What is cervical cancer? Why do we care?

- 2nd leading cause of cancer deaths among women worldwide (after breast cancer)
- 500,000 new cases annually; 280,000 deaths
- 85% of deaths occur in developing countries (25% in India)
- Strikes women in prime life when they are most needed by their families and communities
- Disease is theoretically 100% preventable through screening, treatment and (since 2006) vaccination

How do we compare?

**US**
- 11,000 cases; 4,000 deaths
- Median age at dx: 48
- Incidence: 8.2/100,000
- Death rate: 2.5/100,000
- 26.2% dx between 35-44
- NCI funding: 79 million 2004, 71.6 2008
- Hispanic/AA/American Indian: significant disparities

**South Carolina**
- 170 cases, 60 deaths
- Incidence: 8.6/100,000
- Death rate: 2.7/100,000
- AA women: 12.5 inc./4.9 d
- 26.3% dx between 35-44
- 27% dx 45-64
- National rank: 37/50
- Screening rates comparable to US rate – flu care is a major barrier
- Some counties have death rates comparable to some of our poorest nations – Hampton, Allendale, e.g.
US Cervix cancer death rates 2007 (per 100,000) age adjusted

- Dark blue: 2.9 – 4.2
- Light blue: 2.5 – 2.8
- Dark green: 2.1 – 2.4
- Light green: 2.1 – 2.4
- White: < 16 cases reported

Cervical cancer in the developing world

- 80% of deaths: South / South East Asia, sub-Saharan Africa, South & Central America. Fewer than 5% screened.
- Underestimated: no reliable system of counting/registries
- Age adjusted incidence: 25/100000 (US: 8.2/100,000) 2008
- Age adjusted mortality: 10-25/10000 (US: 2.5/100,000)
- 5 year survival rates: tremendous variation
  - Uganda: < 25%, 30-50% Cuba, India, Philippines,
  - 50-60% Costa Rica, Thailand, Turkey (US: 95%)
Incidence, deaths, 5 year prevalence (2002)

<table>
<thead>
<tr>
<th>Region</th>
<th>Cases</th>
<th>Deaths</th>
<th>5 yr prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>World</td>
<td>492,800</td>
<td>273,200</td>
<td>1,409,200</td>
</tr>
<tr>
<td>Developed</td>
<td>83,400</td>
<td>39,500</td>
<td>309,900</td>
</tr>
<tr>
<td>Less developed</td>
<td>409,400</td>
<td>233,700</td>
<td>1,099,300</td>
</tr>
<tr>
<td>South America</td>
<td>48,900</td>
<td>23,400</td>
<td>139,200</td>
</tr>
<tr>
<td>S. Central Asia</td>
<td>137,700</td>
<td>86,500</td>
<td>445,100</td>
</tr>
<tr>
<td>W. Africa</td>
<td>209,000</td>
<td>167,000</td>
<td>535,000</td>
</tr>
<tr>
<td>E. Africa</td>
<td>33,900</td>
<td>27,100</td>
<td>57,200</td>
</tr>
<tr>
<td>E. Europe</td>
<td>308,000</td>
<td>171,000</td>
<td>507,000</td>
</tr>
<tr>
<td>W. Europe</td>
<td>12,700</td>
<td>5,600</td>
<td>35,200</td>
</tr>
</tbody>
</table>

What do we know?

- Cervical cancer is an infectious disease, 99% caused by persistent infection with cancer-causing strains of human papillomavirus (HPV), most commonly types 16/18 (70%)
- Transmitted by intimate, sexual contact; skin to skin
- Infection is ubiquitous: most asymptomatic and self-limiting (80% sexually active acquire HPV)
- > 100 types identified; – 20 are oncogenic
- HPVs cause other genital/non-genital cancers in men and women; and costly burdensome non-genital disease

Human Papillomavirus (HPV)

- Necessary, not sufficient; cancer causing infectious agent
- Most common STI worldwide
- 20 million incident cases worldwide/6 million in US
- 75% new cases occur in ages 15-24, infection rapid following onset of sexual activity
- Most infections transient, asymptomatic; do not result in clinical disease
- Harald zur Hausen: Nobel prize 2008: linked HPV to ca
The Pap test

Role of the Pap test

US/Developed countries
- Introduced 1950s
- Death rates dropped 74% between 1955-1974
- Dropping 4%/year
- Success tied to frequency of screening
- Lack of screening = ↑ risk

Low resource countries
- < 5% of women screened
- Deaths occur at younger ages
- Lack infrastructure, screening, treatment facilities
- Beset by extremes of poverty, turmoil, disease

Sharon Bond, PhD, CNM
### Strategies in low resource nations

**Strategies**
- Use of lay health workers
- Visual inspection methods
- "See and Treat"
- HPV testing
- HPV vaccination
- Pap testing (resource intensive, not proven effective, quality control issues)
- Nothing population-based
- Few treatment facilities

**Cost effectiveness**
- Single lifetime screening in India, age 35, reduces lifetime risk by 25-35% at < $500/year of life saved
- With 2 lifetime screenings, risk of death from cervical cancer decreases by 40% (Sankaranarayanan, 08)

### Visual inspection

**advantages**
- Simple, safe, well accepted
- Low level of infrastructure
- Performed by many types of personnel, including lay health workers
- Training period is short: 1-3 weeks
- Results immediately available

**disadvantages**
- Less effective for women > 50
- Quality control issues
- Standardization not yet fully established
- Wide ranging sensitivity and specificity
  - 30-40% sensitivity
  - 90-99% specificity
- Overtreatment of minor or benign disease

### Visual inspection

![Visual inspection images]
Cervical cancer

HPV Testing

- We can now determine whether women carry "high-risk" HPV types.
- This testing is done for only 3 indications:
  - women > 21 with specific abnormal Pap test results
  - following treatment for dysplasia
  - In conjunction with annual Paps for women > 30.
- We can isolate HR types (16/18) and make decisions about care and treatment
- No indication for testing low risk types

HPV vaccines

- Quadrivalent (6, 11, 16, 18): FDA app: in US 6/06 (Gardasil)
- Bivalent (16 / 18): FDA app: 9/09 (Cervarix)
- Proven efficacy in trials > 30,000 women; highly immunogenic
- High safety profile – VLP vaccines – contain no DNA
- Target: 11-12 yo girls / "catch-up" – 15-26 (9-16);
- Bridge studies
- Approved for men and boys in US: 10/09 (EGW)
- Other multivalent vaccine studies underway; cross protection
Challenges for vaccine implementation

- High costs; private vs. public sector
- Feasibility, acceptability, association as STI
- Logistics of delivery (3 doses in 6 mos), storage concerns
- How to reach target populations (many girls do not attend school in LR nations if school-based program)
- Long term immunogenicity; boosters needed?
- Competing, very real, health priorities

Zooming ahead in the US

- Benefits of new, better technologies for screening and vaccines
- Natural history studies of HPV, vaccine availability driving changes in practice and screening guidelines – supported by cancer associations and women’s health organizations
- Better able to target those at risk; decrease screening (and costs) among those at low risk (e.g. adolescents)
- Better use of resources
- Still... Have yet to reach all women for screening – US populations: immigrants, American Indians, low-income, women with chronic disease, after sterilizations, women in rural areas, ...

References

- Journal of the SC Medical Association; October 2009 (entire issue devoted to cervical ca)
Introduction Global and Public Health

The Global Burden of Parasitic Infections

L.W. Preston Church, MD
Ralph H. Johnson VA
churchlw@musc.edu

Impact of Malaria

• What we have been saying:
  - 300-500 million infections/year
  - 750,000 deaths/year -> 90% in children under age 5 in sub-Saharan Africa
• “New” thinking (modeling)
  - 1.24 million deaths 2010 (1.14 million in Africa)
  - 525,000 deaths in children < age 5
Is this a surprise?

Murray et al, Lancet, 4 Feb 2012

Impact of Malaria

What do we know about prevention efforts?
• Who is the target?
What do we know about malaria prevention efforts?

What are the interventions?
**Impact of Malaria**

What do we know about immunity to malaria?

- Only 33 individuals have been shown to have sterile immunity to *P. falciparum* - none of whom acquired this immunity naturally.
- Malaria naïve adults are immunologically similar to children - should we expect a different response to infection?

**Entomological Inoculation Rate**

\[ \text{EIR} = \frac{M}{a \times S} \]

- \(M\) = # Anopheles/person
- \(a\) = # persons bitten by 1 Anopheles/day
- \(S\) = # Anopheles with infectious sporozoites in salivary glands

Are we going to make a sustainable difference anytime soon?

- The RTS,S/AS01 vaccine
- Other vaccines

Preston Church, MD
The Neglected Tropical Diseases

- Dracunculiasis
- Lymphatic filariasis
- Trachoma
- African trypanosomiasis
- Leprosy
- Soil transmitted helminthias
- Schistosomiasis
- Onchocerciasis
- Chagas Disease
- Visceral Leishmaniasis

Dracunculiasis melinensis

No symptoms x 1 year, then:
- Slight fever
- Itchy rash
- Nausea
- Vomiting
- Diarrhea
- Dizziness
- Blister forms → burning pain → immerse foot in water to soothe → female emerges
**Dracunculis melinensis**

Complications:
- Local or systemic infection
- Tetanus
- Pain and disability

---

**Dracunculiasis Eradication Project**

- 1986 ~ 3.5 million cases in 20 countries
- 2011 ~ 1060 cases
  - 97% southern Sudan
  - 3% Mali, Chad, Ethiopia
- Methodology
  - Surveillance/case containment
  - Safe drinking water (filtration)
  - Vector control
  - Education

---

**Impact of Parasitic Diseases**

- Lymphatic filariasis
  - 110 million infected
  - 40 million disabled – the second leading cause of disability worldwide
- Onchocerciasis
  - 15-25 million infected
  - ~550,000 blind or visually impaired
Onchocerciasis – Cutaneous Manifestations

- Chronic popular dermatitis and subcutaneous nodules
- Leopard Skin

Onchocerciasis – "African River Blindness"

- "Snowflake" opacities of punctate keratitis
**Onchocerciasis**

**Diagnosis**
- skin snips –
  - visualize microfilariae
  - PCR

**Rx:**
- Ivermectin
  - Contraindicated if concomitant loiasis (fatal encephalopathy)
- Doxycycline
- DEC contraindicated – Mazzotti reaction

---

**Lymphatic Filariasis** *(Wuchereria bancrofti, Brugia malayi)*

Epidemiology: tropics/sub-tropics, ~120 million
- vectors - mosquitoes, reservoirs *(B. malayi)*
Lymphatic Filariasis

**Diagnosis:**
- blood smear - 10 pm - 2 am
- serology (TPE) - IgG1 and IgG4
- ultrasound (visualize adults)

**Treatment:**
- DEC
- Ivermectin
- Doxycycline

**Lymphedema management:**
- Antibiotic soap
- Compression
- Surgery
- Doxycycline!

---

**Impact of Parasitic Diseases**

- Intestinal helminths may occupy 2 billion GI tracts worldwide
- Consequences most notable in children - anemia, malnutrition, growth retardation, impaired cognitive development
Parasite Public Health

- Control and eradication are a multicomponent process:
  - Sanitation/water management
  - Education
  - Vector control
  - Antimicrobials:
    - Mass administration
    - Case finding and targeted administration
  - Vaccines

All it takes is political will, manpower and lots of $.

Parasite Immunology

- In general multiple arms of the immune system are involved
  - Sterile immunity is rare
  - Premunition - persistence of viable organisms at low concentration within the host provides continued immune stimulus to control disease and prevent reinfection
A Worm’s Eye View of the Immune System

• Man has co-evolved with parasites for millions of years. Observations pertinent to this relationship include:
  ◦ Lower population risk for asthma in developing countries
  ◦ Lower prevalence of inflammatory bowel disease in emerging nations
  ◦ Higher prevalence of IBD in northern Europe vs. southern Europe, northern US vs. southern US
  ◦ Rising incidence of asthma, IBD, autoimmune diseases

A Worm’s Eye View of the Immune System

• Animal studies give biologic plausibility to a relationship:
  ◦ Schistosomes or schistosomal eggs or antigens prevent type 1 diabetes, Grave’s thyroiditis, experimental allergic encephalomyelitis
  ◦ Trichuris suis prevents Crohn’s Disease
  ◦ Hymenolepis diminuta prevents experimental colitis
  ◦ T. brucei prevents collagen induced arthritis

A Worm’s Eye View of the Immune System

• Human studies suggest parasite infections drive evolution of host immune responses
  ◦ Decreased prevalence of specific interleukin and interleukin receptor genes associated with inflammatory bowel or celiac disease in populations where parasite burdens are higher

Could it be that parasite extermination leads to immune disregulation and an increase in autoimmune or allergic disease?
Introduction Global and Public Health

A Worm’s Eye View of the Immune System

- ~200 million chronically infected with *Schistosoma* spp
- Complex life cycle
- Adult worms survive in the vascular space for up to 40 years
- Immune evasion -
  - Immunomodulating neuropeptides use molecular mimicry in the snail
  - Adults coat themselves with host antigens
  - Enzymatically cleave antibodies

A Worm’s Eye View of the Immune System

- Immune dependence by the parasite?
  - *S. mansoni* eggs must translocate from the portal capillaries to the gut lumen
    - Process does not occur in immunosuppressed mice
    - Egg excretion is reduced in HIV infected individuals proportional to the number of circulating CD4 cells
    - Egg production in female worms appears to depend upon tissue necrosis factor (TNF)
    - Adult worms bear receptors activated by transforming growth factor β and may play a role in growth and development

Murine immune response to *schistosoma* infection:

- *S. mansoni* in the skin secrete prostaglandin D2 which inhibits migration of Langerhan’s cells to lymph nodes
  - Deletion of the PGD2 receptor results in decreased numbers of adult worms and decreased immune responses to eggs
- Eggs are potent inducers of the TH2 response by multiple mechanisms
Murine immune response to schistosoma infection:
- IL10 is generated by several sources and facilitates the development of T_{reg}:
  - One source is schistosome specific phosphatidylserine which activates TLR2 at the cell surface of DCs
- T_{reg} further TH1 responses and polarize the response toward TH2:
  - There is some downregulation of TH2, however, as responses to allergens such as house dust mite decrease

How does this prevent autoimmune responses?
- Skews responses away from TH1
- Increases T_{reg} which can downregulate both types of autoimmune response
- Other parasite secretory products, such as pro-opiomelanocortin-derived peptides and enkephalin, may also modulate immune response
The Burden of HIV/AIDS in Africa:
New Hope, New Challenges

Michael Sweat, PhD
MUSC
Department of Psychiatry and Behavioral Sciences
Family Services Research Center
April 3, 2012

Thanks to Kevin O'Reilly
At WHO who shared some slides

Global summary of the AIDS epidemic | 2009

<table>
<thead>
<tr>
<th>Number of people living with HIV</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total: 33.3 million [31.4 million – 35.3 million]</td>
<td></td>
</tr>
<tr>
<td>Adults: 30.8 million [29.2 million – 32.6 million]</td>
<td></td>
</tr>
<tr>
<td>Women: 15.9 million [14.8 million – 17.2 million]</td>
<td></td>
</tr>
<tr>
<td>Children (&lt;15 years): 2.5 million [1.6 million – 3.4 million]</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>People newly infected with HIV in 2009</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total: 2.6 million [2.3 million – 2.8 million]</td>
<td></td>
</tr>
<tr>
<td>Adults: 2.2 million [2.0 million – 2.4 million]</td>
<td></td>
</tr>
<tr>
<td>Children (&lt;15 years): 370,000 [230,000 – 510,000]</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AIDS deaths in 2009</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total: 1.6 million [1.6 million – 2.1 million]</td>
<td></td>
</tr>
<tr>
<td>Adults: 1.6 million [1.4 million – 1.8 million]</td>
<td></td>
</tr>
<tr>
<td>Children (&lt;15 years): 260,000 [150,000 – 360,000]</td>
<td></td>
</tr>
</tbody>
</table>

Adults and children estimated to be living with HIV | 2009

Total: 33.3 million [31.4 million – 35.3 million]
Fewer people dying of AIDS

- Thanks to expanded treatment efforts

Annual AIDS-related deaths by region, 1990-2009

- Dotted lines represent ranges, solid lines represent the best estimate.

Treatment is increasingly available...

Michael Sweat, PhD, Professor
Dept. of Psychiatry, MUSC
And clearly having an effect

Getting to AIDS treatment
- Addressing an infectious disease with a chronic disease care model
- Innovation
- Health system strengthening
- Funding
- Policies and consideration of social justice

Health system strengthening for AIDS treatment: simplified procedures

Michael Sweat, PhD, Professor
Dept. of Psychiatry, MUSC
Health system strengthening for AIDS treatment: simplified regimens

Health system strengthening for AIDS treatment: improved logistics

And dealing with the continuing challenges

Michael Sweat, PhD, Professor
Dept. of Psychiatry, MUSC
But what about preventing new infections?

Fewer people getting infected with HIV, thanks to prevention efforts

Changes in the incidence of HIV infection, 2001 to 2009

Source: UNAIDS.

To assess changes in incidence, the estimated national incidence rate was compared between 2009 and 2001. Countries with a change (decrease or increase) in the incidence rate of 25% or more during this period were identified. In most cases, the assessment was based on EPP/Spectrum modelling results (1,2). For selected countries, published analyses of country-level incidence were also used. The EPP/Spectrum criteria for including countries in this analysis were as follows. EPP files were available and trends in EPP were not derived from workbook prevalence estimates; prevalence data were available up to at least 2007; there were at least four time points between 2001 and 2009 for which prevalence data were available for concentrated epidemics and at least three data points in the same period for generalized epidemics; for the majority of epidemic curves for a given country, EPP did not produce an artificial increase in HIV prevalence in recent years due to scarcity of prevalence data points; data were representative of the country; the EPP/Spectrum–derived incidence trend was not in conflict with the trend in case reports of new HIV diagnoses; and the EPP/Spectrum–derived incidence trend was not in conflict with modelled incidence trends derived from age-specific prevalence in national survey results.
HIV In developing Countries

Number of people newly infected with HIV

Prevention efforts have expanded around the world

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Dept. of Psychiatry, MUSC
A general lack of consensus on the relative efficacy of interventions,

An ever changing and rapidly growing evidence base on intervention efficacy, and

Lack of shared standards and terminology for intervention approaches

Michael Sweat, PhD, Professor
Dept. of Psychiatry, MUSC
### Topics

- **Individual / Cognitive Interventions** -
  - (1) Provider-Initiated HIV Testing and Counseling (PITC),
  - (2) Drug Treatment,
  - (3) Family Life Education,
  - (4) Interpersonal Skills Training (Empowerment),
  - (5) Behavioral Counseling, and
  - (6) Diffusion & Opinion Leader;

- **Structural and Social-Ecological Interventions** -
  - (1) Free Condom Distribution;
  - (2) Income Generation,
  - (3) Built Environment,
  - (4) Policy Interventions,
  - (5) Social Capital Enhancement,
  - (6) Community Mobilization;

- **Topics Defined by Behavioral Outcomes** -
  - (1) Interventions to Enhance Adherence to Antiretroviral Treatment (ART),
  - (2) Interventions designed to Increase Uptake of AIDS Treatment, Mother to Child Transmission (MTCT) Programs, and HIV Testing, and
  - (3) Interventions that Promote Serosorting.

### Methods

1. Define the topic
2. Develop inclusion criteria
3. Create a list of search terms
4. Systematically search the literature
5. Screen search results
6. Acquire articles
7. Screen full-text articles and select studies for inclusion
8. Extract study data into standardized format (code)
9. Resolve coding discrepancies
10. Assess study rigor
11. Analyze, synthesize and interpret results
12. Conduct meta-analyses when feasible

### Data Extracted

1. Citation Information
2. Study Inclusion Criteria
3. Study Methods
   - Study population characteristics
   - Setting
   - Sampling
   - Study design
   - Unit of analysis
   - Loss to follow up rates
4. Study Group (arms or comparison groups)
   - Characteristics
5. Intervention Characteristics
6. Intervention Topic-Specific Questions
7. Outcome Measures and Primary Outcome Results
8. Additional Information
   - Costs, limitations, potential harms, community acceptance, other relevant information
Key project Outcomes

- Publishing systematic reviews and meta-analyses
- Develop practical guidance
- Developing a comprehensive and consistently coded database on study characteristics, efficacy, intervention characteristics, and population characteristics
  - Now in a position to:
    - Look across variables and intervention types
    - Model population-level effects
New Project: Mathematical Modeling

- Develop Mathematical Models
- Compile Requisite Data on Model Parameters and Intervention Effects
- Stratify Epidemic Settings & Generate Summary Base-Case Model Datasets
- Use Mathematical Modeling to Identify Optimal Prevention Program Strategies

In Collaboration with:
- Imperial College, London
- World Health Organization
- Johns Hopkins School of Public Health

Analytic Goals of Modeling Project

To Examine:
- Timing
- Targeting
- Duration
- Coverage
- Decay
- Inclusion Threshold
- Sequencing
- Cumulative impact
- Combining

What’s new?

Use of antiretroviral drugs for prevention

- For HIV-positives:
  - Treatment as prevention
  - Early Treatment

- For HIV-negatives:
  - Oral pre-exposure prophylaxis (“PreP”)
  - Topical pre-exposure prophylaxis

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HIV In developing Countries
IP724/BMTRY789.05

April 3, 2012

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Treatment as prevention: Recent results from HPTN052

- RCT assessing the effect of early treatment on HIV transmission in serodiscordant couples
- Based on observation that viral load becomes undetectable with successful treatment
- Large international trial
- Results: 96% effective in preventing HIV infection in uninfected partner

Benefits and challenges of HPTN052

- Improved health (?), reduced transmission
- Existing delivery mechanism
- Costs and expansion challenges
- "outside" sources of infection
- What is a "stable sexually-active couple"?
Pre-exposure prophylaxis (PrEP)

- Use of antiretroviral drug by uninfected person to block acquisition of HIV
- Can be taken orally (daily) or topically (coitally-dependent)
- Drugs used are tenofovir/emtricitabine (oral), tenofovir alone (oral) or 1% tenofovir gel (topical)
- Safety profiles well established from treatment
- Efficacy (trial effectiveness) becoming clear; implementation challenges remain

Why PrEP? Does it work?

- Evidence that PrEP may work to prevent HIV
  - Existing uses of ARV for prevention
    - PMTCT (Prevention of Mother to Child Transmission)
    - Post exposure prophylaxis (PEP)
  - Animal models
  - PrEP trials (RCTs)
    - Captsa 004
    - iPrex
    - Partners PrEP
    - TDF2

Pre- and post-exposure ART prevents vertical HIV transmission

Prolonged nevirapine or nevirapine/zidovudine prophylaxis to breastfeeding infants from Malawi decreased postnatal HIV transmission by half

Kumwenda et al. NEJM 2008
Either FTC or TDF were protective
- 70% to 100% Effective/exposure
Emtricitabine + Tenofovir
- The combination was 100% effective
- Even after repeated rectal exposures (14)
The prophylactic activity probably reflects
- Long intracellular half life
- Activity in macrophages
- High concentration in genital tissues

Preclinical Evaluation of Tenofovir (TDF) and TDF-Emtricitabine (FTC) (N=40)


Macaque data indicating intermittent PrEP may be feasible

What have Human PrEP trials found?
- iPrex (MSM, Nov 2010): 42% effective on modified ITT, much higher in regular users
- Partners PrEP (serodiscordant couples):
  - TDF 62% effective, FTC/TDF 73% effective
- TDF2 (heterosexuals): FTC/TDF: 78% effective
- FemPrEP (heterosexual women): stopped for futility
**Topical PrEP trial**
- Caprisa 004 (women, July 2009):
  - coitally-dependent dosing, 1% TDF gel:
  - 39% effective

**Challenges to PrEP Implementation**
- Cost of daily PrEP
  - Possibly greater than treatment for national budgets?
- Diverting treatment to those uninfected
- Motivation for daily PrEP
- Behaviour of those taking PrEP
  - Adherence
  - Risk compensation
- Experience with other daily prevention is poor
- Political challenge of advocating scarce resources for socially marginalized groups
  - Sex workers, MSM, IDU
  - Readily available drug
- Treatment versus prevention
- Development of viral resistance to ARV
  - Low dose
  - Possibility for breakthrough infection

**Effective Targeting**
For the same number of people starting PrEP, effective targeting to those at most risk can substantially amplify impact.
Identifying Optimal HIV Retesting Frequency For PrEP Programs
Preparing for PrEP Meeting
Glion, 29-30 October 2009

Michael Sweat, PhD
The Medical University of South Carolina
Department of Psychiatry and Behavioral Sciences

Thanks to:
Andrew Sadowski, MUSC
Kevin O’Reilly, WHO
Florence Koechlin, WHO

Why is HIV testing frequency important?
• For a feasible program we need to target highest risk populations
• PrEP is low dose = highest likelihood of developing viral resistance to ART when breakthrough infection occurs
• Thus, need to test for incidence, and switch to more complex and higher dose drug regimen when infection occurs.
• Failure to detect viral resistance could ultimately destroy the ability to use ARV for treatment

Method

HIV incidence

HIV infections Averted

Model to estimate HIV incidence
1) Sexual Behavior
2) HIV Prevalence
3) HIV infectivity

Adjusted Values for PrEP
1) Reduced HIV infectivity
2) Potential for risk compensation (adjusted for level of PrEP efficacy)
**Method**

- **Model to estimate HIV incidence:**
  1. Sexual behavior
  2. HIV prevalence
  3. HIV infectivity

- **Adjust values for PrEP:**
  1. Reduced HIV infectivity
  2. Potential for risk compensation (adjusted for level of PrEP efficacy)

**The Incidence of Viral Resistance is Fairly Low (~10/5000 annually)**

- **Annual Number of Secondary Resistant Cases**
  - Minimum: 0.4588
  - Maximum: 46.6183
  - Mean: 9.9874

**ART Resistance is Most Sensitive to Frequency of HIV Testing & Efficacy of PrEP**

- **Frequency of HIV Testing (Months)**
- **Effectiveness of PrEP**
- **Likelihood of Resistance to Developing in Week on PrEP**
- HIV Fox Regular Male Partners
  - Risk compensation multiplier Gender
  - PrEP Fox / Female
  - Risk compensation multiplier Number Partners
  - HIV Prevalence New Male Partners

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HIV In developing Countries

April 3, 2012

Michael Sweat, PhD, Professor
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Summary

- The incidence of ARV resistant cases is likely to be low, even under pessimistic scenarios
  - Approximately 10/5000 annually in base-case model
- The incidence of ARV resistance is highly sensitive to the frequency of HIV testing
  - More frequent testing and rapid removal of HIV incident cases from PrEP program could significantly lower ART resistance

An integrated model of HIV Prevention

<table>
<thead>
<tr>
<th>Intervention Categories</th>
<th>Prong 1</th>
<th>Prong 2</th>
<th>Prong 3</th>
<th>Prong 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioral</td>
<td>Prevent HIV Uninfected</td>
<td>PrEP</td>
<td>Early ART for HIV-infected high CD4</td>
<td>Treatment for HIV-infected low CD4</td>
</tr>
<tr>
<td>Biomedical</td>
<td>HIV testing of partners</td>
<td>PrEP</td>
<td>Partner HIV testing</td>
<td>-</td>
</tr>
<tr>
<td>System-Level</td>
<td>Condom access, policy, structural, cultural</td>
<td>-</td>
<td>-</td>
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</tr>
</tbody>
</table>
Prediction 1:
- Downward trends in HIV incidence and AIDS mortality will continue, as AIDS becomes a manageable condition for many

Prediction 2:
- Search for the "magic bullet" will limit our successes
- Support for behavioral prevention may decline due excitement about new biomedical interventions and lack of appreciation of successes in behavioral prevention

Prediction 3:
- Without vaccine, elimination of HIV will not be possible

Thank you!