

An Overview of Early Cervical Cancer Screening and Treatment: the Future of Diagnose and Treat For Rural America

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Disclosures

- Dr. Sudabeh Moein: Founder and CMO of Moein Health
- Dr. Partha Basu and Dr. Patricia Smith have no conflicts of interest with regards to this presentation

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Osteopathic Medicine (LMU-DCOM)

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(VCEDA)

Health Wagon

International Agency for Research on Cancer/World
Health Organization

Objectives

1. Understand the global burden of cervical precancer/cancer and factors contributing to rising incidence and call to action
2. Review the standard of care for screening/diagnosis/treatment of cervical precancerous condition in low middle income countries (LMICs) vs. USA
3. Delineate the similarities and challenges of cervical cancer screening and management in LMICs and rural USA
4. Highlight current, future, and alternative methods and devices for decreasing the cervical precancer/cancer burden in LMICs and rural USA

Pre CME Lecture Knowledge Check



Global Cervical Cancer Burden, Inequalities, and Solutions

Partha Basu, MD, PhD

Deputy Branch Head Early Detection Prevention and Infections

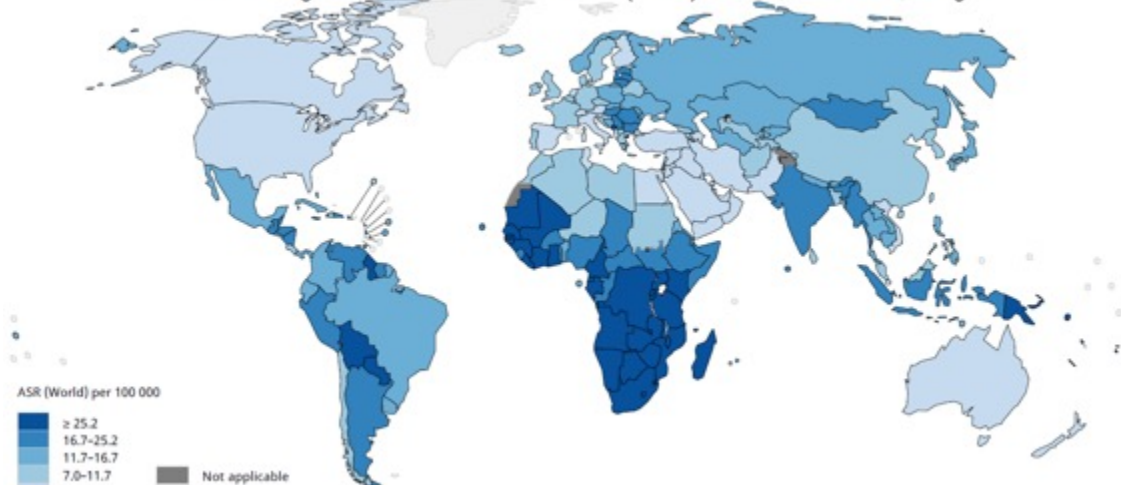
IARC/WHO

No conflict of interest with regards to this presentation

Speaker Objectives

1. Identify statistics demonstrating global inequities in cervical cancer from the World Health Organization
2. List modern diagnostic technology suitable for LMIC rural settings
3. List modern therapeutic technology for cervical cancer, such as thermal ablation

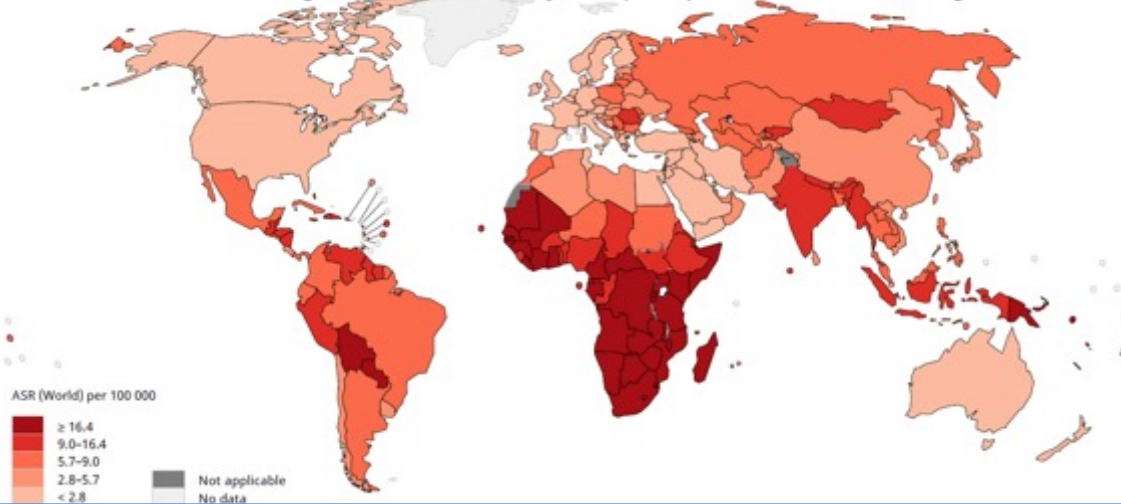
Estimated age-standardized incidence rates (World) in 2020, cervix uteri, all ages



Cervical cancer Worldwide, in 2020

600 000 new cases
340 000 deaths

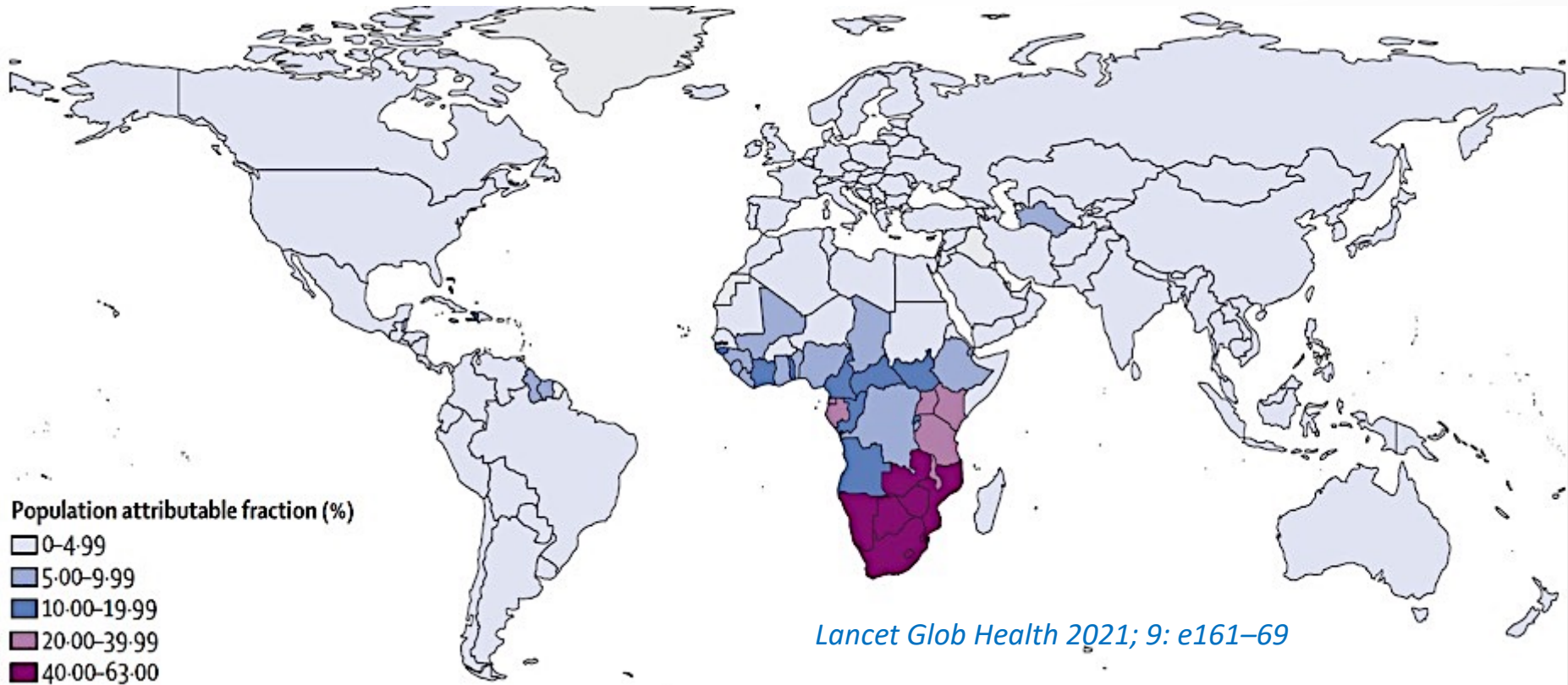
Estimated age-standardized mortality rates (World) in 2020, cervix uteri, all ages



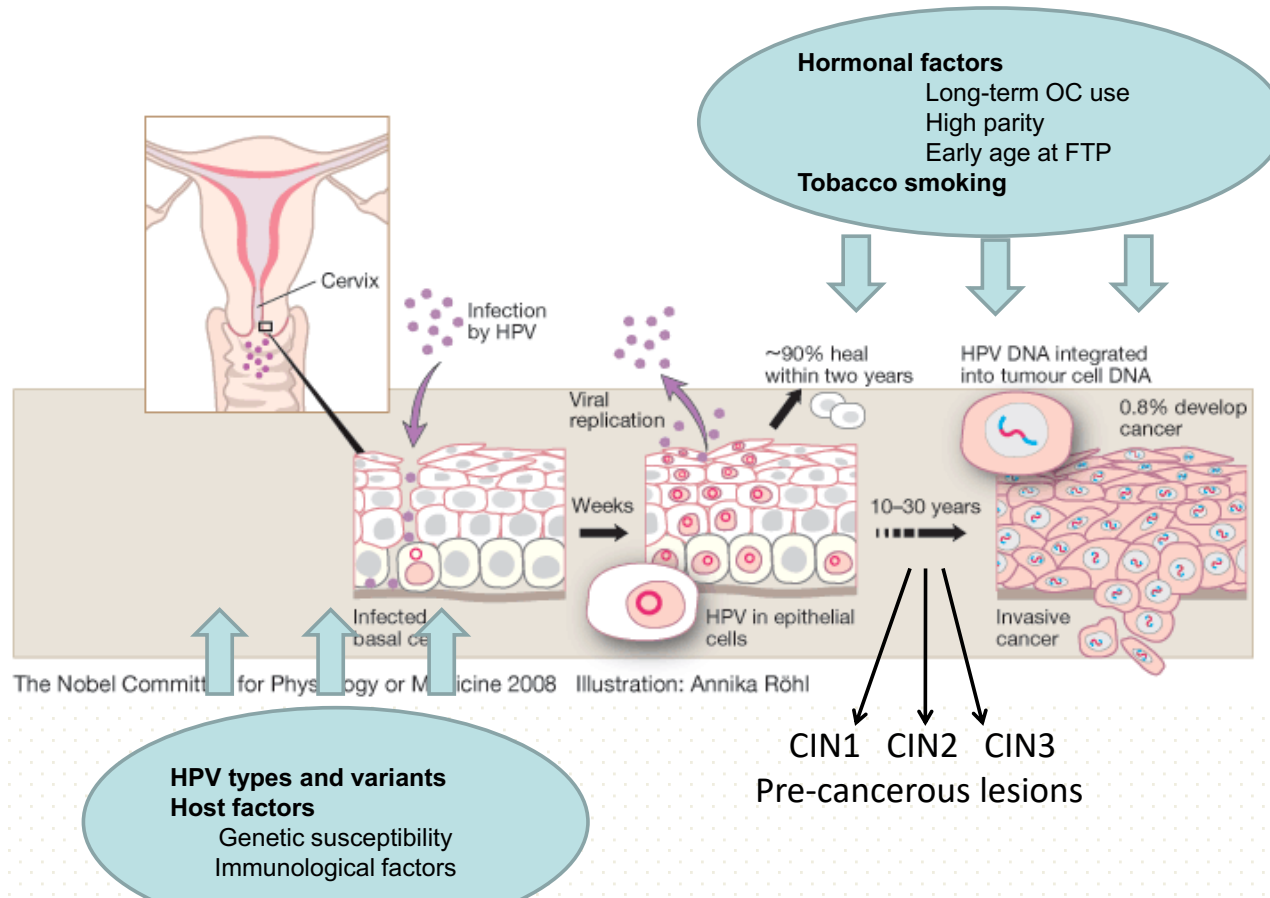
Age-standardised rate of

Incidence: $13,3 \times 100\,000$
Mortality: $7,3 \times 100\,000$

Africa region alone accounts for 85% of CA cx cases attributable to HIV

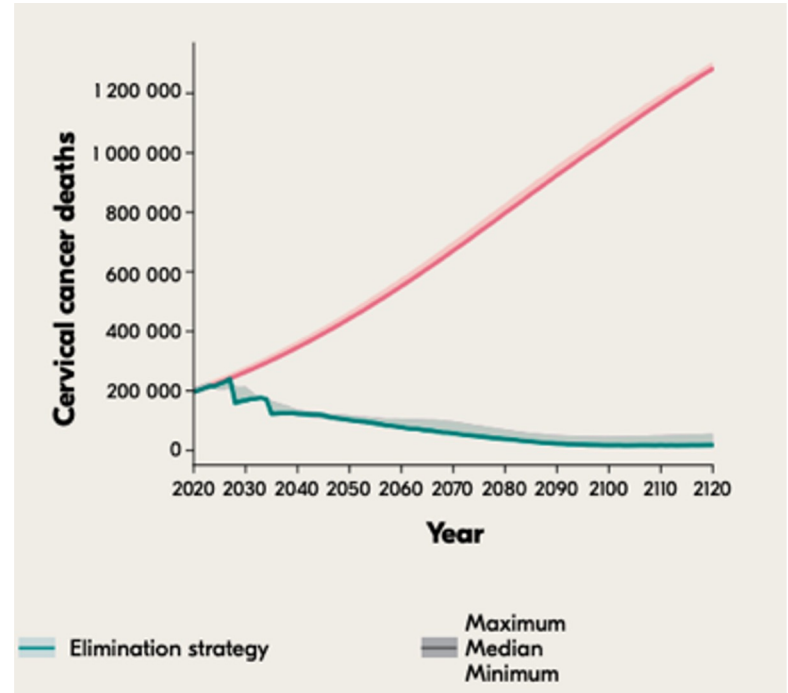


Natural history of cervical cancer



WHO Call to Action

- In 2018, The Director General of the WHO gave a call to eliminate cervical cancer as a public health problem globally
- The aim is to reduce cervical cancer incidence to $<4/100,000$ globally by the end of this millenium
- The WHO has set the 90-70-90 targets for all countries to be achieved by 2030



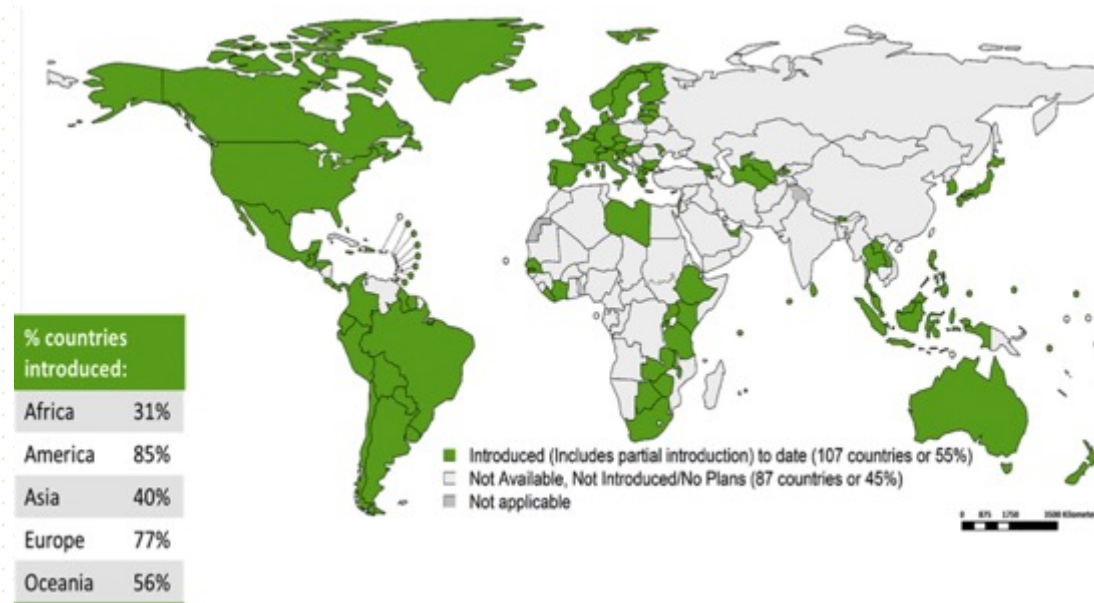
Inequity in Access to HPV Vaccination

112 (58%) countries have HPV vaccination prog

41% of LMICs & 22% of LIC have introduced

70% of 9-14 yr old girls live in countries without program

Only 12% of the girls in LMICs have received 2 doses



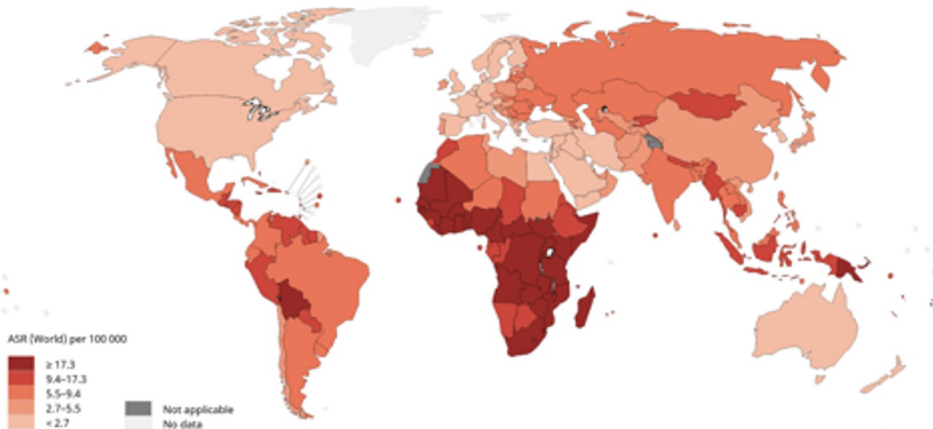
WHO member states with HPV vaccination in their national immunization program, as of June 2020

[Health Topics](#) ▾[Countries](#) ▾[Newsroom](#) ▾[Emergencies](#) ▾[Data](#) ▾[About WHO](#) ▾[Home](#) / [News](#) / One-dose Human Papillomavirus (HPV) vaccine offers solid protection against cervical cancer

One-dose Human Papillomavirus (HPV) vaccine offers solid protection against cervical cancer

Global and USA Map of Inequities

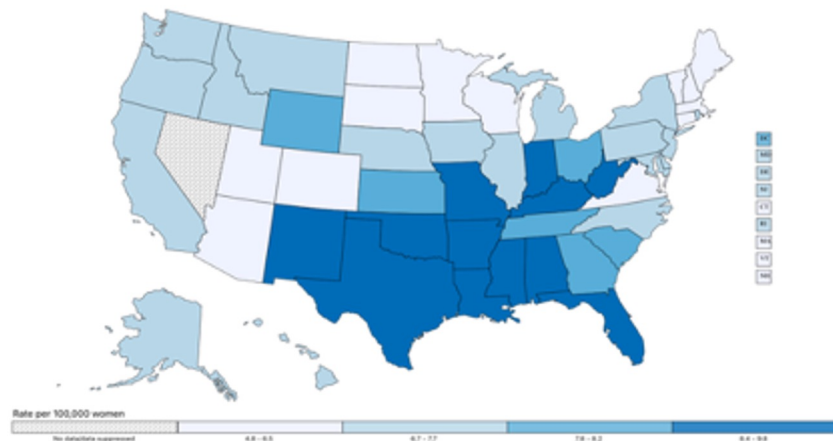
Estimated age-standardized mortality rates (World) in 2018, cervix uteri, all ages



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Data source: GLOBOCAN 2018
Graph production: IARC
[<http://gco.iarc.fr/today>]
World Health Organization

Rate of New Cancers in the United States, 2015-2019
Cervix, All Ages, All Races and Ethnicities, Female

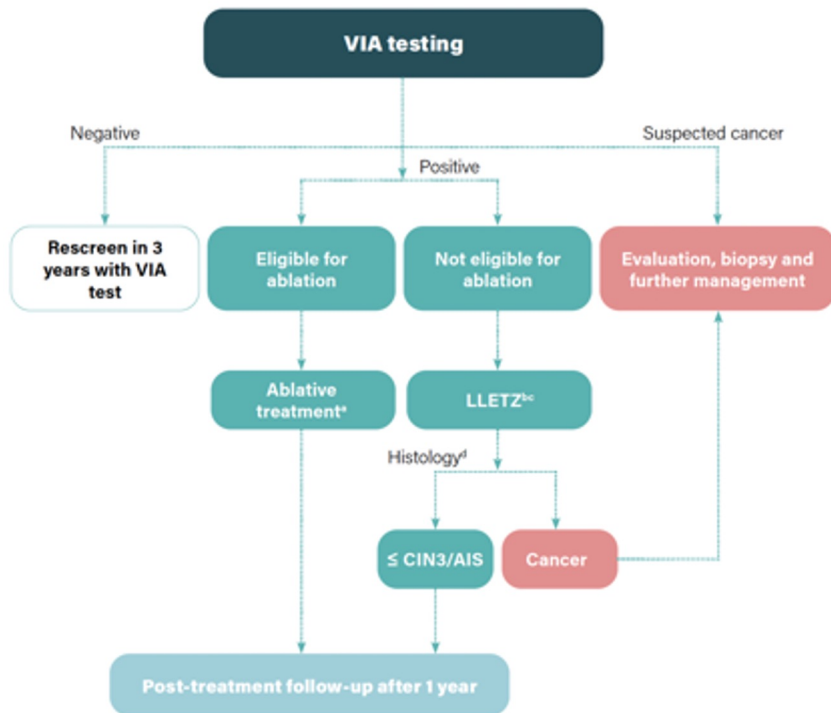


World Health Organization
International Agency for Research on Cancer 2018

Current Standard of Care for Cervical Cancer Screening for LMIC

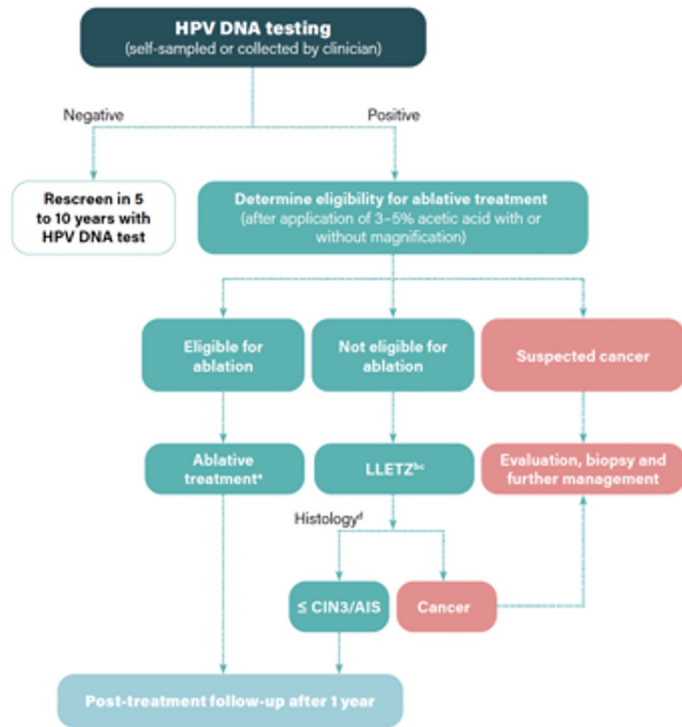
ALGORITHM 1. PRIMARY VIA SCREENING (SCREEN-AND-TREAT APPROACH)

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



ALGORITHM 2. PRIMARY HPV DNA TEST SCREENING (SCREEN-AND-TREAT APPROACH)

For the general population of women



Existing Screening Challenges in LMIC

- Not yet considered as a health priority
- Limited knowledge
- Lack of programme and trained manpower
- Lack of compliance
- No focus on quality of services

Existing Diagnosis Challenges in LMIC

- Access to colposcopy
- Universal need for histopathology in public sector
- Reliance on VIA/VIL in LMIC's; not available in Rural America
- The compliance of the women significantly reduce with the number of visits -
screening, diagnosis and treatment need to be combined in a single visit

Existing Therapeutic Challenges in LMIC

- Few medical care centers that offer LEEP
- Poor quality of LEEP
- Prevalent practices (VIA/VIL) lead to large number of over-treatments
- Possible solutions:
 - Cryotherapy (Not practical in LMIC)
 - Thermal ablation/Ablative treatment
 - Handheld colposcope
 - Limited availability of histopathology post treatment



Cervical Cancer Screening and Management of Premalignancy in the US

Patricia Smith, MD, FACOG

Clinical Assistant Professor of Obstetrics and Gynecology
The George Washington University School of Medicine

No conflict of interest with regards to this presentation

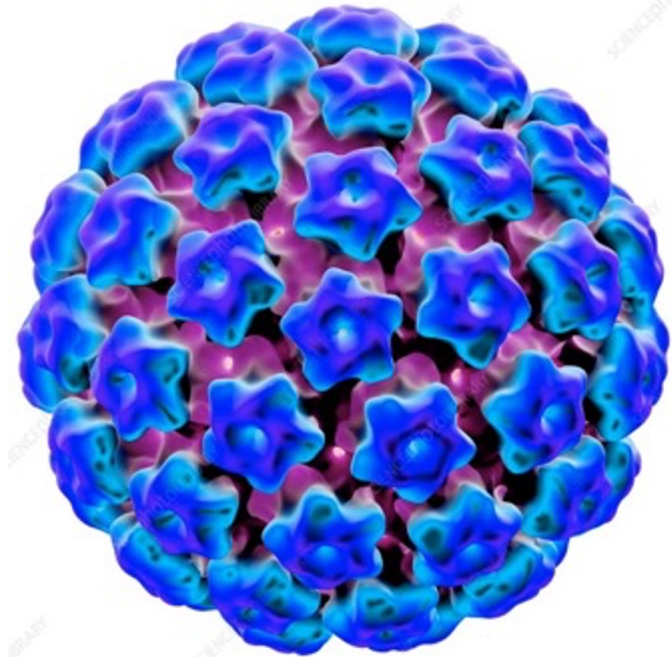
Speaker Objectives

1. Judge the history of pap smears and colposcopy in the US
2. Distinguish different grades of CIN from the basic etiology and science of cervical cancer dysplasia
3. Implement US management of cervical cancer care, such as treatment options and timeline

Human Papilloma Virus (HPV)

- HPV infection is very common
- Major etiologic agent in cervical precancerous lesions/carcinoma
- Non-enveloped double-stranded DNA virus in Papillomaviridae family, >150 genotypes
- 40 genotypes infect anogenital tract - divided into high-risk and low-risk

Oncogenic strains = high risk HPV (hrHPV)

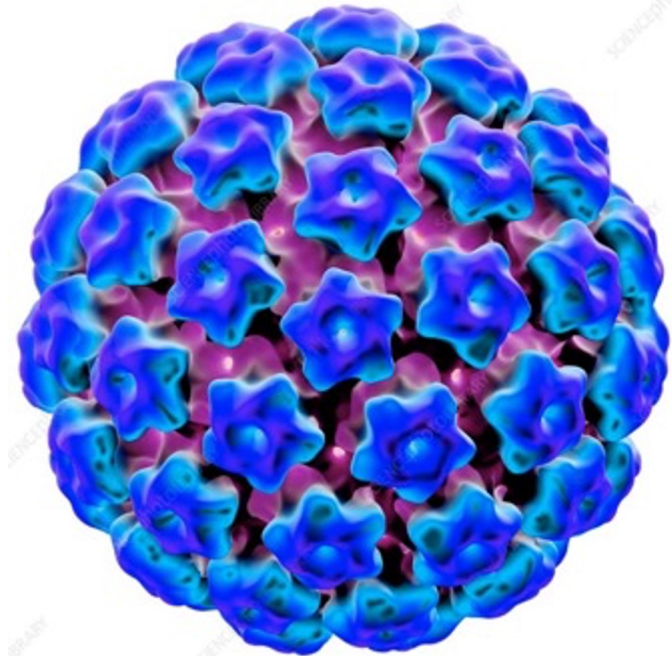


Reference:

Cervical cancer: epidemiology, prevention and the role of human papillomavirus infection. Franco EL, Duarte-Franco E, Ferenczy A CMAJ. 2001;164(7):1017.

Human Papilloma Virus (HPV)

- **HPV16 & HPV18**
 - cause **70% of high-grade cervical lesions**
 - 50% by 16, 20% by 18
 - other hrHPV genotypes - 31, 33, 35, 39, 45, 51, 52, and 58
- **Low-grade squamous intraepithelial lesions (LSIL) – Transient HPV infection**
 - cleared within 2 to 5 years and have a low risk of malignancy
- **High-grade squamous intraepithelial lesions (HSIL) – Persistent infection**
 - greater risk of progression to cervical cancer



Reference:

Cervical cancer: epidemiology, prevention and the role of human papillomavirus infection. Franco EL, Duarte-Franco E, Ferenczy A CMAJ. 2001;164(7):1017.

Cervical Cancer Screening - Standard of Care in US

- Screening recommendation depends on age and presence of cervix in immunocompetent patients
- Endorsed by ASCCP, ACOG, SGO

Population*	Recommendation	USPSTF Recommendation Grade†
Aged less than 21 years	No screening	D
Aged 21–29 years	Cytology alone every 3 years‡	A
Aged 30–65 years	Any one of the following: <ul style="list-style-type: none">• Cytology alone every 3 years• FDA-approved primary hrHPV testing alone every 5 years• Cotesting (hrHPV testing and cytology) every 5 years	A
Aged greater than 65 years	No screening after adequate negative prior screening results§	D
Hysterectomy with removal of the cervix	No screening in individuals who do not have a history of high-grade cervical precancerous lesions or cervical cancer	D

Pap Terminology

Negative for intraepithelial malignancy (NILM) – A specimen that is adequate for evaluation and in which no epithelial abnormality is identified.

Atypical squamous cells of undetermined significance (ASC-US) – Cells that display abnormalities more marked than simple reactive changes but do not display a squamous intraepithelial lesion; in some cases, these lesions are associated with cervical intraepithelial neoplasia (CIN) .

Atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H) – Cells that likely consist of a mixture of true high-grade squamous intraepithelial lesion and other findings that mimic such lesions

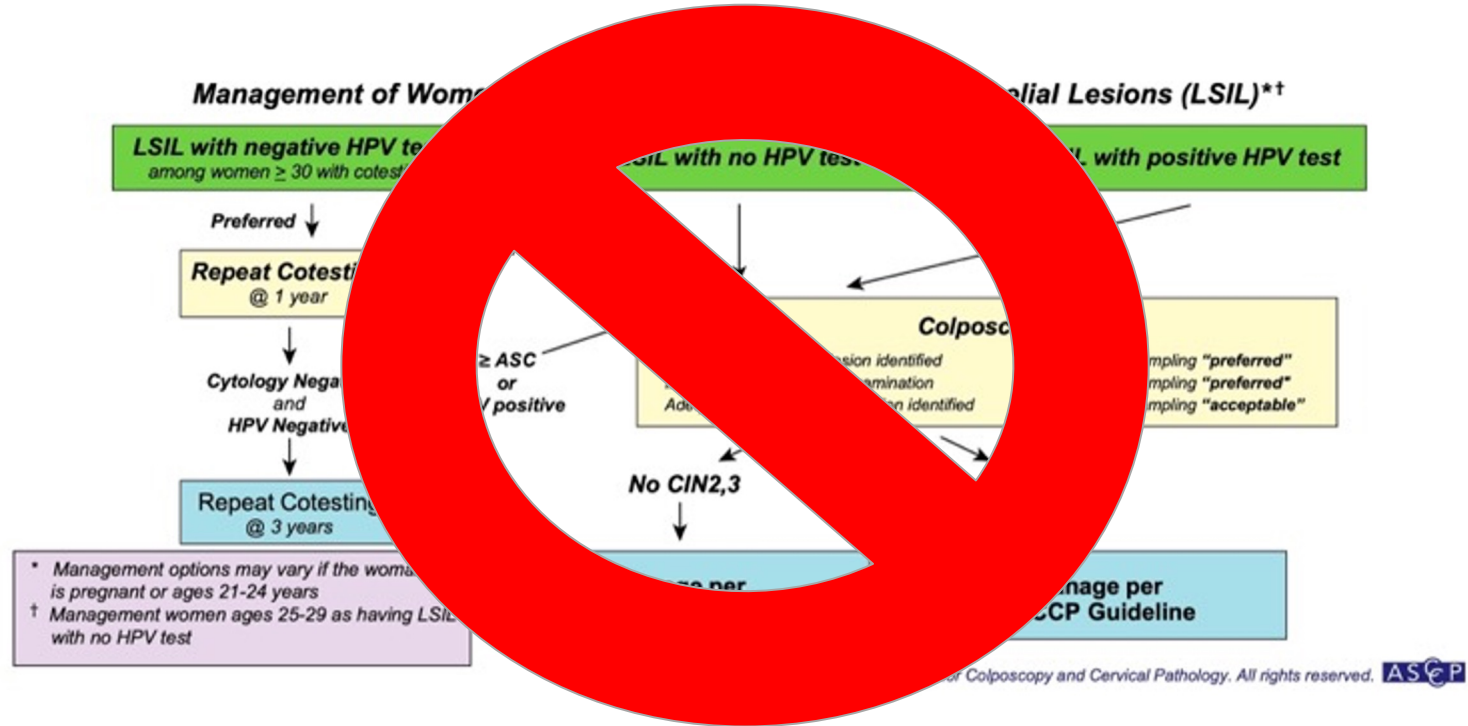
Low-grade squamous intraepithelial lesions (LSIL) – Lesions associated with human papillomavirus (HPV) infection. These tend to be associated with transient changes that regress over time

High-grade squamous intraepithelial lesions (HSIL) – Lesions associated with high-risk types of HPV and that have a high risk of progression to CIN or cancer

Cervical cancer screening co-testing – Testing with both cervical cytology (Pap test) and HPV testing.

Reflex testing – The collection of a specimen for either HPV or cytology testing, and performing the other test **only** if the results of the first test are abnormal

Management: Abnormal Cervical Cancer Screening



Reference: 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH, Garcia F, Huh WK, Kim JJ, Moscicki AB, Nayar R, Saraiya M, Sawaya GF, Wentzensen N, Schiffman M, 2019 ASCCP Risk-Based Management Consensus Guidelines Committee J Low Genit Tract Dis. 2020;24(2):102.

Management: Abnormal Cervical Cancer Screening

- Recommendations based on **risk of CIN3+**, not results
 - determined by a combination of current results and past history (or unknown history)
 - Same current results can have different management recommendations
- Management also takes into factors in patient's age, plans for future childbearing, pregnancy, immunocompetency etc
- Risk estimate tables found online; American Society for Colposcopy and Cervical Pathology (ASCCP) provides a management guidelines app to facilitate use

Depending on above, management recommendations can be **surveillance, colposcopy/cervical biopsy, or expedited treatment**

Age

Under 25
YEARS25 to 29
YEARS30 to 65
YEARSOver 65
YEARS

Clinical Situation

Routine screening (within past 5 years) >

Rarely screened (>5 years ago) >

Evaluation of a colposcopic biopsy >

Management of results during post colposcopy surveillance (within past 7 years) >

Follow-up after treatment >

Special Situation

Unsatisfactory cytology >

Post hysterectomy >

Symptomatic >

Immunosuppressed >

Help me decide Next >



Clinical Situation



Testing



Recommendation

Current testing



HPV



None



Negative

Positive
(untyped)Positive
(genotyped)

Cytology



Normal



ASC-US



LSIL



ASC-H

< Back

Next >



Clinical Situation



Testing



Recommendation

Recommendation

Colposcopy/Treatment¹After treatment, HPV-based testing at 6 months is preferred at follow-up visit²

Risk

Immediate risk of CIN3+ is 26%¹

Colposcopy

Diagnostic procedure with colposcope – provides an illuminated, magnified view of the cervix, vagina, and vulva

Used as follow-up evaluation for abnormal cervical cancer screening tests (dependent on risk) or abnormal findings on gross examination of the cervix, vagina, or vulva.

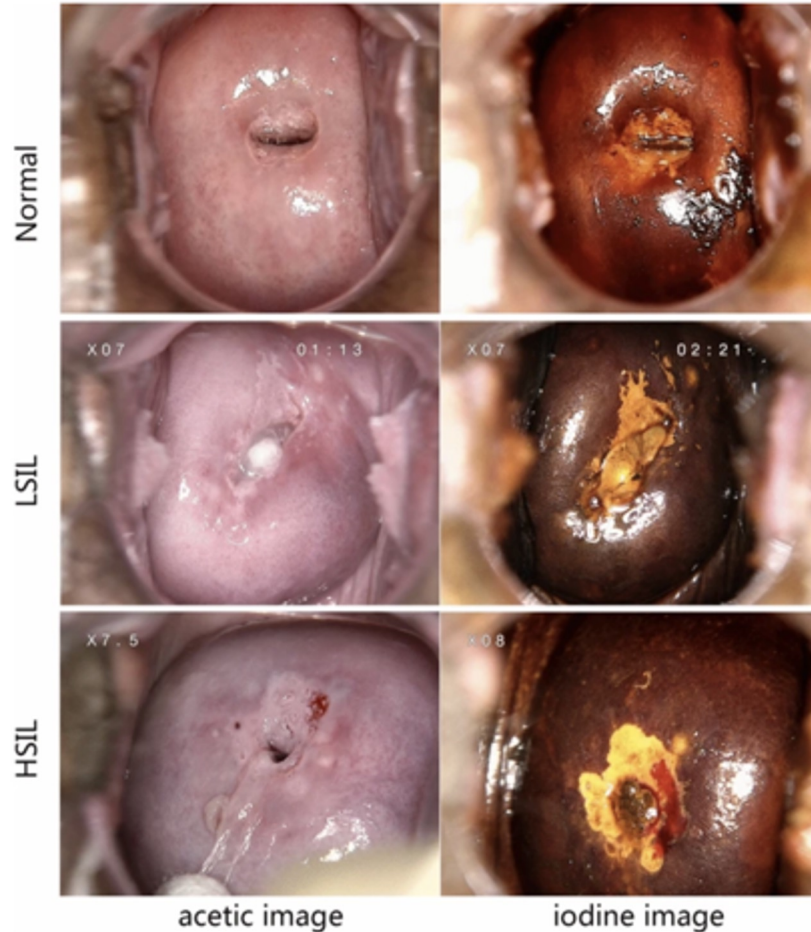
Typically involves application of dilute acetic acid and/or Lugol's iodine – allows delineation of cervical precancerous changes.

Malignant and premalignant epithelium have specific macroscopic characteristics relating to contour, color, and vascular pattern that can be identified by the colposcopist for directed biopsy.

Colposcopy Equipment and Devices



Acetic Acid and Lugol's Staining as Observed by Colposcopy

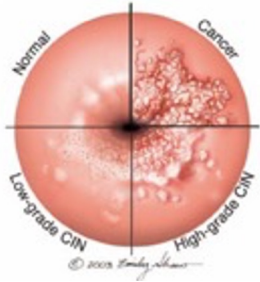


LSIL typically corresponds to CIN 1

HSIL typically corresponds to CIN 2 or CIN 3

The representative acetic and iodine images of the normal, LSIL and HSIL case.

Cervical Intraepithelial Neoplasia (CIN)

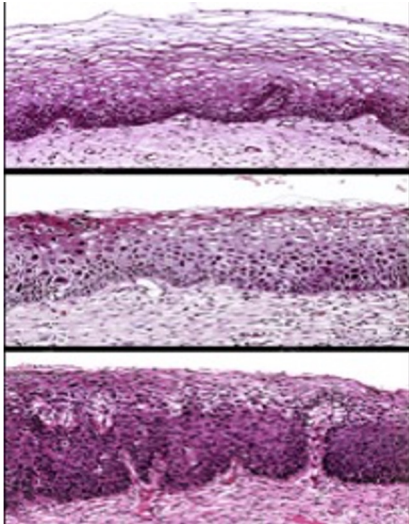


Cervical intraepithelial neoplasia (CIN) Premalignant squamous lesion of the uterine cervix diagnosed by cervical biopsy and histologic examination

TISSUE IS THE ISSUE!!

Classified on a scale from one to three

- CIN 1: Refers to abnormal cells affecting about $\frac{1}{3}$ of the thickness of the epithelium
- CIN 2: Refers to abnormal cells affecting about $\frac{1}{3}$ to $\frac{2}{3}$ of the epithelium
- CIN 3: Refers to abnormal cells affecting $> \frac{2}{3}$ of the epithelium



Cervical Intraepithelial Neoplasia (CIN)

Risk for progression to cancer is related **age** and **CIN grade**

- Patients <25 years have lower risk of developing cervical cancer than patients \geq 25 years
- **CIN 1 - low-grade lesion** that has a low potential for malignancy, high potential for regression; observation preferred for most younger patients
- **CIN 2,3 - high grade lesion** that has a higher potential for progression and a lower potential for regression
 - Observation also an option for some patients with CIN 2, such as those who plan future childbearing and are concerned about the potential adverse obstetric outcomes (eg, preterm delivery) associated with treatment
- **CIN 3 is premalignancy to cervical cancer**, treatment always recommended in non-pregnant patients

References

Wright, J. (2022). Cervical Intraepithelial Neoplasia: Management. Goff, B (Ed.), *UpToDate*. Retrieved July 8, 2022, from <https://www.uptodate.com/contents/cervical-intraepithelial-neoplasia-management>

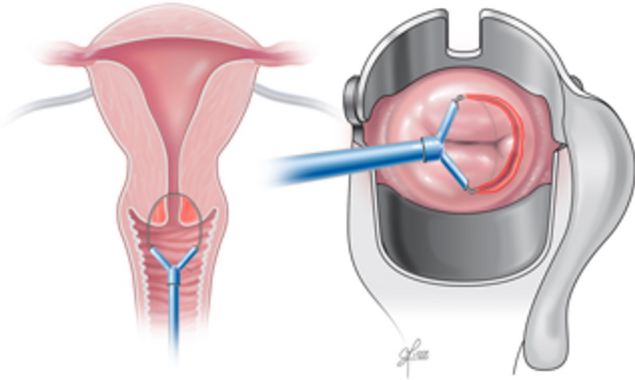
Treatment of CIN3+ in US

Treatment for precancerous lesions of the cervix involve *excision of a cone-shaped portion of the cervix surrounding the endocervical canal and including the entire transformation zone (TZ)*

Two types of excisional treatments:

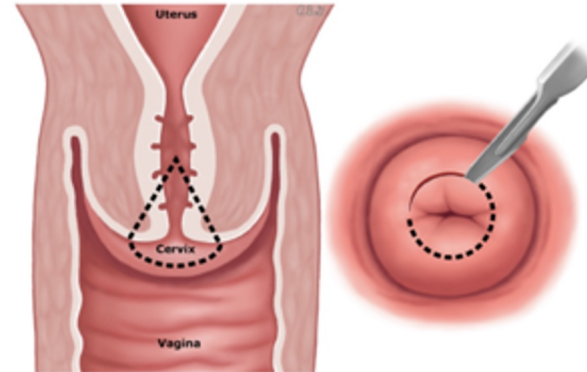
Loop Electrosurgical Excisional Procedure (LEEP)

Electrical loop used to obtain specimen - office procedure
OR

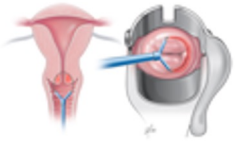


Cold-knife Conization (CKC)

Scalpel used to obtain specimen - need to do in



Treatment of CIN3+ in US: Excisional Procedures



LEEP

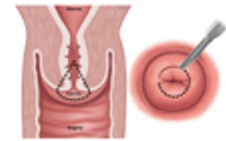
Advantages:

- Easily done in the office setting
- Rapid performance
- Technically easy
- Equipment inexpensive
- Low complication rate
- Good specimen quality
- Healing with minimal distortion

Disadvantages:

- Some thermal damage to specimen, cervix
- A large or deep cone may be difficult to perform in the office and result in more thermal damage if a second loop excision is required

CKC



Advantages

- Technical simplicity
- Excellent specimen quality

Disadvantage

- General or regional anesthetic required - must be done in OR = \$\$\$
- Distortion after healing
- Complication rate higher (e.g. cervical insufficiency, preterm delivery)

Treatment of CIN3+ in US

Excisional treatment is the gold standard and preferred over ablative treatment for histologic HSIL (CIN 2 or CIN 3) in the United States.

Excisional treatment is recommended for adenocarcinoma in situ (AIS).

Observation is preferred management for CIN 1

Reference

Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH, Garcia F, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. 2019 ASCCP Risk-Based Management Consensus Guidelines Committee. J Low Genit Tract Dis 2020;24:102–31. Available at: https://journals.lww.com/jlgt/Fulltext/2020/04000/2019_ASCCP_Risk_Based_Management_Consensus.3.aspx. Retrieved July 7, 2022.

Challenges: Cervical Cancer Screening in US

Patient discomfort and psychosocial consequences – Inconvenient, anxiety provoking

Rising health care costs

False-positive results – Both HPV testing and Pap testing are associated with false-positive results that lead to subsequent testing, follow-up examinations, and downstream interventions.

Risks of treatment on pregnancy outcomes – The harmful effects of treatment (ie, ablation, excision) on pregnancy outcomes include increased risk of second-trimester pregnancy loss, preterm premature rupture of membranes, preterm delivery, and perinatal mortality. This is discussed in more detail separately.

Reference: Feldman S, Goodman A, Peipert J (2022). Screening for cervical cancer in resource-rich settings. Goff, B (Ed.), *UpToDate*. Retrieved July 8, 2022, from <https://www.uptodate.com/contents/screening-for-cervical-cancer-in-resource-rich-settings>

Challenges: Cervical Cancer Screening in US

ACS updated cervical cancer screening guidelines recommend **primary hrHPV testing** as preferred screening option for average-risk individuals aged 25–65

Can greatly improve access to cervical cancer screening, but still investigational in the United States

Despite the demonstrated efficacy and efficiency of primary hrHPV testing (utilized commonly in Europe) slow to be adopted in US

- limited availability of FDA-approved tests
- significant laboratory infrastructure changes

Limited access to primary hrHPV testing is of particular concern in rural and under-resourced communities, communities of color – disproportionately high rates of cervical cancer incidence, morbidity, and mortality



Reference: American College of Obstetricians and Gynecologists. Updated guidelines for management of cervical cancer screening abnormalities. Practice Advisory. Washington, DC: American College of Obstetricians and Gynecologists; 2020. Available at: <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/10/updated-guidelines-for-management-of-cervical-cancer-screening-abnormalities>. Retrieved July 7, 2022.

Diagnosis and Treatment Methodologies and Innovations for Rural USA

Sudabeh Moein, MD, FACOG, ABIHM

Moein Health Foundation

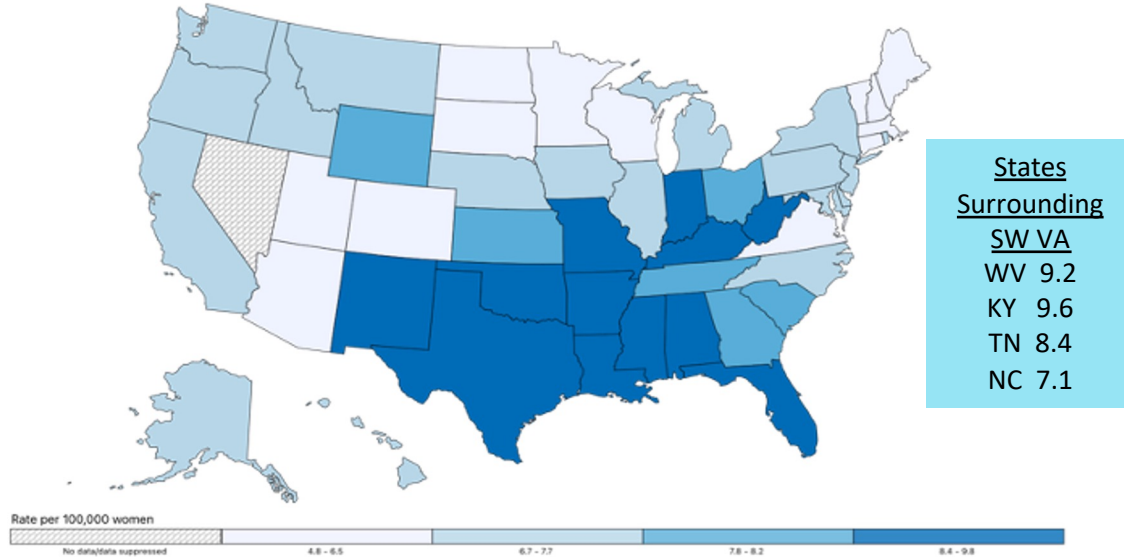
Founder and CMO

Speaker Objectives

1. Compare Moein Health Clinical innovations (begins at slide 34) Research Findings to the standard current standard of care in diagnosis and treatment
2. Distinguish differences between standard colposcopy (non-disposable devices) versus colposcopy with convenience kit (disposable devices)
3. Weigh the novel methods of 1. biopsy in the same visit, and 2. treatment in the same visit
4. By demonstration of current and future methods, will identify gaps and shortcomings with current methods and how future methods overcome these gaps and shortcomings.

Inequities within the US

Rate of New Cancers in the United States, 2015-2019
Cervix, All Ages, All Races and Ethnicities, Female



Source - U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999-2019): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; <https://www.cdc.gov/cancer/dataviz>, released in June 2022.

Reference

CDC, Locklar et al., 2022, Duarte et al., 2022

Inequities within the US



Example: Cumberland Plateau Health District

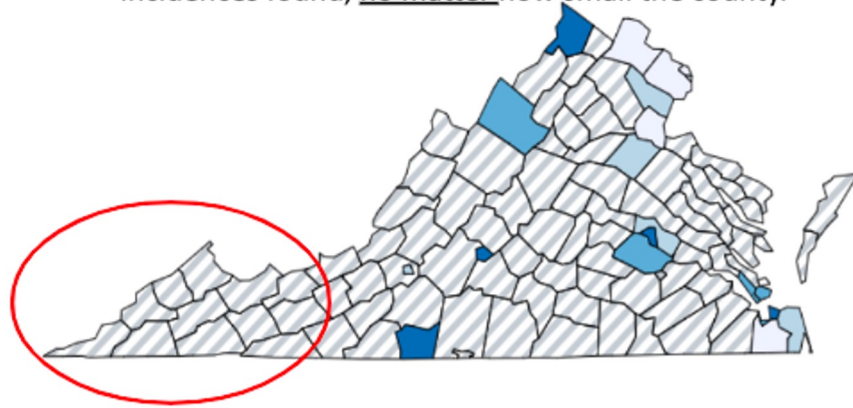
- Ranks 8th in incidence of cervical cancer.
- Ranks 35th (worst) in staging rate for cervical cancer. Later detection means lost lives and more money spent.

Poor ranking (35th) in staging indicates early screening is inadequate

Rate of New Cancers in Virginia

Cervix, All Ages, All Races/Ethnicities, Female, 2013-2017

Values artificially skewed low / suppressed when less than 16 incidences found, no matter how small the county.



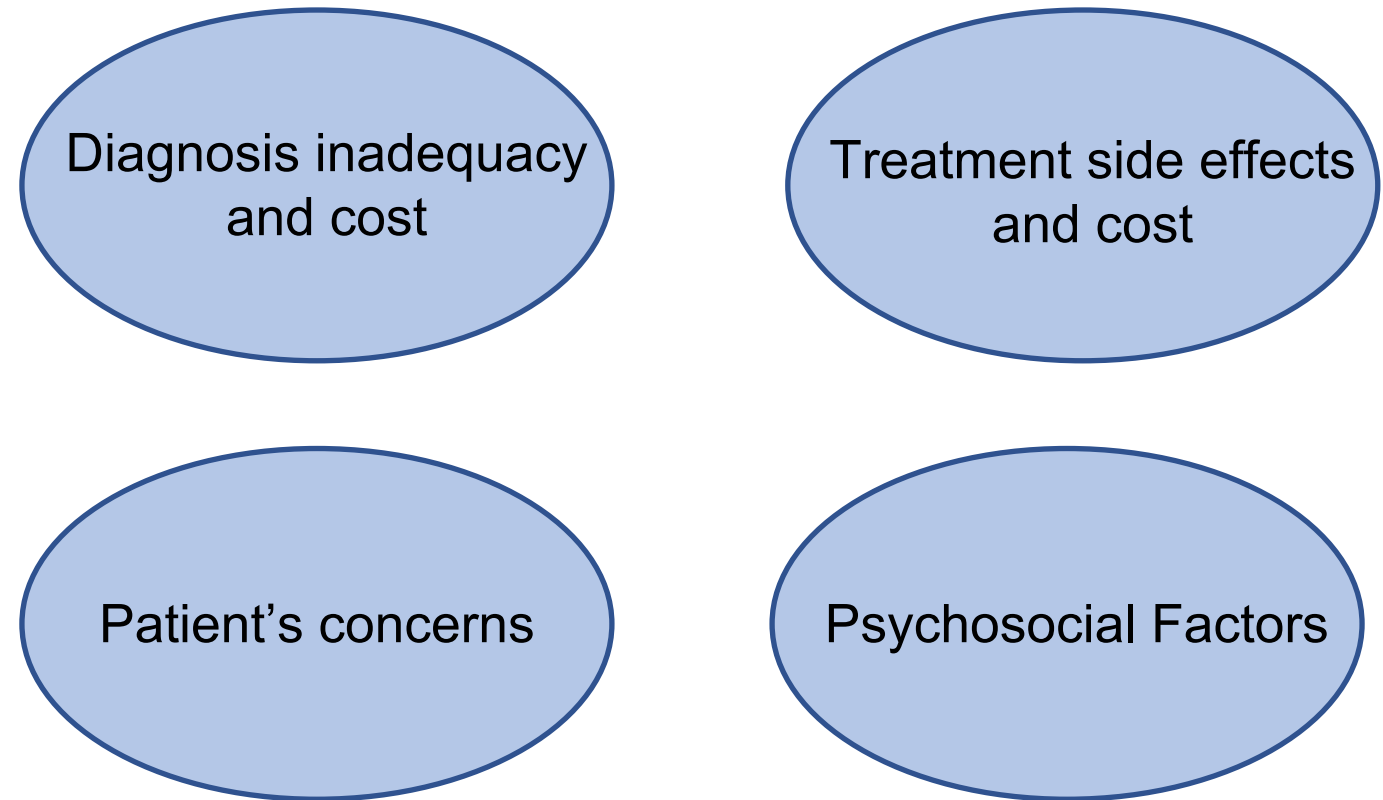
Rate per 100,000 people

Data source – U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on November 2019 submission data (1999-2017); U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; <https://www.cdc.gov/cancer/dataviz/>, June 2020.

US vs LMIC: Highlights

	US	LMIC
Screening	<ul style="list-style-type: none">• Pap +/- HPV	<ul style="list-style-type: none">• Shifting to HPV typing
Diagnosis	<ul style="list-style-type: none">• Colposcopy + Biopsy	<ul style="list-style-type: none">• VIA• Hand held colpo +/- Biopsy
Management	<ul style="list-style-type: none">• LEEP, CKC	<ul style="list-style-type: none">• Thermocoagulation +/- LEEP, referral to tertiary care center

Clinical Challenges and Contributing Factors



Diagnosis inadequacy
and cost

Treatment side effects
and cost

Patient's concerns

Psychosocial Factors

Clinical Challenges and Contributing Factors

Diagnosis inadequacy and cost

- Requires screening visit before diagnosis visit
- AA staining (colposcopy or VIA) is inaccurate

Patients' concerns

- Pain during procedure
- Poor health care access
- Time for multiple visits
- Fear of catching disease

Treatment side effects and cost

- LEEP shortens and scars the cervix
- Preterm births
- Inadequate subsequent colposcopy

Psychosocial factors

- Lack of awareness and education
- Inadequate health resources
- Fear of death from cancer
- Shame and vulnerability
- Social stigma with having HPV or cancer
- Embarrassment with male examiners
- Shortage of physicians in rural USA

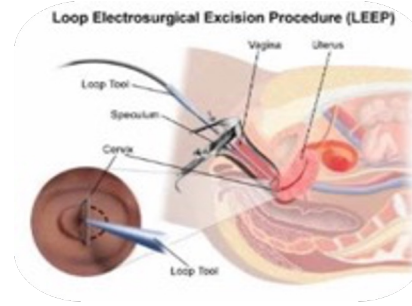
Current Standard of Care



Screening



Diagnosis



Treatment



Follow Up

4 Visits

Diagnosis with AA can be
missed 55% of the time

Innovations, Methods, and Solutions

Screening → Diagnosis → Treatment → Diagnose and Treat

- ColpoKit
- VIA Kit
- FNA Kit
- VIA with FNA Kit
- Topical TCA Kit
- MH D&T Kit
 - FNA = Fluorescein Sodium
 - TCA = Trichloroacetic Acid

Additional Solutions

- Speculum (disposable/hygienic, expandable/comfortable, illuminating)

Nature of the strategy

- Condensed visits without compromising diagnosis or quality of care.
- Easy-to-use disposable kits for all levels of practitioners and clinicians.

Patents

- Moein, et. al.; METHODS AND KIT FOR DIAGNOSING AND TREATING NEOPLASTIC TISSUE. US Patent 10,588,564, 11/5/2019
- Moein, et. al.; ONE-TIME USE EXPANDABLE SPECULUM. US 16/538532, filed August 12, 2019. Patent approved June 9, 2022
- Moein, et. al.; APPLYING THERAPEUTIC AGENTS FOR GENITAL AND ANAL PRE-CANCER TREATMENT, INCLUDING CERVICAL INTRAEPITHELIAL NEOPLASIA, APPLICATION # 63/367,755, Filed: 2022-07-06,

Challenge 1. ColpoKit - Screen & Diagnose

- Challenges that the kit addresses:
 - Need for multiple visits → combines 2 visits to 1
 - Patients' fears of iatrogenic infections → disposable tools
 - Pain → less pain with SoftBiopsy devices (Winter et al., 2012)



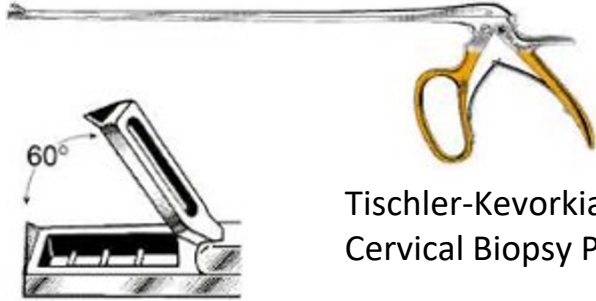
Instructions for use:

1. Place drape sheet on medical tray.
2. Place all items on tray per image below.
3. Unwrap speculum, place on upper left side of tray.
4. Open lubricant packet and squeeze contents near speculum.
5. Place cup 1, cup 2 and amber Lugol's iodine solution jar.
6. Open both saline solutions and pour into cup 1.
7. Open both vinegar packets and pour into cup 2.
8. Remove lid from amber jar.
9. Place 1 pipette next to each cup and jar.
10. Open all cotton swab packets and place as illustrated.
11. Place un-opened Soft ECC® by cotton swabs.
12. Place un-opened SoftBiopsy® brushes by Soft ECC brush®.



For Comments or Questions please contact MoeinHealth.org

Current Devices



Tischler-Kevorkian
Cervical Biopsy Punch



Kevorkian curette

Disposable, Modern Devices



SoftBiopsy® - Gynecological Biopsy Device



Soft-ECC® - Endocervical Curette

Convenience Kit Demonstration

See Video

Upcoming (August 2022) Feasibility Study in Wise County in partnership with LMU and Health Wagon

Are you at risk for Cervical Cancer?

Screening can prevent cervical cancer deaths.



*Every 2 minutes one woman in the world dies of cervical cancer.
In the U.S. most of those women live in rural areas.*

FREE Cervical Cancer Screening with *The Health Wagon* Aug 19 – 24

Participants will receive FREE testing and a women's cervical cancer exam. We are investigating a new screening method that reduces discomfort, allows a quicker exam, and provides rapid results. **Be wise – get tested!**

Who should be screened?

Any woman aged 21-64.

Where can I sign up?

Contact The Health Wagon **276-328-8850** (ext. 2).

Why should I participate?

- You could save your life.
- You will receive follow-up care information on results.
- Your input helps guide future education programs in your community.



Challenge 2 : Diagnosis with Colposcopy

- High inter-observer variability
 - As high as 52.4% (Hopman 1991)
 - Poor kappa values (Massad et al., 2008)
- High rate of false negative and false positive test results (Slawson et al., 1993)
 - FP: 4-33%
 - FN: 40-60%
- Poor staining for high grade lesion leads to increased false negatives for CIN2+ (20% increase) (Huh 2014)
 - “This analysis clearly demonstrates that colposcopy is far from perfect and likely misses clinically significant disease.” (Huh 2014)
 - “Whether taking additional biopsies, random biopsies, or both, colposcopists should strive to optimize disease detection.” (Huh 2014)

Diagnosis Images 2002, 2017

- Challenges that FNa addresses:
 - Access to healthcare
 - Cost and complexity
 - Limitations of colposcopy

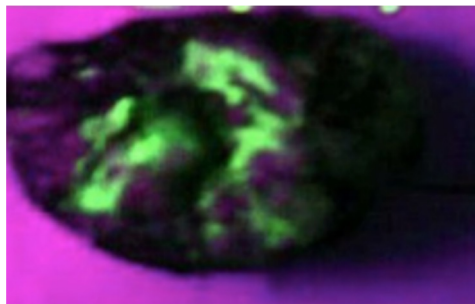
WHO Colposcopy Workshop, 2017

Images by Dr. Moein in Dhaka, Bangladesh,

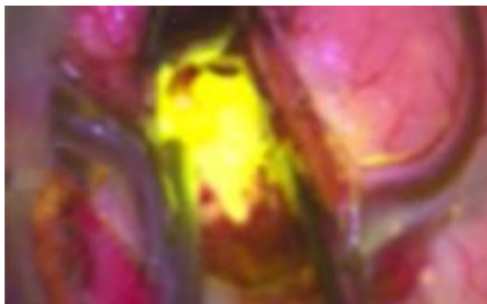
WHO Colposcopy Workshop, 2017

Fluorescein Sodium (FNa) as Diagnostic Contrast Staining Agent

First Use of FNa to Diagnose Cervical Cancer, 2002 (R. Mohajer, S. Moein)



Fluorescein Guidance in Glioblastoma Resection, 2017

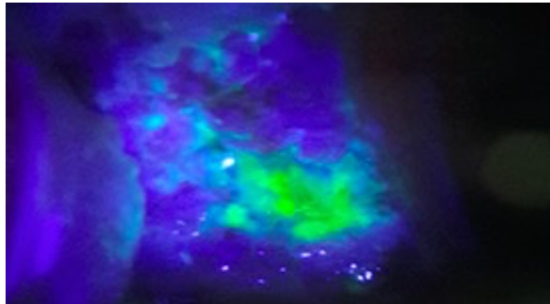


Diagnosis Study and Images: Mexico, 2017

2016 – 2017 Fluorescein Sodium Study Universidad de Monterrey, Mexico (>1500 screened)

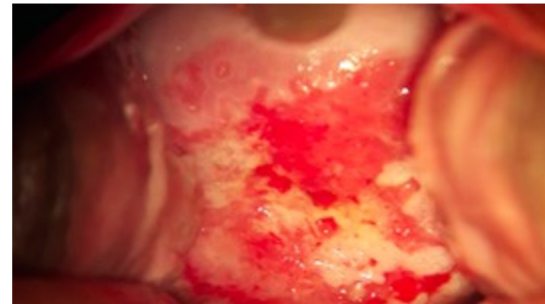
Fluorescein Sodium

- Sensitivity = 94.4%
- **Specificity = 100%**
- Positive Predictive Value = 100%
- Negative Predictive Value = 60%



Acetic Acid

- Sensitivity = 98.6%
- **Specificity = 50%**
- Positive Predictive Value = 95.9%
- Negative Predictive Value = 75%



References: Lopez , A. Moein S. Thesis published at Universidad de Monterrey in 2017. Images courtesy of UDM, Dept of Colposcopy, 8/31/2017, Statistical Analysis courtesy of Dr. Srabani Mittal, Kolkata, India

Moein Health Clinical Research Findings

Study Title	n=	FNa Sensitivity Specificity PPV NPV	AA Sensitivity Specificity PPV NPV	Results
Harbor UCLA	34 abnormal pap	100.00% 78.95% 78.95% 100.00%	100.00% 42.11% 57.69% 100.00%	FNa is more specific than AA. Null hypothesis rejected, FNa \neq AA.
Mexico	1500 screened 78 abnormal pap	94.4% 100% 100% 60%	98.6% 50% 95.9% 75%	FNa is more specific than AA
India	207 screened 70 abnormal screen	82% 65% 60% 85%	59% 95% 95% 79%	FNa results diminished by separating staining intensity levels.

Analogous Research on FNa

Novel Use of Fluorescein Dye in Detection Of Oral Dysplasia and Oral Cancer

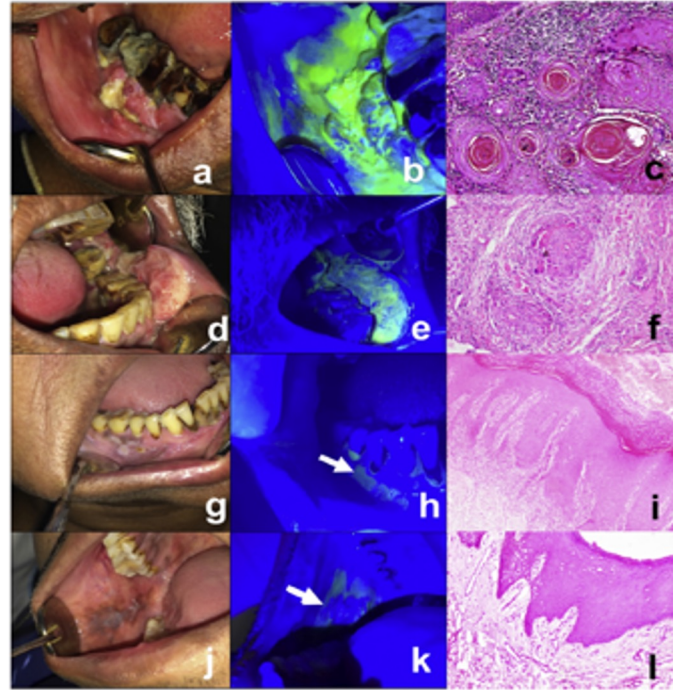
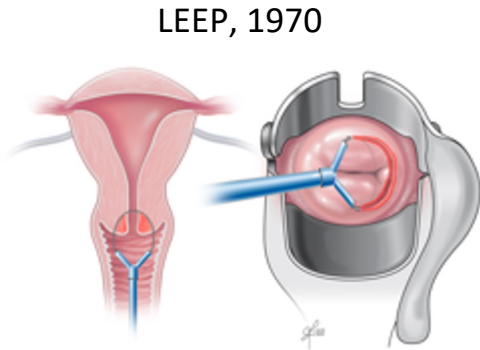


Fig. 1. Case subject of histopathologically diagnosed Oral squamous cell carcinoma (OSCC) depicting intense fluorescein staining intensity (a, b, c). Case subject of OSCC depicting moderate fluorescein staining intensity (d, e, f). Case subject of oral potentially malignant disorder (OPMD) histopathologically diagnosed as moderate dysplasia depicting mild fluorescein staining intensity (white arrow; g, h, i). Case subject of tobacco induced keratosis with no dysplasia depicting absence of fluorescein staining (white arrow; j, k, l).

Challenge 3: Treatment

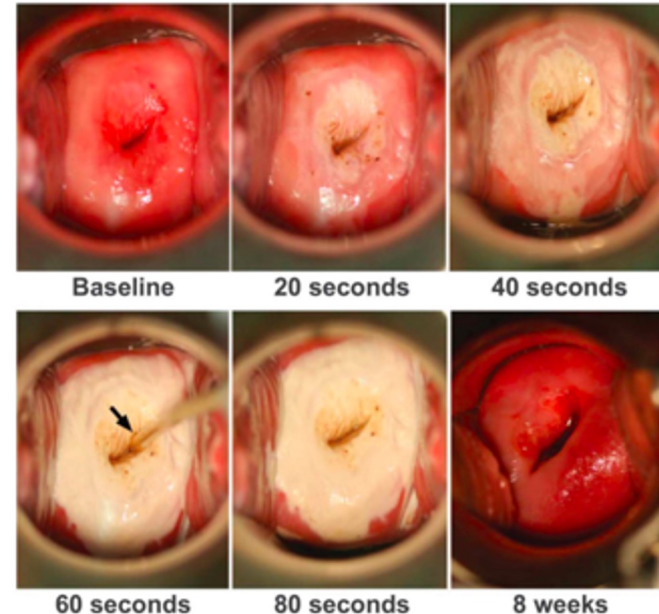
- Challenges that TCA addresses:
 - Access to healthcare → No need for tertiary care center
 - Cost and complexity → “Simple, safe, and cost-effective with high efficacy” (Winata et al., 2022)
 - Side effects → High HPV clearance (CIN1-3) (Geisler et al., 2016)



Geisler et al.,
2016

Fig. 1. Treatment of high-grade cervical intraepithelial neoplasia (CIN) with topical 85% trichloroacetic acid. The first (baseline) photograph was taken after the application of 3% acetic acid. The photographs at the time of 20, 40, 60, and 80 seconds were taken after the application of 85% trichloroacetic acid. The photograph at 60 seconds shows the treatment of the endocervical canal with the wooden end of a cotton tip (arrow) saturated with 85% trichloroacetic acid. The final photograph was taken 8 weeks after treatment.

Geisler, Efficacy of Trichloroacetic Acid in the Treatment of CIN. Obstet Gynecol 2016.



Additional Innovations

- Challenges of speculums:
 - Pain → self application empowerment
 - Fear of catching disease during exam → disposable



Graves speculum, 1878

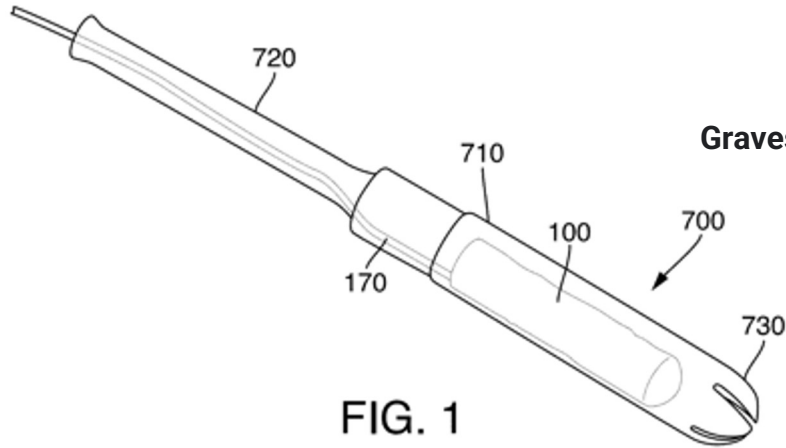
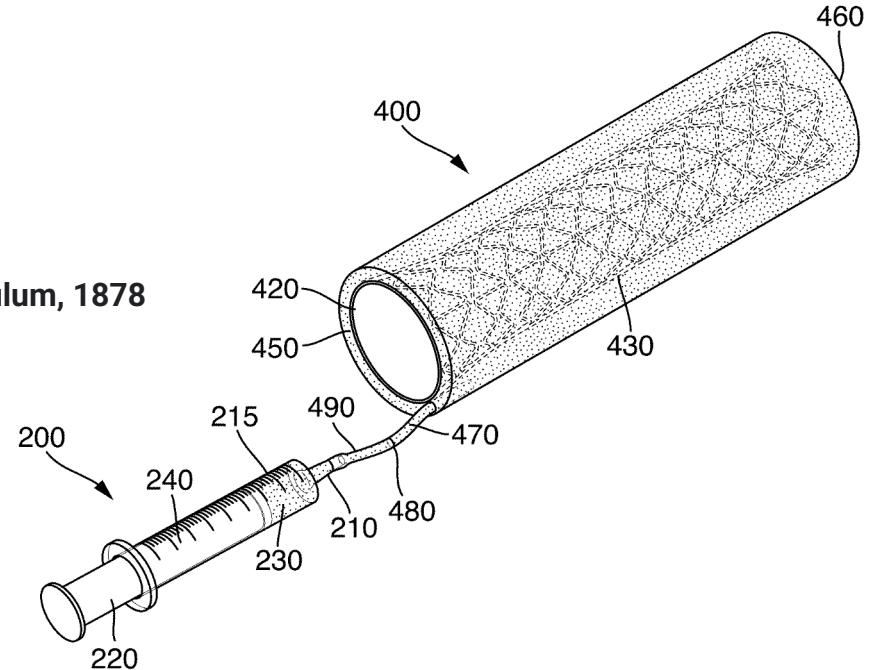


FIG. 1



Conclusion and Future Work

- Cervical Cancer is still on the rise despite it being preventable and treatable.
- Challenges in rural USA are similar LMICs
- Moein Health Innovations (FNA, TCA, etc.) extend practices from other medical fields into women's health
- Moein Health Innovations address nearly all the challenges
 - Convenience kit with AA combines screening and diagnosis
 - Adding FNA improves diagnostic accuracy (potentially eliminating need for colposcopy)
 - Adding TCA provides rapid treatment and fewer side effects
 - Adding single use expandable speculum reduces pain and eliminates iatrogenic infection
 - Trains and empowers full service from local, mid-level care providers
- Our next steps are large prospective trials in rural America, starting with Southwest Virginia, for further optimization of our products.

Post CME Lecture Knowledge Check



Q&A

Thank you!

References

- American College of Obstetricians and Gynecologists. Updated guidelines for management of cervical cancer screening abnormalities. Practice Advisory. Washington, DC: American College of Obstetricians and Gynecologists; 2020.
- Cervical cancer: epidemiology, prevention and the role of human papillomavirus infection. Franco EL, Duarte-Franco E, Ferenczy A CMAJ. 2001;164(7):1017.
- Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, et al. Screening for cervical cancer: U.S. Preventive Services Task Force recommendation statement. U.S. Preventive Services Task Force. JAMA 2018;320:674-86.
- Duarte, M. 10.1200/GO.21.00371 JCO Global Oncology no. 8 (2022) e2100371. Published online June 13, 2022.
- Feldman S, Goodman A, Peipert J (2022). Screening for cervical cancer in resource-rich settings. Goff, B (Ed.)
- Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN 2012 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>.
- Fusco E, Padula F, Mancini E, Cavaliere A, Grubisic G. History of colposcopy: a brief biography of Hinselmann. J Prenat Med. 2008 Apr;2(2):19-23. PMID: 22439022; PMCID: PMC3279084.
- Hall, Michaela T et al. The Lancet Public Health, Volume 4, Issue 1, e19 - e27 [https://doi.org/10.1016/S2468-2667\(18\)30183-X](https://doi.org/10.1016/S2468-2667(18)30183-X)
- Hoffman, M, Mann W. (2022). Cervical Intraepithelial Neoplasia: Diagnostic Excisional Procedures. Goff, B (Ed.)

References

- Hopman EH, Voorhorst FJ, Kenemans P, Meyer CJLM, Helmerhorst TJM. Observer agreement on interpreting colposcopic images of CIN. *Gynecol Oncol* 1995; 58:206-9.
- Huh, W. K., Sideri, M., Stoler, M., Zhang, G., Feldman, R., & Behrens, C. M. (2014). Relevance of random biopsy at the transformation zone when colposcopy is negative. *Obstetrics and gynecology*, 124(4), 670–678.
- Locklar, L., & Do, D. P. (2022). Rural-urban differences in HPV testing for cervical cancer screening. *The Journal of rural health : official journal of the American Rural Health Association and the National Rural Health Care Association*, 38(2), 409–415.
- Massad, L Stewart MD1; Jeronimo, Jose MD2; Schiffman, Mark MD2 for NIH/ASCCP Research Group Interobserver Agreement in the Assessment of Components of Colposcopic Grading, *Obstetrics & Gynecology*: June 2008 - Volume 111 - Issue 6 - p 1279-1284
- Moein, et. al.; METHODS AND KIT FOR DIAGNOSING AND TREATING NEOPLASTIC TISSUE. US Patent 10,588,564, 11/5/2019
- Moein, et. al.; ONE-TIME USE EXPANDABLE SPECULUM. US 16/538532, filed August 12, 2019. Patent approved June 9, 2022
- Moein, et. al.; TCA Method and Devices for treating, US filed
- Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH, Garcia F, Huh WK, Kim JJ, Moscicki AB, Nayar R, Saraiya M, Sawaya GF, Wentzensen N, Schiffman M, 2019 ASCCP Risk-Based Management Consensus Guidelines Committee *J Low Genit Tract Dis*. 2020;24(2):102.
- Slawson DC, Bennett JH, Herman JM. Follow-up Papanicolau smear for cervical atypia: are we missing significant disease? A HORNET Study. *J Fam Pract* 1993; 36:289-93.
- Sung, H, Ferlay, J, Siegel, RL, Laversanne, M, Soerjomataram, I, Jemal, A, Bray, F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021: 71: 209- 249.
<https://doi.org/10.3322/caac.21660>

References

- Vilos G. A. (1998). The history of the Papanicolaou smear and the odyssey of George and Andromache Papanicolaou. *Obstetrics and gynecology*, 91(3), 479–483. [https://doi.org/10.1016/s0029-7844\(97\)00695-9](https://doi.org/10.1016/s0029-7844(97)00695-9)
- Winter, M., Cestero, R. M., Burg, A., Felix, J. C., Han, C., Raffo, A. M., & Vasilev, S. (2012). Fabric-based exocervical and endocervical biopsy in comparison with punch biopsy and sharp curettage. *Journal of lower genital tract disease*, 16(2), 80–87. <https://doi.org/10.1097/LGT.0b013e318234262d>
- Wright, J. (2022). Cervical Intraepithelial Neoplasia: Management. Goff, B (Ed.), UpToDate. Retrieved July 8, 2022, from <https://www.uptodate.com/contents/cervical-intraepithelial-neoplasia-management>
- 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors.
- <https://www.cdc.gov/cancer/cervical/statistics/index.htm>
- <https://dceg.cancer.gov/news-events/news/2021/cervix-guidelines>
- https://gco.iarc.fr/tomorrow/en/dataviz/bars?types=0&sexes=0&mode=cancer&group_populations=0&multiple_populations=0&multiple_cancers=1&cancers=23&populations=910&apc=cat_ca20v1.5_ca23v-1.5
- <https://histologics.com/softbiopsy.html>
- <https://www.margpharma.com/wp-content/uploads/Kevorkian-Young-Curette-Tip-Only.jpg>
- <https://us.vwr.com/stibo/bigweb/std.lang.all/01/26/17870126.jpg>
- https://www.who.int/health-topics/cervical-cancer#tab=tab_1
- <https://www.who.int/publications/i/item/9789240014107>