

**ECIBC**

*the* **EUROPEAN COMMISSION INITIATIVE**  
on **BREAST CANCER**

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***Il sottoscritto Paolo Giorgi Rossi.***

*ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,*

dichiara

*che negli ultimi due anni ha avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:*

*- Come PI di uno studio indipendente, finanziato dal Ministero della Salute ho condotto trattative con Roche, Hologic, Becton Dickinson, per ottenere reagenti a prezzo ridotto o gratis.*

# Origin of the Initiative

Because of "substantial and persistent **inequalities** in breast cancer **incidence, mortality,** prevalence and survival existing within and between Countries"

2008: the Council of the EU asks the **European Commission** to initiate **ECIBC**



# What is ECIBC?

70 experts in 2 working groups



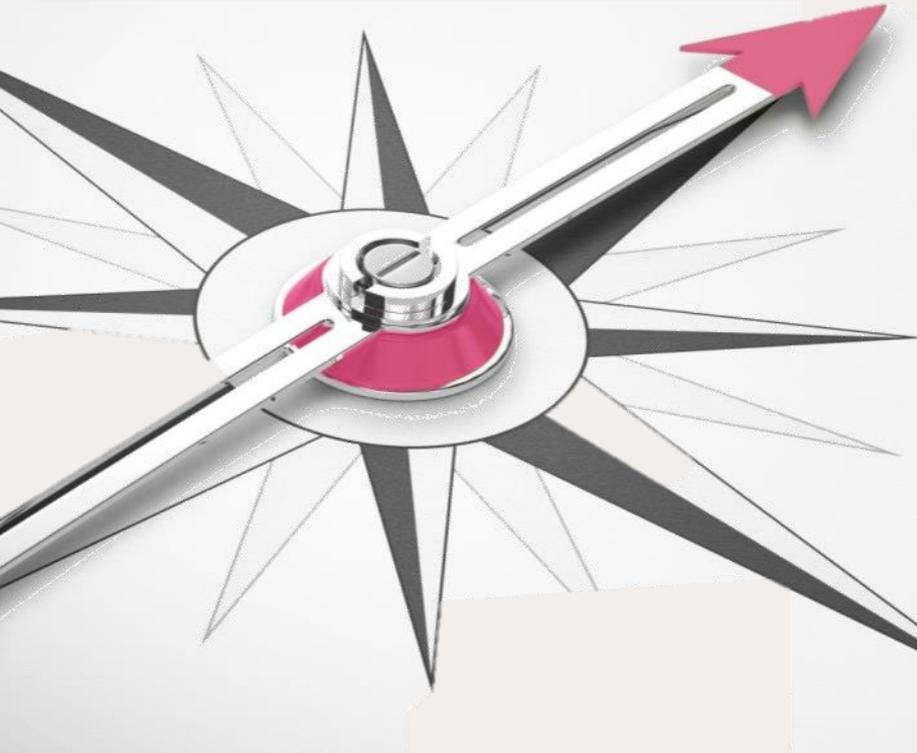
Surveys, papers, bilaterals, events

**35 Countries** (EU28+Island, FYROM, Montenegro, Norway, Serbia, Switzerland and Turkey)

**113 million** women potentially involved

Coordinated by the **European Commission**

# 1. *European Breast Guidelines*



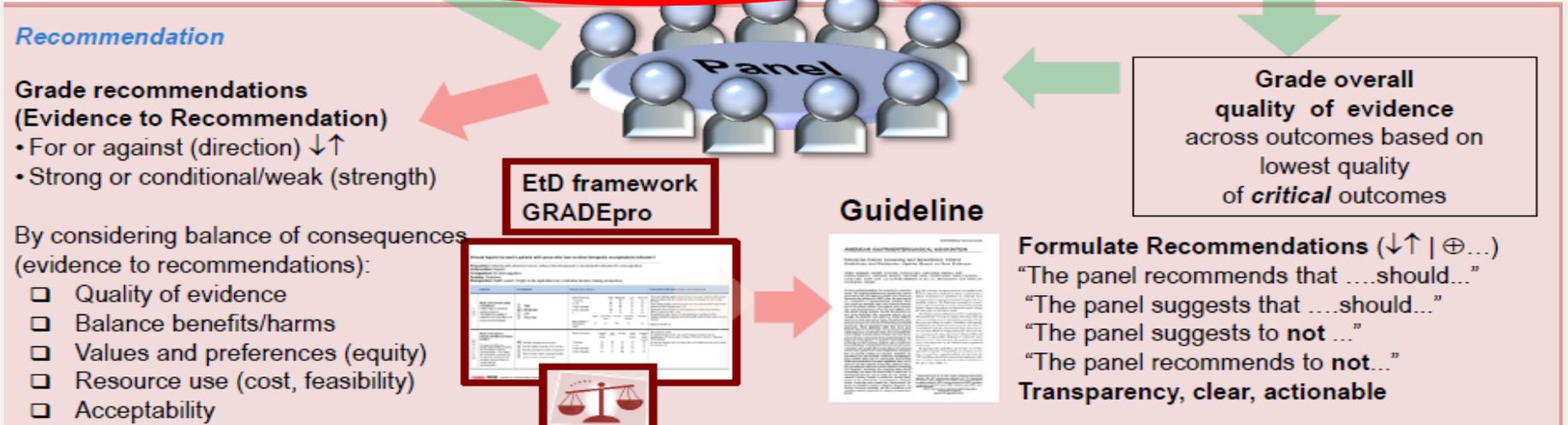
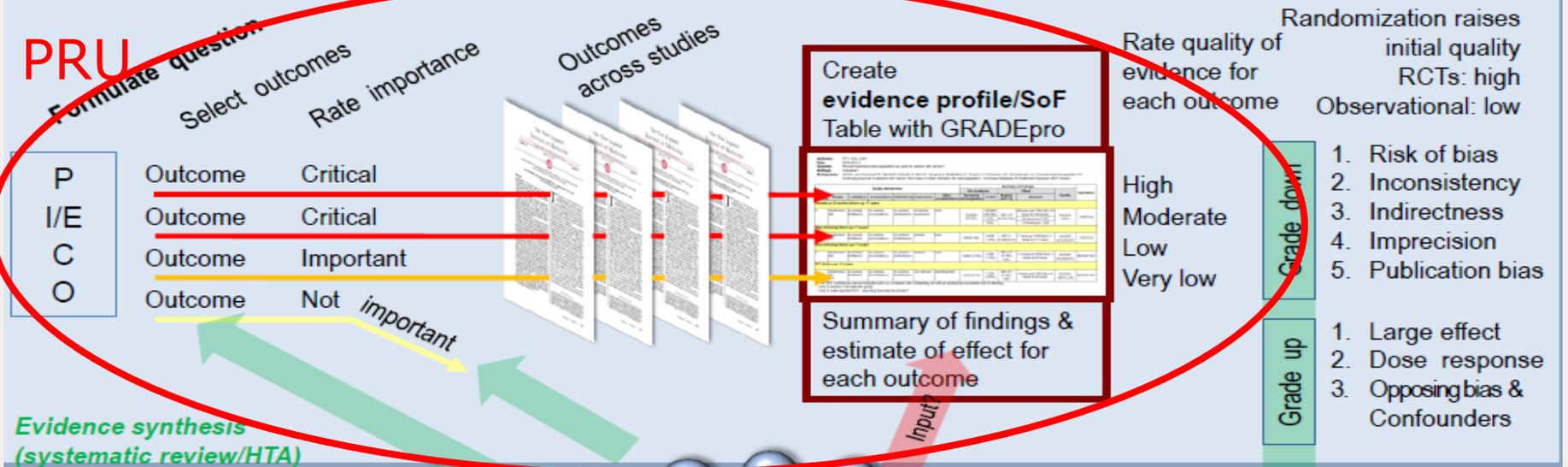
About **90 PICO**s on  
**screening and diagnosis**

**Evidence based**, updated as new  
evidence and priorities emerge

Developed by the **GDG** using **GRADE  
Evidence to Decision Framework**

**Web based** and specifically **tailored** for  
each of three profiles: citizens and  
patients, health professionals, and  
policy makers

# PRU



# Building picos from clinical questions:

## Cyto/histo sampling

**Population:** women with suspicious imaging after Mx, US, eventually tomo and clinical assessment (possible subpopulations: mass, asymmetry, distortion, calcifications)

**Intervention:** Core Needle Biopsy

**Control:** FNAC

**Outcomes:** breast cancer mortality (modelled from false negative), false positive, test related outcomes (bleeding, pain,...), spread of cancer.



# Building picos from clinical questions

Initial formulation of the four PICOs for the literature search	mass lesion or asymmetric density	architectural distortion	microcalcification
NCB vs FNAC (vacuum assisted or not)	PICO 6a	PICO 6b	PICO 7b
Stereotactic NCB vs US-guided NCB (vacuum assisted or not)	Not assessed	Not assessed	PICO 7a

Final formulation of two PICOs for recommendations	mass lesion or asymmetric density	architectural distortion	microcalcification
NCB vs FNAC (vacuum assisted or not)	PICO 6		
Stereotactic NCB vs US-guided NCB (vacuum assisted or not)	Not assessed	Not assessed	PICO 7

# European guidelines on breast cancer screening and diagnosis

The recommendations included in the guidelines are developed starting from relevant "healthcare questions" that below are grouped into main topics. Each topic includes one or more recommendations presented in a question and answer format.

## Breast cancer screening

Screening ages and frequencies

Tomosynthesis use in screening

Additional tests for dense breast screening

How to invite and inform women about screening

How to organise breast cancer screening programmes

## Breast cancer diagnosis

How to inform women about their results

Further assessment after the mammogram

Staging of breast cancer

Surgical planning

Towards the treatment of invasive breast cancer

## PAGE CONTENTS

Test for women recalled due to suspicious lesions

How to obtain a sample from a suspicious breast lesion

Type of guidance for needle core biopsy in individuals with breast calcifications

Communication training for the staff

# How to obtain a sample from a suspicious breast lesion

In women with suspicious breast lesions (including mass lesions, asymmetric breast density, calcifications and/or architectural distortions) in mammography, the ECIBC's Guidelines Development Group (GDG) recommends **needle core biopsy over fine needle aspiration cytology to diagnose breast cancer** (strong recommendation, moderate certainty of the evidence).

## MORE INFORMATION

### **Details for professionals**

[Core biopsy vs. aspiration cytology](#)

### **Summary information for women**

[What you need to know](#)

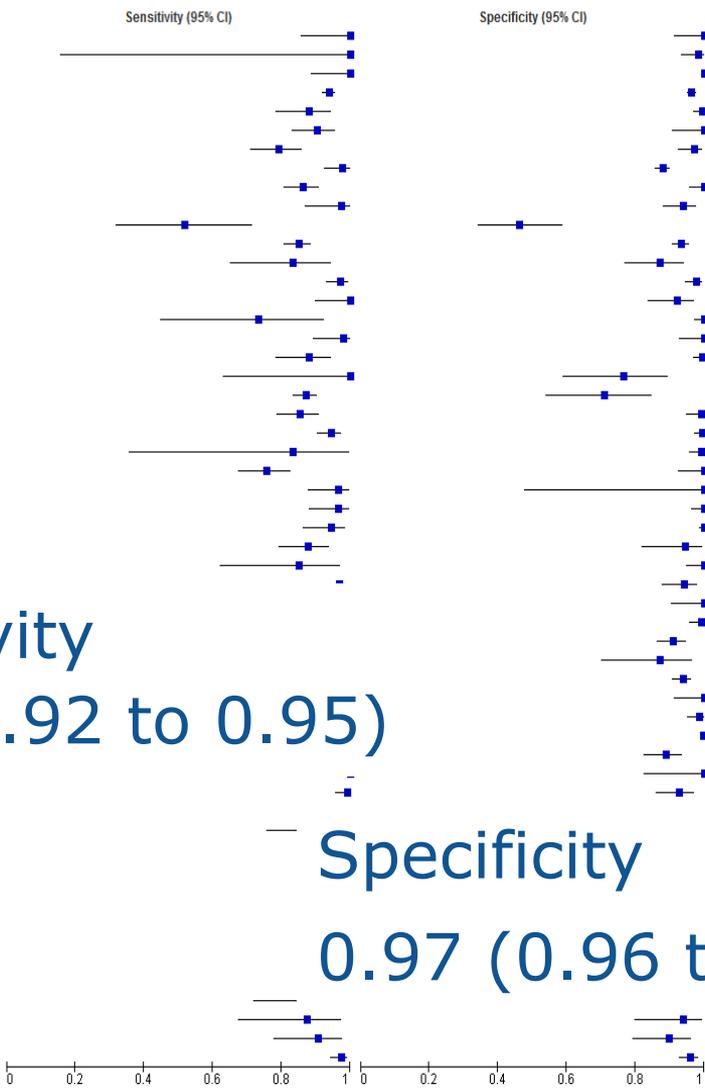
# Fine needle aspiration cytology (FNAC) versus reference standard.

55 datasets, 19.878 participants.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Anwar 2013	24	0	0	40	1.00 [0.86, 1.00]	1.00 [0.91, 1.00]
Apesteguia 1997	2	2	0	107	1.00 [0.16, 1.00]	0.98 [0.94, 1.00]
Baykara 2013	31	0	0	504	1.00 [0.89, 1.00]	1.00 [0.99, 1.00]
Brancato 2012	710	43	47	1150	0.94 [0.92, 0.95]	0.96 [0.95, 0.97]
Chen 2010	66	1	9	176	0.88 [0.78, 0.94]	0.99 [0.97, 1.00]
Dennison 2003	95	0	10	38	0.90 [0.83, 0.95]	1.00 [0.91, 1.00]
Drew 1999	102	4	27	130	0.79 [0.71, 0.86]	0.97 [0.93, 0.99]
Farshid 2008	91	120	2	880	0.98 [0.92, 1.00]	0.88 [0.86, 0.90]
Gao 2005	169	0	27	85	0.86 [0.81, 0.91]	1.00 [0.96, 1.00]
Gent 1986	39	7	1	109	0.97 [0.87, 1.00]	0.94 [0.88, 0.98]
Harvey 1996	14	37	13	32	0.52 [0.32, 0.71]	0.46 [0.34, 0.59]
Huang 2003	305	31	54	436	0.85 [0.81, 0.88]	0.93 [0.91, 0.95]
Iqbal 2015	25	9	5	61	0.83 [0.65, 0.94]	0.87 [0.77, 0.94]
Ishikawa 2007	138	4	4	178	0.97 [0.93, 0.99]	0.98 [0.94, 0.99]
Islam 2015	34	6	0	70	1.00 [0.90, 1.00]	0.92 [0.84, 0.97]
Janet 2010	11	0	4	135	0.73 [0.45, 0.92]	1.00 [0.97, 1.00]
Jia 1986	49	0	1	50	0.98 [0.89, 1.00]	1.00 [0.93, 1.00]
Jiang 2008	66	1	9	176	0.88 [0.78, 0.94]	0.99 [0.97, 1.00]
Kanchanabat 2000	8	8	0	26	1.00 [0.63, 1.00]	0.76 [0.59, 0.89]
Leifland 2003	353	11	52	27	0.87 [0.84, 0.90]	0.71 [0.54, 0.85]
Li 2008	129	1	22	108	0.85 [0.79, 0.91]	0.99 [0.95, 1.00]
Lu 2010	205	1	12	194	0.94 [0.91, 0.97]	0.99 [0.97, 1.00]
Lui 2000	5	1	1	125	0.83 [0.36, 1.00]	0.99 [0.96, 1.00]
Lui 2010	102	0	33	48	0.76 [0.67, 0.83]	1.00 [0.93, 1.00]
Lumachi 1999	55	0	2	5	0.96 [0.88, 1.00]	1.00 [0.48, 1.00]
Ma 2010	56	0	2	99	0.97 [0.88, 1.00]	1.00 [0.96, 1.00]
Ma 2010b	68	0	4	291	0.94 [0.86, 0.98]	1.00 [0.99, 1.00]
Manheimer 1977	79	2	11	35	0.88 [0.79, 0.94]	0.95 [0.82, 0.99]
Masood 1991	17	0	3	71	0.85 [0.62, 0.97]	1.00 [0.95, 1.00]
Moschetta 2014	61	6	2	--	--	--
Nagar 2012	13	0	0	--	--	--
Okamoto 1998	5	1	1	--	--	--
Pisano 2001	59	18	17	--	--	--
Rubin 1997	34	4	0	--	--	--
Sauer 2003	360	21	47	--	--	--
Singh 2013	19	0	2	--	--	--
Tang 1987	144	2	13	--	--	--
Tao 2004	655	5	14	2	--	--
Usman 2015	49	16	8	--	--	--
Walker 1998	91	0	0	19	1.00 [0.90, 1.00]	1.00 [0.92, 1.00]
Wanebo 1983	123	8	1	102	0.99 [0.96, 1.00]	0.93 [0.86, 0.97]
Wang 1981	442	43	60	479	0.88 [0.85, 0.91]	0.92 [0.89, 0.94]
Wang 1995	25	0	2	22	0.93 [0.76, 0.99]	1.00 [0.85, 1.00]
Wang 2005	99	5	0	207	1.00 [0.96, 1.00]	0.98 [0.95, 0.99]
Wang 2010	110	2	7	55	0.94 [0.88, 0.98]	0.96 [0.88, 1.00]
Wang 2010b	96	12	4	498	0.96 [0.90, 0.99]	0.98 [0.96, 0.99]
Wei 2007	91	4	2	78	0.98 [0.92, 1.00]	0.95 [0.88, 0.99]
Yang 2010	79	0	4	259	0.95 [0.88, 0.99]	1.00 [0.99, 1.00]
Yu 2006	1620	116	33	359	0.98 [0.97, 0.99]	0.76 [0.71, 0.79]
Zeng 1999	94	1	2	66	0.98 [0.93, 1.00]	0.99 [0.92, 1.00]
Zhan 2007	32	2	0	44	1.00 [0.89, 1.00]	0.96 [0.85, 0.99]
Zhang 1996	21	1	2	40	0.91 [0.72, 0.99]	0.98 [0.87, 1.00]
Zhang 2006	21	2	3	31	0.88 [0.68, 0.97]	0.94 [0.80, 0.99]
Zhang 2008	39	6	4	53	0.91 [0.78, 0.97]	0.90 [0.79, 0.96]
Zhao 2009	218	10	6	241	0.97 [0.94, 0.99]	0.96 [0.93, 0.98]

Sensitivity  
0.94 (0.92 to 0.95)

Specificity  
0.97 (0.96 to 0.98)

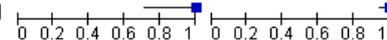


**Needle core biopsy (NCB) versus reference standard.**  
 45 datasets,  
 36.563 participants.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Abdasaleh 2003	104	1	16	18	0.87 [0.79, 0.92]	0.95 [0.74, 1.00]
Ahmed 2010	21	2	2	53	0.91 [0.72, 0.99]	0.96 [0.87, 1.00]
Arazi 2013	10	6	3	90	0.77 [0.46, 0.95]	0.94 [0.87, 0.98]
Brancato 2012	673	69	18	523	0.97 [0.96, 0.98]	0.88 [0.85, 0.91]
Britton 1997	94	2	7	95	0.93 [0.86, 0.97]	0.98 [0.93, 1.00]
Burbank 1994	14	3	0	88	1.00 [0.77, 1.00]	0.97 [0.91, 0.99]
Caruso 1998	67	0	0	7	1.00 [0.95, 1.00]	1.00 [0.59, 1.00]
Cho 2008	17	0	0	83	1.00 [0.80, 1.00]	1.00 [0.96, 1.00]
Ciatto 2007	1158	207	71	1532	0.94 [0.93, 0.95]	0.88 [0.86, 0.90]
Cipolla 2006	182	11	1	232	0.99 [0.97, 1.00]	0.95 [0.92, 0.98]
Cornelis 2009	73	0	3	97	0.96 [0.89, 0.99]	1.00 [0.96, 1.00]
Crowe 2003	694	14	33	91	0.95 [0.94, 0.97]	0.87 [0.79, 0.93]
Dahlstrom 1996	51	0	1	115	0.98 [0.90, 1.00]	1.00 [0.97, 1.00]
Dillon 2005	1299	120	85	461	0.94 [0.92, 0.95]	0.79 [0.76, 0.83]
Doyle 2005	23	2	0	119	1.00 [0.85, 1.00]	0.98 [0.94, 1.00]
Fajardo 2004	358	31	17	1025	0.95 [0.93, 0.97]	0.97 [0.96, 0.98]
Furhman 1998	295	31	3	852	0.99 [0.97, 1.00]	0.96 [0.95, 0.98]
Hao 2015	9470	709	203	1565	0.98 [0.98, 0.98]	0.69 [0.67, 0.71]
Helbich 1997	100	2	3	105	0.97 [0.92, 0.99]	0.98 [0.93, 1.00]
Ioffe 1998	43	0	4	17	0.91 [0.80, 0.98]	1.00 [0.80, 1.00]
Jackman 2002	11	3	0	17	1.00 [0.72, 1.00]	0.85 [0.62, 0.97]
Keranan 2014	74	0	10	74	0.88 [0.79, 0.94]	1.00 [0.95, 1.00]
Kirshenbaum 2003	117	20	2	253	0.98 [0.94, 1.00]	0.93 [0.89, 0.95]
Latosinsky 2000	85	13	6	246	0.93 [0.86, 0.98]	0.95 [0.92, 0.97]
Lieberman 2000						
Loffe 1998						
Makoske 2000						
Margolin 2001						
Meyer 1999						
Nagar 2012						
Nguyen 1996						
Parker 1994						
Parkin 2010	69	0	0	11	1.00 [0.93, 1.00]	1.00 [0.72, 1.00]
Pfeiderer 2003	5	0	1	8	0.83 [0.36, 1.00]	1.00 [0.63, 1.00]
Pistolesse 2009	116	0	0	117	1.00 [0.97, 1.00]	1.00 [0.97, 1.00]
Povoski 2011	1036	1	8	398	0.99 [0.98, 1.00]	1.00 [0.99, 1.00]
Puglisi 1999	32	2	3	63	0.91 [0.77, 0.98]	0.97 [0.89, 1.00]
Smith 2001b	3	0	2	20	0.60 [0.15, 0.95]	1.00 [0.83, 1.00]
Stolier 1997	30	6	2	170	0.94 [0.79, 0.99]	0.97 [0.93, 0.99]
Toth 2012	17	10	0	18	1.00 [0.80, 1.00]	0.64 [0.44, 0.81]
Welle 2000	36	15	0	122	1.00 [0.90, 1.00]	0.89 [0.83, 0.94]
White 2001	231	31	7	464	0.97 [0.94, 0.99]	0.94 [0.91, 0.96]
Yeoman 1996	55	2	30	64	0.65 [0.54, 0.75]	0.97 [0.89, 1.00]
Zhou 2014	498	305	7	145	0.99 [0.97, 0.99]	0.32 [0.28, 0.37]
Zografos 2008	11	0	0	69	1.00 [0.72, 1.00]	1.00 [0.95, 1.00]

**Sensitivity**  
 0.94 (0.92 to 0.95)

**Specificity**  
 0.97 (0.96 to 0.98)

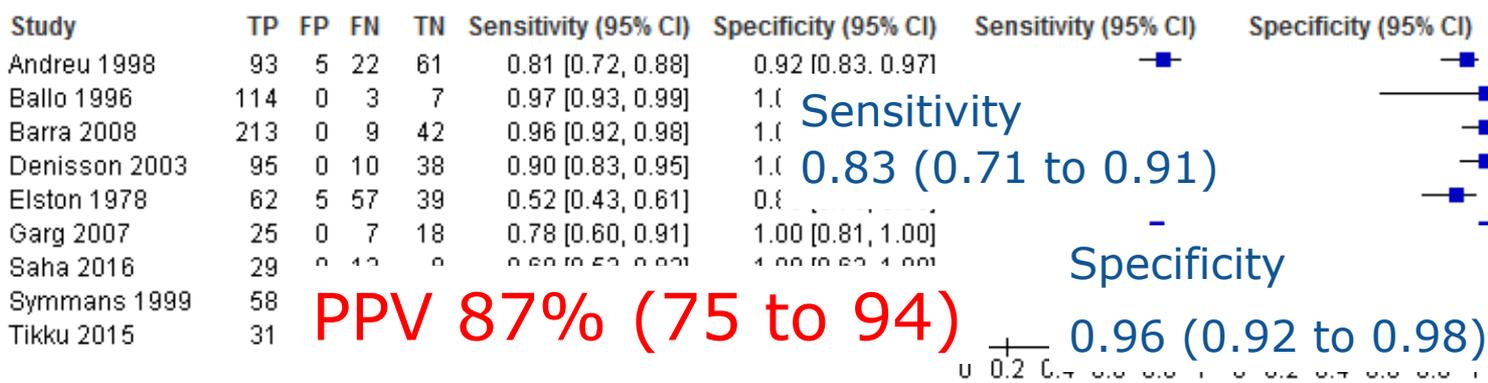


# Fine needle aspiration cytology (FNAC) versus Needle core biopsy (NCB).

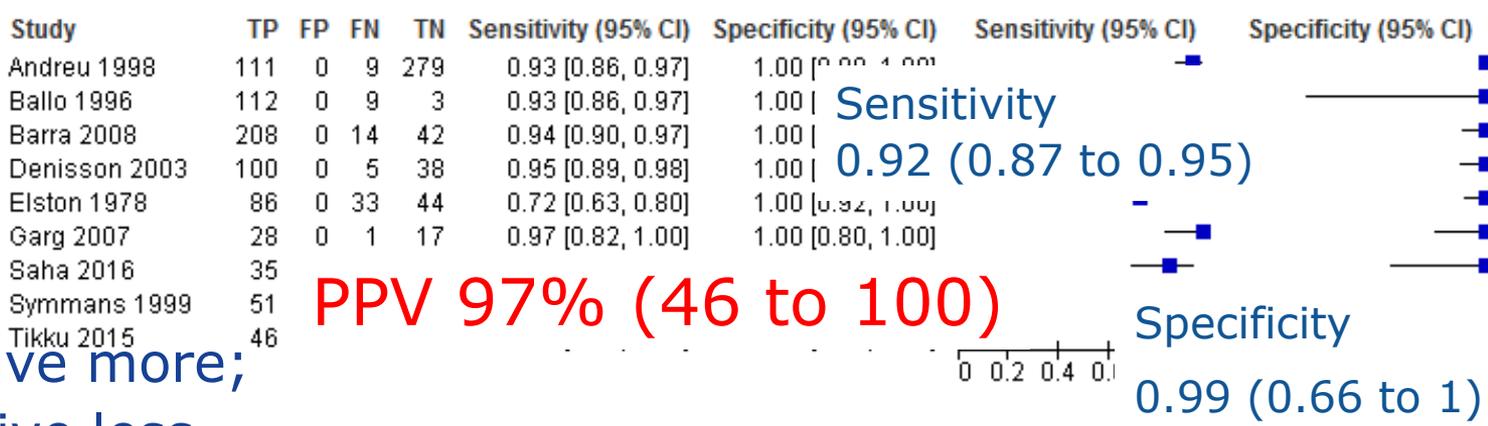
9 datasets, 1498 participants.

31 True Negative more; 19 False Positive less every 1000 tested women (prev. 34%)

## FNAC



## CNB



**Local recurrence:** four retrospective studies found no significant difference between preoperative diagnostic needle core biopsy (863 women) or an excisional biopsy (1022 women). The local recurrence rates varied between 1.1 and 3.7% for the needle core biopsy group and between 2.1 and 10.3% for the excisional biopsy group

Risk of **local and distant recurrence:** an observational study compared recurrence up to 5 years after diagnosis in women who had biopsy and in women who had only surgical assessment, adjusting for all the known prognostic factors (Taxin 1997). The risk was similar in women who received either of the two types of biopsy.

**Adverse events:** the most frequent adverse event is pain although pain leading to test discontinuation is occasional. The absolute incidence of adverse events such as bleeding or infection is low and the incidence of severe complications is less than 1%.

- The certainty of the information for health outcomes is moderate due to uncertainty regarding the management of lesions of undetermined malignancy potential.
- **False negatives** may have additional biopsies but may go undetected for an unknown amount of time.
- **False positive**: all positive biopsies undergo surgery.
- The certainty of the evidence was based on the assumption that there will always be **more desirable health effects** than undesirable ones based on **better typing of breast lesions** with NCB.

# Costs

Study ID	Country (year value)	Test	Average cost per breast lesion case
Hukkinen 2008	Finland (2005)	US-guided FNAC <sup>1</sup>	150 €
		US-guided NCB <sup>1</sup>	176 €
Study ID	Country (year value)	Test	Average cost per biopsy
Vimpeli 2008	Finland (2005, except for the technicians' fees at 2004)	- US-guided FNAB <sup>2</sup>	45 €
		- Palpation guided FNAB <sup>2</sup>	37 €
		- US-guided NCB <sup>2</sup>	83 €
		- Palpation guided NCB <sup>2</sup>	70 €

€: Euros. **US**: ultrasound. **FNAC/B**: fine needle aspiration biopsy. **NCB**: needle core biopsy.

<sup>1</sup>The cost of the initial biopsy was 150 € per lesion for FNAC and 176 € per lesion for CNB. These costs included costs of radiology, pathology and surgery costs of interventions needed for one detected cancer. With the expenses caused by the additional needle biopsies included, the need for surgical biopsies and the unnecessary axillary operations due to false-positive findings corresponding costs per lesion were 294€ with FNAC and 223€ with NCB.

<sup>2</sup>The average biopsy cost per case, regardless the method used to guide the needle to the lesion, were 66 € in the FNAB group and 221 € in the NCB group. All calculations covered the costs of professionals (technicians, radiologists), cytological/ histological analysis of biopsies, radiological and other equipment, disposable supplies, and social security and administrative costs.

## Costs

Two studies conducted in the USA (Masood 2015 and Nagar 2012) reported that biopsy with NCB was more expensive than FNAC.

However, due to the greater number of inconclusive results with FNAC, the initial biopsy with FNAC may require additional biopsies, and surgeries.

# Cost effectiveness

Nº. of studies	Study design	Nº. of women	Incremental costs	Incremental effects	ICER (NCB vs. FNAC)	Quality
Cost per changes in the proportion of pre-surgical malignant diagnoses						
1	Cost-consequences study	572	26 € (2005 value) per biopsy	29% of pre-surgical malignant diagnoses	NCB is more costly and has higher proportion of pre-surgical malignant diagnoses	⊕○○○ VERY LOW*
Cost per changes in the proportion false-positives and false-negatives						
1	Cost-consequences study	688	155 € (2005 value) per biopsy	-8% of false-positives -8% of false-negatives	NCB is more costly false-negative for FNAB 19% and for CNB 11%; false-positive were 9% and 1%, respectively	⊕○○○ VERY LOW*

**ICER:** Incremental cost-effectiveness ratio. **QALY:** Quality adjusted life years. **€:** Euros.

\*Cost-consequence analysis was based on observational data. Both studies were conducted in Finland. The costs, resources used, and cost-effectiveness results may not be applicable to other European settings. The authors did not reported the ICER.

	NCB vs. FNAC
<b>PROBLEM</b>	Yes
<b>ACCURACY OF THE TEST</b>	Accurate
<b>DESIRABLE EFFECTS</b>	Large
<b>UNDESIRABLE EFFECTS</b>	Trivial
<b>CERTAINTY OF EVIDENCE FOR ACCURACY</b>	High
<b>CERTAINTY ABOUT DIRECT EFFECTS</b>	Moderate
<b>CERTAINTY ABOUT MANAGEMENT EFFECTS</b>	Moderate
<b>CERTAINTY ABOUT LINK RESULT AND MANAGEMENT</b>	Moderate
<b>CERTAINTY ABOUT OVERALL EFFECTS</b>	Moderate
<b>VALUES</b>	Probably no important uncertainty or variability
<b>BALANCE OF EFFECTS</b>	Favours the intervention
<b>RESOURCES REQUIRED</b>	Negligible savings and costs
<b>CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES</b>	Low
<b>COST EFFECTIVENESS</b>	Favors the intervention
<b>EQUITY</b>	Varies
<b>ACCEPTABILITY</b>	Yes
<b>FEASIBILITY</b>	Yes
<b>FINAL RECOMMENDATION</b>	Strong in favour of the intervention

# Implications of a *strong* recommendation

- Policy makers: The recommendation can be adopted as a policy in most situations
- Patients: Most people in this situation would want the recommended course of action and only a small proportion would not
- Clinicians: Most patients should receive the recommended course of action
- Screening: we can use participation as proxy of informed decision.

## Implementation considerations

The GDG noted that FNAC may have utility in other medical conditions or contexts (e.g. FNAC of axilla lymph nodes) and as such reinforces that this recommendation applies only to the population addressed in this question.

The GDG noted that there may be resistance to implementation in certain settings where providers are using FNAC over NCB.

Grazie per l'attenzione  
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