

**1st EFC satellite meeting on Quality Assurance in Colposcopy
Berlin, 8-9th April 2011**

Benefits and Harms of Colposcopy

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Burden of Cervical Cancer in the World

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Burden of cervical cancer World, 2008

- **Whole world:**
530,000 cases, 275,000 deaths
- **Developing countries:**
453,000 cases (86%), 242,000 deaths (88%)

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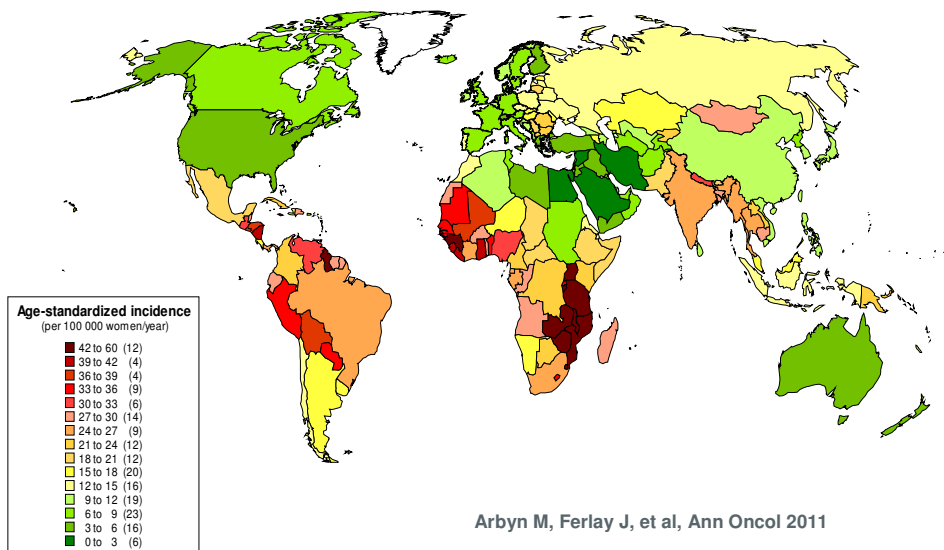
Arbyn, et al, Ann Oncol 2011

Area	Total female population*	Nb of cases	ASIR	SIR	CIR (%)	% of all cancers (all ages)	Rank	Rank (15-44 years)
World	3,357	529,512	15.2	100	1.6	8.8	3	2
Developed countries	632	76,480	9.0	56	0.9	3.0	10	3
Developing countries	2,724	453,032	17.7	116	1.9	13.1	2	2
Eastern Africa	156	31,482	34.5	207	3.9	14.9	1	1
Middle Africa	62	8,209	23.0	140	2.5	22.0	2	2
Northern Africa	102	5,278	6.6	40	0.7	6.4	2	6
Southern Africa	29	6,500	26.8	167	3.0	16.9	2	1
Western Africa	145	28,903	33.7	198	3.9	25.9	2	2
Caribbean	20	4,592	20.8	141	2.1	13.0	2	1
Central America	76	15,606	22.2	150	2.3	16.9	2	1
South America	195	47,888	24.1	160	2.6	14.4	2	2
Northern America	175	12,488	5.7	35	0.5	1.6	13	4
Eastern Asia	762	90,768	9.6	64	0.9	5.7	7	2
South-Eastern Asia	289	44,351	15.8	103	1.7	11.4	2	2
South Central Asia	845	174,129	24.5	156	2.6	22.5	1	2
Western Asia	104	3,454	4.2	26	0.5	3.8	9	6
Eastern Europe	156	31,012	14.5	90	1.4	6.3	4	2
Northern Europe	50	5,325	8.3	50	0.8	2.3	9	3
Southern Europe	78	8,645	8.0	50	0.8	2.7	10	3
Western Europe	96	9,318	6.9	43	0.7	2.0	14	4
Australia/New Zealand	13	798	5.0	31	0.5	1.4	14	5
Melanesia	4	724	23.7	156	2.3	19.5	1	1
Micronesia/Polynesia	0.3	42	14.6	96	1.5	7.7	4	2

* In millions; ASIR: age-standardised rate (world reference); SIR: standardised incidence ratio; CIR: cumulative incidence ratio

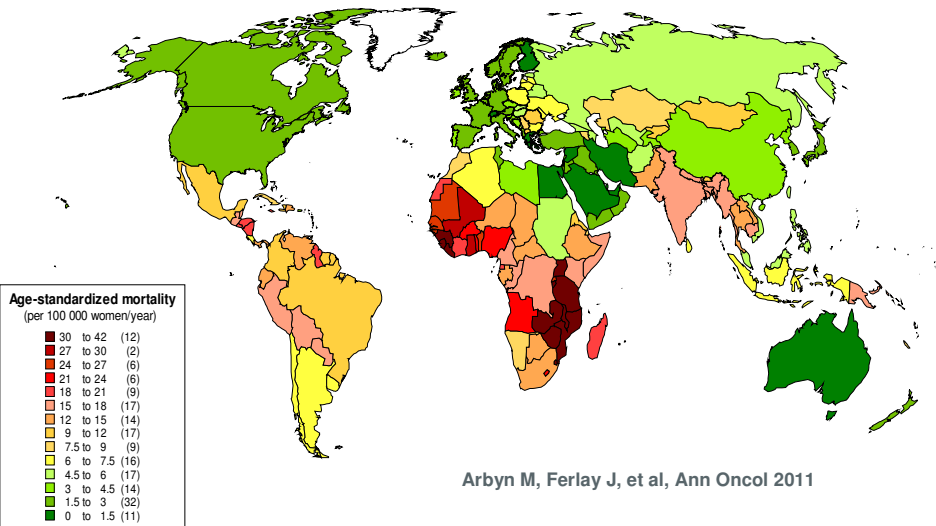
Arbyn M, Ferlay J, et al, Ann Oncol 2011

Incidence of Cervical Cancer (number of cases/100 000 women-years, 2008)



Mortality from Cervical Cancer

(number of cases/100 000 women years, 2008)

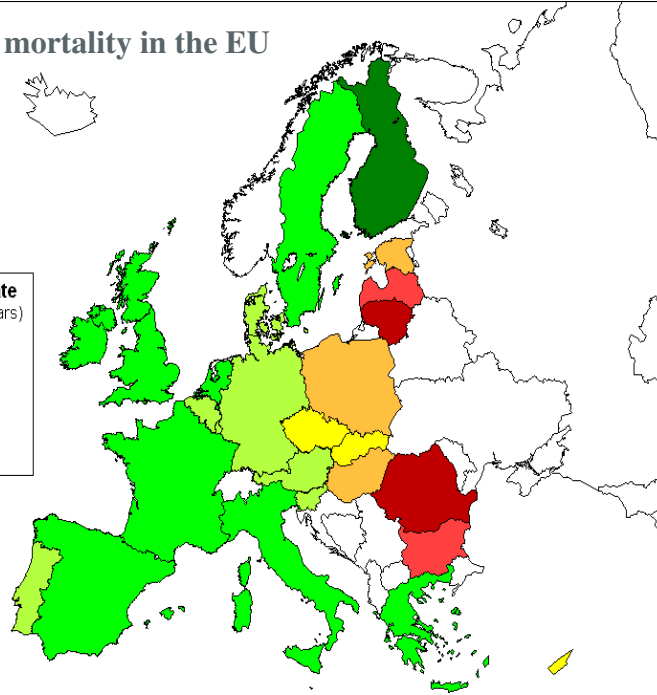
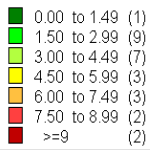


Burden of Cervical Cancer in the Europe

Cervical cancer mortality in the EU (2004)

Number of cases: 34,300
Number of deaths: 16,300

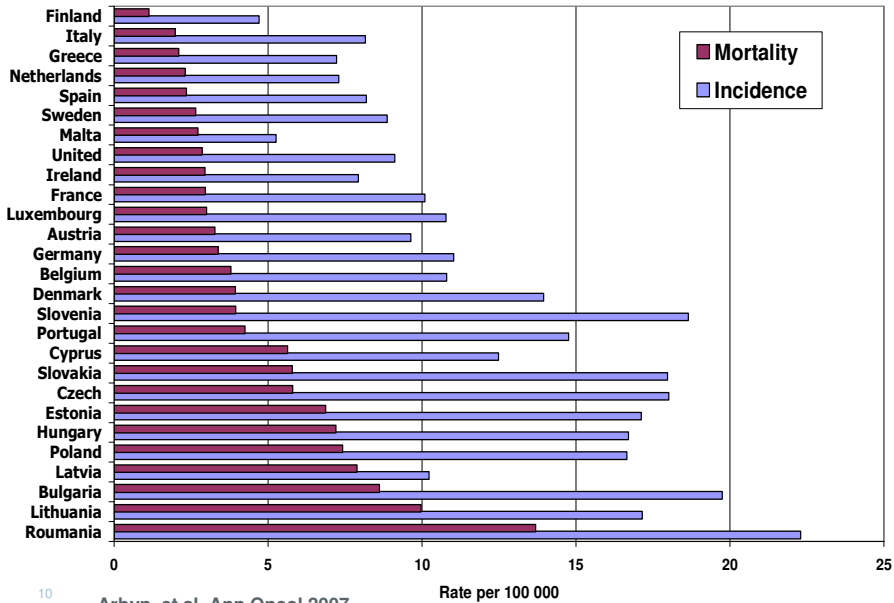
W-age standardised rate
(deaths / 100,000 women-years)



Arbyn, Ann Oncol 2007

W-Age standardised mortality and incidence of cervical cancer

27 Member states of the EU (2004)



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Arbyn, et al, Ann Oncol 2007

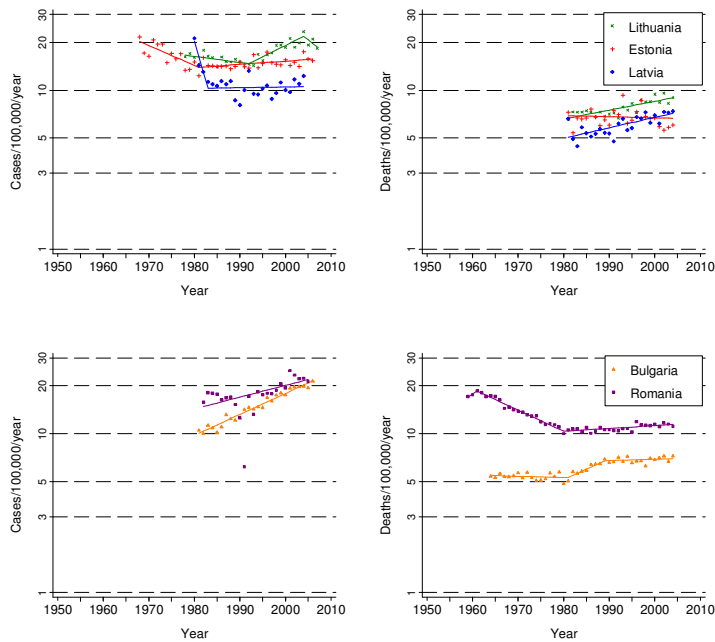
Burden of cervical cancer Europe, 2004

- European continent:
52,000 cases, 27,000 deaths
- EU:
34,300 cases, 16,300 deaths

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Arbyn, et al, Ann Oncol 2007

Trend I & M (Baltic countries, BUL, ROM)



Arbyn, Tumori 2010

East European countries

- Highest burden: Baltic countries, BUL, ROM
- Trends Incidence & mortality from CC ↑
- Contrast with most W-European countries, where I & M ↓

Arbyn EJC 2009

Arbyn IJC 2010

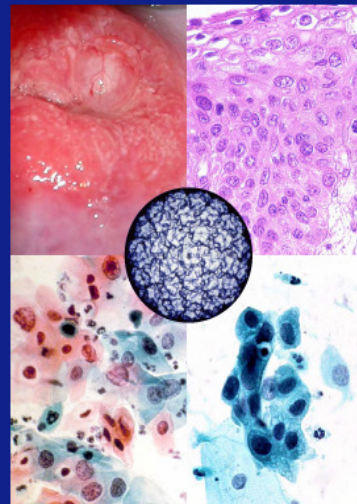
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Management of abnormal cervical cytology

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European guidelines for quality assurance
in cervical cancer screening *Second Edition*



European Commission

Role of colposcopy

- 1. To determine the precise geographical/ anatomical position of the TZ,**
- 2. To confirm or refute the cytological suspicion of CIN**
- 3. To recognize or rule out invasive cancer,**
- 4. To recognize or rule out glandular disease,**
- 5. To facilitate treatment of and monitor progression or regression of CIN.**

EU Guidelines (CH6) Jordan et al, 2008

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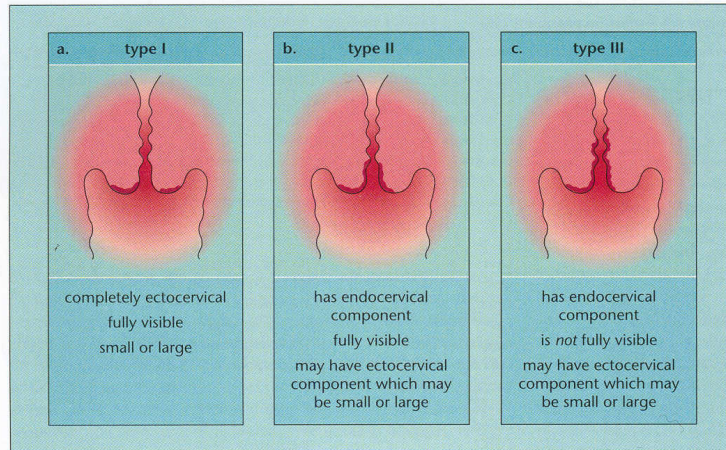
Who should get colposcopy?

- 1. HSIL+**
- 2. ASC-H**
- 3. LSIL, or repeated LSIL**
- 4. hrHPV+ ASC-US, repeated ASC-US**
- 5. AGC**

EU Guidelines (CH6) Jordan et al, 2008

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TZ types



A colposcopist should distinguish the TZ types

17 TZ types should be component of the coploscopy report

Accuracy of colposcopy

- **Conceptual problem**
 - Accuracy assessment requires verification with independent gold standard
 - Colposcopy is part of gold standard
 - Often negative colposcopy is accepted as negative disease ascertainment
 - => automatically: high sensitivity
 - **Meta-analysis: Mitchell** (Obstet Gynecol 1998): outcome CIN2+
 - Sensitivity: 98%
 - Specificity: 48%

Accuracy of colposcopy

- **Independent multiple targeted + random biopsies**
 - Women with satisfactory colposcopy (Pretorius, AJOG 2004).
Sensi: 57% (95% CI: 52-62%).
- **Cumulative diagnosis for CIN3+ (2 years, ALTS study)**
 - Sensitivity of colposcopy impression HG lesion at enrollment: 69.9%
 - (Gage Obstet Gynecol 2006)
- **Cumulative diagnosis for CIN2+ (2 years, ALTS study)**
 - Sensitivity considering any AW: 93%, specificity: 26%
 - Sensitivity of colpo impression HG: 30%
 - Management should not depend on colopo grading
 - (Massad JLGTD 2009)

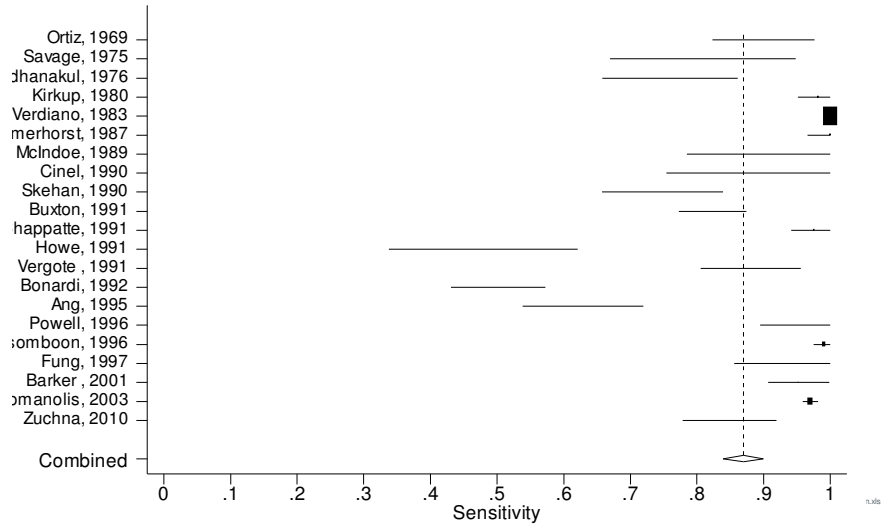
Meta-analysis: accuracy of punch biopsies

- **Martyn Underwood, Charles Redman, Marc Arbyn**
- **Subsequent excision biopsy (LLETZ, Conisation) as gold standard**

Punch biopsies (CIN1+) to detect CIN3+

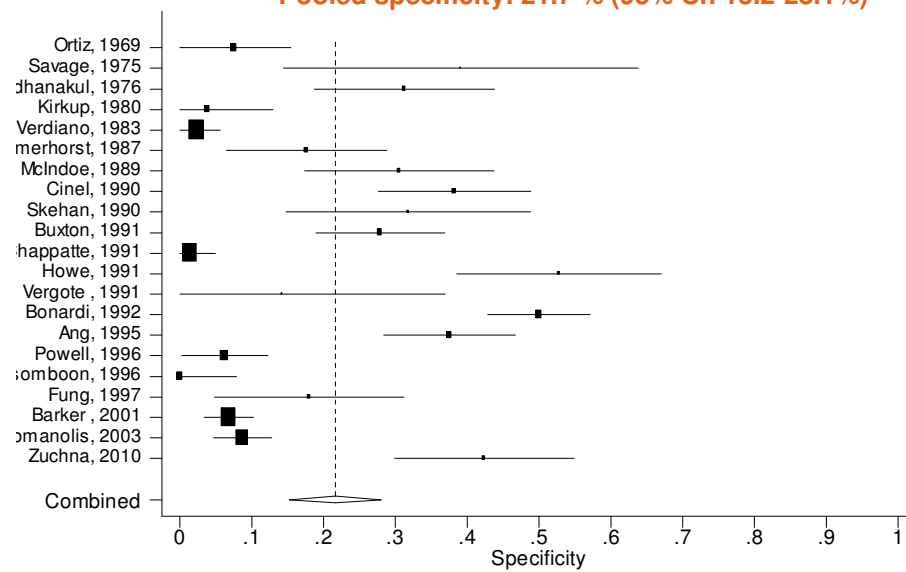
Pooled sensitivity: 86.9 % (95% CI: 83.9-90.0%)

Accuracy of punch biopsies (CIN1+) to detect CIN3+



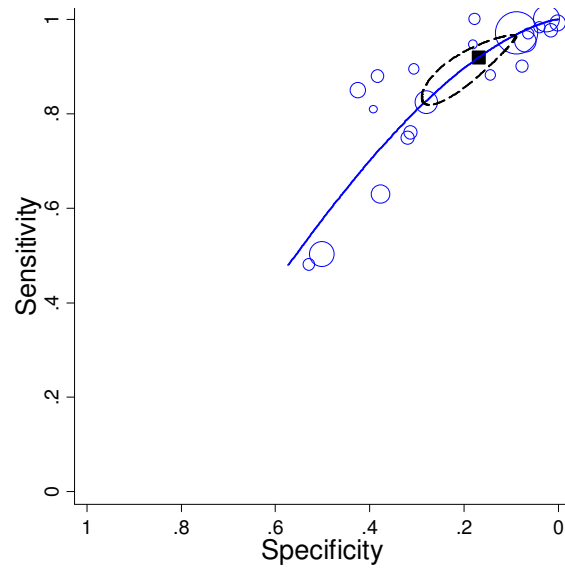
Punch biopsies (CIN1+) to detect CIN3+

Pooled specificity: 21.7 % (95% CI: 15.2-28.1%)



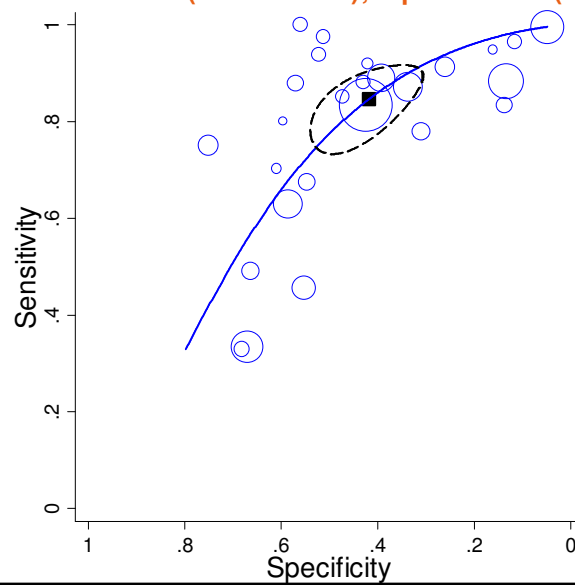
Punch biopsies (CIN1+) to detect CIN3+

Pooled Sensi: 91.9% (CI: 84.8-95.7); Speci: 16.9% (CI: 10.6-25.8)



Punch biopsies (CIN2+) to detect CIN3+

Pooled Sensi: 84.6% (CI: 76.2-90.4); Speci: 41.8% (CI: 33.0-51.2)



Accuracy of colposcopy and colposcopy-targeted biopsies

- Sensitivity substantially lower than previously thought when using random biopsy verification.
- Recent findings might suffer from over-diagnosis (small non progressing CIN2/3).
- Other (European) findings: indicate rather good longitudinal negative predictive value after non-suspicious colposcopy.
- No hard evidence to recommend systematic random biopsies in EU guidelines

Colposcopy practice in Europe

Colposcopy practice in Europe

- Still used as a screening tool (Eastern Europe)
- Specialised quality controlled colposcopy centres in UK
- **Belgium: 1996-2006: 1,980,927** colposcopies vs 6,417,936 Pap smears. One colpo/3 smears
- **Not monitored mixture of well and low performing colposcopy services in EU countries**
- **Good idea to document practice in all member countries of EFC**

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Colposcopy

- **Guidelines for data collection**
- **Quality indicators**

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European guidelines: data collection for treatment of CIN

- **Personal identification (ID, date of birth)**
- **Diagnosis**
 - Date, Diagnosis code
 - Stage & grade
- **Treatment**
 - Date, treating physician, hospital
 - Treatment: (hysterectomy), local excisional, ablative procedure
 - Compliance with follow-up, treatment
 - Linkable with maternity files

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EU guidelines 2008, CH6

Miscan.xls

European guidelines: data collection for treatment of CIN

- **Personal identification (ID, date of birth)**
- **Diagnosis: date, diagnosis code, stage & grade**
- **Treatment**
 - Date, treating physician, hospital
 - Treatment: (hysterectomy), local excisional, ablative procedure
 - Compliance with follow-up, treatment
 - Linkable with maternity files
- **Audit of screening and follow-up history for each cancer case** (link with Cancer Registry)

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EU guidelines 2008, CH6

Miscan.xls

Performance indicators for CC screening (CH7 EU guidelines, Ronco et al)

- **20 quality/performance indicators**
 - Programme enrollment
 - Participation in screening, response to invitation
 - Screen test consumption
 - Distribution screen test results,
 - Screen test performance, PPV of positive cytology/triage (cyto/histological correlation)

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Miscan.xls

Performance indicators for CC screening (CH7 EU guidelines, Ronco et al)

- **Indicators ~ management of screen+ women**
 - % screened women referred to colposcopy
 - % screened women with histoconfirmed CIN
 - Compliance with referral to colposcopy
 - % of detected CIN2+ treated
 - % of detected CIN2+ treated with Hectomy
 - % of CIN1 treated
 - Incidence of invasive Ca after abn cyto
 - Normal follow-up after treatment CIN
- **No quality indicators for Colposcopy!!!**

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EU guidelines 2008, CH7

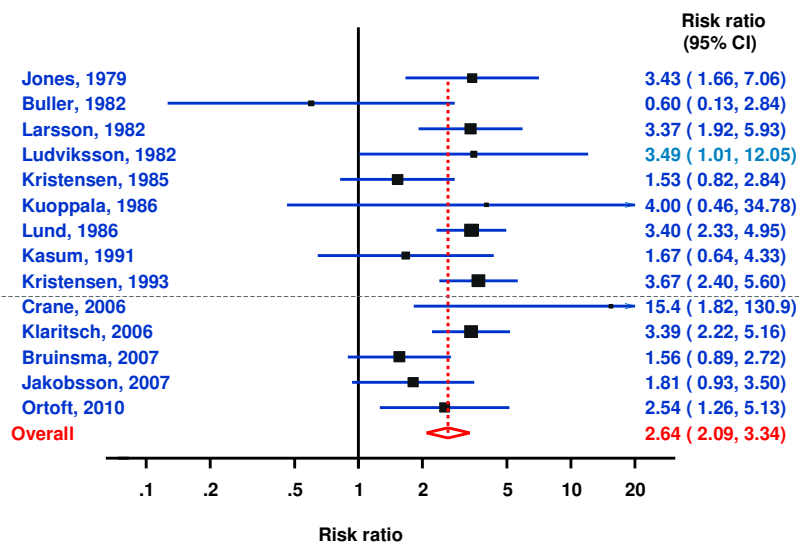
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Adverse obstetrical outcomes associated with treatment of CIN

Kyrgiou, Lancet 2006
Arbyn, BMJ, 2008

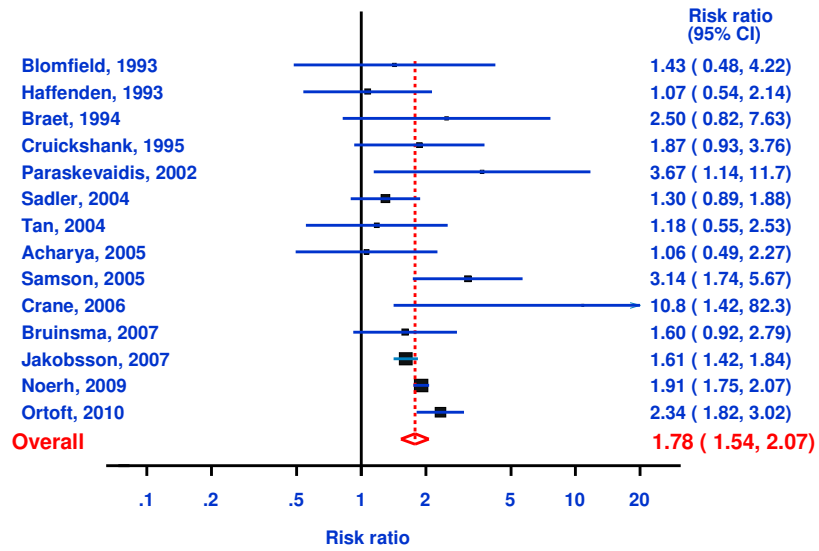
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Preterm delivery (<37W): cold knife conisation vs no treatment

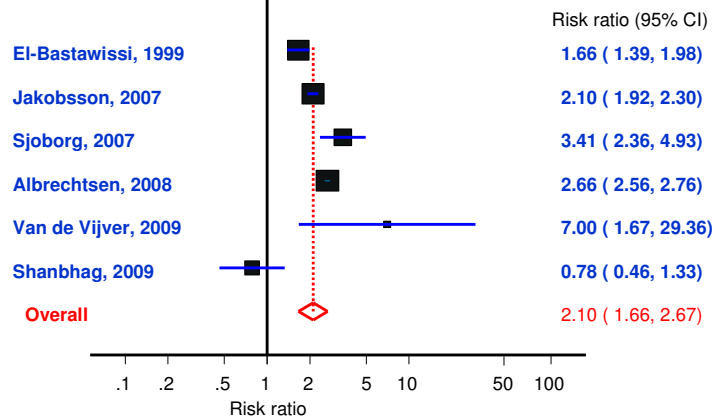


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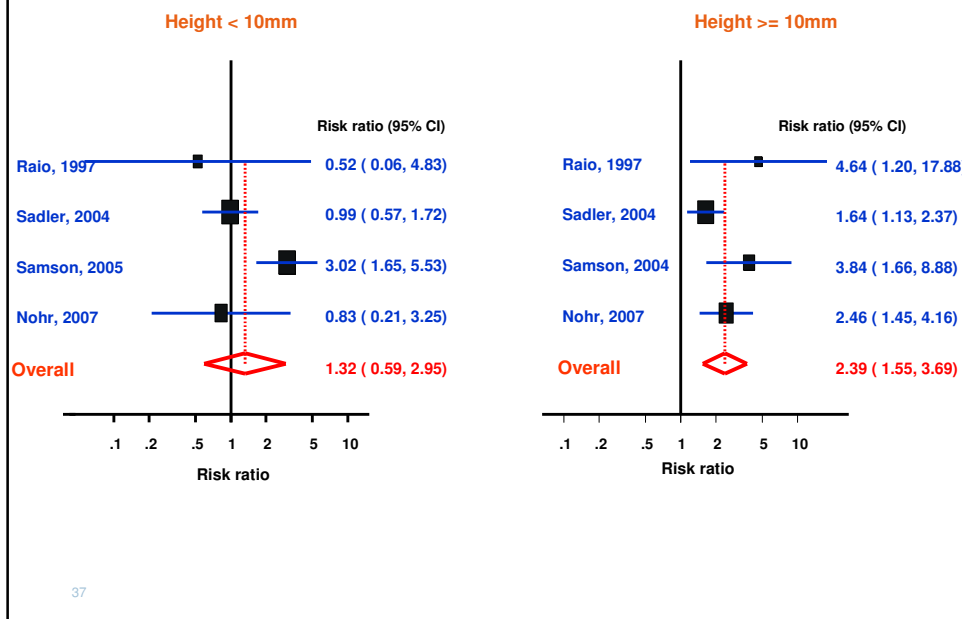
Preterm delivery (<37W): LLETZ vs no treatment



Preterm delivery (<37W): Excisional treatment (NOS) vs no treatment



Preterm delivery (<37W): Excision vs no treatment ~height



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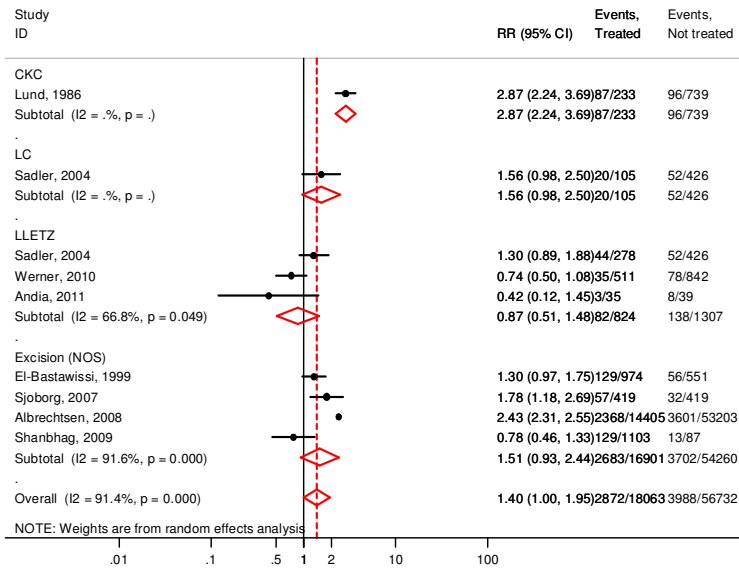
Adverse obstetrical outcomes associated with treatment of CIN

- Risk of preterm delivery might be inflated due to use of inappropriate control groups (Shanbhag 2009; Werner 2010, Bruinsma 2011)
- New meta-analyses ongoing:
 - risk CKC confirmed,
 - risk LLETZ ~ depth, absolute or relative volume of cone (small excisions (minimal size?) probably safe)
- Individual patient data meta-analysis
- Better data needed: standardised report for data collection ~ treatment of CIN

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Control group restricted to women with CIN (pregnancy before CIN diagnosis and non-treated women with CIN)

Preterm delivery at <37 W (Excisional treatment: Post- vs Pre-treatment)



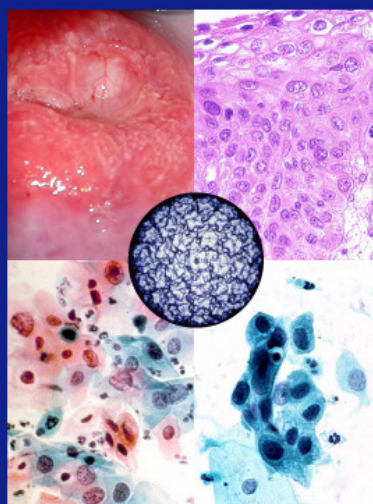
Colposcopy: conclusions

- Inadequate as a screening instrument
- Essential to orient diagnosis and treatment
- Quality assurance indicators needed
- Compliance with colposcopy referral and outcomes after colposcopy should be monitored (necessary component of an organised screening programme)

Supplements to EU guidelines on HPV screening and vaccination

- Ready by 2011

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