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HPV Global Action
In partnership with the
Consortium for Infectious Disease Control
Presents

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Will Canada's HPV prevention plan be on track with WHO 2030 elimination targets?

Presenter: Dr. Marc Steben MD, CCFM, FCFM
Co-President, HPV Global Action
Chair, Canadian Network on HPV Prevention
Board Member, International Papillomavirus Society

Presenter: Dr. Nancy Durand MDCM, FRCS
Associate Professor, Department of Obstetrics and Gynaecology, University of Toronto
Dept Obstetrics and Gynaecology,
Sunnybrook Health Sciences Centre

Moderator: Amélie McFadyen MA
Chief Executive Officer,
HPV Global Action/VPH Action Globale

March 29, 2023

This educational program is made possible through the support of **Merck Canada**

Moderator

Amélie McFadyen, M.A. Sexology

Chief Executive Officer,
HPV Global Action/VPH Action Globale

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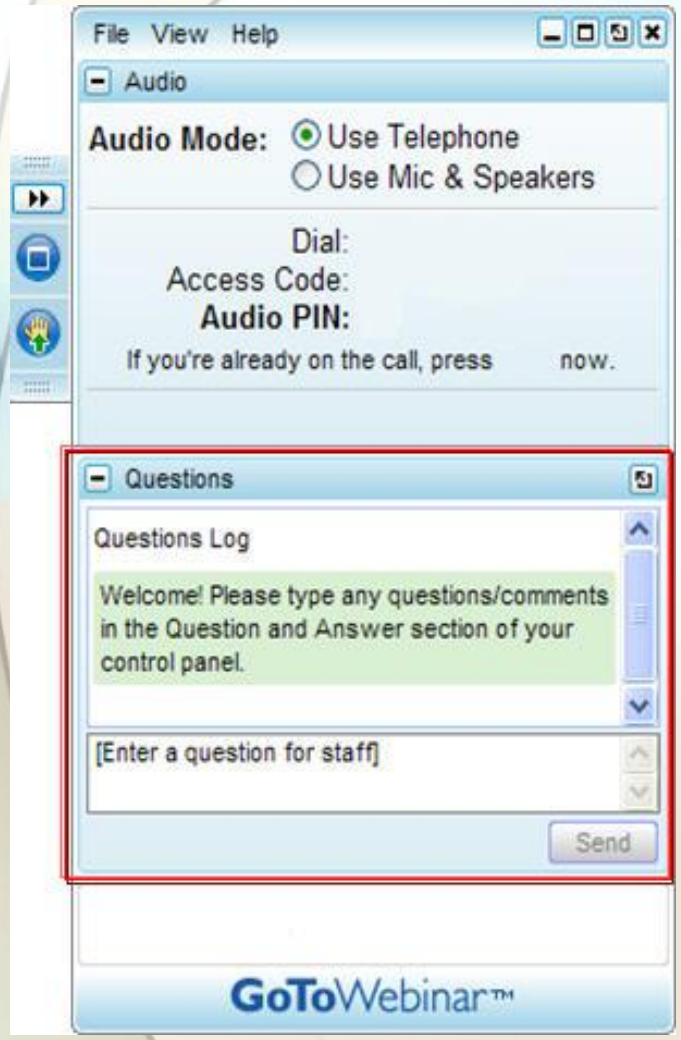
Webinar Objectives

- Enumerate reasons why Canada is at risk of not reaching the 2030 screening targets for elimination of cervical cancer
- Present actions on what Canada can do NOW to reach 2030 screening elimination targets
- Enumerate reasons why Canada is at risk of not reaching the 2030 vaccine targets for elimination of cervical cancer
- Compare Canadian provinces and territorial coverage rates and obstacles
- Discuss potential actions on how to increase Canadian vaccine coverage

Administrative Information



How to participate:

- You can hear the audio for today's webinar via your computer by selecting "Use Mic & Speakers"
- Submit questions at any time by typing in the "Questions" pane on the control panel & click 'Send' button
- Questions will be answered at the end of the presentation

NOTE: For mobile device users:

- To open the questions pane, tap on the "?" or "Questions"
- To change your audio setting, tap on the "Settings" icon

Note: A recording of the presentation will be made available at www.CIDCgroup.org and hpvglobalaction.org

Recording and Evaluation

Slides and Video Recording

The webinar **Slides and Recording** will be archived at:
hpvglobalaction.org and www.CIDCgroup.org

Complete the Evaluation Survey at:

https://forms.gle/Awz8gaHuGAzs52hY8

Completion of survey is requested to receive a certificate of participation

– all registered participants will receive an email with this link

Presenter

Dr. Marc Steben MD, CCFM, FCFM

- Co-President, HPV Global Action
- Chair, Canadian Network on HPV Prevention
- Board Member, International Papillomavirus Society

Will Canada's HPV prevention plan be on track with WHO 2030 elimination targets?

STATE OF THE SCIENCE ON CERVICAL CANCER SCREENING

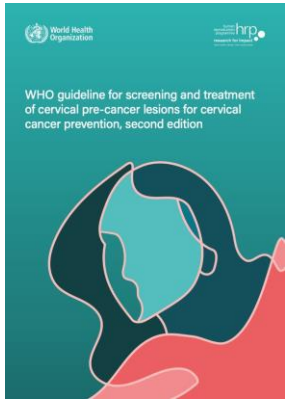
Dr Marc Steben

- *Member of the Board and Chair of Education Committee of the International Papillomavirus Society*
- *2023 president elect, International society for STD research*
- *Chair, Canadian network for HPV prevention*
- *School of public health, Université de Montréal*
- *Co-president, HPV global Action*
- *marc@marcsteben.com*

Disclosure Statement for the last 3 years

Disclosure of Relationship	Company/Organization
I am a member of an Advisory Board or equivalent with a commercial organization.	Merck, GSK, Lupin
I am a member of a Speaker Bureau.	Merck, GSK
I have received payment from a commercial organization (including gifts or other consideration or 'in kind' compensation).	Bayer, Lupin, GSK, Paladin, Roche molecular systems, Merck.
I have received a grant(s) or an honorarium from a commercial organization.	Abbott, Bayer, Beckton-Dickinson, Biofire, Gen-Probe/Hologic, GSK, Lupin, Merck/Merck Sharp Dohme/Sanofi-Pasteur, Paladin, Roche molecular systems.
I hold a patent for a product referred to in the CME/CPD program or that is marketing by a commercial organization	No
I hold investments in a pharmaceutical organization, medical devices company or communications firms.	I own a communication company (Communications Action-Santé Inc.)
I am currently participating in or have participated in a clinical trial within the past two years).	Project PAVE, National Cancer Institute, NIH and project INTEGRATE, Eswatini

- Most of the available evidence on cervical cancer is based on study populations of cisgender women
- We need to recognize that cisgender women, transgender men, non-binary, gender fluid and intersex individuals born with a female reproductive system require cervical cancer prevention services.
- However, to be concise and facilitate readability, the term “women” is used to refer to all gender diverse people at risk for cervical cancer.



WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. Geneva: World Health Organization; 2021. Licence: *CC BY-NC-SA 3.0 IGO*.

Cervical cancer rates **have not decreased appreciably** in the last several years

The incidence and proportion of adenocarcinomas of the cervix is **rising**

The current screening tests are **not designed for detection of non-squamous cervical cancer**[1]

The proportion of women diagnosed with invasive cervical cancer within 3 years of their last screening test is **increasing**[2]

1. Pimenta et al, BMC Cancer 2013;13:553; **2.** Canadian Partnership Against Cancer. Cervical Cancer Screening in Canada 2016 May

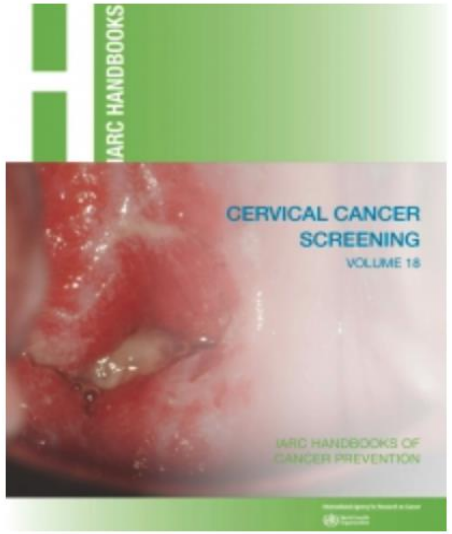
The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

The IARC Perspective on Cervical Cancer Screening

Véronique Bouvard, Ph.D., Nicolas Wentzensen, M.D., Ph.D., Anne Mackie, M.B., B.S., Johannes Berkhof, Ph.D., Julia Brotherton, M.D., Ph.D., Paolo Giorgi-Rossi, Ph.D., Rachel Kupets, M.D., Robert Smith, Ph.D., Silvina Arrossi, Ph.D., Karima Bendahhou, M.D., M.P.H., Karen Canfell, D.Phil., F.A.H.M.S., Z. Mike Chirenje, M.D., Michael H. Chung, M.D., M.P.H., Marta del Pino, M.D., Ph.D., Silvia de Sanjosé, M.D., Ph.D., Miriam Elfström, Ph.D., Eduardo L. Franco, M.P.H., Dr.P.H., Chisato Hamashima, M.D., Dr.Med.Sc., Françoise F. Hamers, M.D., Ph.D., M.P.H., C. Simon Herrington, D.Phil., F.R.C.P., F.R.C.P.E., F.R.C.Path., Raúl Murillo, M.D., M.P.H., Suleeporn Sangrajrang, Ph.D., Rengaswamy Sankaranarayanan, M.D., Mona Saraiya, M.D., M.P.H., Mark Schiffman, M.D., M.P.H., Fanghui Zhao, M.D., Ph.D., Marc Arbyn, M.D., Ph.D., Walter Prendiville, F.R.C.O.G., Blanca I. Indave Ruiz, M.D., Ph.D., M.P.H., Isabel Mosquera-Metcalfe, Ph.D., and Béatrice Lauby-Secretan, Ph.D.

Bouvard V et al. The IARC Perspective on Cervical Cancer Screening. N Engl J Med 2021;385(20):1908-1918.



https://publications.iarc.fr/604

Cervical Cancer Screening

IARC Handbooks of Cancer Prevention Volume 18

IARC

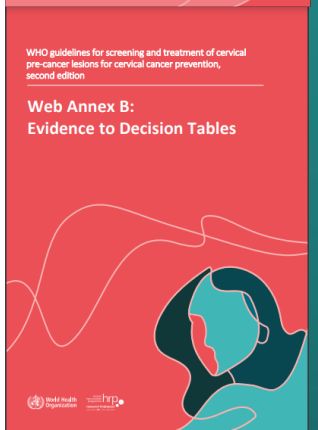
2022

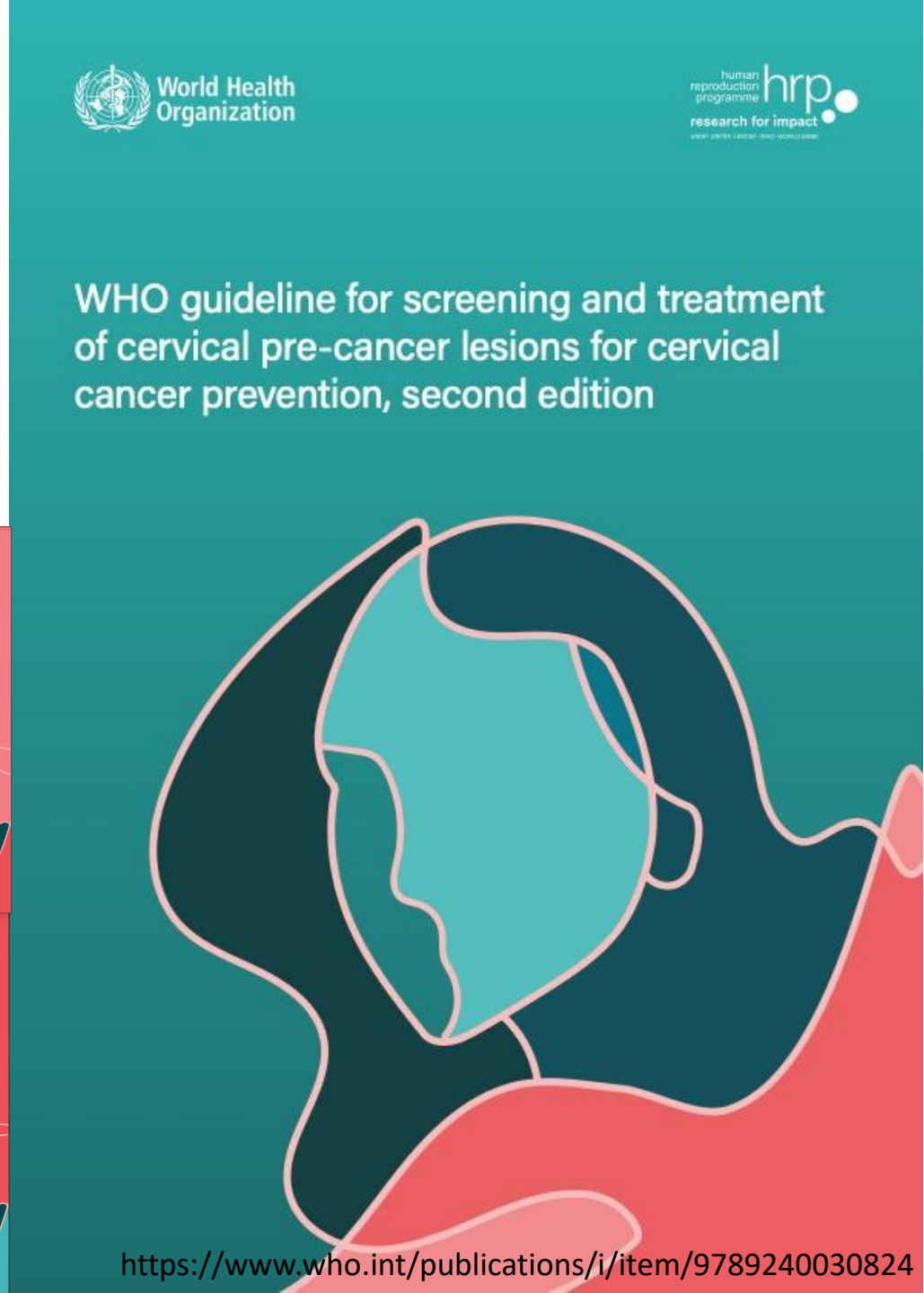
ISBN-13

978-92-832-3025-0

ISBN-13

978-92-832-3024-3





https://www.who.int/publications/i/item/9789240030824

Screening
When is it appropriate and how can we get it right?

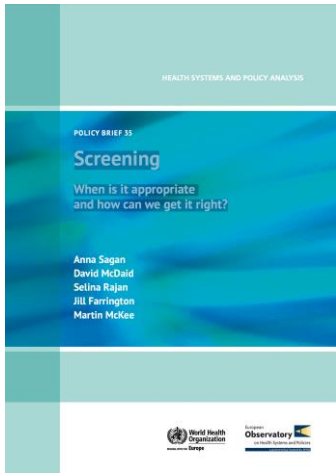
- Key messages
  - Screening may bring benefits but also harm
    - just because it can be done does not mean that it should be done
    - and the same resources may be better used in other ways.
  - Population screening should be done within an organized screening programme
    - There is no justification for unorganized (cervical cancer included!)screening.
  - Wilson & Jungner's screening principles remain the gold standard when deciding on implementing, continuing or discontinuing screening programmes
    - expert judgement
    - as well as high quality evidence,
    - including consideration of resource implications, effectiveness and cost effectiveness,
    - as well as adaptation to country context.

https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf

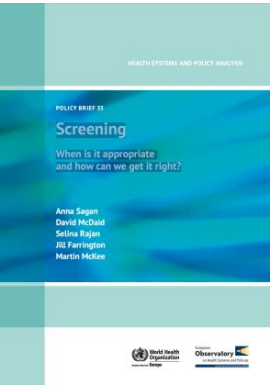
Screening
When is it appropriate and how can we get it right?

- Key messages
  - Care is needed when deciding to implement a screening programme to protect against the potential for commercially driven vested interests and supplier-induced patient demand.
  - It is also important to identify barriers to maximizing the effectiveness of programmes and put in place measures to overcome them.
  - Potential barriers may relate to health system structures, such as payment models and availability of human, physical and financial resources.
  - Potential solutions include financing models that encourage appropriate use, improving information flows, ensuring health workers have appropriate skills, and removing logistical barriers.

https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf



Screening
When is it appropriate
and how can we get it right?



https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf

Box 3: Wilson & Jungner principles (Wilson & Jungner, 1968)

(1) The condition sought should be an important health problem.

(2) There should be an accepted treatment for patients with recognized disease.

(3) Facilities for diagnosis and treatment should be available.

(4) There should be a recognizable latent or early symptomatic stage.

(5) There should be a suitable test or examination.

(6) The test should be acceptable to the population.

(7) The natural history of the condition, including development from latent to declared disease, should be adequately understood.

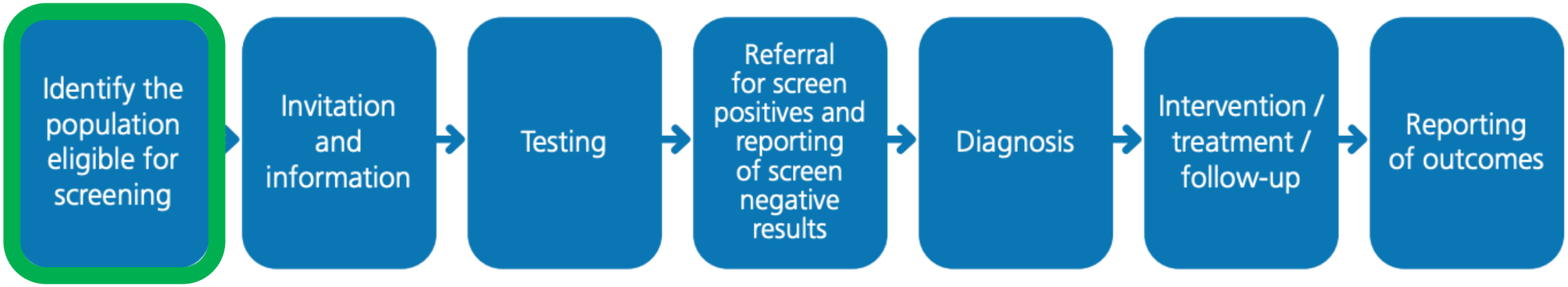
(8) There should be an agreed policy on whom to treat as patients.

(9) The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.

(10) Case-finding should be a continuing process and not a 'once and for all' project.

Screening
When is it appropriate and **how can we get it right?**

Figure 1: Core steps of a screening pathway

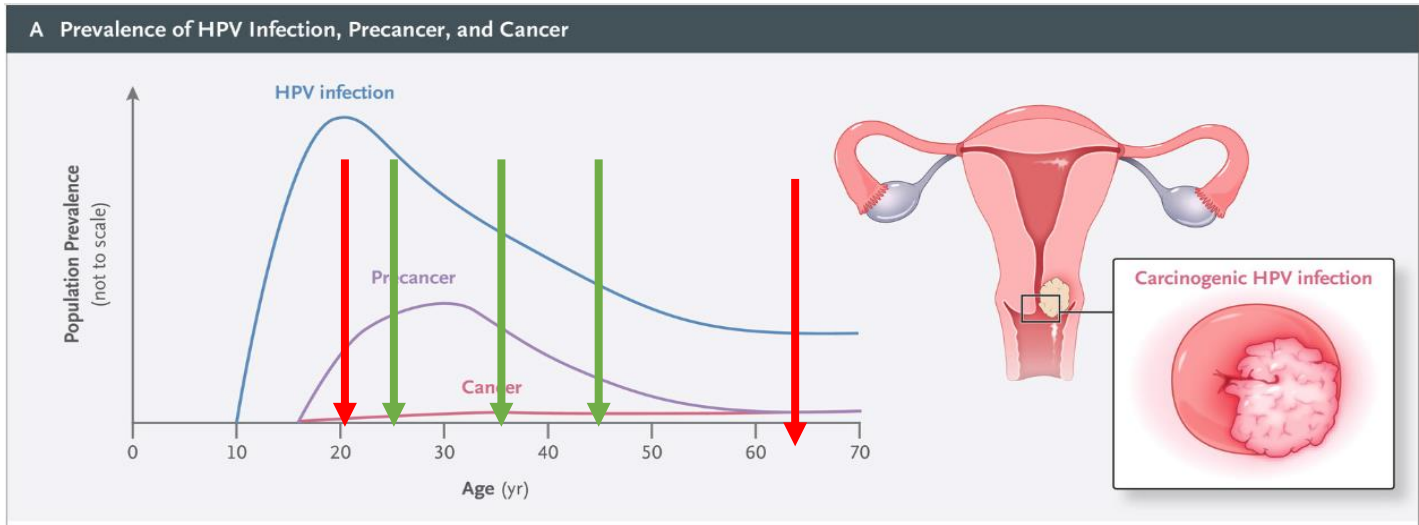


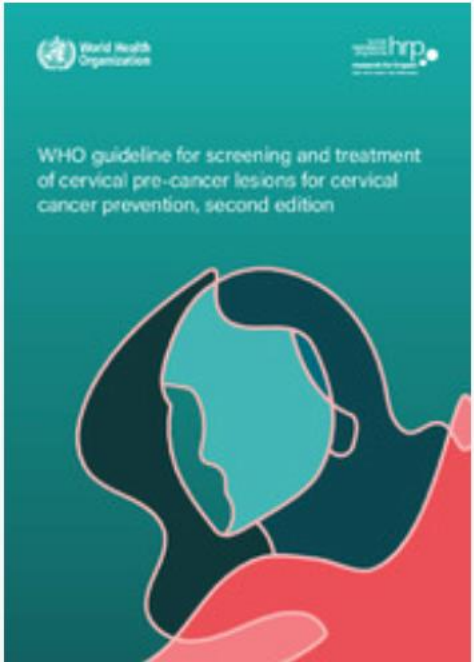
Source: Adapted from WHO Regional Office for Europe, 2020.

https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf

Identify the population eligible for screening

- Depending on HIV status?
- Depending on age?
- Depending on frequency of screening
  - Start time
    - HIC from 25? 30?
    - LMIC only twice in a lifetime
      - 35 and 45?
  - Stop time
    - HIC at 65? 70?
    - LMIC at 50?
- Good registry to identify
  - Overscreened
  - Underscreened



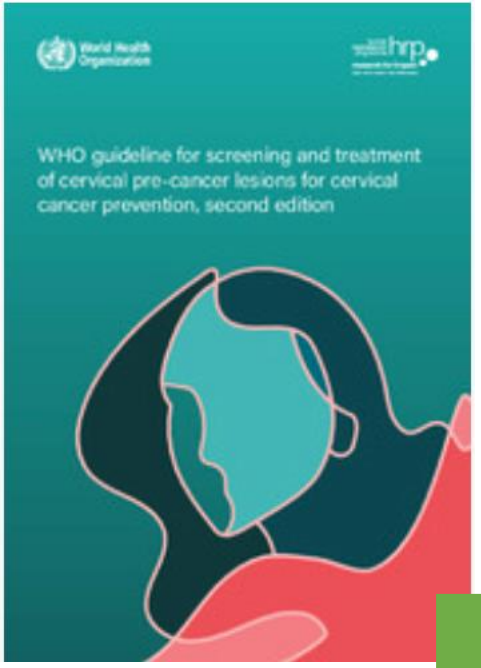


Summary recommendation for the general population of women

WHO suggests using either of the following strategies for cervical cancer prevention among the general population of women:

HPV DNA detection in a screen-and-treat approach starting at the **age of 30 years** with regular screening **every 5 to 10 years**.

HPV DNA detection in a screen, triage and treat approach starting at the **age of 30 years** with regular screening **every 5 to 10 years**.



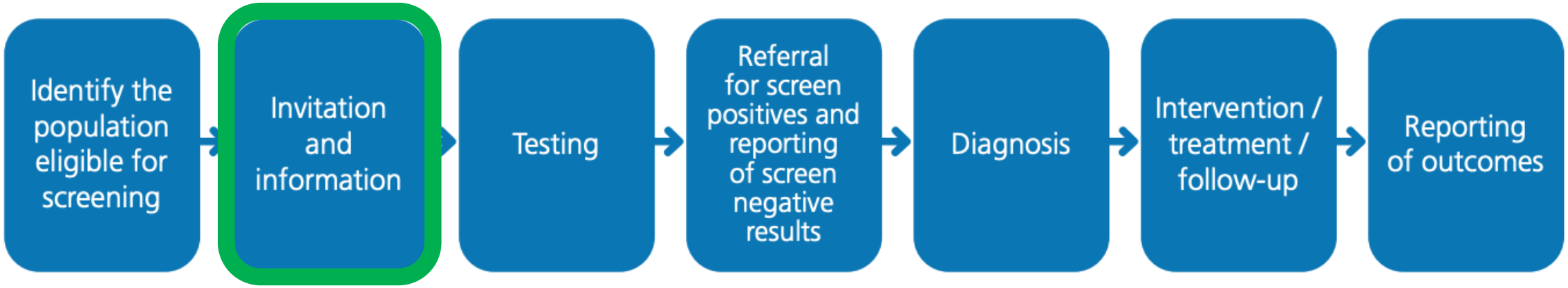
Summary recommendation for women living with HIV

WHO suggests using the following strategy for cervical cancer prevention among women living with HIV:

- HPV DNA detection in a **screen, triage and treat approach** starting at the age of 25 years with regular screening every 3 to 5 years.

Screening
When is it appropriate and **how can we get it right?**

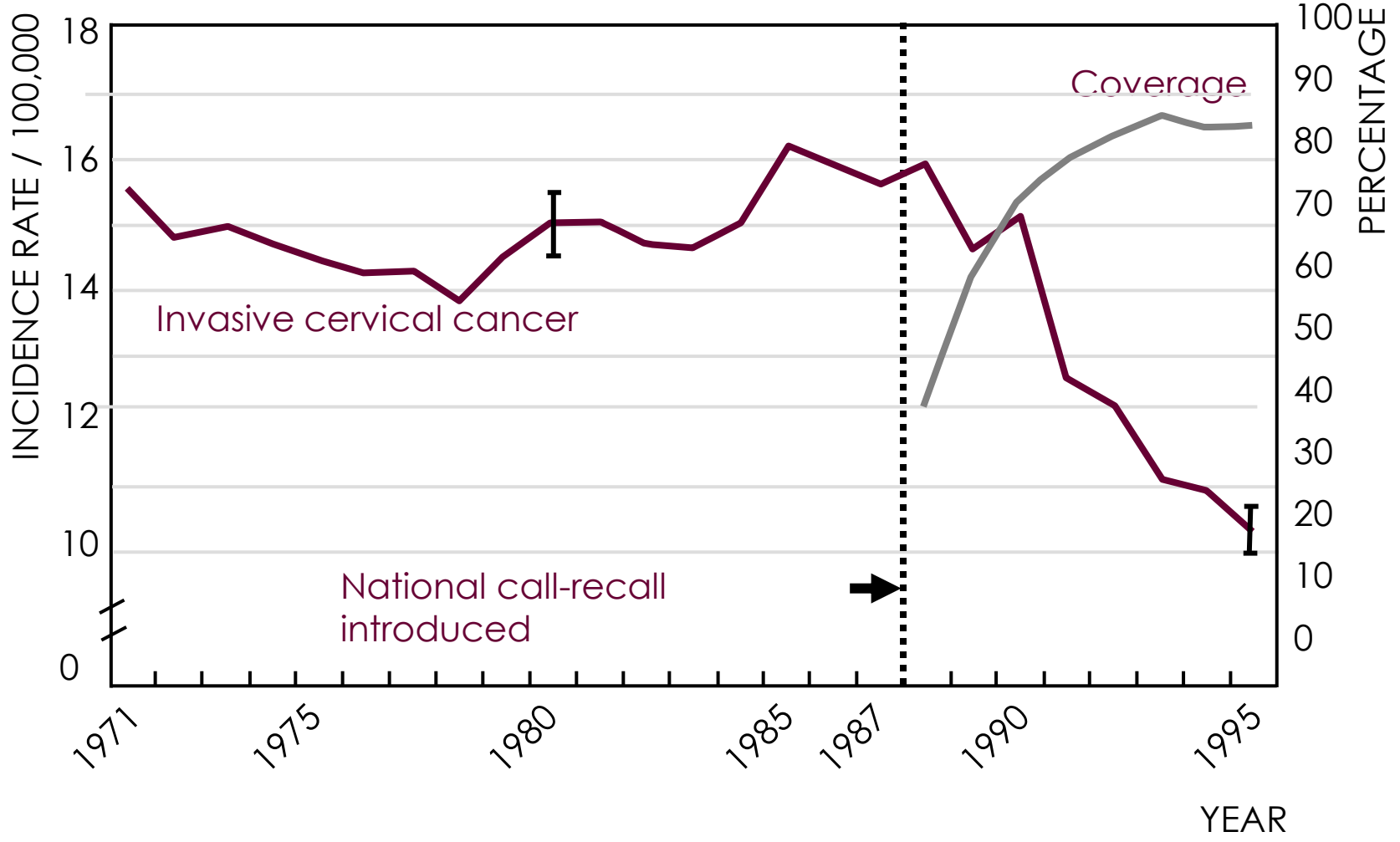
Figure 1: Core steps of a screening pathway



Source: Adapted from WHO Regional Office for Europe, 2020.

https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf

AGE-STANDARDIZED INCIDENCE OF INVASIVE CERVICAL CANCER AND COVERAGE OF SCREENING, ENGLAND, 1971–1995



Reprinted from Quinn M et al. BMJ 1999;318(7188):904–8 with permission from BMJ Publishing group.

Invitation and information

- Opportunistic vs organized
- Self sample made possible
- Do we reach the good people?
- Need to be opportunistic for hard to reach/vulnerable populations or organized in specific medical or social services

- Right sensitivity
- Right information
- Potential benefits
- Potential harms
- Right channels
- Hard to reach population need specific informations but do not use the same information channels if at all

Vulnerable populations = opportunistic vs organized

Medically vulnerable people

- People living with
  - HIV
  - Transplant
  - Immune suppression
  - Auto immune disease
  - Cancer
- In STI Clinics
- Partners of HPV+
- HPV unvaccinated

Socially vulnerable

- Marginalized
  - People with mental health issues
  - Street involved
  - Migrants, refugees and displaced people
  - First nations
  - People with less access to care and education
  - People in jails
  - Institution
- Last mile/km patient

WHO global strategy
to accelerate the elimination of cervical cancer as a public health problem

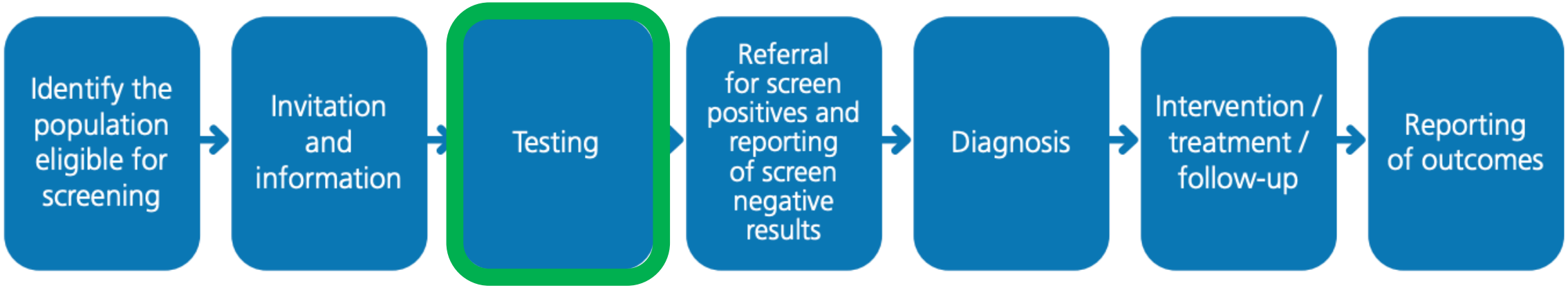
- **The targets of the global strategy are, by 2030:**
  - **to vaccinate 90% of eligible girls against HPV;**
  - **to screen 70% of eligible women at least twice in their lifetimes; and**
  - **to effectively treat 90% of those with a positive screening test or a cervical lesion, including palliative care when needed**

Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Heatlh Organization; 2020 (*https://www.who.int/publications/i/ item/9789240014107*).

to screen 70% of eligible women at least twice in their lifetimes

Screening
When is it appropriate and **how can we get it right?**

Figure 1: Core steps of a screening pathway



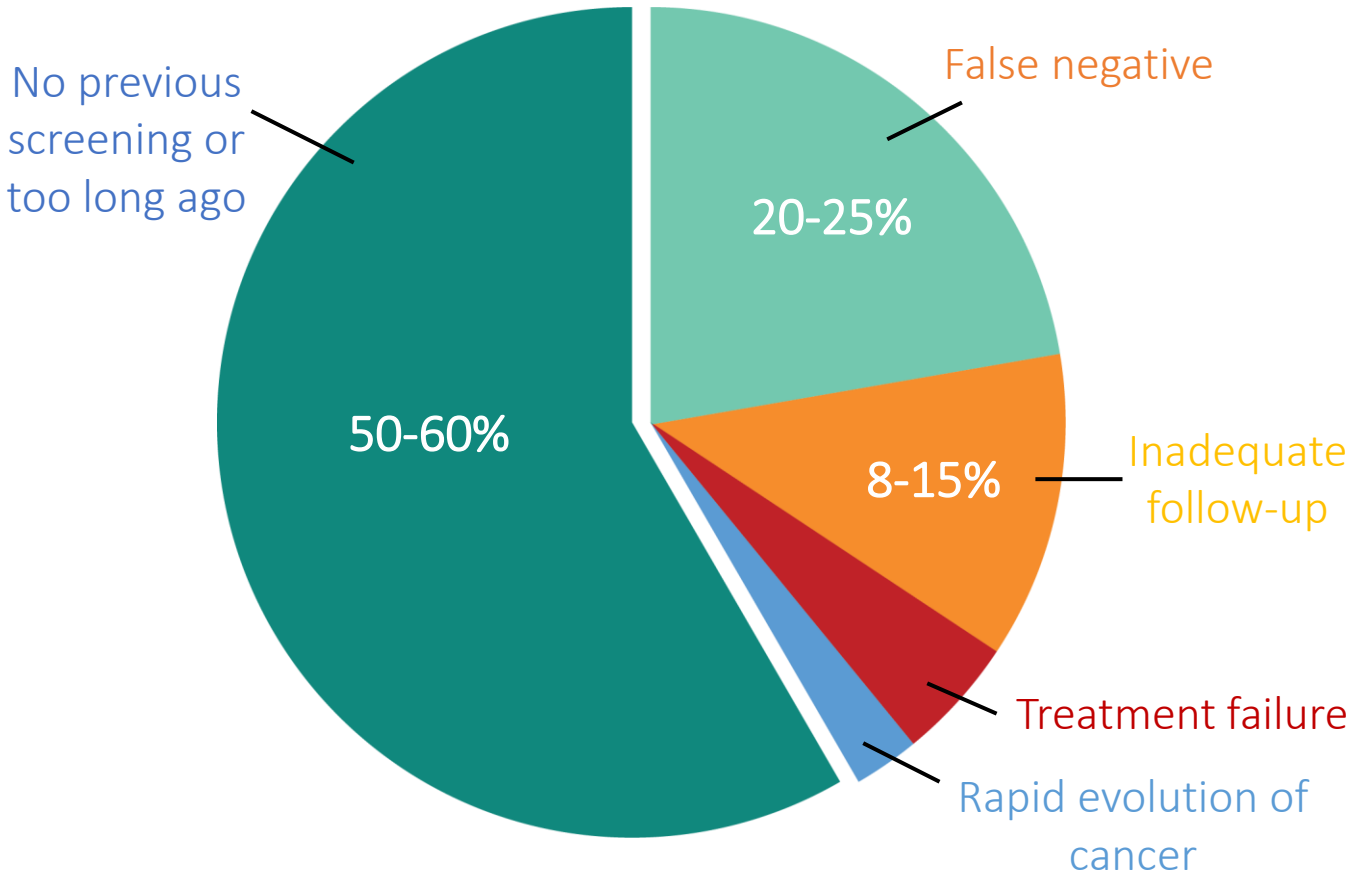
Source: Adapted from WHO Regional Office for Europe, 2020.

https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf

LIMITATIONS OF CYTOLOGIC SCREENING

Cytologic screening is **not sufficient** for prevention of cervical cancer, considering the high, bimodal incidence of HPV infection.

Also, it **does not prevent** genital warts or non-cervical cancer.



Spence AR et al. Prev Med. 2007 Aug-Sep;45(2-3):93-106. Epub 2007 Jun 22.

We will cause more harm than benefit if we dot not change our screening paradigm!

REVIEW ARTICLE

The Expected Impact of HPV Vaccination on the Accuracy of Cervical Cancer Screening: The Need for a Paradigm Change

Eduardo L. Franco,[a,b] Salaheddin M. Mahmud,[a,c,h] Joseph Tota,[a,b] Alex Ferenczy,[d,e,f] and François Coutlée[a,g]

REVIEW ARTICLE

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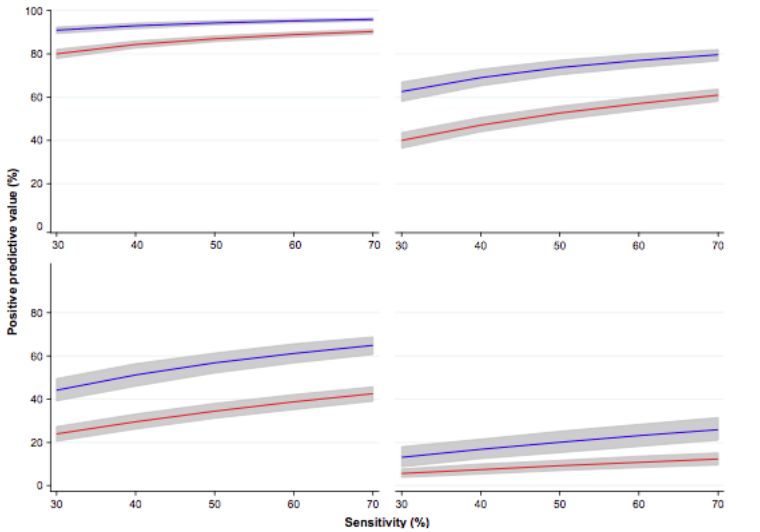
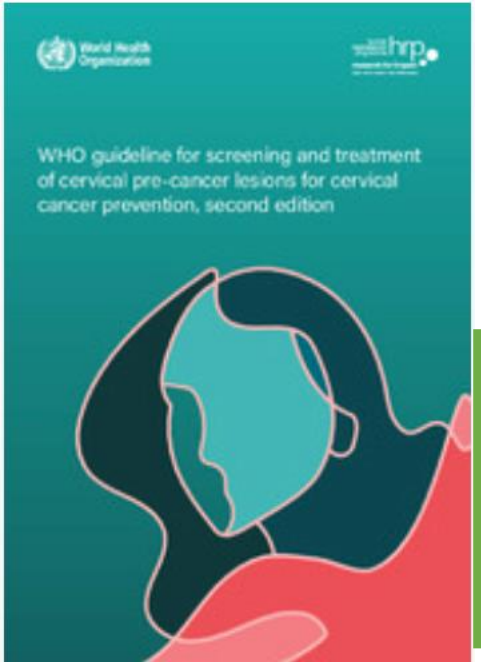


Figure 2. Joint effects of changes in sensitivity, specificity, and cervical lesion prevalence on the positive predictive value of cytology as a primary screening test. The two curves in each graph represent different specificity values of 98% (blue line) and 95% (red line). Each graph represents a different prevalence rate as follows: upper left: 40%, upper right: 10%, lower left: 5%, and lower right: 1%. The gray bands represent 95% credibility intervals (see text and legend for Figure 1 for details). Three of the prevalence scenarios are intended to illustrate situations found in Pap cytology screening in different settings as well as the ones anticipated post-vaccination. A 40% prevalence is shown to represent the situation found in triage following an initially positive referral HPV test.

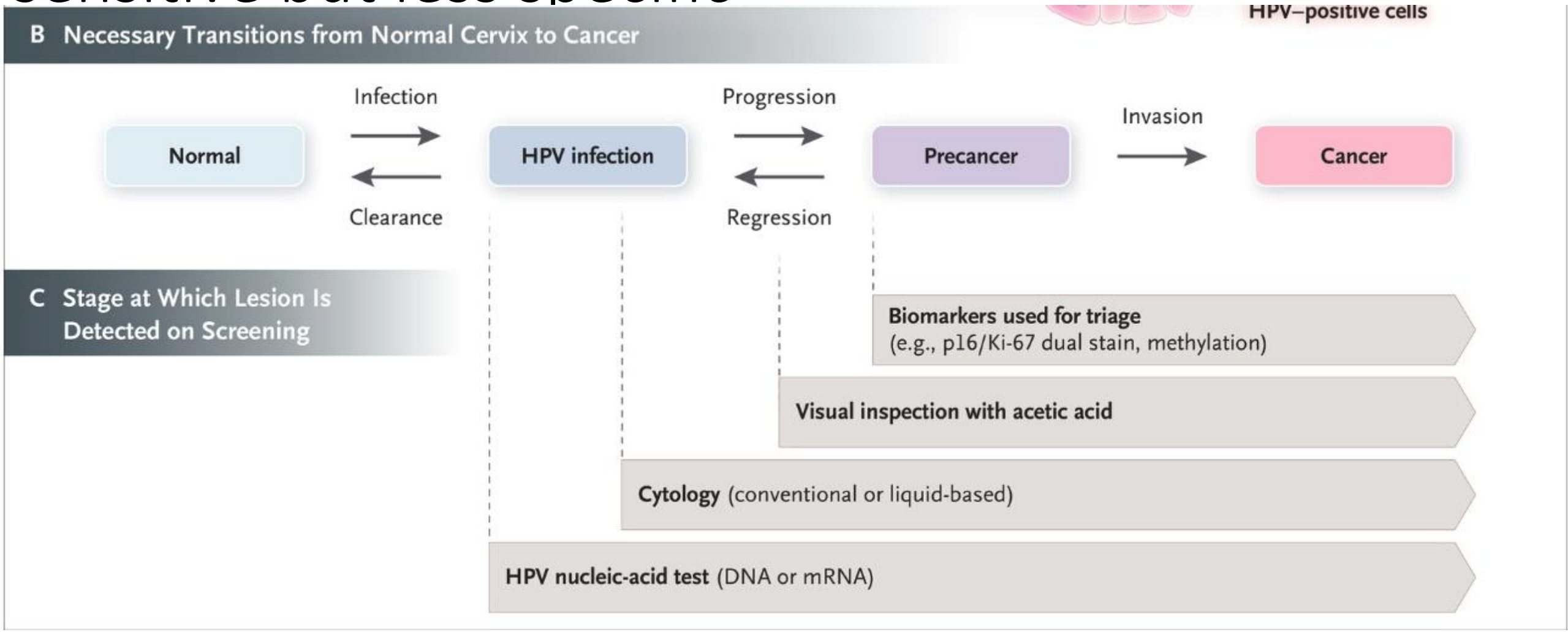
Healthcare system reluctance to change the diagnostic paradigm

- Conservative
- Heavily regulated
- «MD knows best»
- Paternalistic
- Needs to prevent all harms at all cost
- Self-collection for HPV screening have been shown safe, effective, preferred and saves precious/rare healthcare resources



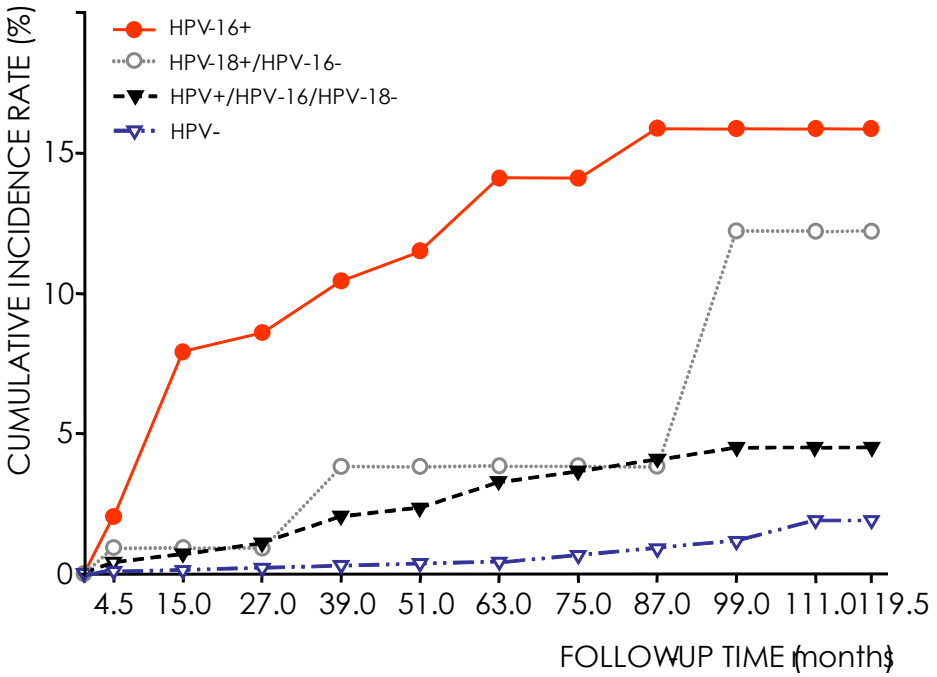
HPV DNA detection as the primary screening test among the general population of women, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test (*Annex 4*). *Remarks: The benefits, harms and programmatic costs of the triage options are similar; 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*		23. **In a screen, triage and treat approach** using HPV DNA detection as the primary screening test among women living with HIV, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test (*Annex* *Remarks: The benefits, harms and programmatic cos 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 integrate 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	24. When providing HPV DNA testing, WHO sugges using either samples taken by a health-care provide or self-collected samples among both the general population of women and women living with HIV.
5. WHO recommends starting regular cervical cancer screening at the **age of 30 years** among the general population of women.	Strong recommendation, moderate-certainty evidence	25. WHO suggests starting regular cervical cancer screening at the **age of 25 years** among women liv with HIV. *Remarks: Low-certainty evidence found that there ar*

Triage options needed since HPV testing is more sensitive but less specific



CUMULATIVE INCIDENCE OF CIN-3 OR GREATER OVER A 10-YEAR PERIOD ACCORDING TO ONCOGENIC HPV STATUS AT ENROLLMENT

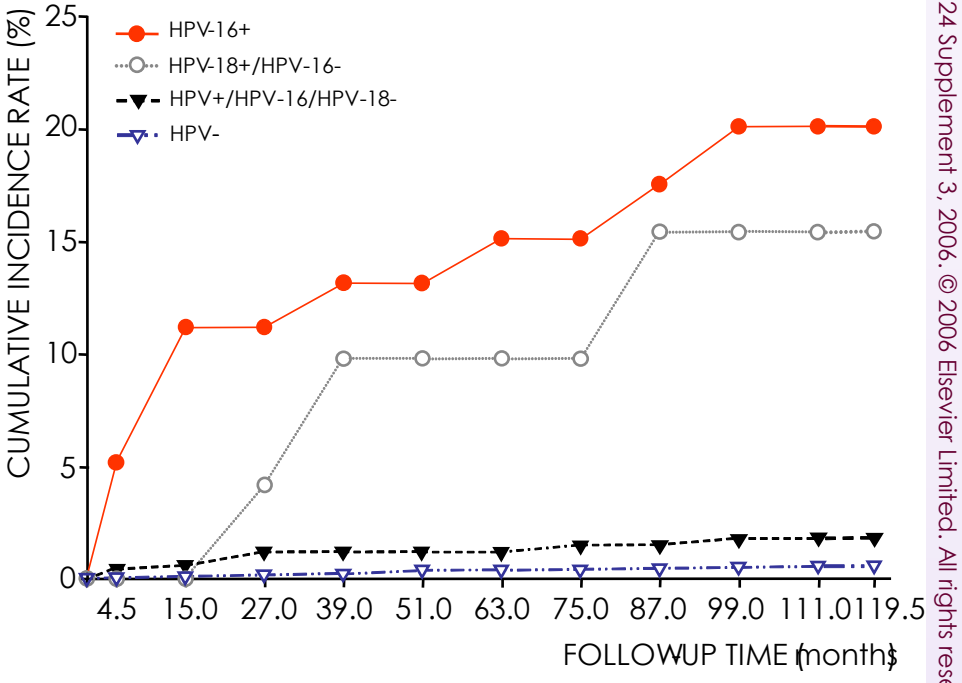
(A) 7,285 WOMEN < 30 YEARS OF AGE



(A) NO. OF WOMEN SEEN DURING FOLLOW-UP INTERVAL

HPV-16+	339	184	140	99	84	68	61	49	57	21	1
HPV-18+/HPV-16-	110	62	50	34	26	26	26	21	23	13	1
HPV+/HPV-16/HPV-18-	1,249	663	514	407	352	312	261	228	229	112	7
HPV-	5,498	2,896	2,349	1,957	1,695	1,493	1,285	1,214	1,083	543	23

(B) 13,229 WOMEN ≥30 YEARS OF AGE



(B) NO. OF WOMEN SEEN DURING FOLLOW-UP INTERVAL

HPV-16+	116	63	50	45	41	44	33	35	32	14	2
HPV-18+/HPV-16-	44	23	24	17	17	15	10	16	12	3	0
HPV+/HPV-16/HPV-18-	962	545	502	455	403	389	339	300	318	144	10
HPV-	11,893	6,863	6,323	5,856	5,441	4,986	4,675	4,337	4,195	2,078	133

Reprinted from Khan MJ, *et al.* J Natl Cancer Inst 2005;97(14):1072–9 with permission from Oxford University Press.

Vaccine, Vol 24 Supplement 3, 2006. Chapter 05, Figure 3

MODELLING 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

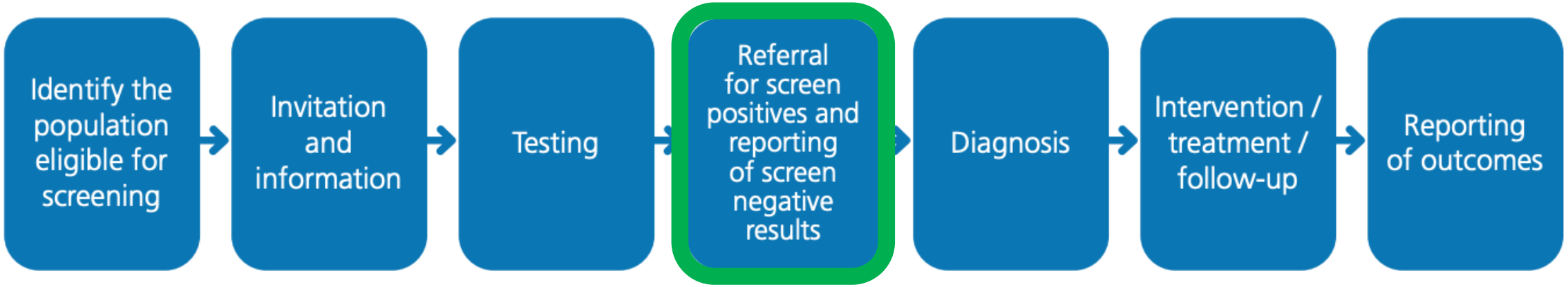
*Outcomes represent total events over the lifetime of a cohort of 100,000 women

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

Web Annex B. Evidence-to-decision tables. In: WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. Geneva: World Health Organization; 2021. p.2

Screening
When is it appropriate and **how can we get it right?**

Figure 1: Core steps of a screening pathway



Source: Adapted from WHO Regional Office for Europe, 2020.

https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf

The appropriate management of screen positive and negative results

- Ensuring that there is an adequate and accessible referral system for those identified as possibly having the condition being screened for.
- A screening programme will have limited value if those who are identified as requiring further investigation and treatment are unable to access these services
- A screening programme should ensure that the system for referring participants is as seamless as possible to ensure that no one falls through the gaps
- With failsafe checks in place to catch those who do

WHO global strategy
to accelerate the elimination of cervical cancer as a public health problem

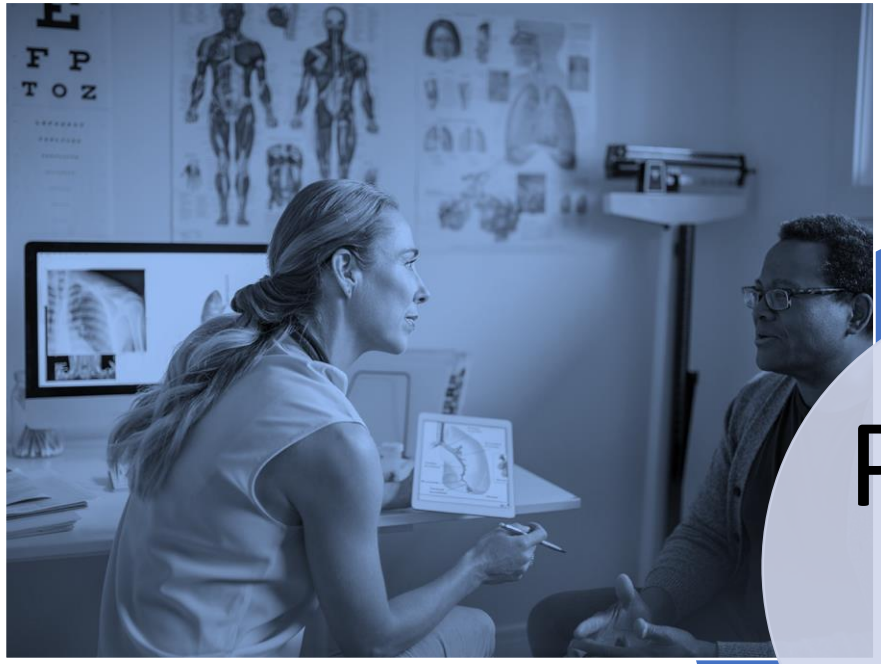
- **The targets of the global strategy are, by 2030:**
  - **to vaccinate 90% of eligible girls against HPV;**
  - **to screen 70% of eligible women at least twice in their lifetimes; and**
  - **to effectively treat 90% of those with a positive screening test or a cervical lesion, including palliative care when needed**

Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Heatlh Organization; 2020 (*https://www.who.int/publications/i/ item/9789240014107*).

to effectively treat 90% of those with a positive screening test or a cervical lesion, including palliative care when needed

90%

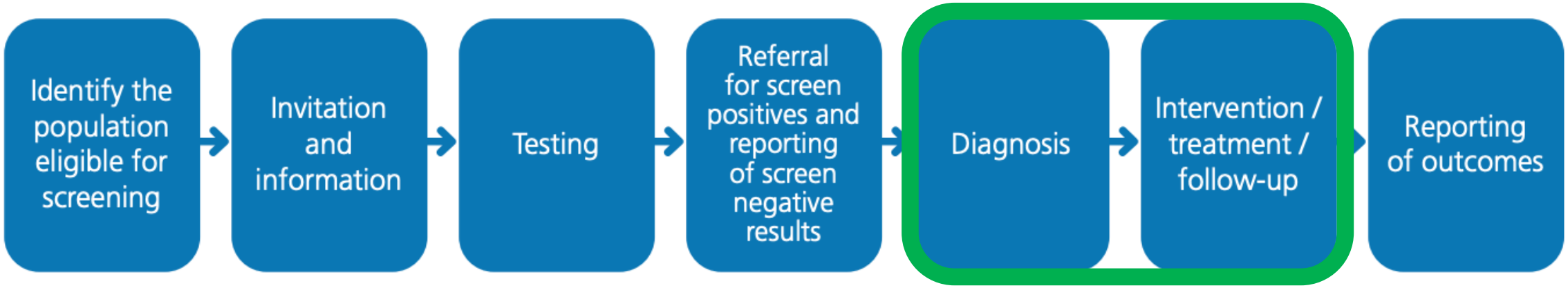
of all individuals with an abnormal screening result should have a clear plan of **appropriate follow-up**



Priority #3

Screening
When is it appropriate and **how can we get it right?**

Figure 1: Core steps of a screening pathway



Source: Adapted from WHO Regional Office for Europe, 2020.

https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf

Ensuring that all those who require treatment receive it

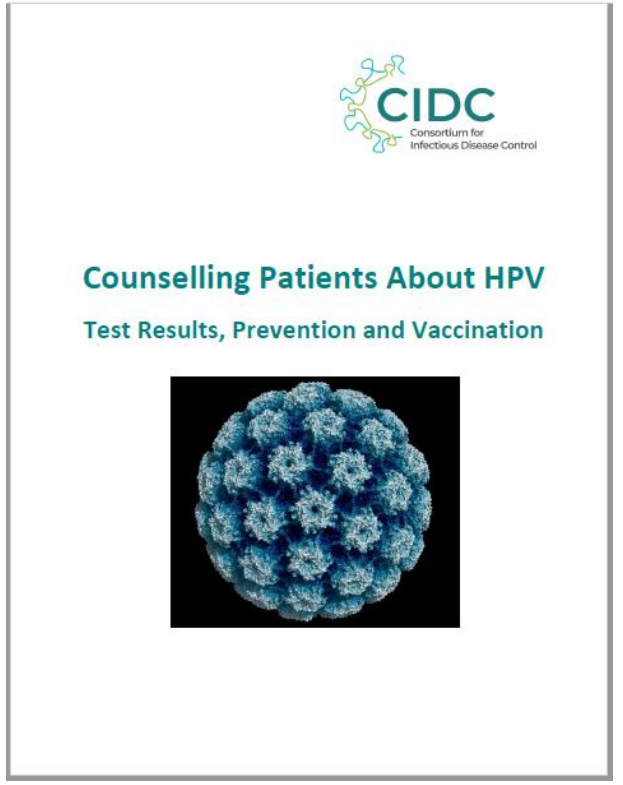
- And do so in the most effective, appropriate and timely way
- Ultimately, there is no point in offering a screening programme if there are insufficient facilities or health personnel to provide treatment for those who need it.
- In some cases, these patients will require follow-up at specified intervals to repeat screening as part of a wider surveillance exercise

Those who are identified as screen positive promptly access adequately staffed diagnostic services.

- Triage for rapid access for those who need it the most especially if there is a long wait list
  - Ex: High grade disease or glandular disease with HPV 16 or 18 gets priority
- Counseling may be needed for anxious patients or couple's turmoil
  - HPV+ is different from High grade disease
  - STI vs pre cancer…
- Opening toward diversified populations
  - Ex: Transgendered patients, mutilated,
- Trauma free intervention…

Resistance to change

- Change of paradigm =
  - From pre-cancerous cells finding to an STI finding
  - Counseling of couple
  - Lengthier to explain
- More expensive?
- Yes but so much better value!
  - For patients
  - For the healthcare system



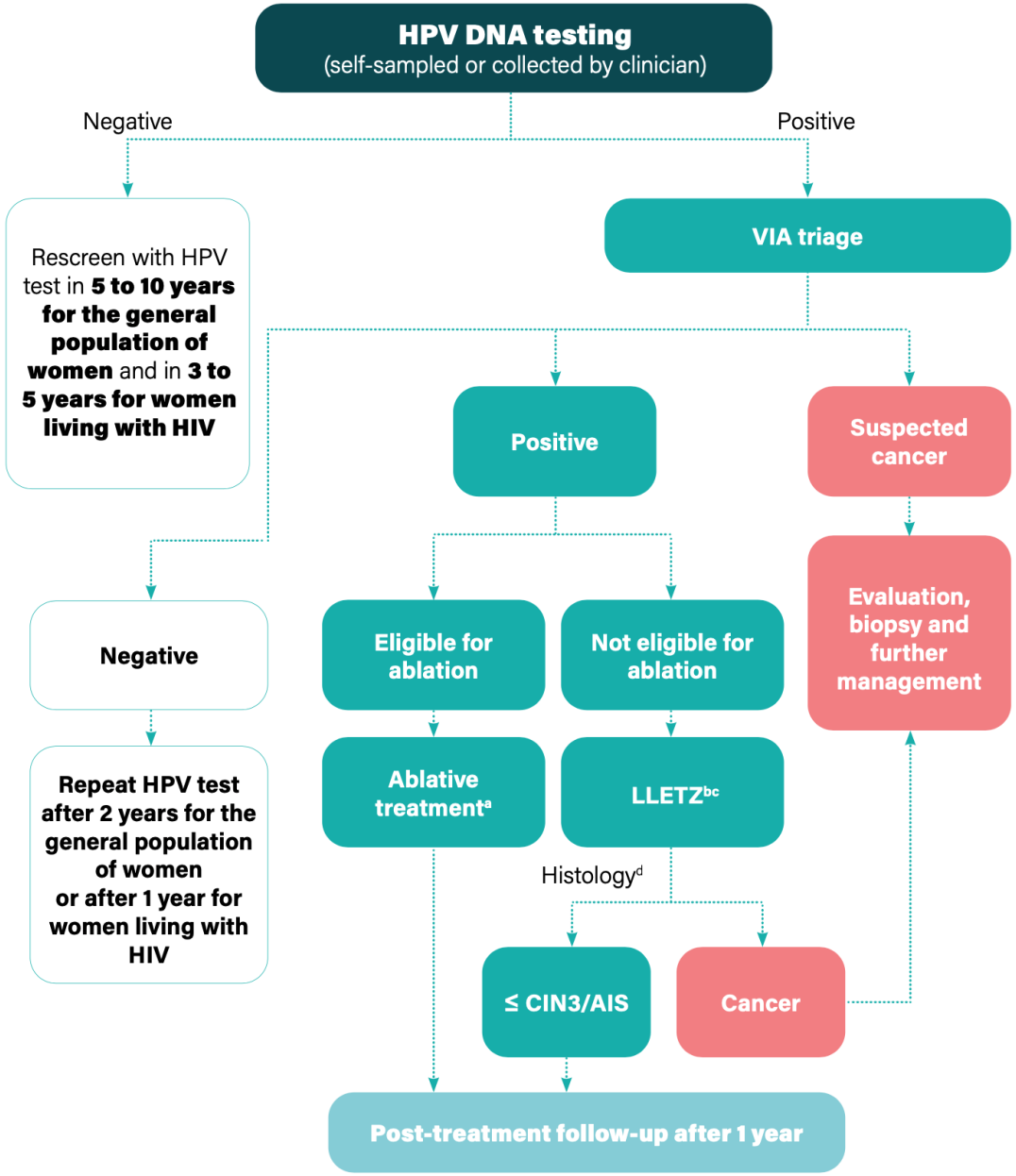
WHO guidelines for the use of thermal ablation for cervical pre-cancer lesions

Outcomes per 1 000 000 women screened

	HPV sensitivity: 95% specificity: 84%		VIA sensitivity: 60%* specificity: 84%*		HPV then VIA	
	Cryotherapy	Thermal ablation	Cryotherapy	Thermal ablation	Cryotherapy	Thermal ablation
Women treated (TP, FP)	175 800		168 800		36 500	
Missed cases (FN)	1 000		8 000		8 600	
Mortality	46	40	121	117	128	124
Cervical Cancer	65	56	170	164	179	173
CIN2-3 recurrence	2600	2 200	6800	6 560	7 160	6 932
Major bleeding	2 989	1758	2870	1 688	620	365
Pain	114 973	106 886	110 395	102 630	23 863	22 185
Major infections	527	352	506	338	109	73

ALGORITHM 5. PRIMARY HPV DNA SCREENING AND VIA TRIAGE (SCREEN, TRIAGE AND TREAT APPROACH)

For both the general population of women and women living with HIV

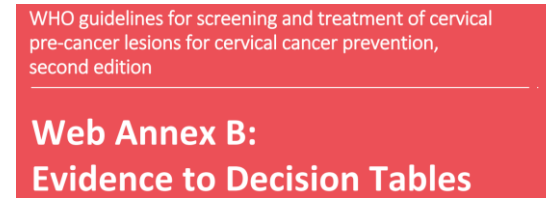


Follow-up after negative triage test or after treatment (Recommendations 31, 32, 33 and 34): The evidence for follow-up screening after a positive HPV DNA primary screening test and negative triage test was based on modelling of follow-up screening at 12 or 24 months, or both (*Web annex A, Supplementary material 13*). There is low-certainty evidence showing that after a negative triage test, there are greater benefits when retesting at 12 months compared with 24 months, but similar harms; and similar benefits and harms at 12 months compared with retesting at both 12 and 24 months. Therefore, screening at 12 months is suggested.

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%

Web Annex B. Evidence-to-decision tables. In: WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. Geneva: World Health Organization; 2021. p.2

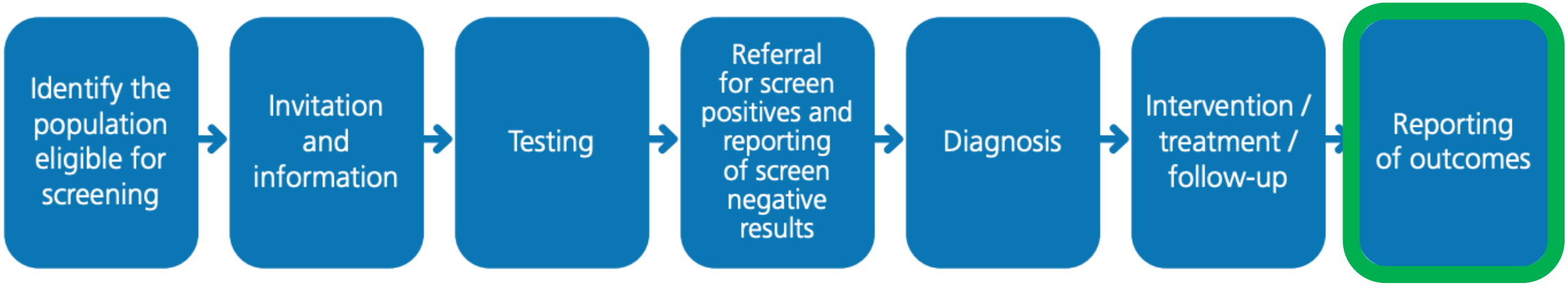


Decisions are also needed about when and who to contact for follow-up care. This guideline makes recommendations that distinguish between three clinical scenarios in routine screening programmes:

- **Regular screening intervals: This applies to women who either had negative screening results or have completed the recommended additional follow-up after treatment and who are thus eligible to return to regular screening intervals.**
- **Follow-up of women with a positive primary screening test but a negative triage test.**
- **Follow-up of women after treatment.**

Screening
When is it appropriate and **how can we get it right?**

Figure 1: Core steps of a screening pathway



Source: Adapted from WHO Regional Office for Europe, 2020.

https://apps.who.int/iris/bitstream/handle/10665/330810/Policy-brief-35-1997-8073-eng.pdf

Reporting of outcomes through a system for monitoring and evaluation

- To identify whether the overall programme is meeting its objectives
- And identify whether the different elements are functioning as well as they should
- These include ensuring:
  - a high level of uptake by different groups in the population;
  - that those undergoing screening have a positive experience so that they will encourage others to participate;
  - and that those in whom problems are identified are referred for further investigation and treatment, leading to health gains.
- Requires linkage to other data sources.
- For example, a cervical cancer screening registry should always be linked to the cancer and HPV vaccine registry.
- Monitoring and evaluation should also take account of changes in technology, such as new investigations that perform better than those that preceded them.

Additional needed information

Quality assurance

- A quality-assured programme is one that is monitored to give assurance that the results consistently achieve the highest level of accuracy and reliability for the detection and treatment of cervical abnormalities by the modality chosen.

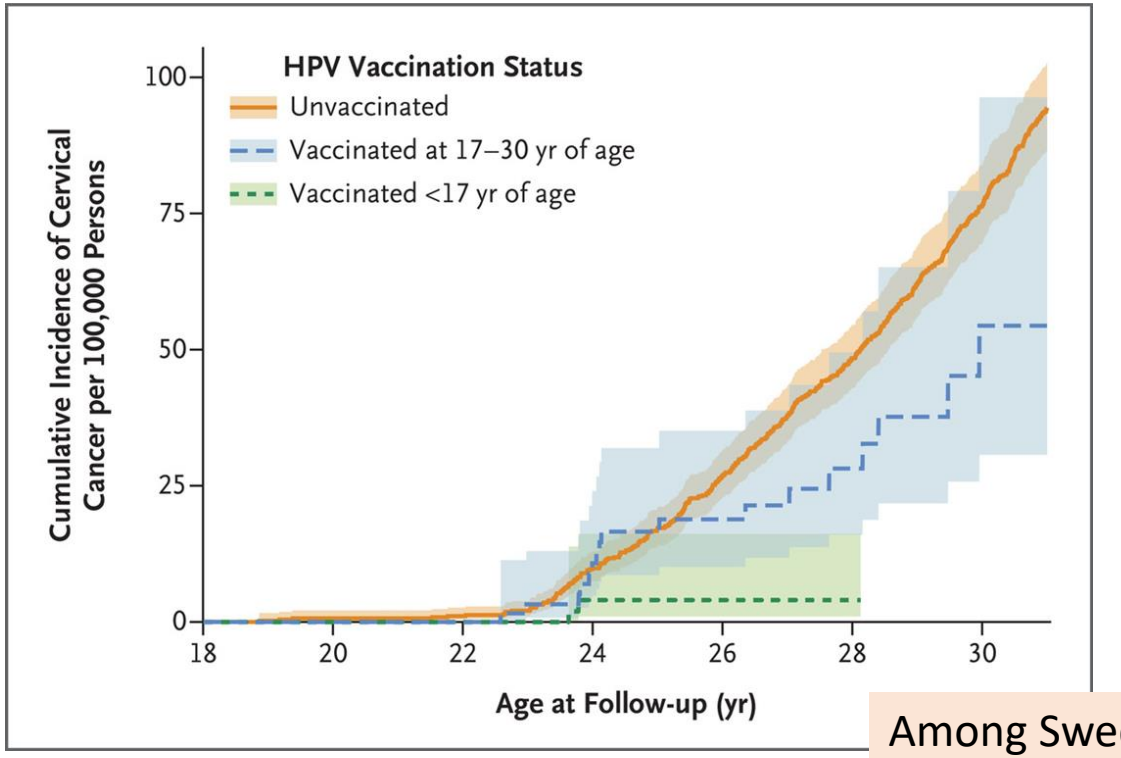
Other programme information

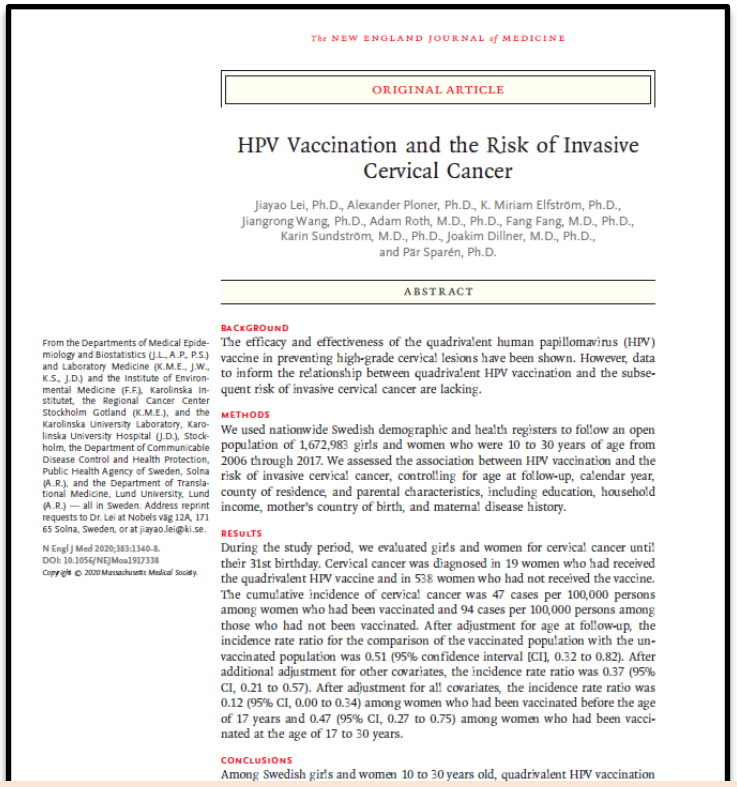
- Screening registries
- Call-and-recall efforts log to ensure that women are managed appropriately are essential for both organized and opportunistic programmes.
- Strong links need to be established between individual patients and the multiple levels of health services (primary care level, hospital level) to ensure the continuity and completion of care.

Trauma free values of cervical cancer screening programs

- Cervical cancer is an intrusive medical act
- All individuals have the right to equality and non-discrimination in sexual and reproductive health care
- Many individuals have been traumatized by abuse, molestation, mutilitation, pain, marginalized and health care…
- Most of the available evidence on cervical cancer is based on study populations of cisgender women
- We need to recognize that cisgender women, transgender men, non-binary, gender fluid and intersex individuals born with a female reproductive system require cervical cancer prevention services.
- However, to be concise and facilitate readability, we use the term “women” to refer to all gender diverse people at risk for cervical cancer.
- Consider the needs of – and provide equal care to – all individuals independently of gender identity or its expression

Impact of vaccination on cancer incidence (Sweden)





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

HPV Vaccination and the Risk of Invasive Cervical Cancer

Jiayao Lei, Ph.D., Alexander Ploner, Ph.D., K. Miriam Elfström, Ph.D., Jiangrong Wang, Ph.D., Adam Roth, M.D., Ph.D., Fang Fang, M.D., Ph.D., Karin Sundström, M.D., Ph.D., Joakim Dillner, M.D., Ph.D., and Pär Sparén, Ph.D.

ABSTRACT

From the Departments of Medical Epidemiology and Biostatistics (J.L., A.P., P.S.) and Laboratory Medicine (K.M.E., J.W., K.S., J.D.) and the Institute of Environmental Medicine (F.F.), Karolinska Institutet, the Regional Cancer Center Stockholm Gotland (K.M.E.), and the Karolinska University Laboratory, Karolinska University Hospital (J.D.), Stockholm, the Department of Communicable Disease Control and Health Protection, Public Health Agency of Sweden, Solna (A.R.), and the Department of Translational Medicine, Lund University, Lund (A.R.) — all in Sweden. Address reprint requests to Dr. Lei at Nobels väg 12A, 171 65 Solna, Sweden, or at jiayao.lei@ki.se.

N Engl J Med 2020;383:1340-8.
DOI: 10.1056/NEJMoa1917338

BACKGROUND
The efficacy and effectiveness of the quadrivalent human papillomavirus (HPV) vaccine in preventing high-grade cervical lesions have been shown. However, data to inform the relationship between quadrivalent HPV vaccination and the subsequent risk of invasive cervical cancer are lacking.

METHODS
We used nationwide Swedish demographic and health registers to follow an open population of 1,672,983 girls and women who were 10 to 30 years of age from 2006 through 2017. We assessed the association between HPV vaccination and the risk of invasive cervical cancer, controlling for age at follow-up, calendar year, county of residence, and parental characteristics, including education, household income, mother's country of birth, and maternal disease history.

RESULTS
During the study period, we evaluated girls and women for cervical cancer until their 31st birthday. Cervical cancer was diagnosed in 19 women who had received the quadrivalent HPV vaccine and in 538 women who had not received the vaccine. The cumulative incidence of cervical cancer was 47 cases per 100,000 persons among women who had been vaccinated and 94 cases per 100,000 persons among those who had not been vaccinated. After adjustment for age at follow-up, the incidence rate ratio for the comparison of the vaccinated population with the unvaccinated population was 0.51 (95% confidence interval [CI], 0.32 to 0.82). After additional adjustment for other covariates, the incidence rate ratio was 0.37 (95% CI, 0.21 to 0.57). After adjustment for all covariates, the incidence rate ratio was 0.12 (95% CI, 0.00 to 0.34) among women who had been vaccinated before the age of 17 years and 0.47 (95% CI, 0.27 to 0.75) among women who had been vaccinated at the age of 17 to 30 years.

CONCLUSIONS
Among Swedish girls and women 10 to 30 years old, quadrivalent HPV vaccination

Among Swedish girls and women 10 to 30 years old, 4vHPV vaccination was **associated with a substantially reduced risk of invasive cervical cancer** at the population level.

J Lei et al. N Engl J Med 2020;383:1340-1348.

When are we going to achieve cervical cancer elimination?

We have a choice: When do we want to eliminate oncogenic HPV types and cervical cancer?

1. **Now**. Catch-up vaccination up to age 30 to reduce R0, inducing elimination of vaccine HPV types. If followed by a one-time HPV screening = permanent elimination of cervical cancer.

2. **Later.** Effective vaccination, but only in children + Screening as usual = The oncogenic HPVs eliminated several decades later. Cervical cancer eliminated a lifetime later.

3. **Never.** Ineffective vaccination (e.g. disorganized, only girls, low coverage) allowing continued circulation of oncogenic HPV.

Courtesy of Dr Joakim Dillner

Conclusion

- We have the tools
- We have the WHO objectives
- We need your commitments
- Allgother we eliminate cervical cancers

Presenter

Dr. Nancy Durand MDCM, FRCS

- Associate Professor, Department of Obstetrics and Gynaecology, University of Toronto
- Dept Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre

Canada's HPV prevention plan:
are we on track for 2030 elimination targets?

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Associate Professor, University of Toronto
Department of Obstetrics and Gynaecology
Toronto, Ontario, Canada

Presenter Disclosure:

- **Presenter:**

  Dr. Nancy Durand
  Sunnybrook Health Sciences Centre
  Toronto, Ontario, Canada

- **Relationships with commercial interests:**
  - Speakers Bureau/Honoraria: Merck Canada, Merck Global
  - Consulting Fees: Merck Canada Advisory Board
    Merck Global Advisory Board
    Moderna Global Advisory Board

- **Other:**

  Associate Professor,
  University of Toronto
  Dept. of Obstetrics and Gynaecology
  Sunnybrook Health Sciences Centre

Are we on track to reach Canada's 90% HPV vaccination targets by 2030?

Learning Objectives:

- Canada’s current HPV vaccine coverage
- Increasing HPV vaccine access
- Changing behaviors through education

HPV Vaccine Approval and Recommendations

Health Canada: HPV Vaccines
approved indications

Gardasil 9 - 2015

9vHPV (4v+31,33,45,52,58)

- females age 9-45
  - CIN; AIS cervix, cervix CA
  - VIN and vulvar CA
  - VaIN and vaginal CA
  - AIN, anal cancer
  - External genital warts
  - Oropharyngeal CA
- males age 9-45 (2020)
  - External genital warts
  - AIN, anal CA
  - Oropharyngeal CA

Cervarix - 2010

2vHPV (types 16, 18)

- females age 10-45
  - CIN
  - AIS cervix
  - Cervix cancer

Cervarix Canadian Product Monograph, GlaxoSmithKline Inc.; November 25, 2014; Gardasil Canadian Product Monograph, Merck Canada Inc.; March 10, 2015; Gardasil 9 Canadian Product Monograph, Merck Canada Inc.; Aug 30, 2020

NACI Recommendations
(National Advisory Committee on Immunization)

- Recommends HPV vaccination in individuals age 9-26
- Supports vaccination over age 26 (no upper age limit)
- Recommends vaccination of those with current or past history of HPV-related disease

https://www.canada.ca/en/public-health/services/publications/healthy-living/updated-recommendations-human-papillomavirus-immunization-schedule-immunocompromised-populations.html

GOC (Society of Gyn Oncology of Canada)

Opportunistic HPV Vaccination: An Expanded Vision

June 2018

- Actively recommend **universal HPV vaccination** in Canada
- Health care systems, institutions and care providers should encourage opportunistic HPV vaccination

https://g-o-c.org/wp-content/uploads/2015/01/18_EEE_WhitePaper_FINAL_Jun18-1.pdf

Joint Statement: CSOHNS – SOGC - GOC
Jan 2021

Our Ongoing and Neglected HPV Cancer Challenge:

Call to action to achieve elimination:

- Vaccination
- Screening
- Early detection and treatment of HPV cancers

CANADIAN SOCIETY OF OTOLARYNGOLOGY - HEAD & NECK SURGERY

THE SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA
LA SOCIÉTÉ DES OBSTÉTRICIENS ET GYNÉCOLOGUES DU CANADA

GOC
LA SOCIÉTÉ DE GYNÉCO-ONCOLOGIE DU CANADA
THE SOCIETY OF GYNECOLOGIC ONCOLOGY OF CANADA

Provincial HPV Vaccination Programs in Canada

Provincial HPV Vaccination Programs

All 13 provinces and territories:

- Gender neutral programs
- 2 doses 9VHPV vaccine except
- Quebec: 1st dose 9vHPV; 2nd dose 2vHPV
- Range between grades 4-7 (age 9-12)

Catch Up Programs

- Ontario – funded HPV vaccine up to grade 12
  - (special add'l catch-up 3 years post high-school until Aug 2023)
- Quebec – girls only catch-up to age 18

- **Alberta, Yukon, NWT:**
  - **Funded vaccine up to / including age 26**

Provincial HPV Vaccination Programs

All have funded doses: MSM

- 6 regions have funded doses for PLWH
  - BC age 26
  - SK males 9-17
  - MB age 26
  - QC age 26
  - NS age 45
  - YK age 45

Ontario HPV Vaccination Program – low uptake

School-Based Immunization Programs among 12-Year-Olds

Figure 9. Immunization coverage for quadrivalent meningococcal conjugate vaccine (MCV4), human papillomavirus (HPV) and hepatitis B among 12-year-olds in Ontario: 2013–14 to 2018–19 school years

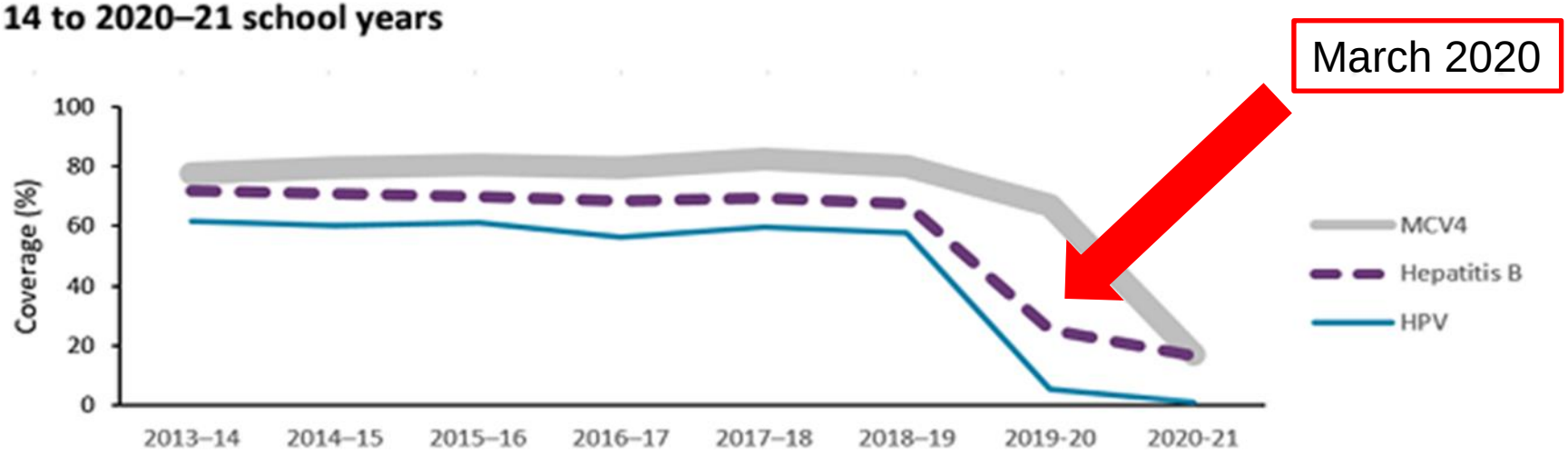
	2013–14	2014–15	2015–16	2016–17	2017–18	2018–19
MCV4	77.5	79.4	80.6	79.6	82.4	80.1
Hepatitis B	71.7	70.7	69.9	68.6	69.2	67.3
HPV	61.5	60.4	61.0	56.3	59.9	57.9

https://www.publichealthontario.ca/-/media/documents/i/2020/immunization-coverage-2018-19.pdf?la=en

Effect of Covid 2020 – 2021 on Ontario Program

Provincial Coverage Estimates for School-based Programs

Figure 1. Immunization coverage for quadrivalent meningococcal conjugate (MCV4), human papillomavirus (HPV) and hepatitis B (Hep B) vaccines among 12-year-olds in Ontario: 2013–14 to 2020–21 school years



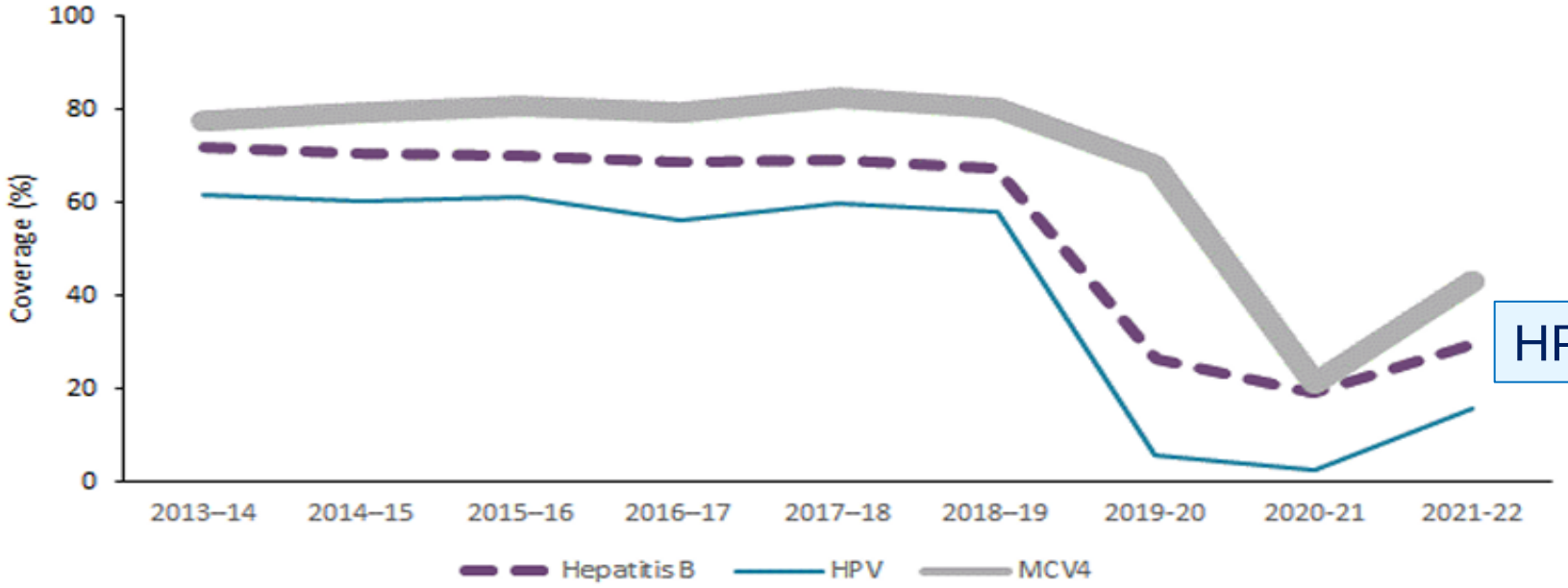
HPV 0.8% 2020-2021

https://www.publichealthontario.ca/-/media/documents/i/2021/immunization-coverage-2019-2021.pdf?sc_lang=en
https://www.theglobeandmail.com/canada/article-routine-vaccination-rates-children-teens/

Post-Covid Catchup Ontario to 2021-2022

Temporal Trends in Coverage

Figure 1. Up-to-date (UTD) immunization coverage for hepatitis B (Hep B), human papillomavirus (HPV) and quadrivalent meningococcal conjugate (MCV4) vaccines among 12-year-olds in Ontario: 2013-14 to 2021-22 school years

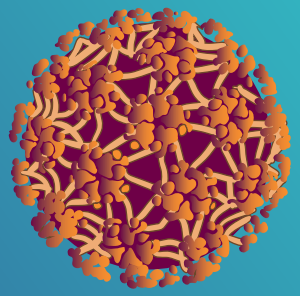


HPV 15.6% 2021-2022

https://www.publichealthontario.ca/-/media/Documents/I/2023/immunization-coverage-2019-2022.pdf?rev=8c17516457604f77aff7e0321157e536&sc_lang=en

HPV Immunization Outside of School-based Provincial Programs

Rationale for Adult HPV Vaccination



Risk of new exposure

Efficacy of vaccination at reducing disease

Vaccination reduces recurrence in previously exposed adults

Clinical Data in Adult Women

4vHPV: Mid-Adult Women Trial
Females Aged 24–45 Years

Randomized controlled trial
(N=3,692)
Years 1–4 of follow-up

89%

Efficacy against persistent infection, abnormal paps and genital warts[a,b]

Castellsagué et al 2011[1]

Long-term extension trial years 4-10
(N=599)

0

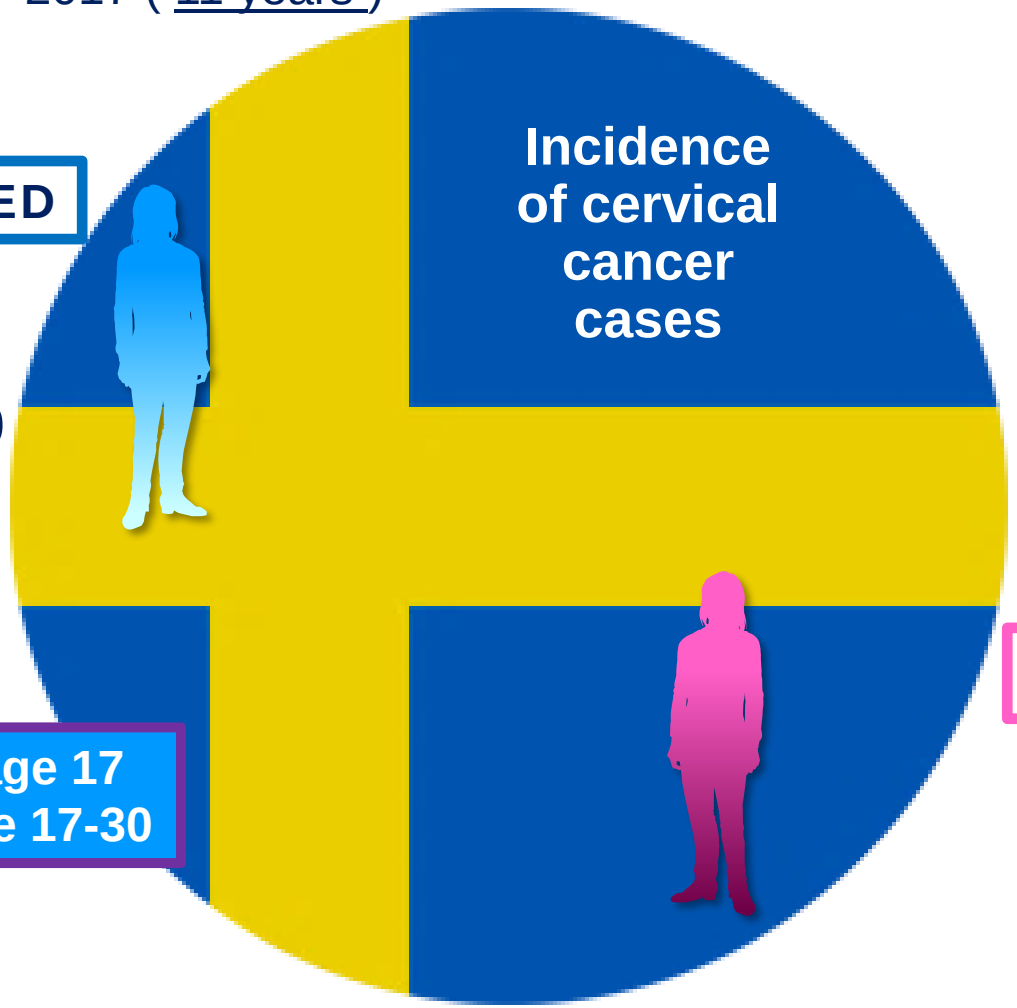
Cases of HPV abnormal paps or genital warts

Data on file. MSD[2];
Walia A 2019[3]

[a]Related to HPV types 6, 11, 16, and 18.
[b]EGL includes condyloma, VIN, and VaIN.
4vHPV = 4-valent human papillomavirus; CIN = cervical intraepithelial neoplasia; DOF = data on file; EGL = external genital lesions; ASCUS = atypical squamous cells of undetermined significance; LSIL = low-grade squamous intraepithelial lesion; VIN = vulvar intraepithelial neoplasia; VaIN = vaginal intraepithelial neoplasia.
1. Castellsagué X et al. *Br J Cancer*. 2011;105:28–37. **2.** Data on File. MSD. **3.** Data presented by Walia A on Nov 14, 2019 at “6th NCI cancer centers HPV Vaccination Summit.”

Swedish Females: Trends in Cervical Cancer[1]

Swedish Health Registry: 2006 - 2017 (11 years)



VACCINATED

19

47/100,000
by age 30

88% reduction if vaccinated < age 17
53% reduction if vaccinated age 17-30

UNVACCINATED

538

94/100,000
by age 30

Per 100,000 woman-years
527,871 vaccinated females aged 10-30 years
1,145,112 non-vaccinated females aged 10-30 years.

1. Lei, J et al. NEJM.Oct 2020; 383;14: 1340-1348.

The Effects of the National HPV Vaccination Programme in England

Nov 2021 Lancet

- Observational study 2006-2013 of cancer registry data of cervix cancer and CIN3 compared to cohorts before pre-vaccination era
- 13.7 million years of follow-up
- Compared rates in vaccinated cohorts to rates prior to vaccination
- In cohort vaccinated age 12-13:

87% reduction in cervix cancer
97% reduction in CIN3

Falcaro M et al. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study. Lancet published online: November 03, 2021; DOI:https://doi.org/10.1016/S0140-6736(21)02178-4

Clinical Data in Adult Males

Clinical Data in Adult Males

Aug 2020: 9vHPV was approved by Health Canada for males over age 26

4vHPV Male Trial Against EGW and HG-AIN Males (16–26 Years)[1,a]

89%
reduction in genital warts[b]

≈3 years

75%
reduction in AIN 2/3 (MSM subset)[b]

≈2 years

10 years

Long-term extension trial years 4-10

0
Cases of EGL or HG-AIN

Seropositivity rates for HPV 6/11/16/18 remained high

[a]Base study in males vaccinated between the ages of 16 and 26 years; [b]Related to HPV types 6, 11, 16, and 18.
4vHPV = 4-valent human papillomavirus; HPV = human papillomavirus; AIN = anal intraepithelial neoplasia; MSM = men who have sex with men; AE = adverse event; ISR = injection-site reaction; SAE = serious adverse event.

Giuliano AR et al. *N Engl J Med*. 2011;364:401–411; Goldstone S, et al. EUROGIN 2018. FC 4-2.

HPV Vaccine Impact on Oral HPV

USA, UK:
Real World Impact on Oral HPV Prevalence Post-Vaccination

- Declining oral HPV prevalence among males and females age 18-33 in USA
- Declining oral HPV prevalence among males and females age 12-24 in UK

Chaturvedi et al JCO 2018; N, et al PLoS One, 2012; Hirth JM, et al Vaccine, 2017; Brouwere AF, et al Prev Med 2019; Schlecht N, et al JAMA Network Open 2019 ; Castillo A, et al PVR 2019; Grun N, et al Scand. J Inf Dis, 2014; Mehanna H, et al. CID 2019.

9vHPV vaccine V503-049 Phase III Trial

- 6000 adult males age 20-45
- USA, Mexico, Columbia, Peru and Brazil; 105 sites
- Feb 2000 – July 2024
- Randomized placebo controlled trial

Objectives:

1. Efficacy against vaccine type oral persistent infection 6 months +
2. Type-specific antibody response at month 7
3. Safety and tolerability

www.clinicaltrials.gov; V503-049, NCT04199689

HPV Vaccination in Those with History of HPV Disease

4vHPV Vaccine Reduces Disease Recurrence in Adult Females With Previous Disease

HPV vaccination reduces recurrence of abnormal paps

70-80%

HPV vaccination reduces recurrence of genital warts

75%

HPV vaccination reduces recurrence of VIN2/3

78%

[a]Related to HPV types 6, 11, 16, and 18.
[b]Women previously treated for cervical squamous intraepithelial lesion.
4vHPV = 4-valent human papillomavirus; CIN = cervical intraepithelial neoplasia; LEEP = loop electrosurgical excision procedure.
1. Kang WD et al. *Gynecol Oncol*. 2013;130:264–268. **2.** Ghelardi A et al. *Gynecol Oncol*. 2018;151:229–234. **3.** Pieralli A et al. *Arch Gynecol Obstet*.. 2018;298:1205–1210; **4.** Ghelardi A et al. Vaccines 2021; 9:83-94.

4vHPV Vaccine Reduces Disease Recurrence in Adult Males With Previous Disease

HPV vaccination reduces recurrence of high-grade anal pre-cancerous cells

52%

HPV vaccination reduces recurrence of genital warts

50%

4vHPV = 4-valent human papillomavirus; MSM = males who have sex with males; HGAIN = high-grade anal intraepithelial neoplasia.

1. Swedish KA et al. *Clin Infect Dis*. 2012;54:891–898. **2.** Swedish KA et al. *PLoS One*. 2014;9:e93393.

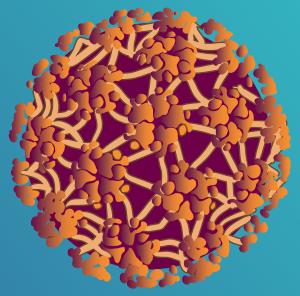
Recommendations for HPV vaccination within colpo setting

- Spain
- Italy
- Austria
- Manitoba (bx proven HSIL)
- PEI (anyone with HPV dx)

Counselling and Communication

How can we improve vaccine uptake?

Rationale for Adult HPV Vaccination

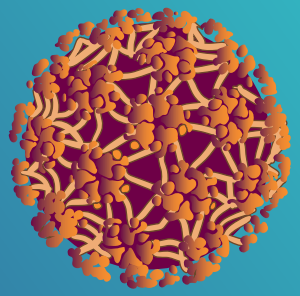


Risk of new exposure

Efficacy of vaccination at reducing disease

Vaccination reduces recurrence in previously exposed adults

Rationale for Adult HPV Vaccination



Risk of new exposure

Efficacy of vaccination at reducing disease

Vaccination reduces recurrence in previously exposed adults

Partners should also be vaccinated for HPV

Why should you get vaccinated for HPV?

This is a vaccine to protect you against *cancer*

HPV cancers are *preventable*

We don’t want to *lose you to this disease*

Counseling for Adult HPV Vaccination

- Don’t assume a young adult (female or male) was already vaccinated
- Remember that the adults you counsel about HPV vaccination are also the parents of children

HPV Vaccination Counselling – “The Message”

Keep it simple

- **Effective**
- **Safe**
- **Recommended**

Opening the HPV Vaccination Discussion

Looking for the opportunities:

- Contraception discussion
- STI testing – EGW prevention
- Travel vaccination
- Flu shot
- Mental health visit
- Change in relationship
- Executive physicals
- Awareness campaigns like Movember

Keys to Improving HPV Vaccine Coverage in Canada

- Increase school-based uptake rates
- Coverage for special populations:
  - Those living with HIV
  - Dx of HPV, HPV-diseases
- Aim for funded vaccine to age 26 (like Alberta, Yukon, NWT)
- Education that gender-neutral adult HPV immunization is of value

Canada's HPV prevention plan:

Are we on track for 2030 elimination targets?

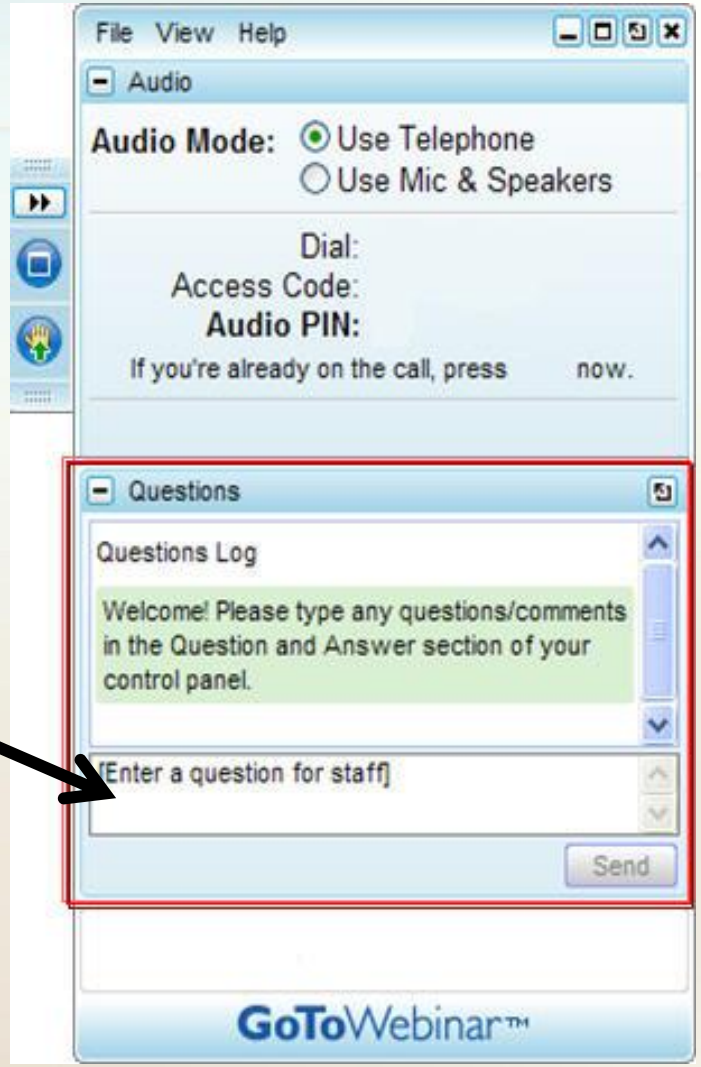
No, we must all do more

Nancy Durand, MDCM, FRCSC
Sunnybrook Health Sciences Centre
Associate Professor, University of Toronto
Department of Obstetrics and Gynaecology
Toronto, Ontario, Canada

Question & Answer Period

On a computer, submit your text question using the Questions pane

NOTE: On a mobile device, tap on the “?” or “Questions” to open the questions pane



Will Canada's HPV prevention plan be on track with WHO 2030 elimination targets?

Evaluation: https://forms.gle/Awz8gaHuGAzs52hY8

- **Slide Set, Video recording, HPV documents at:**
  hpvglobalaction.org & **www.CIDCgroup.org**

Thank you for participating!

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