EVIDENCE TO DECISION TABLE (ETD) PICO 1 AND 2 GENERAL POPULATION

Should HPV DNA detection algorithms vs. other algorithms be used for screening (triage) and treating women in the general population?

POPULATION:	screening (triage) and treating women in the general population
INTERVENTION:	HPV DNA detection algorithms
COMPARISON:	other algorithms
MAIN OUTCOMES:	•Cervical cancer •Mortality •CIN 2+ •HPV infection •Preterm birth (early/late) •Acceptability (to all stakeholders) •Pre-cancer treatments •Adverse events related to pre-cancer treatments - Major infections or bleeding, Procedure associated pain, Cervical stenosis, Infertility, Spontaneous abortions (1st trimester/ 2nd trimester), Perinatal deaths, Premature rupture of membrane, Unnecessary interventions, Increased viral shedding in HIV infected women and, costs (number of tests), feasibility (Coverage of treatment, Coverage of screening), acceptability (stigmatization), equity
SETTING:	
PERSPECTIVE:	Population
BACKGROUND:	There are many strategies (algorithms) that can be used to screen, triage and treat women to prevent cervical cancer. The GDG prioritised the following algorithms to evaluate (other algorithms will be assessed in future): 1.VIA 2.HPV DNA (self or clinician) 3.Cytology then colposcopy 4.HPV DNA then HPV 16/18 (only when already part of the HPV test) and VIA 5.HPV DNA then VIA triage 6.HPV DNA then colposcopy (triage) 7.HPV DNA then cytology (triage) – colposcopy [full description of algorithms is available at
CONFLICT OF INTERESTS:	

ASSESSMENT

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	**REVIEWS OF LONGITUDINAL STUDIES** were conducted by IARC: HPV versus VIA: HPV-and-treat approach achieved greater reduction on the prevalent CIN2+ at 6 months of follow-up compared with VIA-and-treat (77% vs 37%) based on the RCT conducted in South Africa (Denny 2005). Greater reduction of cervical cancer incidence and mortality of a single round of screening with HPV DNA test compared with VIA has been identified at the Osmanabad India RCT (age-standardized incidence [ASR]: 47.4 vs 58.7 per 100 000 person-year, age-standardized mortality: 12.7 vs 20.9 per 100 000 person-year) (Sankaranarayanan 2005, 2009). In addition, HPV DNA test has dramatically reduced the incidence of stage II or higher cervical cancer compared to VIA in the trial (ASR 14.5 vs 32.2 per 100 000 person-year). Regarding diagnostic harms, no absolute trend of higher or lower colposcopy referral rate and PPV were identified between the two screening modalities across different studies. HPV versus cytology: Eight out of nine randomized controlled trials (Ronco 2008, Ogilvie 2018, leinonen 2012, Canfell 2017, Rijkaart 2012, Naucler 2007, Kitchener 2009, Chan 2020) have shown that HPV-based screening by HPV alone, or followed by triage with cytology or colposcopy, or co-testing detects more CIN2+ in screening than cytology, and five out of six trials have shown a decrease in CIN2+ in the next screening round. In a pooled analysis of four of these randomized trials with a median follow-up of 6.5 years, cervical cancer risk was 40% lower in the HPV-based testing arm (Ronco 2014). In one other randomized trial in a previously unscreened population, cervical cancer mortality was 41% lower in the HPV-based testing arm than in the cytological screening arm after a cumulative follow-up of 8 years. The increased CIN2+ detection of HPV-based screening was confirmed in twelve real-world HPV implementation cohorts. These studies evaluated different HPV DNA screening with or without triage (including cytology, co-testing with cytology, and/or colposcopy). These studies also observed an	The GDG agreed on the following based on the modelling: • Primary HPV testing every 5-years from ages 30-50 years, regardless of triaging strategy, resulted in the largest reductions in cervical cancer incidence and mortality rates, with >50% reduction in cervical cancer incidence and >55% reduction in cervical cancer mortality. • Primary VIA testing could reduce cervical cancer incidence rates by up to 46% but required more frequent testing (3-yearly intervals) and high test performance (sustained, population-level sensitivity to CIN2+ of 60%).

increase in the number of screen positives and colposcopy referrals in the HPV screening arm, but the effect on the positive predictive value of CIN3+ was limited.

REVIEWS OF REVIEWS in LMICs for loss to follow-up, triage, treatment

'loss to triage'

- systematic review of *VIA* screening programmes in India
- large variation in loss from 10 to 70% when colposcopy used as triage
- less loss (0 to 1.4%) when colposcopy offered same day

'loss to active surveillance'

- systematic review measuring follow-up after *histological confirmation* - 19% loss at 6 months, 15% loss at 12 months

'loss to treatment'

- systematic review of studies in women with *histological confirmation* - variation in loss from 58 to 100%
- systematic review of *HPV* screening - follow-up may be hindered by access to health care

REVIEWS OF THE ACCURACY OF SCREENING AND TRIAGE TESTS were conducted:

VIA for CIN2+: sensitivity 66%; specificity 87%; extreme heterogeneity (variability) in studies, likely due to subjectivity of interpretation

HPV compared to cytology for CIN2+: relative sensitivity 1.35 [HPV has greater sensitivity); relative specificity 0.94 (HPV slightly lower specificity)

HPV vaginal self versus cervical clinician samples: self PCR similar sensitivity and specificity; self signal amplification lower sensitivity and specificity; self mRNA HPV lower sensitivity but similar specificity

Cytology (ASCUS+) as triage after HPV for CIN2+: sensitivity 71%; specificity 75%

VIA as triage after HPV for CIN2+: sensitivity 65%; specificity 73%

HPV 16/18 (and VIA for negative) as triage for CIN2+: sensitivity 53%; specificity 75%

Colposcopy as triage for CIN2+: sensitivity 83%; specificity 75%

MODELLING was conducted to calculate benefits and harms of different algorithms starting at different ages and with different frequency intervals:

Summary table: General population

	Screening ages	Cervical Cx cases* (% reduction)	Cervical Cx deaths* (% reduction)	Pre-cancer treatments*	Additional pre-term deliveries due to pre-cancer treatment*	NNT to avert a cervical cancer death	Discounted lifetime cost (2019 $US)
No Screening	-	1,950 (-)	1,456 (-)	0	0	-	$3
Primary VIA (high sens)	3yrly, 30-50 yrs (7X)	1,046 (46%)	714 (51%)	147,349	180	199	$54
	5yrly, 30-50 yrs (5X)	1,181 (39%)	803 (45%)	120,442	139	184	$41
Primary VIA	3yrly, 30-50 yrs (7X)	1,194 (39%)	838 (42%)	137,172	167	222	$51
	5yrly, 30-50 yrs (5X)	1,351 (31%)	949 (35%)	111,915	127	221	$39
Primary HPV	5yrly, 30-50 yrs (5X)	851 (56%)	572 (61%)	50,179	88	57	$52
	10yrly, 30-50 yrs (3X)	1,048 (46%)	720 (51%)	40,090	74	54	$35
	10yrly, 35-45 yrs (2X)	1,237 (37%)	883 (39%)	18,528	28	32	$21
Cytology, HPV triage	3yrly, 30-50 yrs (7X)	1,101 (44%)	756 (48%)	20,922	43	30	$60
	5yrly, 30-50 yrs (5X)	1,200 (38%)	822 (44%)	18,516	34	29	$59
HPV, 16/18 triage	5yrly, 30-50 yrs (5X)	877 (55%)	591 (59%)	34,408	67	40	$51
	10yrly, 30-50 yrs (3X)	1,069 (45%)	737 (49%)	27,880	56	39	$34
	10yrly, 35-45 yrs (2X)	1,253 (36%)	897 (38%)	13,119	21	23	$21
HPV, VIA triage	5yrly, 30-50 yrs (5X)	940 (52%)	638 (56%)	30,186	61	37	$51
	10yrly, 30-50 yrs (3X)	1,144 (41%)	792 (46%)	24,239	51	37	$35
	10yrly, 35-45 yrs (2X)	1,318 (32%)	945 (35%)	11,621	18	23	$21
HPV, colp triage	5yrly, 30-50 yrs (5X)	940 (52%)	625 (57%)	33,265	64	40	$57
	10yrly, 30-50 yrs (3X)	1,141 (41%)	779 (47%)	26,633	54	39	$39
	10yrly, 35-45 yrs (2X)	1,308 (33%)	929 (36%)	12,398	20	24	$23
HPV, cytology triage	5yrly, 30-50 yrs (5X)	966 (50%)	648 (56%)	22,352	48	28	$61
	10yrly, 30-50 yrs (3X)	1,166 (40%)	799 (45%)	18,075	40	27	$42
	10yrly, 35-45 yrs (2X)	1,329 (32%)	947 (35%)	8,693	15	17	$25

*Outcomes represent total events over the lifetime of a cohort of 100,000 women

Note: costs of preterm deliveries with thermal ablation was estimated from the risk after ablation from systematic review by Kyrgiou 2017.

- Primary HPV testing approaches resulted in substantially fewer precancer treatment events and fewer adverse obstetric outcomes when compared to primary VIA strategies, even when we assume favourable VIA test performance.
- Of the Primary HPV approaches, no triage (where visual assessment is used to determine eligibility for ablative treatment) had the highest reduction in incidence of cervical cancer (56% reduction). Different triaging options resulted in similar reductions in cervical cancer rates (range 50-55% reduction in incidence), and at least 31% fewer precancer treatment events when compared with no triage.
- Although, not modelled, the sensitivity and specificity of clinically validated PCR-based high risk HPV DNA for detection of CIN2+ on self-collected upper vaginal versus health provider-taken cervical samples are likely similar.
- A 5-year screening interval resulted in greater benefits, fewer harms and lower costs than 10 years when providing HPV DNA testing with or without triage. These effects were similar to cytology (followed by colposcopy) every 3 years, but better than every 5 years; and better than VIA every 5 years.
- Previous modelling for the WHO Global Strategy towards the elimination of cervical cancer demonstrated benefits with screening twice in a lifetime compared to once.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	**See above.**	See above.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Evidence for the desirable and undesirable effects of HPV DNA based testing compared to VIA or cytology based screening is from longitudinal studies and modelling. The evidence from longitudinal studies was reviewed in the IARC Handbook and found moderate certainty evidence when HPV DNA based testing (with or without triage) was used. The modelled evidence provided low certainty evidence and supported the effects from the longitudinal studies: there was some concern for risk of bias in the credibility of the model (e.g., assumptions of adherence and lost to follow-up after screening), but most of the model inputs were of moderate or high certainty evidence (e.g., diagnostic accuracy of HPV).	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	The outcomes previously identified in the 2014 screening and treatment guidelines, using methods from the WHO Handbook for Guideline Development were agreed on by the GDG as the outcomes of importance for these new PICO questions. The importance of the outcomes was identified as: •Cervical cancer •Mortality •Preterm birth (early/late) •Pre-cancer treatments (and related adverse events, see below) •CIN 2+ •HPV infection •Adverse events related to pre-cancer treatments - Major infections or bleeding, Procedure associated pain, Cervical stenosis, Infertility, Spontaneous abortions (1st trimester/ 2nd trimester), Perinatal deaths, Premature rupture of membrane, Unnecessary interventions, Increased viral shedding in HIV infected women •Acceptability (to all stakeholders) A systematic review of qualitative research was conducted and included 43 studies. There was however very little data reporting the value of the outcomes (data was primarily about the acceptability of the different tests and treatments – see below).	The Guideline Development Group agreed that greater value should be placed on cervical cancer incidence and mortality, and less value on treatment of CIN (and subsequent harms) and reproductive outcomes. However, in young women of reproductive age, although more value is placed on reproductive outcomes, there was still greater value placed on cervical cancer and mortality.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ Don't know	The GDG agreed that • HPV DNA as a primary test is favoured over VIA or cytology as a primary test. • HPV DNA testing alone or followed by a triage test are similarly favoured. • HPV DNA testing every 5 or 10 years is probably favoured over every 3 years, and every 3 years with cytology or VIA.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	**Modelling** of outcomes was conducted and the following costs were used: **Summary of aggregate costs (average across all 78 LMIC+)** Event / Cost (US$ 2019) Primary VIA^ 7.13 Primary HPV (+/- 16/18)* 15.20 Primary cytology^ 18.13 VIA triage^{O} 3.03 Cytology triage^{O} 15.74 HPV triage^{O} 8.15 Colposcopy$^{O,\#}$ 9.98 Ablative treatment 11.77 Excisional treatment 41.71 Event / Cost (US$ 2019) Histology @ 18.14 Punch biopsy/Biopsy 11.67 Cancer diagnosis and treatment– FIGO 1[a] 263.23 Cancer diagnosis and treatment– FIGO 2[a] 546.28 Cancer diagnosis and treatment– FIGO 3[a] 683.08 Cancer diagnosis and treatment– FIGO 4[a] 312.77 Palliative care[a] 116.92 Yearly surveillance after treatment[a] 58.36 * Includes workforce, consumables/equipment ^ Includes cost of test, sample drop-off and transport, laboratory staff time, lab supplies, general administration and overhead costs using WHO-CHOICE methodology and database O Same as primary, but includes a proportion of the labour, programmatic and utilisation costs from primary visits due to not requiring another visit. # Includes consumables/equipment, workforce @Includes consumables/equipment, workforce including pathologist and biomedical scientist [a]Cancer costs are only applied to the proportion of cancers that are treated, and assumed to apply to 90% of screen-detected cases. Yearly surveillance assumed to apply up to 10 years after diagnosis or death, whichever comes first. + The average across 78 LMIC sum the country-level costs weighted by the population of each country, and divides by the total population of those countries combined. Additional costs considered: - programmatic costs - cancer specific equipment - variations in health care worker wages and training (but not staff turnover) - HPV and thermal ablation costs are based on recently negotiated prices	

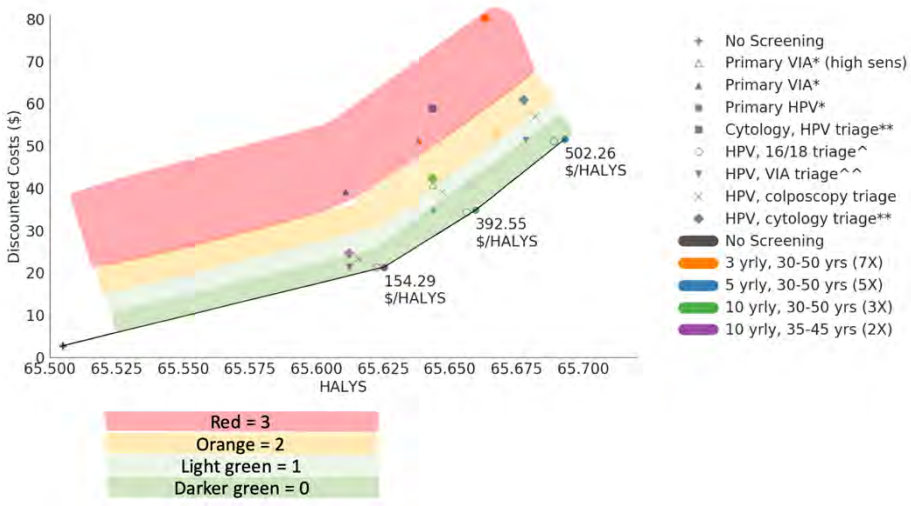
Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	Based on modelling.	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	**Modelling** was conducted to compare cost-effectiveness. Figure below illustrates where each algorithm falls when comparing Health Adjusted Life Years (HALYs, a combination of mortality and morbidity) against discounted costs:  	The GDG agreed about the following when comparing HPV testing to VIA or cytology testing: Primary HPV testing without triage was on the cost-effectiveness frontier: ● 10-yearly intervals at ages 35-45 (ICER =$154/HALY saved), ● 10-yearly intervals at ages 30-50 (ICER = $393/HALY saved), ● 5-yearly intervals at ages 30-50 ($502/HALY saved) Primary HPV 16/18 triage had similar costs and effects and could be considered to have similar cost-effectiveness outcomes. As a reference point for a potential willingness-to-pay

		(WTP) threshold in this population, the population-weighted average GDP per capita (pc) for 2019 across the 78-LMIC is US$1,999. Also, 68 of 78 LMIC (87%) had a GDP/pc >$500. The findings were robust to lower compliance assumptions. The GDG noted that the costs of HPV alone and HPV with HPV 16/18 triage were similar. The reason for this is greater treatments with HPV alone but fewer treatments with HPV 16/18 triage but greater cost of additional testing with triage.

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence found	While there is no evidence yet, the GDG agreed that providing HPV DNA testing may lead to greater access to screening.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	**A survey of GDG members** was conducted to explore concern for costs and integration of different algorithms: • respondents were moderately to very concerned about the ability to finance ALL algorithms (cyto>HPV>VIA) for scale-up and sustainability • more were very concerned about ability to minimize cost to patient for HPV and cytology algorithms **A survey of 561 women** was conducted online via SurveyMonkey in 2020, and was completed anonymously. All women aged 15 years and older, regardless of their prior cervical cancer screening or treatment status were eligible to participate. Survey results found that • most women (82.56%) in the general population stated that they would not face problems in attending a screening program • clear and strong preference for immediate treatment following a diagnosis of a cervical intraepithelial lesion (78%) among all women • follow-up visits after treatment for a cervical lesion were likely to cause difficulties to the respondents • aversion for the use of a speculum during screening • request from the community for better counselling, patient education, availability of choices of treatment and screening tests A systematic review of qualitative studies was conducted and included 43 studies. The results showed that the studies consistently demonstrate very high acceptability (70% or higher, several with 90%) across the studies for self-sampling, VIA, HPV DNA tests or a triage-based method. Studies also showed that women desired to decide whether to receive treatment, few said they would prefer to consult with their partner and few felt that they felt obligated to consult prior to treatment. Factors lowering acceptability included lack of reminders, payment of test, no tertiary education, no children, recent HIV diagnosis, poor awareness of cervical cancer, poor provider patient relationships. **Systematic review of reviews of provider perspectives** was conducted <u>VIA</u> • perceived limitations of VIA – low sensitivity and specificity and subjectivity - leading to missed cases and unnecessary referral to colposcopy or treatment • perceived incompetency – standardised training needed • lack of criteria for VIA positive	The GDG also considered that it may be difficult to change perceptions of providers to NOT use cytology; however, there may be increasing positive attitudes to HPV

	HPV • Lack of understanding about HPV tests and meaning of positive result • In LMICs, perception that implementing HPV would increase uptake, lead to more treatment (if same day) and be more sensitive to detect precancerous lesions • Self-sampling could reduce opportunities to see women for other care	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	**A survey of GDG members** was conducted to explore feasibility/implementations issues: • >70% of respondents were moderately to very concerned about generating demand for screening for all algorithms; ~80% was the highest for VIA • more were very concerned about access to HPV or cytology screening (30-40%) compared with VIA • more were moderately or very concerned about scale-up and sustainability of maintaining a trained workforce for VIA and cytology (~90%) vs. HPV (~55%) • over 50% of respondents were moderately or very concerned about ability to meet infrastructural demands for HPV or cytology • ability to maintain registry (aggregate or patient level) was moderately or very concerning in all algorithms (>75%) • variable concerns about integration with other programs (by level of concern cyto>HPV>VIA)	The GDG also considered: • complexity of algorithm may mean difficulty implementing • multiple steps in algorithm and across health sectors may reduce feasibility • political will appears to be a large factor in implementation • training providers and sustaining a skilled workforce is a large factor

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	●

CONCLUSIONS

Recommendation

1. WHO recommends using HPV DNA detection as the primary screening test rather than VIA or cytology in screening and treatment approaches among both the general population of women and women living with HIV.*
[Strong recommendation, moderate certainty of evidence in effects]

Remarks: Existing programmes with quality-assured cytology as the primary screening test should be continued until HPV DNA testing is operational; existing programmes using VIA as the primary screening test should transition rapidly because of the inherent challenges with quality assurance.

2. WHO suggests using an HPV DNA primary screening test either **with triage or without triage** to prevent cervical cancer among the general population of women.
[Conditional recommendation, moderate certainty of evidence in effects]

3a. **In a screen-and-treat approach** using HPV DNA detection as the primary screening test, WHO suggests treating women who test positive for HPV DNA among the general population of women.
3b. **In a screen, triage and treat approach** using HPV DNA detection as the primary screening test among the general population of women, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test (Annex 4).
[Conditional recommendation, moderate certainty of evidence in effects]

Remarks: The benefits, harms and programmatic costs of the triage options are similar; therefore, the choice of triage method will be dependent on feasibility, training, programme quality assurance and resources in countries. HPV16/18 genotyping could be integrated into the HPV DNA test (refer to Annex 4 for specific details of the algorithms).

4. When providing HPV DNA testing, WHO suggests using either samples taken by a health-care provider or self-collected samples among both the general population of women and women living with HIV.*
[Conditional recommendation, low-certainty evidence in effects]

8. WHO suggests a regular screening interval of every 5 to 10 years when using HPV DNA detection as the primary screening test among the general population of women.
[Conditional recommendation, low-certainty evidence in effects]

9. Where HPV DNA testing is not yet operational, WHO suggests a regular screening interval of every 3 years when using VIA or cytology as the primary screening test among both the general population of women and women living with HIV.*
[Conditional recommendation, low-certainty evidence in effects]

10. While transitioning to a programme with a recommended regular screening interval, screening even just twice in a lifetime is beneficial among both the general population of women and women living with HIV.*
[Good-practice statement]

Justification

A strong recommendation was made for using HPV DNA detection as a primary screening test when part of a screen-and-treat approach or a screen, triage and treat approach because a higher value was placed on the greater reductions in cervical cancer and deaths that are likely with HPV DNA detection compared with using VIA or cytology as a primary screening test (moderate-certainty evidence). There may also be fewer harms, such as preterm deliveries, when screening with an HPV DNA test compared with VIA. HPV DNA testing by the provider or by self-sampling may have similar effects, so either method of testing was suggested (low-certainty evidence). HPV DNA testing is largely acceptable to women and providers, is feasible and is more likely to lead to more equitable access to screening.

A conditional recommendation was made to use either HPV DNA detection followed by treatment or HPV DNA detection with a triage test because the balance of benefits and harms may be similar for either approach (moderate-certainty evidence). The benefits and harms may also be similar with any of the triage tests considered (moderate-certainty evidence), but the choice of approach should be made depending on context, because the feasibility and the resources needed for triage tests vary across settings.

Conditional recommendations were made on the screening intervals and the age at which to stop screening based on modelled evidence showing greater benefits and fewer harms with 5- to 10-year screening intervals with HPV DNA testing, compared with more frequent screening or similar intervals using cytology or VIA (low-certainty evidence).