Immunising older cohorts
Pros and cons

Margaret Stanley

HPV Prevention and Control Board
Antwerp November 2019
Vaccines depend for their impact at the population level by reducing transmission and true herd immunity.

Transmission has to be blocked without transmission disease disappears irrespective of whether those vulnerable to infection have serum antibody or not.

This why catch up programmes are so important.

Immunising older women is a catch up programme.
As an example
Meningococcal vaccines
Immunising infants
The UK story

Slides courtesy Adam Finn@adamhfinn
University of Bristol UK
Age – UK 1998/9
One off “catch up” programme 2000

- One dose MenC conjugate
- All children up to the age of 20y
- (Eventually extended to 23y)
MenC disease carried on disappearing but not by inducing long lasting antibody in vulnerable recipients.
UK Students - carriage

The catch up programme worked by blocking transmission
immunising teenagers protected younger children
teenagers are the group with highest rates of carriage
young children have the highest rates of disease
Transmission was blocked

Take home message
• Think fundamentally
• blocking transmission is the name of the game
Immunising older women

Pros

• Transmission of vaccine types blocked rapidly
• Rapid impact on disease in older cohorts – herd protection

Cons

• Cost – current models predict even 1 dose vaccination not cost effective in >26 year olds
• What about those already infected and shedding virus will serum antibody block transmission? Possibly
How does serum neutralising antibody against HPV L1 prevent virus entry?
Proposed mode of HPV entry

Virus binds to the BM\textsuperscript{1,2,3} via L1 undergoes shape change\textsuperscript{4}

L2 is exposed, cleaved, binds to the keratinocyte\textsuperscript{3,4}

The L1 receptor is now exposed\textsuperscript{3,4} virus binds to the wound keratinocyte and enters the cell

Neutralisation after HPV 16L1 VLP immunisation

Antibody binds to virus and prevents BM binding and conformational change.

Antibody binds to virus and prevents binding via L1 to the epithelial cell.

Basement Membrane (BM)

Wound keratinocyte

HPV 16 L1 antibodies that prevent conformational change neutralise at very low concentrations ($10^{-12}M$).

Passive immunisation shows very low levels of antibody prevent virus entry.

Very low levels of antibody are needed to prevent HPV infection.
Antibody to L1 can prevent HPV infection by

Blocking binding to the basement membrane

Blocking binding to the epithelial cell receptor

Both types of antibody are generated after vaccination with HPV VLPs

Passive immunisation experiments show that very low levels of these antibodies are sufficient to prevent HPV entry into cervical epithelial cells

Immunising older women

Pros
• Transmission of vaccine types blocked rapidly
• Rapid impact on disease in older cohorts - herd protection

Cons
• Cost – current models predict even 1 dose vaccination not cost effective in >26 year olds

• What about those already infected and shedding virus will serum antibody block transmission? Possibly
If virus is shed as free particles into the vaginal lumen in a productive infection then antibody in the cervico/vaginal mucus and fluids should coat the particle and prevent autoinoculation and/or infection of the sexual partner.

Transmission would be blocked.

If cell associated virus is shed this mechanism would not operate.