# Recommendation 9

**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 an HPV test followed by colposcopy (with or without biopsy) and treat with cryotherapy (or LEEP when not eligible)**
**(conditional recommendation, ⊕⊖⊖⊖ evidence)**

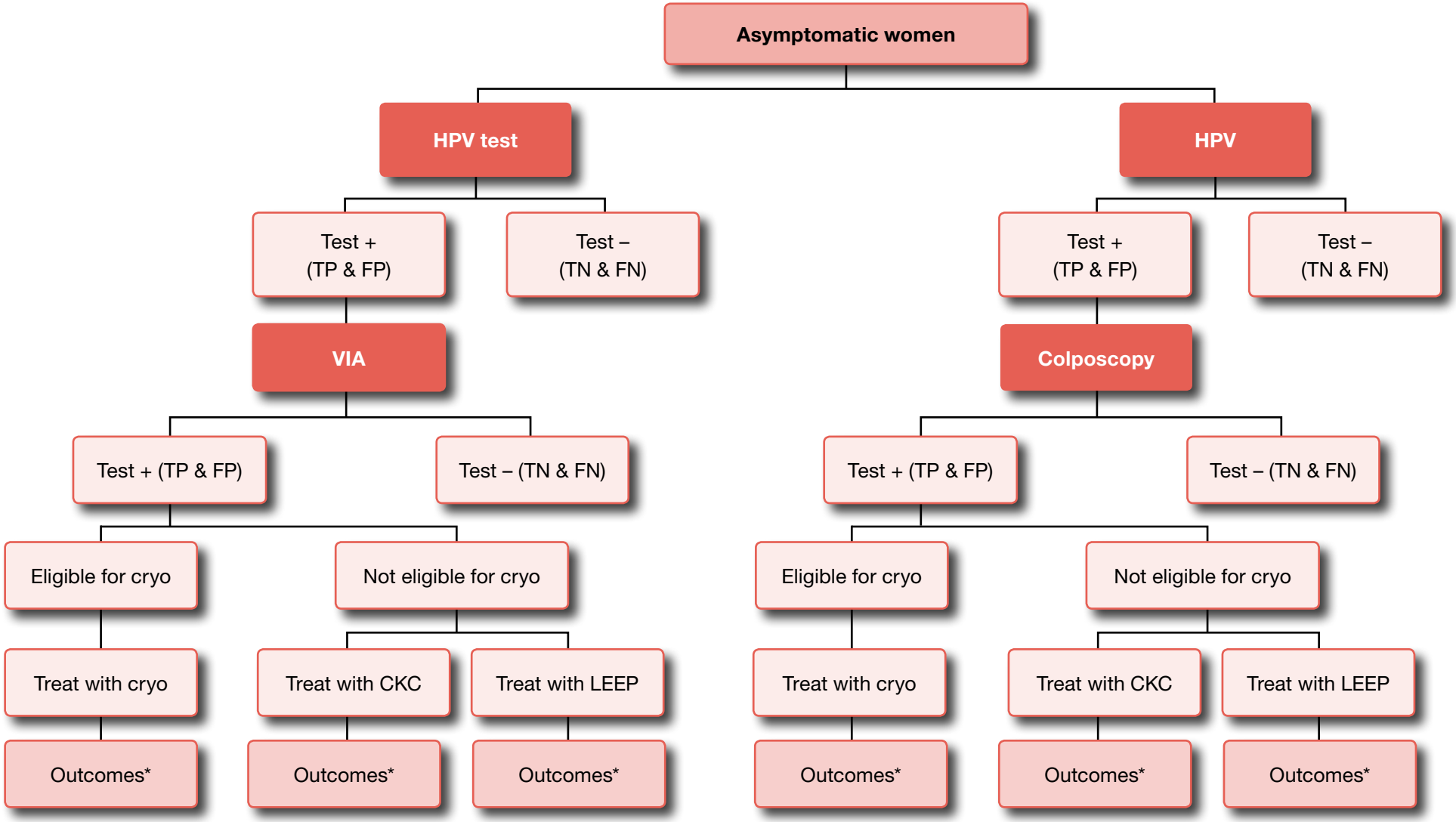
**Remarks:** The reductions in cancer and related mortality of screen-and-treat with an HPV test followed by colposcopy (with or without biopsy) may be slightly greater compared to an HPV test followed by VIA. The panel agreed that the benefits of either strategy outweigh the harms and costs; however, the difference in costs between the strategies is uncertain. There may be more resource implications with colposcopy due to increased training of providers, quality control, waiting time, and the potential for more women to be lost to follow-up. It is also unclear whether women would perceive a difference between VIA and colposcopy; however, a biopsy during colposcopy may be less acceptable than VIA. This recommendation applies to women regardless of HIV status.

## Evidence-to-recommendation table

| Decision domain | Judgement | Summary of reason for judgement |
|---|---|---|
| **Quality of evidence**<br>*Is there high- or moderate-quality evidence?* | Yes ☐ / No ☒ | There is low-quality evidence for the diagnostic test accuracy of both triage tests and a comparison between the strategies. 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. Also the link between test accuracy data and treatment effects is very uncertain. |
| **Balance of benefits versus harms and burdens**<br>*Are you confident that the benefits outweigh the harms and burdens for the recommended strategy?* | Yes ☐ / No ☒ | The benefits of HPV test followed by colposcopy (reduction in CIN recurrence, cervical cancer, and related mortality) may be greater than with HPV test followed by VIA. But there may be greater overtreatment with HPV test followed by colposcopy without biopsy. Little or no difference in cancers detected. |
| **Values and preferences**<br>*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 greater number of women overtreated and potential complications. High value was placed on women finding a biopsy less acceptable than visual inspection. |
| **Resource implications**<br>*Is the cost small relative to the net benefits for the recommended strategy?* | Yes ☐ / No ☒ | There may be greater resource implications by adding colposcopy than with adding VIA to the HPV test due to increased training of providers, quality control, waiting time, and potential for more women lost to follow up. |

# Evidence for an HPV test followed by VIA compared to an HPV test 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 HPV test followed by colposcopic impression

## Diagnostic test accuracy

| | | | | | |
|---|---|---|---|---|---|
| Pooled sensitivity HPV test | 95% (95% CI: 84 to 98) | Pooled sensitivity VIA | 69% (95% CI: 54 to 81) | Pooled sensitivity colposcopic impression | 95% (95% CI: 86 to 98) |
| Pooled specificity HPV test | 84% (95% CI: 72 to 91) | Pooled specificity VIA | 87% (95% CI: 79 to 92) | 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 HPV test followed by 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 | HPV test followed by colposcopic impression | |
| True positives (patients with CIN2+) | 5 studies (8921 patients) | Cross-sectional and cohort studies | Serious[b] | None[c] | Serious[d] | None[e] | Undetected | ⊕⊕⊖⊖ low | 13 | 18 | CRITICAL |
| **TP absolute difference** | | | | | | | | | 5 fewer | | |
| True negatives (patients without CIN2+) | 5 studies (8921 patients) | Cross-sectional and cohort studies | Serious[b] | None[c] | Serious[d] | None[e] | Undetected | ⊕⊕⊖⊖ low | 960 | 889 | CRITICAL |
| **TN absolute difference** | | | | | | | | | 71 more | | |
| False positives (patients incorrectly classified as having CIN2+) | 5 studies (8921 patients) | Cross-sectional and cohort studies | Serious[b] | None[c] | Serious[d] | None[e] | Undetected | ⊕⊕⊖⊖ low | 20 | 91 | CRITICAL |
| **FP absolute difference** | | | | | | | | | 71 fewer | | |
| False negatives (patients incorrectly classified as not having CIN2+) | 5 studies (8921 patients) | Cross-sectional and cohort studies | Serious[b] | None[c] | Serious[d] | None[e] | Undetected | ⊕⊕⊖⊖ low | 7 | 2 | CRITICAL |
| **FN absolute difference** | | | | | | | | | 5 more | | |

**Footnotes:**

[a] This is the number of studies that assessed DTA data for HPV test and VIA.

[b] We used QUADAS to assess risk of bias. Many studies only performed one biopsy of an abnormal lesion. 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 for HPV test followed by colposcopic impression were calculated based on sensitivity and specificity of the two tests. Direct data were not available.

[d] Estimates of HPV test and VIA sensitivity and specificity were variable despite similar cut-off values; inconsistency could not be explained by quality of studies. This was downgraded. This judgement was considered in the context of other factors, in particular imprecision.

[e] Wide CI for HPV test sensitivity and VIA specificity, 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 HPV test followed by 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 | HPV→colp imp +/– CKC | HPV→colp imp +/–LEEP | HPV→colp imp +/– cryo | No screen[10] |
| **Mortality from cervical cancer**[1] | 91 | 99 | 99 | 31 | 41 | 42 | 250 |
| **Cervical cancer incidence**[2] | 128 | 138 | 138 | 44 | 58 | 58 | 350 |
| **CIN2+ recurrence**[3] | 4905 | 5311 | 5311 | 1704 | 2263 | 2263 | 13 400 |
| **Undetected CIN2+ (FN)** | 7000 | | | 2000 | | | |
| **Major bleeding**[4] | 288 | 76 | 11 | 937 | 246 | 37 | 0 |
| **Premature delivery**[5] | 540 | 514 | 521 | 631 | 546 | 568 | 500 |
| **Infertility**[6] | – | – | – | – | – | – | – |
| **Major infections**[7] | 30 | 43 | 5 | 97 | 140 | 15 | 0 |
| **Minor infections**[8] | 314 | 202 | 217 | 1022 | 658 | 706 | 0 |
| **Unnecessarily treated (FP)** | 20 000 | | | 91 000 | | | – |
| **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).

*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)
- HPV test: pooled sensitivity 95% (95% CI: 84 to 98), pooled specificity 84% (95% CI: 72 to 91)
- 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 | HPV→colp imp +/– CKC | HPV→colp imp +/– LEEP | HPV→colp imp +/– cryo | No screen[10] |
|---|---|---|---|---|---|---|---|
| **15–39 years[a]** | | | | | | | |
| **Mortality from cervical cancer** | 26 | 28 | 28 | 9 | 12 | 12 | 71 |
| **Cervical cancer incidence** | 37 | 39 | 39 | 13 | 17 | 17 | 100 |
| **CIN2+ recurrence** | 5052 | 5459 | 5459 | 1745 | 2305 | 2305 | 13 829 |
| **40–49 years[a]** | | | | | | | |
| **Mortality from cervical cancer** | 170 | 183 | 183 | 58 | 77 | 77 | 464 |
| **Cervical cancer incidence** | 237 | 256 | 256 | 82 | 108 | 108 | 650 |
| **CIN2+ recurrence** | 4728 | 5134 | 5134 | 1653 | 2213 | 2213 | 12 886 |
| **50–74 years[a]** | | | | | | | |
| **Mortality from cervical cancer** | 313 | 338 | 338 | 108 | 142 | 142 | 857 |
| **Cervical cancer incidence** | 438 | 473 | 473 | 151 | 199 | 199 | 1200 |
| **CIN2+ recurrence** | 4403 | 4809 | 4809 | 1562 | 2121 | 2121 | 11 943 |
| **Complications (same across all groups)** | | | | | | | |
| **Major bleeding[4]** | 288 | 76 | 11 | 937 | 246 | 37 | 0 |
| **Premature delivery[5]** | 540 | 514 | 521 | 631 | 546 | 568 | 500 |
| **Infertility[6]** | – | – | – | – | – | – | – |
| **Major infections[7]** | 30 | 43 | 5 | 97 | 140 | 15 | 0 |
| **Minor infections[8]** | 314 | 202 | 217 | 1022 | 658 | 706 | 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 HPV test followed by colposcopy with biopsy

## Diagnostic test accuracy

| | | | |
|---|---|---|---|
| Pooled sensitivity HPV test | 95% (95% CI: 84 to 98) | Pooled sensitivity VIA | 69% (95% CI: 54 to 81) |
| Pooled specificity HPV test | 84% (95% CI: 72 to 91) | Pooled specificity VIA | 87% (95% CI: 79 to 92) |

(Reference standard: colposcopy with biopsy when indicated)

## 3.1 Diagnostic test accuracy (DTA) evidence profile: HPV test followed by VIA vs HPV test followed by colposcopy with biopsy

| 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 | HPV test followed by colposcopy with biopsy | |
| True positives (patients with CIN2+) | 5 studies (8921 patients) | Cross-sectional and cohort studies | Serious[b] | None[c] | Serious[d] | None[e] | Undetected | ⊕⊕⊖⊖ low | 13 | 19 | CRITICAL |
| **TP absolute difference** | | | | | | | | | 6 fewer | | |
| True negatives (patients without CIN2+) | 5 studies (8921 patients) | Cross-sectional and cohort studies | Serious[b] | None[c] | Serious[d] | None[e] | Undetected | ⊕⊕⊖⊖ low | 960 | 980 | CRITICAL |
| **TN absolute difference** | | | | | | | | | 20 fewer | | |
| False positives (patients incorrectly classified as having CIN2+) | 5 studies (8921 patients) | Cross-sectional and cohort studies | Serious[b] | None[c] | Serious[d] | None[e] | Undetected | ⊕⊕⊖⊖ low | 20 | 0 | CRITICAL |
| **FP absolute difference** | | | | | | | | | 20 more | | |
| False negatives (patients incorrectly classified as not having CIN2+) | 5 studies (8921 patients) | Cross-sectional and cohort studies | Serious[b] | None[c] | Serious[d] | None[e] | Undetected | ⊕⊕⊖⊖ low | 7 | 1 | CRITICAL |
| **FN absolute difference** | | | | | | | | | 6 more | | |

**Footnotes:**

[a] This is the number of studies that assessed DTA data for HPV test and VIA.

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

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

[d] Estimates of HPV test and VIA sensitivity and specificity were variable despite similar cut-off values; inconsistency could not be explained by quality of studies. This was downgraded. This judgement was considered in the context of other factors, in particular imprecision.

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

## 3.2 GRADE evidence table for patient-important outcomes following different screen-and-treat strategies: HPV test followed by VIA compared to HPV test followed by colposcopy with biopsy

| 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 | HPV→colp biopsy +/– CKC | HPV→colp biopsy +/–LEEP | HPV→colp biopsy +/– cryo | No screen[10] |
| **Mortality from cervical cancer**[1] | 91 | 99 | 99 | 20 | 30 | 31 | 250 |
| **Cervical cancer incidence**[2] | 128 | 138 | 138 | 28 | 43 | 43 | 350 |
| **CIN2+ recurrence**[3] | 4905 | 5311 | 5311 | 1088 | 1677 | 1677 | 13 400 |
| **Undetected CIN2+ (FN)** | 7000 | | | 1000 | | | |
| **Major bleeding**[4] | 288 | 76 | 11 | 163 | 43 | 6 | 0 |
| **Premature delivery**[5] | 540 | 514 | 521 | 523 | 508 | 512 | 500 |
| **Infertility**[6] | – | – | – | – | – | – | – |
| **Major infections**[7] | 30 | 43 | 5 | 17 | 24 | 3 | 0 |
| **Minor infections**[8] | 314 | 202 | 217 | 178 | 115 | 123 | 0 |
| **Unnecessarily treated (FP)** | 20 000 | | | 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).

*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)
- HPV test: pooled sensitivity 95% (95% CI: 84 to 98), pooled specificity 84% (95% CI: 72 to 91)
- 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.

## 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 | HPV→colp biopsy +/– CKC | HPV→colp biopsy +/–LEEP | HPV→colp biopsy +/– cryo | No screen[10] |
|---|---|---|---|---|---|---|---|
| **15–39 years[a]** | | | | | | | |
| **Mortality from cervical cancer** | 26 | 28 | 28 | 6 | 9 | 9 | 71 |
| **Cervical cancer incidence** | 37 | 39 | 39 | 8 | 12 | 12 | 100 |
| **CIN2+ recurrence** | 5052 | 5459 | 5459 | 1109 | 1698 | 1698 | 13 829 |
| **40–49 years[a]** | | | | | | | |
| **Mortality from cervical cancer** | 170 | 183 | 183 | 37 | 57 | 57 | 464 |
| **Cervical cancer incidence** | 237 | 256 | 256 | 52 | 79 | 79 | 650 |
| **CIN2+ recurrence** | 4728 | 5134 | 5134 | 1062 | 1651 | 1651 | 12 886 |
| **50–74 years[a]** | | | | | | | |
| **Mortality from cervical cancer** | 313 | 338 | 338 | 68 | 105 | 105 | 857 |
| **Cervical cancer incidence** | 438 | 473 | 473 | 96 | 146 | 146 | 1200 |
| **CIN2+ recurrence** | 4403 | 4809 | 4809 | 1015 | 1604 | 1604 | 11 943 |
| **Complications (same across all groups)** | | | | | | | |
| **Major bleeding[4]** | 288 | 76 | 11 | 163 | 43 | 6 | 0 |
| **Premature delivery[5]** | 540 | 514 | 521 | 523 | 508 | 512 | 500 |
| **Infertility[6]** | – | – | – | – | – | – | – |
| **Major infections[7]** | 30 | 43 | 5 | 17 | 24 | 3 | 0 |
| **Minor infections[8]** | 314 | 202 | 217 | 178 | 115 | 123 | 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

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.

De Vuyst H et al. Comparison of Pap smear, visual inspection with acetic acid, human papillomavirus DNA–PCR testing and cervicography. *International Journal of Gynecology & Obstetrics*, 2005, 89(2):120–126.

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.

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 Obstetric 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.