Elimination of HPV-associated Cancers: Routine Universal HPV Vaccination and the Role of Anal Screening

Antwerp, Belgium (hybrid meeting)

5 and 6 June 2025

marc.baay@p-95.com

HPV Prevention and Control Board

www.hpvboard.org

DISCLAIMER

“If you want me to give you a two-hour presentation,

I am ready today.

If you want only a five-minute speech,

it will take me two weeks to prepare.”

Mark Twain

Gender-neutral vs routine vs universal vaccination

- Routine = systematic (as opposed to a campaign, which is meant for risk groups or an outbreak)
- Universal = without any discrimination
- Should an age range be added? E.g., universal adolescent vaccination? With the focus on MACs, this may be confusing.

Context HPV related disease

- 662K new cases of cervical cancer and 349K deaths in 2022
- Correlation with level of income
- China and India together - 40% of cases
- HPV-related cancer - 4.5% of all cancer cases; 8.6% in women, 0.8% in men
- In 2023, vaccination coverage 27% in girls and 7% in boys
- HPV-based screening 7%, any screening 32%
- Far from WHO targets of 90% and 70%, respectively

Context anal cancer

- Anal cancer is a rare cancer (1-2/100,000), with the highest incidence rate in high-risk groups; PLWH, MSM, women with other HPV-related lesions, transplant recipients, people with autoimmune diseases. But in absolute numbers, anal cancer occurs most frequently in women.
- The anal cancer risk scale helps to define groups most likely to benefit from screening
- HPV persists much longer in the anus than in the cervix
- The HPV vaccine is very effective in preventing anal cancer but mostly so when provided before sexual debut; vaccinate boys, not MSM

Context anal cancer

- Secondary prevention of anal cancer is possible; the ANCHOR study was stopped prematurely to offer the control group the same advantage as the intervention group (57% reduction in progression).
- Anal cancer screening: who / when / with what / how to manage positive cases?
- Risk Category A (Incidence ≥ 10-fold compared to the general population (i.e., 17/100,000)) => always screen
- Risk Category B (Incidence up to 10-fold higher compared to the general population) => screen if sufficient high resolution anoscopy (HRA) capacity is available

Context HPV vaccination in male cohorts

- MSM with HIV have a higher HPV 16 incidence and a lower clearance rate
- Anal Intraepithelial Neoplasia 3 (AIN3) is more frequently associated with HPV 16 than AIN2
- Knowledge gaps: timing, host immune factors, reliable biomarkers, longitudinal incidence data, …
- The HPV incidence with age stays high in men but goes down in women.
- Men have a low seroconversion rate after natural HPV-16 infection (4%) compared to women (60%)

Context HPV vaccination in male cohorts

- Efficacy and effectiveness of HPV shown in randomized controlled trials and observational studies
- Similar serum and oral IgG levels in MSM living with HIV
- Community-randomized implementation trial in Finland (girls-only vs girls and boys vs control) showed that moderate universal HPV vaccination coverage provides superb herd effect and protective effectiveness
- Nevertheless, LMIC may have to make different decisions based on limited resources; females have the highest burden and are therefore prioritized for vaccination. With sufficient supply and resources -> vaccinate boys as well

Context HPV vaccination in male cohorts

- However, universal vaccination:
  - Ensures protection of unvaccinated women and men
  - Will tackle the male reservoir
  - Provides resilience in case of vaccine disruptions (pandemic, vaccine confidence crisis)

Context HPV vaccine availability

- More companies, more vaccines, including higher-valent vaccines (up to 14-valent)
- If 1-dose schedule in boys and girls, approximately 130M doses of vaccine/year needed
- With current base supply no risk of shortage
- For most LMIC, the price of the vaccine is not the issue, but the cost of delivery
- From 2017 to 2024, demand exceeded supply, necessitating countries to pause introduction. Now catching up to age 18.
- Projected supply will exceed demand, leaving room for routine universal vaccination

Context HPV vaccine availability

- Not all vaccines have an indication for use in males
- Not all vaccines in the pipeline will reach the market, based on limited previous experience of the companies.
- Overproduction may lead to restructure in industry. Try to ensure demand, offer long-term forecasts of how the market may evolve, although many factors play a role.
- Maybe a golden opportunity for routine universal vaccination but GAVI only supports vaccination of girls, otherwise vaccine for a higher price.
- Switching from 4-valent to (cheaper) 2-valent. New countries may choose to use cheaper 2-valent vaccine. Some already do (Angola, Nepal?).

Context from data to policy

- Universal vaccination vs risk group vaccination
- Prime example: hepatitis B virus (HBV) vaccination
- Started as risk group vaccination, showed no impact
- 1992, call to integrate HBV into national immunization program
- GAVI helped introduction in 72 poorest countries
- Risk-based also a problem with other vaccines (Flu, pneumococcal vaccines)
- Combining vaccines may help to reach higher coverage

Context from data to policy

- Scotland:
  - 2008: 12–13-year-old girls, school-based + catch up to age 18, 80% uptake
  - 2012: switch 2-valent to 4-valent
  - 2019: universal program
  - 2022: switch to 9-valent
  - 2023: switch to 1-dose
  - Catch-up possibility for non-school attenders (to age 25)
- Consent process may be a barrier
- Coverage consistently lower in boys, unclear why
- Coverage consistently lower in most deprived

Context from data to policy

- Kenya:
  - Inclusion of boys may facilitate acceptance and messaging
  - Do not forget that the burden is in females
  - In many LMIC vaccine programs, budgets are often limited with little room for mitigating mis-, disinformation
- Cameroon:
  - Early success in pilot and demonstration projects led to national roll-out
  - Covid-19 pandemic and opposition from religious leaders
  - Change to 1-dose schedule and extension to boys

Context implementation

- Big drop-offs in the anal cancer screening cascade signal a problem that needs to be solved.
- Who should do the screening? Primary care for selection, specialized care for screening?
- Many questions to answer along the cascade.
- After HSIL diagnosis only 58% showed up for treatment and of those only 25% returned for follow-up. Black people and PLWH less likely to be treated. What are barriers?
- Inequity in HIC: incidence of cervical cancer twice as high in most deprived compared to least deprived.

Context implementation

- Lower vaccine coverage in boys than in girls, regardless of deprivation or ethnicity.
- Lower awareness of HPV in boys.
- Context-specific modelling framework: 7 clusters based on sexual behavior
- Local versus global perspective: local – later sexual debut allows older upper age for vaccination, global – higher cervical cancer risk allows older upper age for vaccination
- Cost-effectiveness based on one country per cluster
- Based on local perspective – cost-effective in all clusters
- Based on global perspective – cost-effective in 4/6 clusters

Context implementation

- Not cost-effective due to low Gross Domestic Product per capita
- Focus for optimization can differ: elimination (reduction of incidence) – supply constraints (number needed to vaccinate to prevent 1 case of cancer) – budget constraints (cost per Disability-Adjusted Life Year).
- All strategies have the same order: young girls, older girls, boys.
- Inclusion of boys in Thailand leads to a NNV that is 10 times lower than the NNV in HIC

Context implementation

- The current vaccination strategy leads to increased inequity: the LMIC/HIC incidence ratio will increase from 2.5 to 15.
- A vaccine coverage of 90% will keep the ratio at 2.5 but will lead to elimination in LMIC only in 2095.
- Universal vaccination plus MAC will speed up elimination to 2075 and reduce ratio to 1.25
- The WHO targets (90% vaccination, 70% screening) will speed up further (2065) and close the gap between LMIC and HIC
- This strategy will prevent 40 million cases of cervical cancer
- 1-dose vaccination, less expensive vaccines and increased supply can help reduce current inequalities in vaccination coverage

Lessons learned

- US and UK have 30% of global cancer cases but only 5% of global population – underreporting
- The data on HPV-based cancers are not perfect, but the best we currently have
- The negative predictive value of anal cancer screening is currently unknown
- Guidelines facilitate reimbursement
- Reliable biomarkers are needed for regression/progression

Lessons learned

- Treatment after screening reduces progression by 57%, this needs to be further improved.
- Puerto Rico – concordance between self-collected and provider-collected anal sample. This may overcome the shortage of providers.
- Governmental guidelines provide medicolegal support for provider to do anal cancer screening routinely (”have the guts to go to the anus”)
- New HRA trainees take a long time to be ready to actually ‘touch’ patients

Lessons learned

- GAVI will change pricing in 2026. This may be favorable for the cheaper vaccines.
- Girl-only vaccination makes people suspicious of hidden objectives (example – infertility)
- (Some) people believe that HPV vaccination may unleash sexual promiscuity
- Talk to religious leaders
- Do not become complacent when the demo project is a success, keep investing in communication

Lessons learned

- In some European countries, 90% of people look for more information on HPV vaccination; make sure they get it from people who know what they talk about rather than Facebook et al.
- Learn how to implement anal cancer screening together: share (positive and negative) experiences to improve along the way.
- In HIC – equity in access but inequity in uptake.
- Next to vaccination, screening in LMIC is necessary to reach elimination and achieve equity.
- New models for screening need to be developed, think outside the box.
- No screening without proper treatment and follow-up -> see & treat, one-stop shop

Lessons learned

- Vulnerable girls who are not vaccinated will not be reached by vaccinating boys.
- Reach the most vulnerable, also in HIC.
- 90/70/90 is a goal, but not quite reaching this goal may still be highly impactful. 80% vaccination of girls may be enough, if this cannot be reached universal vaccination at 70% may provide the same outcome.

The way forward

- Obtain insight into the burden of HPV-related cancer other than cervical cancer in LMIC
- Living guideline process for anal cancer screening to include new data / new tests as soon as available
- Build screening capacity, reimbursement of screening, quality assurance – quality control, collect real-world data, cost-effectiveness studies (per risk group), investigate impact on quality of life (patient-reported outcomes)
- Further investigate self-sampling for anal cancer screening.
- Patient may prefer provider-collected sample, convince them they can do it right.

The way forward

- A shift to digital consent may increase participation (Scotland).
- The roadmap for anal cancer screening implementation may be applicable to (all) other cancer screening programs.
- As cervical cancer screening is necessary to reach elimination in LMIC, new tests and new algorithms need to be developed.

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Feedback welcome!

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