Recommendation 8

The expert panel suggests a strategy of screen with an HPV test followed by VIA and treat with cryotherapy (or LEEP when not eligible for cryotherapy) over a strategy of screen with cytology followed by colposcopy (with or without biopsy) and treat with cryotherapy (or LEEP when not eligible) **(conditional recommendation, ⊕⊖⊖⊖ evidence)**

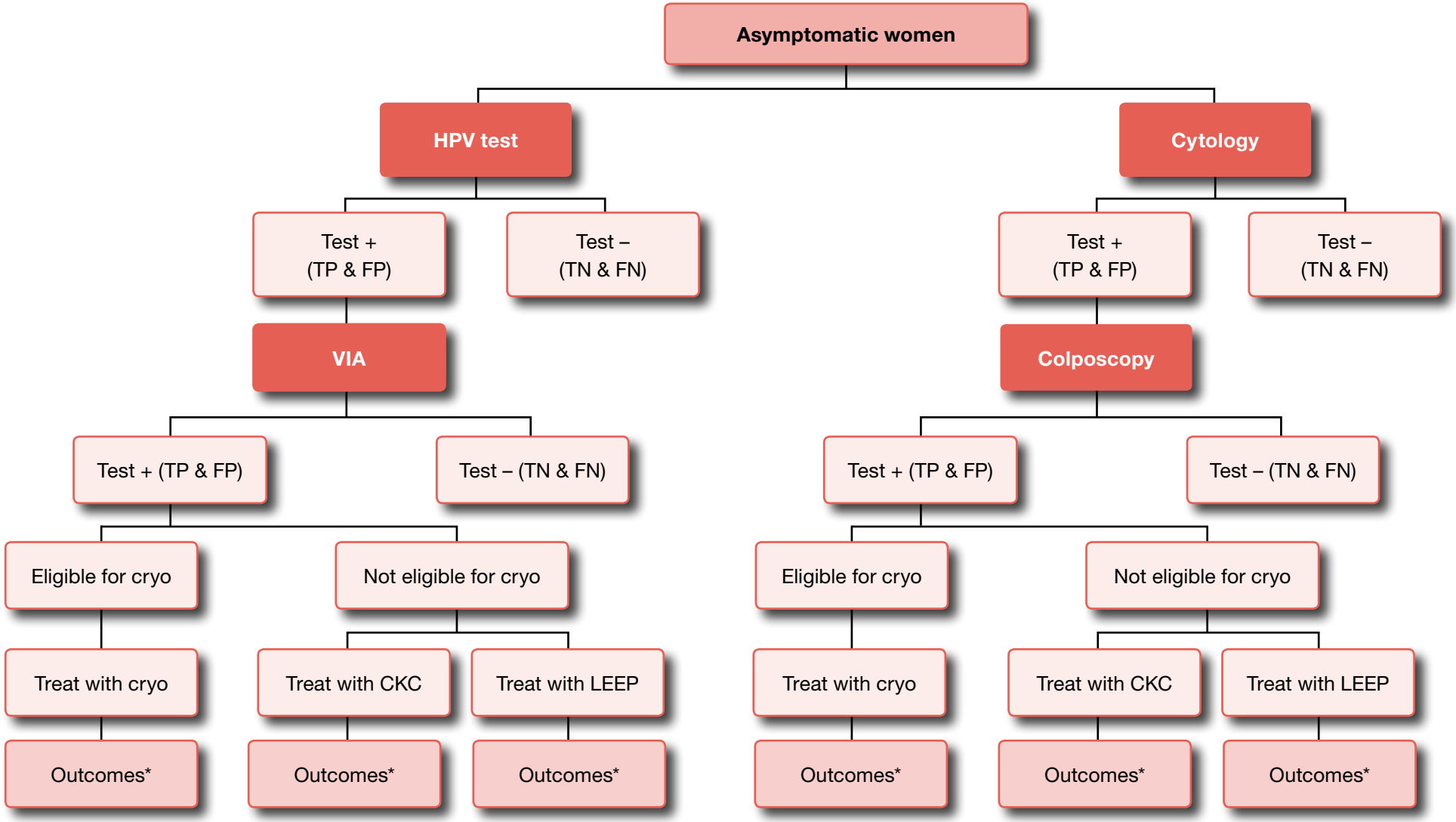
Remarks: The benefits of the two screen-and-treat strategies are similar. However, there may be higher resources required in cytology programmes due to quality control, training, and waiting time. The addition of colposcopy requires a second visit. This recommendation applies to women regardless of HIV status.

Evidence-to-recommendation table

Decision domain	Judgement	Summary of reason for judgement
Quality of evidence *Is there high- or moderate-quality evidence?*	Yes ☐ / No ☒	There is low-quality evidence for the diagnostic test accuracy data for HPV test followed by VIA compared to cytology followed by colposcopy. There is low- to very-low-quality evidence for the effects of treatment and the natural progression of CIN from observational studies often with inconsistent results across studies. The link between test accuracy data and treatment effects is very uncertain.
Balance of benefits versus harms and burdens *Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?*	Yes ☐ / No ☒	The benefits and harms of HPV test followed by VIA and cytology followed by colposcopy may be similar. However, there may be slightly fewer cancers detected with HPV test followed by VIA.
Values and preferences *Are you confident about the assumed or identified relative values and are they similar across the target population?*	Yes ☒ / No ☐	High value was placed on a screen-and-treat strategy versus no screening, since qualitative studies have shown that once women decide to be screened they find the screening tests and immediate treatment acceptable. High value was placed on the resources required.
Resource implications Is the cost small relative to the net benefits for the recommended strategy?	Yes ☒ / No ☐	Fewer resources may be required for HPV test followed by VIA as there may be additional resources required in cytology programmes due to increased training of providers, quality control, and waiting time. Colposcopy following cytology also requires a second visit.

Evidence for an HPV test followed by VIA compared to cytology followed by colposcopy to screen for CIN2+

1. Flowchart of screen-and-treat strategies



*Outcomes are: mortality from cervical cancer, rate of cervical cancer detection, rate of CIN2+ detection, major bleeding, premature delivery, infertility, STI detection, major infections, and minor infections

2. Evidence used for decision-making: HPV test followed by VIA compared to cytology (ASCUS) and colposcopic impression

Diagnostic test accuracy

Pooled sensitivity HPV test	94% (95% CI: 89 to 97)	Pooled sensitivity VIA	69% (95% CI: 54 to 81)
Pooled specificity HPV test	90% (95% CI: 86 to 93)	Pooled specificity VIA	87% (95% CI: 79 to 92)
Pooled sensitivity cytology (ASCUS)	70% (95% CI: 57 to 81)	Pooled sensitivity colposcopic impression	95% (95% CI: 86 to 98)
Pooled specificity cytology (ASCUS)	95% (95% CI: 92 to 97)	Pooled specificity colposcopic impression	42% (95% CI: 26 to 61)

(Reference standard: colposcopy with biopsy when indicated)

2.1 Diagnostic test accuracy (DTA) evidence profile: HPV test followed by VIA compared to cytology (ASCUS) and colposcopic impression

Outcome	No. of studies (No. of patients)[a]	Study design	Factors that may decrease quality of evidence					DTA QoE	Effect per 1000 patients/year for pretest probability of 2%		Importance
			Limitations	Indirectness	Inconsistency	Imprecision	Publication bias		HPV test followed by VIA	Cytology followed by colposcopic impression	
True positives (patients with CIN2+)	14 studies (34 584 patients)	Cross-sectional and cohort studies	Serious[b]	None[c]	Serious[d]	None[e]	Undetected	⊕⊕⊖⊖ low	13	13	CRITICAL
TP absolute difference									0		
True negatives (patients without CIN2+)	14 studies (34 584 patients)	Cross-sectional and cohort studies	Serious[b]	None[c]	Serious[d]	None[e]	Undetected	⊕⊕⊖⊖ low	967	952	CRITICAL
TN absolute difference									15 more		
False positives (patients incorrectly classified as having CIN2+)	14 studies (34 584 patients)	Cross-sectional and cohort studies	Serious[b]	None[c]	Serious[d]	None[e]	Undetected	⊕⊕⊖⊖ low	13	28	CRITICAL
FP absolute difference									15 fewer		
False negatives (patients incorrectly classified as not having CIN2+)	14 studies (34 584 patients)	Cross-sectional and cohort studies	Serious[b]	None[c]	Serious[d]	None[e]	Undetected	⊕⊕⊖⊖ low	7	7	CRITICAL
FN absolute difference									0		

Footnotes:

[a] This is the number of studies that assessed DTA data for: 1. HPV test and VIA; and 2. HPV test and cytology.

[b] We used QUADAS to assess risk of bias. Half of studies only performed one biopsy of an abnormal lesion and had unclear blinding of tests. Colposcopy studies had unclear blinding of index test results. This was downgraded one level in the context of other factors, in particular indirectness.

[c] Data for HPV test followed by VIA and cytology followed by colposcopy were calculated based on sensitivity and specificity of the two tests. Direct data were not available.

[d] Estimates of HPV test, VIA, cytology (ASCUS) and colposcopy sensitivity/specificity were variable despite similar cut-off values; inconsistency was not explained by quality of studies. This was downgraded one level in the context of other factors, in particular imprecision.

[e] Wide CI for sensitivity and specificity of HPV test followed by VIA and cytology followed by colposcopy and therefore wide CI for TP, TN, FP, FN, may lead to different decisions depending on which confidence limits are assumed.

2.2 GRADE evidence table for patient-important outcomes following different screen-and-treat strategies: HPV test followed by VIA compared to cytology (ASCUS) and colposcopic impression

Outcomes	Events in the screen-and-treat strategies for patient-important outcomes (numbers presented per 1 000 000 patients)						
	HPV→VIA +/– CKC	HPV→VIA +/– LEEP	HPV→VIA +/– cryo	Cyto→colp imp +/– CKC	Cyto→colp imp +/– LEEP	Cyto→colp imp +/– cryo	No screen[10]
Mortality from cervical cancer[1]	91	99	99	89	96	96	250
Cervical cancer incidence[2]	128	138	138	125	135	135	350
CIN2+ recurrence[3]	4905	5311	5311	4782	5194	5194	13 400
Undetected CIN2+ (FN)	7000			7000			–
Major bleeding[4]	222	58	9	358	94	14	0
Premature delivery[5]	531	511	516	550	518	526	500
Infertility[6]	–	–	–	–	–	–	–
Major infections[7]	23	33	3	37	53	6	0
Minor infections[8]	242	156	167	391	251	270	0
Unnecessarily treated (FP)	13 000			28 000			–
Cancer found at first-time screening[9]	3168			4794			0

Footnotes:

The colours in the table: In each GRADE evidence table, colour-coding is used to highlight the 'desirability' of the effects for that outcome relative to other outcomes. The continuum runs from dark gray (desirable) through light gray and light pink to dark pink (least desirable).

The numbers in the table are based on

- CIN2+ pretest probability 2%
- VIA: Pooled sensitivity 69% (95% CI: 54 to 81), pooled specificity 87% (95% CI: 79 to 92)
- Cytology (ASCUS): Pooled sensitivity 70% (95% CI: 57 to 81), pooled specificity 95% (95% CI: 92 to 97)
- Colposcopy: Pooled sensitivity 95% (95% CI: 86 to 98), pooled specificity 42% (95% CI: 26 to 61)
- The overall QoE for each of these outcomes is very low ⊕⊖⊖⊖. Our lack of confidence in these effect estimates stems mainly from very low-quality evidence for treatment effects and natural progression/history data.

[1] We assume no mortality from cervical cancer in TN and FP. To calculate the mortality from cervical cancer, we assumed 250 deaths per 350 women with cervical cancer. These numbers are based on Eastern Africa age-standardized rates of cervical cancer and mortality provided by WHO (http://globocan.iarc.fr/, accessed 30 October 2012).

[2] We assume no cervical cancer in TN or FP. To calculate cervical cancer incidence in women with persistent CIN2+, we assumed 350 cervical cancers per 14 000 women who have persistent CIN2+ (i.e. FN). This incidence is based on Eastern Africa age-standardized rate of cervical cancer of 350 cervical cancers per 1 000 000 women, of whom 2% have CIN2+ (20 000 women with CIN2+, and a subsequent 30% regression for a total of 14 000 with persistent CIN2+). These data are available from WHO (http://globocan.iarc.fr/, accessed 30 October 2012).

[3] We assume no CIN2+ in TN and FP. Our calculations in the model are based on 70% natural persistence of CIN2+ with no treatment (30% regression) in FN. The incidence of cervical cancer and mortality are also subtracted from the CIN2+ in FN (see above for calculations). TP are treated and recurrence rates of CIN2+ are 5.3% in cryotherapy and LEEP, and 2.2% in CKC.

[4] We assumed major bleed would be 0 in TN and FN as they were not treated. We assumed 0.000339 of the population treated with cryotherapy, 0.002257 with LEEP, and 0.001705 with CKC, based on pooled proportions in observational studies with no independent controls, will have major bleeding.

[5] We assumed 5% population risk of premature delivery in 1% of women who become pregnant. Based on pooled meta-analysis of controlled observational studies, 0.001125 of the population treated with cryotherapy, 0.000925 with LEEP, and 0.001705 of the population treated with CKC will have premature delivery.

[6] We did not identify any data about the risk of infertility after treatment for CIN2+.

[7] We assumed major infection would be 0 in TN and FN as they were not treated. Based on pooled proportions from studies with no independent control 0.000135 of the population treated with cryotherapy 0.001279 with LEEP, and 0.000888 with CKC will have major infection.

[8] We assumed minor infection would be 0 in TN and FN as they were not treated. Based on pooled proportions from studies with no independent control, 0.006473 of the population treated with cryotherapy, 0.006027 with LEEP, and 0.009368 with CKC will have minor infection.

[9] Cancers detected at first-time screening calculated from Sankaranarayanan et al. (2005). Numbers for single screening tests were calculated as 'screen-detected' cancers in women who participated in the screening programme; and numbers for tests with colposcopy were calculated as 'screen-detected' plus 'clinically detected' cancers. For a sequence of tests (e.g. HPV test followed by VIA), the greater number of cancers detected between tests was used. No cancers would be found in the 'no screen' group. This is not the annual incidence of cervical cancer (which is shown in a row above). It represents the cumulative rate of cancer development before screening started (i.e. the prevalence of cancer at the time when screening is conducted).

[10] 'No screen' numbers were calculated using the same assumptions above for FN, with the exception of premature delivery which was baseline risk in the population.

2.3 GRADE evidence table for patient-important outcomes following different screen-and-treat strategies by age

	HPV→VIA +/– CKC	HPV→VIA +/– LEEP	HPV→VIA +/– cryo	Cyto→colp imp +/– CKC	Cyto→colp imp +/–LEEP	Cyto→colp imp +/– cryo	No screen[10]
15–39 years[a]							
Mortality from cervical cancer	26	28	28	25	28	28	71
Cervical cancer incidence	37	39	39	36	39	39	100
CIN2+ recurrence	5052	5459	5459	4925	5337	5337	13 829
40–49 years[a]							
Mortality from cervical cancer	170	183	183	165	179	179	464
Cervical cancer incidence	237	256	256	231	250	250	650
CIN2+ recurrence	4728	5134	5134	4609	5022	5022	12 886
50–74 years[a]							
Mortality from cervical cancer	313	338	338	305	330	330	857
Cervical cancer incidence	438	473	473	427	462	462	1200
CIN2+ recurrence	4403	4809	4809	4293	4706	4706	11 943
Complications (same across all groups)							
Major bleeding[4]	222	58	9	358	94	14	0
Premature delivery[5]	531	511	516	550	518	526	500
Infertility[6]	–	–	–	–	–	–	–
Major infections[7]	23	33	3	37	53	6	0
Minor infections[8]	242	156	167	391	251	270	0

Footnotes:

[a] Events were calculated similar to Table 2.2. However, events for cervical cancer are based on incidence of cervical cancer in Eastern Africa of 100/1 000 000 cervical cancers per year in women age 15–39 years; 650 for age 40–49 years; and 1200 for age 50–74 years, provided by WHO (http://globocan.iarc.fr/, accessed 30 October 2012). It is assumed that the recurrence of CIN is constant across age groups but the incidence of cervical cancer and associated mortality increases, thus reducing the overall recurrence of CIN (a proportion of those with CIN will develop cancer or die). These data should be used primarily to make comparisons across screen-and-treat strategies, not within columns for different age groups.

[4,5,6,7,8,10] See footnotes for Table 2.2.

3. Evidence used for decision-making: HPV test followed by VIA compared to cytology (ASCUS) and colposcopic impression with biopsy when indicated

Diagnostic test accuracy

Pooled sensitivity HPV test	94% (95% CI: 89 to 97)	Pooled sensitivity VIA	69% (95% CI: 54 to 81)	Pooled sensitivity cytology (ASCUS)	70% (95% CI: 57 to 81)
Pooled specificity HPV test	90% (95% CI: 86 to 93)	Pooled specificity VIA	87% (95% CI: 79 to 92)	Pooled specificity cytology (ASCUS)	95% (95% CI: 92 to 97)

(Reference standard: colposcopy with biopsy when indicated)

3.1 Diagnostic test accuracy (DTA) evidence profile: HPV test followed by VIA compared to cytology (ASCUS) and colposcopy with biopsy when indicated

Outcome	No. of studies (No. of patients)[a]	Study design	Factors that may decrease quality of evidence					DTA QoE	Effect per 1000 patients/year for pretest probability of 2%		Importance
			Limitations	Indirectness	Inconsistency	Imprecision	Publication bias		HPV test followed by VIA	Cytology followed by colposcopy with biopsy	
True positives (patients with CIN2+)	14 studies (34 584 patients)	Cross-sectional and cohort studies	Serious[b]	None[c]	Serious[d]	None[e]	Undetected	⊕⊕⊖⊖ low	13	14	CRITICAL
TP absolute difference									1 fewer		
True negatives (patients without CIN2+)	14 studies (34 584 patients)	Cross-sectional and cohort studies	Serious[b]	None[c]	Serious[d]	None[e]	Undetected	⊕⊕⊖⊖ low	967	980	CRITICAL
TN absolute difference									13 fewer		
False positives (patients incorrectly classified as having CIN2+)	14 studies (34 584 patients)	Cross-sectional and cohort studies	Serious[b]	None[c]	Serious[d]	None[e]	Undetected	⊕⊕⊖⊖ low	13	0	CRITICAL
FP absolute difference									13 more		
False negatives (patients incorrectly classified as not having CIN2+)	14 studies (34 584 patients)	Cross-sectional and cohort studies	Serious[b]	None[c]	Serious[d]	None[e]	Undetected	⊕⊕⊖⊖ low	7	6	CRITICAL
FN absolute difference									1 more		

Footnotes:

[a] This is the number of studies that assessed DTA data for: 1. HPV test and VIA, and 2. HPV test and cytology.

[b] We used QUADAS to assess risk of bias. Half of studies only performed one biopsy of an abnormal lesion and had unclear blinding of tests. This was downgraded one level in the context of other factors, in particular indirectness.

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Outcomes	Events in the screen-and-treat strategies for patient-important outcomes (numbers presented per 1 000 000 patients)						
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Mortality from cervical cancer[1]	91	99	99	81	88	88	250
Cervical cancer incidence[2]	128	138	138	113	124	124	350
CIN2+ recurrence[3]	4905	5311	5311	4328	4762	4762	13 400
Undetected CIN2+ (FN)	7000			6000			–
Major bleeding[4]	222	58	9	120	32	5	0
Premature delivery[5]	531	511	516	517	506	509	500
Infertility[6]	–	–	–	–	–	–	–
Major infections[7]	23	33	3	12	18	2	0
Minor infections[8]	242	156	167	131	84	91	0
Unnecessarily treated (FP)	13 000			0			–
Cancer found at first-time screening[9]	3168			3545			0

Footnotes:

The colours in the table: In each GRADE evidence table, colour-coding is used to highlight the 'desirability' of the effects for that outcome relative to other outcomes. The continuum runs from dark gray (desirable) through light gray and light pink to dark pink (least desirable).

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- Cytology (ASCUS): Pooled sensitivity 70% (95% CI: 57 to 81), pooled specificity 95% (95% CI: 92 to 97)
- The overall QoE for each of these outcomes is very low ⊕⊖⊖⊖. Our lack of confidence in these effect estimates stems mainly from very low-quality evidence for treatment effects and natural progression/history data.

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[3] We assume no CIN2+ in TN and FP. Our calculations in the model are based on 70% natural persistence of CIN2+ with no treatment (30% regression) in FN. The incidence of cervical cancer and mortality are also subtracted from the CIN2+ in FN (see above for calculations). TP are treated and recurrence rates of CIN2+ are 5.3% in cryotherapy and LEEP, and 2.2% in CKC.

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[6] We did not identify any data about the risk of infertility after treatment for CIN2+.

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[8] We assumed minor infection would be 0 in TN and FN as they were not treated. Based on pooled proportions from studies with no independent control, 0.006473 of the population treated with cryotherapy, 0.006027 with LEEP, and 0.009368 with CKC will have minor infection.

[9] Cancers detected at first-time screening calculated from Sankaranarayanan et al. (2005). Numbers for single screening tests were calculated as 'screen-detected' cancers in women who participated in the screening programme; and numbers for tests with colposcopy were calculated as 'screen-detected' plus 'clinically detected' cancers. For a sequence of tests (e.g. HPV test followed by VIA), the greater number of cancers detected between tests was used. No cancers would be found in the 'no screen' group. This is not the annual incidence of cervical cancer (which is shown in a row above). It represents the cumulative rate of cancer development before screening started (i.e. the prevalence of cancer at the time when screening is conducted).

[10] 'No screen' numbers were calculated using the same assumptions above for FN, with the exception of premature delivery which was baseline risk in the population.

3.3 GRADE evidence table for patient-important outcomes following different screen-and-treat strategies by age

	HPV→VIA +/– CKC	HPV→VIA +/– LEEP	HPV→VIA +/– cryo	Cyto→colp biopsy +/– CKC	Cyto→colp biopsy +/– LEEP	Cyto→colp biopsy +/– cryo	No screen[10]
15–39 years[a]							
Mortality from cervical cancer	26	28	28	23	25	25	71
Cervical cancer incidence	37	39	39	32	35	35	100
CIN2+ recurrence	5052	5459	5459	4457	4891	4891	13 829
40–49 years[a]							
Mortality from cervical cancer	170	183	183	150	164	164	464
Cervical cancer incidence	237	256	256	209	229	229	650
CIN2+ recurrence	4728	5134	5134	4174	4608	4608	12 886
50–74 years[a]							
Mortality from cervical cancer	313	338	338	276	303	303	857
Cervical cancer incidence	438	473	473	386	424	424	1200
CIN2+ recurrence	4403	4809	4809	3891	4325	4325	11 943
Complications (same across all groups)							
Major bleeding[4]	222	58	9	120	32	5	0
Premature delivery[5]	531	511	516	517	506	509	500
Infertility[6]	–	–	–	–	–	–	–
Major infections[7]	23	33	3	12	18	2	0
Minor infections[8]	242	156	167	131	84	91	0

Footnotes:

[a] Events were calculated similar to Table 3.2. However, events for cervical cancer are based on incidence of cervical cancer in Eastern Africa of 100/1 000 000 cervical cancers per year in women age 15–39 years; 650 for age 40–49 years; and 1200 for age 50–74 years, provided by WHO (http://globocan.iarc.fr/, accessed 30 October 2012). It is assumed that the recurrence of CIN is constant across age groups but the incidence of cervical cancer and associated mortality increases, thus reducing the overall recurrence of CIN (a proportion of those with CIN will develop cancer or die). These data should be used primarily to make comparisons across screen-and-treat strategies, not within columns for different age groups.

[4,5,6,7,8,10] See footnotes for Table 3.2.

4. References

4.1 References to studies included in meta-analysis of diagnostic test accuracy

Agorastos T et al. Human papillomavirus testing for primary screening in women at low risk of developing cervical cancer. The Greek experience. *Gynecologic Oncology*, 2005, 96(3):714–720.

Belinson J et al. Shanxi Province Cervical Cancer Screening Study: a cross-sectional comparative trial of multiple techniques to detect cervical neoplasia. *Gynecologic Oncology*, 2001, 83(2):439–444.

Bigras G, De Marval F. The probability for a Pap test to be abnormal is directly proportional to HPV viral load: Results from a Swiss study comparing HPV testing and liquid-based cytology to detect cervical cancer precursors in 13 842 women. *British Journal of Cancer*, 2005, 93(5):575–581.

Cardenas-Turanzas M et al. The performance of human papillomavirus high-risk DNA testing in the screening and diagnostic settings. *Cancer Epidemiology Biomarkers and Prevention*, 2008, 17(10):2865–2871.

de Cremoux P et al. Efficiency of the hybrid capture 2 HPV DNA test in cervical cancer screening. A study by the French Society of Clinical Cytology. *American Journal of Clinical Pathology*, 2003, 120(4):492–499.

Depuydt CE et al. BD-ProExC as adjunct molecular marker for improved detection of CIN2+ after HPV primary screening. *Cancer Epidemiology Biomarkers and Prevention*, 2011, 20(4):628–637.

De Vuyst H et al. Comparison of Pap smear, visual inspection with acetic acid, human papillomavirus DNA–PCR testing and cervicography. *International Journal of Gynaecology & Obstetrics*, 2005, 89(2):120–126.Hovland S et al. A comprehensive evaluation of the accuracy of cervical pre-cancer detection methods in a high-risk area in East Congo. *British Journal of Cancer*, 2010, 102(6):957–965.

Mahmud SM et al. Comparison of human papillomavirus testing and cytology for cervical cancer screening in a primary health care setting in the Democratic Republic of the Congo. *Gynecologic Oncology*, 2012, 124(2):286–291.

Monsonego J et al. Evaluation of oncogenic human papillomavirus RNA and DNA tests with liquid-based cytology in primary cervical cancer screening: the FASE study. *International Journal of Cancer*, 2011, 129(3):691–701.

Pan Q et al. A thin-layer, liquid-based Pap test for mass screening in an area of China with a high incidence of cervical carcinoma: a cross-sectional, comparative study. *Acta Cytologica*, 2003, 47(1):45–50.

Petry KU et al. Inclusion of HPV testing in routine cervical cancer screening for women above 29 years in Germany: results for 8466 patients. *British Journal of Cancer*, 2003, 88(10):1570–1577.

Qiao YL et al. A new HPV–DNA test for cervical-cancer screening in developing regions: a cross-sectional study of clinical accuracy in rural China. *Lancet Oncology*, 2008, 9(10):929–936.

Shastri SS et al. Concurrent evaluation of visual, cytological and HPV testing as screening methods for the early detection of cervical neoplasia in Mumbai, India. *Bulletin of the World Health Organization*, 2005, 83(3):186–194.

Sodhani P et al. Test characteristics of various screening modalities for cervical cancer: a feasibility study to develop an alternative strategy for resource-limited settings. Cytopathology, 2006, 17(6):348–352.

4.2 References to studies included for diagnostic test accuracy of colposcopic impression

Belinson J et al. Shanxi Province Cervical Cancer Screening Study: a cross-sectional comparative trial of multiple techniques to detect cervical neoplasia. *Gynecologic Oncology*, 2001, 83(2):439–444.

Cantor SB et al. Accuracy of colposcopy in the diagnostic setting compared with the screening setting. *Obstetrics & Gynecology*, 2008, 111(1):7–14.

Cremer ML et al. Digital assessment of the reproductive tract versus colposcopy for directing biopsies in women with abnormal Pap smears. *Journal of Lower Genital Tract Disease*, 2010, 14(1):5–10.

Cristoforoni PM et al. Computerized colposcopy: results of a pilot study and analysis of its clinical relevance. *Obstetrics & Gynecology*, 1995, 85(6):1011–1016.

Durdi GS et al. Correlation of colposcopy using Reid colposcopic index with histopathology – a prospective study. *Journal of the Turkish German Gynecology Association*, 2009, 10(4):205–207.

Ferris DG, Miller MD. Colposcopic accuracy in a residency training program: defining competency and proficiency. *Journal of Family Practice*, 1993, 36(5):515–520.

Homesley HD, Jobson VW, Reish RL. Use of colposcopically directed, four-quadrant cervical biopsy by the colposcopy trainee. *Journal of Reproductive Medicine*, 1984, 29(5):311–316.

Jones DE et al. Evaluation of the atypical Pap smear. *American Journal of Obstetrics & Gynecology*, 1987, 157(3):544–549.

Kierkegaard O et al. Diagnostic accuracy of cytology and colposcopy in cervical squamous intraepithelial lesions. *Acta Obstetricia et Gynecologica Scandinavica*, 1994, 73(8):648–651.

Mousavi AS et al. A prospective study to evaluate the correlation between Reid colposcopic index impression and biopsy histology. *Journal of Lower Genital Tract Disease*, 2007, 11(3):147–150.

Patil K et al. Comparison of diagnostic efficacy of visual inspection of cervix with acetic acid and Pap smear for prevention of cervical cancer: Is VIA superseding Pap smear? *Journal of SAFOG*, 2011, 3(3):131–134.