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Prevention of HPV-Related Cancers
Females: cervical, vulvar, vaginal, anal, oropharyngeal cancers
Males: penile, anal, oropharyngeal cancers

- Epidemiology
- HPV vaccination
- Screening
- HIV Positive individuals
Does HPV Cause Other Cancers, and if YES, which HPV types, and what proportion of these cancers?

- HPV natural history studies
  - Oral
  - Non-melanoma skin cancer
- Non-melanoma skin cancer
- Larynx
- Lung

Need continued funding for epidemiology and basic science investigations
Females: cervical, vulvar, vaginal, anal, oropharyngeal cancers
Males: anal, oropharyngeal, penile cancers

- Epidemiology
- HPV vaccination – disease control, HPV 16/18 elimination
- Screening

Cancers that the vaccine has proven to protect against
In 2014 publicly funded HPV vaccination programmes existed in 64 countries, regions in 4 countries, and 12 overseas territories.
47 million women worldwide received 3 HPV vaccine doses in national vaccination programs:
- 32M in high resource regions
- 15M in low resource regions

This represents
- 1.4% of the total female population
- 40.0% of targeted female cohorts in countries that vaccinate

The number and percent of males vaccinated is a fraction of that occurring among females.
What Is Needed to Increase Vaccine Uptake Globally Among Females

- Reduced vaccine cost (GAVI, PAHO pricing, tender price)
  - Lower number of vaccine doses
- Increase political will (awareness of need to reduce cervical cancer) to develop national programs in countries with high rates of invasive cervical cancer
- Sustain vaccine uptake – develop strategies to prevent media driven down turns in vaccination rates
- In the US, dissemination and implementation research is needed to develop efficacious strategies to reach 2020 Healthy People Goals (80% vaccinated)
**Males** Remain Susceptible to HPV Infection and Cancers Throughout Their Lifetime

- Oral HPV infection and oropharyngeal cancer is higher in men vs. women
- Anal HPV infection and disease is highest among MSM
- MSM do not benefit from female only vaccine programs
- Men rarely develop immunity following natural HPV infection, regardless of age
- Antibodies acquired from natural HPV infection do not protect against subsequent infection or disease
- No routinely available screening methods for cancers caused by HPV in men

**Vaccination is the only reliable method to ensure protection against HPV in males**
Does HPV Vaccination Prevent all HPV-Related Cancers in Males?

- Vaccination prevents anogenital infection and diseases in men
  - Reduction of **external genital lesions** caused by HPV 6, 11, 16, 18
  - Reduction of **AIN** caused by HPV 6, 11, 16, 18 in men
  - Reduction in **PeIN** caused by HPV 6, 11, 16, 18 – but event rate too small to draw conclusions

- HPV vaccination induces high antibody titers in males (regardless of age and HIV status)

- HPV antibodies are present at oral cavity following vaccination of males

**Need Phase III Trial to provide definitive evidence of vaccine efficacy against oral infections and disease in males**
Clinical Efficacy of HPV Vaccines in High Risk Populations?

- HIV positive men
- HIV positive women
- Pediatric cancer survivors
- Immunosuppressed, other than HIV (transplant patients)

Are immunogenicity data sufficient to draw conclusions regarding vaccine efficacy?

- Despite high antibody response, vaccination of older HIV+ males and females does not protect against AIN incidence (ACTG Trial).
Screening - Anal Cancer Prevention and Control

- Rate of progression/regression of AIN? What percent of AIN progresses to cancer?
- Does identification of AIN through anal cytology and HRA decrease anal cancer incidence, morbidity, mortality? ANCHOR Trial under way led by Palefsky
  - If yes, would require HRA and treatment training
  - Unclear if this is feasible in either low or high resource countries
- Other methods of screening to reduce anal cancer incidence?
  - Screening to detect anal cancer early, followed by aggressive treatment as an alternative to screening for HgAIN?
- Need for more efficacious treatments for HgAIN. Treatment vaccine for HgAIN?
Screening - Oropharyngeal Cancer Prevention and Control

- Rate of progression/regression of oral HPV infections? What percent of infections persist and progress?
- Methods to detect early stage tumors?
  - Antibody based approach
  - Oral gargle base approaches
    - Viral biomarkers
    - Host biomarkers
- Methods to identify highest risk population for future intervention
Cancer Prevention Science – State of the Art

**Females:** cervical, vulvar, vaginal, anal, oropharyngeal cancers

**Males:** anal, oropharyngeal, penile cancers

- Epidemiology
- HPV vaccination
- Screening
  - unvaccinated women
  - combined with vaccination in younger females
Cervical Cancer Screening – *High Resource Countries*

**Existing Cytology Program and HPV Testing Facilities:**

HPV testing, triage to colposcopy or cytology – new standard for the future

- Research to increase specificity and PPV test (10+ year window) (i.e., HPV methylation)

- Ease of implementation

- Overall reduced costs

- Research to overcome barriers to provider and insurance acceptance of new technologies

- Research to optimize screening protocols in the setting of HPV vaccinated populations (e.g., age at initiation of screening, screening interval, optimal test)
Cervical Cancer Screening – Low Resource Countries

Need to establish screening programs?

- Validate low cost, low burden methods for sample collection (i.e., urine)
- Develop and validate low cost, point of care HPV tests
- Optimal number of screens in a lifetime?
- Build public health infrastructure to reach at risk population for routine screening
- Build capacity to diagnose and treat pre-malignant and malignant lesions
- Optimize screening intervention in the setting of vaccinated cohorts
Summary of Research Priorities

- Epidemiology
  - oral and anal HPV natural history
  - case-control and cohort studies evaluating HPV carcinogenicity at suspected anatomic sites
- Phase III Trial testing vaccine efficacy against persistent oral HPV infection
- Develop efficacious cancer screening and early detection interventions
  - Anal and oropharyngeal cancers
- Develop low cost, high specificity cervical cancer screening interventions applicable to low resource countries
- Methods to screen HPV vaccinated cohorts
- Develop efficacious treatment for HgAIN
- Develop evidence based methods to increase HPV vaccine dissemination and assure high and sustained coverage
AACR Collaborations with Other HPV Organizations to Advance Cancer Prevention and Control

Scientific and Health Policy Community:
- IPVS
- ASPO
- ACS
- CDC
- US Preventive Services Task Force
- Pharma

Community at Large
- Legislature (state and federal), WHO (PAHO)
- Foundations (Prevent Cancer, Anal Cancer, Oral Cancer, ACS)