

The role of epidemiology in cervical cancer elimination

The World Epidemiology Conference
Capetown, South Africa
September 2024

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Professor & NHMRC Leadership Fellow
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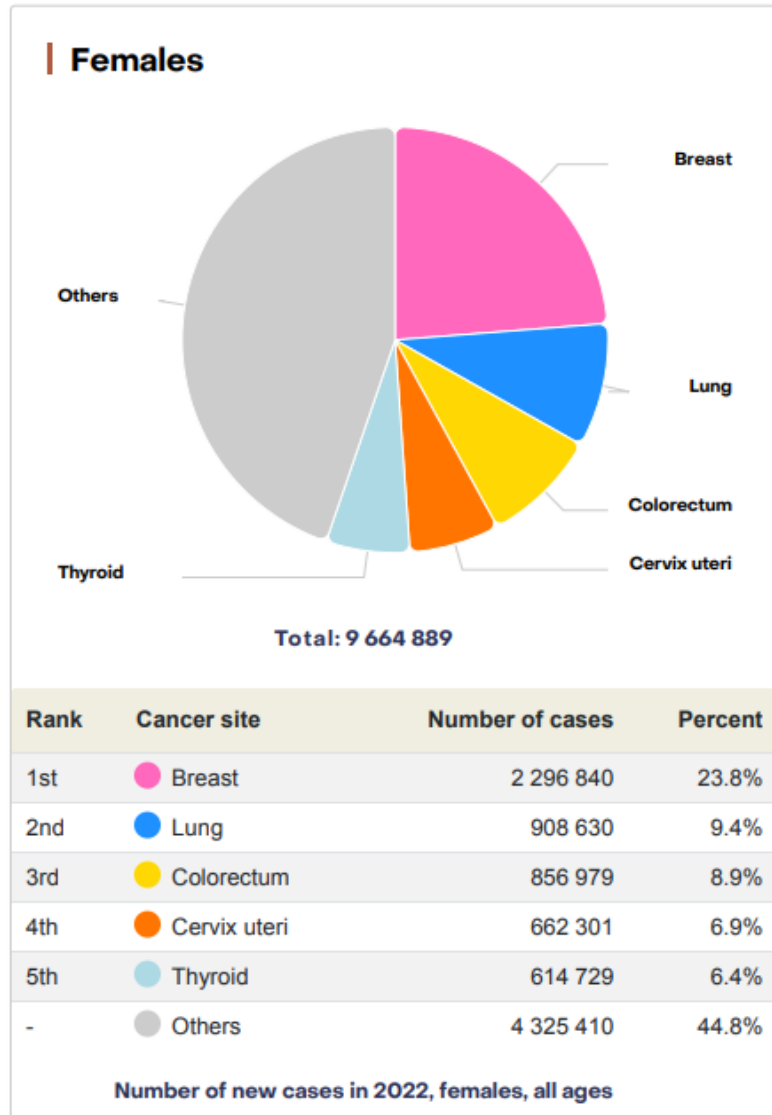


Disclosures

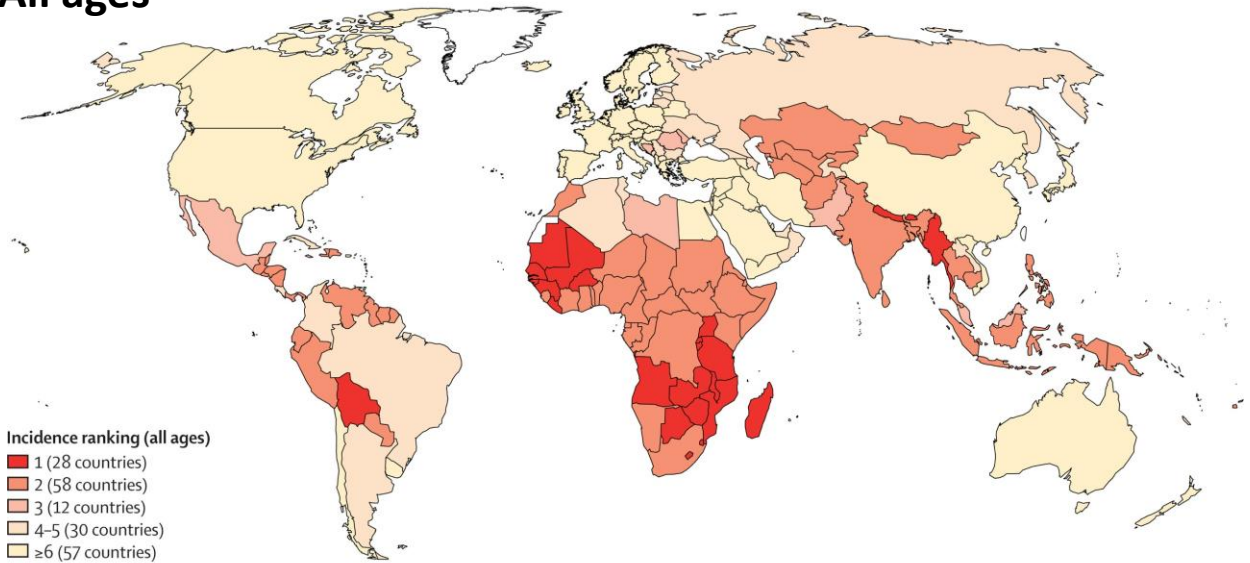
I am co-PI of an investigator-initiated trial of cervical screening, "Compass", run by the Australian Centre for Prevention of Cervical Cancer (ACPCC), which is a government-funded not-for-profit charity. The trial has received support from the Australian government and the ACPCC has received equipment and a funding contribution from Roche Molecular Diagnostics.

I am also co-PI on an implementation program *Elimination of Cervical Cancer in the Western Pacific (ECCWP)/ Elimination Partnership for Cervical Cancer in the Indo-Pacific (EPICC)* which has received support from the Australian government, the Minderoo Foundation and equipment donations from Cepheid Inc.

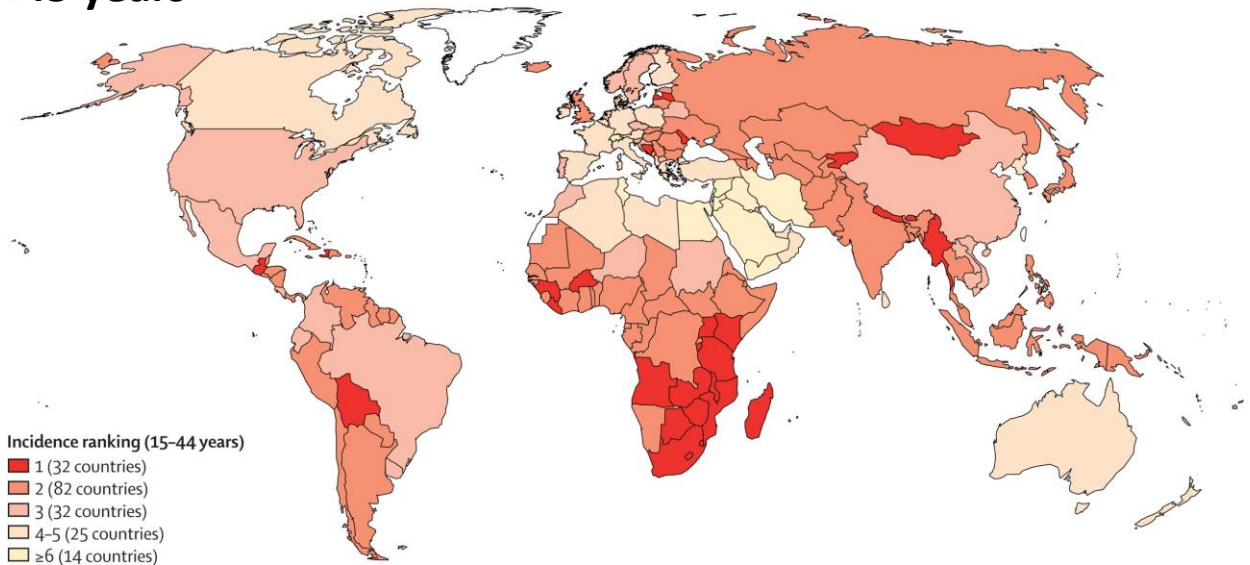
Cervical cancer: High burden, immense inequity



All ages



<45 years



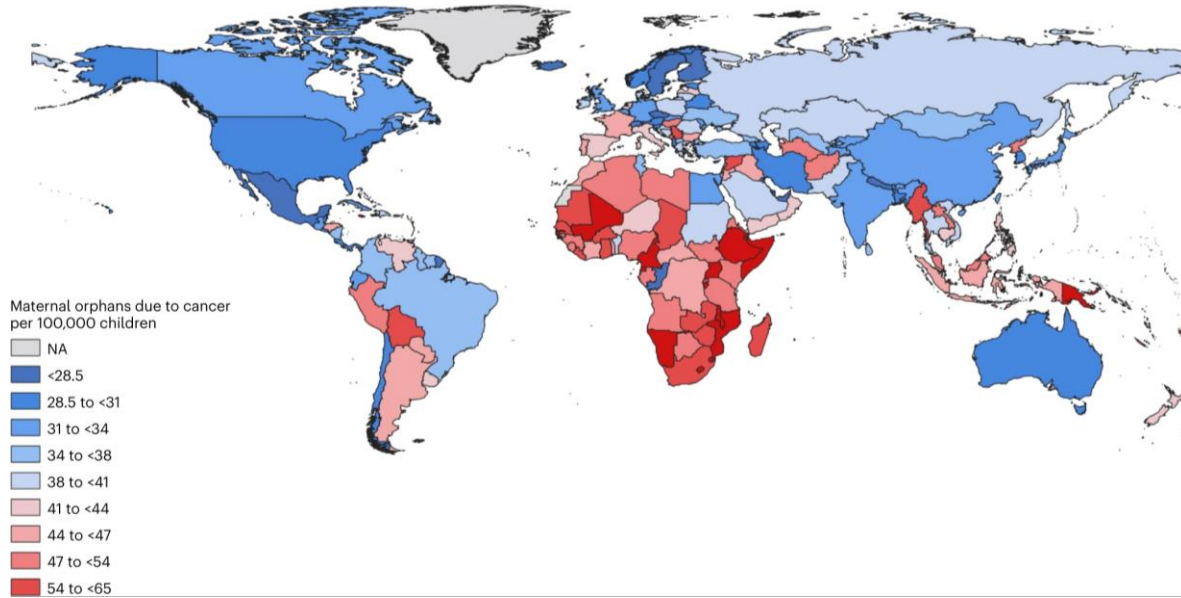
¹The International Agency for Research on Cancer (IARC), Global Cancer Observatory.

²Arbyn M, Weiderpass E, Bruni L, de Sanjose S, Saraiya M, Ferlay J, Bray F, Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis, *Lancet GH* 2019.

There are severe intergenerational consequences

All cancers

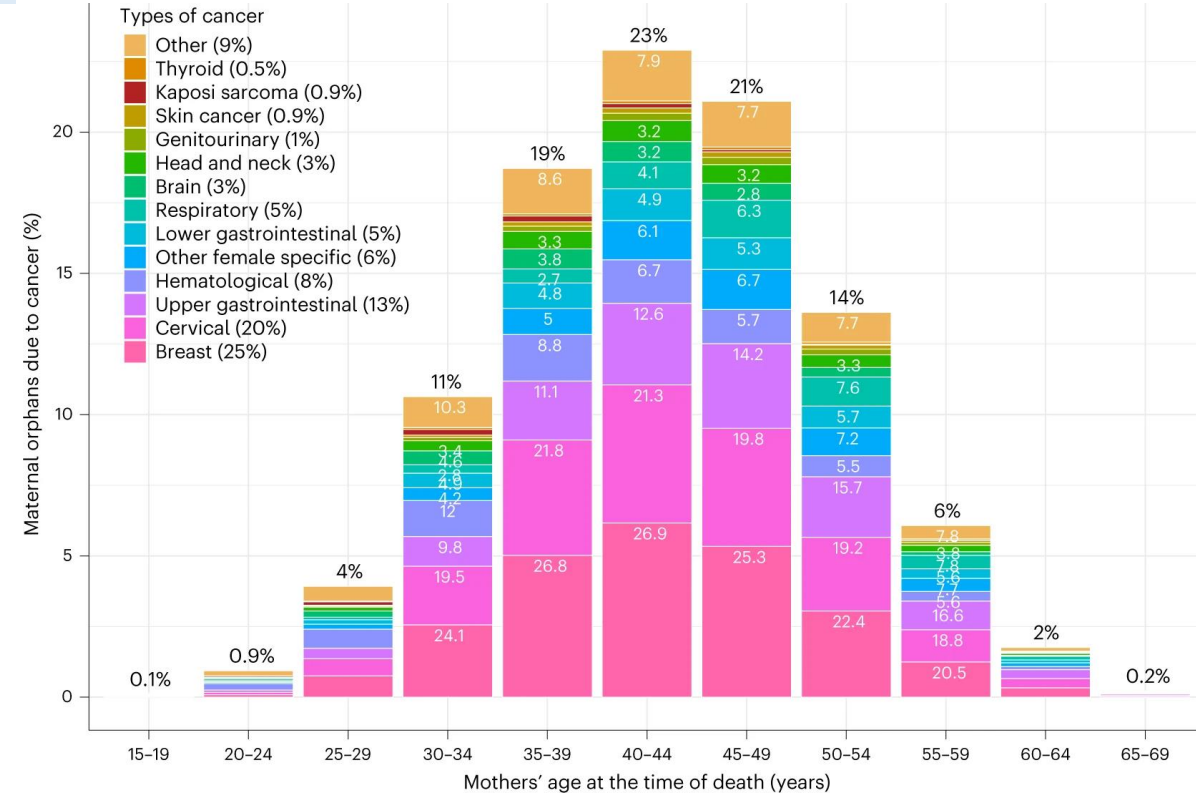
In 2020, 4.4M cancer deaths in women resulted in 1.0M new maternal orphans globally



New maternal orphans due to cancer per 100,000 children in 2020

Cervical cancer

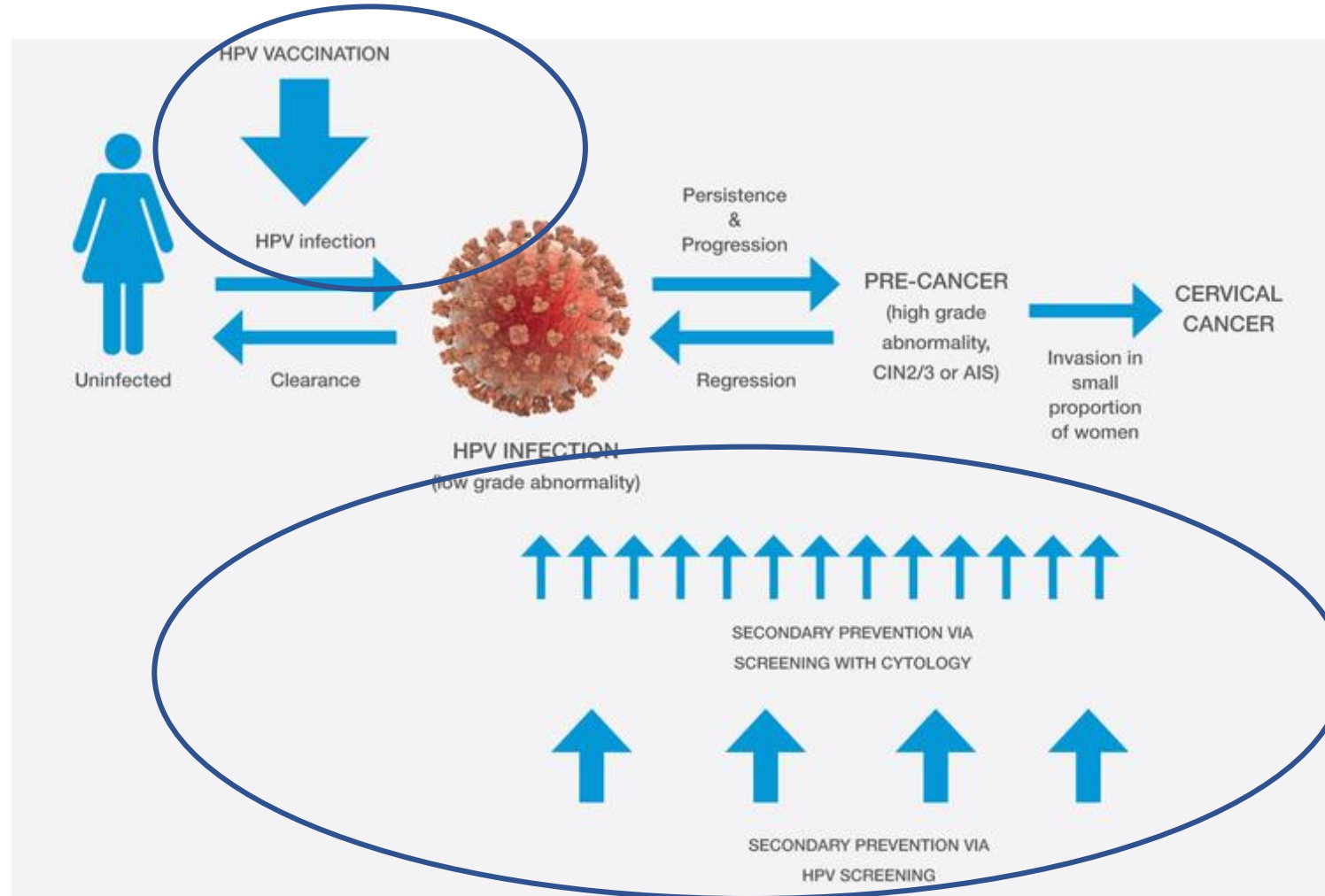
Est. 341,000 cervical cancer deaths, resulting in 210,000 new maternal orphans



Global distribution of maternal orphans due to cancer by mother's age at time of death and type of cancer

Natural history of disease, and intervention effectiveness, are well understood

Primary target population: girls aged 9-14 years



Primary target population: Women aged 25-30+ years

Viral association with cancer identified

Early ecological analysis

Special Article

CANCER OF THE CERVIX: A SEXUALLY TRANSMITTED INFECTION?

VALERIE BERAL

*Department of Medical Statistics and Epidemiology,
London School of Hygiene and Tropical Medicine,
Keppel Street, London WC1E 7HT*

Summary When mortality patterns for cancer of the uterine cervix were compared with trends in incidence of sexually transmitted diseases in both England and Wales and in Scotland, there were striking associations between the temporal, social class, occupational, and geographic distributions of these diseases. The data suggest that exposure to sexually transmitted infection is an important determinant of cervical cancer. Although they are still young, women born after 1940 are already experiencing increased cervical-cancer mortality. If cervical-cancer prevention and therapy remain unchanged, this generation's high risk of death from cervical cancer will probably continue to operate throughout their lives.

Beral V, *Lancet* 1974

Identification of HPV DNA in CaCx

A papillomavirus DNA from a cervical carcinoma and its prevalence in cancer biopsy samples from different geographic regions

(human papillomaviruses/low-stringency hybridization/molecular cloning/genital tumors)

MATTHIAS DÜRST, LUTZ GISSMANN, HANS IKENBERG, AND HARALD ZUR HAUSEN*

Institut für Virologie, Zentrum für Hygiene, Universität Freiburg, Hermann-Herder-Strasse 11, 7800 Freiburg, Federal Republic of Germany

Communicated by Gertrude Henle, March 21, 1983

“DNA from one biopsy sample of invasive cancer of the cervixshowed no homology with DNA of other human HPV types. We therefore propose to designate it tentatively as HPV 16.”

Durst M et al., *PNAS USA* 1983

Attributable fraction of HPV types in cervical cancer now well quantified

HPV type	HPV species	IARC Group ^a	% HPV type prevalence in cancer	% HPV type prevalence in normal	Odds ratio	% Attributable (etiological) fraction
HPV16	α-9	Group 1	55.8	2.6	47.6	62.4
HPV18	α-7	Group 1	14.3	1	15.7	15.3
HPV45	α-7	Group 1	4.8	0.6	8.3	4.8
HPV33	α-9	Group 1	4	0.6	7.1	3.9
HPV58	α-9	Group 1	4	0.8	5.1	3.7
HPV31	α-9	Group 1	3.5	1	3.7	2.9
HPV52	α-9	Group 1	3.2	1	3.3	2.6
HPV35	α-9	Group 1	1.6	0.4	3.9	1.4
HPV59	α-7	Group 1	1.2	0.4	2.9	0.9
HPV39	α-7	Group 1	1.3	0.6	2.0	0.8
HPV68	α-7	Group 2A	0.6	0.4	1.5	0.2
HPV51	α-5	Group 1	1	0.9	1.2	0.2
HPV56	α-6	Group 1	0.8	0.6	1.3	0.2
HPV73	α-11	Group 2B	0.5	0.3	1.8	0.2
HPV26	α-5	Group 2B	0.2	0.1	4.1	0.2
HPV30	α-6	Group 2B	0.2	0.1	2.6	0.1
HPV69	α-5	Group 2B	0.2	0.1	1.4	0.1
HPV67	α-9	Group 2B	0.3	0.2	1.2	< 0.1
HPV82	α-5	Group 2B	0.2	0.1	1.2	< 0.1
HPV34	α-11	Group 2B	0.1	0.1	1.0	Not attributable
HPV66	α-6	Group 2B	0.3	0.6	0.4	Not attributable
HPV70	α-7	Group 2B	0.2	0.8	0.3	Not attributable
HPV53	α-6	Group 2B	0.5	1.1	0.4	Not attributable

Types in first gen vaccines, AF>70%

Additional types in second gen vaccines, AF > 90%

Types commonly included in current assays in bold

Combes, Clifford et al., Int J Cancer 2015

IARC Handbooks: Cervical Cancer Screening 2022.

<https://publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Cervical-Cancer-Screening-2022>

Real-world data on HPV vaccine efficacy has emerged

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

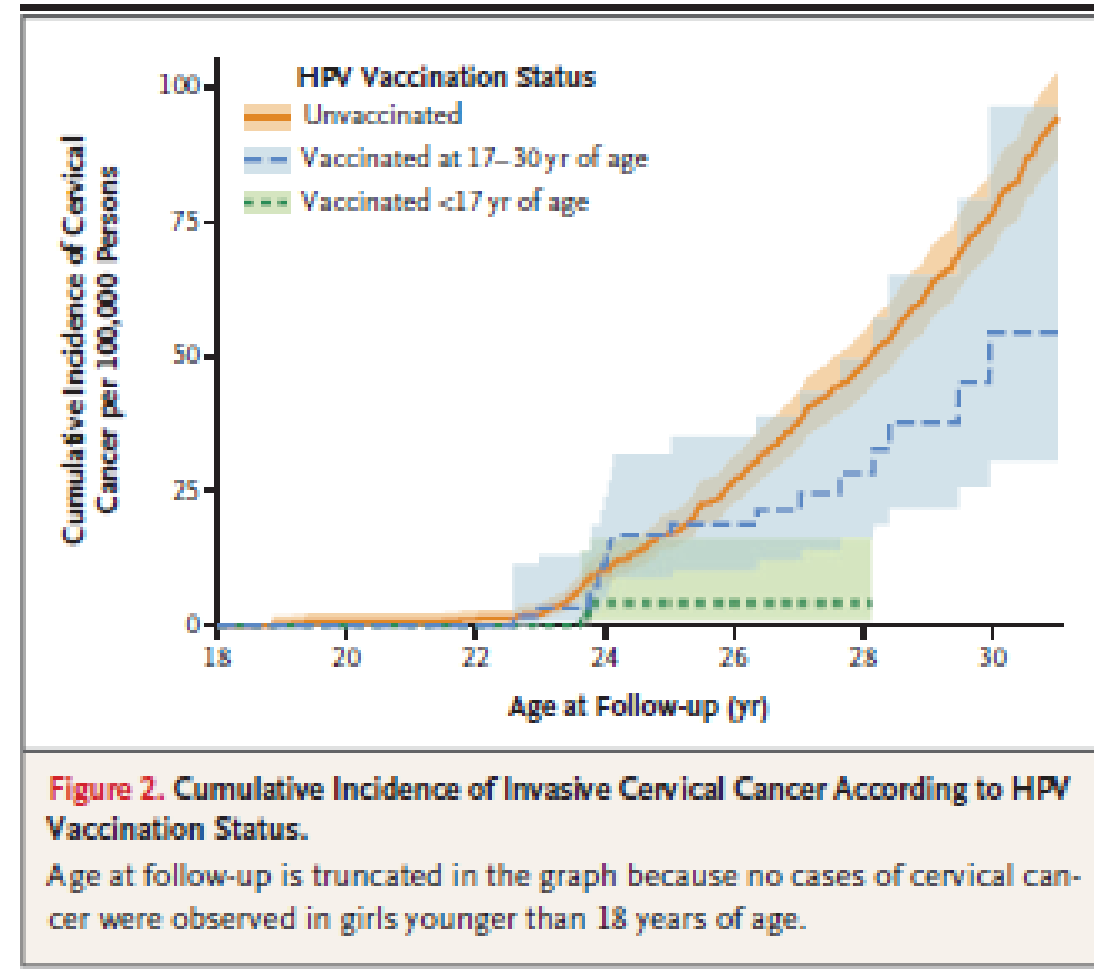
HPV Vaccination and the Risk of Invasive Cervical Cancer

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

IRR for invasive cancer:

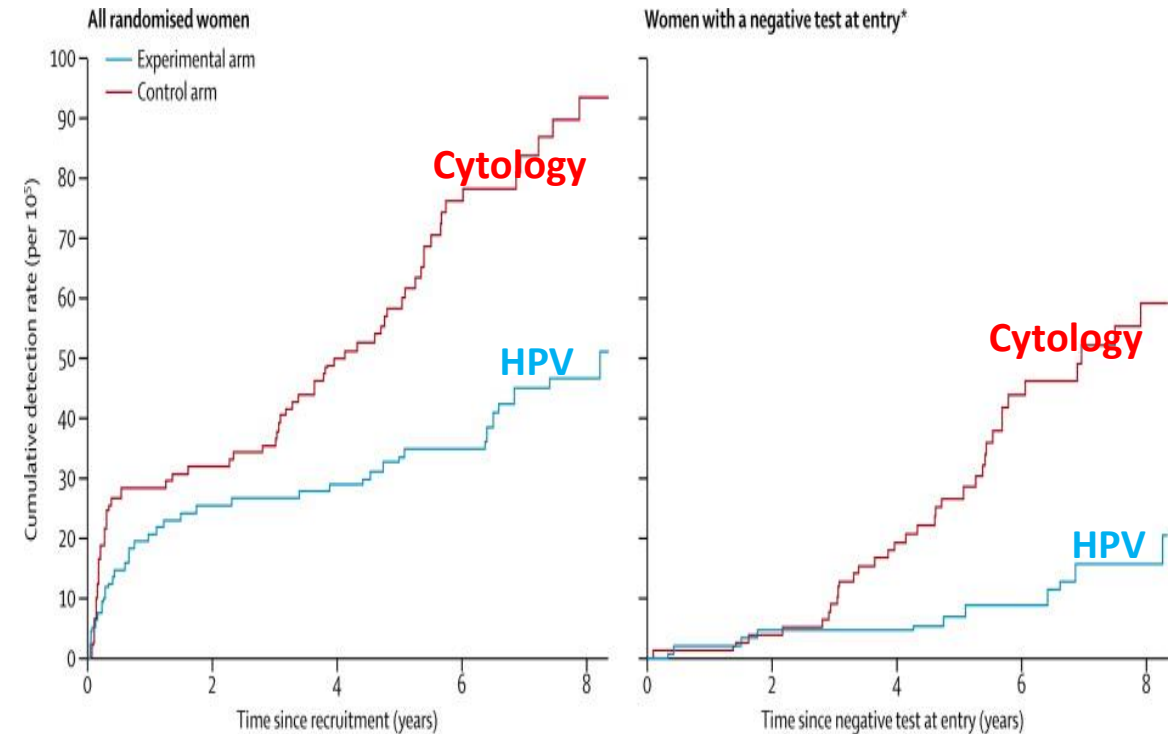
- ***0.12 (95%CI:0.00-0.34) among women who had been vaccinated before the age of 17 years***
- ***0.47 (95%CI:0.27-0.75) among women who had been vaccinated at the age of 17 to 30 years***



Meta-analysis of cross-sectional data and pooled analysis of trial data on HPV vs. cytology screening

Human papillomavirus (HPV) compared to Papanicolaou (Pap) test for detection of cervical intraepithelial neoplasia (CIN 2+) in asymptomatic women					
Patient or population: adult asymptomatic women					
Settings: outpatient screening programmes					
New Test: HPV, HC2 test Cut-off value: 1 pg/mL					
Comparison Test: Pap, liquid-based cytology (LBC) test Cut-off value: atypical squamous cells of undetermined significance (ASCUS)					
Reference Test: a colposcopy exam with or without biopsy as clinically indicated					
HPV	138,230 women (25 studies)	Pooled sensitivity (95% CI)	89.9% (88.6 to 91.1%)	Pooled specificity (95% CI)	89.9% (89.7 to 90.0%)
Pap	82,003 women (15 studies)	Pooled sensitivity (95% CI)	72.9% (70.7 to 75%)	Pooled specificity (95% CI)	90.3% (90.1 to 90.5%)

Koliopoulos G, Nyaga VN, Santesso N, Bryant A, Martin-Hirsch PP, Mustafa RA, Schünemann H, Paraskevaidis E, Arbyn M. Cytology versus HPV testing for cervical cancer screening in the general population. *Cochrane Database Syst Rev.* 2017.



Ronco G, Dillner J, Elfström KM, Tunesi S, Snijders PJ, Arbyn M, Kitchener H, Segnan N, Gilham C, Giorgi-Rossi P, Berkhof J, Peto J, Meijer CJ; International HPV screening working group. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. *Lancet.* 2014

Updated systematic review of observational data and trials

The NEW ENGLAND JOURNAL of MEDICINE

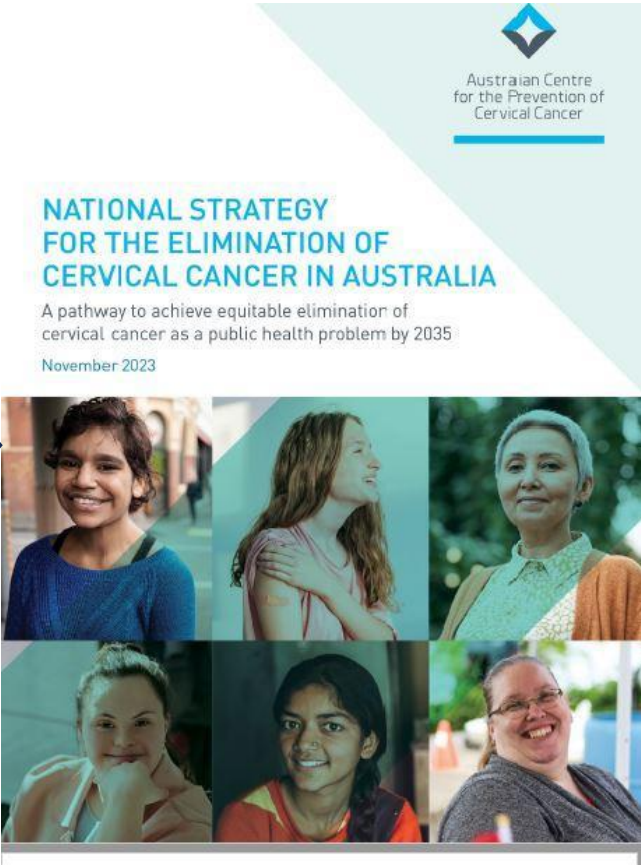
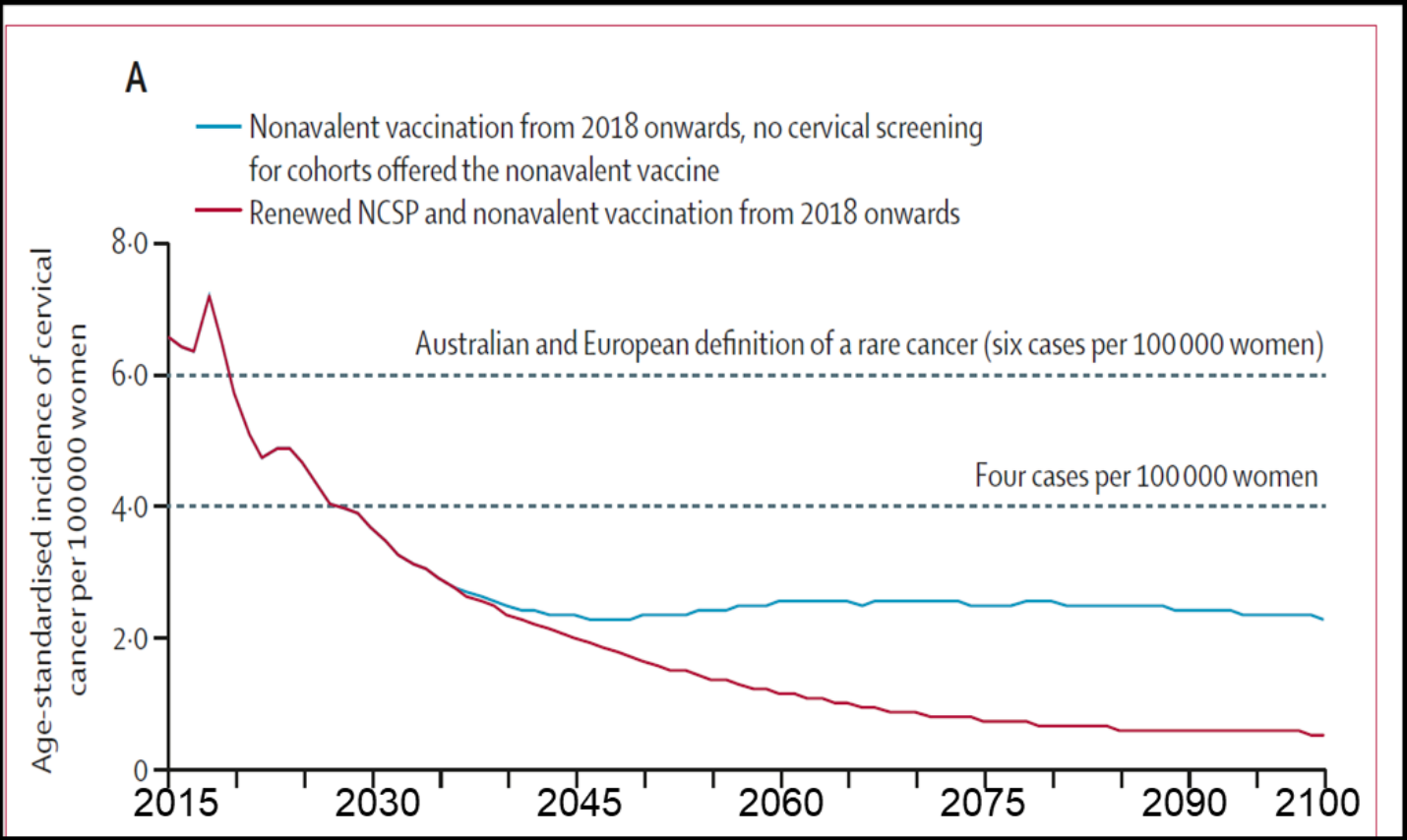
SPECIAL REPORT

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-Metcalf, Ph.D., and Béatrice Lauby-Secretan, Ph.D.

Bouvard et al., NEJM 2022

Understanding the prospects for combining interventions: population-level modelling, Australia



The WHO global strategy

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



The three pillars of cervical cancer control WHO 2030 targets



Vaccination

90%
of girls fully
vaccinated by age 15



Screening

70%
of women HPV screened
at 35 and 45



Treatment

90%
of women identified with
precancer or cervical
cancer treated

Cervical cancer threshold for elimination as a public health problem:
4 cervical cancer cases per 100,000 women per annum

Rol

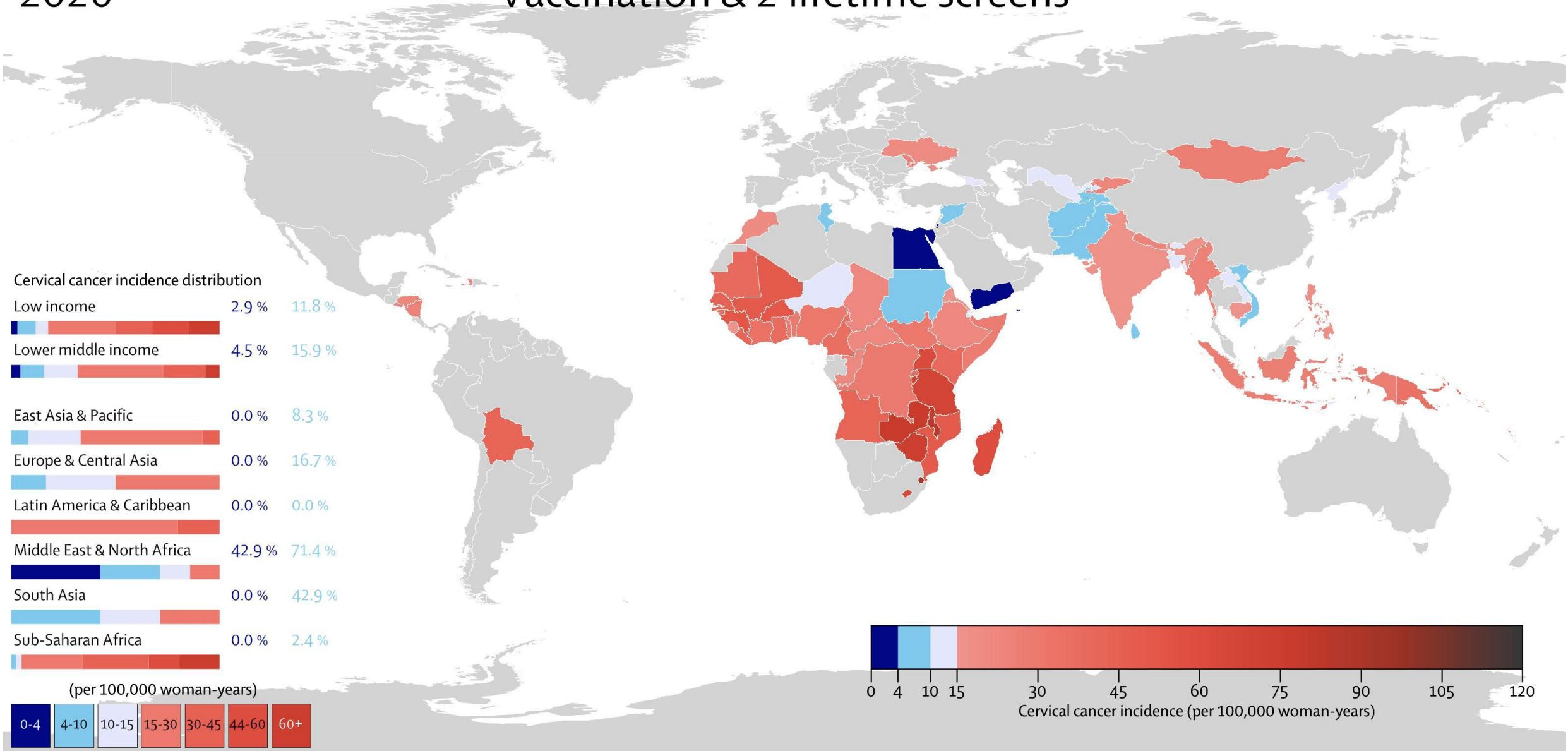
US \$3.20 returned to the economy for every dollar invested through 2050 and beyond.

The figure rises to US \$26.00 when the benefits of women's improved health on families, communities, and societies are considered.

2020

Vaccination & 2 lifetime screens

CCEMC modelling across 78 LMIC



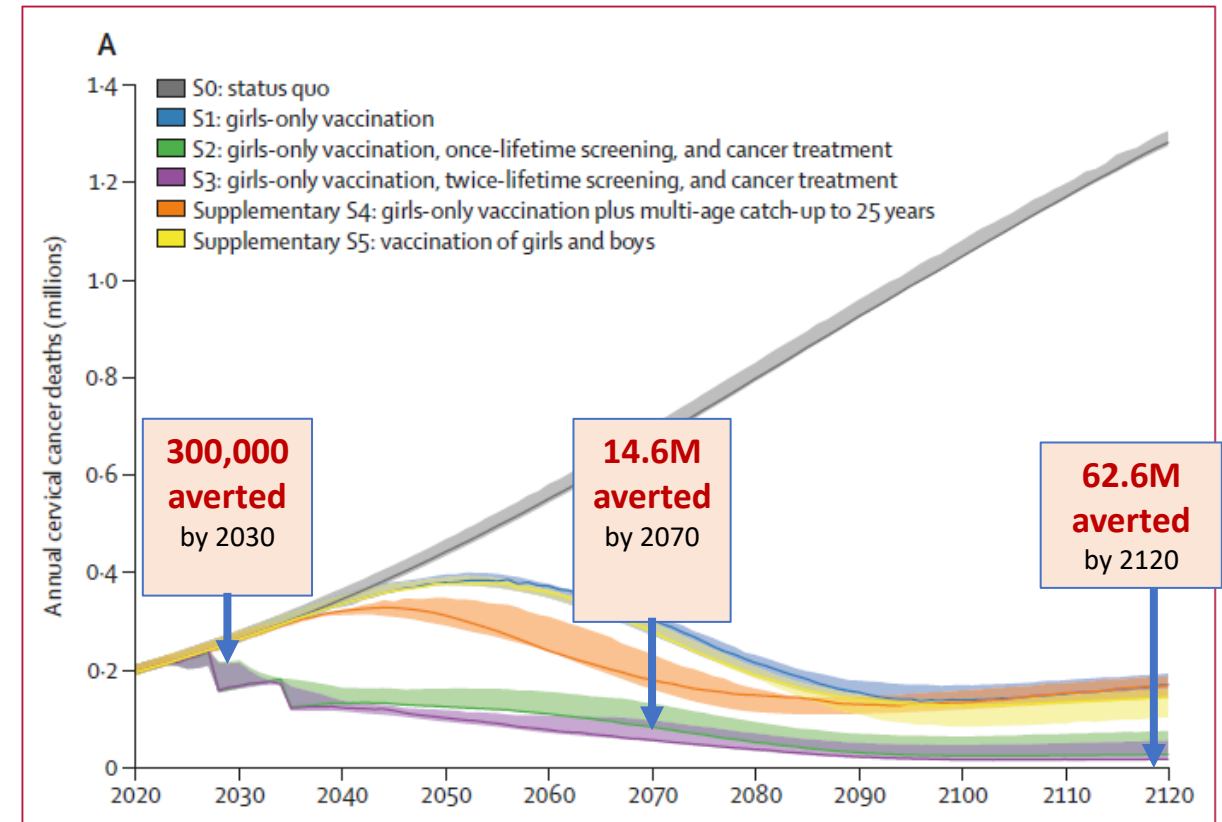
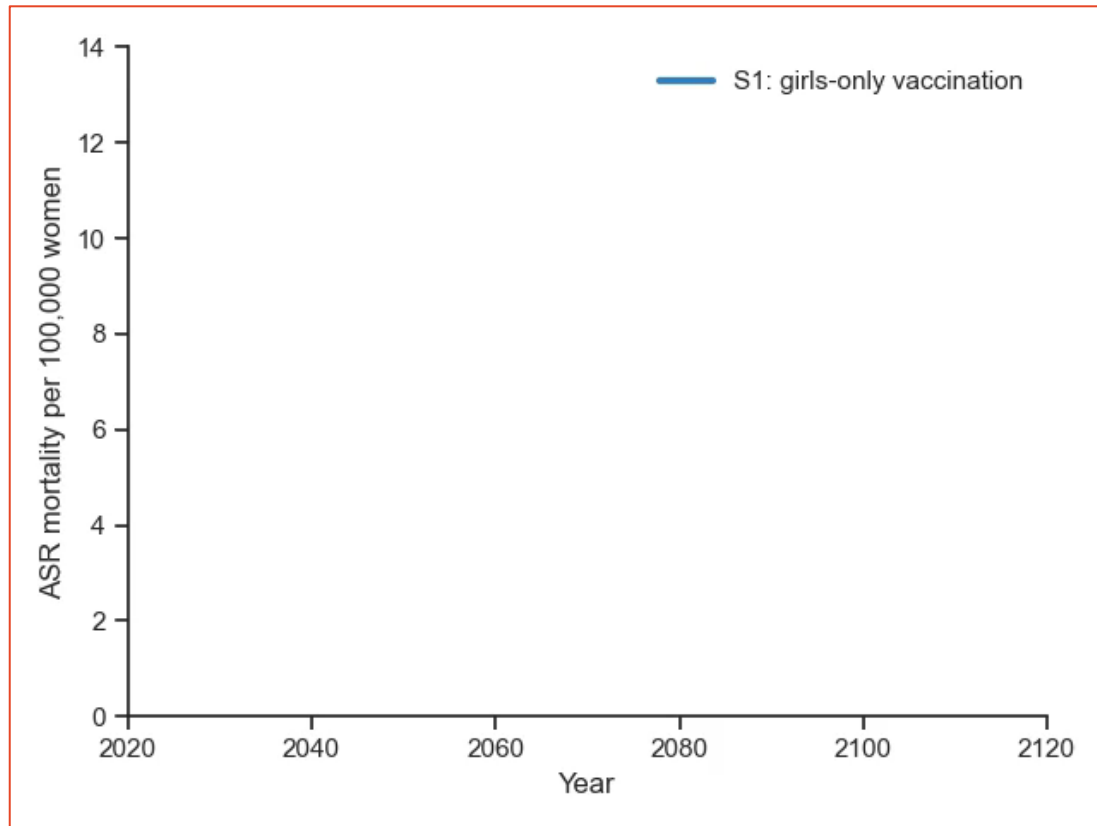
The Daffodil Centre



Brisson M,* Kim JJ,* Canfell K,* Drolet M, Gingras G, Burger EA, Martin D, Simms KT, Bénard É, Boily MC, Sy S, Regan C, Keane A, Caruana M, Nguyen DTN, Smith MA, Laprise JF, Jit M, Alary M, Bray F, Fidarova E, Elsheikh F, Bloem PJN, Broutet N, Hutubessy R. Lancet Jan 30 2020.

The elimination strategy emphasises acting immediately on three fronts

CCEMC modelling across 78 LMIC



Regional-level impact

- Over the next 10 years, about half (48%) of cervical cancer deaths averted in LMIC would be in **Sub-Saharan Africa** and almost a third (32%) would be in **South Asia** (including India, Afghanistan, Bangladesh, Bhutan, Nepal, Pakistan, Sri Lanka).
- Over the next century, almost 90% of deaths averted would be in these two regions.

Averted deaths by region, over 10, 50 & 100 year periods

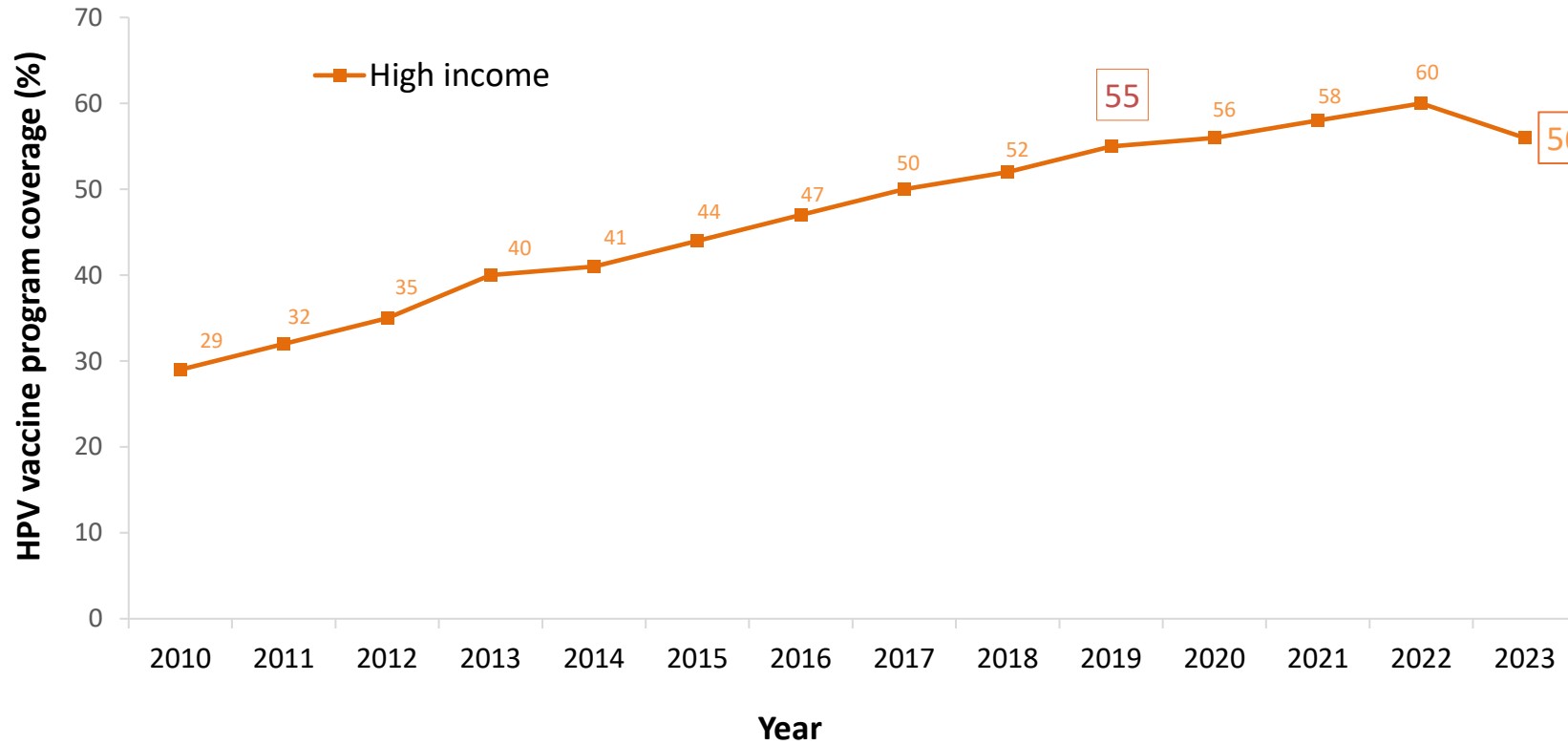
	All 78 LMICs	East Asia & Pacific	Europe & Central Asia	Latin America & Caribbean	Middle East & North Africa	South Asia	Sub-Saharan Africa
By 2030 (2020-2030)	0.3 (0.3-0.4)	0.0 (0.0-0.1)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.1 (0.1-0.1)	0.1 (0.1-0.2)
% of averted deaths in All-78 LMICs	-	16% (13-18%)	0% (0-1%)	1% (1-1%)	3% (1-3%)	32% (29-34%)	48% (45-55%)
By 2070 (2020-2070)	14.6 (14.1-14.6)	1.8 (1.6-1.8)	0.1 (0.1-0.1)	0.2 (0.2-0.2)	0.2 (0.2-0.3)	4.2 (3.9-4.4)	8.0 (7.9-8.1)
% of averted deaths in All-78 LMICs	-	12% (11-13%)	1% (1-1%)	1% (1-1%)	2% (1-2%)	29% (28-30%)	55% (54-57%)
By 2120 (2020-2120)	62.6 (62.1-62.8)	5.3 (4.9-5.4)	0.3 (0.3-0.3)	0.5 (0.5-0.5)	0.8 (0.7-0.9)	12.4 (11.8-12.7)	43.5 (43.0-43.7)
% of averted deaths in All-78 LMICs	-	9% (8-9%)	1% (0-1%)	1% (1-1%)	1% (1-1%)	20% (19-20%)*	69% (69-70%)*

Implementation: The next challenge



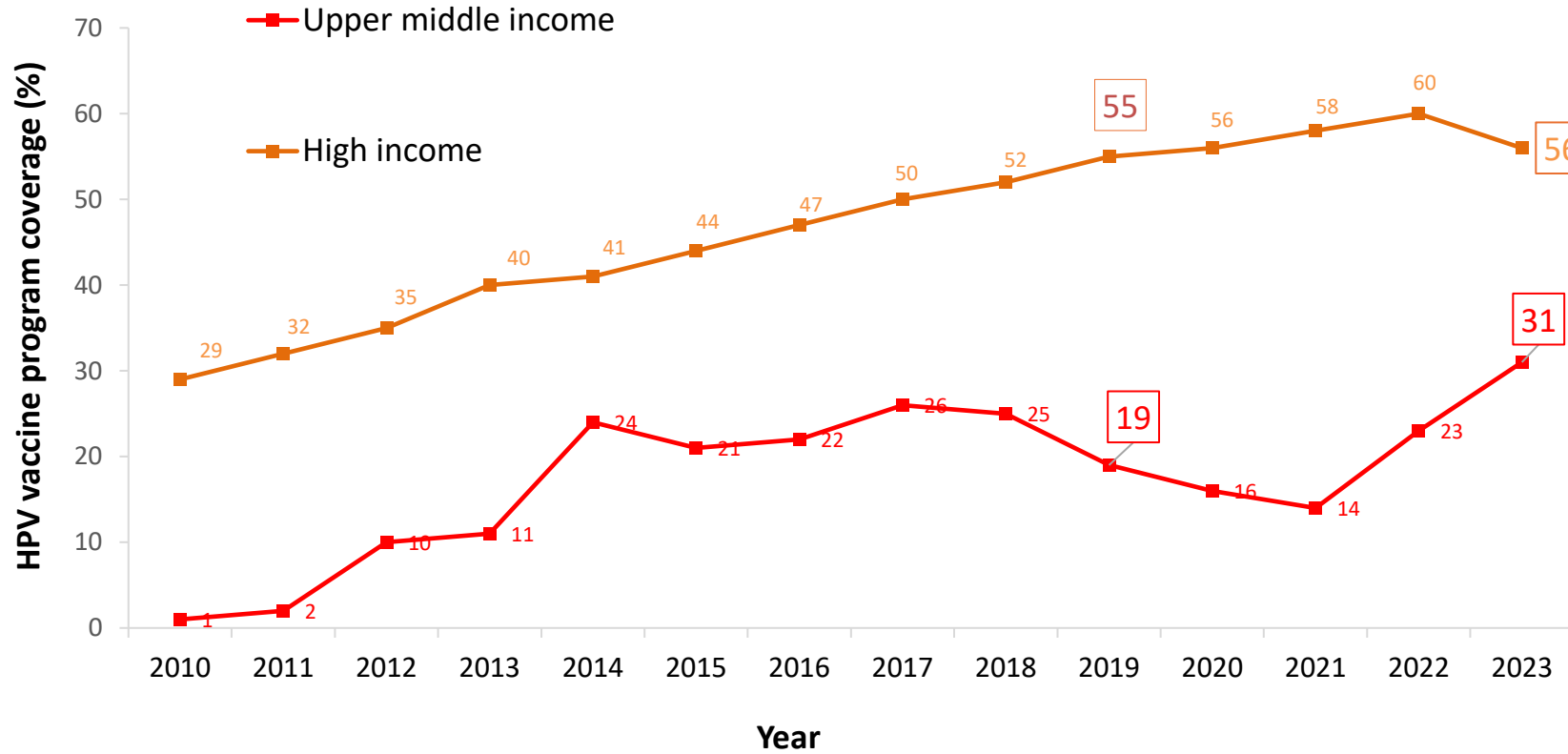
HPV vaccination coverage by country income category

Dose 1 coverage (girls to age 14 years)



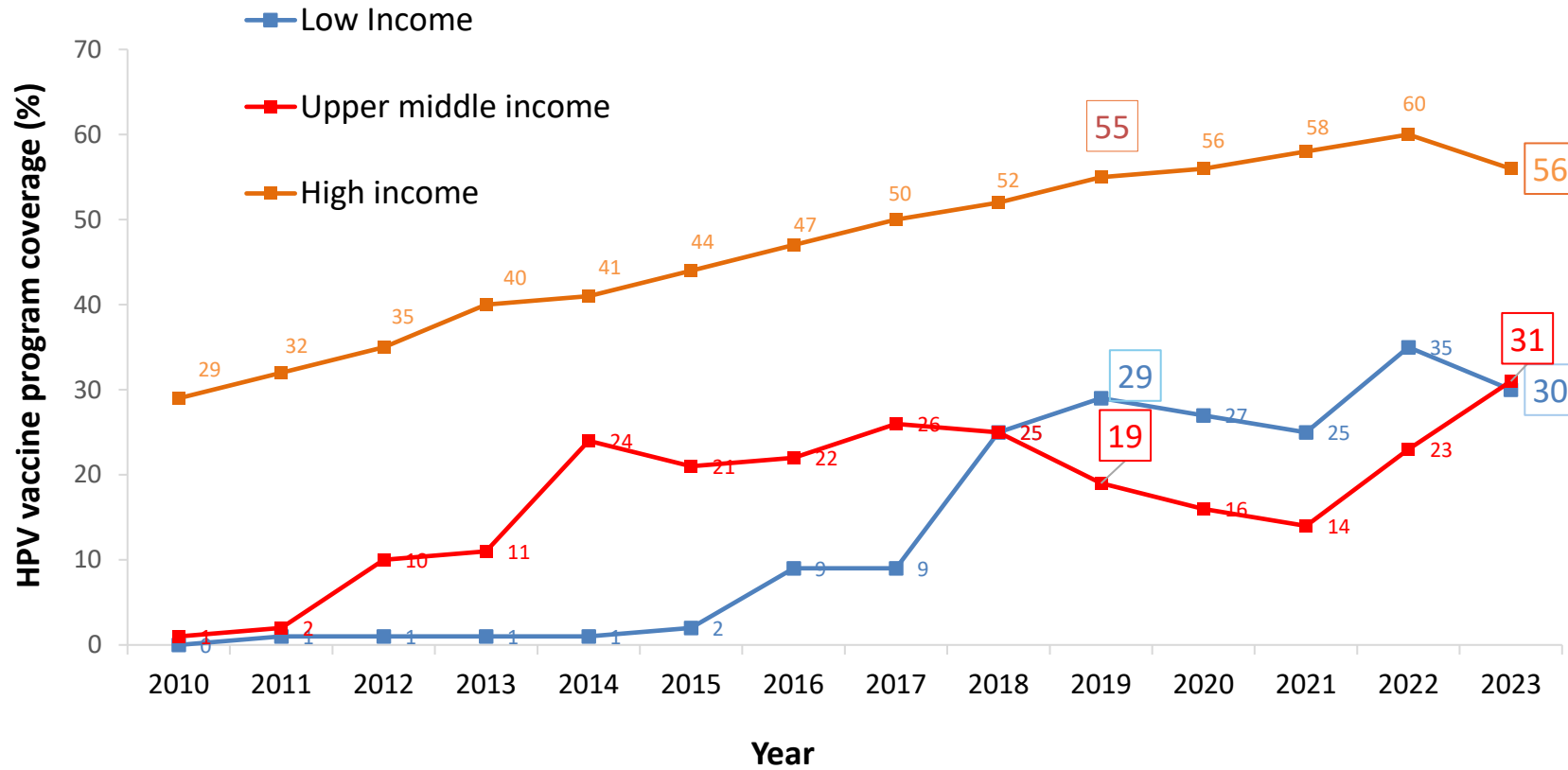
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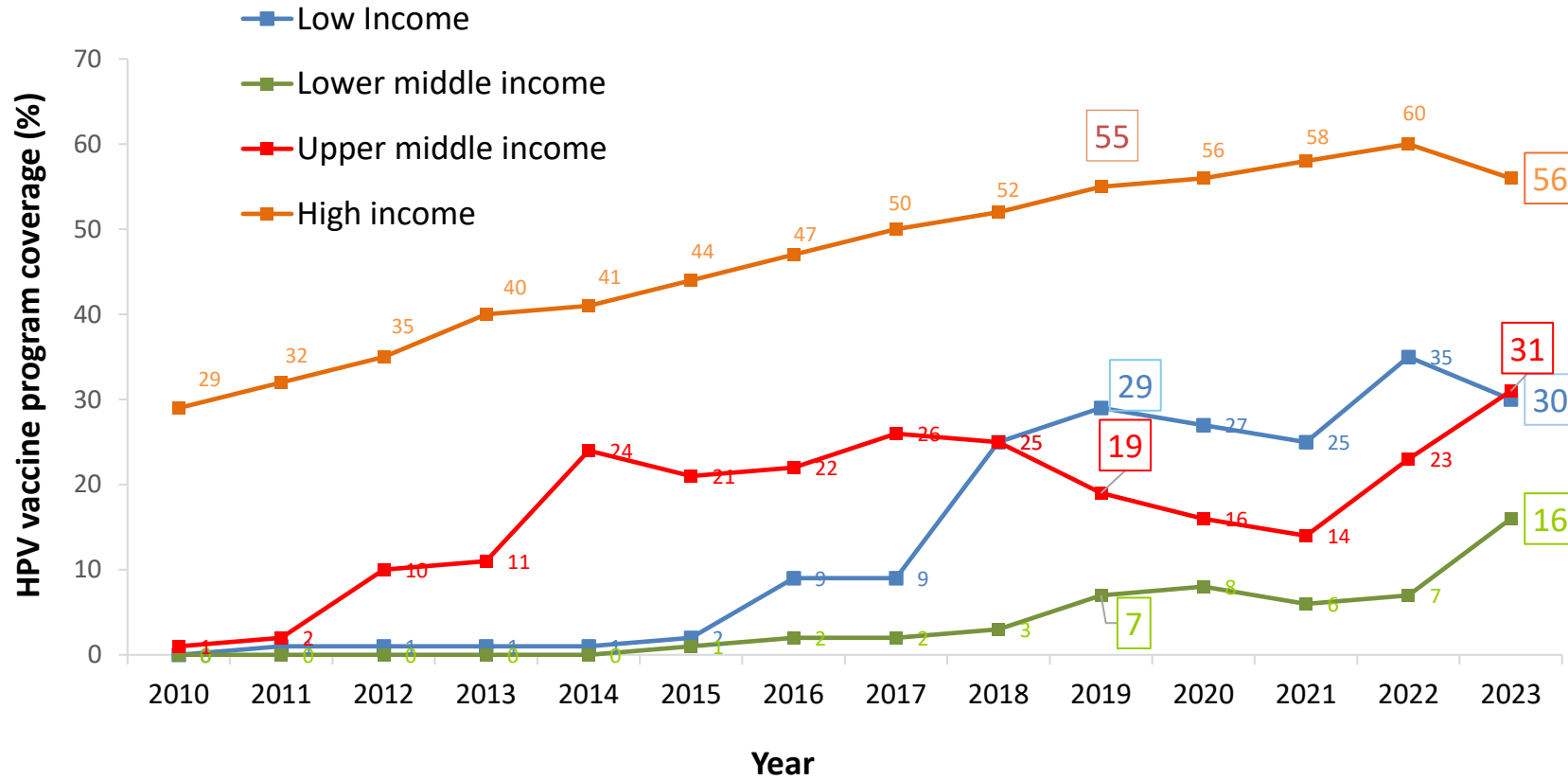
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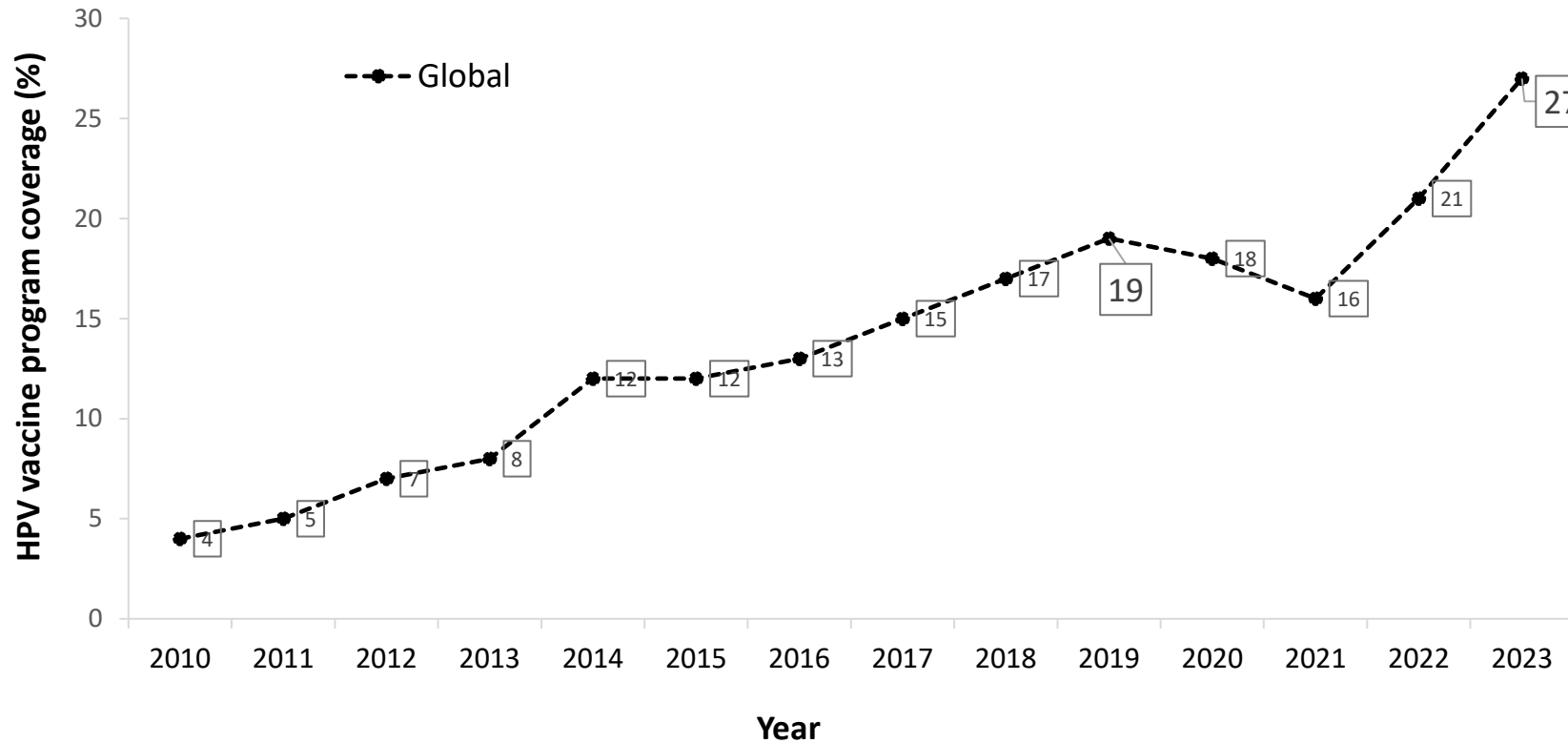
HPV vaccination coverage by country income category

Dose 1 coverage (girls to age 14 years)



HPV vaccination coverage by country income category

Dose 1 coverage (girls to age 14 years)



Global coverage dipped during the COVID-19 crisis but has recovered and increased overall:

From 19% in 2019 to 27% in 2023

WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition

nature medicine



Article

<https://doi.org/10.1038/s41591-023-02600-4>

Benefits, harms and cost-effectiveness of cervical screening, triage and treatment strategies for women in the general population

Received: 19 December 2022
Accepted: 19 September 2023
Published online: 12 December 2023
Check for updates

Kate T. Simms^{1,2*}, Adam Keane^{1,2}, Diep Thi Ngoc Nguyen¹, Michael Caruana³, Michaela T. Hall⁴, Gigi Lui⁵, Cindy Gauvreau^{6,7}, Owen Demk⁸, Marc Arbyn⁹, Partha Basu¹⁰, Nicolas Wentzensen¹¹, Beatrice Lauby-Secretan¹², Andre Tibawi¹³, Raymond Hutubessy¹⁴, Maribel Almonte¹⁵, Silvia De Sanjose¹⁶, Helen Kelly¹⁷, Shona Dalal¹⁸, Linda O. Eckert¹⁹, Nancy Santesso²⁰, Nathalie Broutet²¹ & Karen Canfell²²

nature medicine



Article

<https://doi.org/10.1038/s41591-023-02601-3>

Benefits and harms of cervical screening, triage and treatment strategies in women living with HIV

Received: 22 December 2022
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Check for updates

Michaela T. Hall^{1*}, Kate T. Simms², John M. Murray³, Adam Keane⁴, Diep T. N. Nguyen⁵, Michael Caruana⁶, Gigi Lui⁷, Helen Kelly⁸, Linda O. Eckert⁹, Nancy Santesso¹⁰, Silvia de Sanjose¹¹, Edwin E. Swal¹², Ajay Rangaraj¹³, Morkor Newman Owiredu¹⁴, Cindy Gauvreau¹⁵, Owen Demk¹⁶, Partha Basu¹⁷, Marc Arbyn¹⁸, Shona Dalal¹⁹, Nathalie Broutet²⁰ & Karen Canfell²¹

A critical enabler: new screening guidelines from WHO

“WHO recommends using HPV 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”

EPICC: Elimination Partnership for Cervical Cancer in the Indo-Pacific



ELIMINATION PARTNERSHIP IN THE
INDO-PACIFIC FOR CERVICAL CANCER

The ffodil Centre

A partnership between



THE UNIVERSITY OF
SYDNEY



Kirby Institute



Australian Centre
for the Prevention of
Cervical Cancer



Unitaid



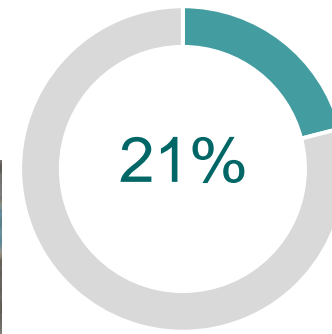
family
planning
australia



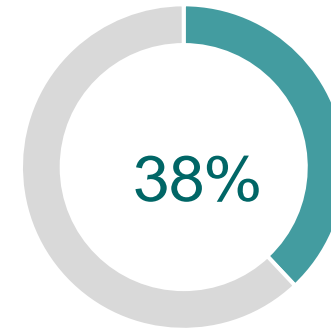
EPICC in Vanuatu



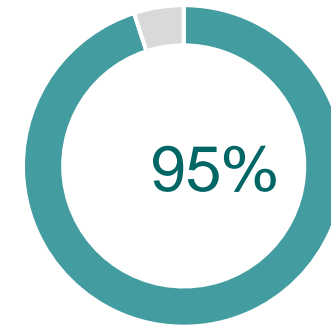
20,000 age-eligible girls for HPV vaccination and 34,000 age-eligible women for HPV screening



HPV vaccination



HPV-based cervical screening



Treatment of cancer and precancer



MINISTRY OF HEALTH
GOVERNMENT OF VANUATU



**ELIMINATION PARTNERSHIP IN THE
INDO-PACIFIC FOR CERVICAL CANCER**

March 5th, 2024



Wave of new commitments marks historic step towards the elimination of cervical cancer

New country, policy and program commitments, plus nearly US\$ 600 million in new funding, at first-ever global forum offer a chance to save hundreds of thousands of lives by 2030.

5 March 2024 | News release | Cartagena de Indias, Colombia | Reading time: 7 min (1828 words)

Governments, donors, multilateral institutions, and partners today announced major new policy, programmatic and financial commitments, including nearly US\$ 600 million in new funding, to eliminate cervical cancer. If these ambitions to expand vaccine coverage and strengthen screening and treatment programs are fully realized, the world could eliminate a cancer for the first time.

September 21st, 2024



[Administration](#)

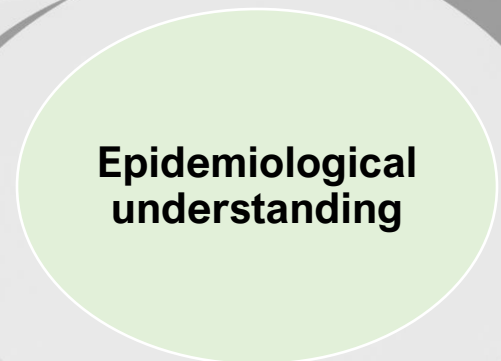
SEPTEMBER 21, 2024

Fact Sheet: Quad Countries Launch Cancer Moonshot Initiative to Reduce the Burden of Cancer in the Indo-Pacific

[BRIEFING ROOM](#) | [STATEMENTS AND RELEASES](#)

Today, the United States, Australia, India, and Japan are launching a groundbreaking effort to help end cancer as we know it in the Indo-Pacific, starting with cervical cancer, a largely preventable disease that continues to be a major health crisis in the region, and laying the groundwork to address other forms of cancer as well. This initiative is part of a broader set of announcements made at the [Quad Leaders Summit](#).





**Epidemiological
understanding**

**Implementation in both high & low-
income settings, supported by
localized evidence & modelling**

**Population modelling
of outcomes and costs
if interventions
combined and scaled**

**Systematic review &
meta-analysis of
intervention
effectiveness**

**Ecological
analysis of STI
association**

**Real-world
outcomes
data**

**Molecular
analyses of
HPV in cancer**

**RCTs of
vaccination &
screening**

**Global strategic planning
& WHO call-to-action**

**Global advocacy for
increased resourcing
and coordination of
activities**

**Major commitments by
governments, the NFP
and private sectors**



Save the date

FOR THE FIRST TIME EVER,

**the world has committed
to eliminate a cancer.**

EVERYONE IS INVITED TO JOIN THE LAUNCH

Since Dr. Tedros' Call to Action in May 2018, the world has responded: in August 2020, the World Health Assembly passed a resolution calling for elimination of cervical cancer and adopting a strategy to make it happen.

On November 17, following the close of the 73rd World Health Assembly, WHO will mark this historic announcement and officially launch the elimination strategy.

Women who have survived cervical cancer from all regions of the world - women who have fought the disease - will open the event. All around the world, companion events and launch activities will mark a day of action.

The moment has arrived for an ambitious, concerted and inclusive strategy to accelerate eliminating cervical cancer as a public health problem.

**17th
November
2020**

1430-1600 CET

EVERYONE IS INVITED
TO JOIN THE LAUNCH

FIND OUT MORE

**CERVICAL
CANCER
FREE
FUTURE**



World Health
Organization

With grateful acknowledgement to:

The Cervical and HPV Stream at The Daffodil Centre: Dr Kate Simms, A/Prof Megan Smith, Prof Deborah Bateson, Ms. Chloe Jennet, Ms. Caitlin McLachlan, Mr. Timothy Balshaw, Ms. Laura Sergeant, Dr Adam Keane, Dr James Killen, Dr Diep Nyugen, Dr Michaela Hall, Dr Xin An, Ms. Susan Yuill, Ms. Dominique Louw, Dr Daniela Rivas, Dr, Louiza Velentzis, Dr, Michael Caruana, Dr Telma Costa, Dr, Matthew Palmer, Dr Monjura Nisha, Dr Rubana Islam, Dr Elizabeth Kennedy, Dr Lauren Winkler, Ms. Kay Rimalos, Ms. Helen Liang, Ms. Gigi Lui, and special thanks to Anna Kelly.

Members of the NHMRC Centre for Research Excellence in Cervical Cancer Control (C4)

Other leads for the WHO Global Cervical Cancer Elimination Modelling Consortium (CCEMC): Dr. Jane Kim, Dr. Marc Brisson and Dr. Raymond Hutubessy & their teams

The I-PaRCS consortium members and Steering Group: Dr Isabelle Soerjomataram, Dr Freddie Bray, Mr Rami Rahal, Dr Julie Torode, A/Prof Iris Lansdorp-Vogelaar, Dr. Ophira Ginsberg & Prof Richard Sullivan..

Mirabel Alimante, Nathalie Broutet, Linda Elkhart and the WHO Cervical Screening & Treatment Guidelines Working Group and Guidelines Development Group

The International Cancer Benchmarking Partnership; Cancer Research UK: Elle Pearson, Alexander Wright

Other CISNET-Cervical PIs and their teams: Jane Kim, Shalini Kulasingam, Inge de Kok & Ruanne Barnabas

Other EPICC Leads: Andrew Vallely, Deborah Bateson, Marion Saville, Kristine Macartney, Ted Trimble, Vanessa Price, Anne Stuart, Kirstie Graham, Sanchia Aranda

Other collaborators whose work I have highlighted here: Dr Florence Guida & Prof Valerie McCormack, Dr Hiroki Akaba, Dr. Emily Burger.

The women and people, families and communities impacted by cervical cancer

