

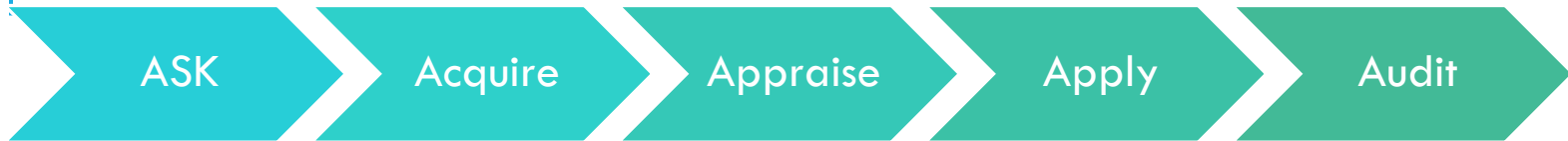
EVIDENCE BASED MEDICINE

三軍總醫院 麻醉科部

成員：曾韋程 黃_王念慈 吳少筠

2017/05/11

STEPS OF EBM



- Formulate an answerable question
- Tracking down the best Evidence
- Critically Appraise Evidence
- Apply to your patient
- Evaluation your performance

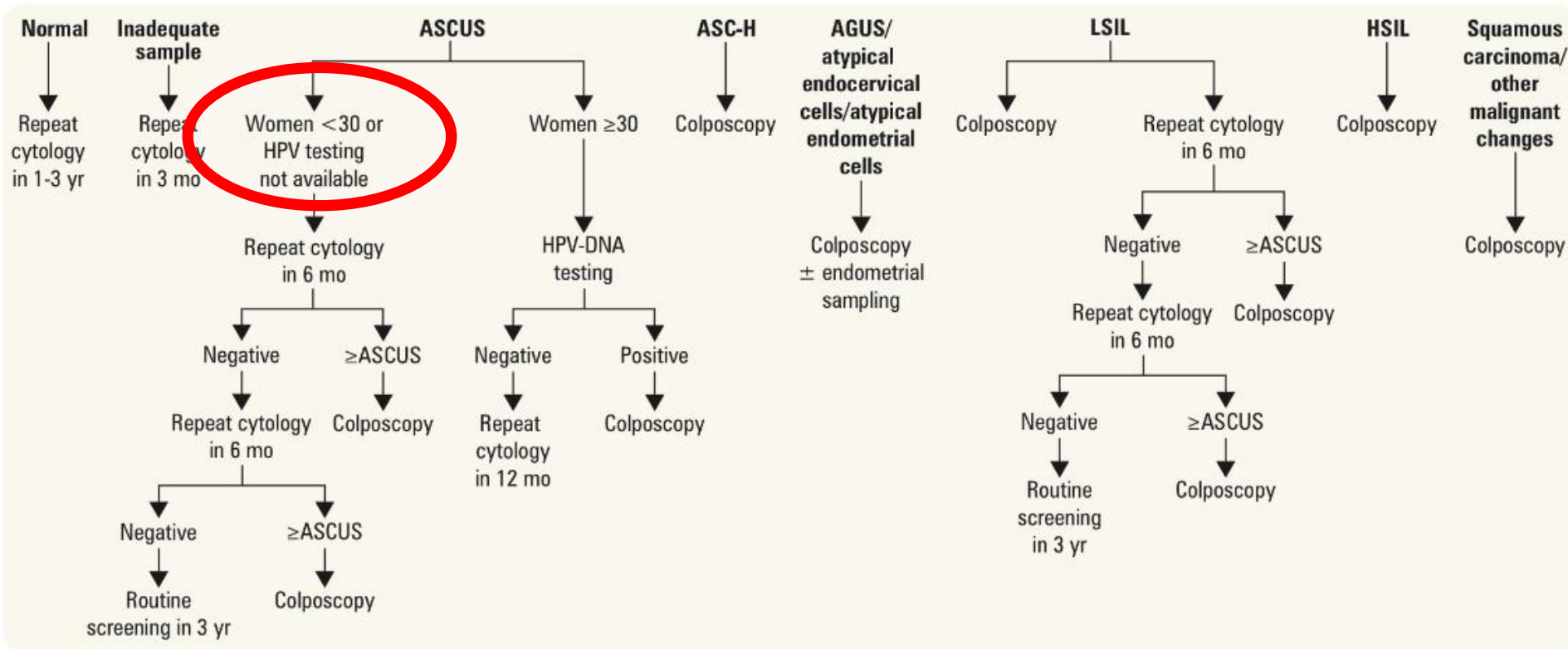
CLINICAL SCENARIO

- 54歲母親因為子宮頸癌過世，姐姐已婚25歲及妹妹未婚16歲至婦產科要求做子宮頸抹片檢查
- 無性行為的妹妹施打價數愈高的子宮頸癌疫苗是否對子宮頸癌的預防愈有效？
- 有性行為的姐姐除了自費做子宮頸癌抹片檢查外是否有其他檢查方式可預防子宮頸癌的發生率？

CONSIDER THE PROBLEM

- 價數愈高的子宮頸癌疫苗對子宮頸癌預防愈有效？
- 有其他更優於抹片的檢查方式來做子宮頸癌的篩檢？

CERVICAL CANCER



PICO1.

問題:有過性行為的女性除了子宮頸抹片檢查還有沒有其他檢查方式偵測子宮頸病變?

Patient	25歲有過性行為女性
Intervention	只作抹片檢查
Comparison	抹片檢查+其他診斷方式
Outcome	子宮頸病變診斷敏感度

Type of question: 治療/預防型 傷害型 診斷型 預後型問題

最適合回答此問題的研究設計為:系統性回顧 (Systematic review)

PICO-2.

問題:無性行為女性是否施打價數愈高的子宮頸癌疫苗愈可降低子宮頸癌的發生率?

Patient	無性行為女性
Intervention	施打兩價、四價的子宮頸癌疫苗
Comparison	施打最新九價的子宮頸癌疫苗
Outcome	子宮頸癌發生率

問題類型:此為治療/預防型傷害型診斷型預後型問題
最適合回答此問題的研究設計為:系統性回顧 (Systematic review)

Article types
Clinical Trial
Review
Customize ...

Text availability
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Free full text
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10 years
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Species
Humans
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Search Tip

Sort by **Best Match** to display results from highest to lowest relevance to your search terms.

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Results by year



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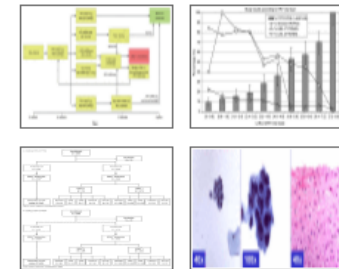
Search results

Items: 1 to 20 of 3410 Selected: 1

<< First < Prev Page 1 of 171 Next > Last >>

- [Human papillomavirus association is the most important predictor for surgically treated patients with oropharyngeal cancer.](#)
Wagner S, Wittekindt C, Sharma SJ, Wuerdemann N, Jüttner T, Reuschenbach M, Prigge ES, von Knebel Doeberitz M, Gattenlöhner S, Burkhardt E, Pons-Kühnemann J, Klusmann JP.
Br J Cancer. 2017 May 4. doi: 10.1038/bjc.2017.132. [Epub ahead of print]
PMID: 28472822
[Similar articles](#)
- [\[Sorting role of p16\(INK4a\)/Ki-67 double immunostaining in the cervical cytology specimens of ASCUS and LSIL cases\].](#)
Yu J, Zhu HT, Zhao JJ, Su JZ, Xia YD.
Zhonghua Bing Li Xue Za Zhi. 2017 May 8;46(5):323-326. doi: 10.3760/cma.j.issn.0529-5807.2017.05.008. Chinese.
PMID: 28468038
[Similar articles](#)
- [Pooled analysis on the necessity of random 4-quadrant cervical biopsies and endocervical curettage in women with positive screening but negative colposcopy.](#)
Hu SY, Zhang WH, Li SM, Li N, Huang MN, Pan QJ, Zhang X, Han Y, Zhao FH, Chen W, Qiao YL.
Medicine (Baltimore). 2017 Apr;96(17):e6689. doi: 10.1097/MD.0000000000006689.
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- [Diagnostic Value of the CareTM HPV Test in Screening for Cervical Intraepithelial Neoplasia Grade 2 or Worse](#)
Karimi Zarchi M, Heydari E, Tabatabaie A, Moghimi M, Kooti W.
Asian Pac J Cancer Prev. 2017 Mar 1;18(3):687-693.
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Sensitivity of APTIMA HPV E6/E7 mRNA test in comparison with hybrid capture [J Med Virol. 2016]

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ORIGINAL ARTICLE

Year : 2016 | Volume : 12 | Issue : 1 | Page : 283-289

Diagnostic value of combination of HPV testing and cytology as compared to isolated cytology in screening cervical cancer: A meta-analysis

[Tong Li](#), [Yan Li](#), [Guo-Xian Yang](#), [Peng Shi](#), [Xiao-Ying Sun](#), [Yu Yang](#), [Ying-Ying Li](#), [Yang Liu](#)

Department of Gynecology and Obstetrics, Central Hospital Affiliated to Shenyang Medical College, Shenyang, China

Date of Web Publication

13-Apr-2016

CASP

10 questions to help you make sense of a review

How to use this appraisal tool

Three broad issues need to be considered when appraising the report of a systematic review:

- **Are the results of the review valid?** (Section A)
- **What are the results?** (Section B)
- **Will the results help locally?** (Section C)

The 10 questions on the following pages are designed to help you think about these issues systematically.



1. DID THE REVIEW ADDRESS A CLEARLY FOCUSED QUESTION?

Objectives: The objective of this study was to assess the diagnostic value of combination of human papillomavirus (HPV) testing and cytology as compared to isolated cytology in screening cervical cancer

P: woman

I: cytology

C: isolated or combined

O: screen for cervical cancer



2. DID THE AUTHORS LOOK FOR THE RIGHT TYPE OF PAPERS?

Data sources

The publication year ranged from 2003 to 2012. Of the eight articles, **two studies were randomized controlled trial (RCT) and six articles were cross-sectional study.**

The region of these studies included France, America, Canada, Italy, Brazil, etc., The source of subjects was mainly conventional census.



3. DO YOU THINK THE IMPORTANT, RELEVANT STUDIES WERE INCLUDED?

- PubMed and Embase (Embase).

- The keyword

- ("cervical cancer" or "cervical neoplas

- ("Pap test" or "Pap

- ("TCT" or "Thinprep" or "cytological tech

- ("HPV" or "human

- The deadline for the search was September 30, 2014.



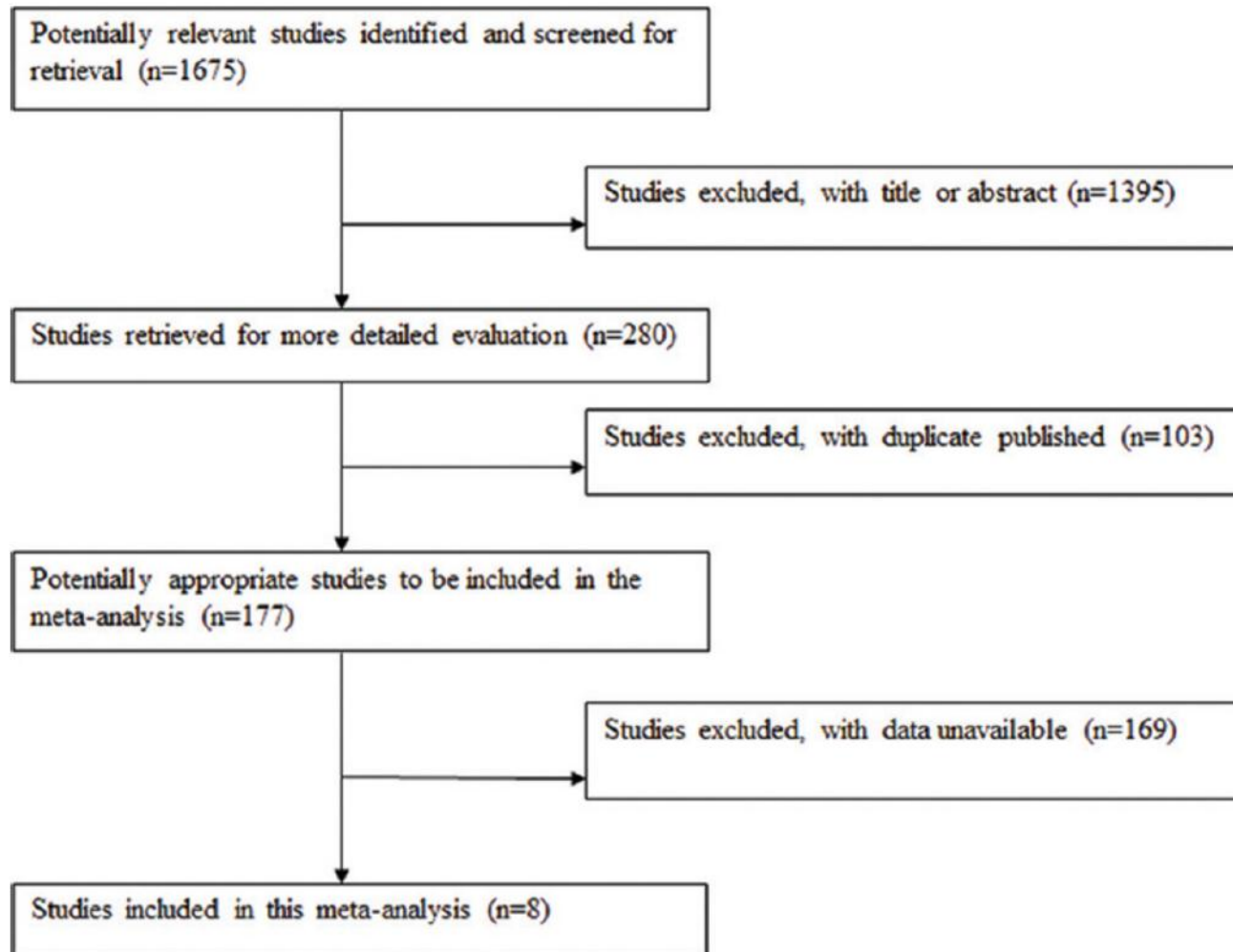
er" or "Carcinoma of cervix"

smear")

l Cytology Test" or "cytology"

METHODS

Figure 1: Search results and process of selecting studies of the study



4. DID THE REVIEW'S AUTHORS DO ENOUGH TO ASSESS THE QUALITY OF THE INCLUDED STUDIES?

Table 3: Quality assessment of the included articles

Studies												Total (/14)			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Coste <i>et al.</i>	+												-	+	11
Garcia <i>et al.</i>	+												+	+	12
Kitchener <i>et al.</i>	+												+	+	12
Rijkaart <i>et al.</i>	+												+	+	12
Ronco <i>et al.</i>	+												-	+	11
Ratnam <i>et al.</i>	+												+	+	12
Pereira <i>et al.</i>	+												+	+	13
Kumar <i>et al.</i>	+	+	+	+	+	+	+	+	+	+	+	+	+	0	13



QUADAS=Quality Assessment of Diagnostic Accuracy Studies, + = Yes, - = No, 0=Not clear

5. IF THE RESULTS OF THE REVIEW HAVE BEEN COMBINED, WAS IT REASONABLE TO DO SO?

Statistical analyses

Meta-DiSc (Version 1.4) was used to calculate summary estimates such as sensitivity, specificity, likelihood ratio (LR), diagnostic odds ratio (DOR), 95% confidence intervals (CI), and summary receiver operating characteristic (SROC) curves. The I^2 test was utilized to assess the heterogeneity of the studies. A Q statistic (Q statistic) and/or $I^2 > 50%$ were considered to indicate heterogeneity. If $I^2 > 50%$, a random-effects Simonian–Laird was performed to calculate the pooled effect, otherwise a fixed effect model of Mantel–Haenszel would be used.^[16] A two-sample Z-test was conducted to evaluate the differences between the two diagnostic modalities.^[17]



analysis. The effect index, LR, diagnostic odds ratio, receiver operating characteristic (ROC) curve, and the I^2 test were used. A P - value < 0.05 was considered statistically significant. Simonian–Laird was used to calculate the pooled effect, otherwise a fixed effect model of Mantel–

6. WHAT ARE THE OVERALL RESULTS OF THE REVIEW?

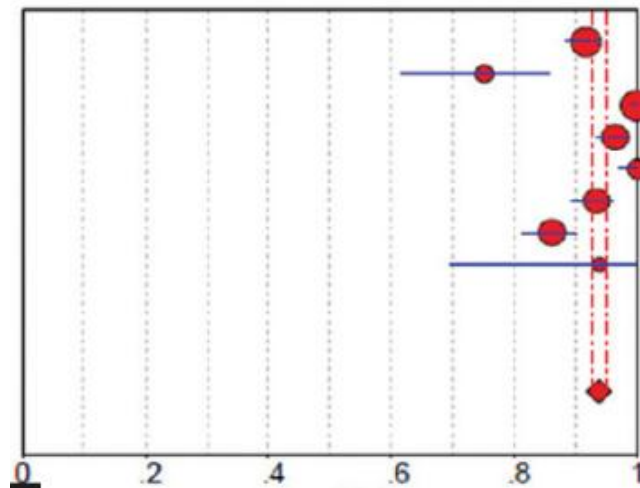


Table 4: Pairwise comparison between cytology method and combination of HPV and cytology method

Diagnosis index	Cytology group	HPV and cytology group	Z value	P
Sensitivity	0.743 (95% CI: 0.716-0.768)	0.937 (95% CI: 0.925-0.948)	13.375	<0.01
Specificity	0.951 (95% CI: 0.949-0.953)	0.858 (95% CI: 0.855-0.860)	56.935	<0.01
Positive LR	6.408 (95% CI: 2.322-17.683)	3.924 (95% CI: 2.037-7.559)	0.597	0.56
Negative LR	0.226 (95% CI: 0.112-0.460)	0.083 (95% CI: 0.033-0.210)	1.436	0.15
DOR	30.897 (95% CI: 7.170-133.150)	51.563 (95% CI: 14.682-181.090)	0.388	0.70
AUC	0.855 (95% CI: 0.842-0.868)	0.884 (95% CI: 0.690-1.000)	0.294	0.77
Cochran-Q	0.786 (95% CI: 0.774-0.798)	0.876 (95% CI: 0.678-1.000)	0.893	0.37

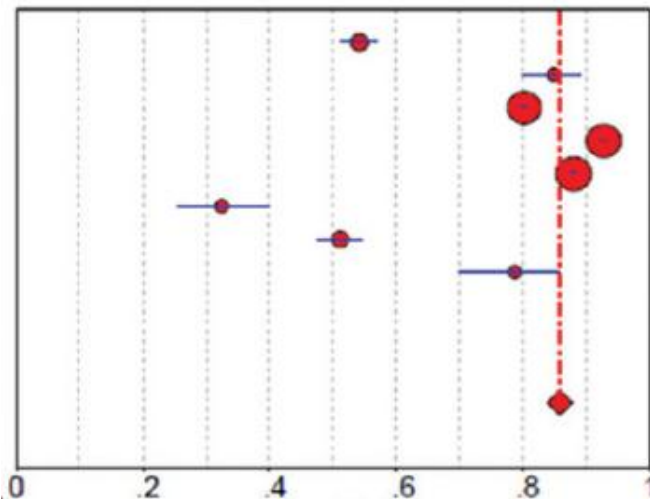
LR=Likelihood ratio, DOR=Diagnostic odds ratio, AUC=Area under a receiver operating characteristic curve, CI=Confidence interval, HPV=Human papillomavirus

7. HOW PRECISE ARE THE RESULTS?



	Sensitivity (95% CI)	
Coste. Joel	0.92	(0.88 - 0.94)
Garcia. Francisco	0.75	(0.62 - 0.86)
Kitchener. Henry C	1.00	(0.99 - 1.00)
Rijkaart. Dorien C	0.96	(0.93 - 0.98)
Ronco. Guglielmo	1.00	(0.97 - 1.00)
Ratnam. Samuel	0.93	(0.89 - 0.96)
Pereira. Sonia Maria Mirand	0.86	(0.81 - 0.90)
Kumar. Kamlesh	0.94	(0.70 - 1.00)

Pooled Sensitivity = 0.94 (0.92 to 0.95)
 Chi-square = 112.92; df = 7 (p = 0.0000)
 Inconsistency (I-square) = 93.8 %



	Specificity (95% CI)	
Coste. Joel	0.54	(0.51 - 0.57)
Garcia. Francisco	0.85	(0.80 - 0.89)
Kitchener. Henry C	0.80	(0.80 - 0.81)
Rijkaart. Dorien C	0.93	(0.92 - 0.93)
Ronco. Guglielmo	0.88	(0.87 - 0.88)
Ratnam. Samuel	0.32	(0.25 - 0.40)
Pereira. Sonia Maria Mirand	0.51	(0.48 - 0.55)
Kumar. Kamlesh	0.79	(0.70 - 0.86)

Pooled Specificity = 0.86 (0.86 to 0.86)
 Chi-square = 3010.86; df = 7 (p = 0.0000)
 Inconsistency (I-square) = 99.8 %

8. CAN THE RESULTS BE APPLIED TO THE LOCAL POPULATION?

Table 1: Characteristics of the eligible

Author	Publication year	Study year	Age (years)	Study types	Study location	Testing items	TP	FP	FN	TN
Coste <i>et al.</i>	2003	1999.9.1-2000.5.30	33.3±11.1	Cross-sectional study	France	HPV+cytology	368	622	34	733
						cytology	75	142	27	1510
Garcia <i>et al.</i>	2003	1999.1-2000.6	36.9 (18-67)	Cross-sectional study	United States, Mexico, Peru	HPV+cytology	42	42	14	235
						cytology	55	38	46	195
Kitchener <i>et al.</i>	2009	2001.6-2003.9	20-64	RCT	UK	HPV+cytology	452	3567	1	14366
						cytology	133	653	2	5336
Rijkaart <i>et al.</i>	2012	1999.1-2002.9	29-56	RCT	Netherlands	HPV+cytology	257	1478	10	18552
						cytology	193	513	22	19351
Ronco <i>et al.</i>	2006	2002-2003	25-34	Cross-sectional study	Italy	HPV+cytology	117	2660	0	19335
						cytology	84	771	5	20196
Ratnam <i>et al.</i>	2000	1996.9-1998.8	30 (18-69)	Cross-sectional study	Canada	HPV+cytology	222	115	16	55
						cytology	76	86	93	153
Pereira <i>et al.</i>	2006	2002.1-2002.12	33.5 (16-73)	Cross-sectional study	Brazil	HPV+cytology	239	397	39	415
						cytology	195	222	83	580
Kumar <i>et al.</i>	2007	2003.1-2004.12	NA	Cross-sectional study	India	HPV+cytology	15	25	1	92
						cytology	15	18	8	86

RCT=Randomized control trial, TP=True positive, FN=False negative, FP=False positive, TN=True negative, NA=Not applicable, HPV=Human papillomavirus. Age (years): Median (range); Mean±standard deviation (SD)

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Kitchener <i>et al.</i>	2009	2001.6-2003.9	20-64	RCT	UK	HPV+cytology cytology	452 133	3567 653	1 2	14366 5336
Rijkaart <i>et al.</i>	2012	1999.1-2002.9	29-56	RCT	Netherlands	HPV+cytology cytology	257 193	1478 513	10 22	18552 19351
Ronco <i>et al.</i>	2006	2002-2003	25-34	Cross-sectional study	Italy	HPV+cytology cytology	117 84	2660 771	0 5	19335 20196
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Age (years): Median (range); Mean±standard deviation (SD)

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Author	Year	Study period	Age (years)	Study design	Study location	Testing items	TP	FP	FN	TN
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文章內容對象非東方人種
年齡區間類似
應可引用

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Age (years): Median (range); Mean±standard deviation (SD)

9. WERE ALL IMPORTANT OUTCOMES CONSIDERED?

未將Cost-effects納入考量
未將腫瘤stages納入考量

10. ARE THE BENEFITS WORTH THE HARMS AND COSTS?



STEPS OF EBM

- Asking answerable Clinical Question
- Tracking down the best Evidence
- Critically Appraise Evidence
- **Apply to your patient**
- Evaluation your performance

ANSWERS

- 小姐你好，根據目前最新的實證醫學，採用 Combination 檢查方式可以提升診斷率，雖然診斷特異度可能較單純做抹片檢查較低，但是可以符合蘇小姐的期待擁有較高的敏感度。

