MPCA

Cervical Cancer Screening and Prevention

Objectives

- Describe epidemiology of cervical cancer
- Review cervical cancer screening guidelines
- Highlight recent changes in cervical cancer screening and prevention guidelines
- Identify strategies to increase screening and preventative care in practice

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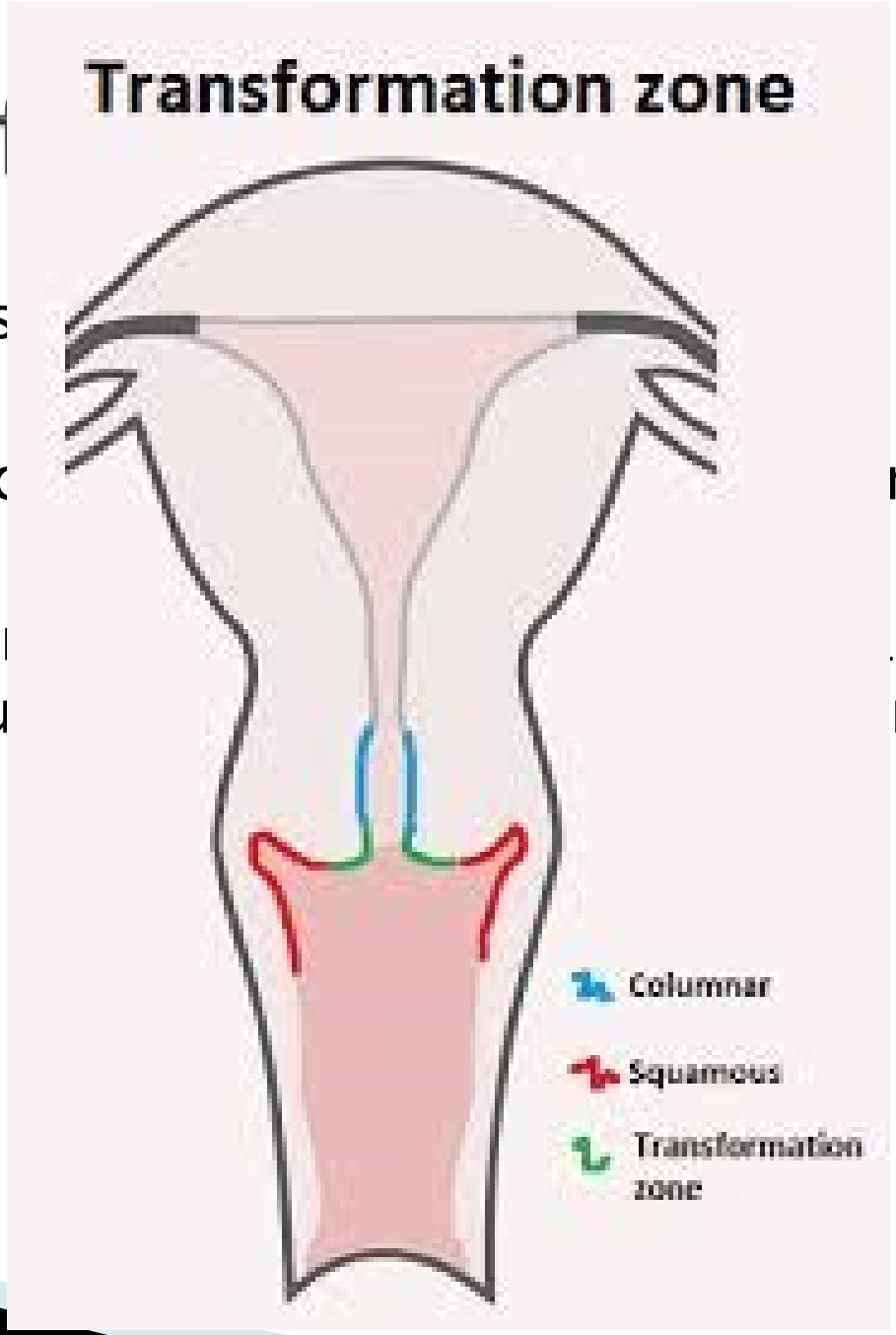


World view

- Second most common type of cancer in women
  - **17.8 cases per 100,000 women** (2012)
- Second most common cause of cancer deaths
  - **9.8 per 100,000** (2012)
- 528,000 new cancer cases worldwide and 266,000 deaths from cervical cancer in 2012
- Most cases occur in developing countries
- In Africa and Central America cervical cancer is the *leading cause* of cancer-related mortality among women
- Less common in developed countries ***because*** *of* cervical cancer screening and HPV vaccination efforts

The US View

- **3rd** most common gynecologic cancer
- **11th** most common cancer overall
- **12,845** new cases of Cervical Cancer in 2015(CDC)
- **4,175** individuals died of Cervical Cancer in 2015 (CDC)

- The lifetime risk of developing cervical cancer in the US was **0.76 percent** (based upon national data from 2000 to 2004)

Risks for Cervical Cancer

- ***HPV***
  - Detected in 99.7 percent of cervical cancers
- Smoking
- History of STI (Chlamydia, Gonorrhea)
- Conditions causing immunosuppression
  -includes HIV
- ***Not getting screened***

HPV

- Infection with high-risk strains of HPV and *persistence* of HPV infection are the **most important** determinants of progression to cervical cancer

HPV types

- High Risk (oncogenic/cancer associated)
  - 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, 82
  - **HPV 16 and 18 are found in over 70 percent of all cervical cancers**
- Low Risk (non-oncogenic)
  - 6, 11, 40, 42, 43, 44, 54, 61, 72, 81

For the pathophysiology nerds…

- Most important HPV proteins in the pathogenesis of malignant disease are E6 and E7
- E6 and E7 proteins are consistently expressed in HPV-carrying anogenital malignant tumors
  - Act cooperatively with growth regulating host cell proteins (p53 and retinoblastoma (Rb)) to immortalize infected epithelial cells

Goals of screening

- To reduce morbidity and mortality by detecting and treating precursors and early stage cervical cancer
  - Prevent progression to invasive disease and reduce mortality
  - Goal is NOT to find HPV infection or abnormal Paps
    - These are *surrogate risk markers*, not inevitable cancer precursors—useful but not determinative

Importance of balancing benefits versus risks

- Benefits
  - Early detection of treatable lesions and reduction in incidence and mortality of cervical cancer
- Risks
  - False positives leading to unnecessary procedures and other harms including increased anxiety

Cervical Cancer Screening (CCS) Comparison of Guidelines

Recommendation	USPSTF (2018)	ASCCP (2012/2015 interim guidelines)
Age to start	Age 21	Age 21
Women ages 21–29	Cytology every 3 years	Cytology every 3 years
Women ages 30–65	Co-testing every 5 years OR hrHPV testing alone every 5 years OR Cytology alone every 3 years	Co-testing every 5 years OR hrHPV testing every 3 years OR Cytology alone every 3 years
Women ages > 65	Discontinue after age 65 if adequate screening	Discontinue after age 65 if adequate screening
Post-Hysterectomy	Discontinue if for benign reason	Discontinue if for benign reason

CCS Guidelines
Who do these apply to?

- Most screening recommendations focus on individuals who are at *average* risk for cervical cancer:
  - Asymptomatic
  - Immunocompetent
  - Adequate prior screening

Who falls outside guidelines?

- Symptomatic individuals w/ a cervix
- Individuals with HIV
- Immunosuppressed individuals with a cervix
- History of DES exposure
- History of abnormal screening
  - History of cervical pre-cancer or cancer (including those who have undergone a hysterectomy)

Who NOT to screen

- Asymptomatic individuals w/ a cervix < 21
- Individuals who have had a hysterectomy for *benign* reasons
- Individuals w/ a cervix > 65 (Maybe?)

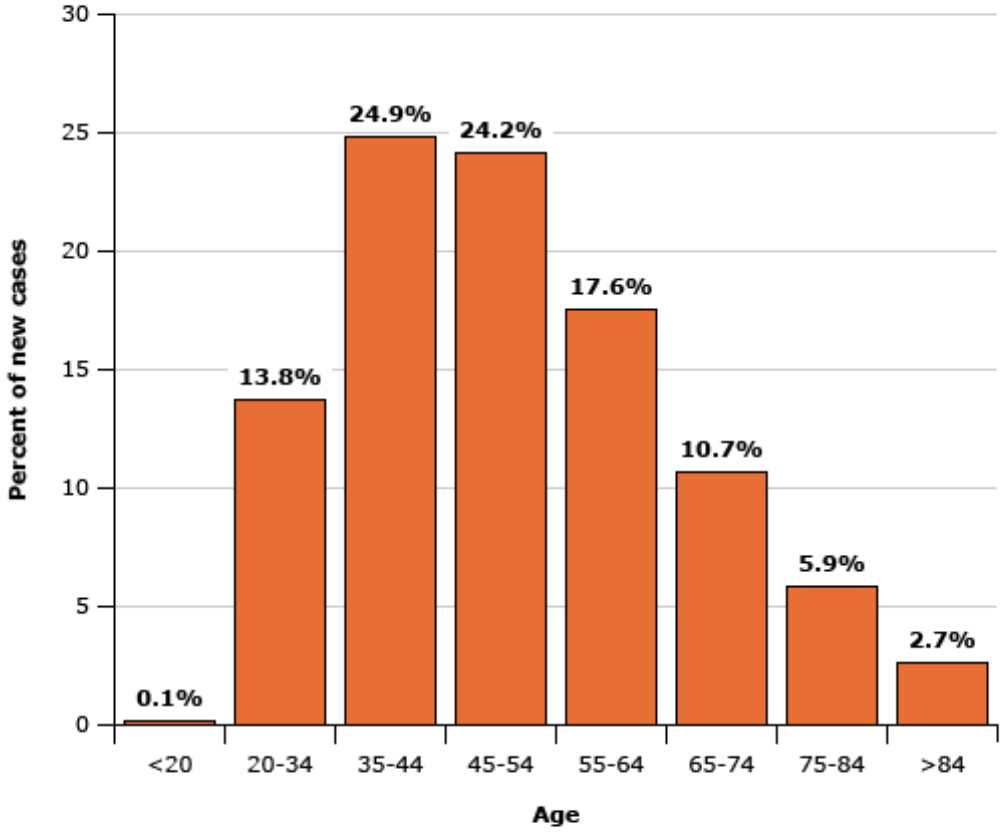
Hysterectomy – Importance of WHY

- Individuals with a history of CIN2 or CIN3 should continue to have testing for at least 20 years after the abnormality was found.

DON'T screen under age 21

- Incidence of cervical cancer in ages 15 to 19 years in the United States is 0.1 per 100,000
- Adolescents are more likely to spontaneously clear HPV infection and associated cytological abnormalities
- 90 to 95 percent of low-grade lesions in adolescents (and many high-grade lesions) regress spontaneously

Percent of new cases by age group: Cervix uteri cancer*



Infection of the cervix with human papillomavirus (HPV) is the most common cause of cervical cancer, although not all women with HPV infection will develop cervical cancer. The number of new cases of cervix uteri cancer was 7.8 per 100,000 women per year based on 2007 to 2011 cases. Cervix uteri cancer is most frequently diagnosed among women aged 35 to 44. Median age at diagnosis is 49.

* SEER 18 2007 to 2011, all races, females.

Reproduced from: SEER Cancer Statistics Factsheets: Cervix Uteri Cancer. National Cancer Institute. Bethesda, MD. Available at: http://seer.cancer.gov/statfacts/html/cervix.html (Accessed on December 8, 2014).

UpToDate®

Who NEEDS screening

- All individuals with a cervix between the ages of 21-65
- This includes:
  - WSM
  - Women who report never having sex
  - Transgender men with a cervix
  - Women and transgender men who have received the HPV vaccination
  - Individuals who have had a partial hysterectomy and still have cervix

Cervical Cancer screening Frequency of screening?

Recommendation	USPSTF (2018)	ASCCP (2012/2015 interim guidelines)
Age to start	Age 21	Age 21
Women ages 21-29	Cytology every 3 years	Cytology every 3 years
Women ages 30-65	Co-testing every 5 years OR hrHPV testing alone every 5 years OR Cytology alone every 3 years	Co-testing every 5 years OR hrHPV testing every 3 years OR Cytology alone every 3 years
Women ages > 65	Discontinue after age 65 if adequate screening	Discontinue after age 65 if adequate screening
Post-Hysterectomy	Discontinue if for benign reason	Discontinue if for benign reason

Frequency of screening

- 21-29
  - Every 3 years
- 30-65
  - Every 3-5 years depending on type of screening used

Why not screen annually?

Most abnormal screens represent transient HPV infection, not pre-cancer

- Cancer risk 18 mo after 3 neg Paps = 1.5/100,000
- Cancer risk 36 mo after 3 neg Paps = 4.7/100,000
- →99,997 women screened unnecessarily to diagnose 3 cancers

Risk of HSIL/cancer <3y after negative Pap not significantly higher than risk after 1y

Cervical Cancer screening Type of screening?

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Cervical Cancer screening
How to screen

- Pap/cytology only
  - Generally recommended for younger women
- Co-testing with pap/cytology and HPV testing
- Primary HPV testing

Why not include HPV testing in screening for younger women?

- Infection with HPV may be transient and cervical dysplasia may regress spontaneously, *particularly in young women*
  - Poor specificity and correspondingly poor positive predictive value of HPV testing limit its usefulness as a screening modality in this age group

Primary HPV testing – What do the guidelines say?

- USPSTF (2018)
  - Can consider primary HPV testing every years for women age ≥30
- ACOG (2016)
  - Can consider primary HPV testing every 3 years for women age ≥25
- ASCCP/SGO (2015 interim guidelines)
  - hrHPV testing alone every 3 years for women ≥ 30

NOTE for FQHCs: As of 2018 the UDS manual does NOT consider primary HPV testing as satisfying the metric for cervical cancer screening

What's the best test?

- No high-quality data indicating that one screening strategy is clearly superior to another with regard to clinical outcomes

- HPV infection is more likely to be persistent in women ≥30 years than in younger women and has a greater likelihood of clinical significance than in younger age groups

FDA Approved HPV tests

- Hybrid capture 2
- Cervista HPV HR
- **cobas HPV**
  - **ONLY one approved for primary HPV testing**
- Aptima mRNA

Cervical Cancer Screening When to stop screening?

- Evidence Grey Zone…

Evidence Grey Zone

- A 2013 systematic review of 24 studies found no conclusive evidence to support a specific age to stop cervical cancer screening, as none of the reviewed studies looked specifically at this question

- **Women aged 65 years or older who have never been screened have the highest incidence of and mortality from cervical cancer and benefit the most from screening**

When to stop screening??

- Depends on:
  - Patient's prior results
  - Life expectancy
  - Preferences

When to stop screening??

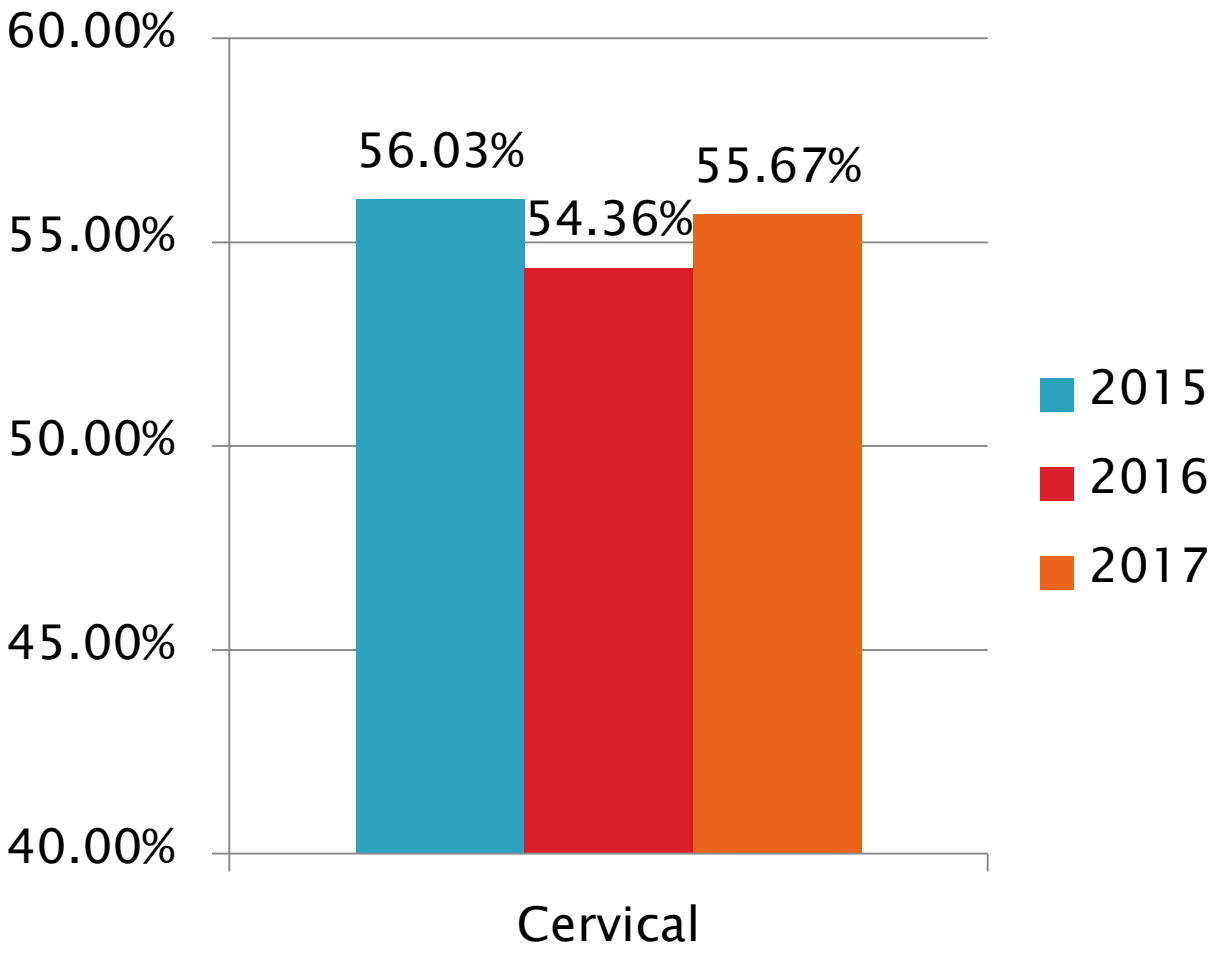
- US guidelines recommend discontinuing screening at age 65 in patients with a history of "adequate results"
  - Two consecutive negative co-tests (Pap tests with human papillomavirus [HPV] testing) within the past 10 years, with the most recent test within the previous five years; **or**
  - Three consecutive negative Pap tests within the past 10 years, with the most recent test within the previous three years; **or**
  - Two consecutive negative primary HPV tests within the past 10 years, with the most recent test within the previous five years
- Some countries and clinicians continue screening until age 74 in women with a life expectancy > 10 years (controversial – again need to weigh risks versus benefits)

Follow up on abnormal results

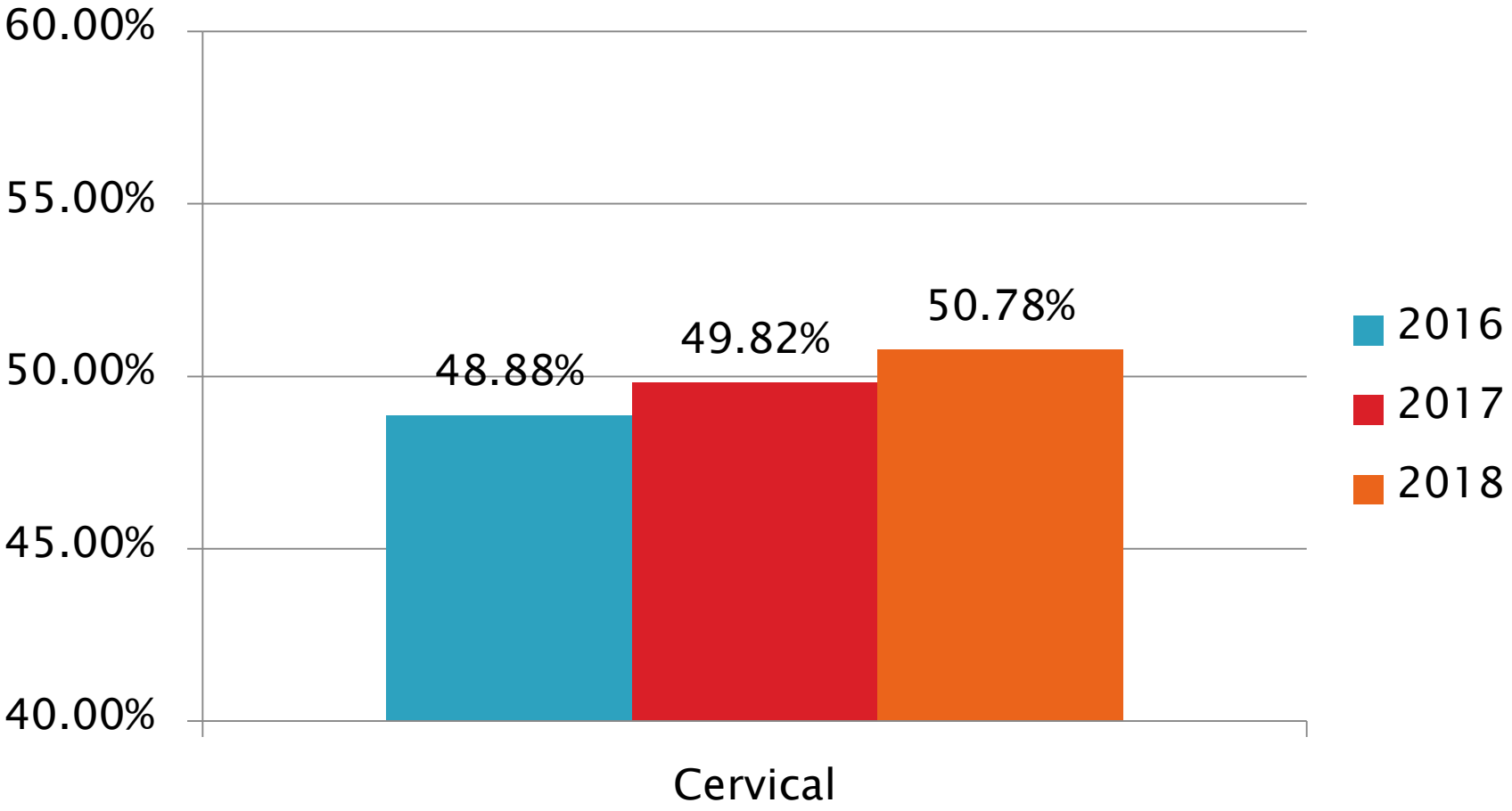
- http://www.asccp.org/asccp-guidelines

- **IMPORTANT**: Inadequate follow-up of abnormal Pap tests performed months or years before the diagnosis of cancer was found in up to *13 percent* of women with invasive cervical cancer

How are we doing Nationally? (HRSA date)



How are we doing in MT? (MPCA data)



Challenges/Barriers to screening

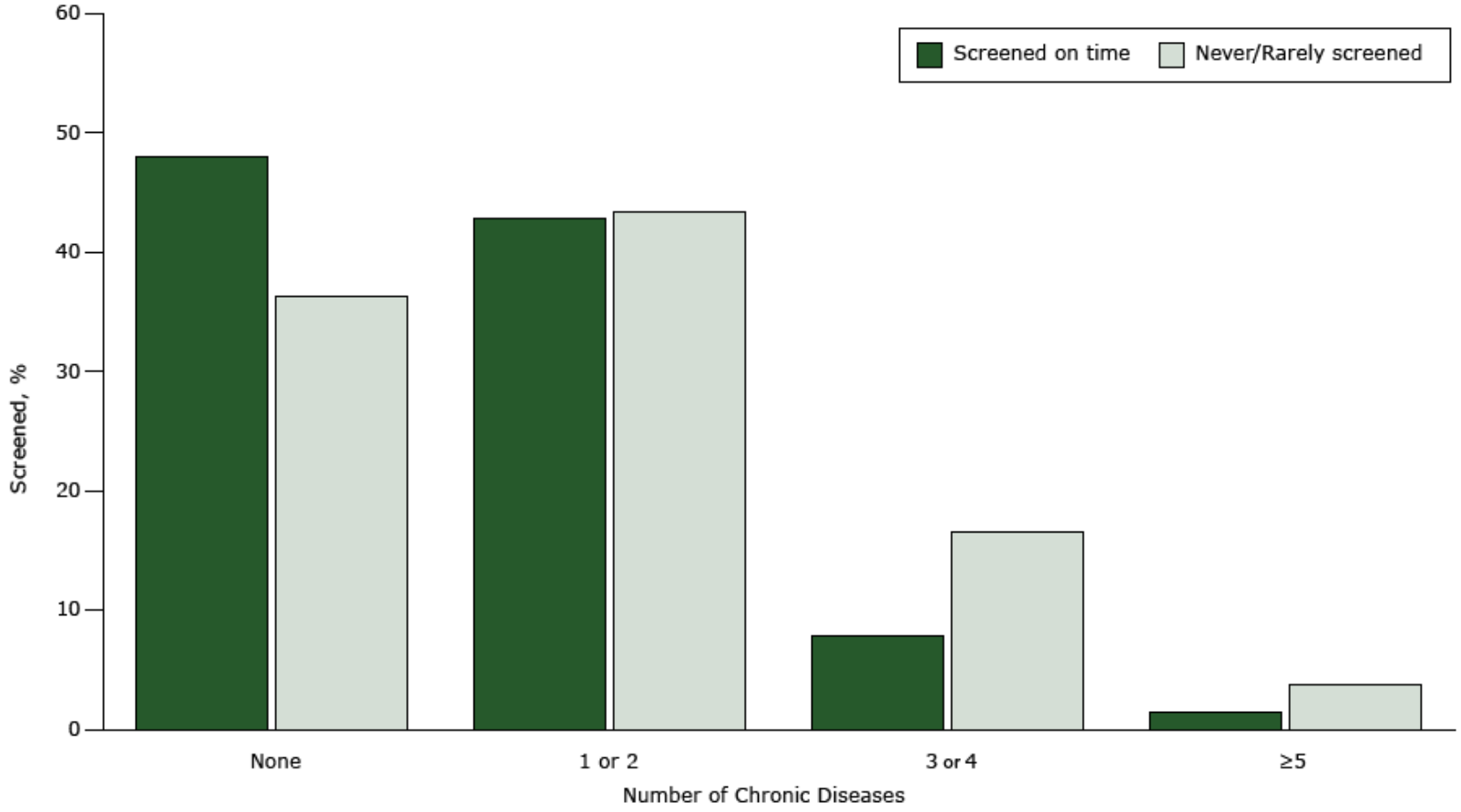
- Access to healthcare
  - Cost (Importance of expanded Medicaid and MCCP)
  - Transportation
- Lack of education/awareness of benefits
- History of trauma
- Fatalistic health beliefs
- Data accuracy
- TIME

PublicHealth IN THE 406

MONTANA CANCER CONTROL PROGRAMS

Challenges/Barriers to screening

- Complexity of patient needs



Disparities in screening

- The rate of screening was similar among the African American (86%) and white population (85%)
- However, among individuals of all races, screening rates are lower in
  - older individuals
  - individuals with no health insurance
  - individuals with less education
  - recent immigrants

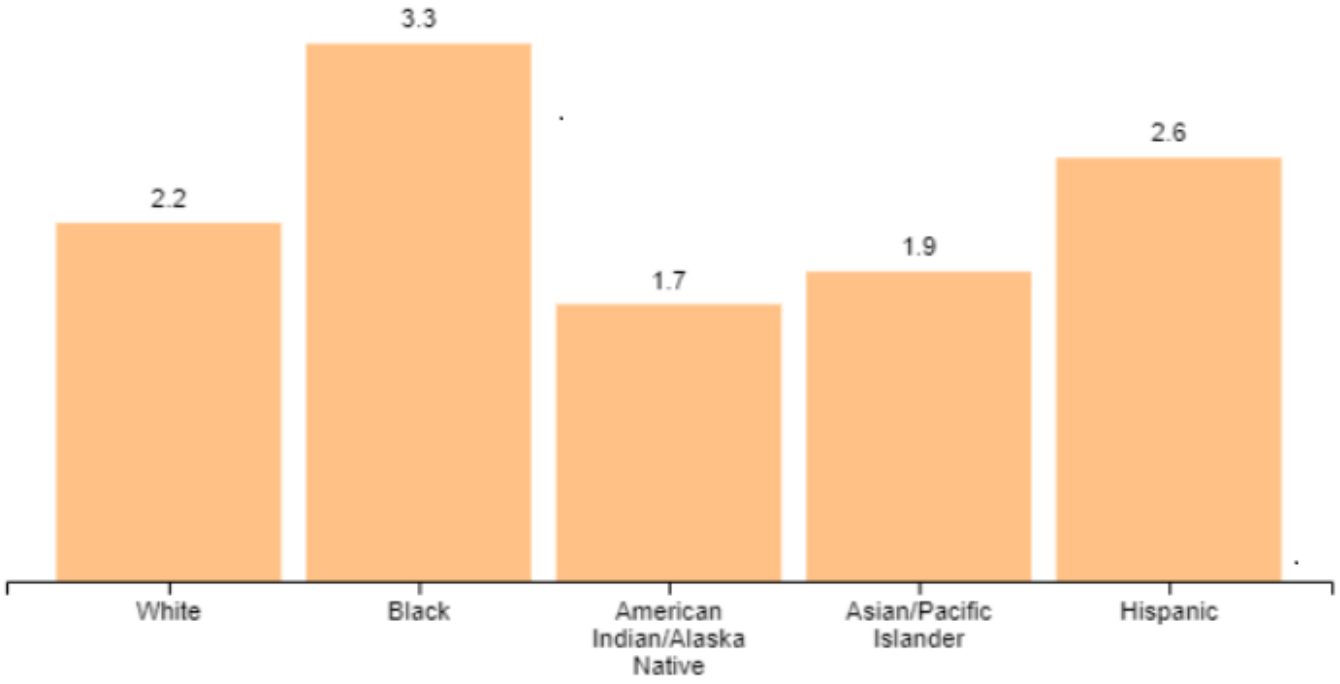
Disparities in outcomes

- Overall 5-year relative survival rate for cervical cancer among African American women is 56%, compared to 69% among white women
- African American women are also more likely to be diagnosed with regional- or distant-stage disease despite similar screening rates
- Racial differences in stage at diagnosis may be due to differences in the quality of screening and follow-up after abnormal results
- Lower socioeconomic status is also associated with lower screening rates, increased risk of late-stage diagnosis, and poorer survival

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Rate of Cancer Deaths by Race/Ethnicity, Female

Cervix, United States, 2015



Rate per 100,000 women

Upstream Prevention – HPV vaccination!!!

The HPV vaccine is cancer prevention!

Boys and Girls

Boys and girls should get the HPV vaccine series by age 13. It can be started at age 9.

It works!

Since the release of the vaccine, infections that cause most HPV cancers and genital warts have dropped 71% among teen girls.

Increase Rates

Make it your goal for every age-eligible patient you care for to be vaccinated against HPV.

HPV vaccination: When?

- Routine vaccination of all children (regardless of gender) at age 11–12 years
- May vaccinate as young as age 9
- Can be administered safely at the same visit as other vaccines recommended for children at ages 11 or 12 years

HPV vaccination: How many?

- 2 Dose schedule: 2 injections when 1st dose given by age 15 (0 and 6-12 month schedule)
  - Minimum interval between the first and second dose is 5 months.
  - If the second dose is administered at a shorter interval, a third dose should be administered 6-12 months after the first dose and a minimum of 12 weeks after the second
- 3 Dose schedule: If 1st dose given after age 15 needs 3 doses (0, 1-2 month, and 6-12 month schedule)
  - 3 dose series also recommended in immunocompromised individuals

10/2018: FDA approves HPV vaccination for adults up to age 45

No change to guidelines yet…

- CDC and ACIP still only recommending HPV vaccination up to age 26 in women and individuals with certain conditions (e.g. HIV)
- Up to age 21 in men at average risk
- Recommend vaccinating MSM and transgender women who have sex with men up until age 26

What's in the current HPV vaccination

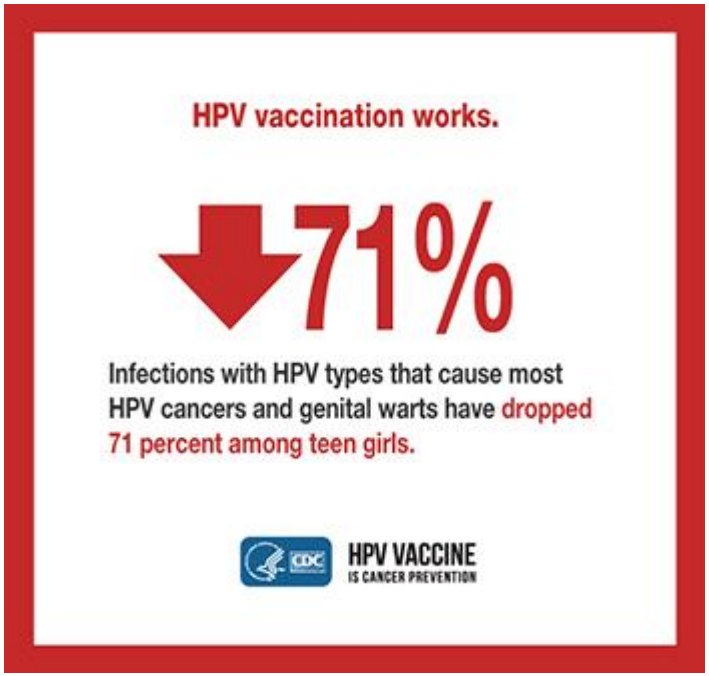
- Since late 2016 the 9-valent HPV (9vHPV) vaccine is the only HPV vaccine currently used in the United States.
- Protects against nine HPV types, including seven types that can cause cancer

HPV vaccine safety

- Most common side effects are mild
  - Pain, redness, or swelling at the injection site
  - Dizziness, fainting, nausea, and headache
- Fainting (syncope) after any vaccine, including HPV vaccine, is more common among adolescents.
  - Adolescents should be seated or lying down during vaccination and remain in that position for 15 minutes after the vaccine is given

HPV vaccine effectiveness

- HPV vaccine was first recommended in the United States in 2006
- By 2014 HPV infections responsible for the majority of HPV cancers and genital warts decreased by **71%** in teen girls and **61%** among young women.



Success Story

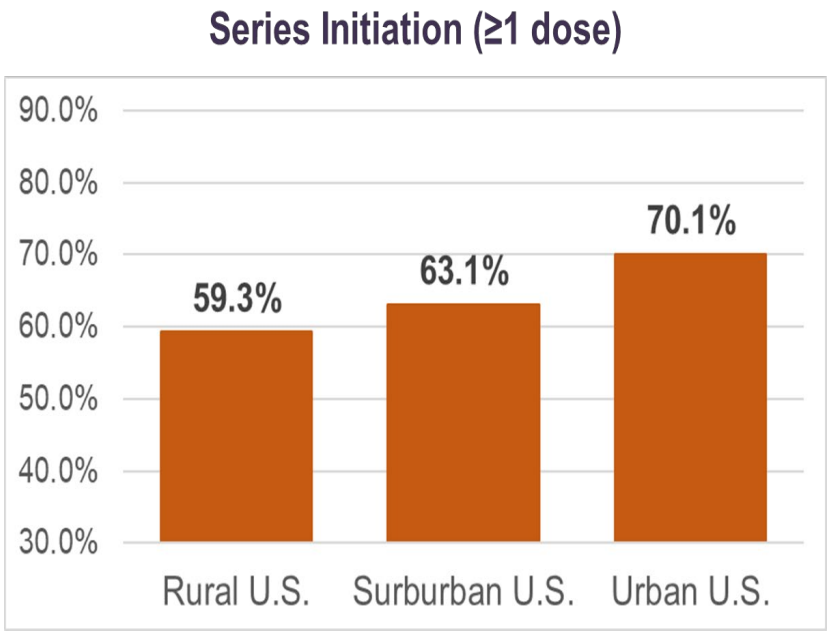
- Australia has the leading rate of cervical cancer screening and HPV vaccination
  - Vaccination rates >70 percent
  - 38 percent reduction in high grade dysplasia

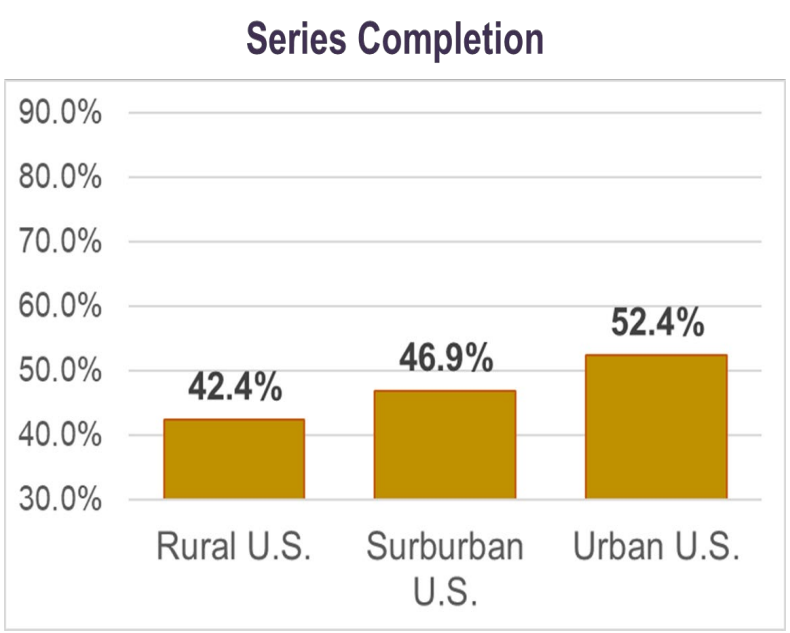
Current State

- In 2017:
  - 49% of adolescents in the US were up to date on the HPV vaccine
  - 66% of adolescents ages 13-17 years received the first dose to start the vaccine series.

- Significant Geographic variability

Adolescent HPV Vaccination Rates*, U.S., National Immunization Survey – Teen 2017





*Among adolescents ages 13-17 years

Data source: CDC's National Immunization Survey-Teen

Results: Adolescent HPV Vaccine Series Initiation, Montana, NIS-Teen 2013-2017

(Data source: CDC's National Immunization Survey-Teen)

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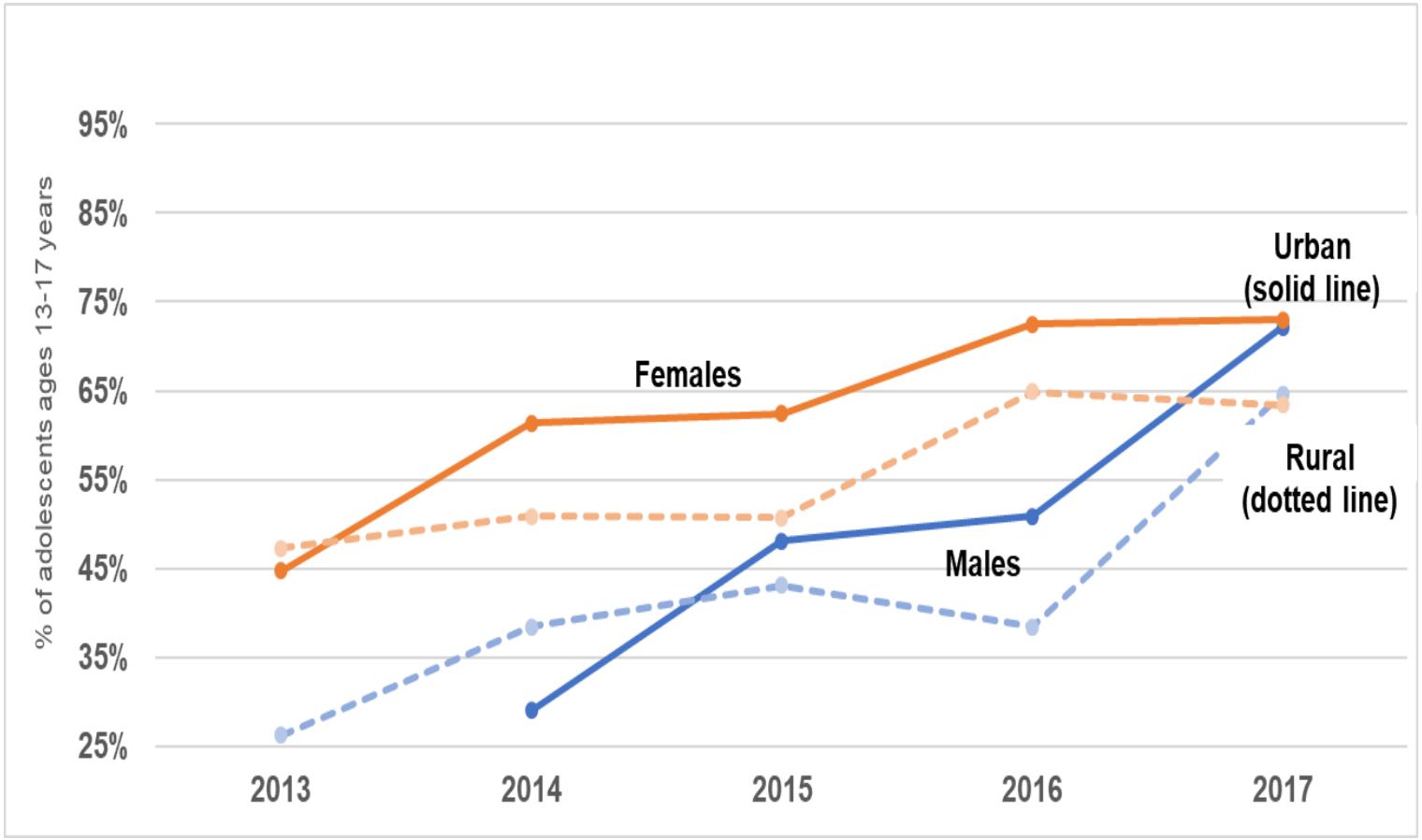
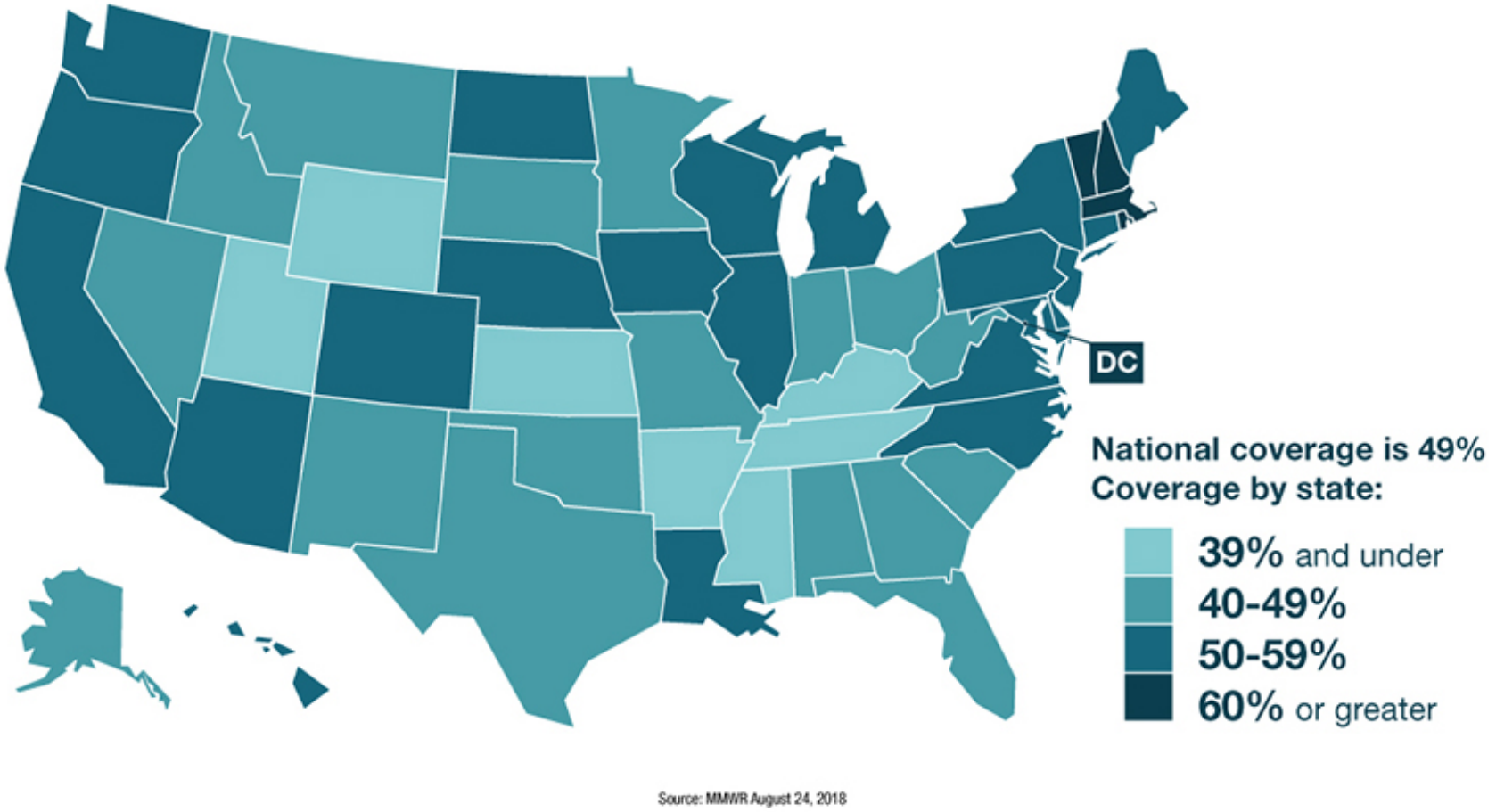
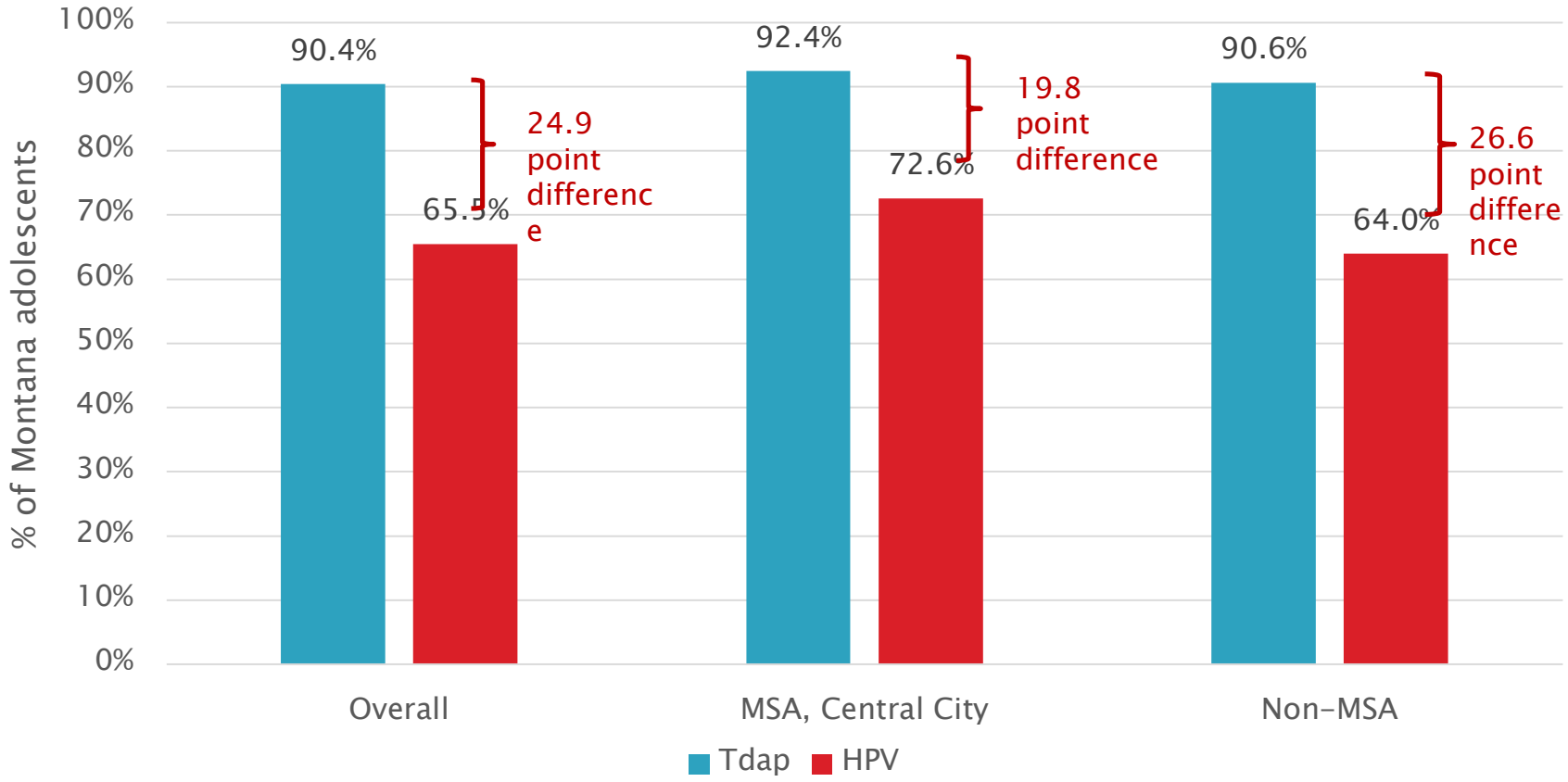


Percentage of adolescents who are up to date on HPV vaccination



Source: MMWR August 24, 2018

Missed opportunities for HPV vaccine initiation in Montana, NIS-Teen 2017 (Data source: CDC's National Immunization Survey-Teen)

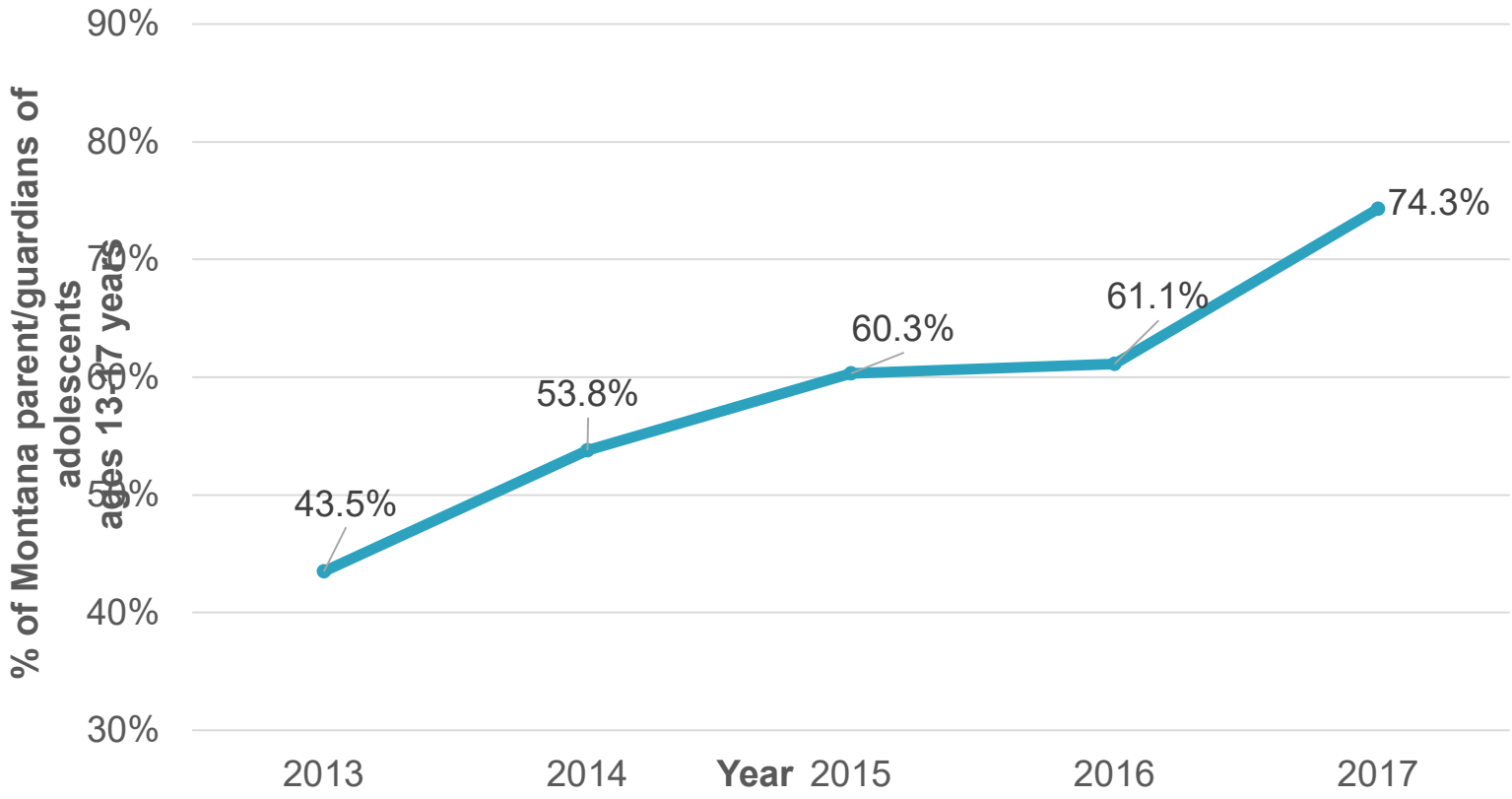


Strategies for HPV Vaccination Success

Action 1

Make a strong and unequivocal recommendation for cancer prevention

Receipt of medical provider recommendation to vaccinate against HPV, Montana, NIS-Teen (Data source: CDC's National Immunization Survey-Teen)



Action 2

Answer parents' questions

Common Questions

- “Why does my child need HPV vaccine?”

- Answer: “HPV vaccine is important because it prevents infections that can cause cancer. That’s why we need to start the shot series today.”

Common Questions

- “How do you know the vaccine works?”
- Answer: “Studies continue to prove HPV vaccination works extremely well, decreasing the number of infections and HPV pre-cancers in young people since it has been available.”

Common Questions

- "Why do they need HPV vaccine at such a young age?"

- Answer: "Like all vaccines, we want to give HPV vaccine earlier rather than later. Getting the vaccine now protects your child long before they are ever exposed. If you wait until your child is older, he/she may end up needing three shots instead of two."

Common Questions

- “I’m worried my child will think that getting this vaccine makes it OK to have sex.”

- Answer: “Studies tell us that getting HPV vaccine doesn’t make kids more likely to start having sex.”

Common Questions

- "I'm worried about the safety of HPV vaccine. Do you think it's safe?"

- Answer: "Yes, HPV vaccination is very safe. Like any medication, vaccines can cause side effects, including pain, swelling, or redness where the shot was given. That's normal for HPV vaccine too and should go away in a day or two. Sometimes kids faint after they get shots and they could be injured if they fall from fainting. We'll have your child stay seated after the shot to help protect him/her."

Top reasons for not intending to vaccinate against HPV, Montana, 2017 (Data Source: Dr. Sophia Newcomer)

- As reported by parents who reported not intending to vaccinate their adolescent in the next 12 months:
  - Safety concerns – 22% (up from 8% in 2016)
  - Not needed or necessary – 17%
  - Adolescent is not sexually active – 10%
  - Lack of knowledge – 7%
  - Adolescent is fearful – 7%
  - Family/parental decision – 5%
  - Not a school requirement – 5%
  - Not recommended – 6%
  - Child should make decision – 2.5%

Framing the HPV Vaccine Conversation

Tips and Time-savers for Talking with Parents about HPV Vaccine

Recommend the HPV vaccine series the same way you recommend the other adolescent vaccines. For example, you can say "Your child needs these shots today," and name all of the vaccines recommended for the child's age.

Parents may be interested in vaccinating, yet still have questions. Taking the time to listen to parents' questions helps you save time and give an effective response. CDC research shows these straightforward messages work with parents when discussing HPV vaccine—and are easy for you or your staff to deliver.

CDC RESEARCH SHOWS:	The "HPV vaccine is cancer prevention" message resonates strongly with parents. In addition, studies show that a strong recommendation from you is the single best predictor of vaccination.
TRY SAYING:	HPV vaccine is very important because it prevents cancer. I want your child to be protected from cancer. That's why I'm recommending that your daughter/son receive the first dose of HPV vaccine today.
CDC RESEARCH SHOWS:	Disease prevalence is not understood, and parents are unclear about what the vaccine actually protects against.
TRY SAYING:	HPV can cause cancers of the cervix, vagina, and vulva in women, cancer of the penis in men, and cancers of the anus and the mouth or throat in both women and men. There are about 26,000 of these cancers each year—and most could be prevented with HPV vaccine. There are also many more precancerous conditions requiring treatment that can have lasting effects.
CDC RESEARCH SHOWS:	Parents want a concrete reason to understand the recommendation that 11–12 year olds receive HPV vaccine.
TRY SAYING:	We're vaccinating today so your child will have the best protection possible long before the start of any kind of sexual activity. We vaccinate people well before they are exposed to an infection, as is the case with measles and the other recommended childhood vaccines. Similarly, we want to vaccinate children well before they get exposed to HPV.
CDC RESEARCH SHOWS:	Parents may be concerned that vaccinating may be perceived by the child as permission to have sex.
TRY SAYING:	Research has shown that getting the HPV vaccine does not make kids more likely to be sexually active or start having sex at a younger age.

Action 3

Minimize missed opportunities

What is a missed opportunity?

A missed opportunity is any patient visit where we could have vaccinated a patient, but missed the chance to do so.

This could be an acute care visit, a school physical, or a walk-in visit.

Strategies to Reduce Missed Opportunities

- Efficient workflows
- Pre-visit planning
- Expand access
- Practice culture
- EHR prompts/Immunization Information System (IIS) reconciliation

Action 4 Take a Team Approach

Team Strategies

- Standing orders
- Consistent messaging
- In-service training
- Huddle reminders
- Practice motivational interviewing
- Schedule follow-up visit

Action 5

Evaluate and sustain success

Evidence-based Strategies to Improve vaccination Coverage

- Reminder/recall system
  - Provider level (e.g., EMR prompts)
  - Parent/patient level (e.g., postcards, telephone calls, text messaging)
- Standing orders
- Provider assessment and feedback
  - Assessment of vaccination coverage levels within the practice and discussion of strategies to improve vaccine delivery
- Utilizing immunization information systems

Take Home Points

- Cervical Cancer Screening is effective at reducing the rates of cervical cancer diagnosis and related mortality
- Important to follow up on abnormal results and only apply guidelines to average risk women
- Inequity still exists in outcomes – we can do better!
- HPV vaccination is effective and safe

Questions?

Acknowledgement – Dr. Sophia Newcomer

- Many of the HPV slides contained NIS – team data.
- The analyses of these NIS-teen data were led by Dr. Sophia Newcomer at the University of Montana's School of Public & Community Health Sciences, conducted in a pilot study funded by the Mountain West Clinical Translational Research – Infrastructure Network under a grant from National Institute of General Medical Sciences of the National Institutes of Health under Award Number 2U54GM104944.

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