

UOG Journal Club: November 2014

Use of IOTA simple rules for diagnosis of ovarian cancer: meta-analysis
应用国际卵巢肿瘤分析简单原则诊断卵巢癌: meta分析

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Journal Club slides prepared by Dr Tommaso Bignardi
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Background背景

- The International Ovarian Tumor Analysis (IOTA) is a multicenter collaboration whose aim is to design tools for the pre-operative diagnosis of ovarian cancer that can be used by non-expert ultrasound operators.
- 国际卵巢肿瘤分析(IOTA)是一个多中心协作组织，其目的是为由非专家的超声人员设计用于术前诊断卵巢癌的工具
- By using standardized terms and definitions to describe morphological features of ovarian tumors, the ‘simple-rules’ model was designed.
- 通过使用标准化的术语和定义描述卵巢肿瘤的形态特征，设计“简单原则”模型。
- According to this model, there are five benign (B) features and five malignant (M) features to determine the nature of an adnexal tumor.
- 根据这个模型，有5个良性（B）特征和5个恶性（M）特征来确定一个附件肿瘤的性质。
- In the original study the rules were applicable in 76% of cases with a sensitivity of 93%, specificity of 90%, positive likelihood ratio (LR+) of 9.45 and negative likelihood ratio (LR-) of 0.08.在原始的研究中，将这个原则应用于76%的案例，敏感性为93%，特异性90%，阳性似然比（LR +）9.45、阴性似然比（LR-）0.08。

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Objectives: 目的

- To present a prospective study on the IOTA ‘simple-rules’ tool for the diagnosis of ovarian cancer**
-演示用IOTA“简单规则”诊断卵巢癌的前瞻性研究
- To perform a meta-analysis of studies that utilized the same diagnostic method**
-对使用相同诊断方法的文献进行meta分析

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Current study: Patients and Methods

当前的研究：患者和方法

Prospective single-center study in a general gynecology clinic within a tertiary unit

Consecutive patients diagnosed with an adnexal tumor were examined by a

single level-II (non-expert) ultrasound operator using the **simple-rules protocol**

在一家三级医院普通妇科门诊进行的前瞻性单一中心研究：诊断为一侧附件肿瘤的病人连续由一个二级(非专家)超声人员使用“简单原则”

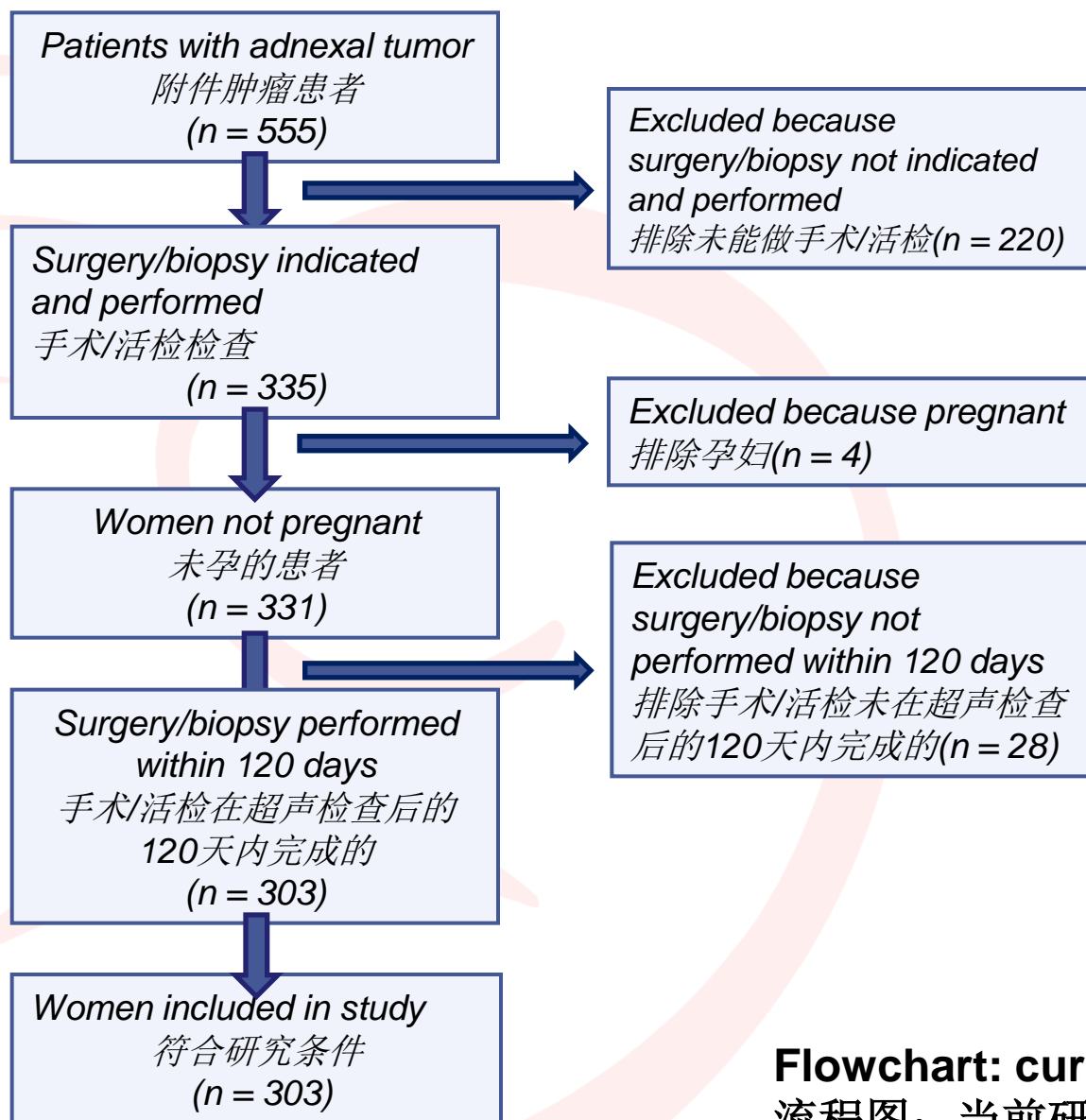
An expert ultrasound operator subsequently used subjective

pattern recognition to classify the tumors as benign or malignant

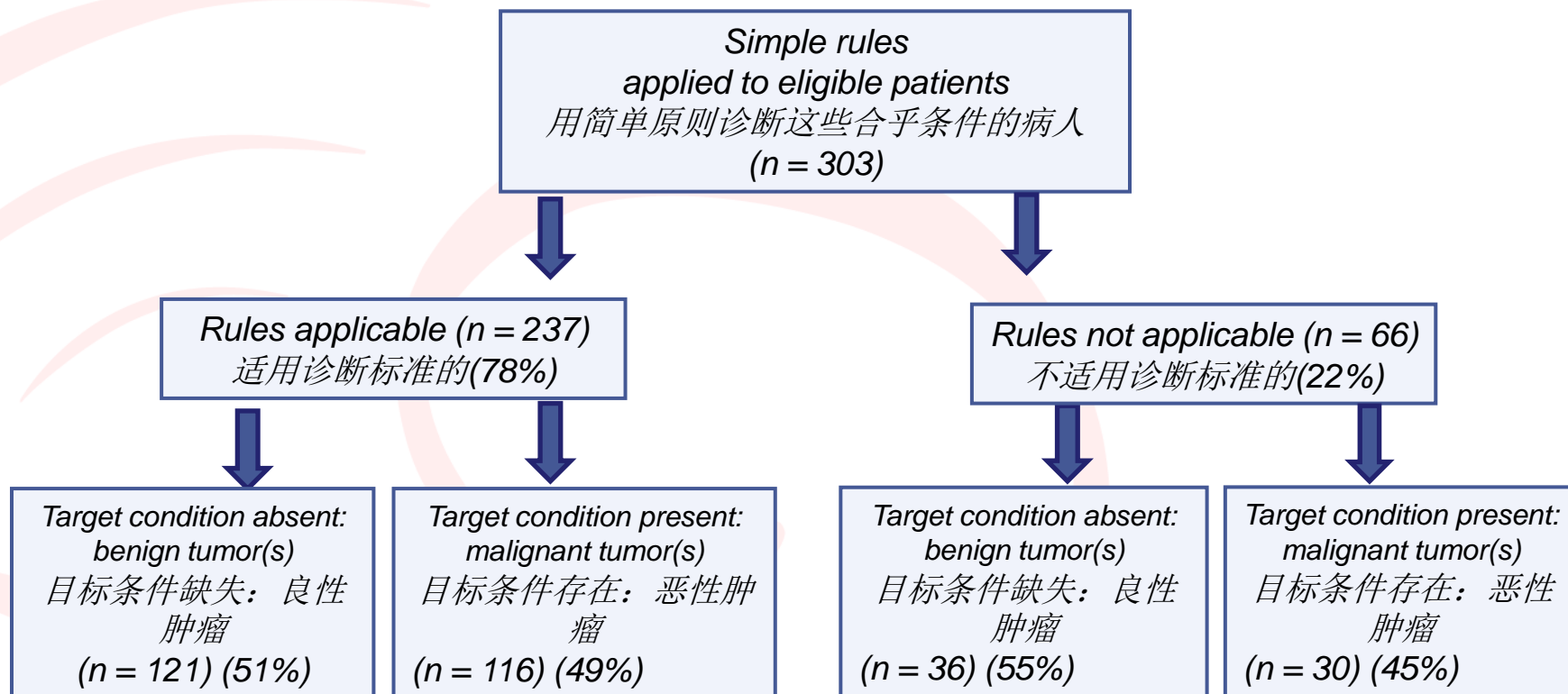
超声专家接着凭借个人主观“模式识别”辨别肿瘤的良恶性

Pregnant women, those unable to undergo a transvaginal scan and those whose surgery date exceeded 120 days from the date of the ultrasound scan were excluded

排除孕妇，无法接受经阴道超声检查和接受超声检查至手术日期超过120天的



Flowchart: current study
流程图：当前研究



Flowchart of results: current prospective study
结果的流程图:当前的前瞻性研究

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Discussion: current study 讨论：目前的研究

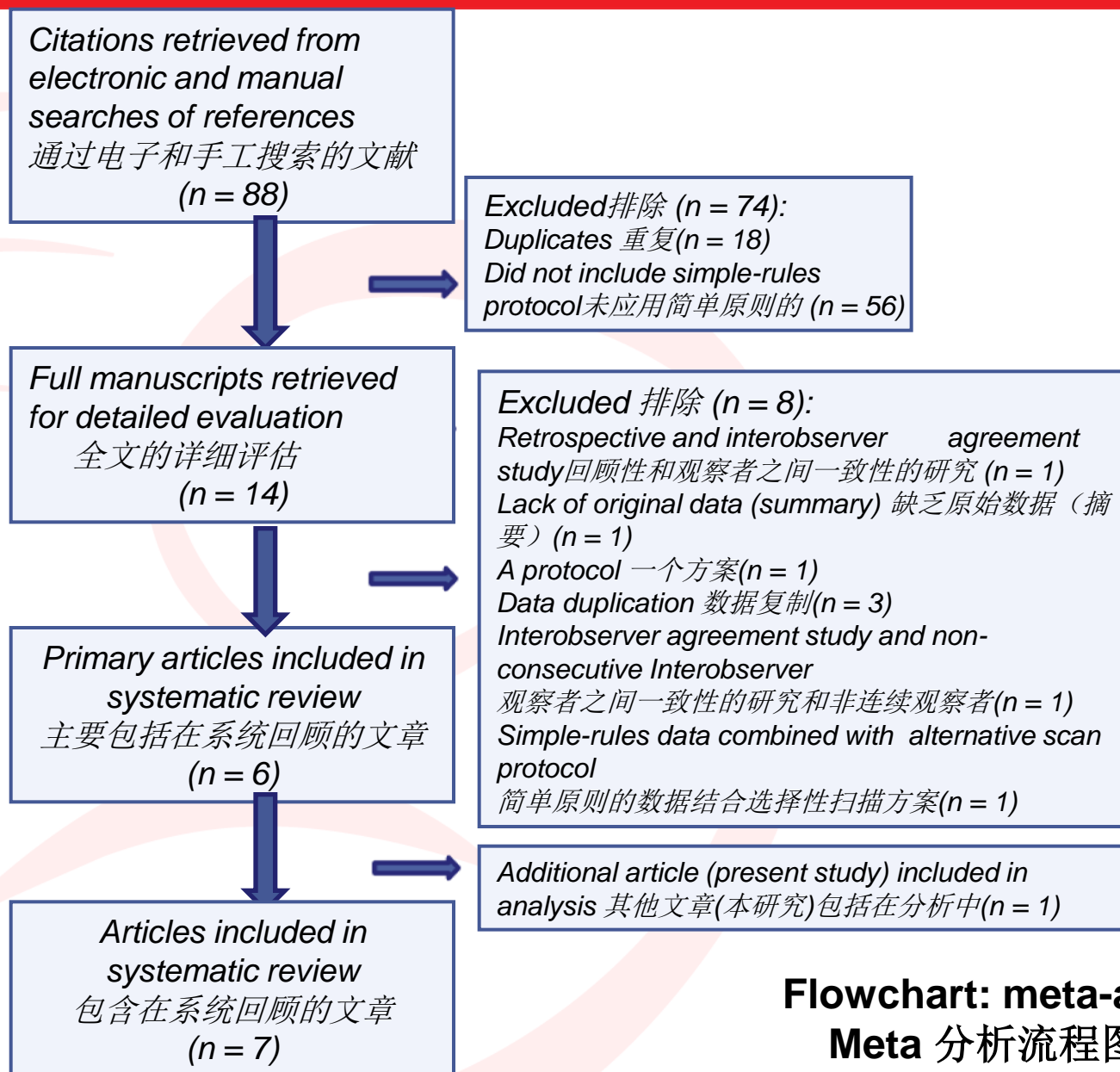
Simple rules were applicable in nearly 80% of women - similar to the findings of the original and subsequent IOTA validation studies.

- 简单原则也适用于近80%的女性——与原始和随后的IOTA有效性研究有类似的发现
- Sensitivity of ovarian cancer diagnosis was not significantly different between the current study and the IOTA studies.
- 卵巢癌诊断的敏感性在目前的研究和 IOTA研究之间没有明显差异。
- Specificity in the current study was significantly lower than in the IOTA validation study ($P < 0.001$), although it was similar to the findings of the original study ($P = 0.48$).
- 特异性当前的研究明显低于IOTA有效性研究($P < 0.001$),尽管在原始的研究中结果相似($P = 0.48$)。
- Pattern recognition performed by the expert operator was superior to the simple rules in cases in which the rules were applicable mainly due to significant differences in specificity (88.6% vs 93.2%, $p = 0.03$).在案例中，专家使用模式识别要优于简单规则，主要是特异性有显著差异(88.6%比93.2%, $p = 0.03$)。

Inclusion criteria: meta-analysis

Meta分析的标准包括

- Search on MEDLINE, EMBASE and Cochrane database
搜索MEDLINE，EMBASE和Cochrane数据库
- Studies had to include data on use of the simple-rules protocol when applied to adnexal tumors for the diagnosis of ovarian cancer
研究必须包括使用简单原则的数据，简单原则适用于附件肿瘤诊断为卵巢癌
- Women must have had surgery and a histological diagnosis for comparison as the gold standard or the reference standard
妇女必须有手术和组织学诊断进行比较作为金标准或参考标准
- Only prospective studies 只包括前瞻性研究
- Studies from 1st January 2008 until 8th November 2013
研究从2008年1月1日到2013年11月8日



Flowchart: meta-analysis
Meta 分析流程图

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- Methodological quality assessment: Quality Assessment of Diagnostic Accuracy Studies (QUADAS) - 2 tool
方法学的质量评价：诊断准确性研究的质量评估(QUADAS)- 2 工具
- Data independently extracted by 2 reviewers 2 审计者独立提取数据
- Sensitivity, Specificity and accuracy of simple rules and pattern recognition were compared using McNemar's test for paired binary outcomes
- 使用McNemar检验成对的二进制结果比较简单原则和模式识别的敏感性、特异性和准确性
- Sensitivity, Specificity and accuracy of simple rules were compared with the original and the validation IOTA studies using the chi-square test for independent binary outcomes

使用卡方检验独立的二进制结果比较简单原则和原始及IOTA有效性研究的敏感性、特异性和准确性

Random-effects meta-analysis was used to calculate univariate pooled estimates of sensitivity and specificity for the IOTA simple-rules tool. A bivariate approach was also investigated to calculate these values. Forest plots were constructed to summarize the results

随机效应的meta分析是用来计算单变量汇总估计IOTA简单原则工具的敏感性和特异性。双变量的方法也是研究计算这些值。总结结果建立了森林图。

Results: Studies included in meta-analysis of accuracy of International Ovarian Tumor Analysis simple rules in diagnosis of malignant adnexal masses

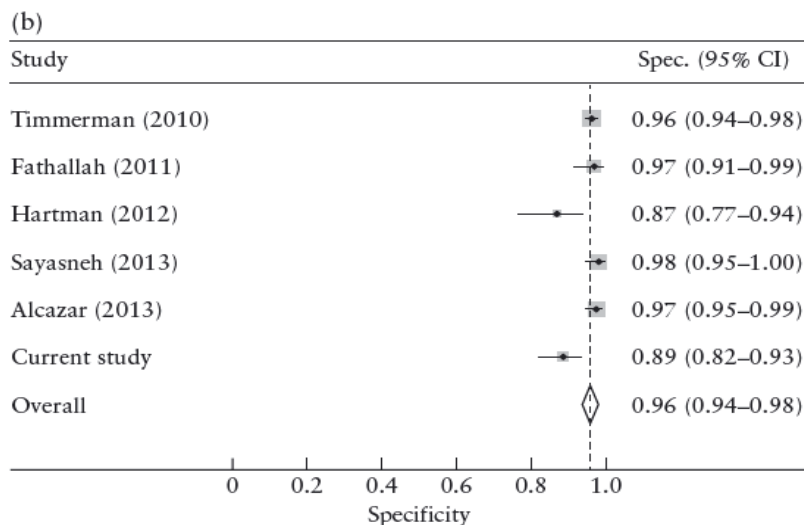
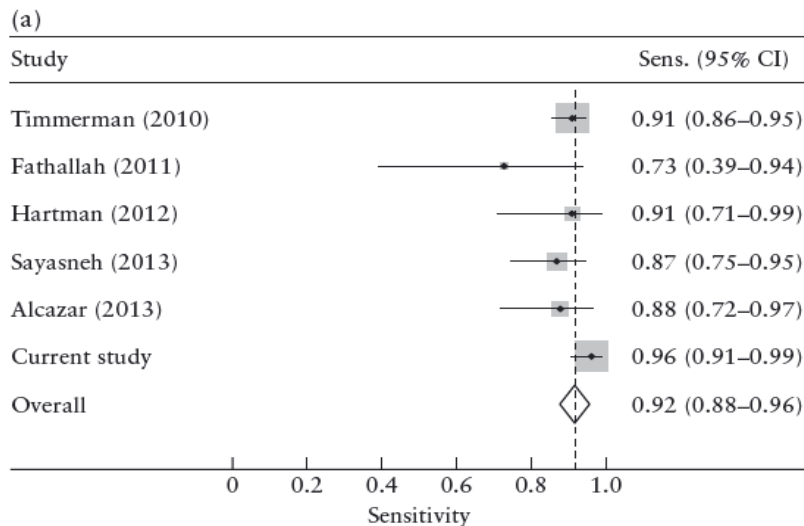
结果：研究包括meta分析国际卵巢肿瘤分析简单原则诊断恶性附件包块

study	n	Patients in whom rules are applicable (n%)* 适用原则的患者	Malignant tumors (n%)* 恶性肿瘤	Benign tumors (n%)* 良性肿瘤	Prevalence of malignancy (%)† 恶性肿瘤的患病率	TP (n) 真阳性	FP (n) 假阳性	FN (n) 假阴性	TN (n) 真阴性	Sensitivity (95% CI) 敏感性	Specificity (95% CI) 特异性
Timmerman 2008	507	386 (76.1)	-	-	29.0	106	25	6	249	0.95 (0.89–0.98)	0.91 (0.87–0.94)
Timmerman 2010	1938	1501 (77.5)	542 (28.0)	1396 (72.0)	24.6	340	49	29	1083	0.92 (0.89–0.95)	0.96 (0.94–0.97)
Fathallah 2011	122	109 (89.3)	14 (11.5)	108 (88.5)	10.1	8	3	3	95	0.73 (0.39–0.94)	0.97 (0.91–0.99)
Hartman 2012	103	91 (88.3)	30 (29.1)	73 (70.9)	24.2	20	9	2	60	0.91 (0.71–0.99)	0.87 (0.77–0.94)
Sayasneh 2013	255	214 (83.9)	74 (29.0)	181 (71.0)	24.8	46	3	7	158	0.87 (0.75–0.95)	0.98 (0.95–1.00)
Alcazar 2013	340	270 (79.4)	55 (16.2)	285 (83.8)	12.2	29	6	4	231	0.88 (0.72–0.97)	0.97 (0.95–0.99)
Current study	303	237 (78.2)	135 (44.6)	168 (55.4)	44.3	101	15	4	117	0.96 (0.91–0.99)	0.89 (0.82–0.93)

Only the first author of each study is given. *Percentage of total population. †Percentage of population in whom rules are applicable. FN, false negative; FP, false positive; TN, true negative; TP, true positive

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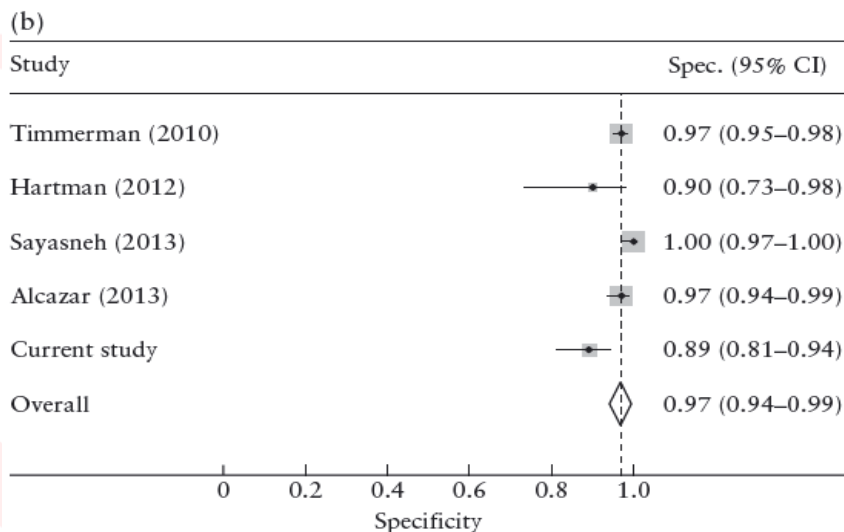
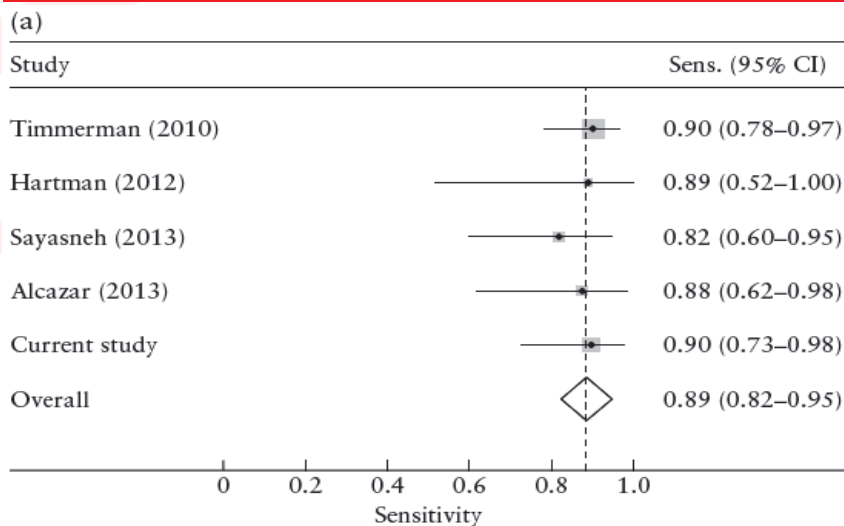


Results: Forest plot of pooled sensitivity (Sens.) (a) and specificity (Spec.) (b) of studies of IOTA simple rules included in subanalysis of externally validated studies. Area of each shaded box is proportional to weighting of study in meta-analysis.

结果:森林图汇集IOTA简单原则的敏感性(a)和特异性(b)研究,包含在外部验证研究的亚组分析.每个阴影框面积与meta分析研究的权重成正比。

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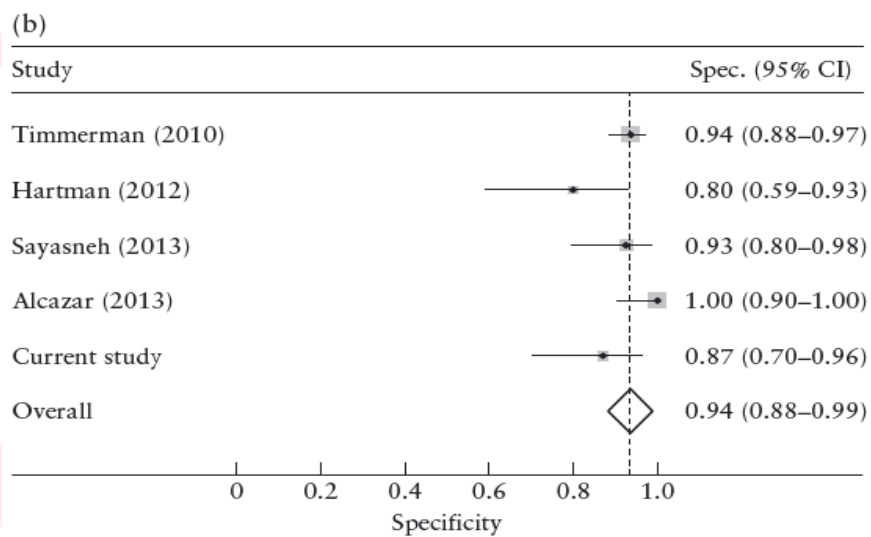
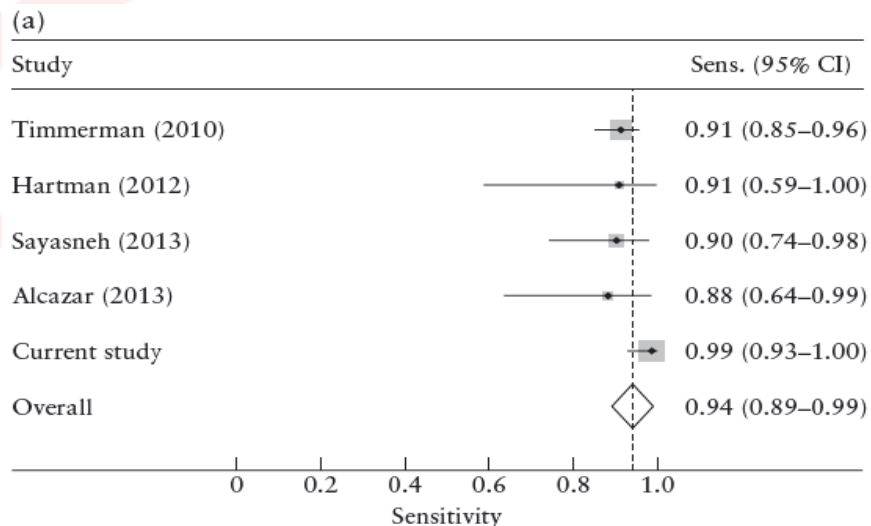


Results: Forest plot of pooled sensitivity (Sens.) (a) and specificity (Spec.) (b) of studies of IOTA simple rules included in subanalysis of externally validated studies in premenopausal women. Area of each shaded box is proportional to weighting of study in meta-analysis.

结果:森林图汇集IOTA简单原则的敏感性(a)和特异性(b)研究, 包含绝经前妇女外部验证研究的亚组分析.每个阴影框面积与meta分析研究的权重成正比。

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Discussion: meta-analysis 讨论: meta分析

- In the meta-analysis, the simple rules performed well overall for the diagnosis of ovarian cancer in the hands of ultrasound operators of varying levels of expertise, with a pooled sensitivity of 93% (95% CI, 90–96%) (I^2 , 32.1%) and a pooled specificity of 95% (95% CI, 93–97%) (I^2 , 78.1%) when internal and external validation studies were included.

在meta分析中，尽管超声操作者的专业知识有很大差异，简单原则用于卵巢癌的诊断表现良好，汇总敏感性为93%(95%可信区间,90-96%)(I^2 32.1%)和汇总特异性为95%(95%可信区间,93 - 97%)(I^2 78.1%)包括内部和外部验证研究。

- The sensitivity and overall accuracy were lower in premenopausal women than in postmenopausal women.

跟绝经后的妇女相比，绝经前妇女的敏感性和整体准确性较低。

- When the rules are applicable, the sensitivity of simple rules increases and the specificity decreases with the increasing prevalence of malignancy in the study population.

当原则适用时，随着人口恶性肿瘤发病率的增加，简单原则的敏感性增加，特异性降低。

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Limitations 不足

- Heterogeneity between studies caused by diversity in study quality, nonconformity in study reporting, differences in study population characteristics.
研究质量的差异，研究报告的不一致，研究人群的特征差异造成了研究之间的异质性。
Not all studies were clear on the exclusion of pregnant women who were not included in any of the original IOTA studies.
并不是所有的研究都明确排除孕妇，但孕妇排除在任何原始的IOTA研究之外。
The prevalence of malignancy ranged from 10% to 44% across the studies.
不同研究之间恶性肿瘤的患病率从10%到44%。
- Diversity in study sizes, ranging from 103 to 1938 women.
研究样本的大小，从103名到1938名妇女。

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Conclusions

- The simple rules protocol could be used in 76–89% of tumors and is an accurate test for the diagnosis of ovarian cancer.
简单原则方案可用于76 - 89%的肿瘤,是一种准确诊断卵巢癌的检查。
- Assessment by an ultrasound expert is required when the protocol cannot be applied.
不适用此方案的情况下,需要通过超声专家评估。

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Discussion points 讨论要点

- Do we need more consensus on how to define expert and non-expert ultrasound operators?
我们是否需要更多的共识定义专家及非专家的超声人员？
- What is the best strategy for tumors that cannot be classified by the simple rules protocol?
对于不能被简单原则分类的肿瘤什么是最好的策略？
- Based on this meta-analysis, do we need further validation for the simple rules protocol?
基于**meta**分析，我们需要进一步验证简单原则的方案吗？
- How to manage tumors in pregnant women, who are not included in any of the IOTA original studies?
如何管理肿瘤孕妇，而她们是不包含在任何IOTA的原始研究中的。