Cervical Cancer Screening and Treatment in a rural hospital in Malawi: A four-year comprehensive review

Presenters: Mai-Linh N. Tran, MD; Mary R. Perry, MD
Authors: Mai-Linh N. Tran, MD; Mary R. Perry, MD; Casey Graybill, MD; Karen Studer, MD, MPH; Marc Debay, MD, MPH, PhD.
Disclosure

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflicts of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

Dr. Mai-Linh Tran, Dr. Mary Perry, Dr. Casey Graybill, Dr. Karen Studer, and Dr. Marc Debay have indicated they have no relevant financial relationships to disclose.
Introductions

Mai-Linh Tran, MD, PGY-3
Family Medicine Resident
Loma Linda University

Mary Perry, MD, PGY-3
Family & Preventive Medicine Resident
Loma Linda University
Case Study Mrs. A

- 65 year old female, translator required
- Heavy vaginal bleeding (chitenje)
- Biopsy of cervix: squamous cell carcinoma
Case Study Mrs. A (Continued)

- Palpable mass extended to lower 1/3 of vagina – Stage 3 Cervical Cancer
- Non-operable, no radiation therapy in Malawi
- Palliative Care – tramadol
- Prayer
Case Study Mrs. B

- 37 year old female coming in for routine pap smear
- Returns 1 week later, results show LSIL
- Colposcopy done with cervical biopsy & endometrial curettage
- Focal CIN 3
- LEEP done – fully excised cancer
Learning Objectives

• Understand the prevalence and outcomes of cervical cancer screening in a rural hospital in Malawi
• Identify the successes and challenges in maintaining and expanding a cytology-based cervical cancer screening program in a rural hospital in sub-Saharan Africa
• Appreciate how residents of a U.S. Family and Preventive Medicine residency program may contribute to the documentation and development of a new program at the training site of a curricular international rotation
Overview

- Burden of cervical cancer
- Prevention and treatment strategies
- Malamulo Adventist Hospital Cervical Cancer Screening Program (MAH CCS)
- Results from the data collection
- Successes and challenges of program implementation
- Resident’s roles
Global Burden of Cervical Cancer

- 2012: ~530,000 new cases, 270,000 deaths worldwide every year
- World population: 2,784 million women aged 15 years and older who are at risk of developing cervical cancer.
- 2\textsuperscript{nd} most common female cancer in the women aged 15 to 44 years in World
- 4\textsuperscript{th} most frequent cause of cancer in women
- 90\% of deaths in 2015 occurred in low-middle income countries
Age-standardized **incidence** rates of cervical cancer in the World (estimates for 2012)

<table>
<thead>
<tr>
<th>Region</th>
<th>Rate per 100,000 women</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>6.6</td>
</tr>
<tr>
<td>East Africa</td>
<td>42.7</td>
</tr>
</tbody>
</table>

*Human Papillomavirus and Related Diseases Report*
*Version posted at www.hpvcentre.net on 27 July 2017*
*©ICO Information Centre on HPV and Cancer (HPV Information Centre), 2017*
Age-standardized **mortality** rates of cervical cancer in the World (estimates for 2012)

- North America: 2.6 per 100,000 women
- East Africa: 27.6 per 100,000 women

Human Papillomavirus and Related Diseases Report
Version posted at www.hpvcentre.net on 27 July 2017
© ICO Information Centre on HPV and Cancer (HPV Information Centre), 2017
Age-standardized **incidence** rates of cervical cancer in Africa (estimates for 2012)

- ~99,038 new cases are diagnosed annually in Africa
- 2nd leading cause of female cancer
- 2nd most common female cancer in women aged 15-44 years
Age-standardized **mortality** rates of cervical cancer in Africa (estimates for 2012)

- ~60,098 cervical cancer deaths occur annually
- 2\(^{nd}\) leading cause of female cancer deaths
- 2\(^{nd}\) most common female cancer deaths aged 15 to 44 years
Age-standardized incidence rate of cervical cancer cases by country in Africa (estimates for 2012)
Cervical Cancer Incidence & Mortality in Malawi (estimates in 2012)

- 4.76 million women ages >15 years at risk of developing cervical cancer
- 3,684 diagnosed with cervical cancer annually
- 2,314 deaths from cervical cancer annually
- 1\textsuperscript{st} most frequent cancer & cause of cancer deaths among women
Perspective

- Malawi has **highest rates** of cervical cancer incidence and mortality in the world
- Limited information about cervical cancer, screening, and treatment programs in Malawi

<table>
<thead>
<tr>
<th>Cervical cancer</th>
<th>Incidence per 100,000</th>
<th>Mortality per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>74.9</td>
<td>49.8</td>
</tr>
<tr>
<td>United States</td>
<td>8.1</td>
<td>2.4</td>
</tr>
</tbody>
</table>
Overview of Prevention Strategies

Prevention

Primary

Male Circumcision

Condom Use

HPV Vaccination

Secondary

Screening & treatment of precancerous lesions

Tertiary

Treatment of cervical CA & palliative care
Cervical Cancer

• Highly preventable in most high income countries
  – screening tests
  – a vaccine to prevent human papillomavirus (HPV) infection

• Highly treatable when found early
  – associated with long survival & good quality of life
Factors Contributing to Developing Cervical Cancer

• High Risk Types Human Papilloma Virus (HPV)

• Risk factors
  – Tobacco smoking
  – High parity
  – Long-term hormonal contraceptive use
  – Co-infection with HIV
  – Co-infection with Chlamydia & Herpes Simplex Virus type 2
  – Immunosuppression
CERVICAL CANCER SCREENING IN LOW RESOURCE SETTINGS
Types of Cervical Cancer Screening

• Visual Inspection with Acetic Acid (VIA)
• Cytology based pap smear
• Human Papilloma Virus (HPV) testing
  – Not available in Malawi
VIA vs. Cytology-based screening

VIA
• Benefits:
  – Low cost, few resources
  – Limited infrastructure needed
  – Same-day treatment
  – Simple to learn
• Constraints:
  – Inter-user variability
  – Need for frequent re-training
  – Easy to miss lesions in post-menopausal women

Cytology-based screening
• Benefits:
  – Widely used in high-income countries
  – Proven effectiveness to decrease cervical cancer
  – Training and quality control methods well established
• Constraints:
  – Higher cost
  – More infrastructure needed: lab, equipment, supplies
  – Results not immediately available
VIA vs Cervical Cytology

AN Fiander. The prevention of cervical cancer in Africa. Women's Health (2011)

Table 3. Results of once in a lifetime cervical screening in rural India.

<table>
<thead>
<tr>
<th>Results</th>
<th>HPV testing</th>
<th>Cervical cytology</th>
<th>VIA</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive screen (%)</td>
<td>10.3</td>
<td>7</td>
<td>13.9</td>
<td>N/A</td>
</tr>
<tr>
<td>Advanced cervical cancer ≥ stage 2</td>
<td>39</td>
<td>58</td>
<td>86</td>
<td>82</td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>0.47</td>
<td>0.75</td>
<td>1.04</td>
<td>1.00</td>
</tr>
<tr>
<td>Deaths</td>
<td>34</td>
<td>54</td>
<td>56</td>
<td>64</td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>0.52</td>
<td>0.89</td>
<td>0.86</td>
<td>1.00</td>
</tr>
<tr>
<td>Negative screen cancers during FU</td>
<td>8</td>
<td>22</td>
<td>25</td>
<td>N/A</td>
</tr>
</tbody>
</table>

FU: Follow up; HPV: Human papillomavirus vaccine; N/A: Not applicable; VIA: Visual inspection with acetic acid.

Table 4. Characteristics of screening tests.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range (%)</td>
<td>Used in model (%)</td>
</tr>
<tr>
<td>VIA</td>
<td>60–90</td>
<td>76</td>
</tr>
<tr>
<td>HPV DNA</td>
<td>65–95</td>
<td>88</td>
</tr>
<tr>
<td>Cytology</td>
<td>45–85</td>
<td>63</td>
</tr>
</tbody>
</table>
Malawi: General CCS Guidelines

- CCS program available
- Type: Visual Inspection with Acetic Acid (VIA)
- Screening age: >25 years old
- Frequency: 2-5 years
- No quality assurance or supervision to monitor screening process
THE CERVICAL CANCER SCREENING PROGRAM AT MALAMULO ADVENTIST HOSPITAL
Background: Malamulo Adventist Hospital (MAH)

- Outpatient department
- Surgery
- Adult Medicine
- Maternity, Gynecology
- Pediatrics
- Radiology, and Laboratory
- Women’s Center for Cancer Screening
- Community Department
- Dental Clinic, Eye Clinic
- several Satellite Clinics
- HIV/AIDS Treatment Center

- Founded in 1902
- 212-bed Christian mission hospital in the rural location of Makwasa, in Southern Thyolo District of Malawi
Cervical Cancer Screening Program: Beginnings

• PAPS Team International, non-profit organization based out of Redlands, CA
  – 1350 patients
  – Cytology based
• Stella Nyirenda, RN and Mary Panulo, LVN
  – Free! Wednesday women’s clinic
  – Outreach to additional communities
  – Same day referrals to OB/GYN
Equipment Needed: Facilities

- Private room
- Exam table/bed
- Gloves
- Clean water / soap to wash hands
- Log books
- Patient record forms
Equipment Needed: Paps

• Speculums (method to clean/maintain), lubricant
• Glass microscope slides, fixatives
• Cytology brush/spatula
• Microscope to review slides
Equipment Needed: Follow-up

- Working electricity
- LEEP instruments
- Tenaculums
- Working colposcopy light
- Referral to surgery for hysterectomy
  - need facility that can manage
People needed

• Secretary, nurses, health workers
  – Enter demographics, intake data
  – Educate women about the process and importance of cervical cancer screening
  – Perform exam, collect pap smears
  – Record and disseminate results, coordinate follow-up

• Cytologist
  – Read pap smear slides

• OB-GYN
  – Follow-up abnormal pap smears

• Pathologist
  – Biopsy results
MAH Women’s Health Clinic Program

- Nurse notify surrounding village chiefs of clinic dates
- Women arrive to clinic in the morning
- Educational class led by nurses
- Pap smears, pelvic & breast exam performed by nurses
- Patient registration & HIV screening
- Return in 2 weeks for results
Pap Smear Results

Results

Normal
- Return for routine screening

Abnormal
- Referral to OB-GYN
  - Colposcopy*
  - LEEP**
  - Surgery: Hysterectomy
  - Palliative Care

*Colposcopy: cervical biopsy, endometrial biopsy, endometrial curettage
**LEEP: Loop Electrosurgical Excision Procedure
DATA COLLECTION
Cervical Cancer Screening Program

- Intake (2 forms)
  - Age
  - Village
  - Pregnancy history
  - LMP
  - Previous pap
  - STD's
  - Symptoms
  - Exam findings
  - Risk factors:
    - Smoking
    - Birth control method
Cervical Cancer Screening Program

- Result forms

<table>
<thead>
<tr>
<th>Patient ID/Number</th>
<th>5599</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registration Date</td>
<td>11-16-16</td>
</tr>
<tr>
<td>Interviewer</td>
<td>Chaim</td>
</tr>
</tbody>
</table>

[Image of a result form showing the fields: Adequacy, Satisfaction, Abnormal, Result, Date, Signature, Patient ID/Number, Registration Date, Interviewer.]
Pathology results

- Negative
- Positive
  - ASCUS, LSIL, ASC-H, HSIL, Cancer (SCC)
- Other: schistosomiasis, candida, cervicitis
Malawian Patient Charts: Health Passports

- Stays with patient
- Summary for each episode of care
- Record pap ID number, date, and results
Transferring Paper into Electronic Data
RESULTS FROM MAH
Overview: by the numbers

• Approximate population served by Malamulo Adventist Hospital:
  – Total population of catchment area: 38,713
  – Women of child-bearing age: 9,804
• Total number of recorded pap smears from 2012 – 2016: 5,899
  – Normal pap smears: 5,577
  – Abnormal pap smears: 322 (5.5%)
Women getting pap smears by month of year

Number of Paps by Month

Number of Paps

Date

Women getting pap smears by month of year

Number of Paps by Month, After Initial

Number of Paps

Date

AMERICAN ACADEMY OF FAMILY PHYSICIANS
Women Screened by Age

- Average age: 38.5 years
- Range: 14-90 years old
Abnormal Pap Smears by Age

% Abnormal by Age

% Abnormal

Age in years

10-19 20-29 30-39 40-49 50-59 60+

Abnormal Pap Smears by Age
Number of Initial visit vs Return visits

- As program became more established, more women came for return visits and repeated pap smears.
- Most given a new ID number, which was not linked to previous pap smears.
- # of initial visits: **5,229**
- # of return visits: **668**
Return Visit Characteristics

Age in years / Percentage

Average Age  % HIV Positive  % Abnormal Pap

Characteristic

Initial Visit  Return Visit
Women Screened by HIV status

- HIV by the numbers
  - Negative: 4,123
  - Positive: 1,479
- Positive HIV rate: **25.1%**
  - Previously reported HIV (+) rate: **26%**
  - Prevalence adult HIV (+) in area: **9%**
- Average age for HIV (+): **39.7 years**
HIV and Abnormal Pap Results

- Abnormal pap:
  - HIV positive: 11.4%
  - HIV negative: 3.3%

- Relative Risk: 3.46, \( p = .000 \)
  - The risk of being HIV+ and having an abnormal pap result was 3.46 times that of being HIV+ and having a normal pap result

- Logistic Regression
  - Unadjusted OR 3.78, \( p = .000 \)
  - Adjusted for age OR 3.57, \( p = .000 \)
  - After controlling for age, the odds of being HIV+ and having an abnormal Pap was 3.57
Abnormal pap smears: Cytology results

![Bar chart showing the number of cases for different cytology results: ASCUS, LSIL, ASCUS-H, HSIL, SCC/Invasive CA, Other.]
2015-2016 Abnormal Pap Smear Outcomes

Abnormal: 84

- ASCUS
  - Hysterectomy: 1
  - Unknown: 4

- Biopsy: 63

- Palliative Care: 1

- Unknown: 15

See next slide
2015-2016 Abnormal Pap Smear Outcomes

Biopsy: 63

- No dysplasia: 9
  - Hysterectomy: 4
- LEEP: 10
- Hysterectomy: 20
- Palliative Care: 3
- Unknown: 23

Death: 1
2015-2016 Abnormal Pap Smear Outcomes

Correlated Totals:
- Abnormal: 84
- Biopsy: 63
- No dysplasia: 9
- LEEP: 10
- Hysterectomy: 24
- Palliative Care: 4
- Death: 1

Log book totals:
- Biopsy: 138
- Hysterectomy: 43
- Palliative Care: 10
SUCCESSSESS AND CHALLENGES
Successes

• Patient benefits
  – Over 6,000 paps completed
  – Screening for HIV
  – Referral for other health concerns
  – Education
  – Free of cost
  – Many life-saving procedures/operations completed

• Technique
  – Only cytology-based screening program in Malawi
Successes

• Facility
  – Dedicated location for Women’s Health Clinic
  – Dedicated location for educational classes
  – Private rooms
  – “No structure” community outreach
  – Community education
Successes

• Partnerships
  – LLU Family/Preventive Medicine, OB-GYN, Internal Medicine, and Surgery residents, Medical students
  – Pan-African Academy of Christian Surgeons (PAACS) training site

• Staff
  – Dedicated, determined, community health workers actively track down patients with abnormal results
  – Outreach to village chiefs from distant villages
  – MAH sponsoring a clinical officer for additional OB/GYN training
Successes

• Sustainability
  – Ongoing donor support
  – 5-year family donor fund specifically for Women’s Center
  – Number of pap smears performed has increased over the years
  – Women coming back for return visits
  – Community ownership: locals comprise majority of staff
Challenges

• Socio-cultural barriers
  – Travelling distance
  – Lack of transportation (most women walk)
  – Language barriers: Limited number of translators available
  – Cultural barriers
    • Outreach to women only with approval from village chief
    • Misconceptions and fear among women

• Treatment
  – Palliative care options limited to pain medication (Tramadol)
  – Limits to treatment, i.e. no radiation therapy
  – Loss to follow-up
Challenges

- Limited time and talent:
  - Secretary for intake and to enter the data into logbooks (borrow from another department), enter results
  - Dedicated pathologist / cytologist (volunteer time)
  - OB-GYN specialist
    - US trained OB-GYN, PAACS* surgical resident, Clinical officers
  - Nurses to collect pap smears, perform pelvic, breast exam
  - Clinic only open once a week
  - Under utilization of the clinic buildings

*Pan-African Academy of Christian Surgeons
Challenges

- Data collection & Management
  - Duplicate patient ID numbers, i.e. new vs. return
  - Multiple locations for documentation:
    - Ministry of Health log book, binders, registries, etc.
  - Inconsistencies with documentation practices
  - Government requirements for data reporting
    - VIA forms
  - Transcribing paper data from various sources to a centralized electronic format
Challenges

• Sustainability:
  – Funding from US donors
  – Cost for the women (currently free)
  – Dedicated staffing (cytologist, OB-GYN)
  – Training health care workers
  – Transportation
Future

- Mobile clinics for women in distant villages
- Expand MAH’s women’s health clinic to more than one day a week
- Possible community needs assessment
- Hospital or community ownership and funding options
- HPV vaccine – coming soon
  - Clinical trials to implement vaccinations underway for 2-shot quadrivalent vaccine series
RESIDENT ROLES
Family & Preventive Medicine Residency Program

• Started in 2006
• 4-year program
• Dual board certification
  – Family Medicine
  – Preventive Medicine
• MPH in Population Medicine
• 4 residents/year
Malamulo Rotation

- PAPS Team International: Sept. 2012
- Site evaluation: May 2013
- Started data evaluation
  - Coded forms, started logging, trained local staff, donated a Macbook
- Became required international OB rotation for residents
- First FPM resident to go: Feb. 2014
Residency Project

• Required rotation x 1-2 years
• 10 residents over course of 4 years
• Assisting with clinic duties
  – Performing pap smears
• Collecting data
• Entering data into computer
Strengths of Resident Project

- Sustainability with consistent resident participation
- Application of statistical and population management principles learned in MPH course work
- Collaboration among residents
Barriers to Residents Participation

• Attendings have multiple clinical duties (limited time)
• Ability to find/access paper data
• Partnering with a person who knows about the project at MAH
• Interest in the project
• No longer required rotation
Opportunities for Future Endeavors

- Continue data analysis of follow-up for patients with abnormal results
- Log and analyze data on longer intake forms
- Expand cervical cancer screening beyond Thyolo district
- Duplicate cervical cancer screening program in other locations in the developing world
Conclusions

• Cervical cancer is a treatable and preventable disease that disproportionately affects those in low-middle income countries

• Cervical cancer screening programs, such as the one in Malawi, are challenging to initiate and maintain, but can be successful in detecting and treating pre-cancerous lesions

• Family Medicine residents can play an important role in data collection and community outreach programs
Acknowledgements: Special Thank You!

• Malamulo Adventist Hospital
• Dr. Casey Graybill, Dr. James Crounse, Dr. Ryan Hayton
• Dr. Marc Debay, Dr. N. Margarete Ezinwa, Dr. Karen Studer
• Stella Nyirenda, RN and Mary Panulo, LVN
• Staff & administrators at MAH
• Residents from Loma Linda University
  – Previous research contributors: Dr. Christina Miller, Dr. Sumedh Mankar, Dr. Jacqueline Uy, Dr. Stewart Wilkey, Dr. Marcus Heisler
  – Additional rotation participants: Dr. Kelsey Cherepuschak, Dr. Jeffrey Cho, Dr. Edward Perry
• Mrs. Kam for helping enter data
Questions?
Resources

- [http://apps.who.int/iris/bitstream/10665/144785/1/9789241548953_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/144785/1/9789241548953_eng.pdf?ua=1)
- [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4989288/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4989288/)
- [http://www.panafrican-med-journal.com/content/article/22/247/full/#.WRptCFTys1I](http://www.panafrican-med-journal.com/content/article/22/247/full/#.WRptCFTys1I)
- [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4989288/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4989288/)
- [http://www.asccp.org/asccp-guidelines](http://www.asccp.org/asccp-guidelines)
Resources

- Lynette Denny, MD, PhD Louise Kuhn, PhD Michelle De Souza, MD Amy E. Pollack, MD, MPH William Dupree, MD Thomas C. Wright, Jr, MD. Screen-and-Treat Approaches for Cervical Cancer Prevention in Low-Resource Settings A Randomized Controlled Trial. JAMA, November 2, 2005—Vol 294, No. 17