The Future of Cervical Cancer Prevention in the United States: The Realities of Evidence Beyond Innovation

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Disclosures

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Worldwide, the recognition that Human Papillomaviruses (HPVs) cause virtually all cervical cancer enabled innovations of HPV vaccination and HPV-based screening

The World Health Organization has promulgated accelerating the elimination of cervical cancer as a global public health problem

World Health Organization (WHO) Call to Action
A Global Strategy for cervical cancer elimination

Dr Tedros Adhanom Ghebreyesus Director-General

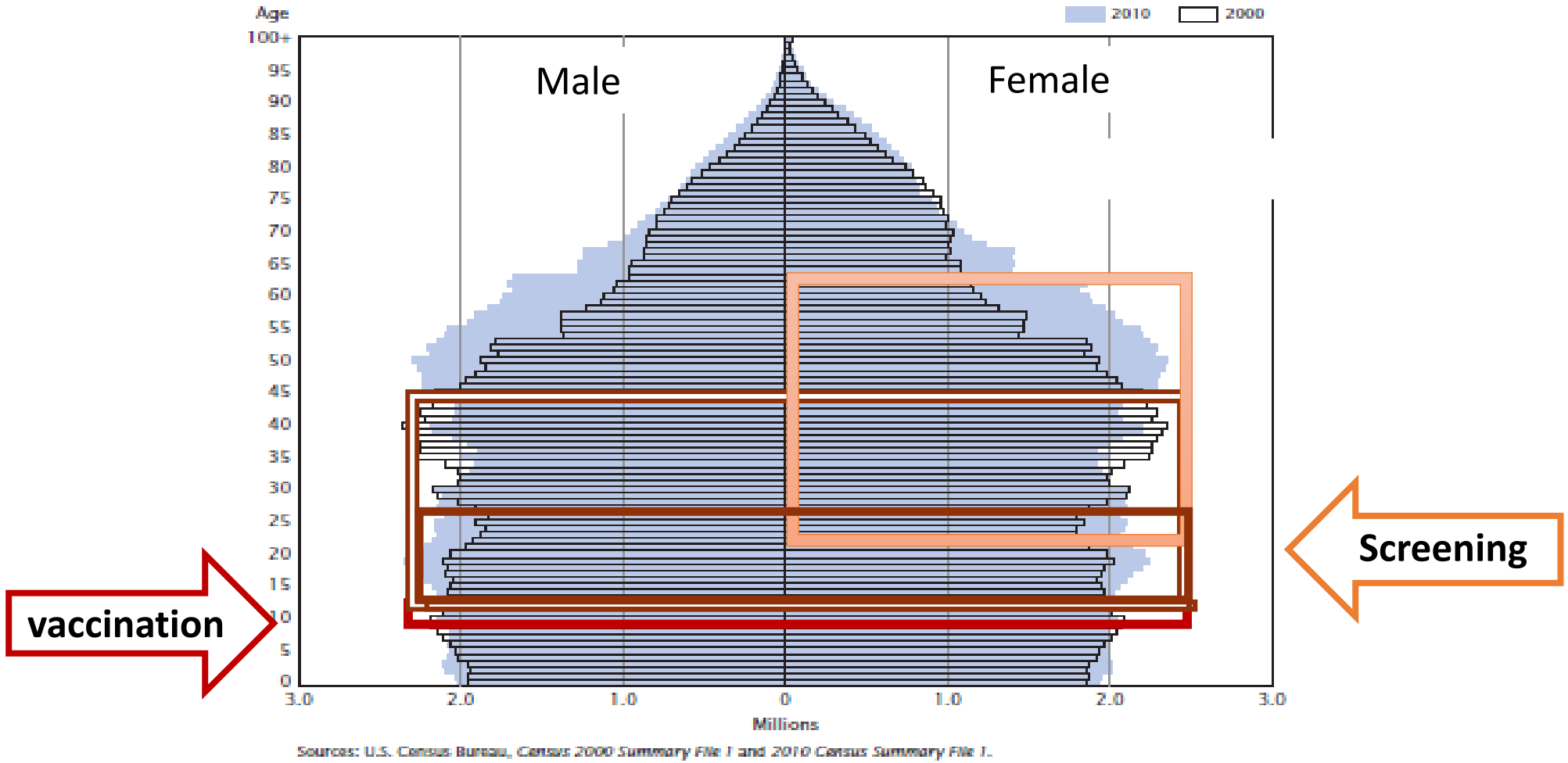
To achieve a threshold of
4 cervical cancer cases per 100 000 women-years

The following 2030 targets were set :

- Vaccination: **90%** of girls fully vaccinated with the HPV vaccine by the age of 15;
- Screening: **70%** of women screened using a high-performance test by the age of 35, and again by the age of 45;
- Treatment: **90%** of women with pre-cancer treated and 90% of women with invasive cancer managed.

To eliminate cervical cancer within the next century will these targets be reached in the US?

Cervical Screening and Vaccination is a MAJOR Health Care Investment but cervical cancer mortality rates have not yet changed for multiple decades ?



Cervical Cancer Prevention has been estimated to cost up to $7-8 billion annually

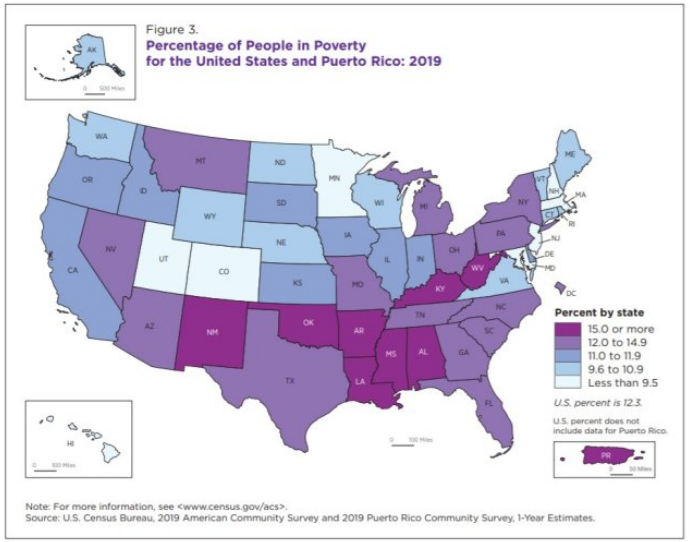
Vaccination adds $1.5 to 2 billion additional costs for 11-12 alone

Vaccination and screening must be integrated

OR it will increase cost by billions annually as will coverage of catch-up vaccination

In the United States, cervical cancer remains primarily a failure
1- to screen women and ….
2- to a lesser extent, a failure to follow-up women with abnormal results

- **Both of these failures have been associated with inequities**

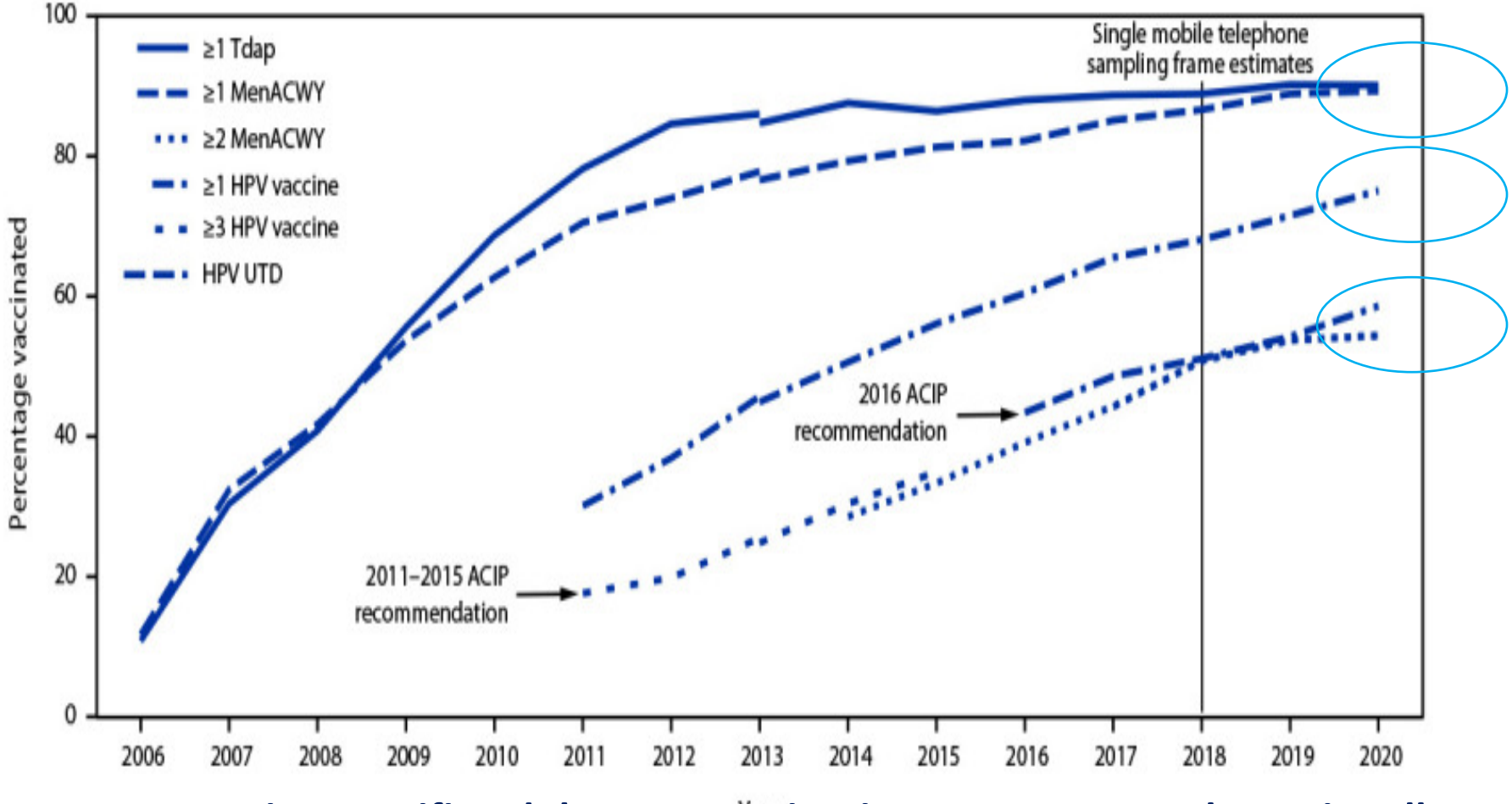


  - racial and ethnic minorities
  - lower educational attainment and health literacy
  - higher levels of poverty
  - living in rural vs urban settings
  - lower levels of acculturation including language
  - being uninsured or covered by public vs private or military insurance
  - not having a usual source of care or medical “home”
  - older age

The focus of the last several decades has been on HPV-based technological innovations to improve primary and secondary prevention

- **PRIMARY PREVENTION (HPV vaccination)**
  - Licensure of HPV vaccine (3 dose [2006] to 2 dose [2016] to 1 dose strategies [ongoing])
  - Substantial research, industry and healthcare dollars have been expended to overcome HPV vaccine uptake barriers to achieve higher population HPV vaccine coverage but we may be coming to a plateau

Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17 years, by year — National Immunization Survey–Teen,[1] USA, 2006–2020



New Mexico-specific Adolescent Vaccination 2020 Data Tracks Nationally

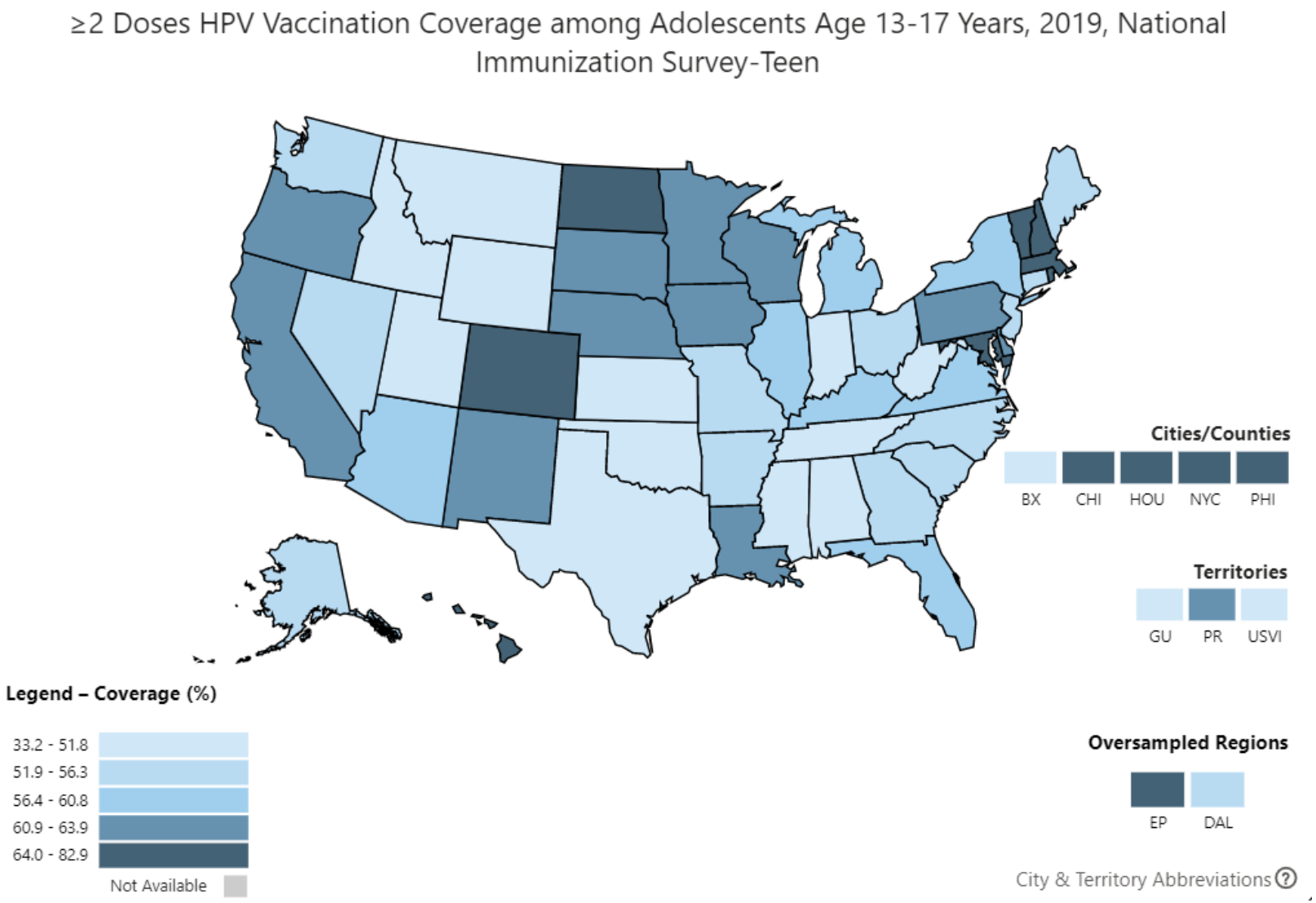
≥1 Tdap	89.3 (84.9–92.6)
≥1 MenACWY	85.2 (80.1–89.2)
≥1 HPV	77.4 (71.9–82.0)
HPV UpToDate (UTD)	59.2 (53.0–65.1)

Will HPV vaccination exceed 70-75% without mandates or will we fail ?

Being HPV vaccinated correlates with getting cervical screening.

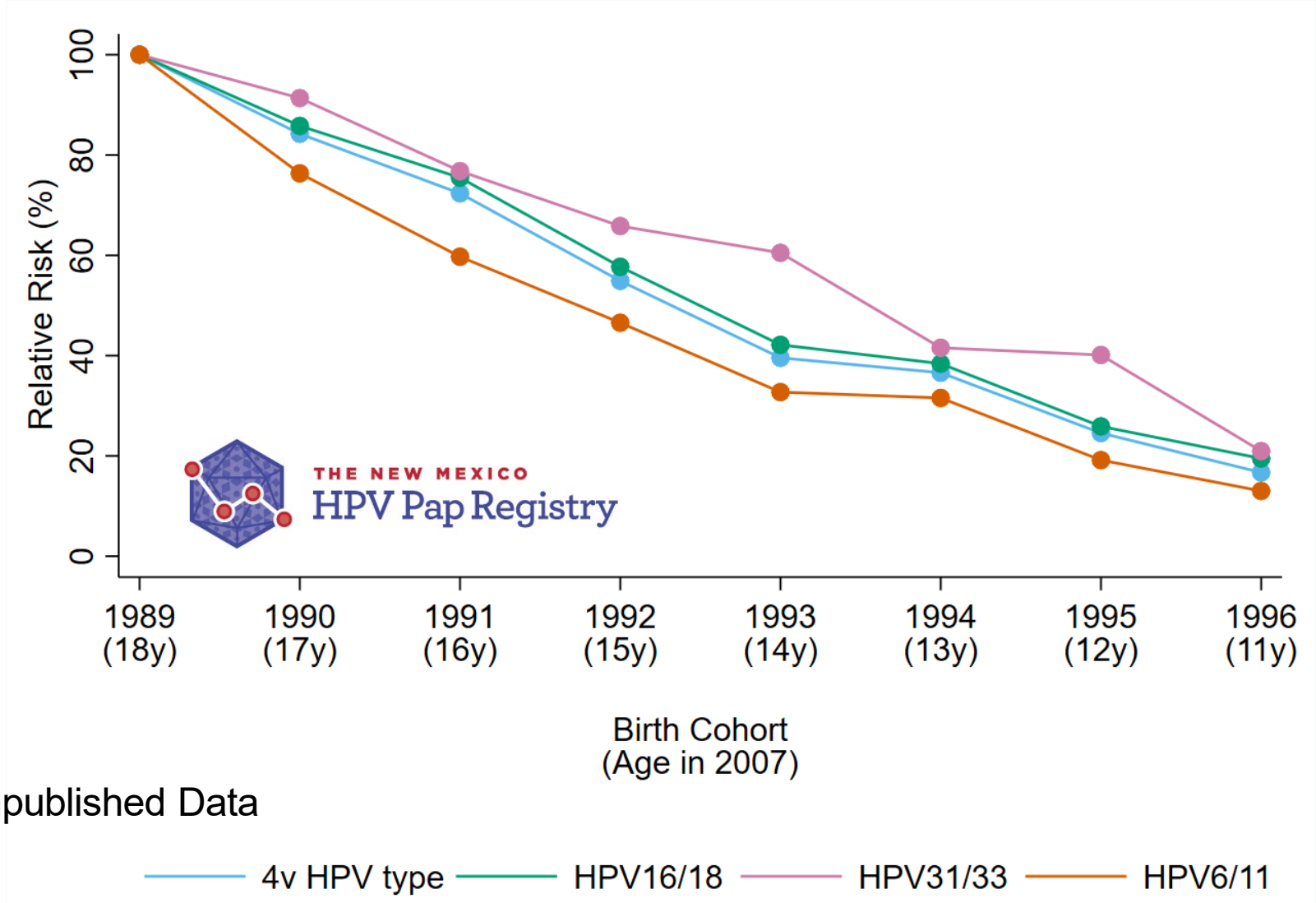
Ultimately, cervical cancer may become a disease of those that are unvaccinated and unscreened.

US HPV Vaccine Population Coverage is Variable by State



Despite lower than targeted HPV vaccine coverage in the US, major reductions in HPV infections have been observed

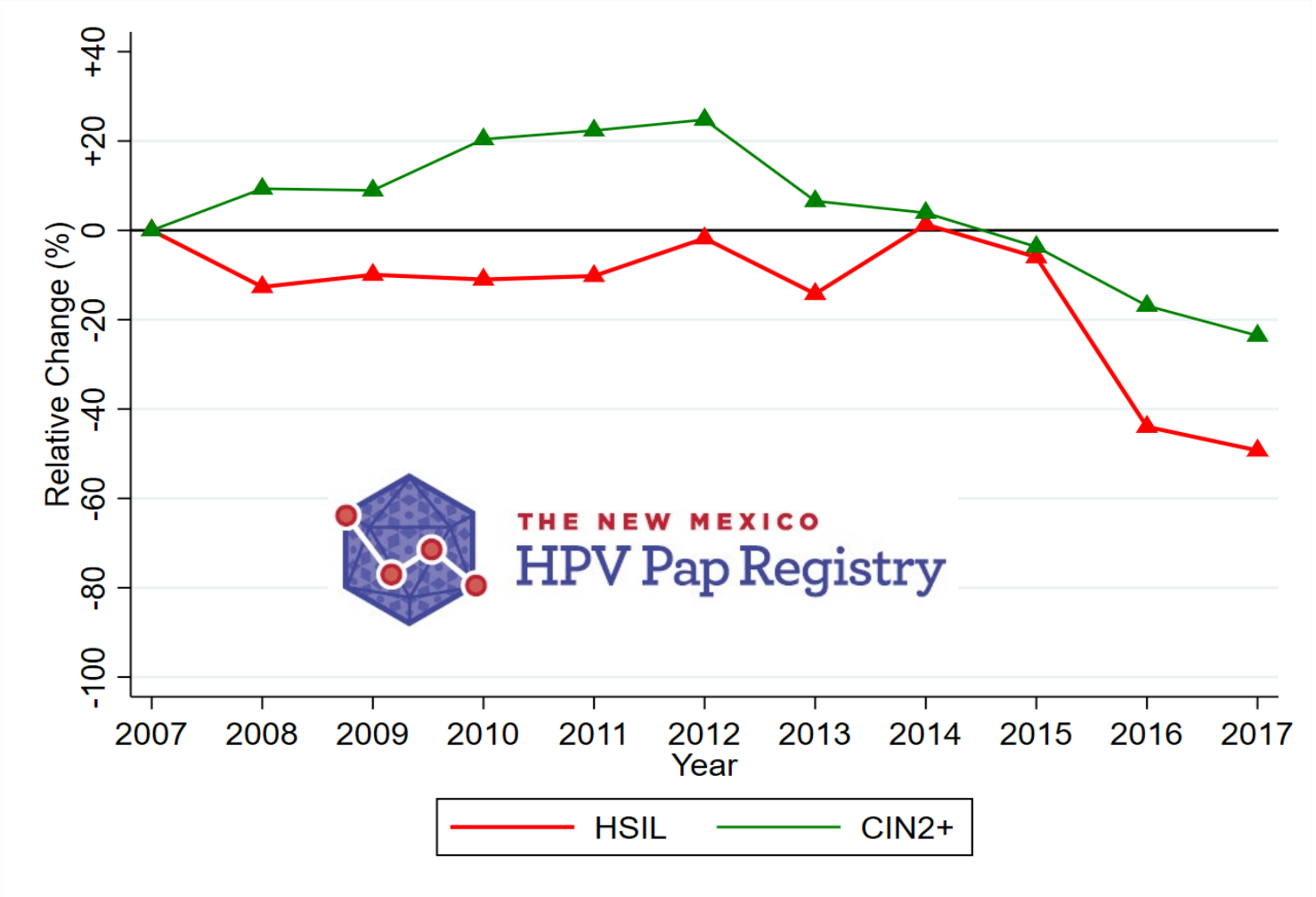
The Impact of HPV Vaccination on HPV Infections

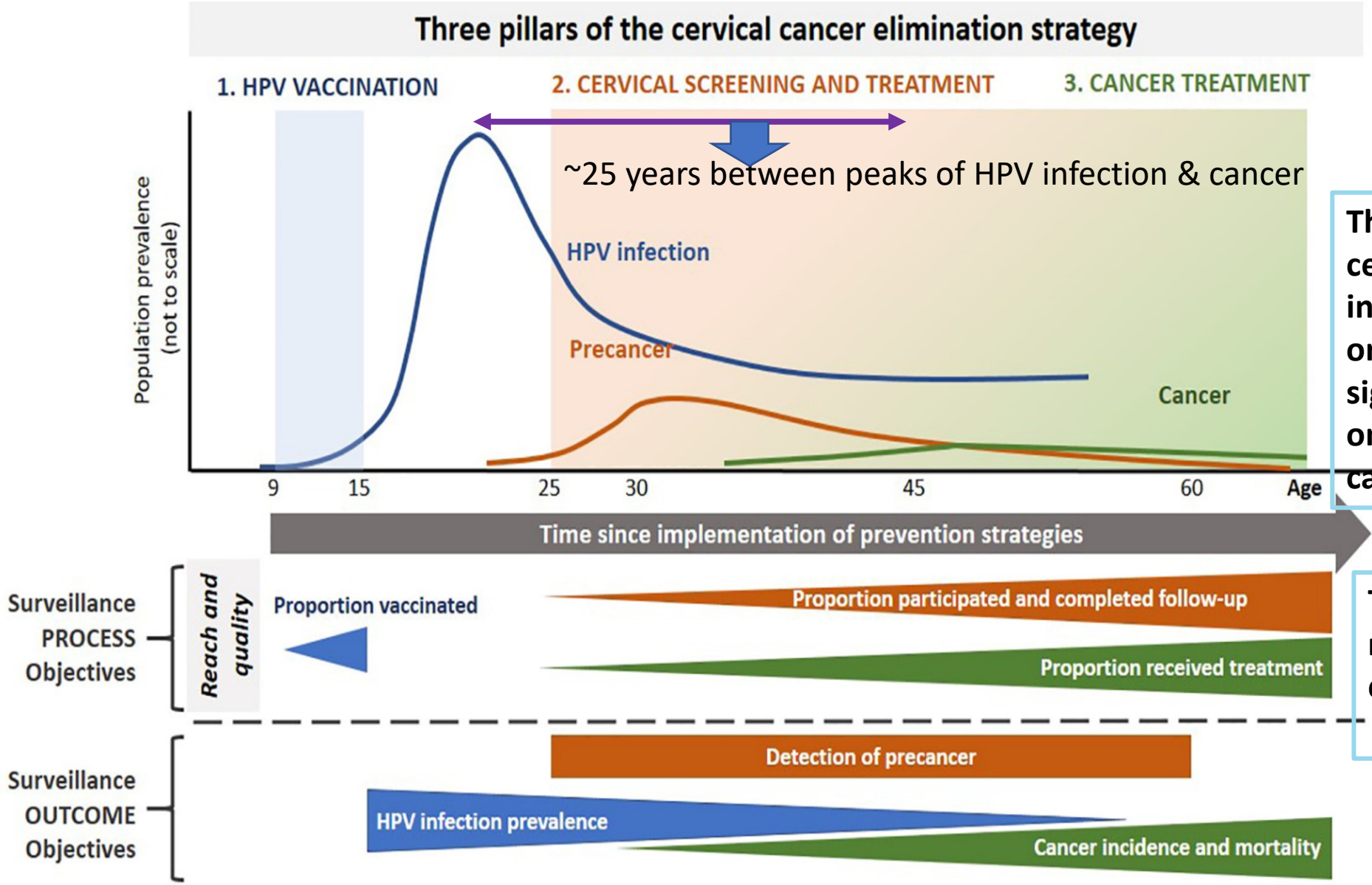


NMHPVPR Unpublished Data

Similarly there was a relative reduction in the percentage of HSIL (high-grade Pap test) and CIN2+ (high-grade precancers)

Among women aged 21-25 years, where vaccine impact is observable, disease declined by year of cervical screening across time, for New Mexico's screening population





The long sojourn time to develop cervical cancer following HPV infection will take another decade or more for the US to observe significant impact of HPV vaccine on any reductions in cervical cancer incidence.

Thus, cervical screening remains necessary for preventing cervical cancer for decades

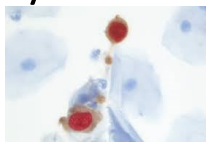
The Natural History of Cervical HPV infection and Disease

Julia ML Brotherton, Cosette M. Wheeler, Gary Clifford, et al.
Prev Med 2021 Mar;144:106293. doi: 10.1016/j.ypmed.2020.106293. Epub 2020 Oct 17

SECONDARY PREVENTION (Screening, Diagnosis, Pre-cancer Treatment)

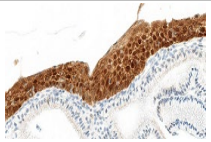
Over several decades, US research and health care resources have focused on

- Efficiencies in screening and triage tests/methods, but have **not focused on population screening coverage and not on (under-screening or over-screening)**
  - Pap Tests → Co-tests (both HPV+Pap) → HPV alone cervical screening
  - Further test innovations (HPV testing with genotyping, p16/Ki-67 dual immunostaining, methylation and HPV sequence variants) to differentiate risk

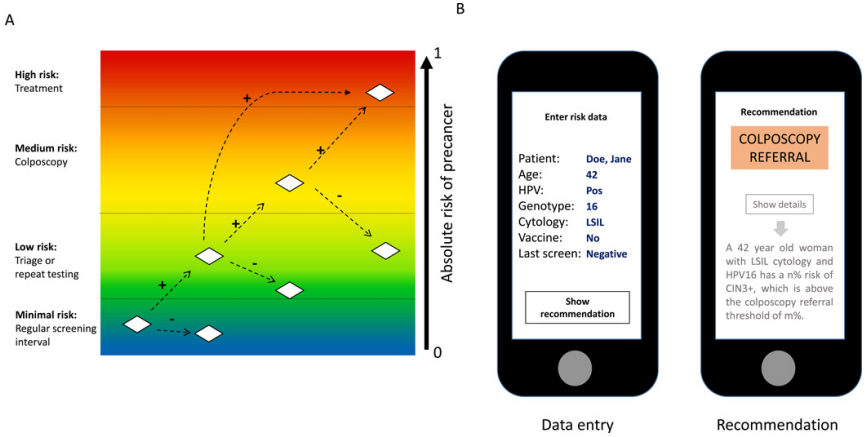


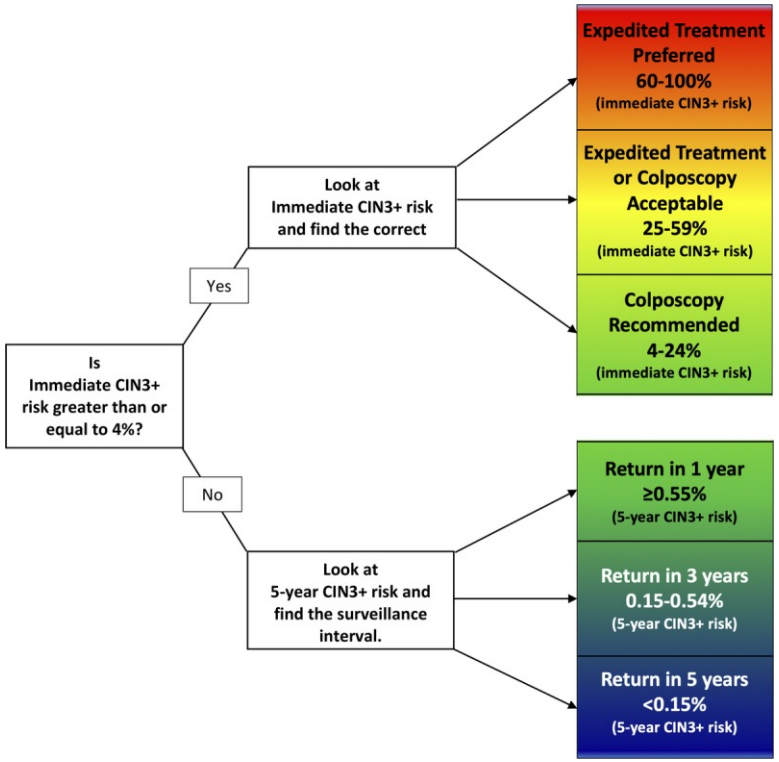
  - Delivery of cervical screening tests by self-sampling (Swab or Urine) to extend screening reach but self-testing is not approved in the U.S. and must consider any harms from losses in overall health benefits obtained through provider encounters

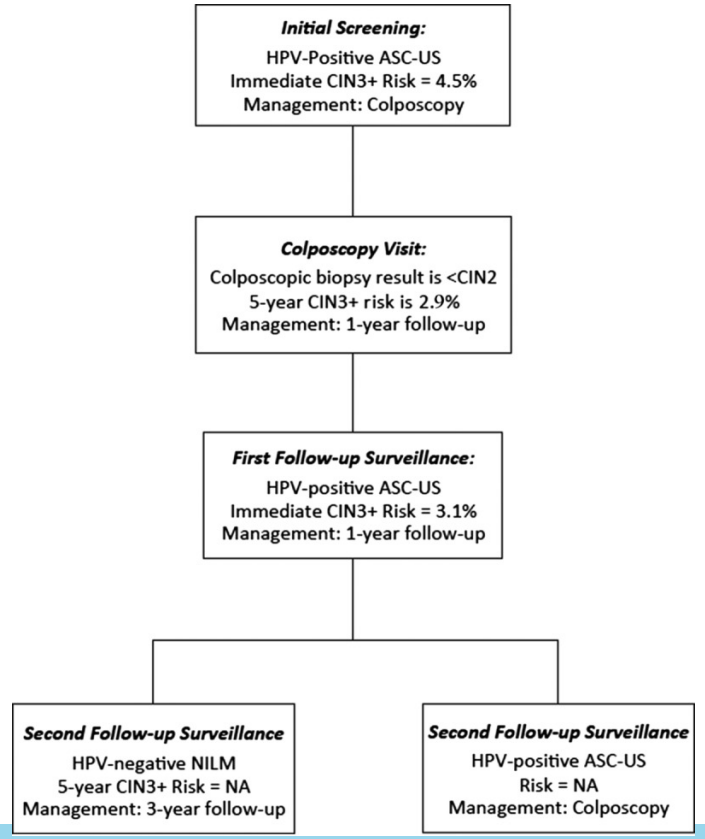
  - Improving the sensitivity of colposcopy (4-quadrant biopsy) and biomarkers to improve on diagnosis and predict cancer risks

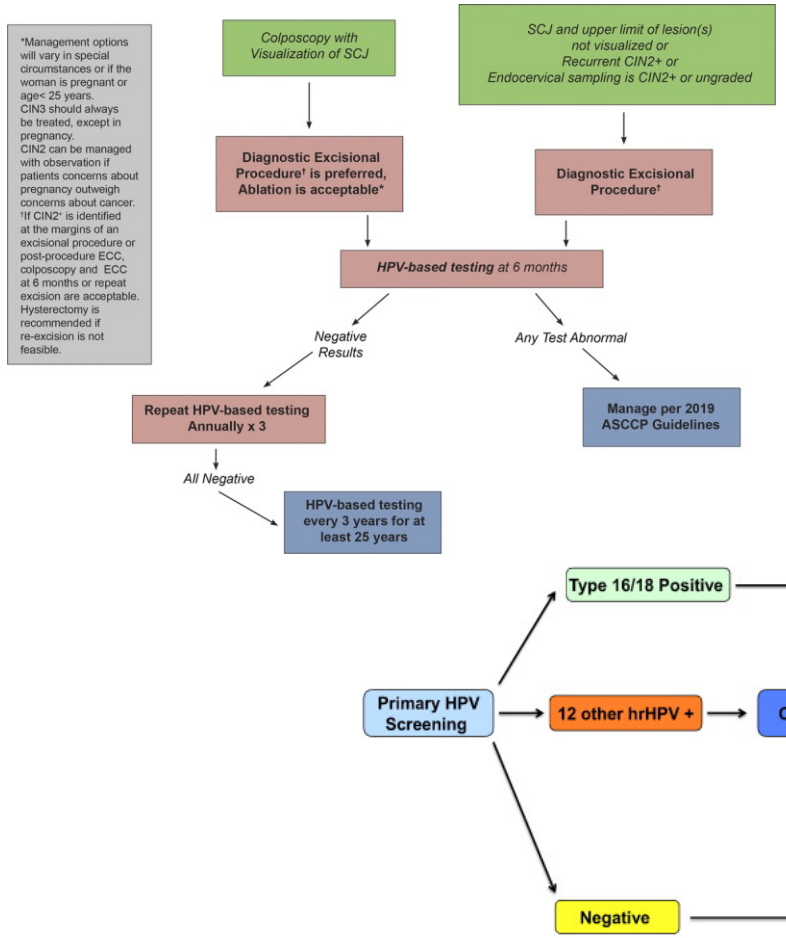


When women do screen, screening and follow-up management algorithms are complex for clinicians and are different for women by different age and different risk profiles



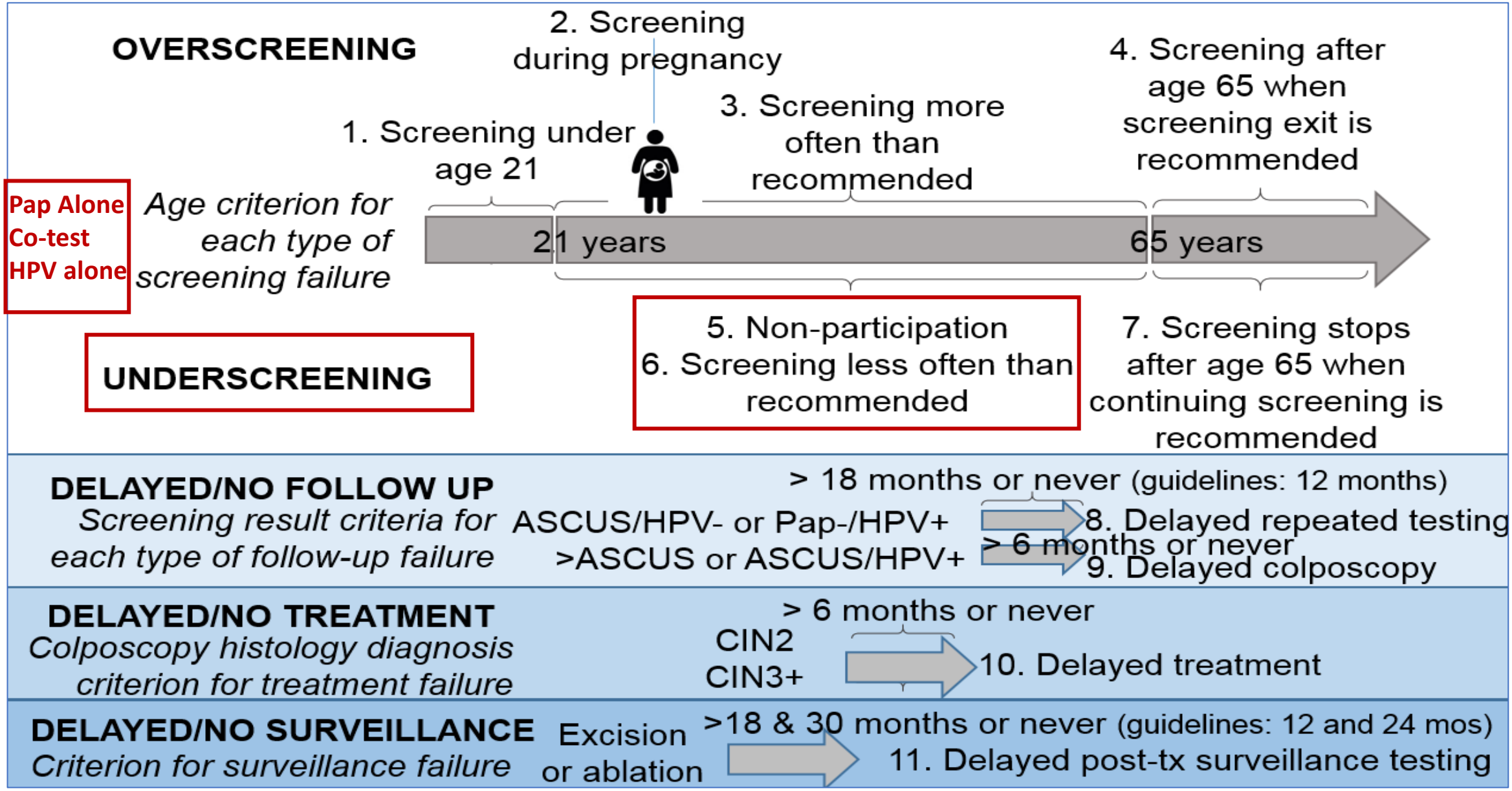




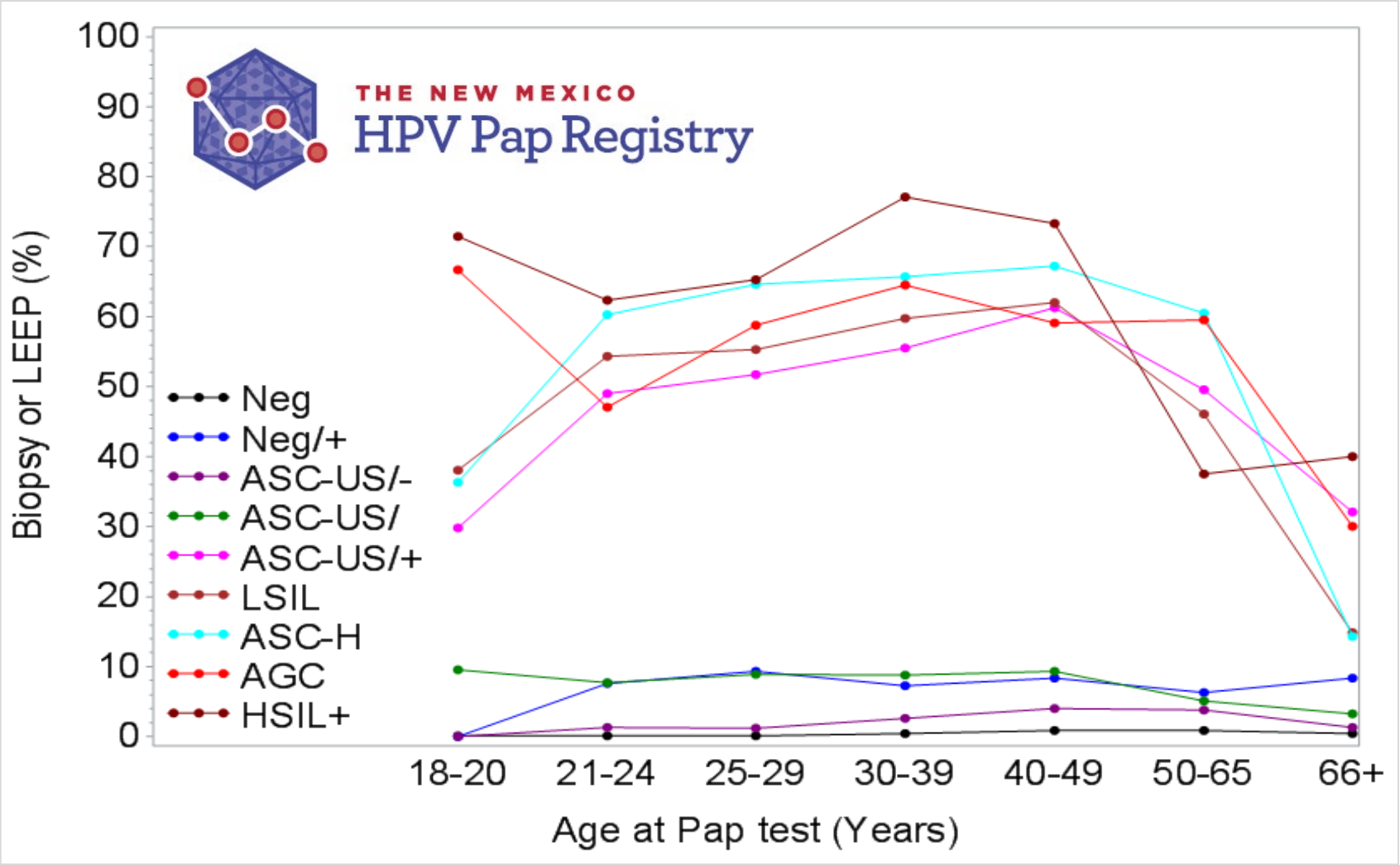


J Low Genit Tract Dis. 2017 Apr; 21(2): 87–90.
Gynecol Oncol. 2015 Feb;136(2):178-82.
J Low Genit Tract Dis. 2020 Apr; 24(2): 102–131.

Failures: Screening and Follow-up (Diagnosis, Treatment & Surveillance)



Failures to follow-up with diagnostic biopsy or to excise precancer within 6 months of abnormal Pap cytology shows decreased follow-up in older women (ASC-US, LSIL, HSIL+, ASC-H, and AGC)



NMHPVPR Unpublished Data

A "Laundry list" of Cervical cancer screening and diagnosis failures

Step	Failures	Causes	Potential Interventions
Screening	• Over-Screening • Under-Screening • Non-Participation	Woman: • Lack of information • Older age • Practical & Financial barriers • Acculturation/Language • Fear of the exam • Anxiety/fear of results • Embarrassment • Association with sex • Prior exam experience • Mistrust of providers/gender Provider: • Screening not discussed • Provider gender • Guideline non-compliance	Woman: • Mass media/local education • No-cost opportunistic screening at other healthcare and non-traditional opportunities • Multi-lingual health workers Population/community-level outreach • Self-collection (swab, urine) Provider: • Provider educational detailing • Provider peer comparison System: • Alternative days/hours • Mobile/Pop-Up units • Electronic surveillance call/recall
Management: Follow-up, Colposcopy, and Diagnosis	• Missed 12-month screen follow-ups • Missed colposcopy • Non-biopsy management • Under-diagnosis • Over-diagnosis	Woman: • Lack of communication • Older age & Comorbidities • Practical & Financial barriers • Acculturation/Language • Fear of colposcopy • Anxiety/fear of results • Missed appointments • Non-compliance with referral • Recent pregnancy • Lower-grade Pap dx Provider: • Guideline non-compliance • Colposcopy is insensitive • Diagnosis can be inaccurate	Woman: • Mass media/local education • No-cost diagnosis (beyond BCCEDP) • Multi-lingual client navigators Provider: • Provider educational detailing • Four-quadrant microbiopsy • Improved endocervical sampling • Pathology. risk-predictive biomarkers System: • Alternative days/hours • Mobile units • Electronic surveillance call/recall

Invasive cervical cancer (ICC) is a disease of the unscreened, under-screened and failures to follow-up abnormalities

In a state-wide population-based study from the New Mexico HPV Pap Registry

- **64% of women with invasive cervical cancer were not screened or had only inadequate screening tests**
- Older women (aged 45–64 years) and women with more advanced cancers were less likely to have been screened, and if screened, were more likely to have a false-negative screening test
- Women with adenocarcinomas vs. squamous cell cervical cancers were more likely to have had a negative screening test (72% vs 45%)
- **Only 32% of all cervical cancers were screen-detected**
- 9% of cancers were diagnosed in women who did not get follow-up with biopsy or treatment recommended after positive screening tests

Gynecol Oncol. 2020 Nov; 159(2): 344–353.
Int J Cancer. 2020 Aug 1; 147(3): 887–896

Opinion - Impacting stagnant cervical cancer survival rates requires bold action to modify the focus of prevention efforts and research directions beyond HPV-based innovations –

Future research resources should focus on:

1. Scale up of interventions to population- and community- levels (e.g., mass media campaigns to screen, diagnose and treat cervical cancer)

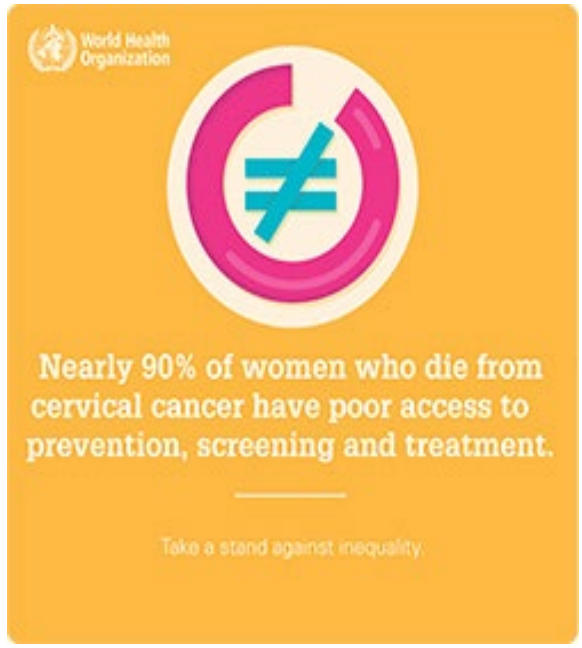
2. Implementing bold interventions to screen and follow-up underserved groups by overcoming the barriers of race, language, poverty and geography

3. Embracing innovative models of service delivery (e.g., non-traditional provider delivery, self-sampling at community venues – Costco, Walmart, Target, mobile units, community pop-ups)

4. Investment in building information systems (state-wide, regional, national) that transcend healthcare systems, clinics, providers and patient locations are needed to support call/recall for screening, diagnosis and cervical pre-cancer treatment.

Some final comments …

- **The US has many forms of health care delivery** (an array of clinicians, hospitals and other health care facilities, insurance plans, and purchasers of health care services, all operating in various configurations of groups, networks, and independent practices)
- **"The health care delivery system," as a term suggests an order, integration, and accountability that doesn't exist**
- **Significant barriers exists for the US to deliver equitable healthcare serving all**
- Often the **poor and other special populations end up reliant on receiving some of their health care, including cervical cancer preventive care from governmental public health agencies with inadequate resource allocation that needs to be addressed**
- The incremental benefits from continued investments in current cervical cancer prevention research cored in HPV-based innovation will likely not address equality and promote empowerment to reduce disparities
- **Larger novel extramural funding programs developed through innovative collaborative investigator-initiated programs** should extend beyond the current models of funding to enable bold population- and community-scaled interventions.

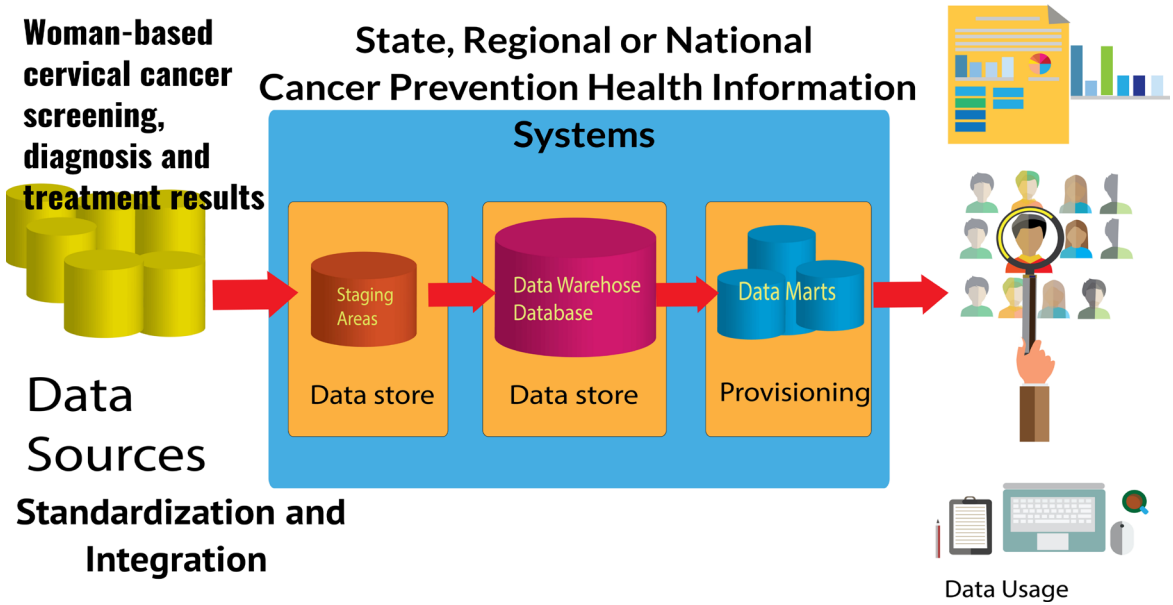

World Health Organization
Nearly 90% of women who die from cervical cancer have poor access to prevention, screening and treatment.
Take a stand against inequality.


DON'T LET CERVICAL CANCER STOP YOU!
GET VACCINATED
GET SCREENED
IT'S TIME TO END CERVICAL CANCER


World Health Organization
Cervical cancer can be prevented.
In addition to vaccination, regular screening of women and treatment of pre-cancerous lesions, protects from cancer.


World Health Organization
Cervical cancer control needs good data.
When high-quality data are collected and used to plan, scale and improve cervical cancer programmes, more women are protected.


PAVING THE ROAD TO HEALTH EQUITY
Health Equity
is when everyone has the opportunity to be as healthy as possible
Programs
Successful health equity strategies
Measurement
Data practices to support the advancement of health equity
Policy
Laws, regulations, and rules to improve population health
Infrastructure
Organizational structures and functions that support health equity
CDC
U.S. Department of Health and Human Services
Centers for Disease Control and Prevention


Woman-based cervical cancer screening, diagnosis and treatment results
State, Regional or National Cancer Prevention Health Information Systems
Staging Areas
Data store
Data Warehose Database
Data store
Data Marts
Provisioning
Data Sources
Standardization and Integration
Data Usage

Thank You !

- Dr. Sarah Temkin
- The Office of Research on Women's Health
- The New Mexico HPV Pap Registry Steering Committee