

EVIDENCE TO DECISION TABLE (ETD): PICO 8 AGE AT INITIATION OF SCREENING WLHIV

Should age 25 years vs. when tested positive for HIV be used for as a threshold to initiate cervical cancer screening in women living with HIV?

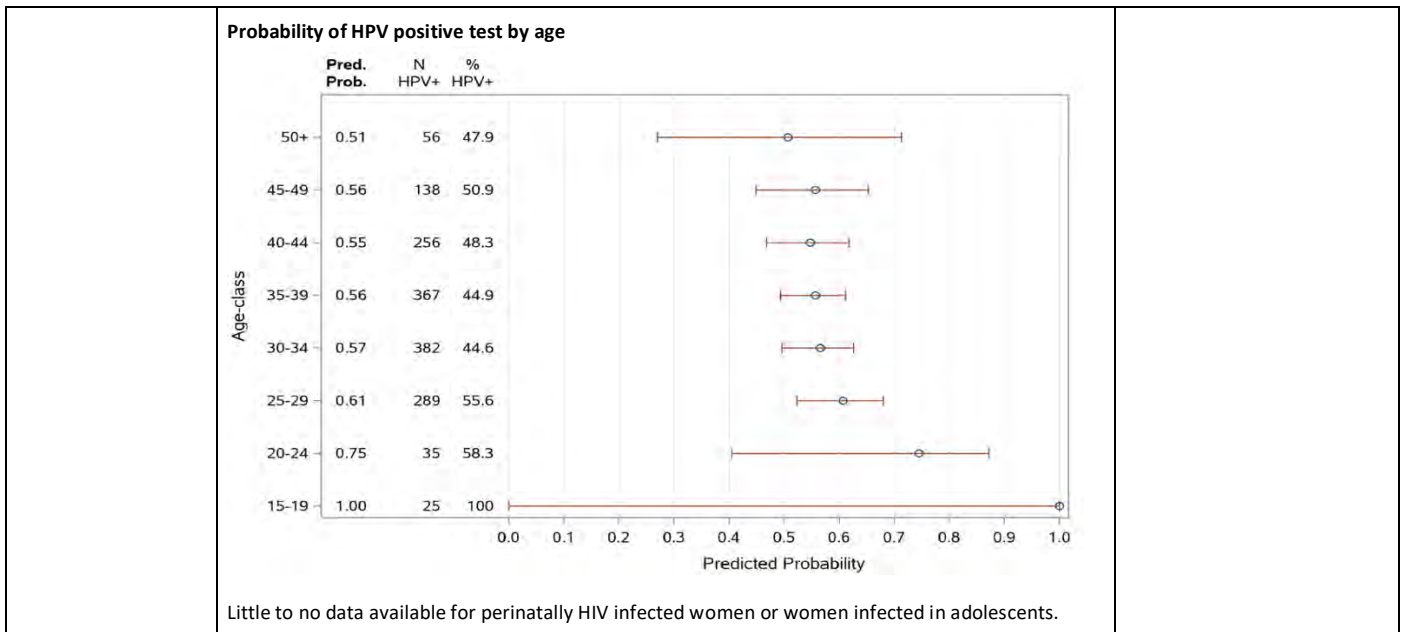
POPULATION:	as a threshold to initiate cervical cancer screening in women living with HIV
INTERVENTION:	age 25 years
COMPARISON:	when tested positive for HIV
MAIN OUTCOMES:	<ul style="list-style-type: none"> •Cervical cancer •Mortality •CIN 2+ •HPV infection •Preterm birth (early/late) •Acceptability (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 <p>and, costs (number of tests), feasibility (Coverage of treatment, Coverage of screening), acceptability (stigmatization), equity</p>
SETTING:	outpatient
PERSPECTIVE:	Population
BACKGROUND:	In 2014, the World Health Organization (WHO) published recommendations for screening and treatment to prevent cervical cancer in all women including women living with HIV (WLHIV). In the context of the WHO strategy towards the elimination of cervical cancer, WHO is updating the current recommendation on screening and treatment of cervical cancer for all women, including for WLHIV. For the PICO questions related to WLHIV, the evidence is limited and the number of publications that present results by age at first screening are scarce.
CONFLICT OF INTERESTS:	

ASSESSMENT

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input type="radio"/> Small <input checked="" type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know	<p>SYSTEMATIC REVIEW OF LITERATURE</p> <p>We conducted a systematic literature search to October 2019 for studies comparing screening to prevent cervical cancer starting at different age groups and/or when individuals tested positive for HIV. Out of 1315 records, 12 studies were included. Studies used varying classification of histologically verified CIN grade as an outcome. It was possible to pool data from three studies by using the category CIN2/3, for a total of 390 cases in 2955 women.</p> <p>Prevalence of CIN 2/3</p> <p>Based on data from 2 studies, the pooled prevalence of CIN2/3 was 11.2% in WLHIV below the age of 30, and 11.5% in WLHIV above the age of 30 (De Vuyst et al, Swanepoel et al).</p> <p>Only one study showed a prevalence of CIN2/3 of 6.7% in WLHIV below 25 years of age, and 9.9% in WLHIV above 25 years of age, respectively (McDonald et al).</p> <p>Prevalence of Invasive Cancer</p> <p>One study reported no cases below 30 years of age (Swanepoel et al), and 3 studies reported a prevalence of 0.3-1.6% in WLHIV below the age of 35-40 (Abraham et al, Kapambwe et al, Swanepoel et al).</p> <p>INDIVIDUAL PATIENT DATA META-ANALYSIS</p> <p>We contacted authors of studies identified from the systematic review that included at least 40 women living with HIV who had CIN2+ and pooled the data from individual patients.</p> <p>Probability of CIN 2/3 by age</p> <p>The probability of having a confirmed diagnosis of CIN 2/3</p> <p>15-19 years: 6% (total participants: 16) 20-24 years: 32% (total participants: 41) 25-29 years: 42% (total participants: 351) 30-34 years: 50% (total participants: 470)</p>	<p>The GDG agreed given the analyses that the group should focus on the numbers of histologically confirmed CIN 2/3.</p> <p>Based on the data, the evidence suggests similar and important numbers of women with CIN 2/3 at 25-29 years and 30-34 years.</p> <p>In addition, there may be lower numbers of CIN 2/3 in WLHIV at 20-24 or 15-19 years, but this is based on very small numbers of women in the analyses.</p>



Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large <input type="radio"/> Moderate <input checked="" type="radio"/> Small <input type="radio"/> Trivial <input type="radio"/> Varies <input type="radio"/> Don't know	See above.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low <input checked="" type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies	A systematic review of primary studies and IPDMA were conducted, but there was little data available comparing the incidence of cervical cancer and CIN lesions resulting in low certainty evidence. There is also low certainty evidence from a large cohort study reporting the proportion of women with cervical cancer by age.	

Values

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input checked="" type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability	<p>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:</p> <ul style="list-style-type: none"> •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) <p>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).</p> <p>A survey of 561 women (which included few women who are living with HIV) was conducted online via SurveyMonkey in 2020, and was completed anonymously. All women aged 15 years and older,</p>	<p>The GDG agreed that the data from the general population would apply to women living with HIV.</p> <p>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.</p> <p>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.</p>

	regardless of their prior cervical cancer screening or treatment status were eligible to participate. Survey results from 275 respondents found that some of the key concerns from women who had never been screened before were fear of the test itself higher costs of test(22.91%) and the fear of having cancer(22.91%).	
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Balance of effects

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	The GDG agreed that the benefits of screening at age 25 probably outweighs the harms of screening at age 20, 30 or 35.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large costs <input type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input checked="" type="radio"/> Moderate savings <input type="radio"/> Large savings <input type="radio"/> Varies <input type="radio"/> Don't know	No research evidence was found about resources. There are likely greater costs when starting earlier than age 25 since more resources are needed for screening and treatment.	

Certainty of evidence of required resources

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input checked="" type="radio"/> No included studies		

Cost effectiveness

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies	Modelling was not conducted for women living with HIV, but the GDG agreed that the costs of screening and treating at age 25 would likely be higher due to the number of women screened positive, but based on the reduction in cervical cancer and related deaths, the costs would probably favour screening at age 25 versus 30 or 35.	

Equity		
What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input checked="" type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know	No research evidence found, but the GDG agreed that there is likely little impact on equity when initiating screening at different ages.	

Acceptability		
Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	There was no research evidence for acceptability of initiating screening. The GDG agreed that age 25 is probably acceptable.	

Feasibility		
Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	There was no research evidence. However, the GDG agreed that initiation of screening will depend on feasibility but initiating at 25 is probably feasible.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
	Trivial	Small	Moderate	Large		Varies	Don't know
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 intervention or 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 intervention or 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 ○
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CONCLUSIONS

Recommendation

25. WHO suggests starting regular cervical cancer screening at the age of 25 years among women living with HIV.
[Conditional recommendation, low-certainty evidence in effects]

Justification

On the age at which to start screening, there was low-certainty evidence from an individual patient data meta-analysis (IPD-MA), mathematical modelling and studies about cervical cancer incidence and CIN by age that supported the initiation of screening at 25 years of age rather than at age 20 or 30. Starting at this age is likely to be acceptable to stakeholders, is feasible and needs fewer resources than starting screening at an earlier age.