementation of virtual unenhanced images? European Journal of Radiology. 2014;83(10):1746-51. | Cannot disaggregate target disorder - >30% pheochromocytomas in malignant group |
| 9 | Hamrahian AH, Ioachimescu AG, Remer EM, Motta-Ramirez G, Bogabathina H, Levin HS, et al. Clinical utility of noncontrast computed tomography attenuation value (Hounsfield units) to differentiate adrenal adenomas/hyperplasias from nonadenomas: Cleveland clinic experience. Journal of Clinical Endocrinology & Metabolism. 2005;90(2):871-7. | Ineligible diagnostic threshold; unenhanced CT (>20HU; data at >10HU excluded due to suspected population overlap with another study (Remer 2006)) |
| 10 | Hida T, Nishie A, Asayama Y, Ishigami K, Ushijima Y, Takayama Y, et al. Apparent diffusion coefficient characteristics of various adrenal tumors. Magnetic Resonance in Medical Sciences. 2014;13(3):183-9. | Cannot disaggregate target disorder - >30% pheochromocytomas in malignant group |
| 11 | Ichikawa T, Ohtomo K, Uchiyama G, Koizumi K, Monzawa S, Oba H, et al. Adrenal adenomas: characteristic hyperintense rim sign on fat-saturated spin-echo MR images. Radiology. 1994;193(1):247-50. | Ineligible diagnostic threshold; MRI (benign=hyperintense rim) |
| 12 | Kastelan D, Kraljevic I, Dusek T, Knezevic N, Solak M, Gardijan B, et al. The clinical course of patients with adrenal incidentaloma: is it time to reconsider the current recommendations? Eur J Endocrinol 2015;173(2):275-82. | Cannot disaggregate target disorder - >30% pheochromocytomas in malignant group |
| 13 | Krestin GP, Freidmann G, Fishbach R, Neufang KF, Allolio B, Krestin GP, et al. Evaluation of adrenal masses in oncologic patients: dynamic contrast-enhanced MR vs CT. Journal of Computer Assisted Tomography. 1991;15(1):104-10. | Cannot disaggregate target disorder - malignant in benign group |
| 14 | Lumachi F, Borsato S, Tregnaghi A, Basso SM, Marchesi P, Ciarleglio F, et al. CT-scan, MRI and image-guided FNA cytology of incidental adrenal masses. European Journal of Surgical Oncology. 2003;29(8):689-92. | Cannot disaggregate target disorder: >10% medullary in benign group |
| 15 | Lumachi F, Borsato S, Tregnaghi A, Marino F, Fassina A, Zucchetta P, et al. High risk of malignancy in patients with incidentally discovered adrenal masses: accuracy of adrenal imaging and image-guided fine-needle aspiration cytology. Tumori. 2007;93(3):269-74. | Cannot disaggregate target disorder: >10% medullary in benign group |
| 16 | Maurea S, Mainolfi C, Bazzicalupo L, Panico MR, Imparato C, Alfano B, et al. Imaging of adrenal tumors using FDG PET: Comparison of benign and malignant lesions. American Journal of Roentgenology. 1999;173(1):25-9. | Ineligible diagnostic threshold; Contrast enhanced CT (qualitative contrast enhancement) |
| 17 | Maurea S, Soricelli A, Salvatore M. Characterization of hypersecreting or non-hypersecreting adrenal adenomas: Comparison between iodine-131 nor-cholesterol scintigraphy and magnetic resonance imaging. Current Radiopharmaceuticals. 2009;2(1):56-62. | Cannot disaggregate target disorder >10% benign in malignant group |
| 18 | Minn H, Salonen A, Friberg J, Roivainen A, Viljanen T, Langsjo J, et al. Imaging of adrenal incidentalomas with PET using (11)C-metomidate and (18)F-FDG. Journal of Nuclear Medicine. 2004;45(6):972-9. | Cannot disaggregate target disorder - malignant in benign group |
| 19 | Nakamura S, Namimoto T, Morita K, Utsunomiya D, Oda S, Nakaura T, et al. Characterization of adrenal lesions using chemical shift MRI: Comparison between 1.5 tesla and two echo time pair selection at 3.0 tesla MRI. Journal of Magnetic Resonance Imaging. 2012;35(1):95-102. | Cannot disaggregate target disorder - >30% pheochromocytomas in malignant group |
| 20 | Pantalone KM, Gopan T, Remer EM, Faiman C, Ioachimescu AG, Levin HS, et al. Change in Adrenal Mass Size As A Predictor of A Malignant Tumor. Endocrine Practice. 2010;16(4):577-87. | Ineligible diagnostic threshold; CT or MRI (>40mm) |
| 21 | Park BK, Kim B, Ko K, Jeong SY, Kwon GY. Adrenal masses falsely diagnosed as adenomas on unenhanced and delayed contrast-enhanced computed tomography: Pathological correlation. European Radiology. 2006;16(3):642-7. | Cannot disaggregate target disorder - >30% pheochromocytomas in malignant group |
| 22 | Park SW, Kim TN, Yoon JH, Kim TH, Chung JM, Jeon UB, et al. The washout rate on the delayed CT image as a diagnostic tool for adrenal adenoma verified by pathology: a multicenter study. International Urology and Nephrology. 2012;44(5):1397-402. | Cannot disaggregate target disorder - >30% pheochromocytomas in malignant group |
| 23 | Prager G, Heinz-Peer G, Passler C, Kaczirek K, Schindl M, Scheuba C, et al., editors. Can Dynamic Gadolinium-enhanced Magnetic Resonance Imaging with Chemical Shift Studies Predict the Status of Adrenal Masses?2001 2001. 2002: Springer; 2002. | Cannot disaggregate target disorder: >10% medullary in benign group |
| 24 | Qin HY, Sun HR, Li YJ, Shen BZ. Application of CT perfusion imaging to the histological differentiation of adrenal gland tumors. European Journal of Radiology. 2012;81(3):502-7. | Cannot disaggregate target disorder - >30% pheochromocytomas in malignant group |
| 25 | Semelka RC, Shoenut JP, Lawrence PH, Greenberg HM, Maycher B, Madden TP, et al. Evaluation of adrenal masses with gadolinium enhancement and fat-suppressed MR imaging. Journal of Magnetic Resonance Imaging. 1993;3(2):337-43. | Ineligible diagnostic threshold; Unenhanced CT (qualitative interpretation), MRI (qualitative interpretation; signal to noise ratio > 0) |
| 26 | Slapa RZ, Jakubowski W, Januszewicz A, Kasperlik-Zaluska AA, Dabrowska E, Fijuth J, et al. Discriminatory power of MRI for differentiation of adrenal non-adenomas vs adenomas evaluated by means of ROC analysis: Can biopsy be obviated? European Radiology. 2000;10(1):95-104. | Cannot disaggregate target disorder - >30% pheochromocytomas in malignant group |
| 27 | Song JQ, Zhang CQ, Liu QW, Yu TF, Jiang XM, Xia QH, et al. Utility of chemical shift and diffusion-weighted imaging in characterization of hyperattenuating adrenal lesions at 3.0T. European Journal of Radiology.  2012;81(9):2137-43. | Cannot disaggregate target disorder: >10% medullary in benign group |
| 28 | Yoo JY, Kelly ML, Carty SE, Stang MT, Armstrong MJ, Howell GM, et al. Adrenal imaging features predict malignancy better than size. Annals of Surgical Oncology. 2015;22(Suppl 3):721-7. | Ineligible diagnostic threshold; CT or MRI (size >=40mm) |

**Suppl. Table 3: Characteristics of the 19 of 37 eligible studies excluded from the meta-analysis**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author, Year  Reason for exclusion | Index Test(s) | Study Design | Population | HU Excl  (HU) | Size Excl  (mm) | Other Exclusions | Patients/  lesions  (N) | Incidental/ Known Malignancy/ Sympto-matic (%) | Hormone excess (con-firmed)  (%) | Reference Standard: Histol/ FU/Other  (%) | Diseased  N; % | No. ACC | No. Mets | Threshold for malignancy |
| Aksakal; 2013  Popl NR | MRI | NC  R | Adrenalectomy series, | No | No | Phaeos, Obvious Mets or ACC, Cushing's, Conn's syndrome | 53/53 | NR/NR/NR | 0% | 100/0/0 | 9; 17% | 6 | 0 | 1. Qualitative SI loss **‡** |
| Bilbey; 1995  Incidental<50% | MRI | NC  P | Imaging series | No | <13mm | No | 38/41 | 47/24/29 | 68% | 68/32/0 | 24; 59% | 5 | 7 | 1. ALR > 0.6 **††** 2. ASR ≥ 80 **‡‡**  3. AMR > 59 **§§** |
| Blake; 2006  Popl NR | CT | NC  R | Imaging series | No | No | Phaeos | 99/122  (117 analysed) | NR/NR/NR | NR | 24/76/0 | 18; 15% | 0 | 14 | 1. APW<52% at 10' (for HU≥0 but ≤43) |
| Boraschi; 1999  Popl NR | MR I | NC  NR | Imaging series | No | No | No | 89/108 | NR/NR/NR | 2% | 43/57/0 | 20; 19% | 5 | 14 | 1. Qualitative adrenal:liver **\*** |
| Chung; 2001  Popl NR | MRI | NC  R | Imaging series | NR | NR | NR | 46/47 | NR/NR/NR | NR | 41/59/0 | 12; 26% | 4 | 8 | 1. Qualitative signal loss **‡** |
| Groussin; 2009  Incidental<50% | CT  PET | WPC  P | Adrenalectomy series | No | No | Phaeos Prior malignancy Clear CT Dx (only included if indeterminate on CT [i.e. unenhanced density >10 HU and REW <50%], or if obvious ACC or symptomatic or growing lesion) | 77/77  (58 analysed for CT; 65 for PET) | 42/0/43  (NR for 12 lesions) | 88% | 100/0/0 | 17; 29% | 17 | 0 | 1. >10HU  2. ALR SUVmax >1.45 **§**  3. SUVmax >3.4 |
| Gust; 2012  Popl NR | PET | NC  R | Adrenalectomy series | NR | NR | NR | 51/51 | NR/NR/NR | 41% | 100/0/0 | 22; 43% | 22 | 0 | 1. ALR ≥ 1.7 **§** |
| Ichikawa; 1993  Popl NR | MRI | NC  NR | NR | NR | NR | Phaeos, all diagnoses other than metastasis and adenoma. | 46/46 | NR/NR/NR | 11% | 67/33/0 | 23; 50% | 0 | 23 | 1. T2 ALR ≥ 2.00 **††** |
| Kamiyamavilar; 2009  Popl NR | CT | WPC  R | Imaging series | No | No | Myelolipoma, hyperplasia | 61/68 | NR/0/NR | NR | 32/68/0 | 15; 22% | 2 | 6 | 1. >10HU 2. APW<45% at 5’ 3. RPW <31% at 5’ |
| Kebapci; 2003  Popl NR | CT | NC  NR | Imaging series | NR | NR | NR; 4 TB moved from D+ to D- by Review team | 65/77 | NR/NR/NR | NR | 43/43/14 | 20; 26% | 0 | 20 | 1. APW <40% at 5’  2. APW <50% at 10’  3. APW <60% at 15’ 4. RPW <35% at 5’ 5. RPW <40% at 10’ 6. RPW <40% at 15’ |
| Launay; 2015  Popl NR | PET-CT | NC (WPC)  R | Adrenalectomy series | <10 | No | an absolute CT washout >60% MR SIII>20% Phaeos, cysts, haematomas | 66/67  (43/43 PET) | NR/NR/NR | ACC: 56% ADA: 87.5% | 100/0/0 | 31; 72% | 23 | 8 | 1. ALR maxSUV>1.29 **§** 2. SUVmax > 3.7 |
| Mayo-Smith; 1995  Popl NR | MRI | NC  NR | Imaging series | No | >50mm | Phaeos | 43/46 | NR/NR/NR | NR | 46/37/17 | 18; 39% | 0 | 18 | 1. ASR ≥ 75 **‡‡**  (Reported in paper as ASR ≥ –25) |
| Nwariaku; 2001  Popl NR | CT | NC  R | Adrenalectomy series | No | No | Contrast-enhanced CT, delayed contrast-enhanced scans, and those with bilateral adrenal masses | 14/14 | NR/NR/NR | 71% of ADA | 100/0/0 | 7; 50% | 2 | 3 | 1. >10HU |
| Park; 2015  Popl NR | CT | NC  R | Adrenalectomy series | No | <30mm (ADA only) | All non-ADA or ACC excluded. ADA exclusions: Extra-adrenal malignancy, bilateral/multiple adrenal lesions nonACC exclusions: any nonACC; | 43/43 | NR/0/NR | NR | 100/0/0 | 12; 28% | 12 | 0 | 1. large ROI: APW<60% or RPW<40% at 15’ |
| Park ; 2007  Popl NR | CT | ??  R | Adrenalectomy series | <-30HU | <10mm | Myelolipoma, CT unreadable or lost, image artefacts presenting ROI measurement; Phaeos (n=12) excluded by Review team | 45/45  33 analysed | NR/NR/NR | NR | 100/0/0 | 8; 24% | 0 | 5 | 1. >10HU |
| Petersenn; 2015  Popl NR | CT | NC  R | Other: cancer registry plus imaging series | No | No | Unclear | 76/76 | NR/NR/NR | NR | 67/33\*/0  (\*histol or FU) | 51; 67% | 51 | 0 | 1. ≥ 10HU |
| Remer; 2006  Popl NR | CT | ??  R | Adrenalectomy series | No | No | NR; Phaeos (n=35) excluded by Bham team | 187/208  (181 unenhanced CT; 146 minus phaeos) | NR/NR/NR | NR | 100/0/0 | 41; 28% | 7 | 34 | 1. >10HU |
| Zettinig; 2004  Popl NR | PET | NR | Not reported | NR | NR | None reported | 16/16 | NR/NR/NR | 69% | 94/6/0 | 4; 25% | 1 | 1 | 1. ALR maxSUV<1.6 **§** 2. SUVmax<3.4 |
| Zielonko; 2008  Popl NR | MRI | NC  NR | Imaging series | No | ≤10 | None reported; Phaeos (n=8) excluded by Review team | 54/57  (49 analysed) | NR/NR/NR | 19% | 67/33/0 | 6; 12% | 1 | 5 | 1. T2 ALR >=1.9 \*\*  2. SII ≤ 3.1% ǁ  (CSI ≤ 0.031) |

ACC – adrenocortical carcinoma; APW – absolute percentage washout; ADC – apparent diffusion coefficient; ALR – adrenal to liver ratio; ASR – adrenal to spleen ratio; AMR – adrenal to muscle ratio; ASR – adrenal to spleen ratio; CT – computed tomography; CS – chemical shift; CSI – chemical shift index; Excl – exclusion; HU – Hounsfield units; IP – in-phase; METS – metastases; MRI – magnetic resonance imaging; NC – non–comparative study; NR – not reported; OP – opposed phase; P – prospective data collection; PET – positron emission tomography; Popl – population; R – retrospective data collection; ROI – region of interest; RPW – relative percentage washout; SI – signal intensity; SII – signal intensity index; SUVmax - maximum standardized uptake value; WPC – within–person comparison (multiple index tests evaluated in all study participants).

\* masses considered to be malignant if their signal was more intense than liver signal

† masses considered to be metastases if their signal was more intense than liver signal and inferior to kidney signal.

‡ masses considered to be malignant if no loss of signal intensity observed on chemical shift

§ALR maxSUV - ratio of SUVmax in the adrenal gland compared to the liver

**Formulae for calculating quantitative thresholds:**

ǁ Signal intensity index = (SI adrenal IP) – (SI adrenal OP)] / (SI adrenal IP)

¶ MRI adrenal to spleen ratio = (SI adrenal OP/SI Spleen OP)/(SI adrenal IP/SI spleen IP)

\*\* MRI adrenal to liver ratio = SI adrenal/SI liver

†† MRI adrenal to liver ratio = [(SI adrenal OP/SI liver OP)/(SI adrenal IP/SI liver IP)]–1) x 100%

‡‡ MRI adrenal to spleen ratio = [(SI adrenal OP/SI Spleen OP)/(SI adrenal IP/SI Spleen IP)]–1) x 100%

§§ MRI adrenal to muscle ratio = [(SI adrenal OP/SI Muscle OP)/(SI adrenal IP/SI Muscle IP)]–1) x 100%]

**Suppl. Table 4: Raw data from studies eligible for meta-analysis (n=18) and excluded from meta-analyses (n=19)**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author; Year | Test and Threshold | Threshold Set\*: | % incidental or malignant | TP | FP | FN | TN | Tot | Sensitivity (95%CI) | Specificity  (95%CI) |
| Studies informing analyses in incidentally detected tumors | | | | | | | | | | |
|  | **Non–contrast CT tumor density** |  |  |  |  |  |  |  |  |  |
| Angelelli; 2013 | >10HU | Retrosp | 74% | 28 | 6 | 0 | 16 | 50 | 1.00 (0.88, 1.00) | 0.73 (0.50, 0.89) |
| Vilar; 2008 | >10HU | Unclear | 100% | 13 | 11 | 0 | 28 | 52 | 1.00 (0.75, 1.00) | 0.72 (0.55, 1.00) |
|  | **CT washout studies** |  |  |  |  |  |  |  |  |  |
| Angelelli; 2013‡ | APW <60% OR RPW <40% at 10' | Retrosp | 74% | 14 | 0 | 1 | 10 | 25 | 0.93 (0.68, 1.00) | 1.00 (0.69, 1.00) |
| Angelelli; 2013‡ | APW <60% OR RPW <40% at 15' | Retrosp | 74% | 13 | 1 | 0 | 11 | 25 | 1.00 (0.75, 1.00) | 0.92 (0.62, 1.00) |
|  | **MR SI loss** |  |  |  |  |  |  |  |  |  |
| Maurea; 2004 | qualitative | Prosp | 67% | 8 | 3 | 0 | 15 | 26 | 1.00 (0.63, 1.00) | 0.83 (0.59, 0.96) |
| Sandrasegaran; 2011 | SII ≤ 23% | Retrosp | 69% | 8 | 5 | 4 | 32 | 49 | 0.67 (0.35, 0.90) | 0.86 (0.71, 0.95) |
|  | **MR SI loss ratios** |  |  |  |  |  |  |  |  |  |
| Maurea; 2004 | qualitative adrenal:liver | Prosp | 67% | 8 | 10 | 0 | 8 | 26 | 1.00 (0.63, 1.00) | 0.44 (0.22, 0.69) |
| Sandrasegaran; 2011 | ASR ≥ 62 | Retrosp | 69% | 7 | 5 | 5 | 32 | 49 | 0.58 (0.28, 0.85) | 0.86 (0.71, 0.95) |
|  | **PET maxSUV** |  |  |  |  |  |  |  |  |  |
| Nunes; 2010 | > 3.4 | Review† | 65% | 3 | 5 | 0 | 15 | 23 | 1.00 (0.29, 1.00) | 0.75 (0.51, 0.91) |
| Tessonnier; 2008 | > 3.28 | Retrosp | 100% | 11 | 8 | 1 | 21 | 41 | 0.92 (0.62, 1.00) | 0.72 (0.53, 0.87) |
|  | **PET ALR maxSUV** |  |  |  |  |  |  |  |  |  |
| Nunes; 2010 | > 1.6 | Retrosp | 65% | 3 | 3 | 0 | 17 | 23 | 1.00 (0.29, 1.00) | 0.85 (0.62, 0.97) |
| Tessonnier; 2008 | > 1.8 | Retrosp | 100% | 12 | 0 | 0 | 29 | 41 | 1.00 (0.74, 1.00) | 1.00 (0.88, 1.00) |
|  |  |  |  |  |  |  |  |  |  |  |
| Studies informing analyses in participants with current or prior non-adrenal malignancy | | | | | | | | | | |
|  | **Non–contrast CT tumor density** |  |  |  |  |  |  |  |  |  |
| Choi; 2013 | >10HU | Prosp | 100% | 19 | 15 | 0 | 6 | 40 | 1.00 (0.82, 1.00) | 0.29 (0.11, 0.52) |
| Frilling; 2004 | >10HU | Unclear | 100% | 25 | 8 | 6 | 5 | 44 | 0.81 (0.63, 0.93) | 0.38 (0.14, 0.68) |
| McNicholas; 1995 | >10HU | Review† | 100% | 19 | 1 | 0 | 17 | 37 | 1.00 (0.82, 1.00) | 0.94 (0.73, 1.00) |
| Porte; 1999 | >10HU | Prosp | 100% | 16 | 3 | 2 | 11 | 32 | 0.89 (0.65, 0.99) | 0.79 (0.49, 0.95) |
| Uemura; 2013 | >10HU | Review† | 100% | 5 | 1 | 1 | 8 | 15 | 0.83 (0.36, 1.00) | 0.89 (0.52, 1.00) |
|  | **CT washout studies** |  |  |  |  |  |  |  |  |  |
| Choi; 2013 | APW at 15’ <60% | Prosp | 100% | 3 | 3 | 16 | 18 | 40 | 0.16 (0.03, 0.40) | 0.86 (0.64, 0.97) |
| Choi; 2013 | RPW at 15’ <40% | Prosp | 100% | 3 | 1 | 16 | 20 | 40 | 0.16 (0.03, 0.40) | 0.95 (0.76, 1.00) |
|  | **MR SI loss** |  |  |  |  |  |  |  |  |  |
| Ream; 2015 | qualitative | Retrosp | 78% | 9 | 4 | 1 | 23 | 37 | 0.90 (0.55, 1.00) | 0.85 (0.66, 0.96) |
|  | **MR SI loss - ALR** |  |  |  |  |  |  |  |  |  |
| Burt; 1994 | qualitative adrenal:liver | Prosp | 100% | 9 | 2 | 1 | 24 | 36 | 1.00 (0.40, 1.00) | 0.24 (0.08, 0.47) |
| Ream; 2015 | > 0.674 | Retrosp | 78% | 4 | 16 | 0 | 5 | 25 | 0.90 (0.55, 1.00) | 0.92 (0.75, 0.99) |
| Schwartz; 1995 | ≥ 1.5 | Retrosp | 100% | 20 | 22 | 3 | 23 | 68 | 0.87 (0.66, 0.97) | 0.51 (0.36, 0.66) |
|  | **MR SI loss - ASR** |  |  |  |  |  |  |  |  |  |
| McNicholas; 1995 | ≥ 75 | Prosp | 100% | 19 | 4 | 0 | 14 | 37 | 1.00 (0.82, 1.00) | 0.78 (0.52, 0.94) |
| Ream; 2015 | > 64.1 | Retrosp | 78% | 9 | 2 | 1 | 25 | 37 | 0.90 (0.55, 1.00) | 0.93 (0.76, 0.99) |
| Schwartz; 1995 | ≥ 55 | Retrosp | 100% | 23 | 9 | 0 | 36 | 68 | 1.00 (0.85, 1.00) | 0.80 (0.65, 0.90) |
|  | **MR SI loss - AMR** |  |  |  |  |  |  |  |  |  |
| Ream; 2015 | > 70.7 | Retrosp | 78% | 9 | 2 | 1 | 25 | 37 | 0.90 (0.55, 1.00) | 0.93 (0.76, 0.99) |
|  | **PET SUVmax** |  |  |  |  |  |  |  |  |  |
| Villar Del Moral; 2010 | > 6 | Retrosp | 53% | 6 | 0 | 5 | 4 | 15 | 0.55 (0.23, 0.83) | 1.00 (0.40, 1.00) |
| Kunikowska; 2014 | >5.2 | Retrosp | 100% | 29 | 7 | 3 | 63 | 102 | 0.91 (0.75, 0.98) | 0.90 (0.80, 0.96) |
| Lang; 2015 | > 2.65 | Retrosp | 100% | 26 | 3 | 3 | 7 | 39 | 0.90 (0.73, 0.98) | 0.70 (0.35, 0.93) |
|  | **PET ALR maxSUV** |  |  |  |  |  |  |  |  |  |
| Villar Del Moral; 2010 | >1.8 | Retrosp | 53% | 6 | 0 | 5 | 4 | 15 | 0.55 (0.23, 0.83) | 1.00 (0.40, 1.00) |
| Kunikowska; 2014 | >1.53 | Retrosp | 100% | 32 | 4 | 2 | 64 | 102 | 0.94 (0.80, 0.99) | 0.94 (0.86, 0.98) |
|  |  |  |  |  |  |  |  |  |  |  |
| Studies excluded from analyses due to study population | | | | | | | | | | |
|  | **Non–contrast CT tumor density** |  |  |  |  |  |  |  |  |  |
| Groussin; 2009 | >10HU | Review † | 42% incidental | 16 | 29 | 1 | 12 | 58 | 0.94 (0.71, 1.00) | 0.29 (0.16, 0.46) |
| Kamiyama 2009 | >10HU | Prosp | NR | 15 | 23 | 0 | 30 | 68 | 1.00 (0.78, 1.00) | 0.57 (0.42, 0.70) |
| Nwariaku; 2001 | >10HU | Prosp | NR | 7 | 4 | 0 | 3 | 14 | 1.00 (0.59, 1.00) | 0.43 (0.10, 0.82) |
| Park; 2007 | >10HU | Prosp | NR | 8 | 16 | 0 | 9 | 33 | 1.00 (0.63, 1.00) | 0.36 (0.18, 0.57) |
| Petersenn; 2015 | >10HU | Prosp | NR | 51 | 10 | 0 | 15 | 76 | 1.00 (0.93, 1.00) | 0.60 (0.39, 0.79) |
| Remer; 2006 | >10HU | Prosp | NR | 41 | 76 | 0 | 29 | 146 | 1.00 (0.91, 1.00) | 0.28 (0.19, 0.37) |
|  | **CT washout studies** |  |  |  |  |  |  |  |  |  |
| Kamiyama 2009 | APW <45% at 5’ | Retrosp | NR | 15 | 12 | 0 | 41 | 68 | 1.00 (0.78, 1.00) | 0.77 (0.64, 0.88) |
| Kebapci; 2003 | APW <35% at 5’ | Unclear | NR | 17 | 12 | 3 | 45 | 77 | 0.85 (0.62, 0.97) | 0.79 (0.66, 0.89) |
| Kamiyama 2009 | RPW <31% at 5’ | Retrosp | NR | 15 | 9 | 0 | 44 | 68 | 1.00 (0.78, 1.00) | 0.83 (0.70, 0.92) |
| Kebapci; 2003 | RPW <50% at 5’ | Unclear | NR | 20 | 10 | 0 | 47 | 77 | 1.00 (0.83, 1.00) | 0.82 (0.70, 0.91) |
| Blake; 2006 | APW <52% at 10’ (plus HU) | Retrosp | NR | 18 | 1 | 0 | 98 | 117 | 1.00 (0.81, 1.00) | 0.77 (0.64, 0.88) |
| Kebapci; 2003 | APW <50% at 10’ | Unclear | NR | 17 | 12 | 3 | 45 | 77 | 0.85 (0.62, 0.97) | 0.79 (0.66, 0.89) |
| Kebapci; 2003 | RPW <40% at 10’ | Unclear | NR | 20 | 10 | 0 | 47 | 77 | 1.00 (0.83, 1.00) | 0.82 (0.70, 0.91) |
| Kebapci; 2003 | APW <60% at 15’ | Unclear | NR | 17 | 11 | 3 | 46 | 77 | 0.85 (0.62, 0.97) | 0.81 (0.68, 0.90) |
| Kebapci; 2003 | RPW <40% at 15’ | Unclear | NR | 20 | 7 | 0 | 50 | 77 | 1.00 (0.83, 1.00) | 0.88 (0.76, 0.95) |
| Park; 2015 | APW <60% or RPW<40% at 15’ | Prosp | NR | 12 | 11 | 0 | 20 | 43 | 1.00 (0.74, 1.00) | 0.65 (0.45, 0.81) |
|  | **MR SI loss** |  |  |  |  |  |  |  |  |  |
| Aksakal; 2013 | qualitative (T NR) | Unclear | NR | 8 | 9 | 1 | 35 | 53 | 0.89 (0.52, 1.00) | 0.80 (0.65, 0.90) |
| Boraschi; 1999 | qualitative (0.5T) | Prosp | NR | 18 | 6 | 2 | 82 | 108 | 0.90 (0.68, 0.99) | 0.93 (0.86, 0.97) |
| Chung; 2001 | qualitative (1.5T) | Prosp | NR | 11 | 5 | 1 | 30 | 47 | 0.92 (0.62, 1.00) | 0.86 (0.70, 0.95) |
| Zielonko; 2008 | SII ≤ 3.1% (0.5T) | Retrosp | NR | 6 | 2 | 0 | 41 | 49 | 1.00 (0.54, 1.00) | 0.95 (0.84, 0.99) |
| Marin; 2012¶ | SII ≤ 23% (OP/IP dataset) (3.0T) | Unclear | 100% incidental | 16 | 10 | 1 | 35 | 62 | 0.94 (0.71, 1.00) | 0.80 (0.66, 0.90) |
|  | **MR SI loss ratios** |  |  |  |  |  |  |  |  |  |
| Bilbey; 1995 | ALR >0.6 (0.5T) | Unclear | NR | 24 | 2 | 0 | 15 | 41 | 1.00 (0.86, 1.00) | 0.88 (0.64, 0.99) |
| Ichikawa; 1993 | ALR ≥2.00 (0.5T) | Retrosp | NR | 18 | 0 | 5 | 23 | 46 | 0.78 (0.56, 0.93) | 1.00 (0.85, 1.00) |
| Porte; 1999¶ | ALR qualitative (T NR) | Prosp | 100% malignancy | 18 | 7 | 0 | 7 | 32 | 1.00 (0.81, 1.00) | 0.50 (0.23, 0.77) |
| Zielonko; 2008 | ALR ≥ 1.9 (0.5T) | Retrosp | NR | 2 | 7 | 4 | 36 | 49 | 0.33 (0.04, 0.78) | 0.84 (0.69, 0.93) |
| Bilbey; 1995 | ASR ≥80 (0.5T) | Unclear | 44% incidental | 24 | 0 | 0 | 17 | 41 | 1.00 (0.86, 1.00) | 1.00 (0.80, 1.00) |
| Mayo-Smith; 1995 | ASR >=75 (1.5T) | Retrosp | NR | 18 | 5 | 0 | 23 | 46 | 1.00 (0.81, 1.00) | 0.82 (0.63, 0.94) |
| Bilbey; 1995 | AMR >59(0.5T) | Unclear | NR | 24 | 2 | 0 | 15 | 41 | 1.00 (0.86, 1.00) | 0.88 (0.64, 0.99) |
|  | **PET maxSUV** |  |  |  |  |  |  |  |  |  |
| Groussin; 2009 | >3.4 | Review † | NR | 22 | 13 | 0 | 30 | 65 | 1.00 (0.85, 1.00) | 0.70 (0.54, 0.83) |
| Launay; 2015 | >3.7 | Retrosp | NR | 30 | 2 | 1 | 10 | 43 | 0.97 (0.83, 1.00) | 0.83 (0.52, 0.98) |
| Zettinig; 2004 | >4.0 | Review † | NR | 4 | 0 | 0 | 12 | 16 | 1.00 (0.40, 1.00) | 1.00 (0.74, 1.00) |
|  | **PET ALR maxSUV** |  |  |  |  |  |  |  |  |  |
| Groussin; 2009 | >1.45 | Review † | NR | 22 | 5 | 0 | 38 | 65 | 1.00 (0.85, 1.00) | 0.88 (0.75, 0.96) |
| Gust; 2012 | ≥ 1.7 | Prosp | NR | 21 | 1 | 1 | 28 | 51 | 0.95 (0.77, 1.00) | 0.97 (0.82, 1.00) |
| Launay; 2015 | >1.29 | Retrosp | NR | 30 | 2 | 1 | 10 | 43 | 0.97 (0.83, 1.00) | 0.83 (0.52, 0.98) |

ALR maxSUV – ratio of SUVmax in the adrenal gland compared to the liver; APW – absolute percentage washout; ADC – apparent diffusion coefficient; ALR – adrenal to liver ratio; ASR – adrenal to spleen ratio; AMR – adrenal to muscle ratio; ASR – adrenal to spleen ratio; CI – confidence interval; CT – computed tomography; FN – false negative; FP – false positive; HU – Hounsfield units; MRI – magnetic resonance imaging; NC – non–comparative study; NR – not reported; OP – opposed phase; P – prospective data collection; PET – positron emission tomography; RPW – relative percentage washout; SI – signal intensity; SII – signal intensity index; SUVmax - maximum standardized uptake value; TN – true negative; TP – true positive.

**\*** indicates whether diagnostic threshold was set prospectively or retrospectively by study authors;

**†** no threshold was selected by study authors but individual participant data was presented such that the review team could extract according to common threshold

**‡** Angelelli % incidentaloma is for full study sample; not reported for subgroups according to washout

**¶** Datasets not included in pooled analyses because they did not report using 1.5 Tesla MRI

**Suppl. Figure 1: Studies evaluating CT - Risk of bias and concerns about applicability per study (based on adapted QUADAS-2 (**[**19**](#_ENREF_19)**))**



**Suppl. Figure 2: Studies evaluating MRI - Risk of bias and concerns about applicability per study (based on adapted QUADAS-2 (**[**19**](#_ENREF_19)**)**



**Suppl. Figure 3: Studies evaluating PET - Risk of bias and concerns about applicability per study (based on adapted QUADAS-2 (**[**19**](#_ENREF_19)**))**

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