ECIBC

the EUROPEAN COMMISSION INITIATIVE on BREAST CANCER

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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

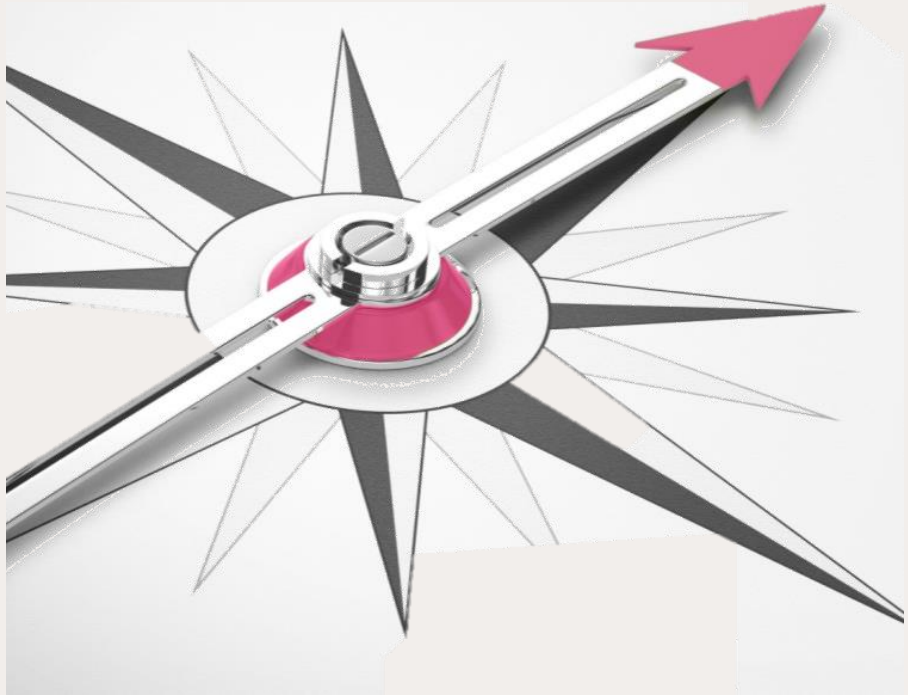
35 Countries (EU28+Island, FYROM, Montenegro, Norway, Serbia, Switzerland and Turkey)

113 million women potentially involved

Coordinated by the **European Commission**

European Commission

Objectives (1)

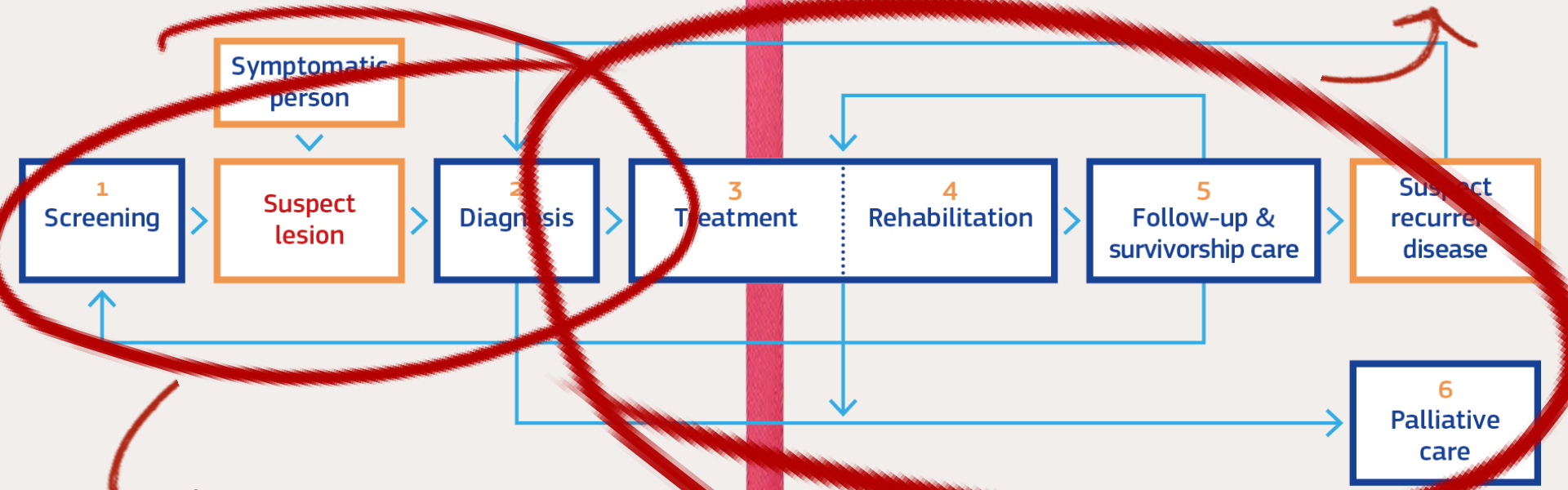


Evidence based Breast Cancer
Guidelines

Objectives (2)

European **Quality Assurance scheme** for breast cancer services

Breast Cancer Guidelines



2. GUIDELINES PLATFORM
FROM TREATMENT TO PALLIATIVE CARE

1. EUROPEAN BREAST CANCER GUIDELINES ON SCREENING AND DIAGNOSIS

European Quality Assurance scheme for Breast Cancer Services: the *European QA scheme*

Addresses **all care processes**

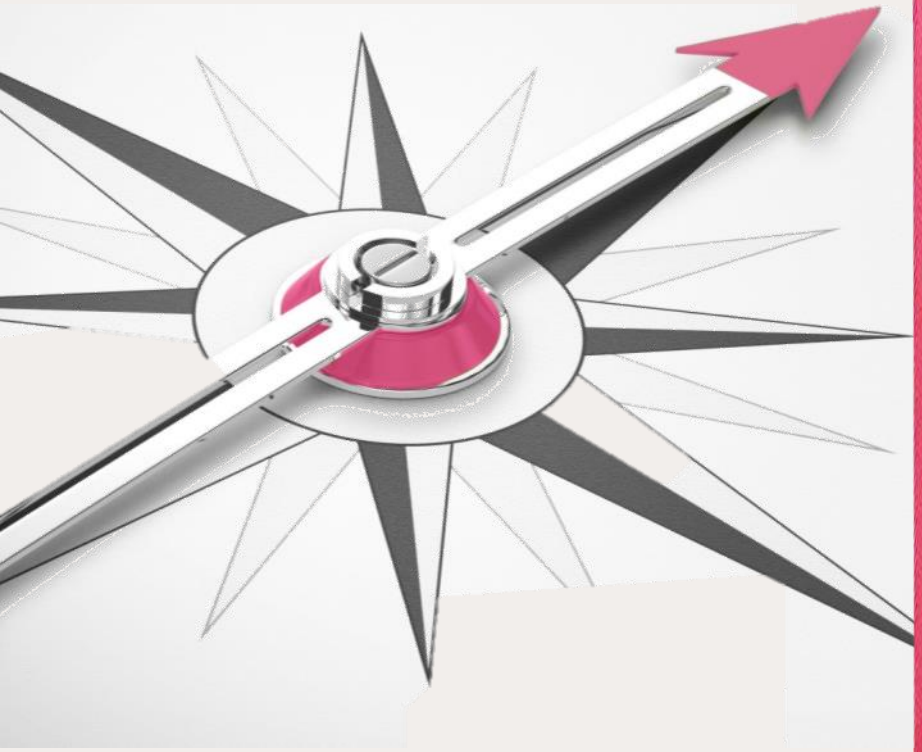
Voluntary application, modular and **adaptable** to national contexts

Using requirements and indicators based on the **evidence** from the *European Breast Guidelines*

Embedded in the **European accreditation framework**

Developed by the **QASDG**

1. *European Breast Guidelines*



About **90 PICOs 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

2. *Guidelines Platform*

Evidence based recommendations covering the **whole care pathway**

Inclusive and comprehensive with only high-quality and "trustworthy" guidelines

Systematic review (Iberoamerican Cochrane Centre)

Now screening and diagnosis

In future: Treatment, rehabilitation, survivorship, and palliative care

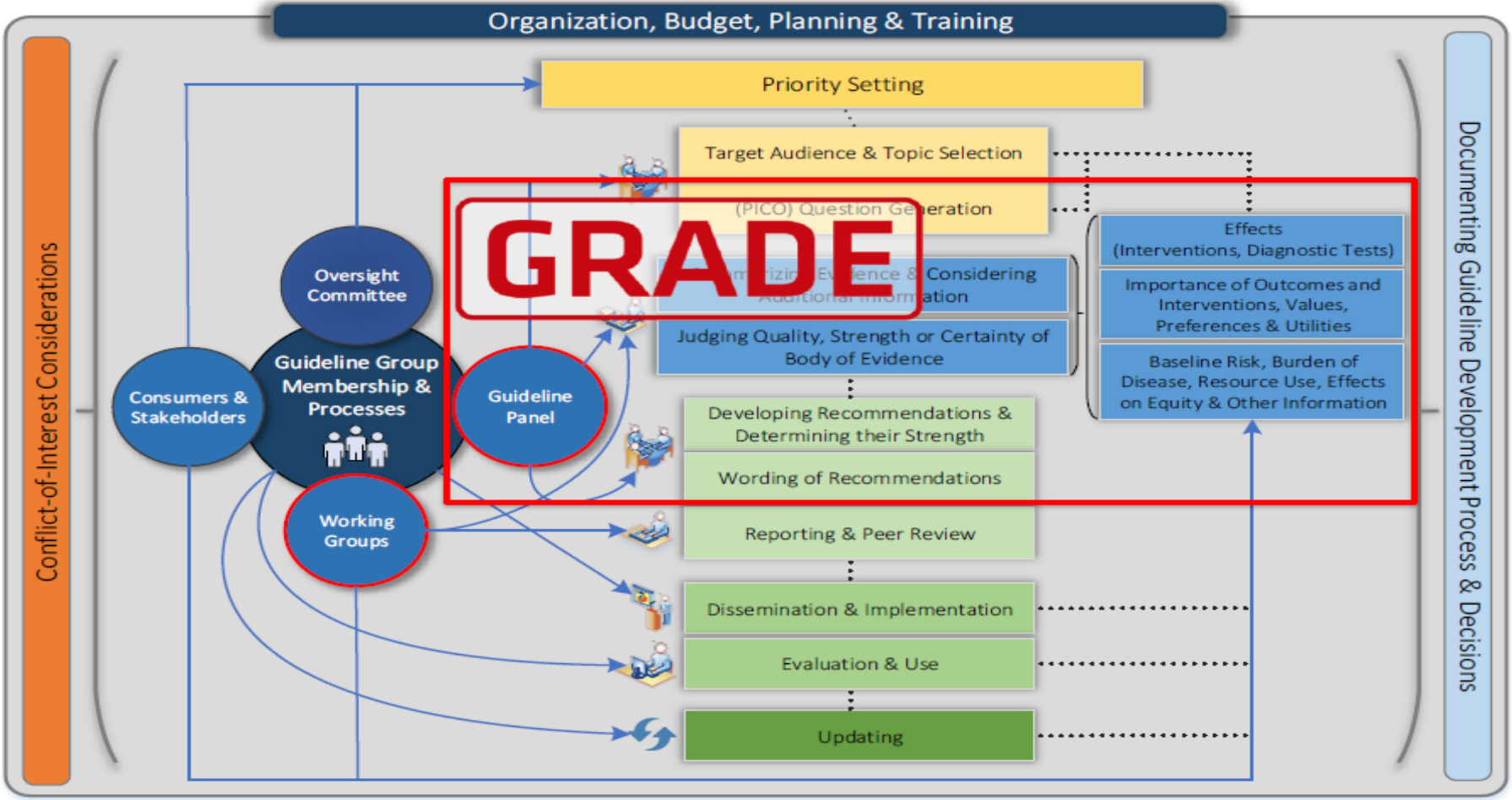
- All the aspects of screening and diagosis
- No high risk and familial breast cancer
- No males

Chapters:

1. Screening
2. Diagnosis
3. Communication and inequalities
4. Training
5. Monitoring and evaluation

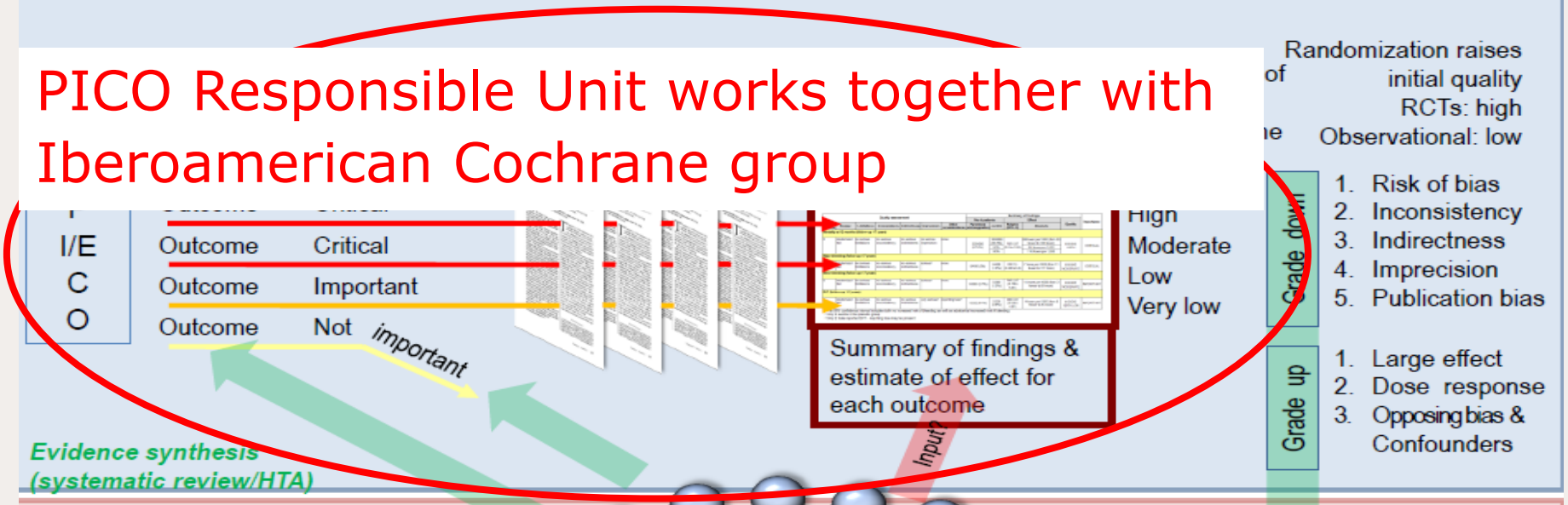
- Glossary

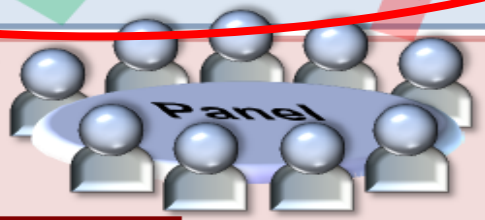
Guidel … rise. CMAJ. 2014 Feb 18;186(3):E123-42.
http://cebgrade.mcmaster.ca/guidecheck.html



Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. CMAJ. 2014 Feb 18;186(3):E123-42.
http://cebgrade.mcmaster.ca/guidecheck.html

PICO Responsible Unit works together with Iberoamerican Cochrane group





Recommendation

Grade recommendations (Evidence to Recommendation)
- For or against (direction) ↓↑
- Strong or conditional/weak (strength)

By considering balance of consequences (evidence to recommendations):
- ❑ Quality of evidence
- ❑ Balance benefits/harms
- ❑ Values and preferences (equity)
- ❑ Resource use (cost, feasibility)
- ❑ Acceptability

EtD framework GRADEpro

Guideline

Grade overall quality of evidence across outcomes based on lowest quality of ***critical*** outcomes

Formulate Recommendations (↓↑ | ⊕…)
"The panel recommends that ….should..."
"The panel suggests that ….should..."
"The panel suggests to **not** ..."
"The panel recommends to **not**..."
Transparency, clear, actionable

Building picos from clinical questions: Easy one

Population: asymptomatic women age 50-69

Intervention: mammography screening

Control: no screening

Outcomes: breast cancer mortality, overall mortality, QoL, false positives, false positive with invasive assessment, overdiagnosis, rate of mastectomy, rate of chemotherapy.

Building PICOs from clinical questions

For some clinical questions framing a PICO was not immediate.

Examples:

- At what age start screening?
- What is the best interval?
- What is the best way to obtain cytological/histological samples?

Building picos from clinical questions: Cyto/histo sampling

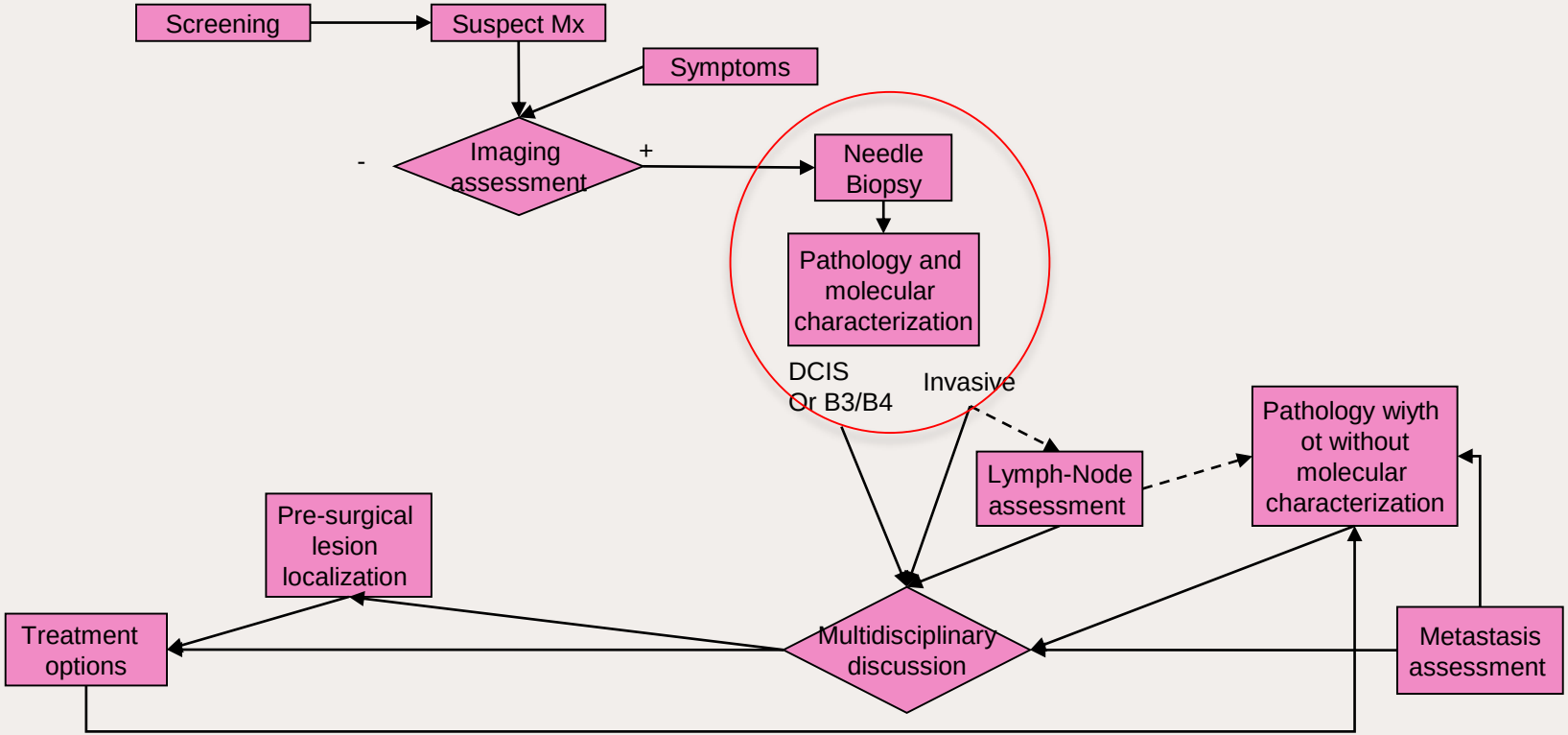
Population: women with suspicious imaging after Mx, US, eventually tomo and clinical assessment (possible subpopulations: mass, asymmetry, distorsion, calcifications)

Intervention: Core Needle Biopsy or Vacuum Assisted CNB, or a two step strategy (FNAC, if not conclusive CNB, if not conclusive VACNB)

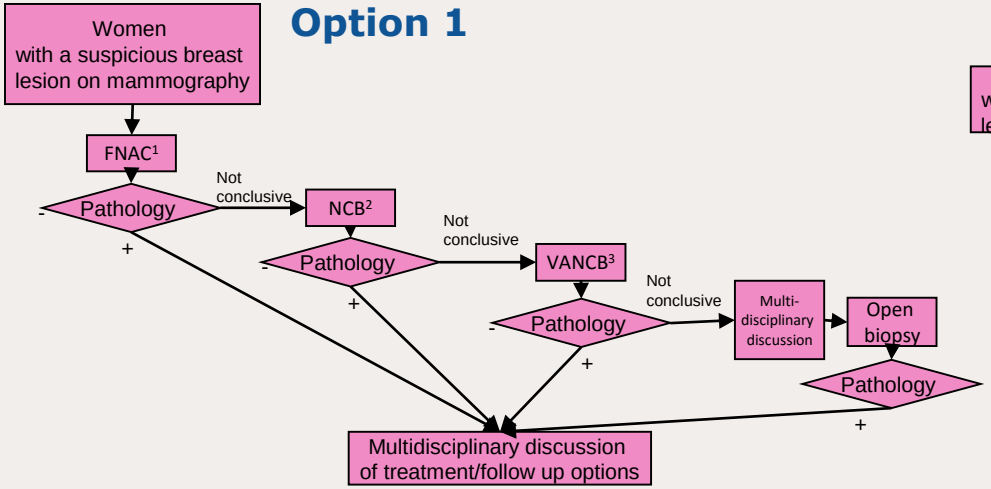
Control: FNAC

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

Building picos from clinical questions: Cyto/histo sampling



Option 1



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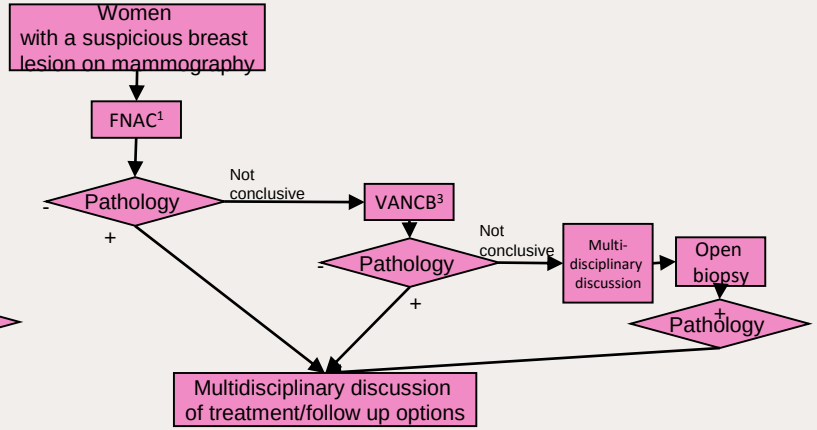
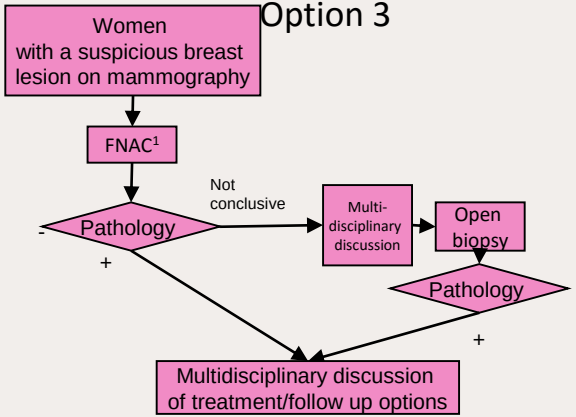
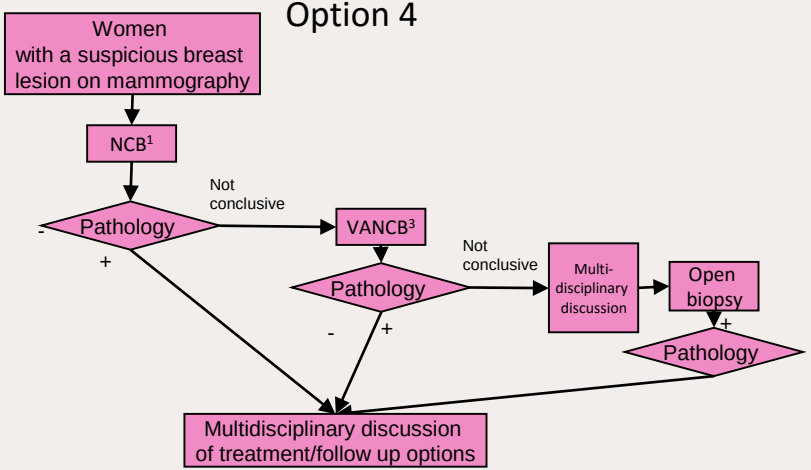


Option 3

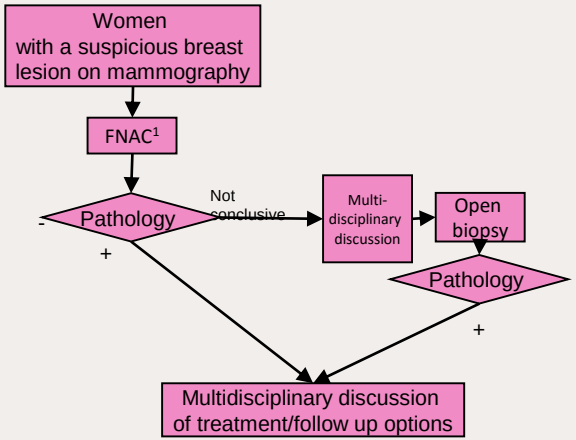


Option 4



1. Fine Needle Aspiration Cytology. Usually under US guidance.
2. Core Needle Biopsy. Can be either US or stereotactic guidance
3. Vacuum Assisted Biopsy. Usually under stereotactic guidance.

Option 6



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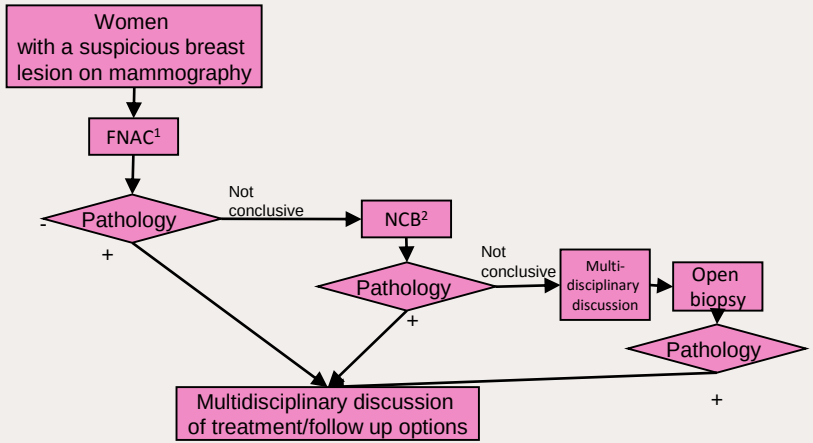
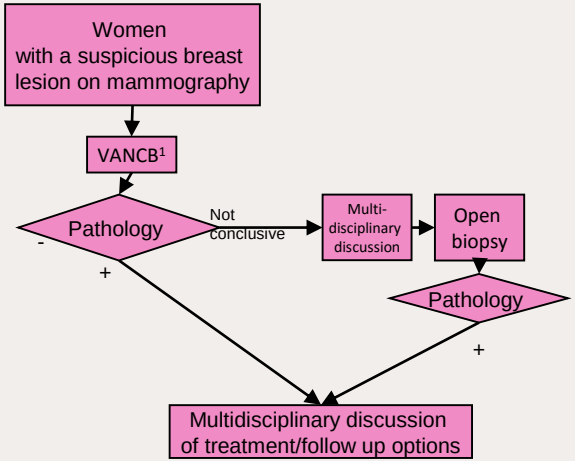


Option 5



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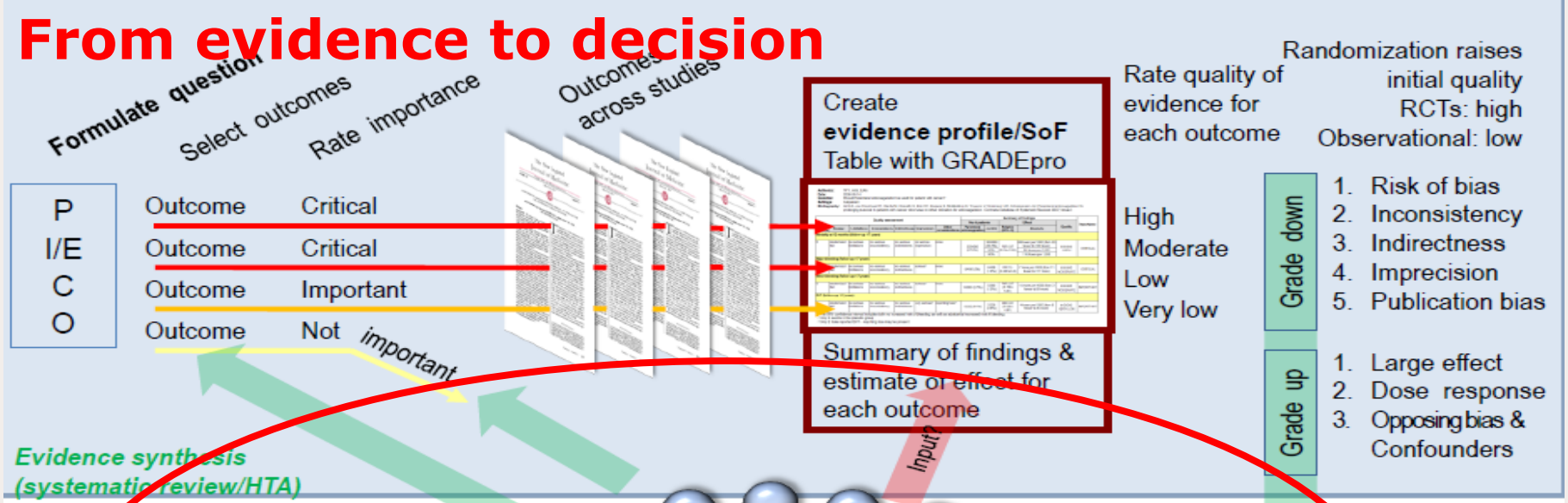
Building picos from clinical questions

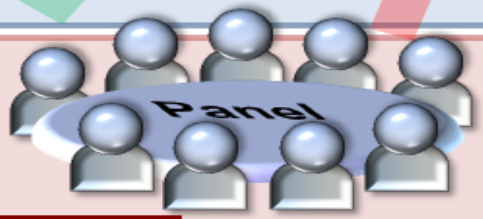
Initial formulation of the four PICOs for the literature search	mass lesion or asymmetric densitiy	architectural distortion	microcalcification
NCB vs FNAC (vacuum assisted or not)	PICO 6a	PICO 6b	PICO 7b
Stereotactic NCB vs US-guided NCB (vacuum assisted or not)	Not assessed	Not assessed	PICO 7°

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

From evidence to recommendation
The work of the Guidelines Development Group

From evidence to decision





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Evidence profile 1. Example: Mammography screening compared to no mammography screening for detecting breast cancer in women 50-69

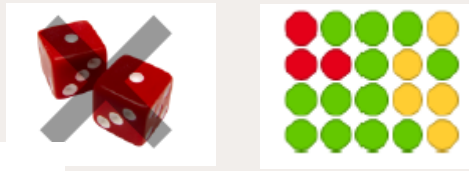
Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography screening	Baseline risk in control group	Relative (95% CI)	Absolute (95% CI)		
Breast cancer mortality (short case accrual) (follow up: mean 18 years)												
6	randomised trials	serious [1]	not serious	serious [2]	not serious	none	578/134,512 (0.4%)	0.6%	**RR 0.76** (0.64 to 0.90)	**144 fewer per 100,000** (from 60 fewer to 216 fewer)	⊕⊕◯◯ LOW	CRITICAL
Breast cancer mortality (longest case accrual available) (follow up: mean 17.3 years)												
6	randomised trials	serious [1]	not serious	serious [2]	not serious	none	774/134,680 (0.6%)	0.8%	**RR 0.78** (0.67 to 0.90)	**167 fewer per 100,000** (from 76 fewer to 251 fewer)	⊕⊕◯◯ LOW	CRITICAL
Breast cancer stage IIA or higher												
4	randomised trials	serious [3]	serious [4]	serious [2]	serious [5]	none	652/143,016 (0.5%)	0.7%	**RR 0.80** (0.64 to 1.00)	**140 fewer per 100,000** (from 0 fewer to 252 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Breast cancer stage III+ or tumour size ≥40 mm												
3	randomised trials	not serious	not serious	serious [2]	not serious	none	99/93,452 (0.1%)	0.2%	**RR 0.62** (0.48 to 0.80)	**65 fewer per 100,000** (from 34 fewer to 88 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

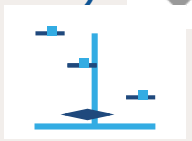
Determinants of certainty in a body of evidence: GRADE

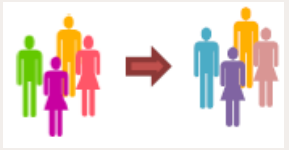
A body of evidence starts as: high ⊕ ⊕ ⊕ ⊕

- **5 factors that can lower quality**

1. 1.Risk of bias criteria
    1. Lack of randomization (observational studies)
2. Inconsistency *(or heterogeneity)*
3. Indirectness *(PICO and applicability)*
4. Imprecision
5. Publication bias

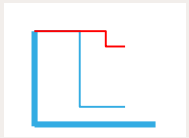


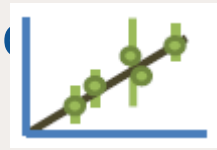


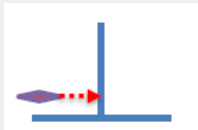


- **3 factors can increase quality**

1. large magnitude of effect
2. opposing plausible residual bias or (nding
3. dose-response gradient

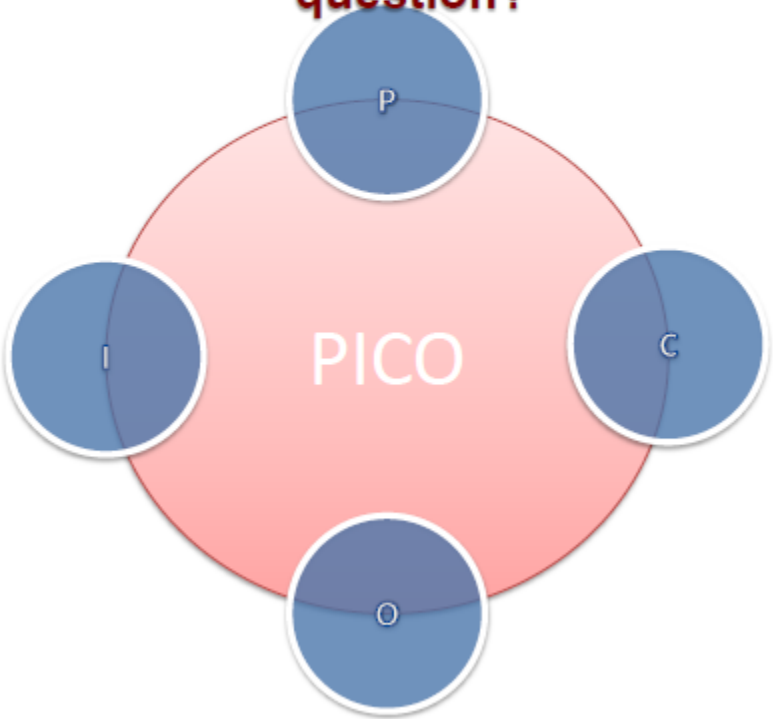


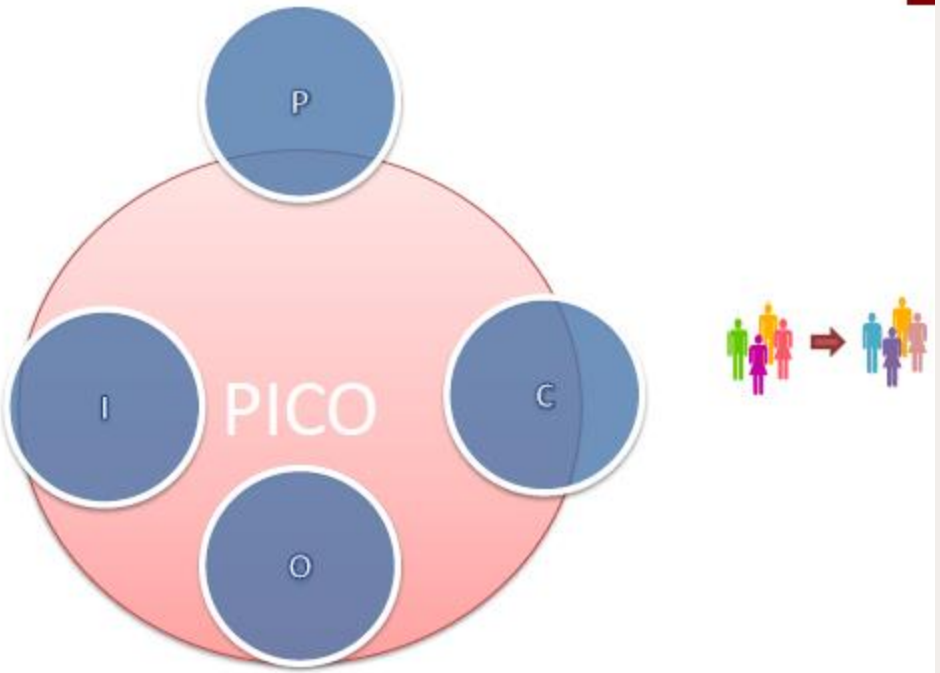




Relation between PICO and available evidence - indirectness

How well does the available information answer the question?

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Evidence profile 2. Example: Mammography screening compared to no mammography screening for detecting breast cancer in women 50-69

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography screening	Baseline risk in control group	Relative (95% CI)	Absolute (95% CI)		
Other cause mortality (follow up: mean 9.6 years)												
3	randomised trials	not serious	not serious	serious [2]	serious [5]	none	4,479/66,432 (6.7%)	6.6%	**RR 0.99** (0.95 to 1.04)	**66 fewer per 100,000** (from 264 more to 330 fewer)	⊕⊕◯◯ LOW	CRITICAL
Overdiagnosis (long case accrual)												
2	randomised trials	not serious	not serious	serious [2]	not serious	none	-	-	-	**Overdiagnosis 10,120 more per 100,000** (from 8,600 more to 11,640 more)	⊕⊕⊕◯ MODERATE	
Overdiagnosis (short case accrual)												
2	randomised trials	not serious	not serious	serious [2]	not serious	none	-	-	-	**Overdiagnosis 17,320 more per 100,000** (14,670 more to 19,960)	⊕⊕⊕◯ MODERATE	

Evidence profile 3. Example: Mammography screening compared to no mammography screening for detecting breast cancer in women 50-69

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Should mammography screening	Baseline risk in control group	Relative (95% CI)	Absolute (95% CI)		
Rate of mastectomies												
5	randomised trials	not serious [6]	not serious	very serious [2,7]	not serious	none	1542/145536 (1.1%)	0.9%	**RR 1.20** (1.11 to 1.30)	**180 more per 100.000** (from 99 more to 270 more)	⊕⊕◯◯ LOW	
Provision of chemotherapy												
2	randomised trials	not serious	serious [8]	very serious [2,7]	serious [5]	none	252/60293 (0.4%)	0.4%	**RR 0.86** (0.52 to 1.41)	**56 fewer per 100.000** (from 164 more to 192 fewer))	⊕◯◯◯ VERY LOW	

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
DESIRABLE EFFECTS	**How substantial are the desirable anticipated effects?** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	**DESIRABLE EFFECTS** Six trials of invitation to mammography screening provided breast cancer mortality data from 249,160 women 50-69 years (short case accrual). Mammography, compared to no screening, reduced the risk of breast cancer mortality (RR=0.76, 95%CI 0.64-0.90; I2=52%, p=0.06) (*low qua* fewer breast cancer dea 5 fewer). Mar se accrual available (RR=0.78, 95%CI 0.67-0.90; I2=54%, p=0.05; 167 fewer breast cancer deaths per 100,000 women over 17.3 years, from 76 fewer to 251 fewer) (*low quality*) and breast cancer stage III+ or tumour size ≥ 40 mm (RR=0.62, 95%CI 0.48-0.80; I2=0%, p=0.69) (*moderate quality*). Mammography, compared to no screening, did not reduce significantly the risk of all-cause mortality (RR = 0.98, 95%CI 0.93, 1.04; I2=34%, p=0.22) (*low quality*), other cause mortality (RR=0.99, 95%CI 0.95-1.04; I2=14%, p=0.31) (*low quality)* or breast cancer stage IIA or higher (RR=0.80 95%CI 0.64-1.00; I2=70%, p=0.02) (*very low quality evidence*).	
UNDESIRABLE EFFECTS	**How substantial are the undesirable anticipated effects?** ○ Large ○ Moderate ○ Small ○ Trivial ○ Varies ○ Don't know	**UNDESIRABLE EFFECTS** Women aged 40-74 years randomised to invitation to screening were more likely to undergo mastectomy (RR = 1.20, 95%CI 1.11-1.30; I2=0%, p=0.86; 180 more mastectomies per 100,000 women, from 99 more to 270 more) (*low quality*). Pooled estimates of overdiagnosis from 2 RCTs were 10.1% (95%CI 8.6-11.6; I2=0%, p=0.61) (*moderate quality*) from a population perspective (long case accrual). From the perspective of woman invited to screening the overdiagnosis proportion was 17.3% (95%CI 14.7- 20.0; I2=10%, p=0.29) (*moderate quality*). Sc 74 (*v* A systematic review of observational studies (Brett 2005) reported that women who had further investigations following their routine mammogram experienced significant anxiety in the short term. According to the systematic review by Hofvind (2012), the estimated cumulative risk of a false-positive screening result in women aged 50–69 undergoing 10 biennial screening tests was 19.7%. In addition the EUNICE Project showed that 2.2% of women had a needle biopsy after the initial screening mammogram. False positive mammograms are also associated with greater anxiety and distress about breast cancer (Salz 2010) and the negative psychological consequences may last up to three years (Bond 2013) (*low quality*).	

Desirable effects: **large**

Undesirable effects: **moderate**

	JUDGEMENT	RESEARCH EVIDENCE	CONSIDERATIONS
CERTAINTY OF EVIDENCE	**What is the overall certainty of the evidence of effects?** ○ Very low ○ Low ○ Moderate ○ High ○ No included studies	Quality of evidence is *moderate* for breast cancer stage III+ or tumour size ≥40 mm and overdiagnosis; *low* for breast cancer mortality, all cause and other cause mortality and rate of mastectomies; *very low* for breast cancer stage IIA or higher and provision of chemotherapy.	
VALUES	**Is there important uncertainty about or variability in how much people value the main outcomes?** ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes	Our systematic review (JRC Techncal Report PICO 10-11, contract FWC443094012015) shows that women place a low value on the psychosocial and physical effects of false positive results and overdiagnosis. However, women generally consider these undesirable effects acceptable (*low confidence*). These findings are of limited value mainly given the significant concerns regarding the adequacy of the information provided to the participants, in order to take an informed decision. Also, acceptability of false positive results is based on studies of patients who have already received a false positive result, who… can… psy… Reg… One… anxiety caused by delays in the receipt of results of diagnostic procedures, or by a lack of understanding of the tests due to suboptimal communication with physicians (*moderate confidence*). Also, women have a higher overall preference towards more comfortable, brief diagnostic procedures (*moderate confidence*).	

Certainty of the evidence: **moderate**

Variability in how much people values outcomes: **possibly important**

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
BALANCE OF EFFECTS	**Does the balance between desirable and undesirable effects favor the intervention or the comparison?** ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	Balance Desirable/Undesirable effects: **favors screening**	To be discussed by the GDG.
RESOURCES REQUIRED	**How large are the resource requirements (costs)?** ○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Based on the results of Sankatsing et al. (Sankatsing 2015), the total costs due to br[illegible] es[illegible] dis[illegible] programme of a cohort of 50 [illegible] women, followed up for 35 years, was 24.0m for each year screened. Moreover, the same study assessed that the absolute cost of treating one overdiagnosis of breast cancer was £1800. The study of Carles et al. (Carles 2011) found that the screening programme is related to a cost of 10.6 ×106€ higher than no screening. In addition, the costs of diagnostics, in de Gelder's study, were 300 million euros compared to no screening.	Resource requirements: **moderate**

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	**What is the certainty of the evidence of resource requirements (costs)?** ○ Very low ○ Low ○ Moderate ○ High ○ No included studies	On the one hand, parameters used in the model of Sankatsing et al. (Sankatsing 2015), Carles et al. (Carles 2011) and de Gelder et al. (de Gelder 2009) were based on data from a biennial screening. On the other hand, parameters used in Pharoah et al. (Pharoah 2013) and [illegible] (Rojnik 2008) did not report any costs (*moderate quality*).	
COST EFFECTIVENESS	**Does the cost-effectiveness of the intervention favor the intervention or the comparison?** ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	Based on the evidence provided by Sankatsing et al. (Sankatsing 2015), the [illegible] wit[illegible] (£2[illegible] Findings from Pharoah et al. (Pharoah 2013) show that screening for women from 50 to 70 was cost effective at a threshold of £20,000 per QALY gained in 2260 (45%) scenarios, but in 588 (12%) scenarios, screening was associated with a reduction in QALYs. Furthermore, Carles et al. (Carles 2011) selected the biennial strategies [illegible] as cost-effective for both effect measures (LYG or QALYs). The findings of Roijnik et al. (Roijik 2008) show that based on commonly quoted thresholds of society's willingness-to-pay of $50,000 per QALY, the optimal cost effective approach in the Slovenian population would be screening women aged 40 to 80 years every 3 years.	Differences in the cost-effectiveness results [illegible]s in [illegible]ology [illegible]whereas Sankatsing et al. (Sankatsing 2015) reported the ICER per LY; Pharoah et al. (Pharoah 2013) and Roijnik (Roijnik 2008) considered the ICER per QALY; Carles et al. (Carles 2011) reported the ICER per QALY, LE and LY. Sankatsing et al. assessed digital mammography while other studies assessed screen-film mammography.

Evidence on resources requirements: **low**

Cost/effectiveness: **favors screening**

	JUDGEMENT	RESEARCH EVIDENCE	ADD CONS
EQUITY	**What would be the impact on health equity?** ○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ← ○ Don't know	Effect on equity: **varies**	To be discussed by the GDG.
ACCEPTABILITY	**Is the intervention acceptable to key stakeholders?** ○ No ○ Probably no ○ Probably yes ○ Yes ← ○ Varies ○ Don't know	In our systematic review we observed the following barriers associated with breast cancer screening: (1) Lack of knowledge and misperceptions regarding preventive medicine and breast health (*high confidence*), (2) Poor communication skills of healthcare providers (*high confidence*), (3) Poor accessibility to breast screening especially among women with disabilities (*high con* Acceptable: **yes** cedure and the possibility of cancer diagnosis (*hig* the procedure (*moderate confidence*), (6) Eml (*moderate confidence*), (7) Lack of support and encouragement from family members, caregivers and social network (*moderate confidence*), (8) Lack of information regarding the available resources (*low confidence*) and (9) Low prioritization of breast cancer screening (*low confidence*). Women and relevant stakeholders expressed similar opinions.	
FEASIBILITY	**Is the intervention feasible to implement?** ○ No ○ Probably no ○ Probably yes ← ○ Yes ○ Varies ○ Don't know	Feasible: **probably yes**	To be discussed by the GDG.

Should mammography screening vs. no mammography screening be used for detecting breast cancer in women between the ages of 50 and 69?

TYPE OF RECOMMENDATION				
Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

RECOMMENDATION
JUSTIFICATION
SUBGROUP CONSIDERATIONS
IMPLEMENTATION CONSIDERATIONS
MONITORING AND EVALUATION
RESEARCH PRIORITIES

For asymptomatic women aged 50 to 69 with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) recommends mammography screening over no mammography screening, in the context of an organised screening programme (strong recommendation, moderate certainty in the evidence)

Implications of a *strong* recommendation

- Policy makers: The recommendation can be adapted 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 participation.

Should mammography screening vs. no mammography screening be used for detecting breast cancer in women between the ages of 50 and 69?

Strong recommendation against the intervention

○

RECOMMENDATION

JUSTIFICATION

SUBGROUP CONSIDERATIONS

IMPLEMENTATION CONSIDERATIONS

MONITORING AND EVALUATION

RESEARCH PRIORITIES

Individual version: This recommendation, having mammography to screen for breast cancer when you are between 50 and 69 years old, is strong because there are greater benefits than harms.
The risk of dying from breast cancer is reduced by between 10 (low risk population) and 50 (high risk population) per ten thousand women offered screening. This corresponds to a **reduction of 10 to 60 breast cancer deaths per ten thousand** in women actually screened. Your risk of developing breast cancer stage III or higher may be lower. There would be little or no effect on your risk of death from other causes.
There will be **140 breast cancers overdiagnosed**. An overdiagnosed cancer is a cancer diagnosed by screening which is so slow-growing that it would never have been diagnosed in a person's lifetime if the person had not been screened.

Target age PICOS

- Should **organised mammography screening** vs. **no mammography screening** be used for early detection of breast cancer in women aged **40 to 44**?

✓Conditional recomm. against the intervention

- Should organised mammography screening… In women aged **45 to 49**?

✓Conditional recomm. for the intervention

- Should organised mammography screening … in women aged **50 to 69**?

✓Strong recomm. for the intervention

- Should organised mammography screening … in women aged **70 to 74**?

✓Conditional recomm. for the intervention

Implications of a *weak* recommendation

- Policy makers: There is a need for substantial debate and involvement of stakeholders
- Patients: The majority of people in this situation would want the recommended course of action, but many would not
- Clinicians: Be more prepared to help patients to make a decision that is consistent with their own values/decision aids and shared decision making
- Screening: we cannot consider participation a benefit per se.

Emphasis on research needs

- Evidence will be emerging from ongoing and newly starting screening trials.
- Implementation challenges of DBT-based screening programmes.
- Information on harms of DBT, including rates of overdiagnosis.
- Benefits and harms, including impacts of interval cancer incidence, stage of breast cancer at detection and mortality reduction.
- Cost-effectiveness.
- Define the quality parameters that need to be fulfilled.

Tailored screening PICOs

- Should **tailored** screening with **automated breast ultrasound** system (**ABUS**) based on **high** mammographic breast **density**, in addition to mammography, vs. mammography alone be used for early detection of breast cancer in asymptomatic women?

✓Conditional recomm. against the intervention

- … with digital breast **tomosynthesis** based on **high** mammographic breast **density**, …, vs. mammography alone… ?

✓Conditional recomm. for the intervention

- … with **hand-held ultrasound (HHUS)** based on **high** mammographic **breast** density,…, vs. mammography alone…?

✓Conditional recomm. against the intervention

- … with magnetic resonance imaging (**MRI**) based on **high** mammographic breast **density**, …, vs. mammography alone?

✓Conditional recomm. against the intervention

Cyto/histo sampling PICOs

- Should **needle core biopsy** vs. **fine needle aspiration** cytology be used to diagnose breast cancer in women with a suspicious breast lesion in mammography?

✓Strong recomm. for the intervention

- Should **stereotactic-guided needle core biopsy** or stereotactic-guided vacuum assisted needle core biopsy vs. **ultrasound-guided needle core biopsy** or ultrasound-guided vacuum assisted needle core biopsy be used to diagnose breast cancer in individuals with breast **calcifications**?

✓Strong recomm. for the intervention

Interval PICOs

Outcomes	Annual/biennial mammography	Triennial/biennial mammography	Annual/Triennial mammography
45 - 49	Conditional against annual	Either of them	Conditional against annual
50 - 69	Strong against annual	Conditional in favor of biennial	Strong against annual
70 - 74	Strong against annual	Conditional in favor of triennial	Strong against annual

Outcomes	Annual mammography	Biennial mammography	Relative	Difference	Quality
Age: 40 to 49 years					
Breast cancer mortality (5 studies) ¶	Rate Ratio 0.89 (0.77 to 1.02) [1-3]	Rate Ratio 0.92 (0.63 to 1.35) [4-5]	Rate Ratio: 0.96 (0.64 to 1.44)	74 fewer per 100,000 women (322 fewer to 341 more)	⊕◯◯◯ VERY LOW
			OR: 1.18 (1.04 to 1.34) ¶¶	---	⊕◯◯◯ VERY LOW
			---	80 more per 100,000 women	⊕◯◯◯ VERY LOW
			---	23,000 more per 100,000 women	⊕◯◯◯ VERY LOW
			---	5,000 more per 100,000 women	⊕◯◯◯ VERY LOW
			Ratio 1.75 to 2.31	51 to 30 more per 100,000 women	⊕◯◯◯ VERY LOW
			Not possible	200 more per 100,000 women	⊕◯◯◯ VERY LOW
			Ratio 1.45	480 more per 100,000 women	⊕◯◯◯ VERY LOW
			Ratio 1.78	14 more per 100,000 women	⊕◯◯◯ VERY LOW
			Ratio 1.5	2 more per 100,000 women	⊕◯◯◯ VERY LOW

¶ Pooled results for each interval comes for different and not related randomized clinical trials. Rate ratio comparing annual screening relative to biennial screening was estimated by an indirect meta-analysis. Absolute effects were calculated taken as basal risk the proportion of breast cancer mortality in

A sensitivity analysis excluding CNBSS-1 from the annual mammography trials (Rate ratio 0.95; 95%CI 0.63 – 1.44)

Estimates of incremental over-diagnosis are from modelling studies non-consistent with recent evidence from UK age trial

Critical issues

- Coverage vs. clinical recommendation framework (lack of a «research only option»)
- Use of indirect evidence (natural history, overdiagnosis and UK age trial)
- Use of results of modeling (impossible to assess how the model includes all the available evidence)
- Very poor literature on costs and cost/effectiveness: impossible to assess gray literature
- Equity, values and feasibility often assessed on old fashion «expert opinion»

Next steps

- Screening:
  - Organized vs. opportunistic
  - Double reading vs. single
- Diagnosis:
  - Imaging assessment
  - Pathology (biomarkers, thresholds, multigene tests)
  - MRI and CESM pre-surgery assessment
- Communication:
  - Letters, other menthods incl. new electronic tools, decision aids…
- Monitoring and evaluation
  - Outcome Indicators
  - Link with QASDG

Thank you and keep in touch!

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