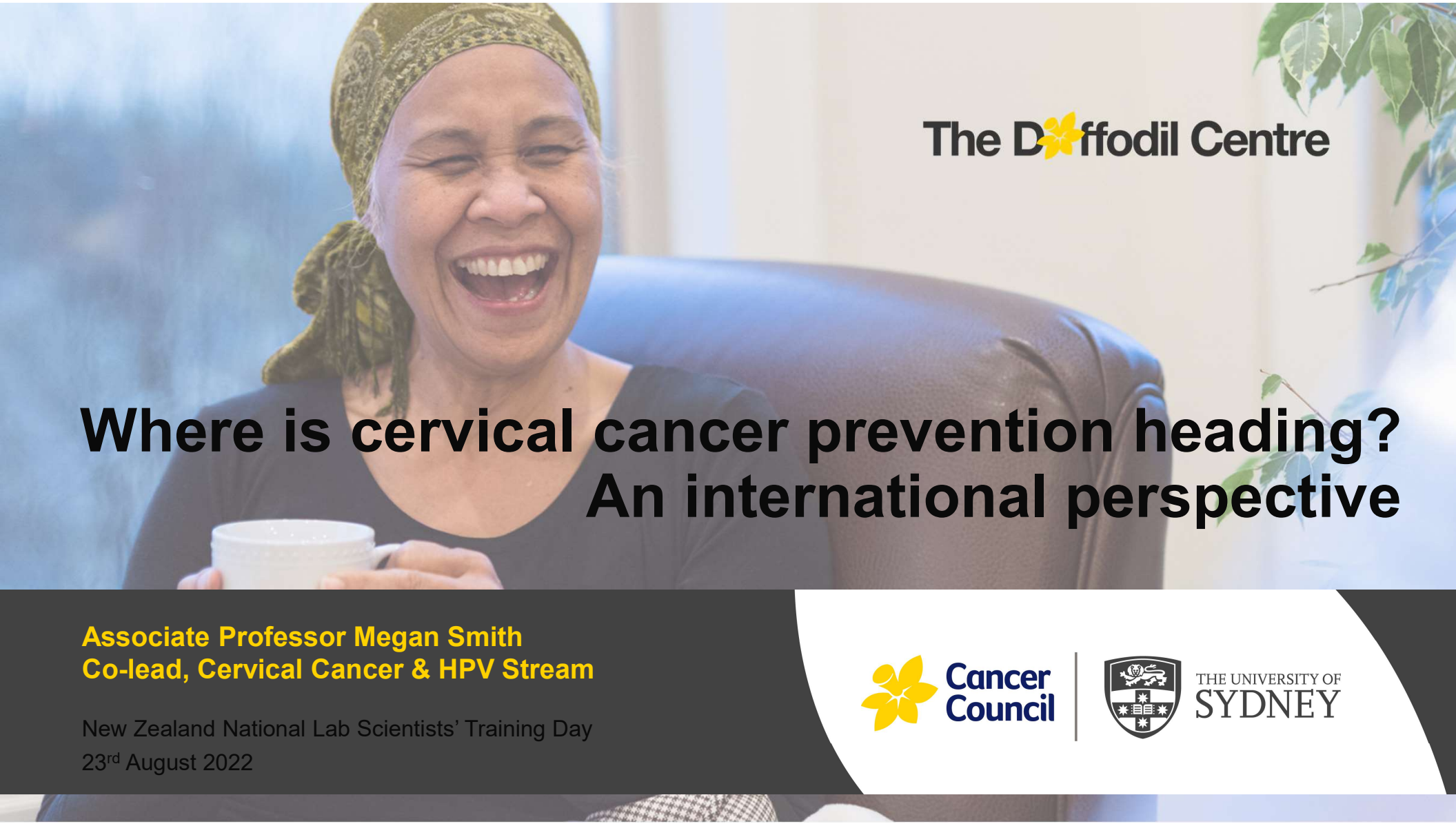
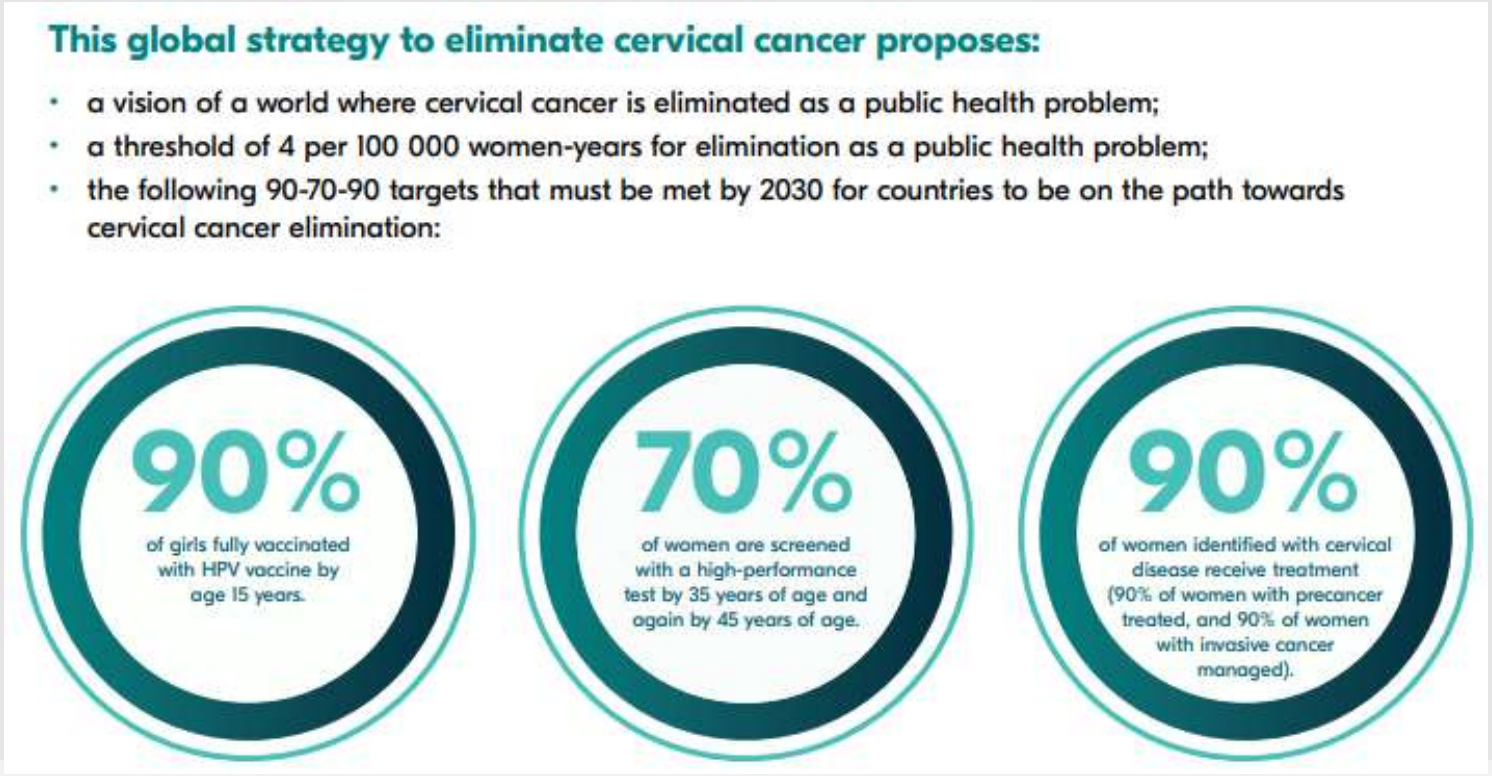


Where is cervical cancer prevention heading? An international perspective

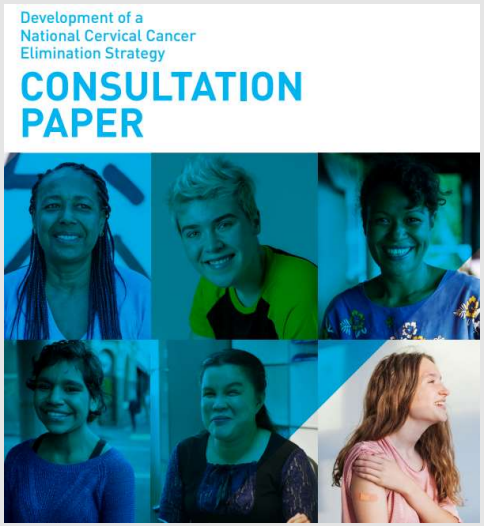
Associate Professor Megan Smith
Co-lead, Cervical Cancer & HPV Stream

New Zealand National Lab Scientists' Training Day
23rd August 2022

World-first – eliminating a cancer

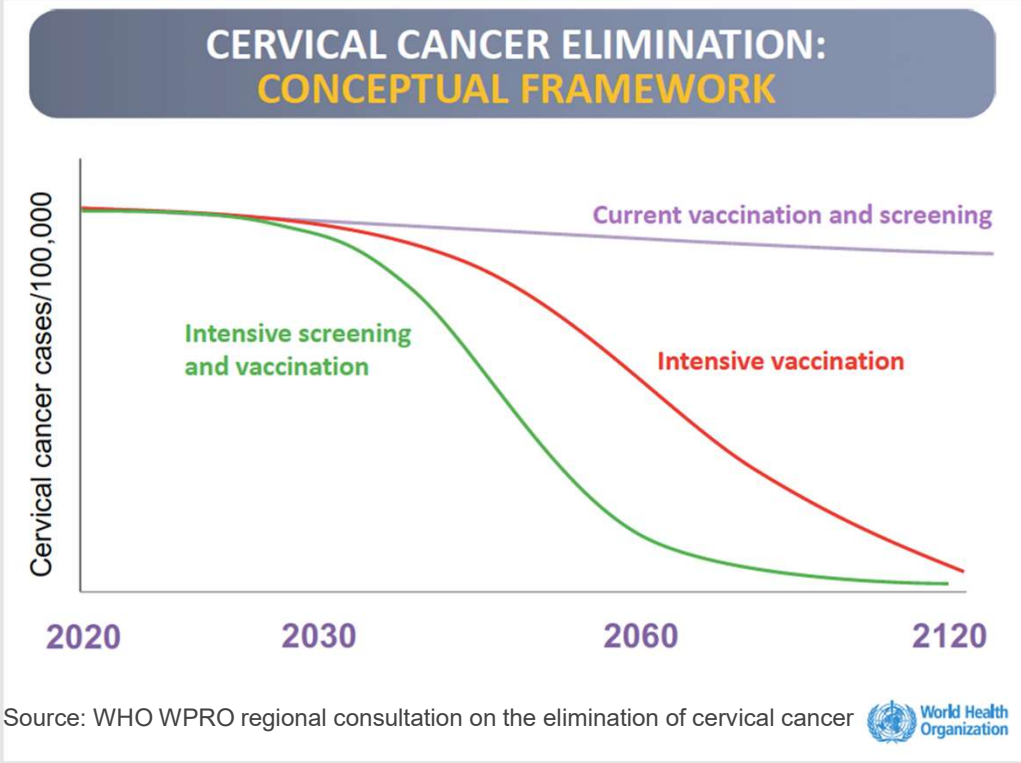


High-performance test = HPV test (or potential future equivalent)



Country-specific strategies and action plans

Cervical screening drives elimination timing



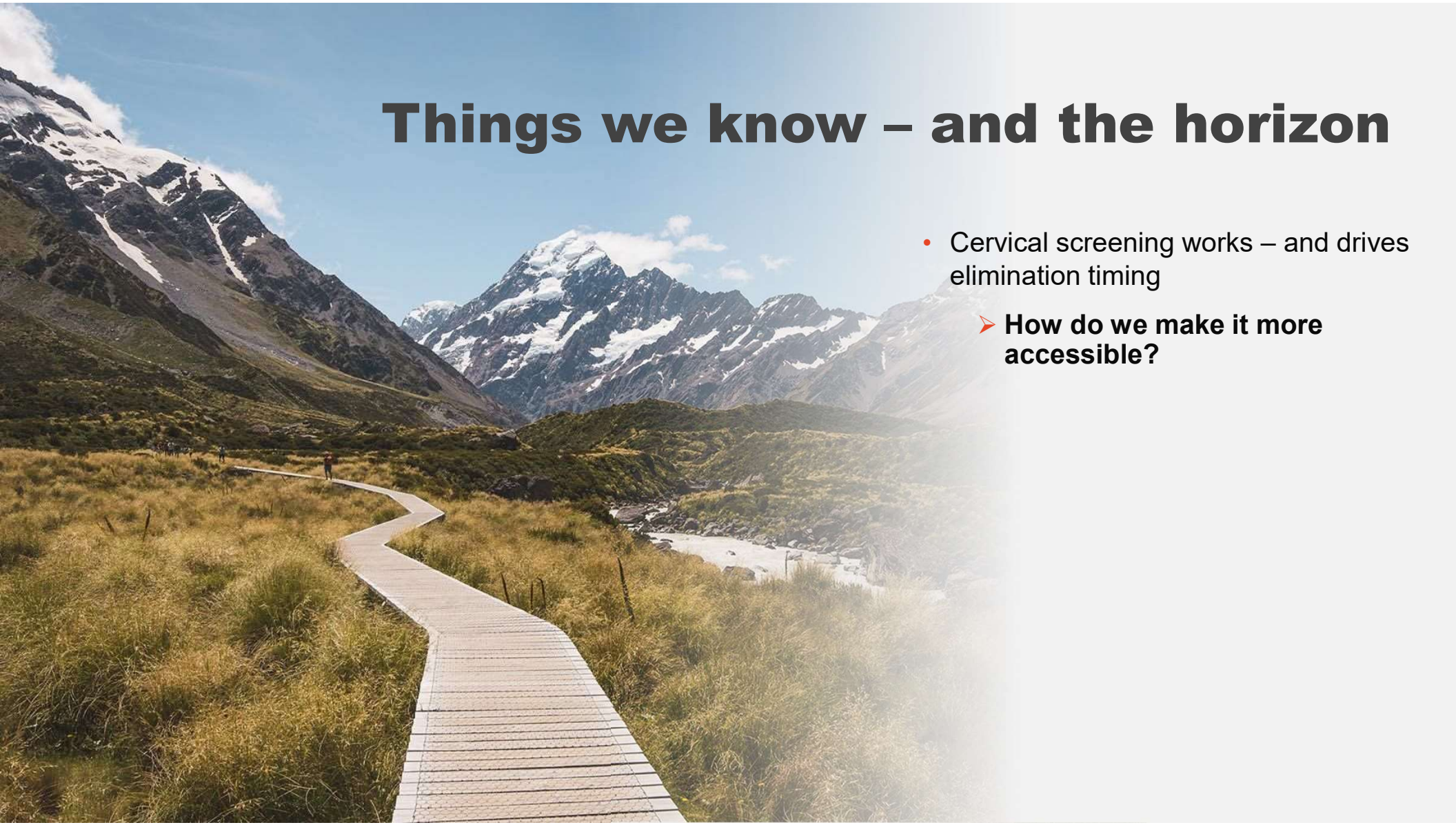
Source: WHO WPRO regional consultation on the elimination of cervical cancer

Different starting points, same pattern

NZ: screening only

NZ: screening + vaccination

NZ: **scaled-up** screening + vaccination



Things we know – and the horizon

- Cervical screening works – and drives elimination timing
  - **How do we make it more accessible?**

Who misses out on screening?

International studies

Who you are

- Indigenous people
- Culturally and linguistically diverse communities
- LGBTIQ+
- People with disabilities
- People who have experienced sexual violence

Where you live

- More remote areas
- More disadvantaged areas

Socioeconomic status

- Financial barriers
- Education/ health literacy
- Awareness
- Competing priorities

Making screening more accessible

- Self-collection
- Accessible clinics
  - Outreach, mobile
  - People with a disability
  - Point-of-care tests
  - Community-controlled services
  - Peer-led services LGBTQI+
- Non-medical providers

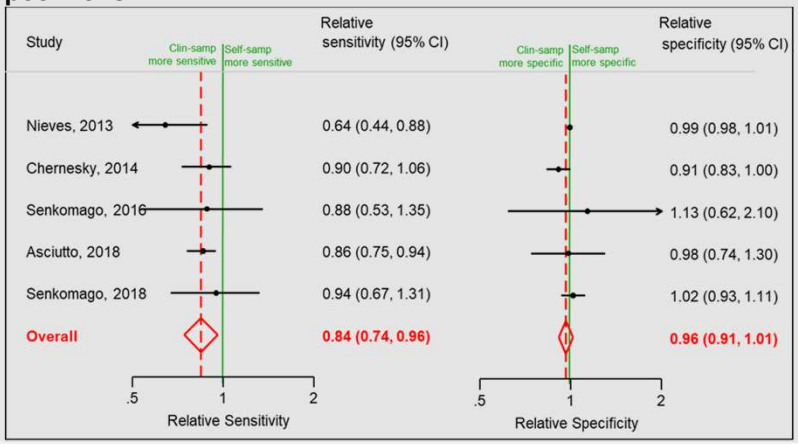
Things we know – and the horizon

- Cervical screening works – and drives elimination timing
  - **How do we make it more accessible?**
- HPV testing is risk-based screening
  - **How can we make it better?**

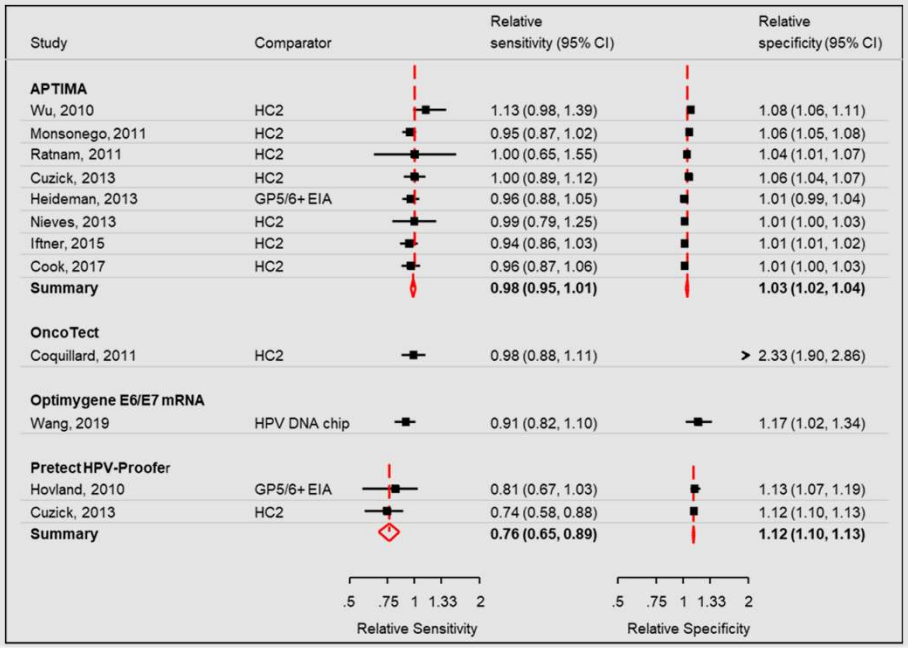
Improving risk identification

- HPV mRNA vs DNA
  - Clinician cervical samples: mRNA equivalent sensitivity, slightly higher specificity
  - Self-collected vaginal samples: lower sensitivity

Relative sensitivity (left) and specificity (right) to detect CIN2+ of hrHPV mRNA testing versus hrHPV DNA on self-collected vaginal specimens



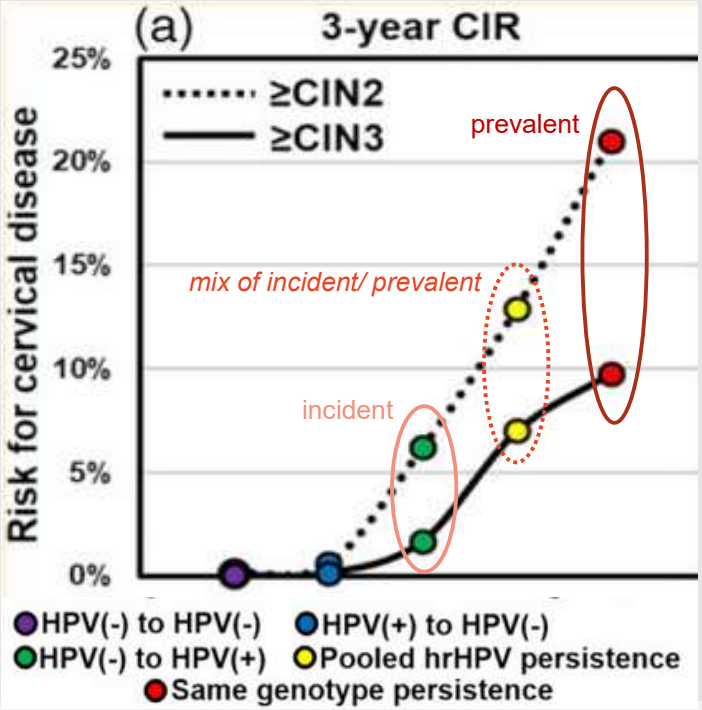
Relative sensitivity (left) and specificity (right) to detect CIN2+ of hrHPV mRNA testing versus hrHPV DNA on clinician-collected cervical specimens



Improving risk identification

- HPV mRNA vs DNA
- Prevalent vs incident HPV detection/ screening round
  - screening round vs detection in an individual
  - ~half of those persistently positive on a pooled test had genotype switch

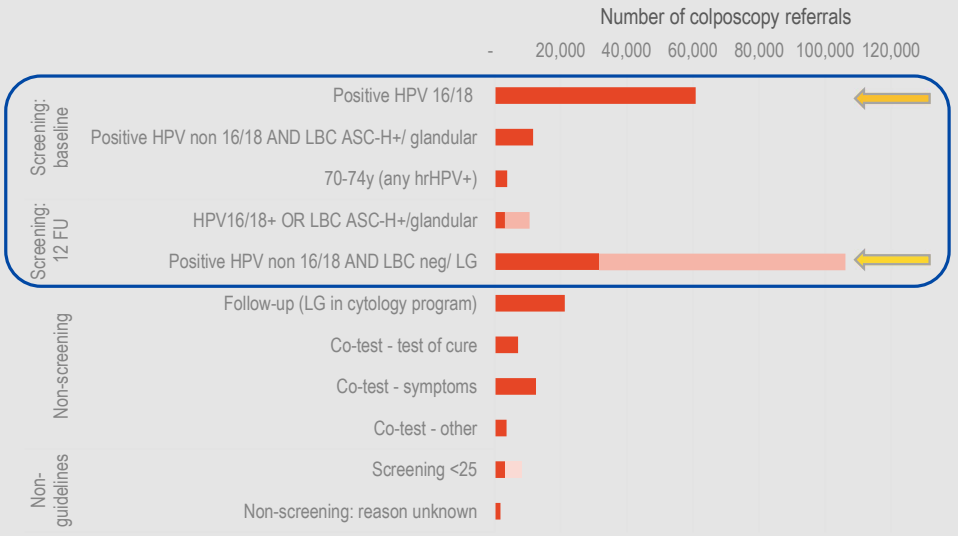
Cumulative incident risk for high-grade cervical disease according to HPV status at the first and subsequent test



Bonde *et al*, J Low Genit Tract Dis. 2021. Human Papillomavirus Same Genotype Persistence and Risk: A Systematic Review.

Improving risk identification

- HPV mRNA vs DNA
- Prevalent vis incident HPV detection/ screening round



Triage

- LBC
  - HPV16/18+: ~30% referrals (decreasing; <15% 25-29y)
  - Non-16/18 without ASC-H+: ~56% referrals (>70% 25-29y)

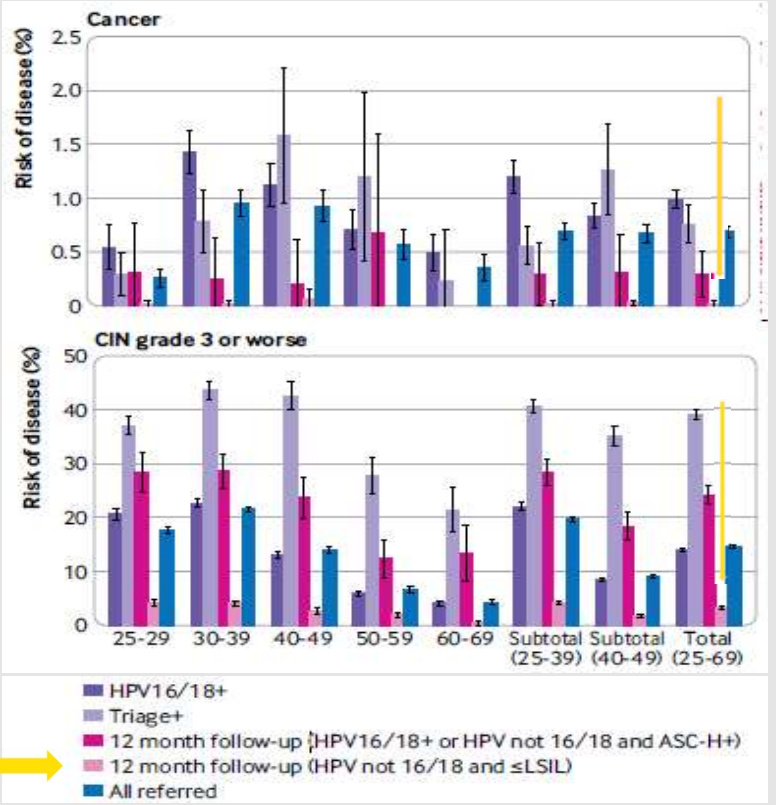
Smith *et al*, BMJ 2022. National experience in the first two years of primary HPV cervical screening in an HPV vaccinated population in Australia: observational study

Improving risk identification

- HPV mRNA vs DNA
- Prevalent vis incident HPV detection/ screening round

Triage

- LBC
  - HPV16/18+: ~30% referrals (decreasing; <15% 25-29y)
  - Non-16/18 without ASC-H+: ~56% referrals (>70% 25-29y)
  - Low risk, even with 12m persistence
    - Updated guidelines in Au; incorporated in NZ draft



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Improving risk identification

- HPV mRNA vs DNA
- Prevalent vis incident HPV detection/ screening round

Triage

- LBC
- Extended genotyping

Adapted from: Bonde *et al*, Journal of Lower Genital Tract Disease. 2021;25(1):27-37 and Demarco *et al*, E Clinical Medicine 2020;22:100293.

HPV type	Rationale	7-year CIN3+ risk	Suggested management
16	uniquely carcinogenic and should be individually distinguished	22%	Colposcopy
18,45	Risk of SCC and adenocarcinoma	>5%	Closely monitor
31,33		>5%	Closely monitor
52,58	Higher risk than remaining types	>5%	Repeat testing; 18-month CIN3+ risk <5% for LG cytology
39,51,56,59,68 (66)	Very little risk if precancer is not immediately found	<5%	Repeat testing unless associated with HG cytology

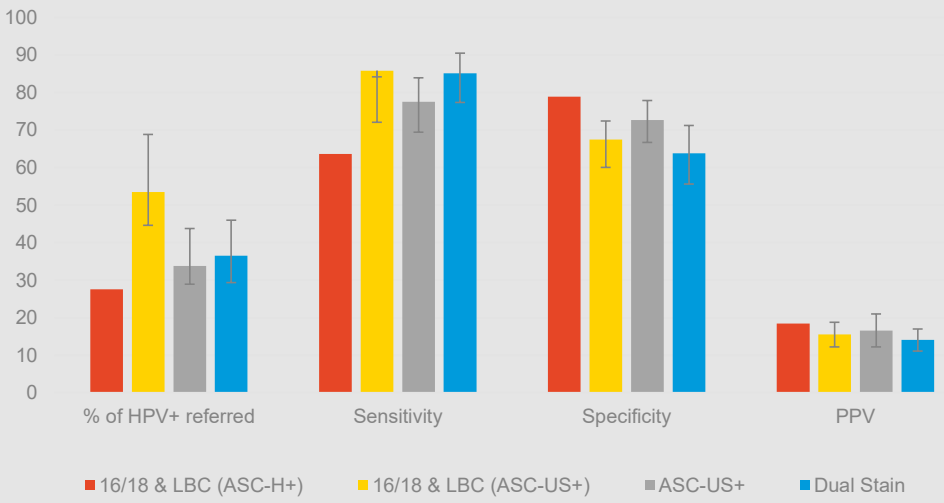
Improving risk identification

- HPV mRNA vs DNA
- Prevalent vis incident HPV detection/ screening round

Triage

- LBC
- Extended genotyping
- p16/ki67 dual-stained cytology

Performance measures for different <u>one-time</u> triage approaches (CIN3+)



Adapted from: IARC Handbook of Cancer Prevention 18 Cervical Cancer Screening (2022) and Smith *et al*, BMJ 2022 (results for 16/18 & LBC (ASC-H+).

Improving risk identification

- HPV mRNA vs DNA
- Prevalent vis incident HPV detection/ screening round

Triage

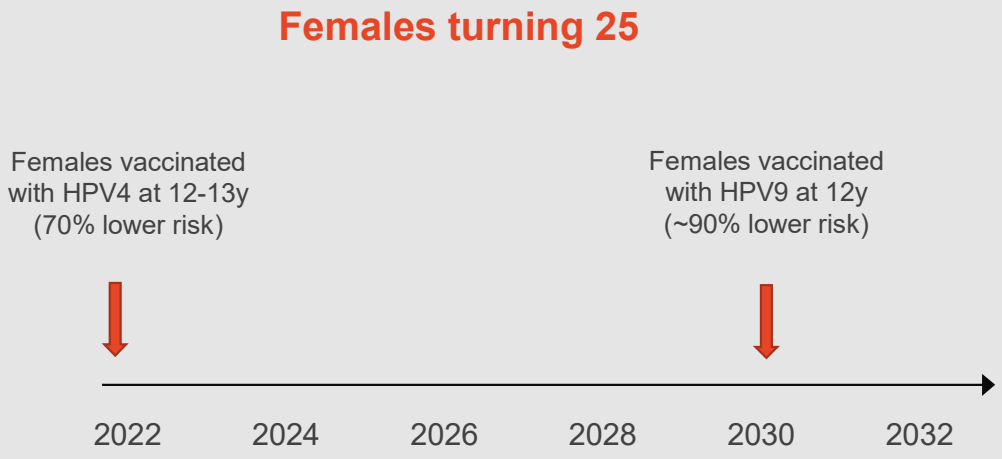
- LBC
- Extended genotyping
- p16/ki67 dual-stained cytology
- Methylation

Things we know – and the horizon

- Cervical screening works – and drives elimination timing
  - **How do we make it more accessible?**
- HPV testing is risk-based screening
  - **How can we make it better?**
- HPV vaccination is maturing
  - **What will future generations need?**

Cohorts vaccinated at 12-13y are entering screening

- Oldest vaccinees in NZ in 2022 aged ~32y



Simms *et al*, Int J Cancer 2016. Will cervical screening remain cost-effective in women offered the next generation nonavalent HPV vaccine? Results for four developed countries.

Vaccination changes screening trade-offs

Cancer type	Screening strategy	Population	Estimated outcomes per annum [a]			NNT per cancer death prevented [b]	CER ($ per life-year saved) [b,c,d]
			# of cancer deaths prevented [b]	# of diagnostic assessments [b]	Cost [b,c]		
Cervical Cancer	Renewed NCSP	Not vaccinated	1,279	121,575 colp.	$214 million	95	$16,632
	Renewed NCSP	HPV4 vaccinated	302	46,630 colp.	$156 million	154	$66,893
	Renewed NCSP	HPV 9 vaccinated	153	22,175 colp.	$126 million	145	$102,897
Bowel cancer	NBCSP	Average-risk	2,519	114,015 col.	$1,410 million	42	$3,380
Breast Cancer	BreastScreen Australia	Average-risk	580	41,763 assessments	$316 million	62	$23,713 - $38,302
Lung Cancer	Three rounds of annual LDCT Screening for high-risk smokers aged 55-74 years	High-risk smokers	N/A	N/A	N/A	N/A	$154,776

CER - cost-effectiveness ratio; col. – colonoscopy; colp. - colposcopy; HPV4- quadrivalent HPV; HPV9-nanvalent HPV; LDCT = low-dose computed tomography; NBCSP- National Bowel Cancer Screening program NCSP- National Cervical Screening Program; NNT- number-needed-to-treat.

[a] Assuming the projected 2020 Australian population

[b] Compared with no screening

[c] In 2018 AUD

[d] In 2009 AUD. After inflation to 2018 AUD, the cost-effectiveness ratios are $40 279/LYS (>40 years) and $65 065 (>20 years)

NNT: for cervical screening, this is the number of COLPOSCOPIES per death prevented

Lew *et al*, Pub Health Res Prac 2019. Benefits, harms and cost-effectiveness of cancer screening in Australia: an overview of modelling estimates.

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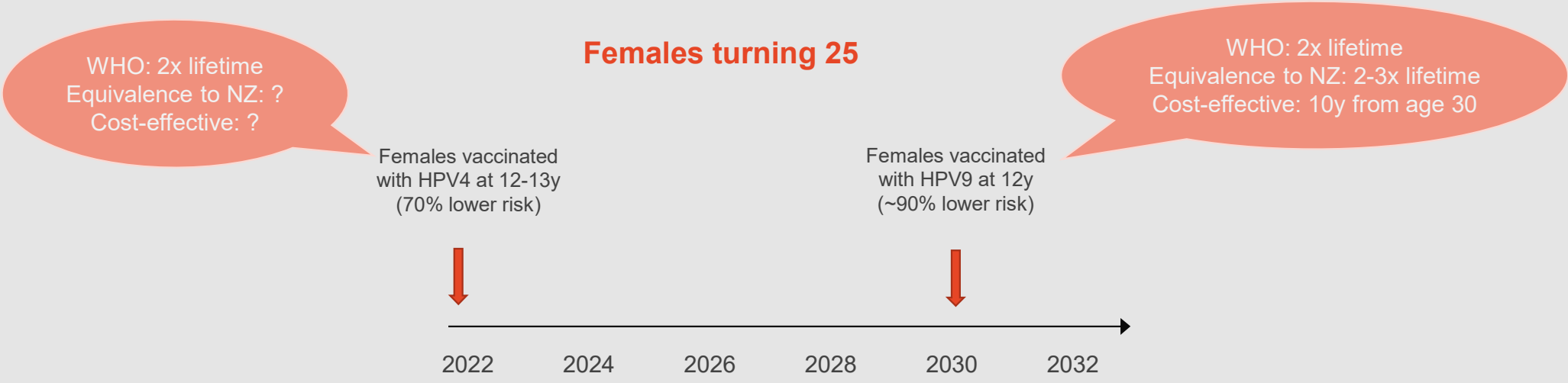
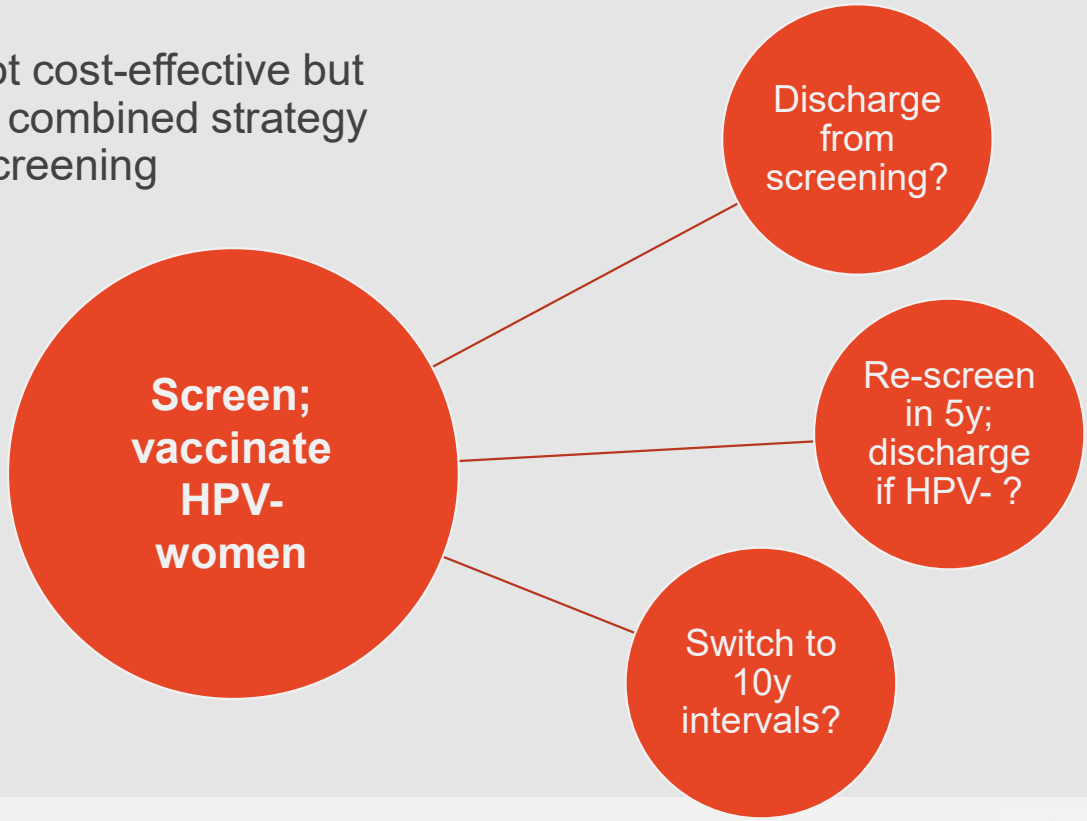


Simms *et al*, Int J Cancer 2016. Will cervical screening remain cost-effective in women offered the next generation nonavalent HPV vaccine? Results for four developed countries.

Screening and vaccination

Vaccination at older ages not cost-effective but could become so if part of a combined strategy to reduce/ discharge from screening

Example:



Simms *et al*, manuscript in preparation

Things we know – and the horizon

- Change will continue
  - **Opportunities**

Thank you

The Daffodil Centre

Cancer Council | THE UNIVERSITY OF SYDNEY