

# Minimale dataset colposcopie

Deel 1: inventarisatie  
richtlijnen en standaarden

Deel 2: systematische  
review colposcopie  
indicatoren

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## Lijst met gebruikte afkortingen

|       |  |
|-------|--|
| ASCCP | American Society for Colposcopy and Cervical Pathology                           |
| CIN   | Cervical Intraepithelial Neoplasia (intra-epitheliale afwijkingen van de cervix) |
| EFC   | European Federation for Colposcopy   |
| HPV   | Humaan papilloma virus   |
| IFCPC | International Federation for Cervical Pathology and Colposcopy                   |
| NEATS | National Guideline Clearinghouse Extent of Adherence to Trustworthy Standards    |
| SCJ   | Squamocolumnar junction (grens tussen plaveisel- en cilinderepitheel)            |
| VIA   | Visuele inspectie met azijnzuur  |
| VILI  | Visuele inspectie met lugol  |

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## Inleiding

In het kader van het programma Zinnige Zorg heeft Zorginstituut Nederland een systematische werkwijze ontwikkeld om de zorg die uit het verzekerde basispakket wordt vergoed, door te lichten. Het uiteindelijke doel hiervan is te beoordelen of diagnostiek en behandelingen op een patiëntgerichte, effectieve en doelmatige manier worden ingezet. Het Zorginstituut gaat daarbij uit van het patiëntenperspectief, de opvattingen van goede zorg zoals weergegeven in richtlijnen of blijkend uit wetenschappelijk onderzoek, en betrokkenheid van relevante partijen gedurende het gehele traject.

Dit heeft geleid tot het verbeter signalement Baarmoederhalsafwijking CIN d.d. 24 september 2019 (1). Aanleiding voor het huidige project is verbeterafpraak 2 uit dit verbeter signalement: “De betrokken partijen gaan onderzoeken op welke wijze colposcopiedata uniform geregistreerd kan worden en wat de financiële consequenties hiervan zijn. Ook zal onderzocht worden of een koppeling met de PALGA [Pathologisch-Anatomisch Landelijk Geautomatiseerd Archief]-databank (technisch en praktisch) haalbaar is.”

Uniforme registratie van colposcopiebevindingen zal beter zicht geven op ongewenste praktijkvariatie die niet verklaard kan worden door variatie in kenmerken (*casemix*) en voorkeuren van patiënten. Ook kunnen verbeteracties ondernomen worden die leiden tot vermindering van ongewenste praktijkvariatie, overdiagnose en overbehandeling. Het uiteindelijke doel is het voorkomen van een directe behandeling (*see and treat*) bij vrouwen met een licht afwijkend uitstrijkje.

Dit heeft geleid tot de volgende onderzoeksvraag: “Welke ongeveer vijf colposcopie indicatoren geven (op zichzelf of in combinatie) de beste voorspelling van de uitslag van het op de colposcopie volgend histologisch onderzoek van het biopt en/of de liexcisie?”. Hierbij zal, indien mogelijk, onderscheid worden gemaakt tussen colposcopisch onderzoek in het kader van bevolkingsonderzoek of op indicatie. Om deze onderzoeksvraag te beantwoorden is eerst een inventarisatie gedaan van de aanbevelingen van beroepsverenigingen op het gebied van rapportage van colposcopie (“colposcopie indicatoren”) beschreven in richtlijnen en standaarden. Deel 1 van dit rapport beschrijft de bevindingen van deze inventarisatie. Dit heeft uiteindelijk geleid tot selectie van acht indicatoren waarvan een systematisch overzicht van de literatuur werd gemaakt, en de diagnostische waarde van deze indicatoren werd bepaald. De bevindingen hiervan worden beschreven in deel 2 van dit rapport.

## Deel 1: inventarisatie richtlijnen en standaarden

### 1. Vraagstelling

De vraagstelling van dit deel van het rapport luidt “Welke aanbevelingen op het gebied van de rapportage van colposcopiebevindingen zijn er gedaan in richtlijnen en standaarden betreffende afwijkingen van de cervix (CIN) en cervixcarcinoom?”.

### 2. Methoden

#### 2.1 Identificatie en selectie van relevante onderzoeken

We zochten in de TRIP-database en Google Scholar naar richtlijnen en standaarden met betrekking tot de rapportage van colposcopiebevindingen en we beperkten ons hierbij tot richtlijnen en standaarden verschenen tussen 1 Januari 2010 en 8 januari 2021. De zoekstrategieën zijn weergegeven in Bijlage 1. Daarnaast werden de websites van de volgende beroepsverenigingen doorzocht: de Nederlandse Vereniging voor Obstetrie en Gynaecologie (NVOG), oncoline.nl, de Scottish Obstetrics and Gynaecology Society, de Society of Obstetricians and Gynaecologists of Canada (SOGC), de National Institute for Health and Care Excellence (NICE), de Royal Australian and New Zealand College of Obstetricians and Gynaecologists, de American Society for Colposcopy and Cervical Pathology (ASCCP) en de International Federation for Cervical Pathology and Colposcopy (IFCPC).

Criteria werden geformuleerd voor de in- en exclusie van richtlijnen en standaarden op het gebied van colposcopie. We includeerden richtlijnen en standaarden geschreven in het Engels of Nederlands, waarin aanbevelingen werden gedaan op het gebied van de rapportage van colposcopiebevindingen bij patiënten verdacht van afwijkingen van de cervix (CIN) en cervixcarcinoom. Zowel richtlijnen voor colposcopie naar aanleiding van een screeningsuitslag, als richtlijnen voor colposcopie op indicatie werden ingesloten. Richtlijnen en standaarden die enkel naar colposcopierapportage beschreven in een andere richtlijn of standaard verwezen, zonder zelf nieuwe of aangepaste criteria voor te stellen, werden geïdentificeerd en in een overzicht gepresenteerd, maar werden niet nader uitgewerkt. Selectie van richtlijnen en standaarden vond plaats door twee onderzoekers onafhankelijk van elkaar. Beoordeling van relevantie van richtlijnen en standaarden uit Google Scholar werden eerst gedaan op basis van titel en abstract en vervolgens op basis van het volledige artikel. De resultaten uit de TRIP-database werden direct op basis van het volledige artikel beoordeeld op relevantie.

#### 2.2 Data-extractie en analyses

De kwaliteit van de geselecteerde richtlijnen en standaarden werd beoordeeld met het NEATS-instrument (2). We verzamelden beschrijvende gegevens over de methodologie die de richtlijnen hanteerden voor het verkrijgen van het bewijs dat ten grondslag lag aan de aanbevelingen (de zoekstrategie), het beoordelen van het bewijs (level of evidence) en het formuleren van aanbevelingen. Daarnaast werden details betreffende de aanbevelingen op gebied van rapportage van colposcopiebevindingen verzameld, inclusief de definitie van de indicator, de manier waarop gegevens gerapporteerd dienen te worden (bijvoorbeeld als vrije tekst of als ja/nee), of de indicator

gekozen is op basis van bewijs of consensus, wat het niveau van bewijs is en welk bewijs ten grondslag ligt aan de indicator.

De beoordeling van de methodologische kwaliteit en de extractie van de gegevens werden uitgevoerd door twee onderzoekers onafhankelijk van elkaar. Verschillen tussen twee beoordelaars werden bediscussieerd. In geval geen overeenstemming bereikt werd, werd een derde onderzoeker ingeschakeld, wiens/wier oordeel leidend was. Vervolgens werden de colposcopie-indicatoren en wetenschappelijke onderbouwingen zoals beschreven in de geselecteerde richtlijnen en standaarden, met elkaar vergeleken.

Tenslotte werden de indicatoren in het overzicht geclusterd op basis van frequentie (beschreven in minstens 3 richtlijnen vs. in minder dan 3 richtlijnen beschreven) en tijdens een online bijeenkomst gepresenteerd aan een klankbordgroep van vier medisch specialisten (een gynaecoloog, een gynaecoloog-oncoloog, een gynaecoloog in opleiding en een patholoog). De deelnemers van de klankbordgroep zijn door de opdrachtgever (het Zorginstituut) uitgenodigd op basis van hun kennis en expertise. De bijeenkomst werd geleid door het Zorginstituut, waarbij advies werd ingewonnen om tot een consensus-based selectie van acht tot tien indicatoren te komen die verder uitgewerkt zullen worden in Deel 2 van het project 'Minimale dataset colposcopie'. Op basis van dit advies selecteerde het Zorginstituut in overleg met Cochrane Netherlands de indicatoren die vervolgens ter goedkeuring werden voorgelegd aan de klankbordgroep en definitief werden vastgesteld.

### 3. Resultaten

#### 3.1 Selectie van onderzoeken

In totaal werden 335 potentieel relevante referenties gevonden (Bijlage 2). Nadat referenties van voor 2010 geëxcludeerd waren, bleven er 260 over. De referenties geïdentificeerd via Google Scholar werden eerst gescreend op basis van titel en/of abstract, en hiervan werden er 90 uitgesloten. Van de overige referenties, alsmede alle referenties geïdentificeerd via de TRIP-database en referenties gevonden d.m.v. het handmatig doorzoeken van relevante websites, werd het volledige artikel bekeken. Hierbij werden zes relevante richtlijnen en standaarden gevonden die allen werden ingesloten. De belangrijkste uitgesloten artikelen en de redenen voor exclusie staan samengevat in Bijlage 3.

De zes geselecteerde referenties omvatten vijf standaarden van beroepsverenigingen, namelijk de colposcopieterminologie van de International Federation for Cervical Pathology and Colposcopy (IFCPC) uit 2011 (3), de prestatiestandaarden colposcopie van de European Federation for Colposcopy (EFC) uit 2017 (4) en drie colposcopiestandaarden van de American Society for Colposcopy and Cervical Pathology (ASCCP) gepubliceerd in 2017 (5-7). Daarnaast werd de Nederlandse richtlijn CIN, AIS en VAIN uit 2015 geselecteerd (8). Deze richtlijn wordt op het moment van schrijven herzien en geactualiseerd, maar deze herziening is nog onder embargo en kan derhalve niet gebruikt worden voor de onderhavige analyse.

In totaal werden zeven referenties uitgesloten, omdat zij aanbevelen de colposcopie te rapporteren volgens eerder gepubliceerde richtlijnen en standaarden zonder zelf nieuwe criteria te ontwikkelen. Al deze zeven referenties verwezen naar de IFCPC standard (Tabel 1).



**Tabel 1: Referenties die geen rapportagecriteria voor indicatoren ontwikkelden, maar wel refereerden naar andere standaarden voor rapportage bij colposcopie**

| Society / Author, year   | Title  | Reference to   |
|--|--|----------------|
| Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2020 (9) | Cervical cancer screening in Australia and New Zealand   | IFCPC Standard |
| Public Health England, 2020 (10)   | Cervical screening: programme and colposcopy management  | IFCPC Standard |
| Society of Obstetricians and Gynaecologists of Canada, 2012 (11)                       | Colposcopic Management of Abnormal Cervical Cytology and Histology   | IFCPC Standard |
| Cancer Council Australia, 2016 (12)  | Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding   | IFCPC Standard |
| Bentley, 2012 (13)   | SOGC Joint Clinical Practice Guideline. Colposcopic Management of Abnormal Cervical Cytology and Histology   | IFCPC Standard |
| Jeronimo, 2017 (14)  | Secondary Prevention of Cervical Cancer: ASCO Resource-Stratified Clinical Practice Guideline  | IFCPC Standard |
| Reich, 2018 (15)   | Joint Guideline of the OEGGG, AGO, AGK and OGZ on the Diagnosis and Treatment of Cervical Intraepithelial Neoplasia and Appropriate Procedures When Cytological Specimens Are Unsatisfactory | IFCPC Standard |

### 3.2 NEATS beoordelingen van de geselecteerde richtlijnen en standaarden

Een overzicht van de zes richtlijnen en standaarden en de methodologie die ze hanteerden, is weergegeven in Tabel 2. In Tabel 3 is een overzicht gepresenteerd van de kwaliteit van de richtlijnen, beoordeeld met het NEATS-instrument. De details van de NEATS-beoordelingen per richtlijn of standaard zijn te vinden in Bijlage 4.

In alle richtlijnen, met uitzondering van de Nederlandse richtlijn en de EFC-standaard, werd de bron van financiering beschreven. In de standaarden van de ASCCP werd beschreven dat een deel van de richtlijnwerkgroep financiering ontving van farmaceutische bedrijven, echter was onduidelijk hoe daarmee omgegaan is binnen het richtlijnontwikkelingsproces. De richtlijnwerkgroepen bestonden alle geheel uit clinici, met uitzondering van de werkgroep van de Nederlandse richtlijn waarin drie patiënten en een wetenschappelijk onderzoeker betrokken werden. De manier waarop het patiëntenperspectief meegenomen was bij de ontwikkeling van de richtlijn verschilde tussen de richtlijnen. Bij de Nederlandse richtlijn werden patiënten dus betrokken in de werkgroep en daarnaast namen patiëntenverenigingen deel aan de commentaarronde op de conceptrichtlijn. Bij de ASCCP-standaarden werd een conceptrichtlijn op een openbare website gepubliceerd zodat commentaar gegeven kon worden zonder daarbij actief patiënten te benaderen. In de IFCPC- en de EFC-standaarden werd niet beschreven of en hoe het patiëntenperspectief meegenomen was. Een systematische zoekstrategie uitgevoerd in 2016 lag ten grondslag aan de drie ASCCP-standaarden, de overige drie richtlijnen waren gebaseerd op expert opinie. In geen van de richtlijnen werd een niveau van bewijs toegekend en ook de stap van bewijs naar aanbeveling werd niet

systematisch uitgevoerd. In de Nederlandse richtlijn werden aanbevelingen gevormd op basis van een zogenoemde *consensus-based* methodiek waarbij bewijs door de experts zelf verzameld en verwerkt is. Bij de drie ASCCP-standaarden werden aanbevelingen gebaseerd op expert-opinie en het systematisch verzamelde bewijs. In de IFCPC- en EFC-standaarden werd dit proces niet beschreven. Slechts in één ASCCP-standaard werd elke aanbeveling ondersteund met bewijs (6). Daarnaast werden in de Nederlandse richtlijn, de IFCPC-standaard en de EFC-standaard enkele aanbevelingen ondersteund met bewijs. Alle richtlijnen scoorden redelijk goed op specificiteit en ondubbelzinnigheid van aanbevelingen. Een plan voor het updaten van de richtlijn werd geen enkele keer beschreven.

**Tabel 2: Toegepaste methoden in de geselecteerde richtlijnen**

| Reference  | Country     | Search strategy  | Level of evidence | Formulation of recommendations  |
|--|-------------|--|-------------------|---|
| Bornstein 2012. International Federation for Cervical Pathology and Colposcopy (IFCPC) (3)               | Global      | No systematic search conducted   | Not applicable    | Consensus based recommendations guided by a narrative review of evidence.   |
| Richtlijn CIN, AIS en VAIN 2015. Nederlandse Vereniging voor Obstetrie en Gynaecologie (NVOG) <b>(8)</b> | Netherlands | No systematic search conducted   | Not applicable    | Consensus based recommendations guided by a narrative review of evidence.   |
| Khan 2017. American Society for Colposcopy and Cervical Pathology (ASCCP) (5)                            | USA         | PubMed was searched in June 2016, restricted to English language.                        | Not applicable    | Recommendations were developed based on the abstracted evidence and expert consensus.   |
| Mayeaux 2017. American Society for Colposcopy and Cervical Pathology (ASCCP) (6)                         | USA         | PubMed and guidelines were searched in July 2016. No language restrictions were applied. | Not applicable    | The working group considered all of the indicators in the identified international guidelines as well as recommendations of the other working groups. When there was no evidence to support a recommendation and international guidelines varied, criteria were selected based on expert opinion. |
| Waxman 2017. American Society for Colposcopy and Cervical Pathology (ASCCP) (7)                          | USA         | PubMed and reference lists were searched in June 2016, restricted to English language.   | Not applicable    | Recommendations were developed based on the abstracted evidence and expert consensus.   |
| Petry 2018. European Federation for Colposcopy (EFC) (4)   | Europe      | No systematic search conducted   | Not applicable    | Not described.  |

Tabel 3: NEATS beoordelingen van de geselecteerde richtlijnen en standaarden

|  | 1. Disclosure of guideline funding source | 2. Disclosure and management of financial conflicts of interests | 3a. GDG composition: multidisciplinary | 3b. GDG composition: methodologist | 4. Patient and public perspectives | 5a. Use of a systematic review of evidence – the search strategy | 5b. Use of a systematic review of evidence – the study selection | 5c. Use of a systematic review of evidence – the synthesis of evidence | 6. Grading or rating the quality or strength of evidence | 7. Benefits and harms of recommendations | 8. Evidence summary supporting recommendations | 9. Rating the strength of recommendations | 10. Specific and unambiguous articulation of recommendations | 11. External review | 12. Updating |
|--|---|--|--|------------------------------------|------------------------------------|--|--|--|--|--|--|---|--|---------------------|--------------|
| Bornstein 2012 IFPCP (3)                 | Y   | 5  | U                                      | N                                  | 1                                  | 1  | 1  | 2  | 1  | 1  | 2  | 1   | 4  | 1                   | 2            |
| Richtlijn CIN, AIS en VAIN 2015 NVOG (8) | N   | 5  | Y                                      | Y                                  | 5                                  | 1  | 1  | 1  | 2  | 1  | 1  | 3   | 3  | 5                   | 1            |
| Khan 2017 ASCCP (5)                      | Y   | 3  | N                                      | N                                  | 3                                  | 5  | 1  | 1  | 1  | 1  | 1  | 1   | 4  | 4                   | 1            |
| Mayeaux 2017 ASCCP (6)                   | Y   | 3  | Y                                      | N                                  | 1                                  | 5  | 4  | 5  | 1  | 1  | 4  | 1   | 4  | 3                   | 1            |
| Waxman 2017 ASCCP (7)                    | Y   | 3  | N                                      | N                                  | 3                                  | 4  | 1  | 1  | 1  | 1  | 1  | 1   | 4  | 4                   | 1            |
| Petry 2018 EFC (4)                       | Y   | 1  | U                                      | N                                  | 1                                  | 1  | 1  | 1  | 1  | 1  | 3  | 1   | 4  | 1                   | 2            |

GDG: Guideline development group; CPG: clinical practice guideline; N: No; U: Unknown; Y: Yes. The assessment of some items is on a scale from 1 to 5 where 1 indicates lowest adherence and 5 highest adherence.

### 3.3 Colposcopierapportage volgens de geselecteerde richtlijnen en standaarden

Een overzicht van alle in de geselecteerde richtlijnen en standaarden genoemde indicatoren is gepresenteerd in Tabel 4. In totaal werden 109 aanbevelingen gedaan op het gebied van rapportage die wij hebben ingedeeld in 46 indicatoren. De volgende acht indicatoren werden in drie of meer richtlijnen en standaarden genoemd en zullen in meer detail worden besproken: zichtbaarheid van de cervix, zichtbaarheid van de transformatiezone, colposcopische impressie, een tekening of foto van de bevindingen, azijnzuurwitte afwijkingen, locatie van een eventuele laesie, grootte van de laesie en zichtbaarheid van de laesie. Vervolgens beschrijven we de indicatoren die slechts door één of twee standaarden genoemd werden, maar wel naar onderliggende evidence verwijzen.

#### *Indicatoren in drie of meer richtlijnen en standaarden genoemd*

De zichtbaarheid van de cervix werd genoemd als indicator in de drie ASCCP-standaarden (5-7). In alle drie de standaarden wordt aanbevolen om deze te rapporteren als volledig zichtbaar of niet volledig zichtbaar. In één standaard (6) werd deze aanbeveling voorzien van referenties naar richtlijnen van de World Health Organization - International Agency for Research on Cancer (WHO/IARC), National Health Service (NHS) uit Groot-Brittannië en Nieuw-Zeeland (16-18). Echter, na het raadplegen van deze documenten hebben wij geen aanbevelingen voor de rapportage van de indicator 'zichtbaarheid van de cervix' gevonden.

De zichtbaarheid van de transformatiezone werd als indicator genoemd in de drie ASCCP-standaarden, de IFPCP-standaard en de Nederlandse richtlijn (3, 5-8). De aanbeveling was om deze te beschrijven als volledig zichtbaar of niet volledig zichtbaar, of als volledig zichtbaar, gedeeltelijk zichtbaar of niet zichtbaar. In de ASCCP-standaard van Mayeaux et al. (6) werd deze aanbeveling ondersteund met referenties naar een eerdere versie van de EFC-standaard, richtlijnen van de WHO/IARC en uit Nieuw-Zeeland en Duitsland, en een eerder gepubliceerde ASCCP-standaard (16, 18-21). Ook de Nederlandse richtlijn refereert naar een eerdere versie van de EFC-standaard (19). Echter, alleen in deze EFC-standaard en de richtlijnen van de WHO/IARC en uit Nieuw-Zeeland werd daadwerkelijk een aanbeveling over rapportage van de zichtbaarheid van de transformatiezone gedaan. In de ASCCP-standaarden van Khan et al. (5) en Waxman et al. (7) werd deze indicator tevens gemarkeerd als onderdeel van de minimum set indicatoren voor rapportage.

De colposcopische impressie werd genoemd in de drie ASCCP-standaarden en de Nederlandse richtlijn (5-8). In de Nederlandse richtlijn werd geen aanbeveling gedaan over de wijze van rapportage. De ASCCP-standaarden bevelen de volgende vier categorieën aan: normaal/benigne, laaggradig, hooggradig, kanker. Zowel de Nederlandse richtlijn als de ASCCP-standaard van Mayeaux et al. (6) verwijst naar een richtlijn uit Nieuw-Zeeland (18). De ASCCP-standaard verwijst daarnaast ook nog naar de EFC-standaard en richtlijnen van de WHO/IARC en uit Duitsland (16, 19, 20). De EFC-standaard is het enige document waarin we daadwerkelijk een aanbeveling over de rapportage van deze indicator teruggevonden hebben. Ook deze indicator wordt in de ASCCP-standaarden van Khan et al. (5) en Waxman et al. (7) gemarkeerd als onderdeel van de minimum set indicatoren voor rapportage.

In de Nederlandse richtlijn en twee ASCCP-standaarden (Khan et al. en Waxman et al.) wordt aanbevolen een tekening of foto van de bevindingen vast te leggen (5, 7, 8). De Nederlandse richtlijn

verwijst hiervoor naar de richtlijn van de WHO/IARC (16) waarin inderdaad gesuggereerd wordt dat een tekening van nut kan zijn. De ASCCP-standaard van Waxman et al. (7) noemt deze tevens als minimum set voor rapportage.

De rapportage van azijnzuurwitte afwijkingen wordt genoemd in de drie ASCCP-standaarden en in de IFPCP-standaard (3, 5-7). De ASCCP-standaarden beschrijven dat vastgelegd dient te worden of azijnzuurwitte afwijkingen aanwezig waren (ja of nee). De ASCCP-standaard van Khan et al. (5) en de IFPCP-standaard bevelen aan meer details te rapporteren, bijvoorbeeld of de kleuring snel ontstond, snel verdween, en of het een doorschijnende of dichte kleuring was. In de ASCCP-standaard van Mayeaux et al. (6) werd verwezen naar de ASCCP-standaard van Massad et al. (21) en richtlijnen uit Groot-Britannië, Nieuw-Zeeland en Italië (17, 18, 22). In deze documenten werden echter geen aanbevelingen voor rapportage teruggevonden. In de ASCCP-standaarden van Waxman et al. (7) en Khan et al. (5) werd deze indicator genoemd als minimum set voor rapportage.

In de drie ASCCP-standaarden en de IFPCP-standaard wordt aanbevolen de locatie van een eventuele laesie te rapporteren (3, 5-7). In de ASCCP-standaarden van Mayeaux et al. (6) en Waxman et al. (7) wordt niet beschreven hoe dit gerapporteerd dient te worden. De ASCCP- en IFPCP-standaard geven aan dat de klokpositie genoteerd moet worden en of de laesie binnen of buiten de transformatiezone ligt. De ASCCP-standaard van Mayeaux et al. (6) verwijst opnieuw naar de richtlijn uit Nieuw-Zeeland (18) waarin echter geen aanbeveling teruggevonden kon worden. De IFPCP-standaard verwijst naar een onderzoek waarin een associatie tussen de locatie van de laesie (binnen of buiten de transformatie) en de graad van de laesie staat beschreven (23).

De drie ASCCP-standaarden bevelen aan om te rapporteren of de laesie volledig zichtbaar was (5-7). Dit dient gerapporteerd te worden als volledig of niet volledig. De ASCCP-standaard van Mayeaux et al. (6) refereert hiervoor naar richtlijnen van de WHO/IARC en uit Nieuw-Zeeland en Groot-Brittannië (16-18). In deze documenten werden echter geen aanbeveling gevonden over de rapportage van de zichtbaarheid van de laesie.

Twee ASCCP-standaarden (Khan et al. en Waxman et al.) en de IFPCP-standaard bevelen aan de grootte van de laesie te rapporteren (3, 5, 7). De ASCCP-standaard van Waxman et al. (7) geeft geen verdere details over de wijze van rapportage. De ASCCP-standaard van Khan et al. (5) en de IFPCP-standaard beschrijven dat het aantal kwadranten van de cervix en het percentage oppervlak van de transformatiezone vastgelegd dienen te worden. De IFPCP-standaard verwijst naar een primair onderzoek waarin gevonden werd dat de grootte van de laesie geassocieerd is met de histologische graad (24) en naar een primair onderzoek waarin de associatie tussen verschillende types CIN en azijnzuurwitte veranderingen, patroon van bloedvaten en de laesie marge werden bestudeerd (25).

#### *Indicatoren in minder dan drie richtlijnen of standaarden genoemd, maar wel ondersteund met onderliggende evidence*

Vier indicatoren werden slechts door één of twee standaarden genoemd, maar wel ondersteund met bewijs uit primaire onderzoeken. De EFC-standaard beschreef één colposcopie indicator, namelijk classificatie van de transformatie in drie types. Deze aanbeveling werd ondersteund met verwijzingen naar de IFPCP standaard (3), een richtlijn uit Groot-Brittannië (17) en een primair

onderzoek waarin de reproduceerbaarheid van de indeling van de transformatiezone in deze drie types werd bestudeerd (26). In dit laatste onderzoek werd gevonden dat de indeling op vergelijkbare wijze werd gebruikt in drie verschillende colposcopie klinieken, en er werd geconcludeerd dat de indeling reproduceerbaar en bruikbaar is. De IFCCP-standaard refereerde naar drie primaire onderzoeken waarin de voorspellende waarde van de Schiller's test (kleuring met lugol) voor de histologische bevindingen (maligne of niet-maligne) werd bestudeerd (27-29). Daarnaast werd gerefereerd naar onderzoeken waarin de voorspellende waarde van *Ridge sign* en *Inner border sign* voor type CIN werden beschreven (30, 31). Ook werd het onderzoek van Hammes et al. aangehaald ter ondersteuning van de aanbeveling met betrekking tot leukoplakia (23). In dit onderzoek werd de voorspellende waarde van leukoplakia (aangemerkt als '*miscellaneous*') voor een laesie ongeacht het type (laaggradig, hooggradig, carcinoom) en voor een hooggradige laesie of carcinoom onderzocht.

#### *Overige indicatoren*

De meerderheid van de overige indicatoren (21 van de 34) werd genoemd in zowel de IFCCP-standaard uit 2011 (3) als de ASCCP-standaard uit 2017 van Khan et al. (5). Er blijkt veel inhoudelijke overlap te zijn tussen deze twee standaarden. Details over deze indicatoren en de aanbevolen manier van rapportage zijn te vinden in Tabel 4.

#### *Selectie van indicatoren voor Deel 2*

Na overleg met klinisch experts werd een selectie gemaakt van indicatoren die uitwerkt zullen worden in Deel 2 van het project. De volgende indicatoren werden geselecteerd: colposcopische impressie (eventueel bepaald met een risicoscore), azijnzuurwitte afwijkingen, locatie van de laesie, grootte van de laesie, zichtbaarheid van de transformatiezone, lugol kleuring, vasculaire patronen, en oppervlak en begrenzing van de laesie.

**Tabel 4: Overzicht van indicatoren, aanbevolen manier van rapportage bij colposcopie en onderliggende referenties zoals beschreven in de geïdentificeerde richtlijnen en standaarden.**

| Indicator                              | Guideline                                  | Description / definition  | Recommended way of reporting                         | Evidence or consensus based? | Evidence referenced |
|--|--|---|--|------------------------------|---------------------|
| Cervix visibility                      | Khan 2017                                  | Visualization of the cervix   | Fully visualized / Not fully visualized due to       | Unclear                      | None                |
|  | Mayeaux 2017                               | Cervix visibility   | Fully visualized / Not fully visualized              | Evidence                     | (16-18)             |
|  | Waxman 2017                                | Cervix visibility   | Fully visualized / Not fully visualized              | Unclear                      | None                |
| General assessment of the cervix       | Bornstein 2012                             | General assessment of the cervix, eg, cervix obscured by inflammation, bleeding, scar | Adequate / Inadequate                                | Unclear                      | None                |
| SCJ visibility*                        | Khan 2017                                  | Visualization of the SCJ  | Fully visualized / Not fully visualized              | Unclear                      | None                |
|  | Bornstein 2012                             | Squamocolumnar junction visibility  | Completely visible / Partially visible / Not visible | Unclear                      | None                |
|  | Mayeaux 2017                               | Squamo-columnar junction  | Fully visualized / Not fully visualized              | Evidence                     | (16, 18-21)         |
|  | Waxman 2017                                | SCJ visibility  | Fully visualized / Not fully visualized              | Unclear                      | None                |
|  | Werkgroep richtlijn CIN, AIS en VAIN, 2015 | Transformation zone visibility  | Not specified  | Evidence                     | (19)                |
| SCJ visibility - cervical manipulation | Waxman 2017                                | Cervical manipulation needed to completely visualize the SCJ                          | Not specified  | Unclear                      | None                |
| Transformation zone type               | Bornstein 2012                             | Transformation zone   | Types 1, 2, 3  | Unclear                      | None                |
|  | Petry 2018                                 | Cervical colposcopy Transformation zone (TZ)  | Document type (1,2 or 3)                             | Evidence                     | (3, 17, 26)         |
| Colposcopic impression*                | Khan 2017                                  | Colposcopic impression  | Normal, benign / Low grade / High grade / Cancer     | Unclear                      | None                |
|  | Mayeaux 2017                               | Colposcopic impression  | Normal, benign / Low grade / High grade / Cancer     | Evidence                     | (16, 18, 20, 21)    |



| Indicator           | Guideline                                  | Description / definition   | Recommended way of reporting   | Evidence or consensus based? | Evidence referenced |
|---------------------|--|--|--|------------------------------|---------------------|
|                     | Werkgroep richtlijn CIN, AIS en VAIN, 2015 | Colposcopic impression   | Not specified  | Evidence                     | (18)                |
|                     | Waxman 2017                                | Colposcopic impression   | Normal, benign / Low grade / High grade / Cancer   | Unclear                      | None                |
| Diagram             | Khan 2017                                  | Diagram or marked image annotating the findings                                    | Image  | Unclear                      | None                |
|                     | Werkgroep richtlijn CIN, AIS en VAIN, 2015 | Drawing and/or (digital) photograph  | Not specified  | Evidence                     | (16)                |
|                     | Waxman 2017                                | Diagram or photograph annotating the findings                                      | Diagram or photograph  | Unclear                      | None                |
| Acetowhite changes* | Khan 2017                                  | Acetowhite changes: Any degree of whitening after application of 3%–5% acetic acid | Yes / No   | Unclear                      | None                |
|                     | Waxman 2017                                | Acetowhitening present   | Yes / No   | Unclear                      | None                |
|                     | Khan 2017                                  | Acetowhite features  | Thin and translucent / Rapidly fading / Thick and dense / Rapidly appearing and slowly fading / Cuffed crypt (gland) openings / Variegated red and white | Unclear                      | None                |
|                     | Mayeaux 2017                               | Acetowhite lesion  | Yes / No   | Evidence                     | (17, 18, 21, 22)    |
|                     | Bornstein 2012                             | Visual characteristics: Grade 2 (major) Dense acetowhite epithelium                | Not specified  | Unclear                      | None                |
|                     | Bornstein 2012                             | Not specified  | Unclear  | Unclear                      | None                |
|                     | Bornstein 2012                             | Visual characteristics: Grade 1 (minor) Thin acetowhite epithelium                 | Not specified  | Unclear                      | None                |
| Lugol staining*     | Khan 2017                                  | Lugol staining   | Not used / Stained / Partially stained / Nonstained  | Unclear                      | None                |

| Indicator                       | Guideline      | Description / definition  | Recommended way of reporting | Evidence or consensus based? | Evidence referenced |
|---------------------------------|----------------|---|------------------------------|------------------------------|---------------------|
|                                 | Bornstein 2012 | Lugol's staining (Schiller's test)                                    | Stained or nonstained        | Evidence                     | (27-29)             |
| Original squamous epithelium    | Khan 2017      | Original squamous epithelium: mature, atrophic                        | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Original squamous epithelium: mature, atrophic                        | Not specified                | Unclear                      | None                |
| Columnar epithelium             | Khan 2017      | Columnar epithelium   | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Columnar epithelium   | Not specified                | Unclear                      | None                |
| Ectropy/ectropion               | Khan 2017      | Ectropy/ectropion   | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Ectropy/ectropion   | Not specified                | Unclear                      | None                |
| Metaplastic squamous epithelium | Khan 2017      | Metaplastic squamous epithelium                                       | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Metaplastic squamous epithelium                                       | Not specified                | Unclear                      | None                |
| Nabothian cysts                 | Khan 2017      | Nabothian cysts   | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Nabothian cysts   | Not specified                | Unclear                      | None                |
| Crypt openings                  | Khan 2017      | Crypt (gland) openings  | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Crypt (gland) openings  | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Visual characteristics: Grade 2 (major) Cuffed crypt (gland) openings | Not specified                | Unclear                      | None                |
| Deciduous in pregnancy          | Khan 2017      | Deciduous in pregnancy  | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Deciduous in pregnancy  | Not specified                | Unclear                      | None                |
| Presence of lesion              | Khan 2017      | Lesion(s) present (acetowhite or other)                               | Yes / No                     | Unclear                      | None                |
|                                 | Waxman 2017    | Lesion(s) present   | Yes / No                     | Unclear                      | None                |
| Location of lesion*             | Mayeaux 2017   | Location of lesion(s)   | Not specified                | Evidence                     | (18)                |
|                                 | Waxman 2017    | Lesion location   | Not specified                | Unclear                      | None                |
|                                 | Khan 2017      | Location of each lesion: Clock position                               | Not specified                | Unclear                      | None                |
|                                 | Bornstein 2012 | Location of the lesion: by clock position                             | Clock location               | Evidence                     | None                |

| Indicator                    | Guideline      | Description / definition   | Recommended way of reporting                                      | Evidence or consensus based? | Evidence referenced |
|------------------------------|----------------|--|---|------------------------------|---------------------|
|                              | Bornstein 2012 | Location of the lesion: Inside or outside the transformation zone        | Inside or outside   | Evidence                     | (23)                |
|                              | Khan 2017      | Location of each lesion: at the SCJ                                      | Yes / No  | Unclear                      | None                |
| Location of satellite lesion | Khan 2017      | Location of each lesion: Satellite lesion                                | Not specified   | Unclear                      | None                |
| Visualization of lesion      | Khan 2017      | Lesion visualized  | Fully / Not fully   | Unclear                      | None                |
|                              | Mayeaux 2017   | Extent of lesion visualized  | Fully / Partial   | Evidence                     | (16-18)             |
|                              | Waxman 2017    | Extent of lesion(s) visualized   | Fully / Not fully   | Unclear                      | None                |
| Size of lesion*              | Khan 2017      | Size of each lesion: No. quadrants the lesion involves                   | Number  | Unclear                      | None                |
|                              | Bornstein 2012 | Size of the lesion: number of cervical quadrants the lesion covers       | Number  | Evidence                     | (24, 25)            |
|                              | Khan 2017      | Size of each lesion: Percentage of surface area of TZ occupied by lesion | Percentage  | Unclear                      | None                |
|                              | Bornstein 2012 | Size of the lesion: as percentage of cervix                              | Percentage  | Evidence                     | (24, 25)            |
|                              | Waxman 2017    | Lesion size  | Not specified   | Unclear                      | None                |
| Description of lesion        | Waxman 2017    | Lesion description: Color, contour, border, vascular changes             | Not specified   | Unclear                      | None                |
| Vascular patterns*           | Khan 2017      | Vascular patterns  | Fine mosaic / Fine punctation / Coarse mosaic / Coarse punctation | Unclear                      | None                |
|                              | Bornstein 2012 | Visual characteristics: Grade 1 (minor) Fine mosaic                      | Not specified   | Unclear                      | None                |
|                              | Bornstein 2012 | Visual characteristics: Grade 1 (minor) Fine punctation                  | Not specified   | Unclear                      | None                |
|                              | Bornstein 2012 | Visual characteristics: Grade 2 (major) Coarse mosaic                    | Not specified   | Unclear                      | None                |

| Indicator                    | Guideline      | Description / definition  | Recommended way of reporting  | Evidence or consensus based? | Evidence referenced |
|------------------------------|----------------|---|---|------------------------------|---------------------|
|                              | Bornstein 2012 | Visual characteristics: Grade 2 (major)<br>Coarse punctuation           | Not specified   | Unclear                      | None                |
| Atypical vessels             | Khan 2017      | Atypical vessels  | Yes / No  | Unclear                      | None                |
|                              | Bornstein 2012 | Atypical vessels  | Not specified   | Unclear                      | None                |
| Fragile vessels              | Bornstein 2012 | Fragile vessels   | Not specified   | Unclear                      | None                |
| Submucosal branching vessels | Khan 2017      | Submucosal branching vessels  | Not specified   | Unclear                      | None                |
| Border and surface*          | Khan 2017      | Margins/border  | Irregular or geographic contour /<br>Condylomatous, raised, papillary / Flat /<br>Sharp border / Inner border sign (Internal margin) / Ridge sign / Peeling edges | Unclear                      | None                |
|                              | Khan 2017      | Contour: flat   | Yes / No  | Unclear                      | None                |
|                              | Bornstein 2012 | Visual characteristics: Grade 1 (minor)<br>Irregular, geographic border | Not specified   | Unclear                      | None                |
|                              | Bornstein 2012 | Visual characteristics: Grade 2 (major)<br>Sharp border                 | Not specified   | Unclear                      | None                |
|                              | Bornstein 2012 | Visual characteristics: Grade 2 (major)<br>Inner border sign            | Not specified   | Evidence                     | (30)                |
|                              | Bornstein 2012 | Visual characteristics: Grade 2 (major)<br>Ridge sign                   | Not specified   | Evidence                     | (31)                |
|                              | Khan 2017      | Irregular surface   | Yes / No  | Unclear                      | None                |
|                              | Bornstein 2012 | Irregular surface   | Not specified   | Unclear                      | None                |
|                              | Leukoplakia    | Bornstein 2012  | Leukoplakia (keratosis, hyperkeratosis)   | Not specified                | Evidence            |
| Khan 2017                    |                | Leukoplakia   | Yes / No  | Unclear                      | None                |
| Erosion                      | Khan 2017      | Erosion   | Yes / No  | Unclear                      | None                |
|                              | Bornstein 2012 | Erosion   | Not specified   | Unclear                      | None                |
| Contact bleeding             | Khan 2017      | Contact bleeding  | Yes / No  | Unclear                      | None                |

| Indicator                      | Guideline      | Description / definition             | Recommended way of reporting | Evidence or consensus based? | Evidence referenced |
|--------------------------------|----------------|--------------------------------------|------------------------------|------------------------------|---------------------|
| Friable tissue                 | Khan 2017      | Friable tissue                       | Yes / No                     | Unclear                      | None                |
| Fused papillae                 | Khan 2017      | Fused papillae                       | Yes / No                     | Unclear                      | None                |
| Exophytic lesion               | Bornstein 2012 | Exophytic lesion                     | Not specified                | Unclear                      | None                |
|                                | Khan 2017      | Exophytic lesion                     | Yes / No                     | Unclear                      | None                |
| Ulceration                     | Khan 2017      | Ulceration                           | Yes / No                     | Unclear                      | None                |
|                                | Bornstein 2012 | Ulceration                           | Not specified                | Unclear                      | None                |
| Necrosis                       | Khan 2017      | Necrosis                             | Yes / No                     | Unclear                      | None                |
|                                | Bornstein 2012 | Necrosis                             | Not specified                | Unclear                      | None                |
| Tumor or gross neoplasm        | Khan 2017      | Tumor or gross neoplasm              | Yes / No                     | Unclear                      | None                |
|                                | Bornstein 2012 | Tumor or gross neoplasm              | Not specified                | Unclear                      | None                |
| Congenital Transformation Zone | Khan 2017      | Congenital Transformation Zone       | Yes / No                     | Unclear                      | None                |
|                                | Bornstein 2012 | Congenital transformation zone       | Not specified                | Unclear                      | None                |
| Condyloma                      | Bornstein 2012 | Condyloma                            | Not specified                | Unclear                      | None                |
| Polyp                          | Khan 2017      | Polyp (ectocervical or endocervical) | Yes / No                     | Unclear                      | None                |
|                                | Bornstein 2012 | Polyp (ectocervical or endocervical) | Not specified                | Unclear                      | None                |
| Inflammation                   | Khan 2017      | Inflammation                         | Yes / No                     | Unclear                      | None                |
|                                | Bornstein 2012 | Inflammation                         | Not specified                | Unclear                      | None                |
| Stenosis                       | Khan 2017      | Stenosis                             | Yes / No                     | Unclear                      | None                |
|                                | Bornstein 2012 | Stenosis                             | Not specified                | Unclear                      | None                |
| Congenital anomaly             | Bornstein 2012 | Congenital anomaly                   | Not specified                | Unclear                      | None                |
|                                | Khan 2017      | Congenital anomaly                   | Yes / No                     | Unclear                      | None                |
| Posttreatment consequence      | Khan 2017      | Posttreatment consequence (scarring) | Yes / No                     | Unclear                      | None                |
|                                | Bornstein 2012 | Posttreatment consequence            | Not specified                | Unclear                      | None                |
| Endometriosis                  | Bornstein 2012 | Endometriosis                        | Not specified                | Unclear                      | None                |

| Indicator                       | Guideline   | Description / definition                  | Recommended way of reporting | Evidence or consensus based? | Evidence referenced |
|---------------------------------|-------------|---|------------------------------|------------------------------|---------------------|
| Biopsies location               | Waxman 2017 | Biopsies location                         | Not specified                | Unclear                      | None                |
| Method of endocervical sampling | Waxman 2017 | Method of endocervical sampling performed | Curette / Brush / Both       | Unclear                      | None                |

\*Deze indicatoren zijn geselecteerd voor verdere uitwerking in Deel 2 van het project.

## 4. Conclusies

- Vijf standaarden en één richtlijn werden geïdentificeerd waarin aanbevelingen gedaan werden op het gebied van de rapportage van colposcopie.
- Er werden in totaal 109 aanbevelingen gedaan op het gebied van rapportage van colposcopie, die ingedeeld werden in 46 indicatoren.
- Het aantal aanbevelingen dat werd ondersteund met evidence was beperkt.
- Acht indicatoren werden vermeld in drie of meer standaarden of richtlijnen: zichtbaarheid van de cervix, zichtbaarheid van de transformatiezone, colposcopische impressie, een tekening of foto van de bevindingen, azijnzuurwitte afwijkingen, locatie van een eventuele laesie, grootte van de laesie en zichtbaarheid van de laesie.
- De aanbevolen wijze van rapportage voor deze acht indicatoren kwam grotendeels overeen tussen de richtlijnen.
- Vier indicatoren werden in minder dan drie standaarden of richtlijnen genoemd, maar werden wel onderbouwd met evidence in de vorm van primaire studies naar de voorspellende waarde voor histologieresultaten of reproduceerbaarheid.
- De volgende indicatoren zijn geselecteerd voor verdere uitwerking in Deel 2: colposcopische impressie, azijnzuurwitte afwijkingen, locatie van de laesie, grootte van de laesie, zichtbaarheid van de transformatiezone, lugol kleuring, vasculaire patronen, en oppervlak en begrenzing van de laesie.

## Deel 2: systematische review colposcopie indicatoren

### 1. Vraagstelling

#### PICO 1 m.b.t. diagnostiek

**P** = Vrouwen die een colposcopisch onderzoek ondergaan in het kader van bevolkingsonderzoek of op indicatie (exclusie: nacontrole/vervolgtraject)

**I** = Colposcopie indicatoren: colposcopische impressie, azijnzuurwitte afwijkingen, locatie van de laesie, grootte van de laesie, zichtbaarheid van de transformatiezone, lugol kleuring, vasculaire patronen, oppervlak en begrenzing van de laesie

(**C** = niet van toepassing)

**O** = Positief en negatief voorspellende waarden (GRADE label 9; critical outcome) voor het vaststellen van afwijkingen aan de hand van de referentiestandaard (biopt of lisexcisie); interbeoordelaarsbetrouwbaarheid (GRADE label 8; critical outcome); sensitiviteit (GRADE label 7; critical outcome); en specificiteit (GRADE label 6; critical outcome).

#### PICO 2 m.b.t. klinisch nut

**P** = Vrouwen die een colposcopisch onderzoek ondergaan in het kader van bevolkingsonderzoek of op indicatie (exclusie: nacontrole/vervolgtraject)

**I** = Systematisch vastgelegde colposcopie

**C** = Niet systematisch vastgelegde colposcopie

**O** = Alle epidemiologisch of klinisch relevante uitkomsten, waaronder het percentage behandelde vrouwen volgens *see and treat* met laaggradige CIN.

### 2. Methoden

#### 2.1 Identificatie en selectie van relevante onderzoeken

##### 2.1.1 Systematische reviews

Op 8 maart 2021 werd er gezocht in Epistemonikos (bevat MEDLINE en Embase) naar systematische reviews (SR's) over colposcopie. De zoekstrategie is weergegeven in bijlage 1B. Er werd geen tijdslimiet gehanteerd met betrekking tot de publicatiedatum. In nauw overleg met de medisch inhoudelijk adviseurs en afgestemd met het Zorginstituut werden criteria geformuleerd voor de in- en exclusie van SR's die deze PICO-vraag beantwoorden. Relevante SR's beschreven de diagnostische accuratesse van colposcopie of specifieke colposcopie indicatoren, de accuratesse van risicoscores bij colposcopie of het klinisch nut van gestandaardiseerde rapportage van colposcopie bevindingen. We includeerden relevante publicaties geschreven in het Engels, Nederlands, Frans of Duits. Selectie van SR's vond plaats



door twee onderzoekers onafhankelijk van elkaar. De studies werden eerst op basis van titel en abstract geselecteerd en vervolgens op basis van het volledige artikel.

Voor de selectie van de meest geschikte review werd de volgende procedure gehanteerd (32):

- a. De review betrof de PICO van de onderzoeksvraag.
- b. Er werd gezocht in MEDLINE en tenminste één andere elektronische database.
- c. De risk of bias bepaling werd op studieniveau gerapporteerd en betrof tenminste de voor GRADE benodigde belangrijkste kwaliteitsitems.
- d. De beschrijvende gegevens en resultaten worden op studieniveau gepresenteerd (2\*2 tabellen of effectschattingen met 95% betrouwbaarheidsinterval (95% BI)).

Werd alleen een SR gevonden die aan criterium a) voldeed, maar niet aan b), c) of d), dan werd deze SR alleen gebruikt als bron van onderzoeken die eventueel gemist zijn in onze zoekstrategie naar primaire onderzoeken.

### *2.1.2 Primaire onderzoeken: diagnostische accuratesse van colposcopie indicatoren*

Op 23 maart 2021 werd in MEDLINE en Embase gezocht naar primaire onderzoeken waarin de diagnostische accuratesse of interbeoordelaarsbetrouwbaarheid (mate van overeenstemming tussen verschillende beoordelaars) van de geselecteerde colposcopie indicatoren werd beschreven. Daarnaast werd er op 10 maart 2021 gezocht in Embase naar primaire onderzoeken waarin predictiemodellen worden ontwikkeld of gevalideerd die gebruikt kunnen worden om tot een colposcopische impressie te komen, en werd er op 8 april 2021 gezocht in Scopus en Web of Science naar onderzoeken waarin de Reid Index en Swede score (33-35), twee veelgebruikte predictiemodellen, werden geciteerd. De complete zoekstrategie is beschreven in bijlage 1C.

Onderzoeken werden geïncludeerd wanneer zij de diagnostische accuratesse van minstens één van de volgende colposcopie indicatoren ten opzichte van histologie als referentiestandaard beschreven: colposcopische impressie, azijnzuurwitte afwijkingen, locatie van de laesie, grootte van de laesie, zichtbaarheid van de transformatiezone, lugol kleuring, vasculaire patronen, oppervlak en begrenzing van de laesie. Ook onderzoeken waarin de interbeoordelaarsbetrouwbaarheid van deze indicatoren werd beschreven, werden ingesloten en onderzoeken waarin regressiemodellen werden opgesteld met één of meerdere indicatoren als onafhankelijke variabele(n). Onderzoeken werden ingesloten wanneer zij werden uitgevoerd bij vrouwen met een indicatie voor colposcopie, waaronder een eerdere positieve screeningstest (cytologie, hoog risico humaan papillomavirus (HPV), visuele inspectie met azijnzuur (VIA) of visuele inspectie met lugol (VILI)) of klachten zoals tussentijds bloedverlies, bloederige afscheiding of bloedverlies tijdens of na seksueel contact. Uiteindelijk werden alleen onderzoeken waarin alle ingesloten vrouwen abnormale cytologie hadden, volledig uitgewerkt. Onderzoeken waarin colposcopie als primaire screeningstest werd ingezet, werden uitgesloten. De referentiestandaard om vast te stellen of er sprake was van CIN of cervixcarcinoom diende te bestaan uit histologie van weefsel verzameld met behulp van een biopt, lisexcisie of conisatie. Onderzoeken waarbij digitale colposcopie (bijvoorbeeld een DYSIS colposcoop) werd gebruikt, werden uitgesloten. Ook onderzoeken waarin alleen vrouwen met een diagnose van CIN of cervixcarcinoom werden geïncludeerd, en dus geen vrouwen zonder afwijkingen op basis van histologie, werden uitgesloten. We includeerden relevante publicaties geschreven in het

Engels, Nederlands, Frans of Duits en we hanteerden geen tijdslimiet. Selectie van artikelen vond plaats door twee onderzoekers onafhankelijk van elkaar. De referenties werden eerst op basis van titel en abstract geselecteerd en vervolgens op basis van het volledige artikel.

### *2.1.3 Primaire onderzoeken: klinisch nut van gestandaardiseerde colposcopie rapportage*

Op 19 maart 2021 werd in MEDLINE, Embase en Cochrane Central Register of Controlled Trials (CENTRAL) gezocht naar primaire onderzoeken over het klinisch nut van gestandaardiseerde rapportage van colposcopie. De zoekstrategie is te vinden in bijlage 1D. Onderzoeken werden geïncludeerd wanneer ze een vergelijkende opzet hadden (gerandomiseerde onderzoeken en niet-gerandomiseerde vergelijkende onderzoeken) waarin het gestandaardiseerd rapporteren van de bevindingen van colposcopie werd vergeleken met niet-gestandaardiseerde rapportage. Alle mogelijke uitkomsten werden meegenomen en er werd geen tijdslimiet gehanteerd. We includeerden relevante publicaties geschreven in het Engels, Nederlands, Frans of Duits. Selectie van artikelen vond plaats door twee onderzoekers onafhankelijk van elkaar. De resultaten werden eerst op basis van titel en abstract geselecteerd en vervolgens op basis van het volledige artikel.

## **2.2 Data-extractie en analyses**

Omdat er geen systematische reviews en ook geen primaire onderzoeken betreffende het klinisch nut van gestandaardiseerde colposcopie rapportage werden gevonden (zie paragraaf 3.1.1 en 3.1.3), werden er enkel data geëxtraheerd uit artikelen die de diagnostische accuratesse van colposcopie indicatoren beschreven.

### *2.2.1 Primaire onderzoeken: diagnostische accuratesse van colposcopie indicatoren*

Van alle onderzoeken die voldeden aan de in- en exclusiecriteria werden gegevens verzameld met betrekking tot de geïncludeerde populatie en de ingangstesten, het type colposcoop, de bestudeerde indicatoren, predictiemodellen om tot een colposcopische impressie te komen, en het type gerapporteerde uitkomsten: diagnostische accuratesse, inter-(of intra)beoordelaarsbetrouwbaarheid en/of associatiematen. Vervolgens werden gegevens van de studiepopulaties geëxtraheerd om te kunnen beoordelen of ze vergelijkbaar zijn met de populatie vrouwen die in Nederland een indicatie heeft voor colposcopie: vrouwen met abnormale cytologie in combinatie met een hoog risico HPV en vrouwen met abnormale cytologie in combinatie met klachten.

Vervolgens werden onderzoeken waarin alle vrouwen een abnormale cytologie hadden, verder uitgewerkt. We extraheerden gegevens met betrekking tot de onderzoeksopzet, groepsgrootte, land, volledige in- en exclusiecriteria, leeftijd van de geïncludeerde populatie, uitvoering van colposcopie, referentiestandaard, definities en classificatie van indicatoren en resultaten. Indien mogelijk werd de kruistabel geëxtraheerd met daarin de resultaten van de colposcopie indicator uitgezet tegen de histologische diagnose (de referentiestandaard). Daarnaast werden de gerapporteerde sensitiviteit, specificiteit, positief voorspellende waarde, negatief voorspellende waarde en bijbehorende afkapwaarden verzameld, evenals associatiematen (odds ratio (OR) en relatief risico (RR)), covariaten opgenomen in het regressiemodel en resultaten met betrekking tot interbeoordelaarsbetrouwbaarheid zoals kappa.

De getallen in de kruistabel werden gebruikt om de overeenstemming, voorspellende waarden en diagnostische accuratesse van de indicatoren ten opzichte van de histologische diagnose te bepalen. De overeenstemming werd berekend voor onderzoeken die dezelfde classificatie hadden voor de

indicator en de histologische diagnose, en deze kon alleen bepaald worden voor de colposcopische impressie. De algehele overeenstemming werd berekend door het aantal vrouwen op de diagonaal van de kruistabel bij elkaar op te tellen en te delen door het totaal aantal vrouwen in het onderzoek. De overeenstemming werd ook berekend per categorie van de colposcopische impressie door het aantal vrouwen dat terecht werd ingedeeld in een bepaalde categorie te delen door het totaal aantal vrouwen met die impressie. Daarnaast werd het percentage vrouwen met een overschatte diagnose berekend (de impressie was ernstiger dan de histologische diagnose) en het percentage vrouwen met een onderschatte diagnose (impressie was minder ernstig dan de histologische diagnose).

De voorspellende waarde werd berekend voor de uitkomsten  $\geq$ CIN 2 en  $\geq$ CIN 3/HSIL en kon bepaald worden voor alle indicatoren. Voor elk categorie van de indicator werd het percentage vrouwen berekend dat een histologische diagnose  $\geq$ CIN 2 of  $\geq$ CIN 3/HSIL kreeg. Daarnaast werd de kans op een foutpositieve test berekend bij een colposcopische impressie van  $\geq$ CIN 2 en  $\geq$ CIN 3/HSIL. Met andere woorden de kans op een histologische diagnose  $<$ CIN 2 bij een impressie  $\geq$ CIN 2 en de kans op een histologische diagnose  $<$ CIN 3/HSIL bij een impressie  $\geq$ CIN 3/HSIL. We noemen dit de foutpositief voorspellende waarde.

Ten slotte werden de sensitiviteit, specificiteit, positief voorspellende waarde en negatief voorspellende waarde voor de uitkomsten  $\geq$ CIN 2 en  $\geq$ CIN 3/HSIL berekend voor alle indicatoren. In overleg met de klinisch expert werden de indicatoren gedichotomiseerd. Indien geen kruistabel beschikbaar was, werden deze waarden overgenomen zoals gerapporteerd in het artikel.

Gegevens met betrekking tot de interbeoordelaarsbetrouwbaarheid en resultaten van multivariabele analyses werden overgenomen uit artikelen en gepresenteerd in tabellen.

### 2.3. Kwaliteitsbeoordeling

QUADAS-2 is een instrument dat gebruikt wordt om de methodologische kwaliteit van diagnostisch test accuratesse (DTA) onderzoek te beoordelen (36). Dit instrument bestaat uit vier domeinen (selectie van deelnemers, index test, referentiestandaard en *flow en timing*). Om tot een inschatting van de kans op vertekening en *applicability concerns* op deze vier domeinen te komen, dienen een aantal signalerende vragen beantwoord te worden. Door de strikte criteria die wij hanteerden voor de selectie van artikelen die uiteindelijk werden opgenomen in onze analyses, verwachtten we dat de geselecteerde onderzoeken weinig van elkaar zouden verschillen met betrekking tot de items van QUADAS-2. Daarom werd in overleg met de opdrachtgever besloten om enkel naar die signalerende vragen binnen QUADAS-2 te kijken die mogelijk onderscheidend zouden zijn. Dat betreft de volgende vragen van het QUADAS-2-domein 'Selectie van deelnemers': 'Werd een opeenvolgende (*consecutieve*) of willekeurige steekproef van patiënten geselecteerd?'; en 'Werd niet-gepaste exclusie van deelnemers voorkomen?'; en van het QUADAS-2-domein 'Flow and timing': 'Ondergingen alle deelnemers de referentiestandaard?' en 'Werden alle deelnemers geïnccludeerd in de analyses?'.  
'

Een formele inschatting van de kans op vertekening en *applicability concerns* op de vier domeinen van QUADAS-2 werd niet uitgevoerd.

## 3. Resultaten

### 3.1 Selectie van onderzoeken

#### *3.1.1 Systematische reviews*

De zoekstrategie in Epistemonikos naar SR's over de diagnostische accuratesse van colposcopie of specifieke colposcopie indicatoren, de accuratesse van risicoscores bij colposcopie, of het klinisch nut van gestandaardiseerde rapportage van colposcopie bevindingen resulteerde in 108 resultaten (Bijlage 2B). Op basis van de titel en/of het abstract bleken er 81 niet relevant. Van de overige 27 onderzoeken werd het volledige artikel bekeken. Er werden drie relevante SR's geïdentificeerd naar de diagnostische accuratesse van de colposcopische impressie (37-39). De gehanteerde methodologie in deze SR's was echter van onvoldoende kwaliteit: er werd slechts één database doorzocht en de kwaliteit van de ingesloten onderzoeken werd niet beoordeeld. Om die reden konden de SR's niet gebruikt worden als uitgangspunt. Wel hebben we de referentielijsten doorzocht voor aanvullende onderzoeken die eventueel gemist zijn door onze zoekstrategie naar primaire onderzoeken. Dit leverde geen extra relevante onderzoeken op. Een overzicht van de uitgesloten SR's en de redenen voor exclusie is te vinden in Bijlage 3B.

#### *3.1.2 Primaire onderzoeken: diagnostische accuratesse van colposcopie indicatoren*

De zoekstrategie in MEDLINE, Embase, Web of Science en Scopus naar primaire onderzoeken betreffende de diagnostische accuratesse van colposcopie indicatoren resulteerde in 1842 referenties (Bijlage 2C). Hiervan konden er 1463 worden uitgesloten op basis van titel en/of abstract en 258 op basis van volledig artikel. Een overzicht van deze 258 artikelen en de reden voor exclusie is te vinden in Bijlage 3C. Uiteindelijk voldeden 121 onderzoeken aan de PICO en deze werden ingesloten.

#### *3.1.3 Primaire onderzoeken: klinisch nut van gestandaardiseerde colposcopie rapportage*

De zoekstrategie in MEDLINE, Embase en Central naar onderzoeken betreffende het klinisch nut van gestandaardiseerde rapportage van colposcopie bevindingen resulteerde in 834 referenties, waarvan er op basis van de titel en het abstract 824 konden worden uitgesloten (Bijlage 2D). Van de overige tien referenties werd het volledige artikel bekeken, maar hiervan bleek geen enkel onderzoek te voldoen aan de in- en exclusiecriteria. Een overzicht van deze tien referenties en de redenen voor exclusie is weergegeven in Bijlage 3D.

### 3.2 Diagnostische accuratesse van colposcopie indicatoren

#### *3.2.1 Beschrijving primaire onderzoeken*

De 121 ingesloten onderzoeken betreffende de diagnostische accuratesse van colposcopie indicatoren werden op basis van overeenstemming met de in Nederland geldende indicaties voor colposcopie verdeeld in twee groepen: 29 onderzoeken (beschreven in 30 artikelen) includeerden vrouwen met

abnormale cytologie, de overige 91 onderzoeken includeerden ook vrouwen met andere indicaties voor colposcopie, zoals een positieve hoog risico HPV, abnormale VIA of klachten. In Nederland hebben vrouwen met een hoog-risico HPV test en een abnormale cytologie (bevolkingsonderzoek), en vrouwen met klachten en een abnormale cytologie een indicatie voor colposcopie. Er werden echter geen onderzoeken geïdentificeerd met exact deze ingangspopulatie. Daarom hebben wij ons (in overleg met het Zorginstituut) geconcentreerd op de overlappende conditie voor colposcopie indicatie: een abnormale cytologie.

#### 3.2.1.1 Primaire ingesloten onderzoeken (maar geëxcludeerd voor analyses)

Een overzicht van de 91 onderzoeken die niet werden opgenomen in de analyses, is weergegeven in Bijlage 5. De onderzoeken werden gepubliceerd tussen 1979 en 2021. Verschillende ingangspopulaties werden gehanteerd in deze onderzoeken: acht onderzoeken includeerden vrouwen met abnormale cytologie of klachten, 14 onderzoeken includeerden vrouwen met abnormale cytologie of hoog risico HPV, in vijf onderzoeken werden vrouwen met abnormale cytologie, hoog-risico HPV of klachten ingesloten, drie onderzoeken includeerden vrouwen met hoog-risico HPV, zes onderzoeken includeerden vrouwen met abnormale visuele inspectie met azijnzuur, 11 onderzoeken includeerden vrouwen met klachten, 14 onderzoeken includeerden vrouwen verwezen naar een colposcopie kliniek (indicatie niet gespecificeerd) en in tien onderzoeken was de exacte populatie onduidelijk. In de overige 20 onderzoeken werden wisselende combinaties van ingangstesten gehanteerd, onder andere abnormale cytologie, visuele inspectie met azijnzuur, visuele inspectie met lugol en klachten.

Alle onderzoeken, met uitzondering van één onderzoek (40), beschreven de diagnostische accuratesse van één of meerdere colposcopie indicatoren. In 13 onderzoeken werd de interbeoordelaarsbetrouwbaarheid beschreven (31, 40-51) en in 9 onderzoeken werden univariabele of multivariabele regressiemodellen toegepast (23, 24, 30, 42, 46, 52-55).

De onderzochte indicatoren waren de colposcopische impressie in 81 onderzoeken (34, 41-45, 47-54, 56-122), azijnzuurwitte afwijkingen in 16 onderzoeken (43-46, 53-55, 70, 78, 84, 86, 110, 120, 123-125), locatie van de laesie in twee onderzoeken (46, 78), grootte van de laesie in negen onderzoeken (46, 47, 53, 54, 78, 83-85, 107), zichtbaarheid van de transformatiezone in vijf onderzoeken (42, 49, 54, 86, 126), lugol kleuring in zes onderzoeken (45, 53, 54, 78, 86, 125), vasculaire patronen in 19 onderzoeken (34, 41, 43, 45, 46, 53-55, 58, 70, 78, 84, 86, 110, 112, 119, 123-125), en oppervlak en begrenzing van de laesie in 18 onderzoeken (34, 40, 43, 45, 46, 53-55, 78, 84, 86, 110, 112, 124, 125, 127-129). Van de 81 onderzoeken waarin de colposcopische impressie werd bestudeerd, werd in 35 onderzoeken een risicoscore gebruikt om tot deze impressie te komen. Dit waren de Reid index in 18 onderzoeken, de Swede index in 12 onderzoeken, en de IFCPC criteria in zes onderzoeken. Daarnaast gebruikten vier onderzoeken een aangepaste versie van de Reid index, twee onderzoeken een ingekorte versie van de Reid index, en één onderzoek een aangepaste vorm van de IFCPC-criteria.

#### 3.2.1.2 Primaire ingesloten onderzoeken (geïncludeerd voor analyses)

De karakteristieken van de 29 ingesloten onderzoeken zijn beschreven in Bijlage 6. De onderzoeken werden uitgevoerd tussen 1977 (130) en 2020 (131-133) en hadden alle een cross-sectionele onderzoeksopzet, waarbij vier onderzoeken gebruik maakten van de onderzoekspopulatie van een RCT (27, 134-136). Tien onderzoeken werden uitgevoerd in de Verenigde Staten (27, 130, 135-142), drie in

Thailand (133, 143, 144), twee in Iran (145, 146), twee in Italië (147, 148), twee in Zweden (33, 134) en steeds één onderzoek in Australië (149), Canada (59), China (131), Denemarken (150), Griekenland (151), Indonesië (152), Slowakije (132), Canada en Verenigde Staten (153), Nederland en Spanje (154, 155) en het Verenigd Koninkrijk en Ierland (156).

De grootte van de onderzoekspopulaties varieerde tussen 44 (138) en 6020 (149) deelnemers. De gemiddelde(/mediane) leeftijd van de deelnemers in de onderzoeken liep uiteen van 24 (135) tot 42 jaar (131) en in zes onderzoeken werd geen leeftijd vermeld (27, 130, 136, 146, 149, 152). In alle onderzoeken bestond de ingangspopulatie uit vrouwen met afwijkende cytologie. Voor één onderzoek werd ook rekening gehouden met HPV-status: vrouwen met een laaggradige cytologische afwijking werden alleen geïncludeerd bij hoog risico HPV (134). De onderzoekspopulaties verschilden met betrekking tot de uiteindelijke histologische diagnoses. In sommige onderzoeken had het merendeel van de deelnemers geen afwijkingen (tot 91 % van de vrouwen in het onderzoek van Karimi en collega's (146)) en in andere onderzoeken werden bij een aanzienlijk aantal deelnemers hooggradige afwijkingen gevonden (tot 94% in het onderzoek van Roy en collega's (152)).

De colposcopische procedure die deelnemende vrouwen ondergingen, werd niet in alle onderzoeken in evenveel detail beschreven. Azijnzuur (gerapporteerde sterktepercentages 4%-6%) werd gebruikt in 19 onderzoeken (27, 131-137, 140-145, 147, 148, 150, 153-155) en lugol in vier (132, 134, 142, 147). Negen onderzoeken gaven geen enkele informatie over de gevolgde colposcopieprocedure (33, 59, 130, 139, 146, 149, 151, 152, 156).

In vrijwel alle onderzoeken was de referentiestandaard histologisch onderzoek van weefsel verkregen via biopsie van een laesie. Vijf onderzoeken beschreven daarnaast biopsieën te nemen van gezond weefsel, wanneer er geen (zichtbare) laesie was (131, 133, 150, 153-155). In een aantal onderzoeken werd weefsel voor histologisch onderzoek (tevens) verkregen via een liexcisie (33, 139, 148, 152), conisatie (33, 134, 144) of operatie (niet gespecificeerd) (151). Eén onderzoek keek enkel naar interbeoordelaarsbetrouwbaarheid, zonder vergelijking met een referentiestandaard (136).

Met uitzondering van drie onderzoeken (138, 147, 152), evalueerden alle onderzoeken colposcopische impressie als indicator. Overige onderzochte indicatoren waren azijnzuurwitte afwijkingen in zeven onderzoeken (33, 136, 138, 143-145, 154, 155), locatie van de laesie in één onderzoek (144), grootte van de laesie in vijf onderzoeken (33, 132, 144, 150, 154, 155), zichtbaarheid van de transformatiezone in twee onderzoeken (132, 147), lugol kleuring in twee onderzoeken (33, 145), vasculaire patronen in zeven onderzoeken (33, 136, 138, 143-145, 154, 155), en oppervlak en begrenzing van de laesie in acht onderzoeken (33, 136, 138, 143-145, 152, 154, 155).

Met betrekking tot de items van QUADAS-2 die voor deze onderzoeken bekeken zijn, vonden we voor negen onderzoeken dat de inclusie van patiënten consecutief of in willekeurige volgorde was wat een lage kans geeft op selectiebias (27, 131, 134-136, 141, 147, 150, 156). Voor de overige onderzoeken was dit onduidelijk. Het hebben van een transformatiezone zonder afwijkingen en/of *see-and-treat* als beleid was in twee onderzoeken een reden om deelnemers te excluderen wat een mogelijke kans geeft op bias (143, 145).

In drie onderzoeken was het risico op bias verhoogd omdat niet alle deelnemers de referentiestandaard ondergingen (130, 134, 156) en voor één onderzoek was dit onduidelijk (147). Deelnemers werden uitgesloten vanwege het ontbreken van de referentiestandaard in zes onderzoeken (33, 137-139, 143,

149) of vanwege colposcopie of cervicografisch beeld van onvoldoende kwaliteit in drie onderzoeken (33, 144, 148) wat allebei ook een kans geeft op bias.

### 3.2.2 Resultaten

De kruistabellen voor elke indicator en de histologische diagnose zijn te vinden in Bijlage 7.

#### 3.2.2.1 Colposcopische impressie

De colposcopische impressie werd in 26 van de 29 geïncludeerde onderzoeken bepaald (27, 33, 59, 130-137, 139-146, 148-151, 153-156). De manier waarop deze bepaald werd en de classificatie van de bevindingen varieerde sterk tussen onderzoeken (Bijlage 8).

In drie onderzoeken werd de impressie bepaald aan de hand van de IFCPC-criteria (131, 148, 153), in vier onderzoeken werd de Reid index gebruikt (135, 142, 145, 151), in twee onderzoeken de ingekorte Reid index (27, 143), in twee onderzoeken een aangepaste Reid index (132, 136), in twee onderzoeken werd de Swede score gebruikt (33, 134), in één een aangepaste Swede score (144) en één onderzoek gebruikte de *Second World Congress of Cervical Pathology and Colposcopy* criteria (140). In de overige 11 onderzoeken was niet duidelijk hoe de colposcopische impressie bepaald was (59, 130, 133, 137, 139, 141, 146, 149, 150, 154-156).

In de meeste onderzoeken werden bevindingen geclassificeerd als normaal, laaggradig en hooggradig (133, 135, 139, 148-150, 153-156). In drie onderzoeken werden bevindingen geclassificeerd als benigne, CIN 1, CIN 2, CIN 3 en soms een aparte categorie cervixcarcinoom (59, 137, 142). De onderzoeken die gebruik maakten van de Reid index en Swede score, hanteerden verschillende afkappunten (bijvoorbeeld 0-2, 3, 4-6 voor een aangepaste versie van de Reid index (27)) of hielden de score continu. In twee onderzoeken was onduidelijk of en hoe de impressie werd geclassificeerd (136, 151).

In tien onderzoeken was de classificatie van de colposcopische impressie vergelijkbaar met de classificatie van de uiteindelijke diagnose op basis van histologie (59, 130, 137, 139, 140, 142, 146, 149, 150, 153). In deze onderzoeken kon de overeenstemming tussen verschillende categorieën bepaald worden (Tabel 5). De algehele overeenstemming tussen de impressie en de diagnose varieerde tussen 32,0% en 88,4%, met een mediaan van 56,5%. In het beste geval kwam dus 88,4% van de colposcopische impressies exact overeen met de diagnose op basis van de daaropvolgende histologie.

Met betrekking tot de gebruikte colposcopie/histologie categorieën waren er onder deze tien onderzoeken twee die de impressie en histologische diagnose classificeerden als normaal, CIN 1, CIN 2 en CIN 3 (137, 142), en een derde onderzoek hanteerde cervixcarcinoom als vijfde categorie (59). Een vierde onderzoek hanteerde de indeling normaal, mild abnormaal, matig abnormaal, ernstig abnormaal of suggestief voor invasief carcinoom (130) en in een vijfde onderzoek werden mild en matig abnormaal samengenomen in één categorie (140). Van alle negatieve colposcopische impressies, was in 78,0% tot 87,5% de histologische diagnose inderdaad negatief (9 onderzoeken). Van de colposcopische impressie CIN 1/mild abnormaal werd in 33,3% tot 88,0% inderdaad CIN 1/mild abnormaal vastgesteld op basis van histologie (4 onderzoeken). Voor CIN 2/matig abnormaal was de impressie in 20,0% tot 50,0% in overeenstemming met de histologische diagnose (4 onderzoeken) en voor CIN 3/ernstig abnormaal was dit het geval voor 37,4% tot 85,9% (5 onderzoeken). In het onderzoek van Benedet en collega's werd in 32,4% van de colposcopische impressies cervixcarcinoom inderdaad cervixcarcinoom vastgesteld met behulp van histologie (59). In drie andere onderzoeken werden diagnoses geclassificeerd als normaal, LSIL en HSIL (139, 149, 153), een vierde onderzoek had inflammatie als extra categorie (150). Van de colposcopische impressies LSIL in deze vier onderzoeken werd in 35,6% tot 71,0% van de gevallen

inderdaad LSIL gediagnosticeerd en voor HSIL was dit 60,6% tot 79,6%.

Tot slot werd ook bepaald in hoeveel procent van de gevallen de colposcopische impressie te laag werd ingeschat, en de histologische diagnose dus ernstiger was dan de impressie, en hoe vaak de impressie te hoog werd ingeschat ten opzichte van de histologische diagnose. Het percentage onderschatte colposcopische impressies varieerde tussen 1,9% en 36,% met een mediaan van 15,6%. In 8,2% tot 51,1% (mediaan 20,0%) bleek de histologische diagnose minder ernstig te zijn dan de colposcopische impressie.



**Tabel 5: Overeenstemming tussen colposcopische impressie en histologische diagnose**

| Reference        | Agreement with histologic diagnosis (%) |                 |                        |                            |                                   |                                 | Disagreement with histologic diagnosis (%) |                   |
|------------------|---|-----------------|------------------------|----------------------------|-----------------------------------|---------------------------------|--|-------------------|
|                  | Overall                                 | Normal          | CIN 1                  | CIN 2                      | CIN 3                             | Carcinoma                       | Predicted too high                         | Predicted too low |
| Baum 2006        | 32.0                                    | 87.5            | 33.5                   | 20.0                       | 37.4                              |                                 | 51.1                                       | 16.9              |
| Benedet 2004     | 52.1                                    | 78.0            | 37.9                   | 33.1                       | 68.7                              | 32.4                            | 26.4                                       | 21.5              |
| Reed 1997        | 77.6                                    | 78.6            | 88.0                   | 50.0                       | 50.0                              |                                 | 8.2  | 14.3              |
|                  |   | <i>Normal</i>   | <i>LSIL</i>            |                            | <i>HSIL</i>                       |                                 |  |                   |
| Cantor 2008      | 58.6                                    | 79.9            | 35.6                   |                            | 60.9                              |                                 | 27.1                                       | 14.3              |
| Bekkers 2008     | 54.3                                    | NA              | 51.8                   |                            | 60.6                              |                                 | 34.5                                       | 11.1              |
| Higgins 1994     | 53.7                                    | 0.0*            | 55.4                   |                            | 66.7                              |                                 | 22.3                                       | 23.9              |
|                  |   | <i>Normal</i>   | <i>Inflammation</i>    | <i>LSIL</i>                |                                   | <i>HSIL</i>                     |  |                   |
| Kierkegaard 1994 | 72.4                                    | 67.5            | 10.5                   | 71.0                       |                                   | 79.6                            | 10.3                                       | 17.2              |
|                  |   | <i>Normal</i>   | <i>Cervicitis</i>      |                            | <i>Mild to moderate dysplasia</i> | <i>Severe dysplasia and CIS</i> | <i>Suspicious invasive</i>                 |                   |
| Jahaveri 1980    | 88.4                                    | 93.0            | 87.0                   |                            | 89.4                              | 85.9                            | 60.0                                       | 8.7               |
|                  |   | <i>Normal</i>   | <i>Mildly abnormal</i> | <i>Moderately abnormal</i> |                                   | <i>Severely abnormal</i>        | <i>Suggestive of invasive carcinoma</i>    |                   |
| Ronk 1977        | 46.4                                    | 58.3            | 33.3                   | 35.6                       | 68.5                              | 62.5                            | 17.6                                       | 36.0              |
|                  |   | <i>Negative</i> |                        |                            | <i>Positive</i>                   |                                 |  |                   |
| Karimi 2011      | 80.8                                    | 30.2            |                        |                            | 97.5                              |                                 | 17.4                                       | 1.9               |

\*Studie includeert patiënten die een lisexcisie ondergaan, waarvan 10 patiënten met een normale impressie maar andere indicaties voor een lisexcisie.

De voorspellende waarde van de colposcopische impressie kon bepaald worden in 15 onderzoeken waaronder de tien hierboven besproken (33, 59, 130, 135, 137, 140-142, 146, 148-150, 153-155). Als eerste werd er een foutpositief voorspellende waarde berekend: de kans dat een vrouw de histologische diagnose <CIN 2 of <CIN 3/HSIL krijgt, terwijl de colposcopische impressie afwijkend ( $\geq$ CIN 2 of  $\geq$ CIN 3/HSIL) was (Tabel 6). Dit zijn vrouwen die mogelijk overbehandeld worden, indien de behandelbeslissing genomen wordt op basis van de colposcopische impressie en zonder een biopt te nemen. Het percentage vrouwen met een colposcopische impressie  $\geq$ CIN 2/matige dysplasie en een histologische diagnose <CIN 2 varieerde tussen 15,4% en 56,5% (4 onderzoeken). Het percentage vrouwen met een colposcopische impressie  $\geq$ CIN 3/HSIL/ernstige dysplasie en een histologische diagnose <CIN 3/HSIL/ernstige dysplasie varieerde tussen 9,9% en 63,6%, met een mediaan van 36,2% (12 onderzoeken). In één onderzoek werd gerapporteerd dat bij een Swede score  $\geq$ 5 (de aanbevolen afkapwaarde voor CIN  $\geq$ 2) in 45,1% van de gevallen toch sprake was van <CIN 2 (33) en in een ander onderzoek werd in 14,1% van de vrouwen met een Reid index tussen 4 en 6 een diagnose <CIN 2 gesteld (135). De overige twee onderzoeken hanteerden andere indelingen en zijn te vinden in Tabel 6.

**Tabel 6: Foutpositief voorspellende waarde van colposcopische impressie ten opzichte van histologische diagnose**

| Reference          | False positive predictive value for diagnosing < CIN 2 (unless otherwise indicated) |                             | False positive predictive value for diagnosing < CIN 3 or < HSIL (unless otherwise indicated) |                   |
|--------------------|---|-----------------------------|---|-------------------|
|                    | Histology   | Colposcopy                  | Histology   | Colposcopy        |
|                    |   | ≥CIN 2                      |   | ≥CIN 3            |
| Baum 2006          | <CIN 2  | 56.5                        | <CIN 3  | 62.6              |
| Benedet 2004       | <CIN 2  | 34.1                        | <CIN 3  | 31.0              |
| Reed 1997          | <CIN 2  | 40.0                        | <CIN 3  | 50.0              |
|                    |   | <i>High grade</i>           |   | <i>High grade</i> |
| Massad 2009        | <CIN 2  | 12.5                        | <CIN 3  | 63.6              |
| van der Marel 2014 | <CIN 2  | 27.4                        | <CIN 3  | 61.5              |
| Spinillo 2014      | <CIN 2  | 31.8                        | <CIN 3  | 41.6              |
|                    |   |                             |   | ≥HSIL             |
| Cantor 2008        |   |                             | <HSIL   | 39.1              |
| Bekkers 2008       |   |                             | <HSIL   | 39.4              |
| Higgins 1994       |   |                             | <HSIL   | 33.3              |
| Kierkegaard 1994   |   |                             | <HSIL   | 20.4              |
|                    |   | ≥Mild to moderate dysplasia |   | ≥Severe dysplasia |
| Jahaveri 1980      | <Mild to moderate dysplasia   | 4.0                         | <Severe dysplasia   | 14.2              |
|                    |   | ≥Moderate dysplasia         |   | ≥Severe dysplasia |
| Ronk 1977          | <Moderate dysplasia   | 15.4                        | <Severe dysplasia   | 9.9               |
|                    |   | <i>Suspicious</i>           |   | <i>Suspicious</i> |
| Jones 1987         | <CIN 2  | 94.6                        | <CIN 3  | 98.4              |
|                    |   | <i>Positive</i>             |   |                   |
| Karimi 2011        | Negative  | 69.8                        |   |                   |
|                    |   | <i>Reid 4-6</i>             |   | <i>Reid 4-6</i>   |
| Massad 2009        | <CIN 2  | 14.1                        | <CIN 3  | 65.9              |
|                    |   | <i>Swede ≥5</i>             |   |                   |
| Strander 2005      | <CIN 2  | 45.1                        |   |                   |

Voor elke gerapporteerde categorie van de impressie werd vervolgens bepaald welk percentage uiteindelijk gediagnosticeerd werd met ≥CIN 2 en met ≥CIN 3/HSIL. Zo werd bijvoorbeeld bepaald welk percentage van de vrouwen met een colposcopische impressie CIN 2 uiteindelijk toch de histologische diagnose ≥CIN 3/HSIL kregen. In Tabel 7 is te zien dat in alle onderzoeken voor oplopende categorieën van colposcopische impressie ook een grotere kans op de histologische diagnose ≥CIN 2 en ≥CIN 3/HSIL gevonden werd. In de meeste onderzoeken lag het percentage histologische diagnoses ≥CIN 3/HSIL binnen de groep met een normale colposcopische impressie lager dan 4% (10 onderzoeken) en in drie onderzoeken werden percentages gevonden van 20.0% (139), 7.6% (154, 155) en 5,7% (148). Het

percentage histologische diagnoses  $\geq$ CIN 2 lag, zoals verwacht, hoger in deze groep (0% tot 57,6%; 9 onderzoeken). Van de vrouwen met colposcopische impressie CIN 1/LSIL werd in 12,0% tot 35,0% van de gevallen een histologische diagnose  $\geq$ CIN 2 vastgesteld (5 onderzoeken), en in één studie (135) werd een uitschieter van 79,5% gevonden. Het percentage vrouwen met een colposcopische impressie CIN 2 dat toch  $\geq$ CIN 3 bleek te hebben, was in drie onderzoeken respectievelijk 12,5% (142), 14,5% (137), en 25,6% (59).

**Tabel 7: Voorspellende waarde van colposcopie indicatoren**

| Reference                     | Predictive value in % for diagnosing $\geq$ CIN 2 (unless otherwise indicated) |               |                         |                                   |                                 |   | Predictive value in % for diagnosing CIN $\geq$ 3 or $\geq$ HSIL (unless otherwise indicated) |                         |                                   |                                 |   |       |
|-------------------------------|--|---------------|-------------------------|-----------------------------------|---------------------------------|---|---|-------------------------|-----------------------------------|---------------------------------|---|-------|
|                               | Histology  |               |                         |                                   |                                 |   | Histology   |                         |                                   |                                 |   |       |
| <b>Colposcopic impression</b> | <i>Normal</i>  | <i>CIN 1</i>  | <i>CIN 2</i>            | <i>CIN 3</i>                      | <i>Cervix-carcinoma</i>         |   | <i>Normal</i>   | <i>CIN 1</i>            | <i>CIN 2</i>                      | <i>CIN 3</i>                    | <i>Cervix-carcinoma</i>                 |       |
| Baum 2006                     | $\geq$ CIN 2   | 0.0           | 25.1                    | 34.5                              | 53.5                            |   | $\geq$ CIN 3  | 0.0                     | 7.9                               | 14.5                            | 37.4                                    |       |
| Reed 1997                     | $\geq$ CIN 2   | 21.4          | 12.0                    | 62.5                              | 50.0                            |   | $\geq$ CIN 3  | 0.0                     | 4.0                               | 12.5                            | 50.0                                    |       |
| Benedet 2004                  | $\geq$ CIN 2   | 7.8           | 26.6                    | 58.6                              | 83.0                            | 61.8                                    | $\geq$ CIN 3  | 2.2                     | 9.2                               | 25.6                            | 69.3                                    | 61.8  |
|                               |  |               |                         |                                   |                                 |   | <i>Normal</i>   | <i>Low grade lesion</i> | <i>High grade lesion</i>          |                                 |   |       |
| Cantor 2008                   |  |               |                         |                                   |                                 |   | $\geq$ HSIL   | 1.5                     | 23.2                              | 60.9                            |   |       |
| Bekkers 2008                  |  |               |                         |                                   |                                 |   | $\geq$ HSIL   | NA                      | 15.6                              | 60.6                            |   |       |
| Higgins 1994                  |  |               |                         |                                   |                                 |   | $\geq$ HSIL   | 20.0                    | 22.3                              | 66.7                            |   |       |
|                               |  | <i>Normal</i> | <i>Low grade lesion</i> | <i>High grade lesion</i>          |                                 |   | <i>Normal</i>   | <i>Low grade lesion</i> | <i>High grade lesion</i>          |                                 |   |       |
| van der Marel 2014            | $\geq$ CIN 2   | 17.4          | 35.0                    | 72.6                              |                                 |   | $\geq$ CIN 3  | 7.6                     | 10.5                              | 38.5                            |   |       |
| Spinillo 2014                 | $\geq$ CIN 2   | 9.5           | 20.4                    | 68.2                              |                                 |   | $\geq$ CIN 3  | 5.7                     | 11.8                              | 58.4                            |   |       |
|                               |  |               |                         |                                   |                                 |   | <i>Normal</i>   | <i>Inflammation</i>     | <i>LSIL</i>                       | <i>HSIL</i>                     |   |       |
| Kierkegaard 1994              |  |               |                         |                                   |                                 |   | $\geq$ HSIL   | 2.5                     | 15.8                              | 23.6                            | 79.6                                    |       |
|                               |  | <i>Normal</i> | <i>Metaplasia</i>       | <i>Low grade</i>                  | <i>High grade</i>               |   | <i>Normal</i>   | <i>Metaplasia</i>       | <i>Low grade</i>                  | <i>High grade</i>               |   |       |
| Massad 2009                   | $\geq$ CIN 2   | 57.6          | 70.0                    | 79.5                              | 87.5                            |   | $\geq$ CIN 3  | 3.4                     | 11.5                              | 19.4                            | 36.4                                    |       |
|                               |  | <i>Normal</i> | <i>Cervicitis</i>       | <i>Mild to moderate dysplasia</i> | <i>Severe dysplasia and CIS</i> | <i>Suspicious invasive</i>              | <i>Normal</i>   | <i>Cervicitis</i>       | <i>Mild to moderate dysplasia</i> | <i>Severe dysplasia and CIS</i> | <i>Suspicious invasive</i>              |       |
| Jahaveri 1980                 | $\geq$ Mild to moderate dysplasia  | 0.0           | 4.3                     | 93.4                              | 98.2                            | 100.0                                   | $\geq$ Severe dysplasia   | 0.0                     | 4.3                               | 4.1                             | 85.9                                    | 80.0  |
|                               |  | <i>Normal</i> | <i>Mildly abnormal</i>  | <i>Moderately abnormal</i>        | <i>Severely abnormal</i>        | <i>Suggestive of invasive carcinoma</i> | <i>Normal</i>   | <i>Mildly abnormal</i>  | <i>Moderately abnormal</i>        | <i>Severely abnormal</i>        | <i>Suggestive of invasive carcinoma</i> |       |
| Ronk 1977                     | $\geq$ Mild to moderate dysplasia  | 41.7          | 73.3                    | 89.1                              | 98.6                            | 100.0                                   | $\geq$ Severe dysplasia   | 1.7                     | 19.0                              | 42.6                            | 89.0                                    | 100.0 |

| Reference                 | Predictive value in % for diagnosing $\geq$ CIN 2 (unless otherwise indicated) |                   |                      |                      | Predictive value in % for diagnosing CIN $\geq$ 3 or $\geq$ HSIL (unless otherwise indicated) |                          |                              |                          |                              |
|---------------------------|--|-------------------|----------------------|----------------------|---|--------------------------|------------------------------|--------------------------|------------------------------|
|                           |  |                   |                      |                      |   | Negative                 | Positive                     |                          |                              |
| Karimi 2011               |  |                   |                      |                      | Positive  | 2.5                      | 30.2                         |                          |                              |
|                           |  | <i>Negative</i>   | <i>Suspicious</i>    |                      |   | <i>Negative</i>          | <i>Suspicious</i>            |                          |                              |
| Jones 1987                | $\geq$ CIN 2   | 0.0               | 5.4                  |                      | $\geq$ CIN 3  | 0.0                      | 1.6                          |                          |                              |
|                           |  | <i>Reid 0-3</i>   | <i>Reid 4-6</i>      |                      |   | <i>Reid 0-3</i>          | <i>Reid 4-6</i>              |                          |                              |
| Massad 2009               | $\geq$ 2 CIN   | 73.0              | 85.9                 |                      | $\geq$ CIN 3  | 15.2                     | 34.1                         |                          |                              |
|                           |  | <i>Swede 0-4</i>  | <i>Swede 5-6</i>     | <i>Swede 7-10</i>    |   |                          |                              |                          |                              |
| Strander 2005             | $\geq$ 2 CIN   | 0.0               | 23.2                 | 74.8                 |   |                          |                              |                          |                              |
| <b>Acetowhite changes</b> |  |                   |                      |                      |   |                          |                              |                          |                              |
|                           |  | <i>Snow-white</i> | <i>Inter-mediate</i> | <i>Grey-white</i>    |   | <i>Snow-white</i>        | <i>Inter-mediate</i>         | <i>Grey-white</i>        |                              |
| Follen 1987               | $\geq$ CIN 2   | 45.5              | 50.0                 | 59.1                 | $\geq$ CIN 3  | 18.2                     | 33.3                         | 22.7                     |                              |
|                           |  |                   |                      |                      |   | <i>Shiny, snow white</i> | <i>Shiny, but grey white</i> | <i>Dull, oyster grey</i> |                              |
| Shojaei 2013              |  |                   |                      |                      | High grade  | 2.8                      | 27.7                         | 75.0                     |                              |
|                           |  | <i>Absent</i>     | <i>Translucent</i>   | <i>Inter-mediate</i> | <i>Opaque</i>   | <i>Absent</i>            | <i>Translucent</i>           | <i>Inter-mediate</i>     | <i>Opaque</i>                |
| van der Marel 2014        | $\geq$ CIN 2   | 40.0              | 34.4                 | 60.1                 | 79.5  | $\geq$ CIN 3             | 13.3                         | 10.9                     | 26.8 46.6                    |
| <b>Location of lesion</b> |  |                   |                      |                      |   |                          |                              |                          |                              |
| No results                |  |                   |                      |                      |   |                          |                              |                          |                              |
| <b>Size of lesion</b>     |  |                   |                      |                      |   |                          |                              |                          |                              |
|                           |  | <i>&lt;5 mm</i>   | <i>5-15 mm</i>       | <i>&gt;15 mm</i>     |   | <i>&lt;5 mm</i>          | <i>5-15 mm</i>               | <i>&gt;15 mm</i>         |                              |
| Kudela 2020               | $\geq$ CIN 2   | 34.5              | 50.0                 | 82.6                 |   | $\geq$ CIN 3             | 24.1                         | 35.7                     | 39.1                         |
|                           |  | <i>0%</i>         | <i>&lt;25%</i>       | <i>25-50%</i>        | <i>&gt;50%</i>  |                          | <i>0%</i>                    | <i>&lt;25%</i>           | <i>25-50%</i> <i>&gt;50%</i> |
| van der Marel 2014        | $\geq$ CIN 2   | 44.4              | 38.0                 | 62.9                 | 72.4  | $\geq$ CIN 3             | 0.0                          | 11.7                     | 25.9 43.3                    |
| <b>SCJ visibility</b>     |  |                   |                      |                      |   |                          |                              |                          |                              |
| No results                |  |                   |                      |                      |   |                          |                              |                          |                              |
| <b>Iodine staining</b>    |  |                   |                      |                      |   |                          |                              |                          |                              |

| Reference                 | Predictive value in % for diagnosing $\geq$ CIN 2 (unless otherwise indicated) |                           |                         |                          |                  | Predictive value in % for diagnosing CIN $\geq$ 3 or $\geq$ HSIL (unless otherwise indicated) |                                |   |                                   |  |                  |               |
|---------------------------|--|---------------------------|-------------------------|--------------------------|------------------|---|--------------------------------|---|-----------------------------------|--|------------------|---------------|
|                           |  |                           |                         |                          |                  |   | <i>Mahogany brown staining</i> | <i>Partial uptake</i>                     | <i>Mustard yellow staining</i>    |  |                  |               |
| Shojaei 2013              |  |                           |                         |                          |                  | High grade  | 8.7                            | 39.8                                      | 74.4                              |  |                  |               |
| <b>Vascular pattern</b>   |  |                           |                         |                          |                  |   |                                |   |                                   |  |                  |               |
|                           |  | <i>Absent</i>             | <i>Fine punctation</i>  | <i>Coarse punctation</i> | <i>Mosaiform</i> | <i>Mosaic</i>   |                                | <i>Absent</i>                             | <i>Fine punctation</i>            | <i>Coarse punctation</i>                     | <i>Mosaiform</i> | <i>Mosaic</i> |
| Follen 1987               | $\geq$ CIN 2   | 53.8                      | 62.5                    | 80.0                     | 46.7             | 50.0  | $\geq$ CIN 3                   | 23.1                                      | 12.5                              | 40.0   | 20.0             | 50.0          |
|                           |  |                           |                         |                          |                  |   |                                | <i>Uniform, fine punctation or mosaic</i> | <i>Absence of surface vessels</i> | <i>Definite, coarse punctation or mosaic</i> |                  |               |
| Shojaei 2013              |  |                           |                         |                          |                  |   | High grade                     | 14.0                                      | 26.0                              | 75.7   |                  |               |
|                           |  | <i>Absent</i>             | <i>Fine punctation</i>  | <i>Coarse punctation</i> |                  |   |                                | <i>Absent</i>                             | <i>Fine punctation</i>            | <i>Coarse punctation</i>                     |                  |               |
| van der Marel 2014        | $\geq$ CIN 2   | 48.4                      | 60.5                    | 88.9                     |                  |   | $\geq$ CIN 3                   | 17.2                                      | 32.5                              | 61.1   |                  |               |
|                           |  | <i>Absent</i>             | <i>Fine mosaic</i>      | <i>Coarse mosaic</i>     |                  |   |                                | <i>Absent</i>                             | <i>Fine mosaic</i>                | <i>Coarse mosaic</i>                         |                  |               |
| van der Marel 2014        | $\geq$ CIN 2   | 51.3                      | 57.0                    | 70.6                     |                  |   | $\geq$ CIN 3                   | 23.2                                      | 20.6                              | 43.1   |                  |               |
|                           |  | <i>Absent</i>             | <i>Atypical vessels</i> |                          |                  |   |                                | <i>Absent</i>                             | <i>Atypical vessels</i>           |  |                  |               |
| van der Marel 2014        | $\geq$ CIN 2   | 54.3                      | 70.0                    |                          |                  |   | $\geq$ CIN 3                   | 23.5                                      | 55.0                              |  |                  |               |
| <b>Border and surface</b> |  |                           |                         |                          |                  |   |                                |   |                                   |  |                  |               |
|                           |  | <i>Uneven or granular</i> | <i>Papillo-matous</i>   |                          |                  |   |                                | <i>Uneven or granular</i>                 | <i>Papillo-matous</i>             |  |                  |               |
| Follen 1987               | $\geq$ CIN 2   | 14.3                      | 60.0                    |                          |                  |   | $\geq$ CIN 3                   | 14.3                                      | 0.0                               |  |                  |               |
|                           |  |                           |                         |                          |                  |   |                                | <i>Lazy margin</i>                        | <i>Abrupt peeling margin</i>      |  |                  |               |
| Roy 1997                  |  |                           |                         |                          |                  |   | High grade                     | 57.1                                      | 97.3                              |  |                  |               |
|                           |  |                           |                         |                          |                  |   |                                | <i>Condylo-matous, micro-papillary</i>    | <i>Regular, smooth</i>            | <i>Rolled, peeling edges, sharp margins</i>  |                  |               |

| Reference          | Predictive value in % for diagnosing $\geq$ CIN 2 (unless otherwise indicated) |               |                         | Predictive value in % for diagnosing CIN $\geq$ 3 or $\geq$ HSIL (unless otherwise indicated) |                      |               |                         |      |
|--------------------|--|---------------|-------------------------|---|----------------------|---------------|-------------------------|------|
|                    | <i>Geo-graphical</i>   | <i>Smooth</i> | <i>Internal borders</i> |   | <i>Geo-graphical</i> | <i>Smooth</i> | <i>Internal borders</i> |      |
| Shojaei 2013       |  |               |                         | High grade  | 11.4                 | 38.4          | 72.4                    |      |
| van der Marel 2014 | $\geq$ CIN 2   | 46.3          | 59.6                    | 74.1  | $\geq$ CIN 3         | 18.6          | 28.0                    | 44.4 |

Gegevens met betrekking tot de diagnostische accuratesse van de colposcopische impressie waren beschikbaar voor 24 onderzoeken en zijn beschreven in Bijlage 9 (33, 59, 130-135, 137, 139-146, 148-151, 153-156). De sensitiviteit en specificiteit voor de diagnose  $\geq$ CIN 2 bij vrouwen met een colposcopische impressie  $\geq$ CIN 2 lagen respectievelijk tussen 0,50 en 0,91, en tussen 0,61 en 0,96 (4 onderzoeken). Voor de diagnose  $\geq$ CIN 2 bij vrouwen met een hooggradige colposcopische impressie lag de sensitiviteit tussen 0,26 en 0,74, en de specificiteit tussen 0,66 en 0,95 (4 onderzoeken). De sensitiviteit en specificiteit voor de diagnose  $\geq$ CIN 3/HSIL bij vrouwen met een colposcopische impressie  $\geq$ CIN 3/HSIL varieerden respectievelijk tussen 0,27 en 0,71, en tussen 0,72 en 0,98 (9 onderzoeken). Voor de Reid index (score tussen 0 en 8) werd een sensitiviteit van 0,96 en specificiteit van 0,70 voor het diagnosticeren van  $\geq$ CIN 3 gevonden bij een score van 5 of hoger (145) en voor de aangepaste Reid index was de sensitiviteit 0,58 en de specificiteit 0,97 bij een vergelijkbare afkapwaarde. In twee andere onderzoeken werd een sensitiviteit van 0,20 en 0,44 en een specificiteit van 0,90 en 0,98 gevonden bij een afkapwaarde van 4 of hoger bij de Reid index voor het diagnosticeren van  $\geq$ CIN 2 (135, 143). Voor de Swede score (score tussen 0 en 10) met een afkappunt van 5 of hoger werd een sensitiviteit van 1,00 en 0,74, en specificiteit van 0,31 en 0,59 gerapporteerd voor het diagnosticeren van  $\geq$ CIN 2, en een sensitiviteit van 0,94 en specificiteit van 0,83 voor de diagnose HSIL gevonden (33, 132, 134). Bij een afkappunt van 7 of hoger was de sensitiviteit 0,43 en de specificiteit 0,89 (134).

#### 3.2.2.2 Azijnzuurwitte afwijkingen

De accuratesse van azijnzuurwitte afwijkingen werd onderzocht in zeven onderzoeken (33, 136, 138, 143-145, 154, 155). Verschillende classificaties werden gehanteerd (Bijlage 8). Eén onderzoek classificeerde azijnzuurwitte afwijkingen als aanwezig of afwezig (136), terwijl de overige onderzoeken gebruik maakten van drie (33, 138, 143, 145) of vier categorieën (144, 154, 155).

De voorspellende waarde voor elke categorie ten opzichte van de histologische diagnose kon berekend worden voor drie onderzoeken (138, 145, 154, 155) en is te vinden in Tabel 7. In twee onderzoeken liep het percentage diagnoses  $\geq$ CIN 3 of HSIL op met toenemende azijnzuurwitte afwijkingen (145, 154, 155). In het onderzoek van Van der Marel en collega's bijvoorbeeld werd een  $\geq$ CIN 3 diagnose gesteld bij 13,3% van de vrouwen zonder azijnzuurwitte afwijkingen en bij 46,6% van de vrouwen met ondoorzichtige afwijkingen. In het derde onderzoek was deze trend minder duidelijk aanwezig (138).

In vier onderzoeken (138, 143, 145, 154, 155) kon de sensitiviteit en specificiteit van azijnzuurwitte afwijkingen worden berekend of werd deze gerapporteerd (Bijlage 9). Hierbij werden verschillende afkapwaarden gebruikt. De sensitiviteit voor het diagnosticeren van  $\geq$ CIN 2 varieerde tussen 0,46 en 0,78, en de specificiteit varieerde tussen 0,48 en 0,94 (3 onderzoeken, waarvan één met 2 afkappunten). Voor het diagnosticeren van  $\geq$ CIN 3 of HSIL lag de sensitiviteit tussen 0,56 en 0,96, en de specificiteit tussen 0,39 en 0,55 (3 onderzoeken).

#### 3.2.2.3 Locatie van de laesie

In geen enkel onderzoek werden gegevens gepresenteerd met betrekking tot de voorspellende waarde of diagnostische accuratesse van de locatie van de laesie.

In één onderzoek werd wel beschreven hoe de locatie ingedeeld werd (144) (Bijlage 8). Dit onderzoek hanteerde de volgende classificatie: alleen de buitenste helft van de transformatie zone, zowel de binnenste als de buitenste helft van de transformatie zone, invasie van het endocervicaal kanaal.



#### 3.2.2.4 Grootte van de laesie

De grootte van de laesie werd in vijf onderzoeken vastgelegd (33, 132, 144, 150, 154, 155). Deze werd vervolgens ingedeeld op basis van het percentage aangedane oppervlak van de cervix (0%, <25%, 25–50%, >50%), de grootte in millimeter (<5 mm, 5-15 mm, >15 mm), of het aantal overspannen kwadranten van de cervix (bijlage 8).

In twee onderzoeken kon de voorspellende waarde van de grootte voor de histologische diagnose berekend worden (Tabel 7) (132, 154, 155). Hieruit bleek dat het percentage  $\geq$ CIN 2 en  $\geq$ CIN 3 toenam voor grotere laesies: van de laesies met grootte van <5 mm, 5-15 mm, en >15 mm werd respectievelijk 24,1%, 35,7%, en 39,1% gediagnosticeerd met  $\geq$ CIN 3 (132) en bij vrouwen met 0%, <25%, 25-50%, en >50% betrokkenheid van de cervix werd respectievelijk in 0%, 11,7%, 25,9%, en 43,3%  $\geq$ CIN 3 gevonden (154, 155).

In dezelfde onderzoeken kon ook de diagnostische accuratesse berekend worden (Bijlage 9). Bij een afkapwaarde van >15 mm werden een sensitiviteit en specificiteit van 0,53 en 0,87 gevonden voor het diagnosticeren van  $\geq$ CIN 2, en van 0,43 en 0,69 voor  $\geq$ CIN 3 (132). Bij een afkapwaarde van >50% van het oppervlak van de cervix werden een sensitiviteit en specificiteit van 0,39 en 0,81 voor  $\geq$ CIN 2, en van 0,52 en 0,77 voor  $\geq$ CIN 3 gevonden.

#### 3.2.2.5 Zichtbaarheid van de transformatiezone

In geen van de ingesloten onderzoeken werd de accuratesse of voorspellende waarde van de zichtbaarheid van de transformatiezone gerapporteerd.

In twee onderzoeken werd wel gerapporteerd hoe deze beoordeeld werd (Bijlage 8). In het onderzoek van Sideri en collega's (147) werd de transformatiezone geclassificeerd als zichtbaar of niet zichtbaar en in het onderzoek van Kudela en collega's (132) werd de transformatiezone ingedeeld in drie types. Type 1 betekent dat de transformatiezone volledig zichtbaar is en gelokaliseerd is op de ectocervix, type 2 betekent een volledig zichtbare transformatiezone (met of zonder behulp van een endocervixspreider) die deels of volledig in het endocervicaal kanaal ligt, en type 3 betekent dat de transformatiezone geheel in het endocervicaal kanaal ligt en niet of slechts deels zichtbaar is (zelfs met een endocervixspreider).

#### 3.2.2.6 Lugol kleuring

In twee onderzoeken werd de classificatie van de kleuring met lugol beschreven (Bijlage 8). Het ene onderzoek hanteerde een indeling in drie categorieën vergelijkbaar met de Reid index: mahoniebruin, gedeeltelijke opname en mosterdgele kleuring (145). Het tweede onderzoek beschreef de ontwikkeling van de Swede score en in dit onderzoek werden ook drie categorieën gehanteerd: bruin, zwak of fragmentarisch geel, duidelijk onderscheidend geel (33). Alleen voor het eerste onderzoek konden de voorspellende waarde en diagnostische accuratesse bepaald worden voor de uitkomst  $\geq$ CIN 3 (145). Hieruit bleek dat de voorspellende waarde toenam indien de kleuring donkerder geel was (Tabel 7). Het percentage vrouwen met een histologische diagnose  $\geq$ CIN 3 was 8,7% indien de kleuring mahoniebruin was, 39,8% voor een gedeeltelijke kleuring en 74,4% voor een mosterdgele kleuring. De sensitiviteit en specificiteit van een gedeeltelijke of volledige gele kleuring voor de histologische diagnose  $\geq$ CIN 3 waren respectievelijk 0,84 en 0,68 (Bijlage 9).

### 3.2.2.7 Vasculaire patronen

De classificatie van vasculaire patronen werd beschreven in zeven onderzoeken (Bijlage 8) (33, 136, 138, 143-145, 154, 155). In de Reid index en Swede score wordt hiervoor een indeling in drie categorieën gehanteerd die door veel onderzoeken is overgenomen: uniform en fijn, afwezigheid van vaten, grove punctatie of mozaïek, soms in combinatie met atypische vaten (33, 143-145). In het onderzoek van Van der Marel en collega's (154, 155) werden de vasculaire patronen opgesplitst in drie losse indicatoren: punctatie (afwezig, fijn of grof), mozaïek (afwezig, fijn of grof) en atypische vaten (aanwezig of afwezig).

In afwezigheid van vasculaire patronen werd toch regelmatig de diagnose  $\geq$ CIN 2 of  $\geq$ CIN 3 gesteld (Tabel 7): voor afwezigheid van vasculaire patronen in het algemeen (voor  $\geq$ CIN 2 of  $\geq$ CIN 3 respectievelijk 53,8% en 23,1%), afwezigheid van punctatie (48,4% en 17,2%), afwezigheid van mozaïek (51,3% en 23,2%) en afwezigheid van atypische vaten (54,3% en 23,5%). Voor fijne en grove vasculaire patronen lag het percentage diagnoses  $\geq$ CIN 2 of  $\geq$ CIN 3 hoger, met het hoogste percentage voor grove patronen (Tabel 7).

De sensitiviteit en specificiteit van deze vasculaire patronen voor het vaststellen van  $\geq$ CIN 2 varieerden van 0,06 (atypische vaten (154, 155)) tot 0,82 (afwezigheid van vaten of grove punctatie of mozaïek (143)) en van 0,47 (groeve mozaïek of atypische vaten (138)) tot 0,98 (groeve punctatie (154, 155)). Voor het vaststellen van  $\geq$ CIN 3 lag de sensitiviteit iets hoger en was de specificiteit meestal lager of vergelijkbaar (Bijlage 9).

### 3.2.2.8 Oppervlak en begrenzing van de laesie

Classificatie van oppervlak en begrenzing van de laesie werd beschreven in acht onderzoeken (Bijlage 8) (33, 136, 138, 143-145, 152, 154, 155). In twee onderzoeken werd de classificatie van de Reid index met drie categorieën gehanteerd: condylomateus of micropapillair, regelmatig en glad, en gerolde of scherpe begrenzing (143). Andere onderzoeken hanteerden indelingen zoals oneven en granulair, of papillomateus (138), difuus, scherp maar onregelmatig, scherp en gelijkmatig met een verschil in hoogte (33, 144), of geografisch, glad, met binnengrenzen (154, 155).

De voorspellende waarde van deze indicator kon bepaald worden in vier onderzoeken (Tabel 7). In het eerste onderzoek werd 14,3% van de vrouwen met een oneven of granulair oppervlak gediagnosticeerd met CIN 3 en 60,0% van de vrouwen met een papillomateus oppervlak bleek CIN 2 te hebben (138). In het tweede onderzoek werd 57,1% van de vrouwen met een vage begrenzing en 97,5% van de vrouwen met een abrupte begrenzing gediagnosticeerd met een hooggradige laesie (152). In een derde onderzoek bleek 11,4% van de vrouwen met een condylomateuze of micropapillaire laesie, 38,4% met een regelmatige en gladde laesie en 72,4% met gerolde of scherpe begrenzing een hooggradige histologische diagnose te hebben (145). In het vierde onderzoek kreeg respectievelijk 46,3% en 18,6% van de vrouwen met een scherpe geografische begrenzing, 59,6% en 28,0% met een gladde begrenzing en 74,1% en 44,4% met binnengrenzen een histologische diagnose  $\geq$ CIN 2 of  $\geq$ CIN 3 (154, 155).

De sensitiviteit en specificiteit voor de diagnose  $\geq$ CIN 2 voor de verschillende afkappunten varieëerde tussen 0,08 en 0,77, en tussen 0,68 en 0,96, respectievelijk (Bijlage 9). Voor de diagnose  $\geq$ CIN 3 / HSIL werd meestal een lage sensitiviteit gevonden (drie onderzoeken vonden een waarde lager dan 0,20 (138,

145, 154, 155) met uitzondering van één onderzoek waarin een sensitiviteit van 0,95 werd gevonden voor een abrupte begrenzing (152). De specificiteit in deze onderzoeken lag tussen 0,60 en 0,95.

### 3.2.2.9 Predictieve waarde indicatoren in vergelijking tot elkaar

In drie onderzoeken werden multivariabele analyses gedaan met één of meerdere indicatoren als covariaat (Tabel 8). In het onderzoek van Higgins en collega's (139) werd de associatie tussen de colposcopische impressie en de uitkomst hooggradige laesie geanalyseerd met een model dat ook informatie bevatte met betrekking tot cytologie en biopsie resultaten. Een hooggradige colposcopische impressie bleek te zijn geassocieerd met een hogere kans op een hooggradige laesie ten op zichte van een normale impressie (Relatief risico: 4,89). Het onderzoek van Phianpiset en collega's (133) analyseerde de associatie tussen de colposcopische impressie en de uitkomst  $\geq$ CIN 2 en corrigeerde voor verschillende HPV-types en het aantal genomen bipten. Zowel een laaggradige als een hooggradige colposcopische impressie was geassocieerd met een hogere odds op  $\geq$ CIN 2. In het laatste onderzoek werd de associatie van de indicatoren azijnzuur, vasculaire patronen en oppervlak en begrenzing met de uitkomst  $\geq$ CIN 2 geanalyseerd. Voor alle indicatoren was de derde (meest afwijkende) categorie geassocieerd met de odds op  $\geq$ CIN 2 (odds ratio's van 5,8, 10,0 en 3,2). Voor vasculaire patronen was ook de tweede categorie (afwezigheid van vaten aan het oppervlak) geassocieerd met  $\geq$ CIN 2 (143).

**Tabel 8: Resultaten multivariabele analyses**

| Reference                     | Cut-off reference | Cut-off index                    | OR (95% CI)             | Covariates   |
|-------------------------------|-------------------|----------------------------------|-------------------------|--|
| <b>Colposcopic impression</b> |                   |                                  |                         |  |
| Higgins 1994                  | $\geq$ High grade | Normal                           | Ref                     | Referral Pap smear; repeat pap smear; biopsy results   |
|                               |                   | Low-grade lesion                 | RR: 1.19 (0.42 - 3.39)  |  |
|                               |                   | High-grade lesion                | RR: 4.89 (1.15 - 20.84) |  |
| Phianpiset 2020               | $\geq$ CIN 2      | Normal                           | Ref                     | High-risk HPV-positive, HPV 16/18 positivity, HPV 16 positivity, HPV 18 positivity, HPV 31, HPV 33, HPV 45, HPV 52, HPV 58 risk groups, and number of biopsies |
|                               |                   | Low grade                        | 10.02 (1.36 - 73.78)    |  |
|                               |                   | High grade                       | 47.36 (6.16 - 363.89)   |  |
| <b>Acetowhite changes</b>     |                   |                                  |                         |  |
| Boonlikit 2016                | $\geq$ CIN 2      | Reference (shiny, snow white)    | Ref                     | Margin, Vessel   |
|                               |                   | Shiny, grey white (intermediate) | 1.7 (0.8–3.7)           |  |
|                               |                   | Dull oyster grey                 | 5.8 (2.5–13.4)          |  |
| <b>Location of lesion</b>     |                   |                                  |                         |  |
| No results                    |                   |                                  |                         |  |
| <b>Size of lesion</b>         |                   |                                  |                         |  |
| No results                    |                   |                                  |                         |  |
| <b>SCJ visibility</b>         |                   |                                  |                         |  |
| No results                    |                   |                                  |                         |  |
| <b>Iodine staining</b>        |                   |                                  |                         |  |
| No results                    |                   |                                  |                         |  |
| <b>Vascular pattern</b>       |                   |                                  |                         |  |
|                               | $\geq$ CIN 2      | Reference (uniform, fine)        | Ref                     | Color, Margin  |

|                           |                                       |   |                 |               |
|---------------------------|---------------------------------------|---|-----------------|---------------|
| Boonlikit<br>2016         | Absence of surface vessels            |   | 3.1 (1.5–6.1)   |               |
|                           | Definite coarse punctuation or mosaic |   | 10.0 (4.3–23.2) |               |
| <b>Border and surface</b> |                                       |   |                 |               |
| Boonlikit<br>2016         | ≥CIN 2                                | Reference<br>(Condylomatous,<br>micropapillary) | Ref             | Color, Vessel |
|                           |                                       | Regular, smooth                                 | 1.2 (0.5–2.4)   |               |
|                           |                                       | Rolled, peeling edges,<br>sharp margins         | 3.2 (1.5–6.8)   |               |

In drie andere onderzoeken kon de voorspellende waarde van verschillende indicatoren met elkaar worden vergeleken. Deze resultaten zijn te vinden in Tabel 7, en ook gepresenteerd per studie in bijlage 10.

Het onderzoek van Follen en collega's (138) analyseerde azijnzuurwitte afwijkingen, vasculaire patronen en het oppervlak van de begrenzing. Categorieën van indicatoren met de hoogste voorspellende waarde voor de diagnose ≥CIN 2 waren grove punctatie (80,0%), fijne punctatie (62,5%) binnen de indicator vasculaire patronen, een papillomateus oppervlak (60,0%) en grijswitte kleuring na toepassen van azijnzuur (59,1%). Voor de diagnose ≥CIN 3 werden de hoogste voorspellende waardes gevonden voor de vasculaire patronen mozaïek (50,0%) en grove punctatie (40,0%) en voor de middelste categorie ('intermediate') van de azijnzuurwitte afwijkingen (33,3%).

Het onderzoek van Shojaei en collega's (145) bestudeerde de voorspellende waarde van azijnzuurwitte afwijkingen, kleuring met lugol, vasculaire patronen en de begrenzing van de laesie voor de diagnose hooggradige laesie. Voor elk van deze indicatoren werd in de laatste categorie (meest afwijkend) een vergelijkbare voorspellende waarde gevonden van tussen de 72,4% en 75,7%. De categorie sneeuw witte kleuring na toepassen van azijnzuur kon het beste gebruikt worden om een hooggradige laesie uit te sluiten: slechts 2,8% van de vrouwen in deze categorie werd gediagnosticeerd met een hooggradige laesie.

Het onderzoek van Van der Marel en collega's (154, 155) presenteerde gegevens over de colposcopische impressie, azijnzuurwitte afwijkingen, grootte van de laesie, vasculaire patronen en begrenzing van de laesie. Categorieën met de hoogste voorspellende waarde voor ≥CIN 2 waren 88,9% voor het vasculaire patroon grove punctatie, 79,5% voor ondoorzichtige azijnzuurkleuring, 74,1% voor aanwezigheid van binnengrenzen, 72,6% voor een hooggradige colposcopische impressie en 72,4% voor laesies die meer dan 50% van de cervix besloegen. De categorie met de laagste voorspellende waarde, die dus het beste gebruikt kan worden om een diagnose ≥CIN 2 uit te sluiten, was een normale colposcopische impressie (17,4%). Met betrekking tot de diagnose ≥CIN 3 werden de hoogste voorspellende waardes gevonden voor grove punctatie (61,1%), aanwezigheid van atypische vaten (55,5%), ondoorzichtige azijnzuur kleuring (46,6%) een aanwezigheid van interne begrenzing (44,4%).

### 3.2.2.10 Interbeoordelaarsbetrouwbaarheid

De interbeoordelaarsbetrouwbaarheid van één of meerdere indicatoren werd beschreven in vier onderzoeken (Tabel 9). In het onderzoek van Ferris en collega's (27) werd de overeenstemming bepaald tussen colposcopisten ('live' beoordeling) en beoordelaars die op afstand de afbeeldingen beoordeelden die gemaakt waren door de colposcopist. Er werd een overeenstemming van 86,6% en een kappa van

0,17 gevonden. Wanneer de resultaten gesplitst werden op basis van uiteindelijke diagnose werden kappa's van 0,11 (<CIN 2), 0,12 (CIN 2), en 0,21 ( $\geq$ CIN 3) gevonden. Een ander onderzoek beschreef de interbeoordelaarsbetrouwbaarheid van een gemodificeerde Swede score tussen een oncologisch gynaecoloog in opleiding en een senior oncologisch gynaecoloog, en vond een kappa van 0,7 en een intrabeoordelaarscorrelatiecoëfficiënt van 0,8 (144). Een derde onderzoek presenteerde het percentage vrouwen bij wie de beoordelaars volledig zicht op de transformatiezone rapporteerden (147). Dit percentage varieerde tussen 40% en 80,4%, met een mediaan van 70,3%. Het laatste onderzoek berekende kappa's voor de indicatoren azijnzuurwitte afwijkingen (0,37 (95% BI 0,30 tot 0,45)), vasculaire mozaïek (0,22 (95% BI 0,16 tot 0,29)), vasculaire punctatie (0,17 (95% BI 0,11 tot 0,23)) en atypische vaten (0,11 (95% BI 0 tot 0,22)) (136). De interbeoordelaarsbetrouwbaarheid van de locatie van de laesie, grootte van de laesie en lugol kleuring werd niet beschreven.

**Tabel 9: Interbeoordelaarsbetrouwbaarheid van colposcopie indicatoren**

| Reference                     | Indicator                                     | Interrater variability  |
|-------------------------------|---|---|
| <b>Colposcopic impression</b> |   |   |
| Ferris 2006                   | Colposcopic impression (Reid index)           | Agreement: 86.6%<br>Weighted Kappa: 0.17<br>Weighted kappa in subgroups:<br>Women diagnosed with <CIN 2: 0.11 (95% CI 0.05-0.16)<br>Women diagnosed with CIN 2: 0.12 (95% CI 0.01-0.22)<br>Women diagnosed with ≥CIN 3: 0.21 (95%CI 0.12-0.31)<br>Comparing colposcopists to reviewers of images  |
| Rodpenpear 2019               | Colposcopic impression (modified Swede score) | Kappa: 0.7, intraclass correlation coefficient: 0.8 (95% CI 0.71–0.86).<br>Comparing gynecologic oncological fellow to senior gynecologic oncologist.   |
| <b>Acetowhite changes</b>     |   |   |
| Massad 2008                   | Acetowhite changes                            | Weighted kappa: 0.37 (95% CI 0.30-0.45)   |
| <b>Location of lesion</b>     |   |   |
| No results                    |   |   |
| <b>Size of lesion</b>         |   |   |
| No results                    |   |   |
| <b>SCJ visibility</b>         |   |   |
| Sideri 1995                   | SCJ visibility                                | For 11 operators, the percentage of visualized SCJ ranged between 40% and 80.4% with a median of 70.3%.<br>The rate of reported abnormal transformation zones was not significantly different between the single operators (chi square test, 17.1; P > 0.05), and ranged between 59.3% and 90.2%. |
| <b>Iodine staining</b>        |   |   |
| No results                    |   |   |
| <b>Vascular pattern</b>       |   |   |
| Massad 2008                   | Mosaicism                                     | Weighted kappa: 0.22 (95% CI 0.16–0.29)   |
| Massad 2008                   | Punctation                                    | Weighted kappa: 0.17 (95% CI 0.11–0.23)   |
| Massad 2008                   | Atypical vessels                              | Weighted kappa: 0.11 (95% CI 0-0.22)  |
| <b>Border and surface</b>     |   |   |
| Massad 2008                   | Margin  | Weighted kappa: 0.23 (95% CI 0.18–0.30)   |

## 4. Samenvatting belangrijkste bevindingen

- Er is veel variatie in de classificatie van colposcopie indicatoren en ook voor de classificatie van histologische diagnoses werden verschillende indelingen gehanteerd. Mede door de verschillende classificaties is er ook veel variatie in voorspellende waarden en diagnostische accuratesse van colposcopie indicatoren. Enkele voorbeelden:
  - Indien de colposcopische impressie  $\geq$ CIN 3 was, was in 36,4 tot 79,6% daadwerkelijk sprake van een histologische diagnose  $\geq$ CIN 3 (10 onderzoeken).
  - Bij bijna de helft van de vrouwen met een colposcopische impressie  $\geq$ CIN 2 werd uiteindelijk toch een histologische diagnose  $<$ CIN 2 gesteld (4 onderzoeken). Dit zou kunnen leiden tot mogelijke overbehandeling.
- In 10 onderzoeken werd voor minder dan 4% van de normale colposcopische impressies toch  $\geq$ CIN 3 gevonden, in drie onderzoeken werden hogere percentages gevonden (range 5,7% tot 20,0%). Een normale colposcopische impressie wijst erop dat de kans op een afwijking  $\geq$ CIN 3 zeer klein is.
- Risicoscores kunnen in theorie gebruikt worden om de colposcopische impressie te standaardiseren, maar overtuigend bewijs ontbreekt. De voorspellende waarde kon in slechts twee onderzoeken berekend worden.
- Informatie over de voorspellende waarde en diagnostische accuratesse van de specifieke indicatoren (anders dan colposcopische impressie) is beperkt.
- Vasculaire patronen werden geïdentificeerd als voorspeller van  $\geq$ CIN 2 in drie onderzoeken waarin multivariabele analyses gedaan werden, en in drie andere onderzoeken waarin directe vergelijkingen gedaan werden. Met name grove punctatie lijkt een sterke voorspeller van  $\geq$ CIN 2. Ook een ondoorzichtige azijnzuurkleuring was voorspellend voor een afwijking  $\geq$ CIN 2 en een sneeuwwitte kleuring voorspelde in één onderzoek juist de afwezigheid van een hooggradige laesie.
- Interbeoordelaarsbetrouwbaarheid van colposcopie indicatoren is laag, maar hierover waren weinig gegevens beschikbaar.
- Er zijn geen studies gevonden m.b.t. het klinisch nut van het systematisch vastleggen van colposcopie uitslagen.

## Discussie en conclusie

Het eerste deel van dit project bestond uit een inventarisatie van de aanbevelingen in richtlijnen en standaarden op het gebied van rapportage van colposcopie. Er werden vijf standaarden en één richtlijn geïdentificeerd waarin in totaal 109 aanbevelingen werden gedaan. Deze aanbevelingen betroffen 46 unieke colposcopie indicatoren. Het aantal aanbevelingen dat werd ondersteund met een verwijzing naar primair onderzoek was echter beperkt. Acht colposcopie indicatoren werden vermeld in drie of meer standaarden of richtlijnen en de aanbevolen wijze van rapportage voor deze acht indicatoren kwam grotendeels overeen tussen de richtlijnen. Deze indicatoren waren colposcopische impressie, azijnzuurwitte afwijkingen, locatie van de laesie, grootte van de laesie, zichtbaarheid van de transformatiezone, lugol kleuring, vasculaire patronen, oppervlak en begrenzing van de laesie. Na overleg met klinisch experts werd besloten om deze indicatoren te selecteren voor het tweede deel van het project, waarin een systematische review werd uitgevoerd naar de voorspellende waarde, accuratesse en interbeoordelaarsbetrouwbaarheid van deze acht indicatoren.

In deze systematische review werden 121 onderzoeken geïdentificeerd naar de voorspellende waarde, accuratesse of interbeoordelaarsbetrouwbaarheid van de acht colposcopie indicatoren bij vrouwen verwezen voor colposcopie. De ingangseisen van de onderzoeken verschilden sterk en daarom werd besloten alleen die onderzoeken verder uit te werken waarin alle vrouwen abnormale cytologie hadden. Dit resulteerde in de inclusie van 29 onderzoeken, waarvan de meerderheid (26 onderzoeken) de voorspellende waarde en/of accuratesse van de colposcopische impressie beschreef. Ondanks de in de richtlijnen en standaarden aanbevolen wijze van rapportage varieerde de manier waarop de colposcopie indicatoren werden geclassificeerd sterk tussen onderzoeken, zelfs indien dezelfde richtlijn werd gebruikt. Dit gold ook voor de classificatie van de histologische diagnose (referentiestandaard).

De colposcopische impressie is een eindoordeel van de colposcopist dat gevormd wordt op basis van onder andere de resultaten van de overige zeven indicatoren. Om tot een colposcopische impressie te komen hanteerden studies de IFPCP-criteria, de Reid index, Swede score of eigen criteria. In deel 1 van het project werden ook de ASCCP-criteria geïdentificeerd, maar deze werden in geen van de ingesloten onderzoeken gebruikt. Het gebruik van een richtlijn of risicoscore zal in theorie verschillen tussen colposcopisten verkleinen (hoewel hier geen overtuigend bewijs voor werd gevonden). Het is echter onduidelijk of het ook daadwerkelijk de voorspellende waarde en accuratesse van de impressie verbetert. Ook vonden we geen onderzoeken naar het klinisch nut van gestandaardiseerde colposcopie rapportage, waardoor het onduidelijk is of patiëntgeoriënteerde uitkomsten verbeteren indien er gebruik gemaakt wordt van een richtlijn, standaard of risicoscore.

De uitslag van de cytologie die aan de colposcopie vooraf gaat, speelt een belangrijke rol bij het nemen van beslissingen met betrekking tot behandeling en/of vervolgdagnostiek. Slechts één onderzoek voerde een analyse uit waarbij de resultaten van de colposcopie en cytologie samen bekeken werden. Hierin werd gevonden dat de colposcopische impressie hooggradige laesie voorspellend was voor de aanwezigheid van een hooggradige afwijking, gecorrigeerd voor de uitslag van de cytologie (onafhankelijke voorspeller).

Op basis van de colposcopische impressie (en cytologie) zal besloten worden of een biopt afgenomen moet worden. Indien er ernstige afwijkingen gevonden worden, is een lixexic, waarbij een deel van de cervix wordt weggehaald, de aangewezen behandeling. Er kan op twee momenten besloten worden tot



een lixexisie: na onderzoek van het weefsel afgenomen bij het biopt, of direct na de colposcopie (zonder analyse van het weefsel). Het eerste wordt de getrapte methode genoemd en het laatste *see and treat*. In het verbeteringsignalement (1) van het Zorginstituut is na consultatie van de betrokken stakeholders geconcludeerd dat het percentage *see and treat* behandelingen (waarbij uiteindelijk de diagnose  $\leq$ CIN 1 wordt gesteld) te hoog is. Hierbij werd afgesproken om: 1) bij vermoeden van laaggradige CIN geen *see and treat* toe te passen. Daarnaast werd afgesproken de CIN, AIS en VAIN Landelijke richtlijn (8) beter te implementeren door 2) vrouwen bij wie CIN 1 is aangetoond niet (direct) te behandelen; 3) bij jonge vrouwen bij wie CIN 2 is aangetoond en die mogelijk een (toekomstige) kinderwens hebben, terughoudend te zijn met behandelen; en 4) vrouwen bij wie CIN 3 is aangetoond altijd te behandelen.

In de in het huidige literatuuronderzoek geïdentificeerde onderzoeken werd in 15,4% tot 56,5% van de vrouwen met een colposcopische impressie  $\geq$ CIN 2 toch de histologische diagnose  $<$ CIN 2 gesteld. Indien deze vrouwen direct behandeld zouden zijn zonder de uitslag van een biopt af te wachten (*see and treat*), zou hier dus sprake zijn geweest van overbehandeling. Overbehandeling is ongewenst vanwege het risico op complicaties (bloedverlies, pijn tijdens en na de behandeling, vorming van littekenweefsel) en het kan negatieve gevolgen hebben bij een latere zwangerschap. Met name bij vrouwen met een kinderwens dient overbehandeling dus zo veel mogelijk voorkomen te worden.

Indien de colposcopische impressie normaal was, was het percentage vrouwen dat toch gediagnosticeerd werd met  $\geq$ CIN 3 in de meeste onderzoeken (7/10) lager dan 4%. Eén belangrijke uitzondering hierop was het onderzoek van Van der Marel en collega's, uitgevoerd in Nederland en Spanje, waarbij een percentage van 7.6% gevonden werd (154, 155).

In alle gevallen geldt dat de colposcopische impressie het beste besproken kan worden met de patiënt. Daarbij dienen zaken zoals een kinderwens meegewogen te worden bij het nemen van een beslissing voor eventuele behandeling.

Met behulp van een op te richten landelijk colposcopieregistratiesysteem in Nederland kunnen gegevens verzameld worden om een eenduidiger inzicht te verkrijgen in de relatie tussen colposcopische uitslagen en de uitslagen van andere onderzoeken en behandelkeuzes in de Nederlandse situatie. Cijfers voor de Nederlandse populatie zijn noodzakelijk om adviezen over het beleid (expectatief of behandelen) bij vrouwen met een colposcopische impressie  $\leq$ CIN 2 te evalueren en zo nodig bij te stellen.

De zichtbaarheid van de transformatiezone is noodzakelijk voor een adequate colposcopie. Er werden geen onderzoeken gevonden waarin de accuratesse of voorspellende waarde van de zichtbaarheid van de transformatiezone werd gerapporteerd. De interesse ging daarom uit naar de interbeoordelaarsbetrouwbaarheid van deze indicator. Helaas werd deze slechts in één onderzoek beschreven en hieruit bleek dat er grote verschillen zijn tussen beoordelaars.

De voorspellende waarde van een indicator is direct afhankelijk van de prevalentie van hooggradige laesies in de onderzoekspopulatie. Indien de prevalentie hoog is, zal de positief voorspellende waarde ook hoger zijn. Er werden grote verschillen in prevalentie van verschillende categorieën CIN en cervixcarcinoom gevonden tussen de ingesloten onderzoeken en dit zal een deel van de gevonden verschillen in voorspellende waarden kunnen verklaren. Deze verschillen in prevalentie zijn daarnaast ook weer een mogelijk gevolg van de verschillen in categorisatie van histologische bevindingen. Verder dient opgemerkt te worden dat interbeoordelaarsbetrouwbaarheid, voorspellende waarde en diagnostische accuratesse niet onafhankelijk van elkaar zijn: indien de

interbeoordelaarsbetrouwbaarheid laag is (d.w.z. er zijn grote verschillen tussen beoordelaars) zullen de voorspellende waarde en diagnostische accuratesse ook laag zijn.

Slechts enkele onderzoeken voerden multivariabele analyses uit waarbij meerdere colposcopie indicatoren werden geïncorporeerd in één analyse. Multivariabele analyses zijn noodzakelijk om informatie te verkrijgen over welke indicator de sterkste (onafhankelijke) voorspellende waarde heeft voor de histologische diagnose. Op basis van de resultaten van deze systematische review is het daarom niet mogelijk om uitspraken te doen over welke indicatoren het belangrijkste zijn. Vervolgonderzoek dient zich te richten op het vergelijken van meerdere colposcopie indicatoren en deze met behulp van multivariabele methoden te analyseren om te komen tot een onderbouwde keuze voor een minimale dataset. Wanneer dergelijk onderzoek wordt uitgevoerd binnen het kader van een landelijke colposcopie registratie kan dit een belangrijke rol spelen in het doorontwikkelen van de colposcopie indicatoren in een dergelijke registratie en bijdragen aan de leer- en verbetercyclus .

Concluderend is er een aantal richtlijnen en risicoscores beschikbaar die het standaardiseren van de colposcopierapportage als doel hebben. Echter, bewijs dat dit daadwerkelijk leidt tot een hogere interbeoordelaarsbetrouwbaarheid is beperkt. Bovendien is er geen onderzoek gedaan naar het klinisch nut van gestandaardiseerde colposcopierapportage en is het dus onduidelijk wat het effect is op het aantal onnodige *see and treat* behandelingen. Wel is er veel onderzoek gedaan naar de voorspellende waarde en accuratesse van colposcopie indicatoren, maar hierbij zijn grote verschillen gevonden in classificaties van indicatoren en histologische diagnoses, en het aantal studies waarin meerdere colposcopie indicatoren direct werden vergeleken, is beperkt. Hierop was één uitzondering, een colposcopische impressie zonder ernstige afwijkingen (<CIN3) werd in 7 van de 10 studies zelden (< 4%) gevolgd door een sterk afwijkende histologische uitslag ( $\geq$ CIN3). Dit suggereert dat de colposcopische impressie een rol kan spelen in het voorkomen van overbehandeling van lichte afwijkingen conform een eerdere meta-analyse (1, 157).

Vervolgonderzoek dient gericht te zijn op het verzamelen van accurate cijfers voor de Nederlandse situatie. Dit kan met behulp van een landelijk colposcopieregistratiesysteem waarin gegevens worden verzameld over de indicatoren die onderdeel waren van het onderhavige rapport. Een vervolgstap is dus om afspraken te maken welke indicatoren onderdeel moeten zijn van deze minimale dataset en vervolgens dient de definitie van deze indicatoren gestandaardiseerd te worden zodat verschillen tussen beoordelaars hopelijk kleiner worden. De selectie van indicatoren kan gebaseerd worden op de voorspellende waarde voor de aanwezigheid van een maligniteit (gepresenteerd in het onderhavige rapport). Tevens presenteren we dat er nog weinig standaardisatie is met betrekking tot de rapportage en hier dienen dus afspraken over gemaakt te worden voor de landelijke registratie. Daarnaast dient na een aantal jaar onderzoek te worden gedaan naar het klinisch nut van gestandaardiseerde colposcopierapportage in Nederland.

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## Bijlagen

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## Bijlage 1. Zoekstrategieën

### 1A: Richtlijnen en standaarden

Datum zoekactie: 8 januari 2021

| <b>Google Scholar via publish or perish year &gt;= 2000</b> |  |     |
|---|--|-----|
| Search 1  | colposcopy standards [title]                 | 19  |
| Search 2  | colposcopy cervix cervical guideline [title] | 190 |
|   |  | 209 |
|   | deduplicated                                 | 207 |

| <b>TRIP database</b> |  |     |
|----------------------|--|-----|
| search 1             | (title:cervix) OR (title:cervical) OR (colposc*) |     |
|                      | date limit 2000:2020                             | 121 |

## 1B: Systematische reviews

Datum zoekactie: 8 maart 2021

| <b>Epistemonikos</b> |  |     |
|----------------------|--|-----|
| search 1             | (advanced_title_en:(colposc*) OR advanced_abstract_en:(colposc*)) [Filters: protocol=no, classification=systematic-review] | 108 |

## 1C: Primaire onderzoeken, PICO 1

Datum zoekactie: 23 maart

Medline (Ovid)

| Ovid MEDLINE(R) ALL <1946 to March 23, 2021> |  |         |
|--|--|---------|
| #  | Searches   | Results |
| 1  | Colposcopes/ or Colposcopy/  | 6613    |
| 2  | (colposc* or LuViva or telecolposcop* or (advanced adj3 cervi* adj3 scan*) or microcolpo* or (Enhanced adj3 Visual adj3 Assessment) or EVA or (Gynocular* or (magnifying adj3 device?))).ti,ab,kw.   | 10979   |
| 3  | 1 or 2   | 12951   |
| 4  | exp Uterine Cervical Neoplasms/  | 76515   |
| 5  | (cervi* adj5 (cancer* or tumor* or tumour* or neoplas* or carcinoma* or adenocarcinoma* or malignan*)).ti,ab,kf.   | 95229   |
| 6  | 4 or 5   | 113176  |
| 7  | 3 and 6  | 7646    |
| 8  | "sensitivity and specificity"/ or "mass screening"/ or "reference values"/ or "false positive reactions"/ or "false negative reactions"/ or (sensitiv* or specificit* or screening or false positive* or false negative* or accuracy or predictive value* or reference value* or roc* or likelihood ratio* or (cross-sectional adj stud*)).tw. | 3102853 |
| 9  | (kappa or reproduc* or ((inter-rater or observer) adj2 (variability or reliability or agreement or concordance))).ti,ab,kf.  | 618614  |
| 10   | 8 or 9   | 3592566 |
| 11   | 7 and 10   | 4065    |
| 12   | (acetic* or aceto*).ti,ab.   | 133036  |
| 13   | exp Acetic Acid/   | 11331   |
| 14   | 12 or 13   | 137743  |
| 15   | "Squamous Intraepithelial Lesions of the Cervix"/  | 579     |
| 16   | ((lesion or lesions) adj3 (location* or place* or size* or large or small or medium or fine or quadrant or number or percentage or proportion* or border or surface or inner-border or ridge)).ti,ab,kf.   | 56390   |
| 17   | 15 or 16   | 56958   |
| 18   | (iodine or lugol or schiller*).ti,ab,kf.   | 57293   |
| 19   | exp Iodides/   | 12437   |
| 20   | 18 or 19   | 65335   |
| 21   | (scj or TZ).ti,ab.   | 1972    |
| 22   | (junction or transformation).ti,ab,kf.   | 316339  |
| 23   | 21 or 22   | 318109  |
| 24   | (vasculari?ation or vessel*).ti,ab,kf.   | 337849  |
| 25   | mosa?c.ti,ab.  | 33521   |
| 26   | 24 or 25   | 371051  |
| 27   | (impression or swede or reid).ti,ab,kf.  | 31245   |

|    |                                  |        |
|----|----------------------------------|--------|
| 28 | 14 or 17 or 20 or 23 or 26 or 27 | 963398 |
| 29 | 11 and 28                        | 940    |

### Embase (embase.com)

| No. | Query   | Results | Date      |
|-----|---|---------|-----------|
| #32 | #30 AND [embase]/lim NOT ('conference abstract'/it OR 'conference paper'/it OR 'review'/it)   | 912     | 24-mrt-21 |
| #31 | #30 AND [embase]/lim  | 1311    | 24-mrt-21 |
| #30 | #12 AND #29   | 1461    | 24-mrt-21 |
| #29 | #15 OR #18 OR #21 OR #24 OR #27 OR #28  | 1300600 | 24-mrt-21 |
| #28 | impression:ti,ab,kw OR swede:ti,ab,kw OR reid:ti,ab,kw  | 44088   | 24-mrt-21 |
| #27 | #25 OR #26  | 509629  | 24-mrt-21 |
| #26 | mosa?c:ti,ab,kw   | 37821   | 24-mrt-21 |
| #25 | vasculari?ation:ti,ab,kw OR vessel*:ti,ab,kw  | 472306  | 24-mrt-21 |
| #24 | #22 OR #23  | 390740  | 24-mrt-21 |
| #23 | junction:ti,ab,kw OR transformation:ti,ab,kw  | 388214  | 24-mrt-21 |
| #22 | scj:ti,ab OR tz:ti,ab   | 2891    | 24-mrt-21 |
| #21 | #19 OR #20  | 91875   | 24-mrt-21 |
| #20 | iodine:ti,ab,kw OR lugol:ti,ab,kw OR schiller*:ti,ab,kw   | 69796   | 24-mrt-21 |
| #19 | 'iodine'/exp  | 46948   | 24-mrt-21 |
| #18 | #16 OR #17  | 88482   | 24-mrt-21 |
| #17 | ((lesion OR lesions) NEAR/3 (location* OR place* OR size* OR large OR small OR medium OR fine OR quadrant OR number OR percentage OR proportion* OR border OR surface OR 'inner border' OR ridge)):ti,ab,kw   | 86534   | 24-mrt-21 |
| #16 | 'epithelium lesion'/exp   | 1985    | 24-mrt-21 |
| #15 | #13 OR #14  | 202602  | 24-mrt-21 |
| #14 | acetic*:ti,ab OR aceto*:ti,ab   | 172202  | 24-mrt-21 |
| #13 | 'acetic acid'/exp   | 56049   | 24-mrt-21 |
| #12 | #7 AND #11  | 6490    | 24-mrt-21 |
| #11 | #8 OR #9 OR #10   | 5375940 | 24-mrt-21 |
| #10 | 'interrater reliability'/exp OR 'sensitivity and specificity'/exp OR 'screening'/exp OR 'false positive result'/exp OR 'false negative result'/exp  | 1118560 | 24-mrt-21 |
| #9  | kappa:ti,ab,kw OR reproduc*:ti,ab,kw OR (((('inter rater' OR observer) NEAR/2 (variability OR reliability OR agreement OR concordance)):ti,ab,kw)   | 714285  | 24-mrt-21 |
| #8  | sensitiv*:ti,ab,kw,de OR specificit*:ti,ab,kw,de OR screening:ti,ab,kw,de OR 'false positive*':ti,ab,kw,de OR 'false negative*':ti,ab,kw,de OR accuracy:ti,ab,kw,de OR 'predictive value*':ti,ab,kw,de OR 'reference value*':ti,ab,kw,de OR roc*:ti,ab,kw,de OR 'likelihood ratio*':ti,ab,kw,de OR (('cross sectional' NEAR/1 stud*):ti,ab,kw,de) | 4825300 | 24-mrt-21 |



|    |   |        |           |
|----|---|--------|-----------|
| #7 | #3 AND #6   | 10893  | 24-mrt-21 |
| #6 | #4 OR #5  | 150401 | 24-mrt-21 |
| #5 | (cervi* NEAR/5 (cancer* OR tumor* OR tumour* OR neoplas* OR carcinoma* OR adenocarcinoma* OR malignan*)):ti,ab,kw   | 125525 | 24-mrt-21 |
| #4 | 'uterine cervix cancer'/exp   | 103346 | 24-mrt-21 |
| #3 | #1 OR #2  | 31972  | 24-mrt-21 |
| #2 | colposc*:ti,ab,kw OR luviva:ti,ab,kw OR telecolposcop*:ti,ab,kw OR ((cervi* NEAR/3 scan*):ti,ab,kw) OR microcolpo*:ti,ab,kw OR ((visual NEAR/3 assessment):ti,ab,kw) OR eva:ti,ab,kw OR gynocular*:ti,ab,kw OR ((magnifying NEAR/3 device?):ti,ab,kw) | 27889  | 24-mrt-21 |
| #1 | 'colposcope'/exp OR 'colposcopy'/exp  | 13342  | 24-mrt-21 |

### Extra zoekstrategie naar predictiemodellen

**Datum zoekactie:** 10 maart 2021

#### **Embase (Embase.com)**

| No. | Query  | Results | Date      |
|-----|--|---------|-----------|
| #7  | #6 NOT ('conference abstract'/it OR 'conference review'/it OR 'letter'/it OR 'review'/it)  | 227     | 10/Mar/21 |
| #6  | #1 AND #4 AND #5   | 316     | 10/Mar/21 |
| #5  | colposc*:ti  | 3593    | 10/Mar/21 |
| #4  | #2 OR #3   | 150004  | 10/Mar/21 |
| #3  | 'uterine cervix cancer'/exp  | 103046  | 10/Mar/21 |
| #2  | (cervi* NEAR/5 (cancer* OR tumor* OR tumour* OR neoplas* OR carcinoma* OR adenocarcinoma* OR malignan*)):ti,ab,kw  | 125183  | 10/Mar/21 |
| #1  | validat*:ti,ab OR predict*:ti OR rule*:ti,ab OR (predict*:ti,ab,kw AND (outcome*:ti,ab,kw OR risk*:ti,ab,kw OR model*:ti,ab,kw)) OR ((variable*:ti,ab,kw OR scor*:ti,ab,kw OR factor*:ti,ab,kw) AND (predict*:ti,ab,kw OR model*:ti,ab,kw OR decision*:ti,ab,kw OR identif*:ti,ab,kw OR prognos*:ti,ab,kw)) OR (decision*:ti,ab,kw AND (model*:ti,ab,kw OR clinical*:ti,ab,kw OR statistical) AND ('model'/exp OR model)) OR (prognostic:ti,ab,kw AND (variable*:ti,ab,kw OR scor*:ti,ab,kw OR factor*:ti,ab,kw OR model*:ti,ab,kw)) OR 'stratification':ti,ab,kw OR 'discrimination':ti,ab,kw OR 'discriminate':ti,ab,kw OR 'c-statistic':ti,ab,kw OR 'c statistic':ti,ab,kw OR 'area under the curve':ti,ab,kw OR 'auc':ti,ab,kw OR 'calibration':ti,ab,kw OR 'indices':ti,ab,kw OR 'algorithm':ti,ab,kw OR 'multivariable':ti,ab,kw | 5280423 | 10/Mar/21 |

Citatiezoekstrategie

**Datum zoekactie:** 8 april 2021

|   | <b>Scopus</b> | <b>Web of Science</b> |
|---|---------------|-----------------------|
| Reid R, Stanhope CR, Herschman BR, et al. Genital warts and cervical cancer. IV. A colposcopic index for differentiating subclinical papillomaviral infection from cervical intraepithelial neoplasia. Am J Obstet Gynecol 1984;149:815–23. | 94            | 82                    |
| Reid R, Scalzi P. Genital warts and cervical cancer. VII. An improved colposcopic index for differentiating benign papillomaviral infections from high-grade cervical intraepithelial neoplasia. Am J Obstet Gynecol 1985; 153:611–8.       | 155           | 137                   |
| Strander B, Ellström-Andersson A, Franzén S, et al. The performance of a new scoring system for colposcopy in detecting high-grade dysplasia in the uterine cervix. Acta Obstet Gynecol Scand 2005;84:1013–7.                               | 47            | 41                    |
| <b>Totaal</b>   | <b>296</b>    | <b>260</b>            |

## 1D: Primaire onderzoeken, PICO 2

Datum zoekactie: 19 maart 2021

### Medline (Ovid)

| Ovid MEDLINE(R) ALL <1946 to March 19, 2021>     |  |          |          |
|--|--|----------|----------|
| Search history sorted by search number ascending |  |          |          |
| #  | Searches   | Results  | Type     |
| 1  | Colposcopes/ or Colposcopy/  | 6608     | Advanced |
| 2  | (colposc* or LuViva or telecolposcop* or (advanced adj3 cervi* adj3 scan*) or microcolpo* or (Enhanced adj3 Visual adj3 Assessment) or EVA or (Gynocular* or (magnifying adj3 device?))).ti,ab,kw.   | 10972    | Advanced |
| 3  | 1 or 2   | 12944    | Advanced |
| 4  | exp Uterine Cervical Neoplasms/  | 76473    | Advanced |
| 5  | (cervi* adj5 (cancer* or tumor* or tumour* or neoplas* or carcinoma* or adenocarcinoma* or malignan*)).ti,ab,kf.   | 95176    | Advanced |
| 6  | 4 or 5   | 113119   | Advanced |
| 7  | (terminology or nomenclature or standard* or score or index or swede or reid).ti,ab,kf.  | 2562603  | Advanced |
| 8  | 3 and 7  | 1696     | Advanced |
| 9  | 6 and 8  | 949      | Advanced |
| 10   | (theor* or concept* or framework* or model*).ti,ab,kf.   | 4081957  | Advanced |
| 11   | exp Interrupted Time Series Analysis/ or exp Controlled Before-After Studies/ or exp Implementation Science/ or exp Health Impact Assessment/ or (implement* or impact or value or evaluat* or assess* or (before adj3 after) or CBA or ITS or (interrupted adj3 ser*) or stepped-wedge).ti,ab,kf. | 9954352  | Advanced |
| 12   | 9 and 11   | 686      | Advanced |
| 13   | 10 or 11   | 12049774 | Advanced |
| 14   | 9 and 13   | 701      | Advanced |
| 15   | review.pt.   | 2772432  | Advanced |
| 16   | 14 not 15  | 627      | Advanced |

### Embase (embase.com)

| No. | Query  | Results  | Date      |
|-----|--|----------|-----------|
| #16 | #15 AND [embase]/lim   | 604      | 22-mrt-21 |
| #15 | #14 NOT ('conference abstract'/it OR 'conference review'/it OR 'review'/it)  | 712      | 22-mrt-21 |
| #14 | #9 AND #13   | 1066     | 22-mrt-21 |
| #13 | #10 OR #11 OR #12  | 15587606 | 22-mrt-21 |
| #12 | implement*:ti,ab,kw OR impact:ti,ab,kw OR value:ti,ab,kw OR evaluat*:ti,ab,kw OR assess*:ti,ab,kw OR ((before NEAR/3 | 13198983 | 22-mrt-21 |

|     |   |         |           |
|-----|---|---------|-----------|
|     | after):ti,ab,kw) OR cba:ti,ab,kw OR its:ti,ab,kw OR ((interrupted NEAR/3 ser*):ti,ab,kw) OR 'stepped wedge':ti,ab,kw  |         |           |
| #11 | 'implementation'/exp OR 'impact'/exp  | 238     | 22-mrt-21 |
| #10 | theor*:ti,ab,kw OR concept*:ti,ab,kw OR framework*:ti,ab,kw OR model*:ti,ab,kw  | 5026690 | 22-mrt-21 |
| #9  | #7 AND #8   | 1446    | 22-mrt-21 |
| #8  | terminology:ti,ab,kw OR nomenclature:ti,ab,kw OR standard*:ti,ab,kw OR score:ti,ab,kw OR index:ti,ab,kw OR swede:ti,ab,kw OR reid:ti,ab,kw  | 3784466 | 22-mrt-21 |
| #7  | #3 AND #6   | 10886   | 22-mrt-21 |
| #6  | #4 OR #5  | 150312  | 22-mrt-21 |
| #5  | (cervi* NEAR/5 (cancer* OR tumor* OR tumour* OR neoplas* OR carcinoma* OR adenocarcinoma* OR malignan*)):ti,ab,kw   | 125445  | 22-mrt-21 |
| #4  | 'uterine cervix cancer'/exp   | 103280  | 22-mrt-21 |
| #3  | #1 OR #2  | 31961   | 22-mrt-21 |
| #2  | colposc*:ti,ab,kw OR luvida:ti,ab,kw OR telecolposcop*:ti,ab,kw OR ((cervi* NEAR/3 scan*):ti,ab,kw) OR microcolpo*:ti,ab,kw OR ((visual NEAR/3 assessment):ti,ab,kw) OR eva:ti,ab,kw OR gynocular*:ti,ab,kw OR ((magnifying NEAR/3 device?):ti,ab,kw) | 27879   | 22-mrt-21 |
| #1  | colposcope'/exp OR 'colposcopy'/exp   | 13337   | 22-mrt-21 |

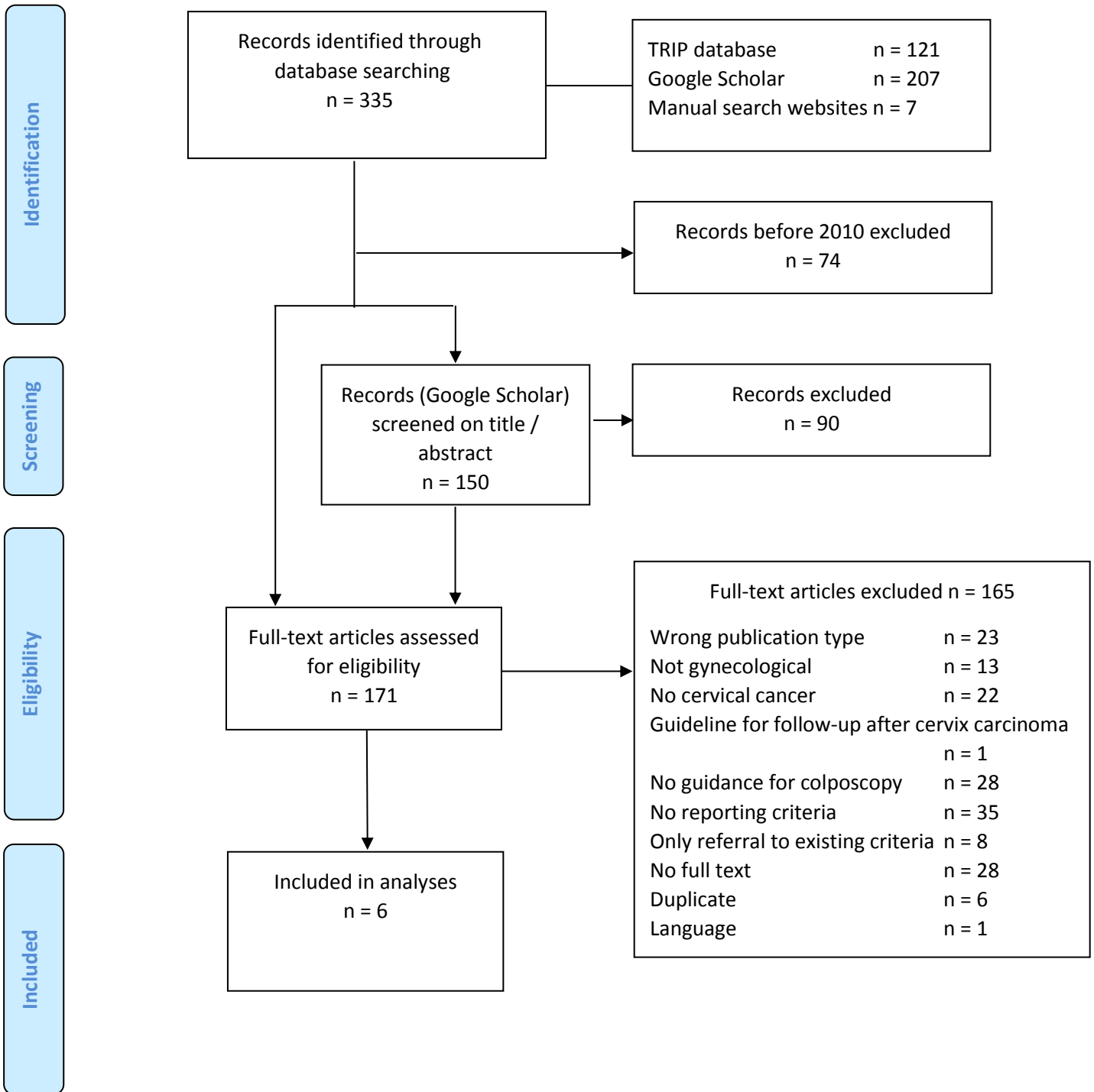
#### Cochrane Central Register of Controlled Trials (CENTRAL)

| #  | Search  | Results |
|----|---|---------|
| #1 | (colposc* or LuViva or telecolposcop* or (advanced adj3 cervi* adj3 scan*) or microcolpo* or (Enhanced adj3 Visual adj3 Assessment) or EVA or (Gynocular* or (magnifying adj3 device?))):ti,ab,kw,eh,mh | 1593    |
| #2 | (cervi* adj5 (cancer* or tumor* or tumour* or neoplas* or carcinoma* or adenocarcinoma* or malignan*)):ti,ab,kw,eh,mh   | 5717    |
| #3 | #1 AND #2   | 643     |
| #4 | (terminology or nomenclature or standard* or score or index or swede or reid):ti,ab,kw  | 391165  |
| #5 | #3 AND #4   | 132     |
| #6 | (clinicaltrials.gov or WHO):so  | 149012  |
| #7 | conference:PT   | 174993  |
| #8 | #6 OR #7  | 324003  |
| #9 | #5 NOT #8   | 114     |

## Bijlage 2. Study flow

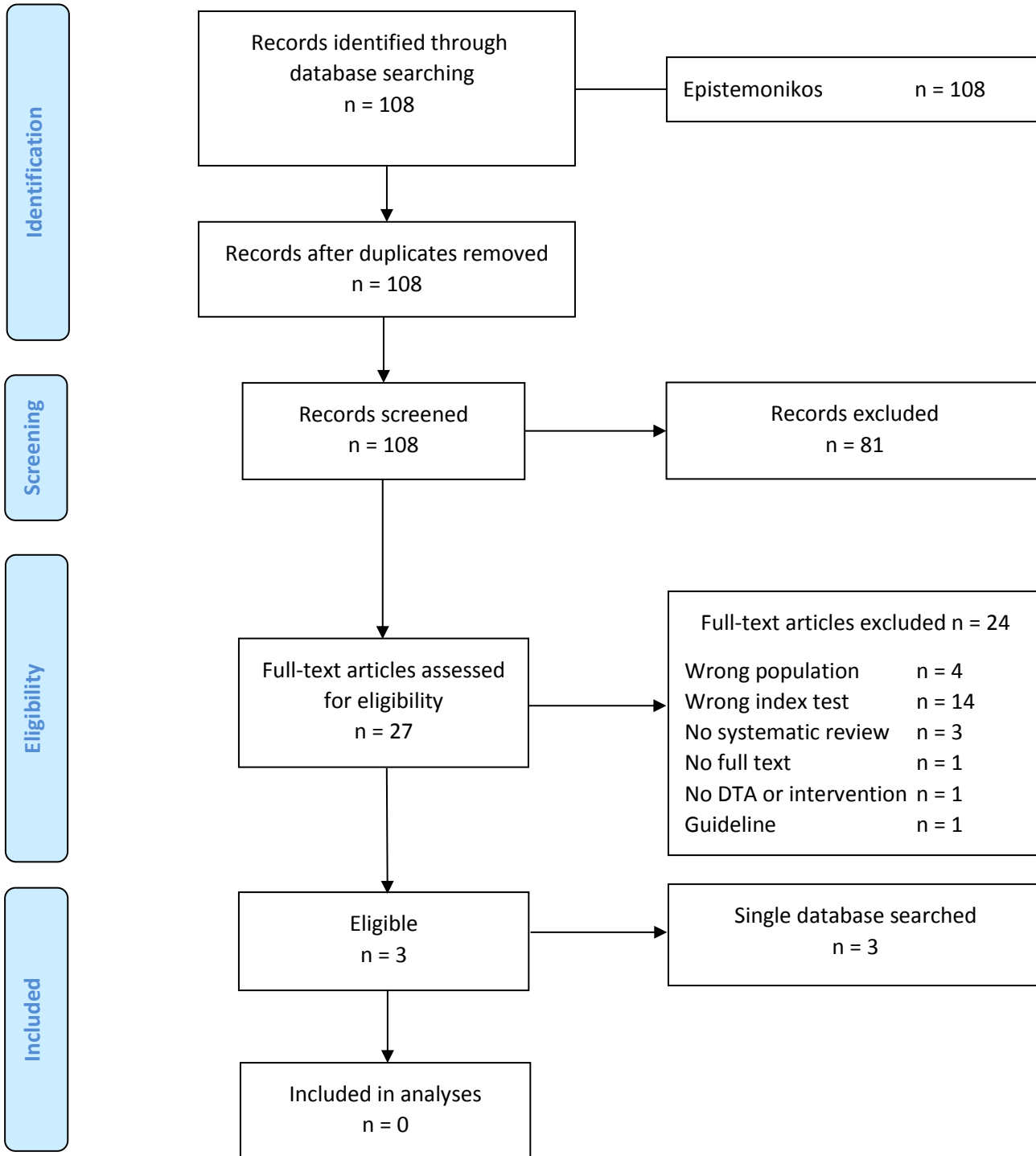
### 2A: Richtlijnen en standaarden

Figuur. Study flow van de selectie van richtlijnen betreffende de rapportage van colposcopie



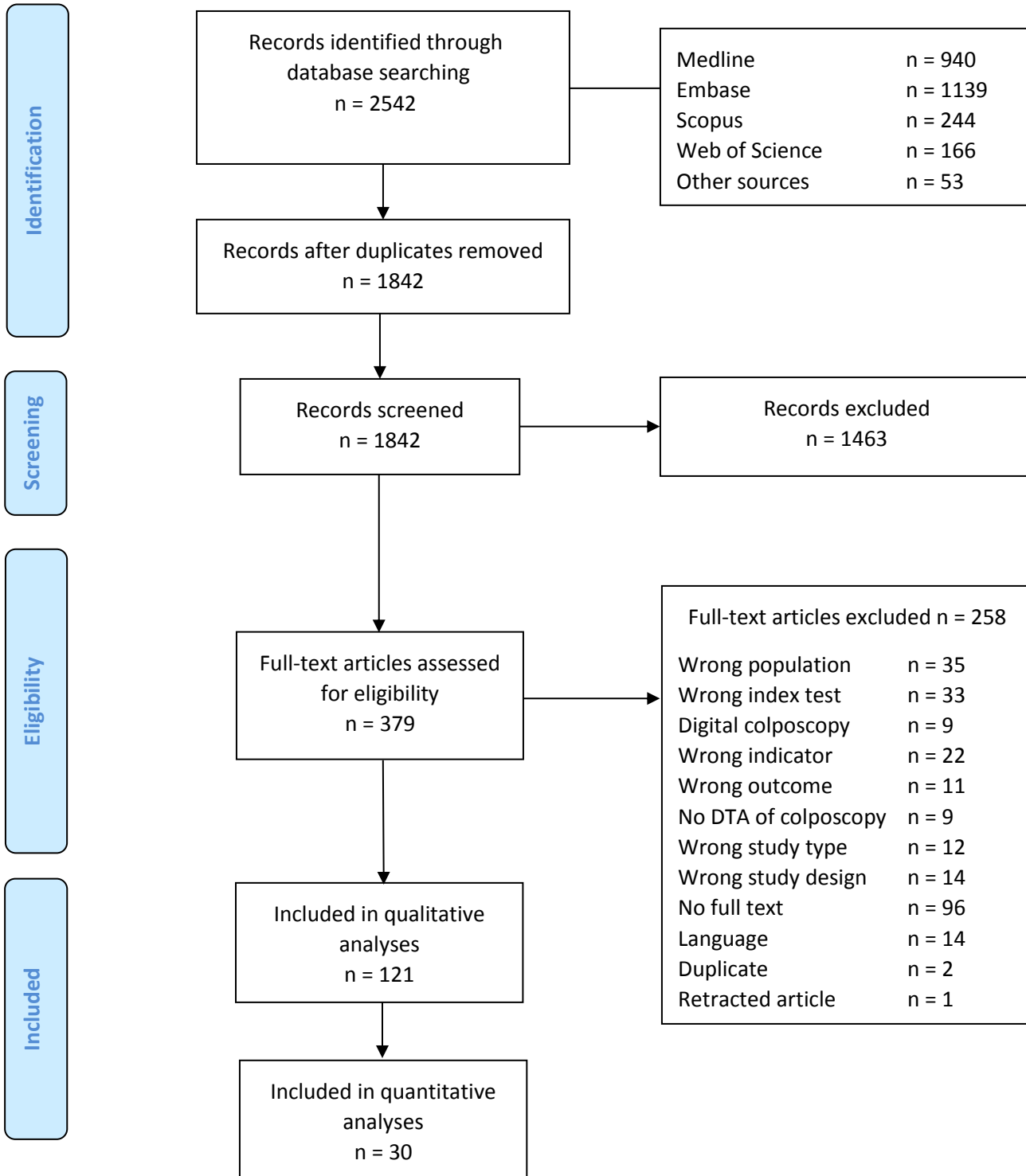
## 2B: Systematische reviews

Figuur. Study flow van de selectie van systematische reviews betreffende de diagnostische accuratesse van colposcopie indicatoren en het klinisch nut van gestandaardiseerde rapportage van colposcopie.



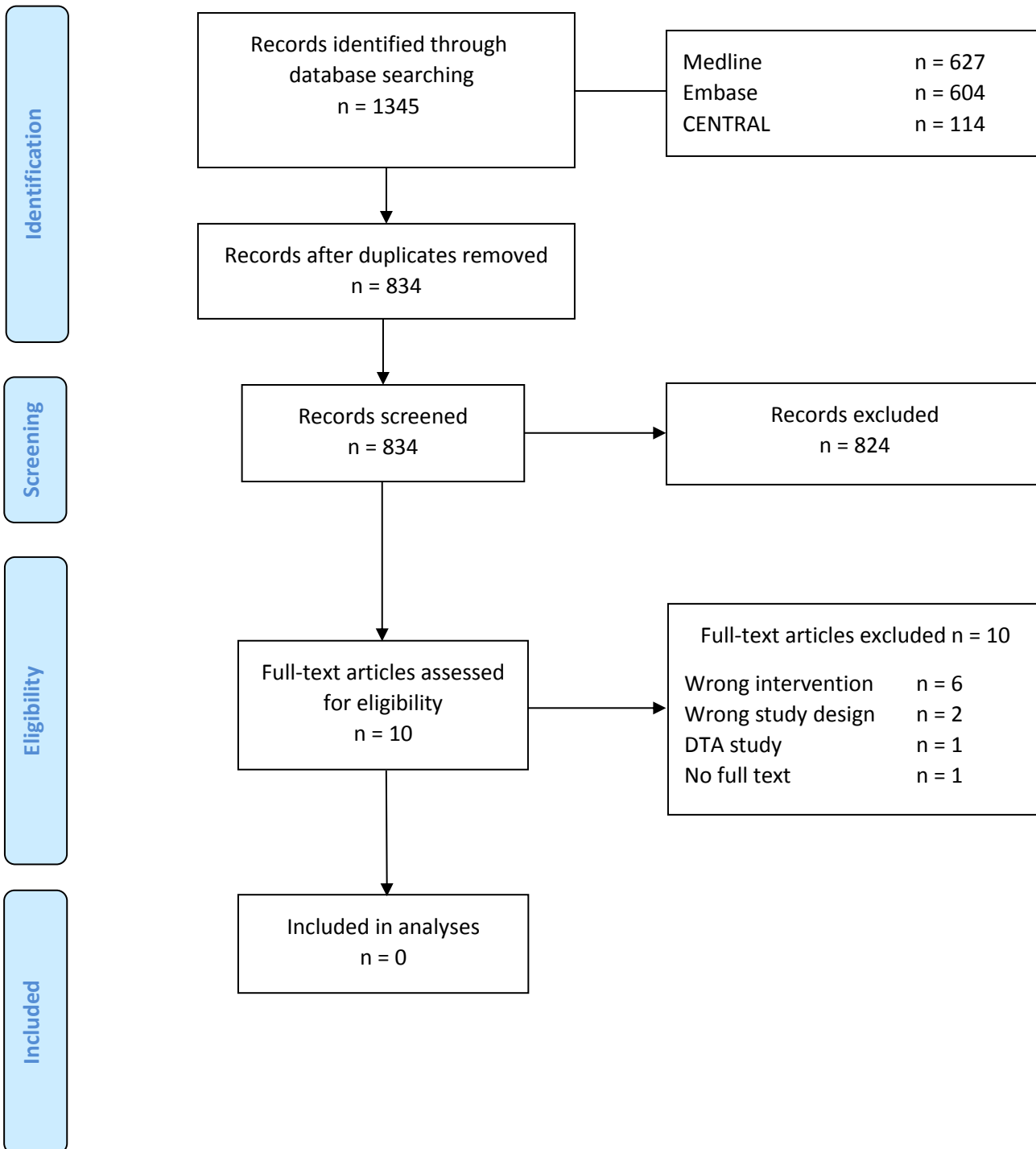
## 2C: Primaire onderzoeken, PICO 1

Figuur. Study flow van de selectie van primaire onderzoeken betreffende de diagnostische accuratesse van colposcopie indicatoren.



## 2D: Primaire onderzoeken, PICO 2

Figuur. Study flow van de selectie van primaire onderzoeken betreffende het klinisch nut van gestandaardiseerde colposcopie rapportage.





## Bijlage 3. Uitgesloten onderzoeken

### 3A: Richtlijnen en standaarden

#### Uitgesloten onderzoeken betreffende richtlijnen voor rapportage van colposcopie

| Reference  | Reason for exclusion                                |
|--|---|
| Accelerating Change Transformation Team 2016 (1)             | No guidance for colposcopy                          |
| American Academy of Pediatrics 2010 (2)                      | No specific reporting criteria regarding colposcopy |
| American College of Obstetricians and Gynecologists 2012 (3) | No guidance for colposcopy                          |
| American College of Obstetricians and Gynecologists 2015 (4) | No guidance for colposcopy                          |
| American College of Obstetricians and Gynecologists 2018 (5) | No guidance for colposcopy                          |
| American College of Obstetricians and Gynecologists 2020 (6) | No guidance for colposcopy                          |
| American College of Physicians 2015 (7)                      | No guidance for colposcopy                          |
| American College of Radiology 2015 (8)                       | No guidance for colposcopy                          |
| American Society for Clinical Pathology 2012 (9)             | No specific reporting criteria regarding colposcopy |
| American Society for Clinical Pathology 2015 (10)            | No guidance for colposcopy                          |
| American Society for Clinical Pathology 2019 (11)            | No guidance for colposcopy                          |
| American Society for Clinical Pathology 2019 (12)            | No guidance for colposcopy                          |
| American Society for Radiation Oncology 2020 (13)            | No guidance for colposcopy                          |
| Arrossi 2017 (14)  | No guidance for colposcopy                          |
| Bentley 2012 (15)  | No new reporting criteria (refer to IFCCP)          |
| Bladé 2014 (16)  | No specific reporting criteria regarding colposcopy |
| Botha 2017 (17)  | No specific reporting criteria regarding colposcopy |
| British Association for Sexual Health and HIV 2013 (18)      | No specific reporting criteria regarding colposcopy |

|  |   |
|--|---|
| British Association for Sexual Health and HIV 2015 (19)                  | No guidance for colposcopy                          |
| Cancer Council Australia 2016 (20)                                       | No new reporting criteria (refer to IFCPC)          |
| Castle 2017 (21)   | No specific reporting criteria regarding colposcopy |
| Clinical Practice Guidelines and Protocols in British Columbia 2014 (22) | No specific reporting criteria regarding colposcopy |
| Clinical Practice Guidelines Portal 2011 (23)                            | No specific reporting criteria regarding colposcopy |
| Clinical Practice Guidelines Portal 2012 (24)                            | No specific reporting criteria regarding colposcopy |
| Clinical Practice Guidelines Portal 2014 (25)                            | No specific reporting criteria regarding colposcopy |
| Clinical Practice Guidelines Portal 2014 (26)                            | No guidance for colposcopy                          |
| College of American Pathologists 2012 (27)                               | No guidance for colposcopy                          |
| CPG Infobase 2013 (28)   | No guidance for colposcopy                          |
| de Sanjose 2017 (29)   | No guidance for colposcopy                          |
| Elit 2016 (30)   | Guideline for follow-up after cervix carcinoma      |
| European Association of Nuclear Medicine 2020 (31)                       | No guidance for colposcopy                          |
| European Society for Medical Oncology 2010 (32)                          | No guidance for colposcopy                          |
| European Society for Medical Oncology 2012 (33)                          | No guidance for colposcopy                          |
| European Society for Medical Oncology 2017 (34)                          | No guidance for colposcopy                          |
| Federal Democratic Republic of Ethiopia Ministry 2015 (35)               | No specific reporting criteria regarding colposcopy |
| Fontham 2020 (36)  | No specific reporting criteria regarding colposcopy |
| Hamashima 2010 (37)  | No specific reporting criteria regarding colposcopy |
| Hillemanns 2019 (38)   | No specific reporting criteria regarding colposcopy |
| Ismail 2020 (39)   | No specific reporting criteria regarding colposcopy |
| Japan Society of Gynecologic Oncology 2011 (40)                          | No guidance for colposcopy                          |
| Jeronimo 2017 (41)   | No specific reporting criteria regarding colposcopy |
| Jeronimo 2016 (42)   | No new reporting criteria (refer to IFCPC)          |

|  |   |
|--|---|
| Kaiser Permanente Clinical Guidelines 2015 (43)  | No specific reporting criteria regarding colposcopy |
| Khodakarami 2014 (44)  | No guidance for colposcopy                          |
| Min 2015 (45)  | No specific reporting criteria regarding colposcopy |
| Murphy 2012 (46)   | No specific reporting criteria regarding colposcopy |
| New Zealand Sexual Health Society 2017 (47)  | No specific reporting criteria regarding colposcopy |
| New Zealand Sexual Health Society 2017 (48)  | No guidance for colposcopy                          |
| Nordic Federation of Societies of Obstetrics and Gynecology 2015 (49)                  | No guidance for colposcopy                          |
| NVOG 2012 (50)   | No specific reporting criteria regarding colposcopy |
| Oncoline 2016 (51)   | No specific reporting criteria regarding colposcopy |
| Oncoline 2018 (52)   | No specific reporting criteria regarding colposcopy |
| Public Health England 2020 (53)  | No new reporting criteria (refer to IFPCPC)         |
| Reich 2018 (54)  | No new reporting criteria (refer to IFPCPC)         |
| Royal Australian and New Zealand College of Obstetricians and Gynaecologists 2020 (55) | No new reporting criteria (refer to IFPCPC)         |
| Royal College of Nursing 2018 (56)   | No specific reporting criteria regarding colposcopy |
| Royal College of Obstetricians and Gynaecologists 2011 (57)                            | No guidance for colposcopy                          |
| Royal College of Obstetricians and Gynaecologists 2014 (58)                            | No specific reporting criteria regarding colposcopy |
| Royal College of Obstetricians and Gynaecologists 2016 (59)                            | No specific reporting criteria regarding colposcopy |
| Royal College of Obstetricians and Gynaecologists 2016 (60)                            | No specific reporting criteria regarding colposcopy |
| Santesso 2016 (61)   | No specific reporting criteria regarding colposcopy |
| Saslow 2012 (62)   | No specific reporting criteria regarding colposcopy |
| Schmidt 2018 (63)  | No specific reporting criteria regarding colposcopy |
| Society of Gynecologic Oncology 2010 (64)  | No guidance for colposcopy                          |
| Society of Gynecologic Oncology 2010 (65)  | No specific reporting criteria regarding colposcopy |
| Society of Obstetricians and Gynaecologists of Canada 2012 (66)                        | No new reporting criteria (refer to IFPCPC)         |

|   |   |
|---|---|
| The National Institute for Health and Care Excellence 2018 (67) | No specific reporting criteria regarding colposcopy |
| University of Michigan Health System 2014 (68)                  | No specific reporting criteria regarding colposcopy |
| Wentzensen 2017 (69)  | No specific reporting criteria regarding colposcopy |
| World Health Organisation Guidelines 2011 (70)                  | No guidance for colposcopy                          |
| World Health Organisation Guidelines 2015 (71)                  | No new reporting criteria                           |
| World Health Organisation Guidelines 2019 (72)                  | No specific reporting criteria regarding colposcopy |

## Referenties

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2. American Academy of Pediatrics. Gynecologic Examination for Adolescents in the Pediatric Office Setting. 2010.
3. American College of Obstetricians and Gynecologists. Tracking and Reminder Systems. 2012.
4. American College of Obstetricians and Gynecologists. Cervical Cancer Screening in Low-Resource Settings. 2015.
5. American College of Obstetricians and Gynecologists. Practice Advisory: Cervical Cancer Screening. 2018.
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7. American College of Physicians. Cervical Cancer Screening in Average Risk Women: Best Practice Advice from the Clinical Guidelines Committee of the American College of Physicians. 2015.
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9. American Society for Clinical Pathology. 2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors. 2012.
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20. Cancer Council Australia. Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. 2016.
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43. Kaiser Permanente Clinical Guidelines. Cervical Cancer Screening. 2015.
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### 3B: Systematische reviews

Uitgesloten systematische reviews betreffende de diagnostische accuratesse van colposcopie indicatoren en het klinisch nut van gestandaardiseerde rapportage van colposcopie.

| Reference                | Reason for exclusion                          |
|--------------------------|---|
| Adsul 2017 (1)           | Wrong index test                              |
| Bentley 2012 (2)         | No systematic review                          |
| Catarino 2018 (3)        | Wrong index test                              |
| Chanthavilay 2015 (4)    | Wrong index test                              |
| Costa-Fagbemi 2019 (5)   | Wrong population                              |
| Ebisch 2016 (6)          | No diagnostic accuracy or intervention review |
| Fokom-Domgoue 2015 (7)   | Wrong index test                              |
| Hermens 2016 (8)         | Wrong index test                              |
| Mayeaux 2017 (9)         | Guideline                                     |
| Mitchell 1998 (10)       | Single database searched                      |
| Mustafa 2016 (11)        | Wrong population                              |
| Nazeer 2011 (12)         | No systematic review                          |
| Nocon 2007 (13)          | Wrong population                              |
| Olaniyan 2002 (14)       | Single database searched                      |
| Onyango Calleb 2020 (15) | Wrong index test                              |
| Peron 2018 (16)          | Wrong index test                              |
| Qiao 2015 (17)           | Wrong index test                              |
| Ren 2020 (18)            | Wrong index test                              |
| Rouzier 2008 (19)        | No full text                                  |
| Sauter 2015 (20)         | No systematic review                          |
| Sauvaget 2011 (21)       | Wrong index test                              |
| Silver 2018 (22)         | Single database searched                      |
| Sritipsukho 2010 (23)    | Wrong index test                              |
| Taghavi 2020 (24)        | Wrong population                              |
| Underwood 2012 (25)      | Wrong index test                              |



|                    |                  |
|--------------------|------------------|
| Wade 2013 (26)     | Wrong index test |
| Williams 2018 (27) | Wrong index test |

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### 3C: Primaire onderzoeken, PICO 1

#### Uitgesloten onderzoeken betreffende diagnostische accuratesse van colposcopie indicatoren

| Reason for exclusion | References |
|----------------------|------------|
| Wrong population     | (1-35)     |
| Wrong index test     | (36-68)    |
| Digital colposcopy   | (69-77)    |
| Wrong indicator      | (78-99)    |
| Wrong outcome        | (100-110)  |
| No DTA of colposcopy | (111-119)  |
| Wrong study type     | (120-131)  |
| Wrong study design   | (132-145)  |
| No Full text         | (146-241)  |
| Language             | (242-255)  |
| Duplicate            | (256, 257) |
| Retracted article    | (258)      |

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### 3D: Primaire onderzoeken, PICO 2

#### Uitgesloten onderzoeken betreffende klinisch nut van gestandaardiseerde rapportage van colposcopie

| Reference         | Reason for exclusion                           |
|-------------------|--|
| Luyten 2015 (1)   | Wrong intervention / no standardized reporting |
| Luyten 2015 (2)   | Wrong intervention / no standardized reporting |
| Marret 1998 (3)   | No full text                                   |
| Min 2020 (4)      | Wrong intervention / no standardized reporting |
| Mueller 2017 (5)  | Wrong study design                             |
| Rema 2019 (6)     | DTA study                                      |
| Simsir 2006 (7)   | Wrong intervention / no standardized reporting |
| Verma 2014 (8)    | Wrong intervention / no standardized reporting |
| White 2013 (9)    | Wrong intervention / no standardized reporting |
| Wieland 2011 (10) | Wrong study design                             |

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## Bijlage 4. Overzicht van de beoordeling met het NEATS-instrument

### Bornstein 2012. International Federation for Cervical Pathology and Colposcopy (IFCPC)

| Item  | Judgement  | Comments  |
|---|--|---|
| 1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.  | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No   |   |
| 2. Financial COIs of guideline development group (GDG) members have been disclosed and managed.   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/> Highest adherence |   |
| 3a. The GDG includes persons from a variety of relevant clinical specialties and other professional groups.   | <input type="checkbox"/> Yes<br><input type="checkbox"/> No<br><input checked="" type="checkbox"/> Unknown   | It seems to be only doctors, though from different countries and from different departments |
| 3b. The guideline states that it included a methodological expert in the GDG, and it identifies the methodologist.  | <input type="checkbox"/> Yes<br><input checked="" type="checkbox"/> No<br><input type="checkbox"/> Unknown   |   |
| 4. The GDG sought the views, perspectives, and preferences of patients, patient surrogates (parents and caretakers), patient advocates, or the public, intended to represent those who have experience with the disease, its treatments, or its complications, or those who could be affected by the guideline. | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 5a. The CPG or a related companion document describes a search strategy that includes a listing of database(s) searched; a summary of search terms used; and the specific time period covered by the literature search, including the beginning date (month and year) and end date (month and year).            | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 5b. The CPG or a related companion document describes the study selection; description includes the number of studies identified, the number of studies included, and a summary of inclusion and exclusion criteria.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 5c. The CPG or a related companion document provides a synthesis of evidence from the selected studies; i.e., an analysis of individual studies and the body of evidence, in the form of a  | <input type="checkbox"/> Lowest adherence<br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/>                   | A couple of studies on items that changed from a previous document                          |

|   |  |                                      |
|---|--|--------------------------------------|
| detailed description or evidence tables, or both.   | <input type="checkbox"/> Highest adherence   |                                      |
| 6. The CPG provides a grading or rating of the level of confidence in or certainty regarding the quality or strength of the evidence for each recommendation.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |                                      |
| 7. The potential benefits and harms of recommended care are clearly described.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |                                      |
| 8. A summary of the relevant supporting evidence is explicitly linked to recommendations.   | <input type="checkbox"/> Lowest adherence<br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |                                      |
| 9. The CPG gives a rating of the strength of each recommendation that takes into account benefits and harms, available evidence, and the confidence in the underlying evidence.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |                                      |
| 10. The recommendations are specific and unambiguous, stating what action should or should not be taken in what situations and for what population groups. Where the CPG recommendations are intentionally vague or underspecified, the CPG clearly describes the rationale behind those recommendations. | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence |                                      |
| 11. The guideline has been reviewed by relevant stakeholders, including scientific and clinical experts, organizations, agencies, and patients.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |                                      |
| 12. The CPG describes a procedure to update the guideline.  | <input type="checkbox"/> Lowest adherence<br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | They just provide an updated version |

**Werkgroep richtlijn CIN, AIS en VAIN, 2015. Werkgroep richtlijn CIN, AIS en VAIN (Nederlandse Vereniging voor Obstetrie en Gynaecologie (NVOG), Nederlandse Vereniging voor Pathologie (NVVP), Nederlandse Vereniging voor Medische Microbiologie (NVVM))**

| Item  | Judgement  | Comments  |
|---|--|---|
| 1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.  | <input type="checkbox"/> Yes<br><input checked="" type="checkbox"/> No   |   |
| 2. Financial COIs of guideline development group (GDG) members have been disclosed and managed.   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/> Highest adherence | <p>P. 99: “Om de beïnvloeding van de richtlijnontwikkeling of formulering van de aanbevelingen door conflicterende belangen te minimaliseren zijn de leden van werkgroep gemandateerd door de wetenschappelijke verenigingen. Alle werkgroepleden hebben bij aanvang en bij de afronding van het richtlijn traject een belangenverklaring ingevuld. Hiermee geven de werkgroepleden aan onafhankelijk gehandeld te hebben bij het opstellen van de richtlijn. Potentiële conflicterende belangen zijn besproken. Waar nodig zijn werkgroepleden met belangenverstremeling vervangen door een ander gemandateerd werkgroep lid.”</p> |
| 3a. The GDG includes persons from a variety of relevant clinical specialties and other professional groups.   | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No<br><input type="checkbox"/> Unknown   |   |
| 3b. The guideline states that it included a methodological expert in the GDG, and it identifies the methodologist.  | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No<br><input type="checkbox"/> Unknown   | <p>P.99: Dr. A. Siebers, wetenschappelijk onderzoeker</p>   |
| 4. The GDG sought the views, perspectives, and preferences of patients, patient surrogates (parents and caretakers), patient advocates, or the public, intended to represent those who have experience with the disease, its treatments, or its complications, or those who could be affected by the guideline. | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/> Highest adherence | <p>p. 94: “De conceptrychtlijn is op 12 februari 2015 ter commentariëring aangeboden op <a href="http://www.richtlijndatabase.nl">www.richtlijndatabase.nl</a> en <a href="http://www.oncoline/">http://www.oncoline/</a> en aan alle voor de knelpuntenanalyse benaderde</p>   |

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|   |   | <p>wetenschappelijke, beroeps- en patiëntenverenigingen en naar de landelijke en regionale tumorwerkgroepen. Ten slotte is de richtlijn ter autorisatie/ter accordering gestuurd naar de betrokken verenigingen/instanties.”</p> <p>P. 99: “Bij de ontwikkeling van deze richtlijn is tijdens alle fasen gebruikt gemaakt van de input van patiënten. Drie patiëntvertegenwoordigers namen zitting in de richtlijnwerkgroep (allen ervaringsdeskundige op het gebied van CIN).”</p> |
| <p>5a. The CPG or a related companion document describes a search strategy that includes a listing of database(s) searched; a summary of search terms used; and the specific time period covered by the literature search, including the beginning date (month and year) and end date (month and year).</p> | <p><input checked="" type="checkbox"/>Lowest adherence<br/> <input type="checkbox"/><br/> <input type="checkbox"/><br/> <input type="checkbox"/>Highest adherence</p> | <p>“Voor consensus based richtlijnteksten is er geen systematisch literatuuronderzoek uitgevoerd en worden de artikelen niet methodologisch beoordeeld. Er wordt geen level of evidence toegekend aan de studies en er wordt geen niveau van bewijs toegekend aan de conclusies.”</p>   |
| <p>5b. The CPG or a related companion document describes the study selection; description includes the number of studies identified, the number of studies included, and a summary of inclusion and exclusion criteria.</p>   | <p><input checked="" type="checkbox"/>Lowest adherence<br/> <input type="checkbox"/><br/> <input type="checkbox"/><br/> <input type="checkbox"/>Highest adherence</p> | <p>“Voor consensus based richtlijnteksten is er geen systematisch literatuuronderzoek uitgevoerd en worden de artikelen niet methodologisch beoordeeld. Er wordt geen level of evidence toegekend aan de studies en er wordt geen niveau van bewijs toegekend aan de conclusies.”</p>   |



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| <p>5c. The CPG or a related companion document provides a synthesis of evidence from the selected studies; i.e., an analysis of individual studies and the body of evidence, in the form of a detailed description or evidence tables, or both.</p> | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | <p>“Voor consensus based richtlijnteksten is er geen systematisch literatuuronderzoek uitgevoerd en worden de artikelen niet methodologisch beoordeeld. Er wordt geen level of evidence toegekend aan de studies en er wordt geen niveau van bewijs toegekend aan de conclusies.”</p>  |
| <p>6. The CPG provides a grading or rating of the level of confidence in or certainty regarding the quality or strength of the evidence for each recommendation.</p>  | <input type="checkbox"/> Lowest adherence<br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | <p>P. 90: “Elke module is uitgewerkt volgens de consensus based methodiek. Consensus based teksten zijn gebaseerd op evidence. Deze evidence is door de werkgroepleden zelf verzameld en verwerkt. Voor consensus based richtlijnteksten is er geen systematisch literatuuronderzoek uitgevoerd en worden de artikelen niet methodologisch beoordeeld. Er wordt geen level of evidence toegekend aan de studies en er wordt geen niveau van bewijs toegekend aan de conclusies. De formulering van de conclusie hangt af van de onderliggende artikelen (zie tabel 1 en 2).”</p> |
| <p>7. The potential benefits and harms of recommended care are clearly described.</p>   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| <p>8. A summary of the relevant supporting evidence is explicitly linked to recommendations.</p>  | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input checked="" type="checkbox"/>   |  |

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|   | <input type="checkbox"/><br><input type="checkbox"/> Highest adherence   |   |
| 9. The CPG gives a rating of the strength of each recommendation that takes into account benefits and harms, available evidence, and the confidence in the underlying evidence.   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | The CPG gives a rating of the strength of each recommendation that takes into account the underlying evidence, by formulating conclusions in a particular way (e.g. 'Het is aangetoond dat...', or 'Er zijn aanwijzingen dat...'). See p. 90-94 |
| 10. The recommendations are specific and unambiguous, stating what action should or should not be taken in what situations and for what population groups. Where the CPG recommendations are intentionally vague or underspecified, the CPG clearly describes the rationale behind those recommendations. | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 11. The guideline has been reviewed by relevant stakeholders, including scientific and clinical experts, organizations, agencies, and patients.   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/> Highest adherence                             |   |
| 12. The CPG describes a procedure to update the guideline.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | P. 98: "Deze module is goedgekeurd op (datum). IKNL bewaakt samen met betrokken verenigingen de houdbaarheid van deze en andere onderdelen van de richtlijn. Zo nodig zal de richtlijn tussentijds op onderdelen worden bijgesteld."            |

### Khan 2017. American Society for Colposcopy and Cervical Pathology Colposcopy Standards

| Item  | Judgement  | Comments   |
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| 1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.    | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No   |  |
| 2. Financial COIs of guideline development group (GDG) members have been disclosed and managed. | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> | Some of the members of the CDG are sponsored by industry. This has been disclosed, but it is unclear |

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|   | <input type="checkbox"/> Highest adherence   | how this was further handled.  |
| 3a. The GDG includes persons from a variety of relevant clinical specialties and other professional groups.   | <input type="checkbox"/> Yes<br><input checked="" type="checkbox"/> No<br><input type="checkbox"/> Unknown   | It seems like mostly clinicians have been included and no other professional groups.   |
| 3b. The guideline states that it included a methodological expert in the GDG, and it identifies the methodologist.  | <input type="checkbox"/> Yes<br><input checked="" type="checkbox"/> No<br><input type="checkbox"/> Unknown   |  |
| 4. The GDG sought the views, perspectives, and preferences of patients, patient surrogates (parents and caretakers), patient advocates, or the public, intended to represent those who have experience with the disease, its treatments, or its complications, or those who could be affected by the guideline. | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | <p>“After further editing and notification of stakeholder professional organizations, recommendations were posted on the ASCCP website for public comments between March 13 and 22, 2017; additional modifications were made in response to the comments”</p> <p>However, patients were not actively involved in the development.</p>  |
| 5a. The CPG or a related companion document describes a search strategy that includes a listing of database(s) searched; a summary of search terms used; and the specific time period covered by the literature search, including the beginning date (month and year) and end date (month and year).            | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/> Highest adherence                             | <p>A systematic literature search was conducted to identify studies with relevant information about the role of colposcopy, benefits, potential harms, and terminology. A separate search for each charge was performed using the search terms appropriate for that charge selected from the following: colposcopy, standards, statistics, numerical data, therapeutic use, therapy, use, uterine cervical neoplasms, cytology, diagnosis, epidemiology, prevention and control, secondary, benefit of colposcopy, adverse effects, contraindications, psychology, classification,</p> |

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|  |  | and pathology. The Colposcopy Standards Steering Committee elected to use PubMed for the literature search because of its comprehensiveness. The PubMed search was performed on June 1, 2016, and yielded 459 citations. |
| 5b. The CPG or a related companion document describes the study selection; description includes the number of studies identified, the number of studies included, and a summary of inclusion and exclusion criteria.                         | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 5c. The CPG or a related companion document provides a synthesis of evidence from the selected studies; i.e., an analysis of individual studies and the body of evidence, in the form of a detailed description or evidence tables, or both. | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 6. The CPG provides a grading or rating of the level of confidence in or certainty regarding the quality or strength of the evidence for each recommendation.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 7. The potential benefits and harms of recommended care are clearly described.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 8. A summary of the relevant supporting evidence is explicitly linked to recommendations.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 9. The CPG gives a rating of the strength of each recommendation that takes into account benefits and harms, available evidence, and the confidence in the underlying evidence.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 10. The recommendations are specific and unambiguous, stating what action should or should not be taken in what  | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/>  |  |

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| situations and for what population groups. Where the CPG recommendations are intentionally vague or underspecified, the CPG clearly describes the rationale behind those recommendations. | <input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence  |  |
| 11. The guideline has been reviewed by relevant stakeholders, including scientific and clinical experts, organizations, agencies, and patients.   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 12. The CPG describes a procedure to update the guideline.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence                             |  |

**Mayeaux 2017. American Society for Colposcopy and Cervical Pathology (ASCCP) Colposcopy Standards**

| Item  | Judgement  | Comments   |
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| 1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.    | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No   | There was no source of financial support for the project. For 1 Author: The project described was partially supported by Grant Number D33HP26995 from the Health Resources and Services Administration (HRSA), an operating division of the U.S. Department of Health and Human Services. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Health Resources and Services Administration or the U.S. Department of Health and Human Services. |
| 2. Financial COIs of guideline development group (GDG) members have been disclosed and managed. | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> | Several authors received support from industry. These are all disclosed. However, the document does not describe how   |

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|   | <input type="checkbox"/> Highest adherence   | these conflicts may have affected the guideline process and any steps taken to manage and minimize their effect (e.g., recusal, divestment).  |
| 3a. The GDG includes persons from a variety of relevant clinical specialties and other professional groups.   | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No<br><input type="checkbox"/> Unknown   | Kim Choma, RN, DNP, APN<br>Women’s Health Nurse Practitioner<br>Genetics, O&G, Cancer epi, MD’s etc. Only people from USA part of authors   |
| 3b. The guideline states that it included a methodological expert in the GDG, and it identifies the methodologist.  | <input type="checkbox"/> Yes<br><input checked="" type="checkbox"/> No<br><input type="checkbox"/> Unknown   | It does not state any person specifically.  |
| 4. The GDG sought the views, perspectives, and preferences of patients, patient surrogates (parents and caretakers), patient advocates, or the public, intended to represent those who have experience with the disease, its treatments, or its complications, or those who could be affected by the guideline. | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | “There were no patients or patient advocates on the working group.”   |
| 5a. The CPG or a related companion document describes a search strategy that includes a listing of database(s) searched; a summary of search terms used; and the specific time period covered by the literature search, including the beginning date (month and year) and end date (month and year).            | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/> Highest adherence | The companion document is a published SR that is referenced in the guideline.   |
| 5b. The CPG or a related companion document describes the study selection; description includes the number of studies identified, the number of studies included, and a summary of inclusion and exclusion criteria.  | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence | The companion document is a published SR that is referenced in the guideline. A bit vague regarding reasons for exclusion in the flowchart. Also one study at the evidence table is missing |
| 5c. The CPG or a related companion document provides a synthesis of evidence from the selected studies; i.e., an analysis of individual studies and the body of evidence, in the form of a detailed description or evidence tables, or both.  | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/> Highest adherence | The companion document is a published SR that is referenced in the guideline.   |

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| 6. The CPG provides a grading or rating of the level of confidence in or certainty regarding the quality or strength of the evidence for each recommendation.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | Both not in the SR and guideline documents  |
| 7. The potential benefits and harms of recommended care are clearly described.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 8. A summary of the relevant supporting evidence is explicitly linked to recommendations.   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence | For each recommendation, it refers to references.   |
| 9. The CPG gives a rating of the strength of each recommendation that takes into account benefits and harms, available evidence, and the confidence in the underlying evidence.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 10. The recommendations are specific and unambiguous, stating what action should or should not be taken in what situations and for what population groups. Where the CPG recommendations are intentionally vague or underspecified, the CPG clearly describes the rationale behind those recommendations. | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence | For the reporting, the recommendations are specific; but they don't state 2) for whom and 3) under which circumstances. |
| 11. The guideline has been reviewed by relevant stakeholders, including scientific and clinical experts, organizations, agencies, and patients.   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | It has not been reviewed by patients, or specifically methodologists. But has been monitored by a steering committee    |
| 12. The CPG describes a procedure to update the guideline.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | An update is not mentioned.   |

**Waxman 2017. American Society for Colposcopy and Cervical Pathology Colposcopy Standards**

| Item   | Judgement  | Comments |
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| 1. The clinical practice guideline (CPG) discloses and states explicitly its funding source. | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No |          |

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| <p>2. Financial COIs of guideline development group (GDG) members have been disclosed and managed.</p>   | <p><input type="checkbox"/>Lowest adherence<br/> <input type="checkbox"/><br/> <input checked="" type="checkbox"/><br/> <input type="checkbox"/><br/> <input type="checkbox"/>Highest adherence</p> | <p>Some members of the GDG were sponsored by industry. COIs have been disclosed, but it is unclear whether the COIs have affected the guideline process.</p>  |
| <p>3a. The GDG includes persons from a variety of relevant clinical specialties and other professional groups.</p>   | <p><input type="checkbox"/>Yes<br/> <input checked="" type="checkbox"/>No<br/> <input type="checkbox"/>Unknown</p>  | <p>The GDG included mostly clinicians and no other professional groups.</p>   |
| <p>3b. The guideline states that it included a methodological expert in the GDG, and it identifies the methodologist.</p>  | <p><input type="checkbox"/>Yes<br/> <input checked="" type="checkbox"/>No<br/> <input type="checkbox"/>Unknown</p>  |   |
| <p>4. The GDG sought the views, perspectives, and preferences of patients, patient surrogates (parents and caretakers), patient advocates, or the public, intended to represent those who have experience with the disease, its treatments, or its complications, or those who could be affected by the guideline.</p> | <p><input type="checkbox"/>Lowest adherence<br/> <input type="checkbox"/><br/> <input checked="" type="checkbox"/><br/> <input type="checkbox"/><br/> <input type="checkbox"/>Highest adherence</p> | <p>“After further editing and notification of stakeholder professional organizations, recommendations were posted on the ASCCP website for public comments between March 13–22, 2017, which resulted in additional modifications in response to the comments.”</p>  |
| <p>5a. The CPG or a related companion document describes a search strategy that includes a listing of database(s) searched; a summary of search terms used; and the specific time period covered by the literature search, including the beginning date (month and year) and end date (month and year).</p>            | <p><input type="checkbox"/>Lowest adherence<br/> <input type="checkbox"/><br/> <input type="checkbox"/><br/> <input checked="" type="checkbox"/><br/> <input type="checkbox"/>Highest adherence</p> | <p>“A systematic literature search was conducted to identify studies with relevant information about colposcopic technique, methods, instrumentation and adjuncts. The literature search terms for these specific areas were generated at the National Cancer Institute and reference lists were provided to the working groups. This PubMed search was performed on June 1, 2016 of English language literature between 1982 and 2015 and yielded 390 abstracts. The working group evaluated these articles for relevant results.”</p> |



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| <p>5b. The CPG or a related companion document describes the study selection; description includes the number of studies identified, the number of studies included, and a summary of inclusion and exclusion criteria.</p>  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| <p>5c. The CPG or a related companion document provides a synthesis of evidence from the selected studies; i.e., an analysis of individual studies and the body of evidence, in the form of a detailed description or evidence tables, or both.</p>  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| <p>6. The CPG provides a grading or rating of the level of confidence in or certainty regarding the quality or strength of the evidence for each recommendation.</p>   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| <p>7. The potential benefits and harms of recommended care are clearly described.</p>  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| <p>8. A summary of the relevant supporting evidence is explicitly linked to recommendations.</p>   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| <p>9. The CPG gives a rating of the strength of each recommendation that takes into account benefits and harms, available evidence, and the confidence in the underlying evidence.</p>   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| <p>10. The recommendations are specific and unambiguous, stating what action should or should not be taken in what situations and for what population groups. Where the CPG recommendations are intentionally vague or underspecified, the CPG clearly describes the rationale behind those recommendations.</p> | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| <p>11. The guideline has been reviewed by relevant stakeholders, including scientific and clinical experts, organizations, agencies, and patients.</p>   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/>  |  |

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|  | <input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence  |  |
| 12. The CPG describes a procedure to update the guideline. | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |

**Petry 2018. European Federation for Colposcopy (EFC)**

| Item  | Judgement  | Comments  |
|---|--|---|
| 1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.  | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No   |   |
| 2. Financial COIs of guideline development group (GDG) members have been disclosed and managed.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 3a. The GDG includes persons from a variety of relevant clinical specialties and other professional groups.   | <input type="checkbox"/> Yes<br><input type="checkbox"/> No<br><input checked="" type="checkbox"/> Unknown   | 34 member societies, but their role is not mentioned. The 5 study authors are from different countries and clinicians |
| 3b. The guideline states that it included a methodological expert in the GDG, and it identifies the methodologist.  | <input type="checkbox"/> Yes<br><input checked="" type="checkbox"/> No<br><input type="checkbox"/> Unknown   |   |
| 4. The GDG sought the views, perspectives, and preferences of patients, patient surrogates (parents and caretakers), patient advocates, or the public, intended to represent those who have experience with the disease, its treatments, or its complications, or those who could be affected by the guideline. | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 5a. The CPG or a related companion document describes a search strategy that includes a listing of database(s) searched; a summary of search terms used; and the specific time period covered by the literature search, including the beginning date (month and year) and end date (month and year).            | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |   |
| 5b. The CPG or a related companion document describes the study selection; description includes the number of studies identified, the number of studies   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/>   |   |

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| included, and a summary of inclusion and exclusion criteria.  | <input type="checkbox"/> Highest adherence   |  |
| 5c. The CPG or a related companion document provides a synthesis of evidence from the selected studies; i.e., an analysis of individual studies and the body of evidence, in the form of a detailed description or evidence tables, or both.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | A review of Luyten et al. (2015) is mentioned, as well as the 2013 Quality Indicator (QI) study. |
| 6. The CPG provides a grading or rating of the level of confidence in or certainty regarding the quality or strength of the evidence for each recommendation.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 7. The potential benefits and harms of recommended care are clearly described.  | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 8. A summary of the relevant supporting evidence is explicitly linked to recommendations.   | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | Scored as such because of the 2013 Quality Indicator (QI) study.                                 |
| 9. The CPG gives a rating of the strength of each recommendation that takes into account benefits and harms, available evidence, and the confidence in the underlying evidence.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 10. The recommendations are specific and unambiguous, stating what action should or should not be taken in what situations and for what population groups. Where the CPG recommendations are intentionally vague or underspecified, the CPG clearly describes the rationale behind those recommendations. | <input type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input checked="" type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 11. The guideline has been reviewed by relevant stakeholders, including scientific and clinical experts, organizations, agencies, and patients.   | <input checked="" type="checkbox"/> Lowest adherence<br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence |  |
| 12. The CPG describes a procedure to update the guideline.  | <input type="checkbox"/> Lowest adherence<br><input checked="" type="checkbox"/>   | Apart from stating that the QIs will undergo continuing  |

|  |  |   |
|--|--|---|
|  | <input type="checkbox"/><br><input type="checkbox"/><br><input type="checkbox"/> Highest adherence | review, there is no information about an expected timeframe or the process that will be followed. |
|--|--|---|

## Bijlage 5. Overzicht primaire ingesloten onderzoeken geëxcludeerd voor analyses

| Reference               | Population   | Study type                |     |                        | Prediction models | Indicators        |                 |                        |                     |                    |                |                |                 |                  |
|-------------------------|--|---------------------------|-----|------------------------|-------------------|-------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|------------------|
|                         |  | Indication for colposcopy | DTA | Interrater variability |                   | Predictor finding | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern |
| Del Pino 2021 (1)       | Abnormal cytology or HPV                                 | X                         |     |                        | Univariable       |                   | X               |                        |                     |                    |                |                |                 |                  |
| Li 2021 (2)             | Abnormal cytology, persistent abnormal HPV or complaints | X                         |     |                        | Univariable       | IFCPC criteria    | X               |                        |                     |                    | X              |                |                 |                  |
| Maringa 2021 (3)        | Abnormal cytology, VIA or VILI, or complaints            | X                         |     |                        | Multivariable     | Swede score       | X               | X                      |                     | X                  |                | X              | X               | X                |
| Nayak 2021 (4)          | Complaints   | X                         |     |                        |                   | Reid index        | X               |                        |                     |                    |                |                |                 |                  |
| Dorji 2020 (5)          | Abnormal VIA or complaints                               | X                         |     |                        |                   |                   | X               |                        |                     |                    |                |                |                 |                  |
| Fatahi 2020 (6)         | Abnormal HPV or complaints                               |                           |     |                        |                   | Reid index        | X               |                        |                     |                    |                |                |                 |                  |
| Najib 2020 (7)          | Complaints   | X                         |     |                        |                   |                   | X               |                        |                     |                    |                |                |                 |                  |
| Parra 2020 (8)          | Abnormal HPV   | X                         |     |                        |                   |                   | X               |                        |                     |                    |                |                |                 |                  |
| Pretorius 2020 (9)      | Abnormal cytology or HPV                                 | X                         |     |                        |                   |                   | X               |                        |                     |                    |                |                |                 |                  |
| Ruan 2020 (10)          | Unclear  | X                         | X   |                        |                   |                   | X               |                        |                     |                    |                |                | X               |                  |
| Suwanthananon 2020 (11) | Abnormal cytology or HPV                                 |                           |     |                        |                   | Reid index,       | X               |                        |                     |                    |                |                |                 |                  |

| Reference                    | Population   | Study type |                        |                   | Prediction models                | Indicators      |                        |                     |                    |                |                |                 |                  |                    |
|------------------------------|--|------------|------------------------|-------------------|----------------------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|------------------|--------------------|
|                              |  | DTA        | Interrater variability | Predictor finding |                                  | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern | Border and surface |
|                              |  |            |                        |                   | Swede score                      |                 |                        |                     |                    |                |                |                 |                  |                    |
| Usmani 2020 (12)             | Abnormal VIA   |            |                        |                   | Modified Reid index, Swede score | X               |                        |                     |                    |                |                |                 |                  |                    |
| Yuan 2020 (13)               | Women referred to colposcopy clinic, not further specified   | X          |                        |                   |                                  |                 |                        |                     |                    | X              |                |                 |                  |                    |
| Bhattachan 2019 (14)         | Complaints   |            |                        |                   | Swede score                      | X               |                        |                     |                    |                |                |                 |                  |                    |
| Boonlikit 2019 (15)          | Abnormal HPV   |            |                        |                   | Modified Reid index              | X               |                        |                     |                    |                |                |                 |                  |                    |
| Dayal 2019 (16)              | Abnormal VIA   |            |                        |                   | Swede score                      | X               |                        |                     |                    |                |                |                 |                  |                    |
| de Castro Hillmann 2019 (17) | Women referred to colposcopy clinic, not further specified   | X          |                        |                   |                                  | X               |                        |                     |                    |                |                |                 |                  |                    |
| Huh 2019 (18)                | Abnormal cytology or HPV, or follow-up after treatment       | X          |                        |                   |                                  | X               |                        |                     |                    |                |                |                 |                  |                    |
| Lockett 2019 (19)            | Abnormal HPV   | X          |                        |                   |                                  | X               |                        |                     |                    |                |                |                 |                  |                    |
| Parra 2019 (20)              | Abnormal cytology or HPV, or a history of cervical dysplasia | X          |                        |                   |                                  | X               |                        |                     |                    |                |                |                 |                  |                    |

| Reference           | Population   | Study type                |     | Prediction models           | Indicators                                       |                   |                 |                        |                     |                    |                |                |                 |                  |
|---------------------|--|---------------------------|-----|-----------------------------|--|-------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|------------------|
|                     |  | Indication for colposcopy | DTA |                             | Interrater variability                           | Predictor finding | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern |
| Pretorius 2019 (21) | Abnormal cytology or HPV                                   | X                         |     |                             |  | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Rema 2019 (22)      | Abnormal cytology or VIA                                   |                           |     |                             | Modified IFCCP criteria                          | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Fan 2018 (23)       | Abnormal cytology or HPV, or complaints                    | X                         |     | Univariable & multivariable |  | X                 | X               |                        | X                   | X                  | X              | X              | X               |                  |
| Taghavi 2018 (24)   | Abnormal HPV or VIA  |                           |     |                             | Swede score                                      | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Wentzen 2018 (25)   | Unclear  | X                         |     |                             |  | X                 | X               |                        |                     |                    |                |                |                 |                  |
| Beyer 2017 (26)     | Women referred to colposcopy clinic, not further specified | X                         |     | Univariable & multivariable |  |                   | X               |                        |                     |                    |                | X              | X               |                  |
| Kashimura 2017 (27) | Abnormal cytology or complaints                            | X                         |     |                             | IFCCP criteria                                   | X                 |                 |                        | X                   |                    |                |                |                 |                  |
| Kushwah 2017 (28)   | Abnormal cytology, VIA or VILI, or complaints              | X                         |     |                             | Reid index, Swede score                          | X                 |                 |                        | X                   |                    |                |                |                 |                  |
| Li 2017 (29)        | Abnormal cytology or HPV, or complaints                    | X                         | X   |                             | IFCCP criteria, Reid Index, modified Reid Index, | X                 | X               |                        |                     | X                  | X              | X              | X               |                  |

| Reference           | Population   | Study type                |     |                        | Prediction models       | Indicators      |                        |                     |                    |                |                |                 |                  |                    |
|---------------------|--|---------------------------|-----|------------------------|-------------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|------------------|--------------------|
|                     |  | Indication for colposcopy | DTA | Interrater variability | Predictor finding       | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern | Border and surface |
|                     |  |                           |     |                        | Swede score             |                 |                        |                     |                    |                |                |                 |                  |                    |
| Macdonald 2017 (30) | Women referred to colposcopy clinic, not further specified | X                         |     |                        |                         | X               |                        |                     |                    |                |                |                 |                  |                    |
| Mueller 2017 (31)   | Abnormal cytology or HPV                                   | X                         | X   |                        |                         | X               | X                      |                     |                    |                |                | X               | X                |                    |
| Penumalli 2017 (32) | Abnormal cytology or complaints                            | X                         |     |                        | Swede score             | X               |                        |                     |                    |                |                |                 |                  |                    |
| Ranga 2017 (33)     | Abnormal cytology, HPV, VIA or VILI                        | X                         |     |                        | Reid index, Swede score | X               |                        |                     | X                  |                |                |                 |                  |                    |
| Baasland 2016 (34)  | Abnormal cytology or HPV                                   |                           |     |                        | Abbreviated Reid index  | X               |                        |                     |                    |                |                |                 |                  |                    |
| Coronado 2016 (35)  | Women referred to colposcopy clinic, not further specified | X                         |     |                        |                         | X               |                        |                     |                    |                |                |                 |                  |                    |
| Fatehi 2016 (36)    | Abnormal cytology, HPV or VIA, or complaints               | X                         |     |                        |                         | X               |                        |                     |                    |                |                |                 |                  |                    |
| Ghosh 2016 (37)     | Abnormal HPV or VIA  | X                         |     |                        |                         | X               |                        |                     |                    |                |                |                 |                  |                    |
| Liu 2016 (38)       | Women referred to colposcopy clinic, not further specified | X                         | X   |                        |                         | X               | X                      |                     |                    |                |                |                 |                  |                    |



| Reference                | Population   | Study type                |     |                        | Prediction models | Indicators        |                 |                        |                     |                    |                |                |                 |
|--------------------------|--|---------------------------|-----|------------------------|-------------------|-------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|
|                          |  | Indication for colposcopy | DTA | Interrater variability |                   | Predictor finding | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining |
| Aue-Aungkul 2015 (39)    | Women referred to colposcopy clinic, not further specified |                           | X   |                        | Reid index        | X                 | X               |                        |                     |                    | X              | X              | X               |
| Barut 2015 (40)          | Complaints   | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                | X              |                 |
| Jeronimo 2015 (41)       | Women referred to colposcopy clinic, not further specified | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |
| Kaban 2015 (42)          | Abnormal cytology or complaints                            |                           |     |                        | Reid index        | X                 |                 |                        |                     |                    |                |                |                 |
| Nooh 2015 (43)           | Complaints   | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |
| Schneider 2015 (44)      | Abnormal cytology or HPV                                   | X                         |     |                        |                   |                   | X               |                        |                     |                    |                | X              | X               |
| Thulaseedharan 2015 (45) | Unclear  | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |
| Vercellino 2015 (46)     | Abnormal cytology or HPV, or complaints                    | X                         |     |                        |                   |                   | X               |                        |                     |                    | X              | X              | X               |
| Zhao 2015 (47)           | Abnormal cytology or HPV, or complaints                    | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |
| Ghosh 2014 (48)          | Abnormal HPV or VIA, or complaints                         | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |
| Nessa 2014 (49)          | Abnormal VIA   |                           |     |                        | Swede score       | X                 |                 |                        |                     |                    |                |                |                 |

| Reference            | Population  | Study type                |     |                        | Prediction models | Indicators        |                 |                        |                     |                    |                |                |                 |                  |
|----------------------|---|---------------------------|-----|------------------------|-------------------|-------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|------------------|
|                      |   | Indication for colposcopy | DTA | Interrater variability |                   | Predictor finding | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern |
| Pimple 2014 (50)     | Abnormal VIA  |                           |     |                        | Reid index        | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Saleh 2014 (51)      | Complaints  |                           |     |                        | Reid index        | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Singh 2014 (52)      | Complaints  | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Ngonzi 2013 (53)     | Abnormal VIA  |                           |     |                        | Swede score       | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Petry 2013 (54)      | Abnormal cytology and HPV, or persistent abnormal cytology or persistent abnormal HPV |                           |     |                        | IFCPC criteria    | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Slama 2013 (55)      | Abnormal cytology or HPV  | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                | X              | X               |                  |
| Vercellino 2013 (56) | Abnormal cytology or HPV  | X                         |     |                        |                   |                   |                 |                        |                     |                    |                |                |                 | X                |
| Yusuf 2013 (57)      | Complaints  | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Boicea 2012 (58)     | Abnormal cytology or complaints   | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Goyal 2012 (59)      | Complaints  |                           |     |                        | Reid index        | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Porras 2012 (60)     | Abnormal cytology or HPV  | X                         |     |                        |                   | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Aggarwal 2011 (61)   | Complaints  |                           |     |                        | Reid index        | X                 |                 |                        |                     |                    |                |                |                 |                  |

| Reference               | Population  | Study type                |     |                             | Prediction models   | Indicators        |                 |                        |                     |                    |                |                |                 |                  |
|-------------------------|---|---------------------------|-----|-----------------------------|---------------------|-------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|------------------|
|                         |   | Indication for colposcopy | DTA | Interrater variability      |                     | Predictor finding | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern |
| Patil 2011 (62)         | Complaints  | X                         |     |                             |                     | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Cagle 2010 (63)         | Abnormal cytology, HPV or VIA   | X                         |     |                             |                     | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Hong 2010 (64)          | Suspected or diagnosed abnormalities by either cervical cytology or cervicography |                           |     |                             | Modified Reid index | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Liu 2010 (65)           | Abnormal cytology or HPV  | X                         |     |                             |                     | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Louwers 2010 (66)       | Abnormal cytology or HPV, or complaints   | X                         | X   | Univariable                 |                     |                   | X               | X                      | X                   |                    |                | X              | X               |                  |
| Pimple 2010 (67)        | Abnormal VIA  |                           |     |                             | Reid index          | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Durdi 2009 (68)         | Abnormal cytology or complaints   |                           |     |                             | Reid index          | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Scheungra ber 2009 (69) | Abnormal cytology or HPV  | X                         |     | Univariable                 |                     |                   |                 |                        |                     |                    |                |                |                 | X                |
| Scheungra ber 2009 (70) | Abnormal cytology or HPV  | X                         | X   |                             |                     |                   |                 |                        |                     |                    |                |                |                 | X                |
| Hammes 2007 (71)        | Abnormal cytology, HPV, VIA or VILI   | X                         |     | Univariable & multivariable |                     | X                 | X               | X                      | X                   |                    | X              | X              | X               |                  |
| Mousavi 2007 (72)       | Women referred to colposcopy clinic, not further specified                        | X                         |     |                             | Reid index          | X                 |                 |                        |                     |                    |                |                |                 |                  |

| Reference            | Population   | Study type                |     |                        | Prediction models      | Indicators        |                 |                        |                     |                    |                |                |                 |                  |
|----------------------|--|---------------------------|-----|------------------------|------------------------|-------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|------------------|
|                      |  | Indication for colposcopy | DTA | Interrater variability |                        | Predictor finding | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern |
| Monsoneg o 2006 (73) | Abnormal cytology or HPV                                   | X                         |     |                        | IFCPC criteria         | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Volante 2006 (74)    | Unclear  | X                         |     |                        |                        | X                 |                 |                        |                     |                    |                | X              |                 |                  |
| Ferris 2005 (75)     | Women referred to colposcopy clinic, not further specified |                           | X   |                        | Reid index             | X                 |                 |                        |                     | X                  |                |                |                 |                  |
| Benedet 2004 (76)    | Abnormal cytology or complaints                            | X                         |     |                        |                        | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Ferris 2004 (77)     | Abnormal cytology or complaints                            | X                         |     |                        |                        | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Ferris 2004 (78)     | Unclear  | X                         | X   |                        |                        | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Sideri 2004 (79)     | Unclear  | X                         | X   |                        |                        | X                 |                 |                        |                     | X                  |                |                |                 |                  |
| Massad 2003 (80)     | Women referred to colposcopy clinic, not further specified | X                         | X   |                        |                        | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Shaw 2003 (81)       | Abnormal cytology or referred to colposcopy clinic         | X                         |     |                        | Abbreviated Reid index | X                 | X               |                        |                     |                    |                | X              | X               |                  |
| Ferris 2002 (82)     | Unclear  | X                         |     |                        |                        | X                 |                 |                        |                     |                    |                |                |                 |                  |
| Valmadre 2002 (83)   | Unclear  | X                         |     |                        |                        | X                 |                 |                        |                     |                    |                |                |                 |                  |

| Reference             | Population   | Study type                |     |                        | Prediction models          | Indicators      |                        |                     |                    |                |                |                 |                  |                    |
|-----------------------|--|---------------------------|-----|------------------------|----------------------------|-----------------|------------------------|---------------------|--------------------|----------------|----------------|-----------------|------------------|--------------------|
|                       |  | Indication for colposcopy | DTA | Interrater variability | Predictor finding          | Validated model | Colposcopic impression | Aceto-white changes | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern | Border and surface |
| Sheshadri 1999 (84)   | Women referred to colposcopy clinic, not further specified | X                         | X   |                        |                            | X               |                        |                     |                    |                |                |                 |                  |                    |
| Kierkegaard 1995 (85) | Women referred to colposcopy clinic, not further specified | X                         |     | Multivariable          |                            | X               | X                      |                     | X                  |                |                | X               | X                |                    |
| Carriero 1991 (86)    | Abnormal HPV or CIN 1, 2, 3 (retrospective)                |                           |     |                        | Reid index, IFCCP criteria | X               |                        |                     |                    |                |                |                 |                  |                    |
| Edebiri 1990 (87)     | Abnormal cytology or complaints                            | X                         |     |                        |                            | X               | X                      |                     |                    |                |                | X               |                  |                    |
| Sellors 1990 (88)     | Unclear  |                           | X   |                        |                            |                 |                        |                     |                    |                |                |                 | X                |                    |
| Reid 1985 (89)        | Unclear  | X                         |     |                        | Reid index (development)   | X               |                        |                     |                    |                |                | X               | X                |                    |
| Noda 1981 (90)        | Women referred to colposcopy clinic, not further specified | X                         |     |                        |                            |                 | X                      |                     |                    |                |                | X               |                  |                    |
| Swan 1979 (91)        | Abnormal cytology and in utero DES exposure                | X                         |     |                        |                            | X               |                        |                     |                    |                |                |                 |                  |                    |

CIN: Cervical Intraepithelial Neoplasia; DES: Diethylstilbestrol; HPV: Human papilloma virus; IFCCP: International Federation for Cervical Pathology and Colposcopy; VIA: Visual inspection with acetic acid; VILI: Visual inspection with Lugol's iodine

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## Bijlage 6. Overzicht primaire ingesloten onderzoeken, geïnccludeerd voor analyses

| Reference          | Country   | Study design  | Sample size and diagnosis, n (%)  | Eligibility criteria  | Age, years                 | Colposcopy procedure and indicators assessed   | Reference standard  |
|--------------------|-----------|---|---|---|----------------------------|--|---|
| Abdulaziz 2020 (1) | China     | Cross-sectional study, retrospective data collection, consecutive patient enrolment | 1246<br>Negative: 839 (67%)<br>CIN 1: 199 (16%)<br>CIN 2: 98 (8%)<br>CIN 3: 96 (8%)<br>Cancer: 14 (1%)      | Age 21-78y; cervical cytology ASCUS.<br><i>Exclusion criteria:</i> pregnancy, immune-suppression, cervical cancer or precancerous lesions treatment previously.   | Mean (range): 41.6 (21-78) | Speculum insertion; flushing with saline, visualization of SCJ and TZ under × 15 magnification; application of 5% acetic acid for visual inspection of the cervix.<br><br><b>Indicator(s):</b> Colposcopic impression. | Punch biopsy for any suspected cervical lesions. Random four quadrant biopsy and/or endocervical curettage if lesion was inadequately visualized or no lesion was seen during colposcopy. |
| Baum 2006 (2)      | USA       | Cross-sectional study, retrospective data collection                                | 456<br>Benign: 168 (37%)<br>CIN 1: 137 (30%)<br>CIN 2: 79 (17%)<br>CIN 3: 72 (16%)                          | Abnormal cytology; colposcopically directed cervical biopsy.  | Mean (range): 25.2 (13-62) | Speculum insertion; application of 5% of acetic acid to cervix and transformation zone; examination of entire transformation zone.<br><br><b>Indicator(s):</b> Colposcopic impression.                                 | Colposcopically directed biopsy for most suspicious area(s).  |
| Bekkers 2008 (3)   | Australia | Cross-sectional study, retrospective data collection                                | 6020<br>No dysplasia: 1680 (28%)<br>LSIL: 2633 (44%)<br>HSIL: 1707 (28%)                                    | Abnormal Pap smear; colposcopically directed cervical biopsy.<br><i>Exclusion criterion:</i> unsatisfactory colposcopy.   | Not reported.              | No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression.   | Punch biopsies.   |
| Benedet 2004 (4)   | Canada    | Cross-sectional study, retrospective data collection                                | 5271<br>Reactive changes (benign): 1548 (29%)<br>CIN 1: 1484 (28%)<br>CIN 2: 1540 (29%)<br>CIN 3: 665 (13%) | Pap test showing moderate dyskaryosis or greater (i.e. HSIL) or with mild atypia or LSIL changes persistent for 2 years or with unsatisfactory Pap test.<br><i>Exclusion criteria:</i> unsatisfactory colposcopy. | All ages were included.    | No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression  | Colposcopically directed biopsies.  |

| Reference          | Country     | Study design   | Sample size and diagnosis, n (%)   | Eligibility criteria   | Age, years                             | Colposcopy procedure and indicators assessed   | Reference standard   |
|--------------------|-------------|--|--|--|--|--|--|
|                    |             |  | Overt cancer: 34 (0.6%)  |  |  |  |  |
| Boonlikit 2016 (5) | Thailand    | Cross-sectional study, retrospective data collection | 349<br><br>Negative: 44 (12.6%)<br>HPV/CIN1: 147 (42.1%)<br>CIN2/CIN3: 155 (44.4%)<br>Micro invasive: 1 (0.3%)<br>Invasive: 2 (0.6%) | Cytologic abnormalities identified at cervical screening and histology report from cytology directed biopsy.<br><i>Exclusion criteria:</i> normal transformation zone, without a lesion; pregnancy; management using a see-and-treat strategy; history of pelvic radiotherapy. | Mean ± SD (range): 36.7 ± 10.9 (15–85) | Application of acetic acid. No further details provided.<br><br><b>Indicator(s):</b> Colposcopic impression (abbreviated Reid Colposcopic Index); acetowhite changes; vascular pattern; border and surface.  | Colposcopically directed biopsy from the worst affected area of the cervix, histologically assessed using 3% acetic acid.  |
| Cantor 2008 (6)    | Canada, USA | Cross-sectional study                                | 797<br><br>Normal: 366 (46%)<br>LSIL: 200 (25%)<br>HSIL, cancer: 231 (29%)   | Abnormal Pap test results.   | Mean: 36.40                            | Application of 6% acetic acid and let it remain for approximately 2 minutes; reapplication of 6% acetic acid to the cervix using cotton balls repeatedly every few seconds over the next 1–2 minutes to detect “fast fader” or “slow uptake” lesions; inspection of cervix and identification of SCJ and TZ.<br><br><b>Indicator(s):</b> Colposcopic impression. | Colposcopically directed biopsies (one or two) of area with worst colposcopic impression and one or two biopsies of squamous and columnar epithelium from an area of normal appearance. If the overall colposcopic impression was normal, biopsies were obtained from one or two normal sites and included both types of cervical epitheliums. |
| Ferris 2006 (7)    | USA         | Cross-sectional analysis within a RCT                | 3549<br><br>Diagnoses not reported.  | Cytologic interpretations of ASC-US or LSIL.   | Not reported.                          | Application of 5% acetic acid; colposcopes with a beam splitter and charged couple device camera to capture 2 digitized cervical images (at 6x and 10x magnification).   | Colposcopically directed biopsy.   |

| Reference          | Country | Study design   | Sample size and diagnosis, n (%)   | Eligibility criteria   | Age, years   | Colposcopy procedure and indicators assessed   | Reference standard  |
|--------------------|---------|--|--|--|--|--|---|
|                    |         |  |  |  |  | <b>Indicator(s):</b> Colposcopic impression (abbreviated Reid Index).  |   |
| Follen 1987 (8)    | USA     | Cross-sectional study                                | 44<br><br>CIN 1: 22 (50%)<br>CIN 2: 13 (30%)<br>CIN 3: 9 (20%)   | Abnormal Pap smear, satisfactory colposcopy, photographic slide, and biopsy results, biopsy samples disclosed presence of papillomaviral DNA.                      | Mean (range): 33 (20-58)   | Colpophotography; colposcopic classification of cervical lesions based on review of the slides. No further details provided.<br><br><b>Indicator(s):</b> Acetowhite changes; vascular pattern; border and surface. | Colposcopically directed biopsies.  |
| Higgins 1994 (9)   | USA     | Cross-sectional study                                | 188<br><br>Normal: 36 (19%)<br>LSIL: 101 (54%)<br>HSIL: 51 (27%)   | Pap smear demonstrating cytologic evidence of dysplasia.<br><br><b>Exclusion criteria:</b> pregnancy, allergy to local anesthesia.                                 | Median (range): 23.8 (15-45)   | No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression.   | Colposcopically directed biopsies of the most suspicious areas and immediate loop excision of the lesion and the transformation zone after injection of the cervix with 1% xylocaine. |
| Javaheri 1980 (10) | USA     | Cross-sectional study                                | 903<br><br>Normal: 177 (20%)<br>Cervicitis: 45 (5%)<br>Mild to moderate dysplasia: 334 (37%)<br>Severe dysplasia and CIS: 344 (38%)<br>Suspicious invasive: 3 (0.3%) | Abnormal Pap smear.<br><b>Exclusion criteria:</b> pregnancy, history of intrauterine exposure to diethylstilbestrol, presence of a lesion in the cervix or vagina. | "All ages were included (majority of the patients were between 20 and 40 years of age)". | Visualization of squamocolumnar junction; application of acetic acid. No further details provided.<br><br><b>Indicator(s):</b> Colposcopic impression.   | Colposcopically directed biopsies (minimum of three) from most prominently abnormal areas.  |
| Jones 1987 (11)    | USA     | Cross-sectional study, consecutive patient enrolment | 236<br><br>Benign: 178 (75%)<br>CIN 1: 48 (20%)  | Class II significant cellular atypia Pap smears.<br><br><b>Exclusion criterion:</b> pregnancy.   | Mean (range): 25 (13-63)   | Application of acetic acid. No further details provided.<br><br><b>Indicator(s):</b> Colposcopic impression  | Biopsy of transformation zone.  |

| Reference             | Country | Study design  | Sample size and diagnosis, n (%)  | Eligibility criteria   | Age, years                 | Colposcopy procedure and indicators assessed  | Reference standard  |
|-----------------------|---------|---|---|--|----------------------------|---|---|
|                       |         |   | CIN 2: 7 (3%)<br>CIN 3: 3 (1%)  |  |                            |   |   |
| Kallner 2015 (12)     | Sweden  | Cross-sectional analysis of one arm of a randomized cross-over clinical trial | 123<br><br>Benign: 36 (29.8%)<br>CIN 1: 33 (27.3%)<br>CIN 2: 31 (25.6%)<br>CIN 3: 11 (9.1%)<br>CIN 3+ (invasive carcinoma): 1 (0.8%)<br>Adenocarcinoma in situ: 1 (0.8%)<br>NB. n=10 no biopsy (no diagnosis) | ASC-US or LSIL and high risk HPV and HPV positivity, or any high grade HSIL of CIN 2 or more, regardless of HPV status.<br><br><i>Exclusion criteria:</i> on-going vaginal bleeding, any previous gynaecological examinations within a week before the examination, pregnancy. | Mean (SD):<br>33.4 (9.9)   | Speculum insertion; review of cervical vessel patterns using red-free (green filter) mode; application of 5% acetic acid; evaluation after 1 minute; application of 5% Lugol's iodine. Standard colposcope (Carl Zeiss Colposcope 150 FC) was used.<br><br><b>Indicator(s):</b> Colposcopic impression (Swede score). | Directed punch biopsy and excisional cone biopsy.   |
| Karimi 2011 (13)      | Iran    | Cross-sectional study   | 213<br><br>Normal: 193 (90.6%)<br>CIN 1: 16 (6.5%)<br>CIN 2: 2 (0.9%)<br>CIN 3: 0<br>SCC: 2 (0.9%)<br>Unsatisfactory: 79<br>ASCUS: 0<br>LSIL: 0   | ASCUS seen on Pap smear.   | Not reported.              | No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression.  | Biopsy / pathology report.  |
| Kierkegaard 1994 (14) | Denmark | Cross-sectional study, consecutive patient enrolment                          | 811<br><br>Normal: 61 (8%)<br>Inflammation: 6 (1%)<br>LSIL: 405 (50%)<br>HSIL: 339 (42%)  | First abnormal cervical smear.   | Median (range): 29 (15-71) | Colposcopic evaluation before and after application of 4 % acetic acid.<br><br><b>Indicator(s):</b> Colposcopic impression.   | Directed biopsies from any area with abnormal colposcopic characteristics or if the cervix appeared normal at 6 and 12 o'clock positions on the cervix supplied with an endocervical curettage from the non-visible part of the TZ. |

| Reference        | Country  | Study design                          | Sample size and diagnosis, n (%)  | Eligibility criteria   | Age, years                 | Colposcopy procedure and indicators assessed   | Reference standard  |
|------------------|----------|---------------------------------------|---|--|----------------------------|--|---|
| Kudela 2020 (15) | Slovakia | Cross-sectional study                 | 66<br><br>Within normal limits: 14 (21%)<br>CIN1: 16 (24%)<br>CIN2: 15 (23%)<br>CIN3/CIS: 21 (32%)  | Cytological result ASC-H [atypical squamous cells – cannot exclude a high-grade lesion].<br><i>Exclusion criteria:</i> age <18 years, pregnancy, previous procedures on the cervix (cryotherapy, laser therapy, conisation), history of pelvic radiotherapy, inflammation of lower genital tract, diagnosed cervical cancer on the cytological specimen. | Mean (SD): 37.59 (8.71)    | Application of acetic acid and iodine. No further details provided.<br><br><b>Indicator(s):</b> Colposcopic impression (modified Reid Index; Swede score); size of lesion; SCJ visibility.   | Colposcopy guided biopsies from all abnormal areas irrespective of the final score.   |
| Massad 2009 (16) | USA      | Cross-sectional analysis within a RCT | 919<br><br><CIN2/HPV negative: 145 (16%)<br><CIN2/non-oncogenic HPV positive: 108 (12%)<br><CIN2/oncogenic HPV positive: 313 (34%)<br><CIN2/HPV 16 positive: 102 (11)<br>CIN 2: 83 (9%)<br>CIN 3: 165 (18%)<br>Cancer: 3 (0.3%) | Cytological report of ASC-US or LSIL.  | Median (range): 24 (18-73) | Application of 5% acetic acid for one minute; two Cervigrams® taken; recording of colposcopic impressions after real-time colposcopic assessment.<br><br><b>Indicator(s):</b> Colposcopic impression (Reid Index).                     | Histologic outcome was defined as the highest grade lesion identified at initial colposcopy or during subsequent follow up. |
| Massad 2008 (17) | USA      | Cross-sectional analysis within a RCT | 862<br><br>≤CIN 1: 442 (51%)<br>CIN 2 or worse: 244 (28.3%)   | Cytological report of ASCUS or LSIL.   | Not reported.              | Application of 5% acetic acid for one minute; two Cervigrams® taken; recording of colposcopic impressions after real-time colposcopic assessment.<br><br><b>Indicator(s):</b> Colposcopic impression (modified Reid Index); acetowhite | Not applicable, only interrater variability was assessed.   |

| Reference            | Country  | Study design   | Sample size and diagnosis, n (%)   | Eligibility criteria   | Age, years                     | Colposcopy procedure and indicators assessed  | Reference standard   |
|----------------------|----------|--|--|--|--------------------------------|---|--|
|                      |          |  | NB. Does not add up to 100%  |  |                                | changes; vascular pattern; border and surface.  |  |
| Petousis 2018 (18)   | Greece   | Cross-sectional study                                | 120<br><br>CIN 1 or less: 44 (37%)<br>CIN 2: 65 (54%)<br>CIN 3: 11 (9%)  | Abnormal cytology at screening, availability of histologic diagnosis of surgical specimen.<br><i>Exclusion criteria:</i> performed ablation or incomplete data.                        | Mean (SD):<br>32.7 (9.0)       | No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression (Reid Index).   | Histologic diagnosis of surgical specimen and histologic diagnosis of punch biopsy specimen whenever obtained.   |
| Phianpiset 2020 (19) | Thailand | Cross-sectional study                                | 697<br><br>Normal or cervicitis: 365 (52%)<br>CIN 1: 254 (36%)<br>CIN 2-3: 75 (11%)<br>AIS (adenocarcinoma in situ): 1 (0.1%)<br>Carcinoma: 2 (0.3%) | ASC-US or LSIL cytology, age 21 years or older.<br><i>Exclusion criteria:</i> pregnancy, previous treatment for cervical neoplasia.  | Median (IQR): 39.7 (32.0-48.9) | Application of acetic acid. No further details provided.<br><br><b>Indicator(s):</b> Colposcopic impression.  | Up to four colposcopy-directed biopsies at all acetowhite areas; biopsy at 12 o'clock position if the squamocolumnar junction had a normal appearance. |
| Reed 1997 (20)       | USA      | Cross-sectional study                                | 49<br><br>Normal: 11 (22%)<br>CIN 1/HPV: 26 (53%)<br>CIN 2: 9 (18%)<br>CIN 3: 3 (6%)   | Abnormal Pap smear   | Mean: 29                       | Application of 4 to 5% acetic acid; application of Lugol. Standard colposcope (Zeiss-OM 1, Carl Zeiss Inc) was used.<br><br><b>Indicator(s):</b> Colposcopic impression (Reid Index).   | Biopsies from areas considered to be abnormal.   |
| Rodpenpear 2019 (21) | Thailand | Cross-sectional study, retrospective data collection | 220<br><br>Benign: 20 (9%) (Normal: 12 [5%]; Cervicitis: 8 [4%])<br>CIN 1: 86 (39%)<br>CIN 2: 26 (12%)   | Abnormal cervical cytology, satisfactory colposcopy with completely visible transformation zone and cervical abnormalities if any.<br><i>Exclusion criteria:</i> pregnancy, no or poor | Mean (SD):<br>40.14 (10.14)    | Colposcopic cervical images before and after application of acetic acid under low-power magnification.<br><br><b>Indicator(s):</b> Colposcopic impression (modified Swede score); acetowhite changes; location of lesion; size of | Not specified, though authors indicate that specimens may have come from conisation, biopsy or curettage.  |



| Reference         | Country   | Study design          | Sample size and diagnosis, n (%)   | Eligibility criteria   | Age, years             | Colposcopy procedure and indicators assessed  | Reference standard                 |
|-------------------|-----------|-----------------------|--|--|------------------------|---|------------------------------------|
|                   |           |                       | CIN 3: 79 (36%)<br>Carcinoma: 9 (4%)   | quality of cervicographic images, no document of colposcopic impression or pathological report.  |                        | lesion; vascular pattern; border and surface.   |                                    |
| Ronk 1977 (22)    | USA       | Cross-sectional study | 376<br><br>Negative: 76 (20%)<br>Mild dysplasia: 63 (17%)<br>Moderate dysplasia: 68 (18%)<br>Severe dysplasia: 62 (16%)<br>Carcinoma in situ 84 (22%)<br>Microinvasive carcinoma: 11 (3%)<br>Invasive carcinoma: 12 (3%) | Abnormal cytology.   | Not reported.          | No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression.  | Cone biopsies, directed biopsies.  |
| Roy 1997 (23)     | Indonesia | Cross-sectional study | 81<br><br>Low-grade: 5 (6%)<br>High-grade: 76 (94%)  | High grade SIL.  | Not reported.          | No details provided. Olympus OCS-2 colposcope with an addition of OB 300 lens was used.<br><br><b>Indicator(s):</b> Border and surface  | LEEP biopsy of colposcopic region. |
| Shojaei 2013 (24) | Iran      | Cross-sectional study | 260<br><br>Normal: 98 (38%)<br>HPV: 35 (13%)<br>CIN1: 53 (20%)<br>CIN2: 15 (6%)  | Abnormal cytological results.<br><b>Exclusion criteria:</b> normal transitional zone, no lesion. | Mean (SD): 40.9 (12.3) | Application of saline; application of 5% acetic acid for 1 minute; in patients with cervical lesion and abnormal colposcopy, assessment of vascular pattern with green filter and recheck of margin and colour application of 5 % | Biopsy from the lesion.            |

| Reference          | Country | Study design  | Sample size and diagnosis, n (%)   | Eligibility criteria  | Age, years                 | Colposcopy procedure and indicators assessed   | Reference standard   |
|--------------------|---------|---|--|---|----------------------------|--|--|
|                    |         |   | CIN3: 24 (9%)<br>Cancer: 35  |   |                            | acetic acid and potassium iodide solution with 1/4 dilution.<br><br>Colposcopic impression (Reid Index); acetowhite changes; iodine staining; vascular pattern; border and surface                             |  |
| Sideri 1995 (25)   | Italy   | Cross-sectional study, retrospective data collection, consecutive patient enrolment | 856<br><br>Benign: 609 (71%)<br>Low grade: 100 (12%)<br>High grade: 147 (17%)  | Pap smear showing mild dysplasia.   | Mean (range): 35.8 (17-70) | Application of saline, 5% acetic acid, and Lugol's stain. Olympus OSC-2 colposcope (Olympus Corp., Tokyo, Japan) used with magnifications ranging from 10X to 50X.<br><br><b>Indicator(s):</b> SCJ visibility. | Cervical biopsies, histology; not further specified.   |
| Spinillo 2014 (26) | Italy   | Cross-sectional study   | 2526<br><br>Negative: 1282 (51%)<br>CIN1: 709 (28%)<br>CIN2: 169 (7%)<br>CIN3: 318 (13%)<br>Invasive cancer: 48 (2%)         | Abnormal Pap smear, age 21-65 years.<br><b>Exclusion criteria:</b> pregnancy, HPV test or treatment for CIN in the last year, total hysterectomy, lack of a recent (1 month) Pap smear, and use of vaginal medication in the previous 2 days. | Median (IQR): 37 (29-45)   | Application of acetic acid. No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression.   | Histological diagnosis of the punch biopsy (2 to 4 targeted cervical biopsies in all cases where CIN was suspected on colposcopy and in all cases of HSIL irrespective of colposcopic impression) or, when more severe, the diagnosis after cone biopsy obtained by loop electro-excision procedure (LEEP) or cold-knife excision. |
| Strander 2005 (27) | Sweden  | Cross-sectional study   | 297<br><br>Benign: 90 (30%)<br>Koilocytosis or CIN1: 75 (25%)<br>CIN2: 39 (13%)<br>CIN3: 84 (28%)<br>Invasive cancer: 9 (3%) | Abnormal cytology.<br><b>Exclusion criteria:</b> no histopathology obtained, pregnancy, atrophy either caused by puerperium or postmenopausal state, unsatisfactory   | Mean (range): 34 (19-59)   | No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression (Swede score); acetowhite changes; size of lesion; iodine staining; vascular pattern; border and surface.                              | Histopathology obtained either by punch biopsy, laser cone or large loop excision of the transformational zone (LLETZ) cone.   |

| Reference                   | Country               | Study design   | Sample size and diagnosis, n (%)  | Eligibility criteria   | Age, years                   | Colposcopy procedure and indicators assessed  | Reference standard   |
|-----------------------------|-----------------------|--|---|--|------------------------------|---|--|
|                             |                       |  |   | colposcopy where SCJ was not visible.  |                              |   |  |
| Tidy 2013 (28)              | UK and Ireland        | Cross-sectional study, non-consecutive patient enrolment | 196<br><br>Low-grade CIN: 109 (56%)<br>High-grade CIN: 87 (44%)                             | Abnormal cytology.<br><i>Exclusion criteria:</i> pregnancy, active menstruation.   | Median (range): 29.5 (20-64) | No details provided.<br><br><b>Indicator(s):</b> Colposcopic impression.  | Biopsies; not further specified.   |
| van der Marel 2014 (29, 30) | Netherlands and Spain | Cross-sectional study                                    | 610<br><br>Negative: 221 (36%)<br>CIN 1: 123 (20%)<br>CIN 2: 144 (24%)<br>CIN 3+: 122 (20%) | Abnormal Pap smear result defined as ASC-US or worse (disregarding HPV status), age ≥17 years.<br><i>Exclusion criteria:</i> previous treatment of cervical pathology, confirmed diagnosis of invasive cervical cancer at the time of referral, pregnant or breast-feeding at the date of colposcopy or 3 months before. | Median (SD): 36.5 (10.9)     | Application of 5% acetic acid for at least 1 minute. Traditional binocular Colposcope was used with a digital camera fixed to it.<br><br><b>Indicator(s):</b> Colposcopic impression; acetowhite changes; size of lesion; vascular pattern; border and surface. | Up to four directed biopsies from different lesions or different regions within 1 lesion. If fewer than 4 directed biopsies were taken, a biopsy from any normal appearing epithelium of the SCJ (non-directed biopsy) was added. If no acetowhitening was observed, only a non-directed biopsy was performed. |

ASC-US: Atypical squamous cells of undetermined significance; CIN: Cervical Intraepithelial Neoplasia; CIS: Carcinoma in situ; HSIL: High grade squamous intraepithelial lesion; HPV: Human papilloma virus; IQR: Interquartile range; LSIL: Low grade squamous intraepithelial lesion; RCT: Randomized controlled trial; SCC: Squamous cell carcinoma; SCJ: Squamocolumnar junction; SD: standard deviation; TZ: Transformation zone.

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## Bijlage 7. Kruistabellen

### Colposcopische impressie

#### Baum 2006 – Colposcopic impression

| Colposcopy results | Histology results |       |       |       |       |
|--------------------|-------------------|-------|-------|-------|-------|
|                    | Negative          | CIN 1 | CIN 2 | CIN 3 | Total |
| Negative           | 7                 | 1     | 0     | 0     | 8     |
| CIN 1              | 99                | 80    | 41    | 19    | 239   |
| CIN 2              | 40                | 32    | 22    | 16    | 110   |
| CIN 3              | 22                | 24    | 16    | 37    | 99    |
| Total              | 168               | 137   | 79    | 72    | 456   |

#### Bekkers 2008 – Colposcopic impression

| Colposcopy results | Histology results |      |      |       |
|--------------------|-------------------|------|------|-------|
|                    | Normal            | LSIL | HSIL | Total |
| Normal             | 0                 | 0    | 0    | 0     |
| LSIL               | 1405              | 2234 | 671  | 4310  |
| HSIL               | 275               | 399  | 1036 | 1710  |
| Total              | 1680              | 2633 | 1707 | 6020  |

#### Benedet 2004 – Colposcopic impression

| Colposcopy results | Histology results |       |       |       |                  |       |
|--------------------|-------------------|-------|-------|-------|------------------|-------|
|                    | Benign            | CIN 1 | CIN 2 | CIN 3 | Cervix carcinoma | Total |
| Benign             | 1207              | 220   | 87    | 34    | 0                | 1548  |
| CIN 1              | 526               | 563   | 258   | 136   | 1                | 1484  |
| CIN 2              | 312               | 325   | 509   | 392   | 2                | 1540  |
| CIN 3              | 49                | 64    | 91    | 457   | 4                | 665   |
| Cervixcarcinoma    | 11                | 2     | 0     | 10    | 11               | 34    |
| Total              | 2105              | 1174  | 945   | 1029  | 18               | 5271  |

### Cantor 2008 – Colposcopic impression

| Colposcopy results | Histology results |      |              |       |
|--------------------|-------------------|------|--------------|-------|
|                    | Normal            | LSIL | HSIL, cancer | Total |
| Normal             | 207               | 48   | 4            | 259   |
| LSIL               | 110               | 95   | 62           | 267   |
| HSIL, cancer       | 49                | 57   | 165          | 271   |
| Total              | 366               | 200  | 231          | 797   |

### Higgins 1994 – Colposcopic impression

| Colposcopy results | Loop electrosurgical excision procedure specimens |       |       |       |
|--------------------|---|-------|-------|-------|
|                    | Normal  | LGSIL | HGSIL | Total |
| Normal             | 0   | 8     | 2     | 10    |
| LGSIL              | 35  | 87    | 35    | 157   |
| HGSIL              | 1   | 6     | 14    | 21    |
| Total              | 36  | 101   | 51    | 188   |

### Jahaveri 1980 – Colposcopic impression

| Colposcopy results         | Biopsy diagnosis |            |                            |                          |                     | Total |
|----------------------------|------------------|------------|----------------------------|--------------------------|---------------------|-------|
|                            | Normal           | Cervicitis | Mild to moderate dysplasia | Severe dysplasia and CIS | Suspicious invasive |       |
| Normal                     | 160              | 12         | 0                          | 0                        | 0                   | 172   |
| Cervicitis                 | 2                | 20         | 0                          | 1                        | 0                   | 23    |
| Mild to moderate dysplasia | 11               | 10         | 286                        | 13                       | 0                   | 320   |
| Severe dysplasia and CIS   | 4                | 3          | 47                         | 329                      | 0                   | 383   |
| Suspicious invasive        | 0                | 0          | 1                          | 1                        | 3                   | 5     |
| Total                      | 177              | 45         | 334                        | 344                      | 3                   | 903   |

### Jones 1987 – Colposcopic impression

| Colposcopy results | Histology results |           |          |          |            |
|--------------------|-------------------|-----------|----------|----------|------------|
|                    | Benign            | CIN 1     | CIN 2    | CIN 3    | Total      |
| Negative           | 50                | 0         | 0        | 0        | 50         |
| Suspicious         | 128               | 46        | 7        | 3        | 184        |
| <b>Total</b>       | <b>178</b>        | <b>46</b> | <b>7</b> | <b>3</b> | <b>234</b> |

### Karimi 2011 – Colposcopic impression

| Colposcopy results | Biopsy     |           |            |
|--------------------|------------|-----------|------------|
|                    | Negative   | Positive  |            |
| Negative           | 156        | 4         | 160        |
| Positive           | 37         | 16        | 53         |
| <b>Total</b>       | <b>193</b> | <b>20</b> | <b>213</b> |

### Kierkegaard 1994 – Colposcopic impression

| Colposcopy results | Histology |              |            |            |            |
|--------------------|-----------|--------------|------------|------------|------------|
|                    | Normal    | Inflammation | LGL        | HGL        | Total      |
| Normal             | 27        | 1            | 11         | 1          | 40         |
| Inflammation       | 0         | 2            | 14         | 3          | 19         |
| LGL                | 21        | 3            | 316        | 105        | 445        |
| HGL                | 3         | 0            | 54         | 222        | 279        |
| <b>Total</b>       | <b>51</b> | <b>6</b>     | <b>395</b> | <b>331</b> | <b>783</b> |



### Massad 2009 – Colposcopic impression

| Colposcopy results | Biopsy     |            |            |            |             |
|--------------------|------------|------------|------------|------------|-------------|
|                    | <CIN2/HPV  | >CIN2/HPV  | CIN2       | CIN3       | Total       |
| Negative           | 136        | 161        | 13         | 11         | 321         |
| Metaplasia         | 118        | 191        | 39         | 45         | 393         |
| Low grade          | 140        | 347        | 63         | 132        | 682         |
| High grade         | 49         | 151        | 50         | 143        | 393         |
| <b>Total</b>       | <b>443</b> | <b>850</b> | <b>165</b> | <b>331</b> | <b>1789</b> |

### Massad 2009 – Reid index score

| Colposcopy results | Biopsy     |            |            |            |             |
|--------------------|------------|------------|------------|------------|-------------|
|                    | <CIN2/HPV  | >CIN2/HPV  | CIN2       | CIN3       | Total       |
| 0-3                | 399        | 730        | 124        | 225        | 1478        |
| 4-6                | 44         | 120        | 41         | 106        | 311         |
| <b>Total</b>       | <b>443</b> | <b>850</b> | <b>165</b> | <b>331</b> | <b>1789</b> |

### Reed 1997 – Standard colposcopic impression

| Colposcopy results | Pathological diagnosis |           |          |          |           |
|--------------------|------------------------|-----------|----------|----------|-----------|
|                    | Normal                 | CIN1/HPV  | CIN2     | CIN3     | Total     |
| Normal             | 11                     | 0         | 3        | 0        | 14        |
| CIN1/HPV           | 0                      | 22        | 2        | 1        | 25        |
| CIN2               | 0                      | 3         | 4        | 1        | 8         |
| CIN3               | 0                      | 1         | 0        | 1        | 2         |
| <b>Total</b>       | <b>11</b>              | <b>26</b> | <b>9</b> | <b>3</b> | <b>49</b> |

### Ronk 1977 – Colposcopy results

|                    |                                  | Histology results |                |                    |                  |                   |                          | Total |                    |
|--------------------|----------------------------------|-------------------|----------------|--------------------|------------------|-------------------|--------------------------|-------|--------------------|
|                    |                                  | Negative          | Mild dysplasia | Moderate dysplasia | Severe dysplasia | Carcinoma in situ | Micro-invasive carcinoma |       | Invasive carcinoma |
| Colposcopy results | Normal                           | 35                | 16             | 8                  | 0                | 1                 | 0                        | 0     | 60                 |
|                    | Mildly abnormal                  | 28                | 35             | 22                 | 10               | 9                 | 0                        | 1     | 105                |
|                    | Moderately abnormal              | 11                | 11             | 36                 | 30               | 12                | 1                        | 0     | 101                |
|                    | Severely abnormal                | 1                 | 5              | 2                  | 19               | 31                | 7                        | 8     | 73                 |
|                    | Suggestive of invasive carcinoma | 0                 | 0              | 0                  | 1                | 2                 | 2                        | 3     | 8                  |
|                    | Total                            | 75                | 67             | 68                 | 60               | 55                | 10                       | 12    | 347                |

### Spinillo 2014 – Colposcopic impression

|                    |                   | Histology results |       |       |        | Total |
|--------------------|-------------------|-------------------|-------|-------|--------|-------|
|                    |                   | Negative          | CIN 1 | CIN 2 | CIN 3+ |       |
| Colposcopy results | Normal            | 789               | 189   | 41    | 62     | 1081  |
|                    | Low grade lesion  | 436               | 486   | 100   | 137    | 1159  |
|                    | High grade lesion | 57                | 34    | 28    | 167    | 286   |
|                    | Total             | 1282              | 709   | 169   | 366    | 2526  |

### Strander 2005 – Swede score

|                    |       | Histology results |        |       |
|--------------------|-------|-------------------|--------|-------|
|                    |       | Benign or CIN1    | ≥CIN 2 | Total |
| Colposcopy results | 0     | 0                 | 0      | 0     |
|                    | 1     | 10                | 0      | 10    |
|                    | 2     | 5                 | 0      | 5     |
|                    | 3     | 13                | 0      | 13    |
|                    | 4     | 23                | 0      | 23    |
|                    | 5     | 36                | 2      | 38    |
|                    | 6     | 37                | 20     | 57    |
|                    | 7     | 22                | 43     | 65    |
|                    | 8     | 11                | 36     | 47    |
|                    | 9     | 5                 | 20     | 25    |
|                    | 10    | 0                 | 14     | 14    |
|                    | Total | 162               | 135    | 297   |

### Van der Marel 2014 – Colposcopic impression

|                    |                   | Histology results |      |      |       |       |
|--------------------|-------------------|-------------------|------|------|-------|-------|
|                    |                   | Negative          | CIN1 | CIN2 | CIN3+ | Total |
| Colposcopy results | Normal            | 118               | 34   | 18   | 14    | 184   |
|                    | Low grade lesion  | 69                | 61   | 49   | 21    | 200   |
|                    | High grade lesion | 34                | 28   | 77   | 87    | 226   |
|                    | Total             | 221               | 123  | 144  | 122   | 610   |

## Azijnzuurwitte afwijkingen

### Follen 1987 – Color

| Colposcopy results | Histology results |           |          |           |
|--------------------|-------------------|-----------|----------|-----------|
|                    | CIN 1             | CIN 2     | CIN 3    | Total     |
| Snow-white         | 6                 | 3         | 2        | 11        |
| Intermediate       | 3                 | 1         | 2        | 6         |
| Grey-white         | 9                 | 8         | 5        | 22        |
| <b>Total</b>       | <b>18</b>         | <b>12</b> | <b>9</b> | <b>39</b> |

### Shojaei 2013 – Acetowhite changes

| Colposcopy results    | Histology results |               |                |            |
|-----------------------|-------------------|---------------|----------------|------------|
|                       | No CIN lesion     | Low grade CIN | High grade CIN | Total      |
| Shiny, snow white     | 95                | 8             | 3              | 106        |
| Shiny, but grey white | 25                | 43            | 26             | 94         |
| Dull, oyster grey     | 13                | 2             | 45             | 60         |
| <b>Total</b>          | <b>53</b>         | <b>133</b>    | <b>74</b>      | <b>260</b> |

### Van der Marel 2014 - Colour

| Colposcopy results | Histology results |            |            | Total      |
|--------------------|-------------------|------------|------------|------------|
|                    | ≤CIN 1            | CIN 2      | ≥CIN 3     |            |
| Absent             | 9                 | 4          | 2          | 15         |
| Translucent        | 84                | 30         | 14         | 128        |
| Intermediate       | 85                | 71         | 57         | 213        |
| Opaque             | 15                | 24         | 34         | 73         |
| <b>Total</b>       | <b>193</b>        | <b>129</b> | <b>107</b> | <b>429</b> |

## Grootte van de laesie

### Kudela 2020 – Lesion size

| Colposcopy results | Biopsy               |      |      |          |       |
|--------------------|----------------------|------|------|----------|-------|
|                    | Within normal limits | CIN1 | CIN2 | CIN3/CIS | Total |
| <5 mm              | 11                   | 8    | 3    | 7        | 29    |
| 5-15 mm            | 3                    | 4    | 2    | 5        | 14    |
| >15 mm             | 0                    | 4    | 10   | 9        | 23    |
| <b>Total</b>       | 14                   | 16   | 15   | 21       | 66    |

### Van der Marel 2014 – Size of lesion

| Colposcopy results | Histology results |       |        |       |
|--------------------|-------------------|-------|--------|-------|
|                    | ≤CIN 1            | CIN 2 | ≥CIN 3 | Total |
| 0%                 | 5                 | 4     | 0      | 9     |
| <25%               | 106               | 45    | 20     | 171   |
| 25-50%             | 43                | 43    | 30     | 116   |
| >50%               | 35                | 37    | 55     | 127   |
| <b>Total</b>       | 189               | 129   | 105    | 423   |

## Lugol kleuring

### Shojaei 2013 – Iodine staining

| Colposcopy results      | Histology results |               |                |       |
|-------------------------|-------------------|---------------|----------------|-------|
|                         | No CIN lesion     | Low grade CIN | High grade CIN | Total |
| Mahogany brown staining | 95                | 31            | 12             | 138   |
| Partial uptake          | 29                | 21            | 33             | 83    |
| Mustard yellow staining | 9                 | 1             | 29             | 39    |
| <b>Total</b>            | 133               | 53            | 74             | 260   |

## Vasculaire patronen

### Follen 1987 – Vascular pattern

|                    |                   | Histology results |           |           |           |
|--------------------|-------------------|-------------------|-----------|-----------|-----------|
|                    |                   | CIN 1             | CIN 2     | CIN 3     | Total     |
| Colposcopy results | Absent            | 6                 | 4         | 3         | 13        |
|                    | Fine punctation   | 3                 | 4         | 1         | 8         |
|                    | Coarse punctation | 1                 | 2         | 2         | 5         |
|                    | Mosaiform         | 8                 | 4         | 3         | 15        |
|                    | Mosaic            | 1                 | 0         | 1         | 2         |
|                    | Atypical vessels  | 0                 | 0         | 1         | 1         |
|                    | <b>Total</b>      | <b>19</b>         | <b>14</b> | <b>11</b> | <b>44</b> |

### Shojaei 2013 – Vascular pattern

|                    |  | Histology results |               |                |            |
|--------------------|--|-------------------|---------------|----------------|------------|
|                    |  | No CIN lesion     | Low grade CIN | High grade CIN | Total      |
| Colposcopy results | Uniform, fine punctuation or mosaic    | 70                | 16            | 14             | 100        |
|                    | Absence of surface vessels             | 55                | 36            | 32             | 123        |
|                    | Definite, coarse punctuation or mosaic | 8                 | 1             | 28             | 37         |
|                    | <b>Total</b>                           | <b>133</b>        | <b>53</b>     | <b>74</b>      | <b>260</b> |

### Van der Marel 2014 – Atypical vessels

|                    |              | Histology results |            |            |            |
|--------------------|--------------|-------------------|------------|------------|------------|
|                    |              | ≤CIN 1            | CIN 2      | ≥CIN 3     | Total      |
| Colposcopy results | Absent       | 187               | 126        | 96         | 409        |
|                    | Present      | 6                 | 3          | 11         | 20         |
|                    | <b>Total</b> | <b>193</b>        | <b>129</b> | <b>107</b> | <b>429</b> |

### Van der Marel 2014 - Mosaic

|                    |        | Histology results |       |        |       |
|--------------------|--------|-------------------|-------|--------|-------|
|                    |        | ≤CIN 1            | CIN 2 | ≥CIN 3 | Total |
| Colposcopy results | Absent | 132               | 76    | 63     | 271   |
|                    | Fine   | 46                | 39    | 22     | 107   |
|                    | Coarse | 15                | 14    | 22     | 51    |
|                    | Total  | 193               | 129   | 107    | 429   |

### Van der Marel 2014 - Punctuation

|                    |        | Histology results |       |        |       |
|--------------------|--------|-------------------|-------|--------|-------|
|                    |        | ≤CIN 1            | CIN 2 | ≥CIN 3 | Total |
| Colposcopy results | Absent | 144               | 87    | 48     | 279   |
|                    | Fine   | 45                | 32    | 37     | 114   |
|                    | Coarse | 4                 | 10    | 22     | 36    |
|                    | Total  | 193               | 129   | 107    | 429   |

### Oppervlak en begrenzing van de laesie

#### Follen 1987 – Surface contour

|                    |                    | Histology results |       |       |       |
|--------------------|--------------------|-------------------|-------|-------|-------|
|                    |                    | CIN 1             | CIN 2 | CIN 3 | Total |
| Colposcopy results | Uneven or granular | 12                | 0     | 2     | 14    |
|                    | Papillomatous      | 2                 | 3     | 0     | 5     |
|                    | Total              | 14                | 3     | 2     | 19    |

### Roy 1997 - Margin

| Colposcopy results    | Histology results |                   |           |
|-----------------------|-------------------|-------------------|-----------|
|                       | Low grade lesion  | High grade lesion | Total     |
| Lazy margin           | 3                 | 4                 | 7         |
| Abrupt peeling margin | 2                 | 72                | 74        |
| <b>Total</b>          | <b>5</b>          | <b>76</b>         | <b>81</b> |

### Shojaei 2013 – Margin of lesion

| Colposcopy results                   | Histology results |               |                |            |
|--------------------------------------|-------------------|---------------|----------------|------------|
|                                      | No CIN lesion     | Low grade CIN | High grade CIN | Total      |
| Condylomatous, micropapillary        | 91                | 26            | 15             | 132        |
| Regular, smooth                      | 34                | 27            | 38             | 99         |
| Rolled, peeling edges, sharp margins | 8                 | 0             | 21             | 29         |
| <b>Total</b>                         | <b>133</b>        | <b>53</b>     | <b>74</b>      | <b>260</b> |

### Van der Marel 2014 - Margins

| Colposcopy results | Histology results |            |            |            |
|--------------------|-------------------|------------|------------|------------|
|                    | ≤CIN 1            | CIN 2      | ≥CIN 3     | Total      |
| Geographical       | 95                | 49         | 33         | 177        |
| Smooth             | 91                | 71         | 63         | 225        |
| Internal borders   | 7                 | 8          | 12         | 27         |
| <b>Total</b>       | <b>193</b>        | <b>128</b> | <b>108</b> | <b>429</b> |



## Bijlage 8. Definities en classificaties van colposcopie indicatoren

| Reference      | Colposcopic impression  | Acetowhite changes   | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern   | Border and surface  |
|----------------|---|--|--------------------|----------------|----------------|-----------------|--|---|
| Abdulaziz 2020 | IFCPC terminology.<br><br>Classified as:<br>- Normal<br>- Minor lesions<br>- Major lesions<br>- Suspicious for invasion | -  | -                  | -              | -              | -               | -  | -   |
| Baum 2006      | Classified as:<br>- Benign<br>- CIN 1<br>- CIN 2<br>- CIN 3   | -  | -                  | -              | -              | -               | -  | -   |
| Bekkers 2008   | Classified as:<br>- Normal<br>- LSIL<br>- HSIL<br><br>Reported threshold:<br>≥ HSIL                                     | -  | -                  | -              | -              | -               | -  | -   |
| Benedet 2004   | Classified as:<br>- Reactive changes<br>- CIN 1<br>- CIN 2<br>- CIN 3<br>- Overt cancer                                 | -  | -                  | -              | -              | -               | -  | -   |
| Boonlikit 2016 | Abbreviated Reid index.<br><br>All scores were used as cut-off: ≥0, ≥1, ≥2, ≥3, ≥4, ≥5, 6.                              | Classified according to Reid index:<br>- Shiny, snow white<br>- Shiny, grey white (intermediate)<br>- Dull oyster grey<br><br>Reported thresholds:<br>≥ Shiny, grey white (intermediate) and<br>≥ Dull oyster grey | -                  | -              | -              | -               | Classified according to Reid index:<br>- Uniform, fine<br>- Absence of surface vessels<br>- Definite coarse punctuation or mosaic<br><br>Reported thresholds:<br>≥ Absence of surface vessels and ≥ Definite | Classified according to Reid index:<br>- Condylomatous, micropapillary<br>- Regular, smooth<br>- Rolled, peeling edges, sharp margins<br><br>Reported thresholds:<br>≥ Regular, smooth and ≥ Rolled, peeling edges, sharp margins |

| Reference     | Colposcopic impression  | Acetowhite changes   | Location of lesion | Size of lesion | SCJ visibility | Iodine staining | Vascular pattern   | Border and surface  |
|---------------|---|--|--------------------|----------------|----------------|-----------------|--|---|
|               |   |  |                    |                |                |                 | coarse punctuation or mosaic   |   |
| Cantor 2008   | IFCPC terminology.<br><br>Classified as:<br>- Normal and benign (inflammatory and metaplasia)<br>- LSIL<br>- HSIL<br>- Cancer   | -  | -                  | -              | -              | -               | -  | -   |
| Ferris 2006   | Abbreviated Reid index.<br><br>Classified as:<br>- 0-2<br>- 3<br>- 4-6  | -  | -                  | -              | -              | -               | -  | -   |
| Follen 1987   | -   | Classified as:<br>- Snow white<br>- Grey-white<br>- Intermediate | -                  | -              | -              | -               | Classified as:<br>- Absent<br>- Mosaiform or horizontal<br>- Fine punctuation or vertical (including warty)<br>- True mosaic<br>- Coarse punctuation<br>- Atypical vessels | Classified as:<br>- Uneven or granular<br>- Papillomatous |
| Higgins 1994  | Classified as:<br>- Normal<br>- LGSIL<br>- HGSIL  | -  | -                  | -              | -              | -               | -  | -   |
| Javaheri 1980 | Second World Congress of Cervical Pathology and Colposcopy criteria.<br><br>Classified as:<br>- Mild white epithelium and minor changes<br>- Moderately irregular surface contour and | -  | -                  | -              | -              | -               | -  | -   |

| Reference        | Colposcopic impression   | Acetowhite changes | Location of lesion | Size of lesion   | SCJ visibility   | Iodine staining | Vascular pattern | Border and surface |
|------------------|--|--------------------|--------------------|--|--|-----------------|------------------|--------------------|
|                  | thicker white epithelium with sharper boundaries<br>- Markedly irregular surface contour with very sharp boundaries, marked variation in intercapillary distances, and areas of mosaicism and punctation |                    |                    |  |  |                 |                  |                    |
| Jones 1987       | Classified as:<br>- Negative<br>- Suspicious<br>- Unsatisfactory.  | -                  | -                  | -  | -  | -               | -                | -                  |
| Kallner 2015     | Swede score.<br><br>Scale from 0 to 10.  | -                  | -                  | -  | -  | -               | -                | -                  |
| Karimi 2011      | Classified as:<br>- Positive<br>- Negative   | -                  | -                  | -  | -  | -               | -                | -                  |
| Kierkegaard 1994 | Classified as:<br>- Normal<br>- Inflammation<br>- Low grade lesion<br>- High grade lesion  | -                  | -                  | Percentage of cervix engaged, classified as:<br>- ≤25%<br>- 25-50%<br>- >50% | -  | -               | -                | -                  |
| Kudela 2020      | Modified Reid index.<br><br>Classified as:<br>- ≥4<br>- ≥5   | -                  | -                  | Classified as:<br>- <5 mm<br>- 5-15 mm<br>- >15 mm                           | Transformation zone classified as:<br>- Type 1<br>- Type 2<br>- Type 3 | -               | -                | -                  |
| Massad 2009      | Reid index.<br><br>Classified as:<br>- Negative<br>- Metaplasia<br>- Low grade<br>- High grade   | -                  | -                  | -  | -  | -               | -                | -                  |

| Reference       | Colposcopic impression  | Acetowhite changes                                 | Location of lesion   | Size of lesion   | SCJ visibility | Iodine staining | Vascular pattern   | Border and surface   |
|-----------------|---|--|--|--|----------------|-----------------|--|--|
| Massad 2008     | Modified Reid Index.<br><br>Classification not provided.  | Classified as:<br>- Present<br>- Absent            | -  | -  | -              | -               | Vascular component (mosaic or punctation)                            | Margins according common definitions similar to those described by Reid and Scalzi that were provided by the prompting software. |
| Petousis 2018   | Reid index.<br><br>Classification not provided.   | -  | -  | -  | -              | -               | -  | -  |
| Phianpiset 2020 | Classified as:<br>- Normal—no acetowhitening or other abnormalities<br>- Low grade—any acetowhite lesion (thin and rapidly fading whitening, fine mosaicism or fine punctation)<br>- High grade—rapid appearing and thick whitening, coarse mosaicism or fine punctation, sharp border.<br><br>Reported threshold:<br>≥ Low grade | -  | -  | -  | -              | -               | -  | -  |
| Reed 1997       | Reid index.<br><br>Classified as:<br>- Normal<br>- CIN1/HPV<br>- CIN2<br>- CIN3   | -  | -  | -  | -              | -               | -  | -  |
| Rodpenpear 2019 | Modified Swede score.<br><br>Reported threshold:<br>≥11 (maximum value 15)  | Classified as:<br>- None or transparent<br>- Shady | Classified as:<br>- Only outer one-half of transformation zone | Classified as:<br>- Involve 1/4 of transformation zone area in single lesion<br>- Involve 2/4 of | -              | -               | Classified as:<br>- Fine, regular<br>- Absent<br>- Coarse or atypica | Classified as:<br>- Diffuse<br>- Sharp but irregular, jagged, geographic satellites  |

| Reference    | Colposcopic impression  | Acetowhite changes   | Location of lesion   | Size of lesion   | SCJ visibility | Iodine staining  | Vascular pattern   | Border and surface  |
|--------------|---|--|--|--|----------------|--|--|---|
|              |   | - Milky neither transparent nor opaque<br>- Distinct, opaque white   | - Both inner and/or outer one half of transformation zone<br>- Invade endocervical canal | transformation zone area in single lesion or involve 2 quadrants in multiple lesion<br>- Involve $\geq 3/4$ of transformation zone area in single lesion or involve 3–4 quadrants in multiple lesion or undefined endocervically |                |  |  | - Sharp and even, difference in surface level includes cuffing  |
| Ronk 1977    | Classified as:<br>- Mildly abnormal<br>- Moderately abnormal<br>- Severely abnormal | -  | -  | -  | -              | -  | -  | -   |
| Roy 1997     | -   | -  | -  | -  | -              | -  | -  | Abrupt peeling margin was a sharp demarcation area on the edge of an area that appeared different in height compared to surrounding adjacent tissues. Lazy margin was the appearance of the edge of such a lesion which rather flat and subtle. |
| Shojaei 2013 | Reid index.<br><br>Reported threshold: $\geq 5$                                     | Classified according to Reid index:<br>- Shiny, snow white<br>- Shiny, grey white (intermediate)<br>- Dull oyster grey<br><br>Reported thresholds: | -  | -  | -              | Classified according to Reid index:<br>- Magahony brown uptake | Classified according to Reid index:<br>- Uniform, fine vessels<br>- Absence of surface punctuation or mosaic | Classified according to Reid index:<br>- Condylomatous, micropapillary<br>- Regular, smooth<br>- Rolled, peeling edges, sharp margins   |

| Reference          | Colposcopic impression   | Acetowhite changes   | Location of lesion | Size of lesion   | SCJ visibility  | Iodine staining  | Vascular pattern  | Border and surface  |
|--------------------|--|--|--------------------|--|---|--|---|---|
|                    |  | ≥ Shiny, grey white and ≥ Dull oyster grey   |                    |  |   | - Mustard yellow staining  |   |   |
| Sideri 1995        | -  | -  | -                  | -  | Squamocolumnar junction, classified as:<br>- Visible<br>- Not visible | -  | -   | -   |
| Spinillo 2014      | IFCPC criteria.<br><br>Classified as:<br>- Negative<br>- Low grade<br>- High grade   | -  | -                  | -  | -   | -  | -   | -   |
| Strander 2005      | Swede score.<br><br>Scale from 0 to 10.  | Classified as:<br>- 0 or transparent<br>- Shady, milk<br>- Distinct, stearin   | -                  | Classified as:<br>- <5 mm<br>- 5–15 mm or 2 quadrants<br>- >15 mm or 3–4 quadrants or endocervically undefined | -   | Classified as:<br>- Brown<br>- Faintly or patchy yellow<br>- Distinct yellow | Classified as:<br>- Fine, regular<br>- Absent<br>- Coarse or atypical vessels   | Classified as:<br>- 0 or diffuse<br>- Sharp but irregular, jagged, 'geographical'.<br>Satellites<br>- Sharp and even, difference in surface level including 'cuffing' |
| Tidy 2013          | Classified as:<br>- Low grade CIN<br>- High grade CIN  | -  | -                  | -  | -   | -  | -   | -   |
| van der Marel 2014 | Classified as:<br>- Normal (including acetowhitening suggestive for metaplastic changes)<br>- Low-grade<br>- High-grade or worse | Classified as:<br>- Absent<br>- Translucent<br>- Intermediate<br>- Opaque<br><br>Reported threshold:<br>≥ Intermediate | -                  | Percentage of cervix involved, classified as:<br>- 0%<br>- <25%<br>- 25–50%<br>- >50%                          | -   | -  | Punctuation, classified as:<br>- Absent<br>- Fine<br>- Coarse<br><br>Mosaicism, classified as:<br>- Absent<br>- Fine<br>- Coarse<br><br>Atypical vessels, classified as:<br>- Absent<br>- Present | Lesion margins, classified as:<br>- Geographical<br>- Smooth<br>- Internal borders  |

## Bijlage 9. Diagnostische accuratesse van colposcopie indicatoren

| Reference                     | Accuracy for diagnosing CIN ≥2 (unless otherwise indicated) |                             |                     |                     |                     |                        |            | Accuracy for diagnosing DTA CIN ≥3 or ≥HSIL (unless otherwise indicated) |                   |             |             |      |      |            |
|-------------------------------|---|-----------------------------|---------------------|---------------------|---------------------|------------------------|------------|--|-------------------|-------------|-------------|------|------|------------|
|                               | Cut-off index   | Cut-off reference           | Sensitivity         | Specificity         | PPV                 | NPV                    | Prevalence | Cut-off index  | Cut-off reference | Sensitivity | Specificity | PPV  | NPV  | Prevalence |
| <b>Colposcopic impression</b> |   |                             |                     |                     |                     |                        |            |  |                   |             |             |      |      |            |
| Baum 2006                     | ≥CIN 2  | ≥CIN 2                      | 0.60                | 0.61                | 0.44                | 0.76                   | 33.1       | ≥CIN 3   | ≥CIN 3            | 0.51        | 0.84        | 0.37 | 0.90 | 15.8       |
| Benedet 2004                  | ≥CIN 2  | ≥CIN 2                      | 0.74                | 0.77                | 0.66                | 0.83                   | 37.8       | ≥CIN 3   | ≥CIN 3            | 0.46        | 0.95        | 0.69 | 0.88 | 19.9       |
| Reed 1997                     | ≥CIN 2  | ≥CIN 2                      | 0.50                | 0.89                | 0.60                | 0.85                   | 24.5       | ≥CIN 3   | ≥CIN 3            | 0.33        | 0.98        | 0.50 | 0.96 | 6.1        |
| Abdulaziz 2020                | ≥CIN 2  | ≥CIN 2                      | 0.911               | 0.961               |                     |                        |            |  |                   |             |             |      |      |            |
| Phianpiset 2020               | any abnormalities   | ≥CIN 2                      | 0.99<br>(0.93-1.00) | 0.18<br>(0.15-0.21) | 0.13<br>(0.13-0.14) | 0.99<br>(0.94-1.00)    |            |  |                   |             |             |      |      |            |
| Massad 2009                   | ≥High grade   | ≥CIN 2                      | 0.26                | 0.66                | 0.63                | 0.28                   | 69.4       |  |                   |             |             |      |      |            |
| van der Marel 2014            | ≥High grade   | ≥CIN 2                      | 0.62                | 0.82                | 0.73                | 0.73                   | 43.6       | ≥High grade  | ≥CIN 3            | 0.71        | 0.72        | 0.38 | 0.91 | 20.0       |
| Spinillo 2014                 | ≥High grade   | ≥CIN 2                      | 0.36                | 0.95                | 0.68                | 0.85                   | 21.2       | ≥High grade  | ≥CIN 3            | 0.46        | 0.94        | 0.58 | 0.91 | 14.5       |
| Tidy 2013                     | ≥High grade   | ≥CIN 2                      | 0.73<br>(0.63-0.83) | 0.84<br>(0.75-0.90) | 0.78<br>(0.68-0.86) | 0.798<br>(0.713-0.868) |            |  |                   |             |             |      |      |            |
| Cantor 2008                   |   |                             |                     |                     |                     |                        |            | ≥HSIL  | ≥HSIL             | 0.71        | 0.81        | 0.61 | 0.87 | 29.0       |
| Bekkers 2008                  |   |                             |                     |                     |                     |                        |            | ≥HSIL  | ≥HSIL             | 0.61        | 0.84        | 0.61 | 0.84 | 28.4       |
| Higgins 1994                  |   |                             |                     |                     |                     |                        |            | ≥HSIL  | ≥HSIL             | 0.27        | 0.95        | 0.67 | 0.78 | 27.1       |
| Kierkegaard 1994              |   |                             |                     |                     |                     |                        |            | ≥HSIL  | ≥HSIL             | 0.67        | 0.87        | 0.80 | 0.78 | 42.3       |
| Petousis 2018                 |   |                             |                     |                     |                     |                        |            | ≥HSIL  | ≥HSIL             |             |             | 0.72 | 0.48 |            |
| Jones 1987                    | Suspicious  | ≥CIN 2                      | 1.00                | 0.22                | 0.05                | 1.00                   | 4.3        | Suspicious   | ≥CIN 3            | 1.00        | 0.22        | 0.02 | 1.00 | 1.3        |
| Jahaveri 1980                 | ≥Mild to moderate dysplasia                                 | ≥Mild to moderate dysplasia | 1.00                | 0.87                | 0.96                | 0.99                   | 75.4       | ≥Severe dysplasia  | ≥Severe dysplasia | 0.96        | 0.90        | 0.86 | 0.97 | 38.4       |
| Ronk 1977                     | ≥Mildly abnormal  | ≥Mild to moderate           | 0.91                | 0.47                | 0.86                | 0.58                   | 78.4       | ≥Severely abnormal   | ≥Severe dysplasia | 0.53        | 0.96        | 0.90 | 0.76 | 39.5       |

| Reference      | Accuracy for diagnosing CIN ≥2 (unless otherwise indicated) |                   |                     |                     |                     |                     | Accuracy for diagnosing DTA CIN ≥3 or ≥HSIL (unless otherwise indicated) |                  |                   |                     |                     |                     |                      |            |
|----------------|---|-------------------|---------------------|---------------------|---------------------|---------------------|--|------------------|-------------------|---------------------|---------------------|---------------------|----------------------|------------|
|                | Cut-off index   | Cut-off reference | Sens-itivity        | Spec-ificity        | PPV                 | NPV                 | Prevalence   | Cut-off index    | Cut-off reference | Sens-itivity        | Spec-ificity        | PPV                 | NPV                  | Prevalence |
|                | erate dysplasia   |                   |                     |                     |                     |                     |  |                  |                   |                     |                     |                     |                      |            |
| Karimi 2011    |   |                   |                     |                     |                     |                     |  | Positive         | Positive          | 0.80                | 0.81                | 0.30                | 0.98                 | 9.4        |
| Massad 2009    | Reid ≥4   | ≥CIN 2            | 0.20                | 0.90                | 0.86                | 0.27                | 75.2   |                  |                   |                     |                     |                     |                      |            |
| Boonlikit 2016 | Reid ≥1   | ≥CIN 2            | 0.89<br>(0.84–0.94) | 0.51<br>(0.45–0.59) | 0.61<br>(0.54–0.67) | 0.85<br>(0.79–0.92) |  |                  |                   |                     |                     |                     |                      |            |
| Boonlikit 2016 | Reid ≥2   | ≥CIN 2            | 0.85<br>(0.79–0.90) | 0.74<br>(0.68–0.81) | 0.73<br>(0.67–0.80) | 0.86<br>(0.80–0.91) |  |                  |                   |                     |                     |                     |                      |            |
| Boonlikit 2016 | Reid ≥3   | ≥CIN 2            | 0.73<br>(0.66–0.80) | 0.87<br>(0.82–0.92) | 0.82<br>(0.76–0.88) | 0.79<br>(0.74–0.85) |  |                  |                   |                     |                     |                     |                      |            |
| Boonlikit 2016 | Reid ≥4   | ≥CIN 2            | 0.62<br>(0.54–0.70) | 0.92<br>(0.88–0.96) | 0.86<br>(0.80–0.92) | 0.74<br>(0.69–0.80) |  |                  |                   |                     |                     |                     |                      |            |
| Boonlikit 2016 | Reid ≥5   | ≥CIN 2            | 0.44<br>(0.36–0.51) | 0.98<br>(0.97–1.00) | 0.96<br>(0.91–1.00) | 0.68<br>(0.62–0.73) |  |                  |                   |                     |                     |                     |                      |            |
| Boonlikit 2016 | Reid ≥6   | ≥CIN 2            | 0.19<br>(0.13–0.25) | 0.99<br>(0.98–1.00) | 0.97<br>(0.91–1.00) | 0.60<br>(0.54–0.65) |  |                  |                   |                     |                     |                     |                      |            |
| Kudela 2020    |   |                   |                     |                     |                     |                     |  | Modified Reid ≥4 | ≥HSIL             | 0.86<br>(0.71–0.95) | 0.83<br>(0.65–0.94) | 0.86<br>(0.70–0.95) | 0.83<br>(0.65–0.947) |            |
| Kudela 2020    |   |                   |                     |                     |                     |                     |  | Modified Reid ≥5 | ≥HSIL             | 0.58<br>(0.41–0.75) | 0.97<br>(0.83–1.00) |                     |                      |            |
| Shojaei 2013   |   |                   |                     |                     |                     |                     |  | Reid ≥3          | ≥CIN 3            | 0.78                | 0.79                | 0.79                | 0.78                 |            |
| Shojaei 2013   |   |                   |                     |                     |                     |                     |  | Reid ≥5          | ≥CIN 3            | 0.96                | 0.70                | 0.89                | 0.86                 |            |
| Strander 2005  | Swede ≥5  | ≥CIN 2            | 1.00                | 0.31                | 0.55                | 1.00                | 45.5   |                  |                   |                     |                     |                     |                      |            |
| Kallner 2015   | Swede ≥1  | ≥CIN 2            | 1.00<br>(0.93–1.00) | 0.03<br>(0.01–0.11) | 1.00<br>(0.16–1.00) | 0.44<br>(0.34–0.53) |  |                  |                   |                     |                     |                     |                      |            |
| Kallner 2015   | Swede ≥2  | ≥CIN 2            | 0.94<br>(0.83–0.99) | 0.11<br>(0.04–0.21) | 0.70<br>(0.35–0.93) | 0.44<br>(0.35–0.54) |  |                  |                   |                     |                     |                     |                      |            |



| Reference                 | Accuracy for diagnosing CIN ≥2 (unless otherwise indicated) |                   |                     |                     |                     |                     | Accuracy for diagnosing DTA CIN ≥3 or ≥HSIL (unless otherwise indicated) |                    |                   |                  |                  |                  |                  |            |
|---------------------------|---|-------------------|---------------------|---------------------|---------------------|---------------------|--|--------------------|-------------------|------------------|------------------|------------------|------------------|------------|
|                           | Cut-off index   | Cut-off reference | Sens-itivity        | Spec-ificity        | PPV                 | NPV                 | Prevalence   | Cut-off index      | Cut-off reference | Sens-itivity     | Spec-ificity     | PPV              | NPV              | Prevalence |
| Kallner 2015              | Swede ≥3  | ≥CIN 2            | 0.90<br>(0.78–0.97) | 0.25<br>(0.15–0.37) | 0.76<br>(0.53–0.92) | 0.47<br>(0.37–0.58) |  |                    |                   |                  |                  |                  |                  |            |
| Kallner 2015              | Swede ≥4  | ≥CIN 2            | 0.82<br>(0.68–0.91) | 0.37<br>(0.25–0.50) | 0.73<br>(0.54–0.87) | 0.49<br>(0.38–0.61) |  |                    |                   |                  |                  |                  |                  |            |
| Kallner 2015              | Swede ≥5  | ≥CIN 2            | 0.76<br>(0.59–0.85) | 0.59<br>(0.46–0.71) | 0.75<br>(0.60–0.86) | 0.57<br>(0.44–0.70) |  |                    |                   |                  |                  |                  |                  |            |
| Kallner 2015              | Swede ≥6  | ≥CIN 2            | 0.55<br>(0.40–0.69) | 0.80<br>(0.68–0.89) | 0.70<br>(0.59–0.80) | 0.68<br>(0.51–0.81) |  |                    |                   |                  |                  |                  |                  |            |
| Kallner 2015              | Swede ≥7  | ≥CIN 2            | 0.43<br>(0.29–0.58) | 0.89<br>(0.79–0.96) | 0.67<br>(0.57–0.77) | 0.75<br>(0.55–0.89) |  |                    |                   |                  |                  |                  |                  |            |
| Kallner 2015              | Swede ≥8  | ≥CIN 2            | 0.20<br>(0.10–0.34) | 0.95<br>(0.87–0.99) | 0.61<br>(0.51–0.71) | 0.77<br>(0.46–0.95) |  |                    |                   |                  |                  |                  |                  |            |
| Kallner 2015              | Swede ≥9  | ≥CIN 2            | 0.12<br>(0.05–0.25) | 1.00<br>(0.95–1.00) | 0.60<br>(0.50–0.70) | 1.00<br>(0.54–1.00) |  |                    |                   |                  |                  |                  |                  |            |
| Kallner 2015              | Swede ≥10   | ≥CIN 2            | 0.02<br>(0.01–0.11) | 1.00<br>(0.95–1.00) | 0.58<br>(0.48–0.67) | 1.00<br>(0.03–1.00) |  |                    |                   |                  |                  |                  |                  |            |
| Kudela 2020               |   |                   |                     |                     |                     |                     |  | Swede ≥5           | ≥HSIL             | 0.94 (0.81-0.99) | 0.83 (0.65-0.94) | 0.87 (0.72-0.95) | 0.93 (0.74-0.99) |            |
| Rodpenpear 2019           | Swede ≥11<br>(range 1-15)                                   | ≥CIN 2            | 0.82                | 0.96                | 0.96                | 0.85                |  |                    |                   |                  |                  |                  |                  |            |
| <b>Acetowhite changes</b> |   |                   |                     |                     |                     |                     |  |                    |                   |                  |                  |                  |                  |            |
| Follen 1987               | ≥Shiny, grey white  | ≥CIN 2            | 0.62                | 0.50                | 0.59                | 0.53                | 53.8   | ≥Shiny, grey white | ≥CIN 3            | 0.56             | 0.43             | 0.23             | 0.76             | 23.1       |
| Boonlikit 2016            | ≥Shiny, grey white  | ≥CIN 2            | 0.64<br>(0.57–0.72) | 0.82<br>(0.77–0.88) | 0.75<br>(0.68–0.82) | 0.74<br>(0.68–0.80) |  |                    |                   |                  |                  |                  |                  |            |
| van der Marel 2014        | ≥Shiny, grey white  | ≥CIN 2            | 0.79                | 0.48                | 0.65                | 0.65                | 55.0   | ≥Shiny, grey white | ≥CIN 3            | 0.85             | 0.39             | 0.32             | 0.89             | 24.9       |

| Reference                 | Accuracy for diagnosing CIN ≥2 (unless otherwise indicated) |                   |                     |                     |                     |                     | Accuracy for diagnosing DTA CIN ≥3 or ≥HSIL (unless otherwise indicated) |   |                   |             |             |      |      |            |
|---------------------------|---|-------------------|---------------------|---------------------|---------------------|---------------------|--|---|-------------------|-------------|-------------|------|------|------------|
|                           | Cut-off index   | Cut-off reference | Sensitivity         | Specificity         | PPV                 | NPV                 | Prevalence   | Cut-off index                             | Cut-off reference | Sensitivity | Specificity | PPV  | NPV  | Prevalence |
| Shojaei 2013              |   |                   |                     |                     |                     |                     |  | ≥Shiny, grey white                        | High grade        | 0.96        | 0.55        | 0.46 | 0.97 | 28.5       |
| Boonlikit 2016            | Dull oyster grey  | ≥CIN 2            | 0.46<br>(0.38–0.54) | 0.94<br>(0.91–0.98) | 0.87<br>(0.80–0.94) | 0.68<br>(0.62–0.74) |  |   |                   |             |             |      |      |            |
| <b>Location of lesion</b> |   |                   |                     |                     |                     |                     |  |   |                   |             |             |      |      |            |
| No results                |   |                   |                     |                     |                     |                     |  |   |                   |             |             |      |      |            |
| <b>Size of lesion</b>     |   |                   |                     |                     |                     |                     |  |   |                   |             |             |      |      |            |
| Kudela 2020               | ≥15 mm  | ≥CIN 2            | 0.53                | 0.87                | 0.83                | 0.60                | 54.5   | >15 mm                                    | ≥CIN 3            | 0.43        | 0.69        | 0.39 | 0.72 | 31.8       |
| van der Marel 2014        | >50%  | ≥CIN 2            | 0.39                | 0.81                | 0.72                | 0.52                | 55.3   | >50%                                      | ≥CIN 3            | 0.52        | 0.77        | 0.43 | 0.83 | 24.8       |
| <b>SCJ visibility</b>     |   |                   |                     |                     |                     |                     |  |   |                   |             |             |      |      |            |
| No results                |   |                   |                     |                     |                     |                     |  |   |                   |             |             |      |      |            |
| <b>Iodine staining</b>    |   |                   |                     |                     |                     |                     |  |   |                   |             |             |      |      |            |
| Shojaei 2013              |   |                   |                     |                     |                     |                     |  | Partial uptake or mustard yellow staining | High grade        | 0.84        | 0.68        | 0.51 | 0.91 | 28.5       |
| <b>Vascular pattern</b>   |   |                   |                     |                     |                     |                     |  |   |                   |             |             |      |      |            |
| Follen 1987               | Coarse, mosaic or atypical vessels                          | ≥CIN 2            | 0.52                | 0.47                | 0.57                | 0.43                | 56.8   | Coarse, mosaic or atypical vessels        | ≥CIN 3            | 0.64        | 0.52        | 0.30 | 0.81 | 25.0       |
| Shojaei 2013              | Coarse punctation or mosaic                                 | High grade CIN    | 0.23                | 0.94                | 0.78                | 0.56                | 48.8   |   |                   |             |             |      |      |            |
| Boonlikit 2016            | ≥Absence of surface vessels                                 | ≥CIN 2            | 0.82<br>(0.76–0.88) | 0.75<br>(0.69–0.81) | 0.73<br>(0.66–0.79) | 0.83<br>(0.78–0.89) |  |   |                   |             |             |      |      |            |
| Boonlikit 2016            | Definite coarse punc-                                       | ≥CIN 2            | 0.53<br>(0.45–0.60) | 0.94<br>(0.90–0.97) | 0.87<br>(0.81–0.94) | 0.70<br>(0.65–0.76) |  |   |                   |             |             |      |      |            |

| Reference                 | Accuracy for diagnosing CIN ≥2 (unless otherwise indicated) |                   |                     |                     |                     |                     |            | Accuracy for diagnosing DTA CIN ≥3 or ≥HSIL (unless otherwise indicated) |                   |             |             |      |      |            |
|---------------------------|---|-------------------|---------------------|---------------------|---------------------|---------------------|------------|--|-------------------|-------------|-------------|------|------|------------|
|                           | Cut-off index   | Cut-off reference | Sensitivity         | Specificity         | PPV                 | NPV                 | Prevalence | Cut-off index  | Cut-off reference | Sensitivity | Specificity | PPV  | NPV  | Prevalence |
|                           | tation or mosaic  |                   |                     |                     |                     |                     |            |  |                   |             |             |      |      |            |
| van der Marel 2014        | Coarse punctuation  | ≥CIN 2            | 0.14                | 0.98                | 0.89                | 0.48                | 55.0       | Coarse   | ≥CIN 3            | 0.21        | 0.96        | 0.61 | 0.78 | 24.9       |
| van der Marel 2014        | Mosaic coarse   | ≥CIN 2            | 0.15                | 0.92                | 0.71                | 0.47                | 55.0       | Coarse   | ≥CIN 3            | 0.21        | 0.91        | 0.43 | 0.78 | 24.9       |
| van der Marel 2014        | Atypical vessels present                                    | ≥CIN 2            | 0.06                | 0.97                | 0.70                | 0.46                | 55.0       | Present  | ≥CIN 3            | 0.10        | 0.97        | 0.55 | 0.77 | 24.9       |
| <b>Border and surface</b> |   |                   |                     |                     |                     |                     |            |  |                   |             |             |      |      |            |
| Follen 1987               | Papillomatous   | ≥CIN 2            | 0.60                | 0.86                | 0.60                | 0.86                | 26.3       | Papillomatous  | ≥CIN 3            | 0.00        | 0.71        | 0.00 | 0.86 | 10.5       |
| Roy 1997                  |   |                   |                     |                     |                     |                     |            | Abrupt peeling margin  | High grade        | 0.95        | 0.60        | 0.97 | 0.43 | 93.8       |
| Shojaei 2013              |   |                   |                     |                     |                     |                     |            | Rolled, peeling edge, sharp margins                                      | High grade        | 0.17        | 0.94        | 0.72 | 0.54 | 48.8       |
| van der Marel 2014        | Internal borders  | ≥CIN 2            | 0.08                | 0.96                | 0.74                | 0.46                | 55.0       | Internal borders   | ≥CIN 3            | 0.11        | 0.95        | 0.44 | 0.76 | 25.2       |
| Boonlikit 2016            | ≥Regular, smooth  | ≥CIN 2            | 0.77<br>(0.70–0.83) | 0.68<br>(0.61–0.74) | 0.66<br>(0.59–0.73) | 0.78<br>(0.71–0.84) |            |  |                   |             |             |      |      |            |
| Boonlikit 2016            | Rolled, peeling edges, sharp margins                        | ≥CIN 2            | 0.50<br>(0.42–0.58) | 0.90<br>(0.85–0.94) | 0.80<br>(0.71–0.88) | 0.68<br>(0.63–0.74) |            |  |                   |             |             |      |      |            |

CIN: Cervical intraepithelial neoplasia; HSIL: High Grade Squamous Intraepithelial Lesion

## Bijlage 10. Directe vergelijking voorspellende waarde van colposcopie indicatoren binnen één onderzoek

| Reference           | Predictive value for diagnosing $\geq$ CIN 2 (unless otherwise indicated) |                        |                          |                  |               | Predictive value for diagnosing DTA CIN $\geq$ 3 or $\geq$ HSIL (unless otherwise indicated) |                                   |  |                  |               |      |      |
|---------------------|---|------------------------|--------------------------|------------------|---------------|--|-----------------------------------|--|------------------|---------------|------|------|
|                     | Cut off   |                        |                          |                  |               | Cut off  |                                   |  |                  |               |      |      |
|                     | <i>Snow-white</i>   | <i>Inter-mediate</i>   | <i>Grey-white</i>        |                  |               | <i>Snow-white</i>  | <i>Inter-mediate</i>              | <i>Grey-white</i>                            |                  |               |      |      |
| <b>Follen 1987</b>  | $\geq$ CIN 2  | 45.5                   | 50.0                     | 59.1             |               | $\geq$ CIN 3   | 18.2                              | 33.3   | 22.7             |               |      |      |
|                     | <i>Absent</i>   | <i>Fine punctation</i> | <i>Coarse punctation</i> | <i>Mosaiform</i> | <i>Mosaic</i> | <i>Absent</i>  | <i>Fine punctation</i>            | <i>Coarse punctation</i>                     | <i>Mosaiform</i> | <i>Mosaic</i> |      |      |
| <b>Follen 1987</b>  | $\geq$ CIN 2  | 53.8                   | 62.5                     | 80.0             | 46.7          | 50.0   | $\geq$ CIN 3                      | 23.1   | 12.5             | 40.0          | 20.0 | 50.0 |
|                     | <i>Uneven or granular</i>   | <i>Papillo-matous</i>  |                          |                  |               | <i>Uneven or granular</i>  | <i>Papillo-matous</i>             |  |                  |               |      |      |
| <b>Follen 1987</b>  | $\geq$ CIN 2  | 14.3                   | 60.0                     |                  |               | $\geq$ CIN 3   | 14.3                              | 0.0  |                  |               |      |      |
|                     |   |                        |                          |                  |               | <i>Shiny, snow white</i>   | <i>Shiny, but grey white</i>      | <i>Dull, oyster grey</i>                     |                  |               |      |      |
| <b>Shojaei 2013</b> |   |                        |                          |                  |               | High grade   | 2.8                               | 27.7   | 75.0             |               |      |      |
|                     |   |                        |                          |                  |               | <i>Mahogany brown staining</i>   | <i>Partial uptake</i>             | <i>Mustard yellow staining</i>               |                  |               |      |      |
| <b>Shojaei 2013</b> |   |                        |                          |                  |               | High grade   | 8.7                               | 39.8   | 74.4             |               |      |      |
|                     |   |                        |                          |                  |               | <i>Uniform, fine punctation or mosaic</i>  | <i>Absence of surface vessels</i> | <i>Definite, coarse punctation or mosaic</i> |                  |               |      |      |
| <b>Shojaei 2013</b> |   |                        |                          |                  |               | High grade   | 14.0                              | 26.0   | 75.7             |               |      |      |
|                     |   |                        |                          |                  |               | <i>Condylo-matous, micro-papillary</i>   | <i>Regular, smooth</i>            | <i>Rolled, peeling edges, sharp margins</i>  |                  |               |      |      |
| <b>Shojaei 2013</b> |   |                        |                          |                  |               | High grade   | 11.4                              | 38.4   | 72.4             |               |      |      |

| Reference                 | Predictive value for diagnosing $\geq$ CIN 2 (unless otherwise indicated) |                         |                          |               | Predictive value for diagnosing DTA CIN $\geq$ 3 or $\geq$ HSIL (unless otherwise indicated) |                         |                          |                |               |                |
|---------------------------|---|-------------------------|--------------------------|---------------|--|-------------------------|--------------------------|----------------|---------------|----------------|
|                           | <i>Normal</i>   | <i>Low grade lesion</i> | <i>High grade lesion</i> |               | <i>Normal</i>  | <i>Low grade lesion</i> | <i>High grade lesion</i> |                |               |                |
| <b>van der Marel 2014</b> | $\geq$ CIN 2  | 17.4                    | 35.0                     | 72.6          | $\geq$ CIN 3   | 7.6                     | 10.5                     | 38.5           |               |                |
|                           | <i>Absent</i>   | <i>Translucent</i>      | <i>Inter-mediate</i>     | <i>Opaque</i> | <i>Absent</i>  | <i>Translucent</i>      | <i>Inter-mediate</i>     | <i>Opaque</i>  |               |                |
| <b>van der Marel 2014</b> | $\geq$ CIN 2  | 40.0                    | 34.4                     | 60.1          | 79.5   | $\geq$ CIN 3            | 13.3                     | 10.9           | 26.8          | 46.6           |
|                           |   | <i>0%</i>               | <i>&lt;25%</i>           | <i>25-50%</i> | <i>&gt;50%</i>   |                         | <i>0%</i>                | <i>&lt;25%</i> | <i>25-50%</i> | <i>&gt;50%</i> |
| <b>van der Marel 2014</b> | $\geq$ CIN 2  | 44.4                    | 38.0                     | 62.9          | 72.4   | $\geq$ CIN 3            | 0.0                      | 11.7           | 25.9          | 43.3           |
|                           | <i>Absent</i>   | <i>Fine punctation</i>  | <i>Coarse punctation</i> |               | <i>Absent</i>  | <i>Fine punctation</i>  | <i>Coarse punctation</i> |                |               |                |
| <b>van der Marel 2014</b> | $\geq$ CIN 2  | 48.4                    | 60.5                     | 88.9          |  | $\geq$ CIN 3            | 17.2                     | 32.5           | 61.1          |                |
|                           | <i>Absent</i>   | <i>Fine mosaic</i>      | <i>Coarse mosaic</i>     |               | <i>Absent</i>  | <i>Fine mosaic</i>      | <i>Coarse mosaic</i>     |                |               |                |
| <b>van der Marel 2014</b> | $\geq$ CIN 2  | 51.3                    | 57.0                     | 70.6          |  | $\geq$ CIN 3            | 23.2                     | 20.6           | 43.1          |                |
|                           | <i>Absent</i>   | <i>Atypical vessels</i> |                          |               | <i>Absent</i>  | <i>Atypical vessels</i> |                          |                |               |                |
| <b>van der Marel 2014</b> | $\geq$ CIN 2  | 54.3                    | 70.0                     |               |  | $\geq$ CIN 3            | 23.5                     | 55.0           |               |                |
|                           | <i>Geo-graphical</i>  | <i>Smooth</i>           | <i>Internal borders</i>  |               | <i>Geo-graphical</i>   | <i>Smooth</i>           | <i>Internal borders</i>  |                |               |                |
| <b>van der Marel 2014</b> | $\geq$ CIN 2  | 46.3                    | 59.6                     | 74.1          |  | $\geq$ CIN 3            | 18.6                     | 28.0           | 44.4          |                |