HPV for Boys

Karina M Butler, MB, FRCPI
Chair, National Immunisation Advisory Committee, RCPI
Our Lady’s Children’s Hospital Crumlin
Temple Street Children’s University Hospital
University College Dublin, Ireland
Disclosures (5 yrs)

• Prof Butler’s institution has received funding to support conduct of influenza adverse event vaccine surveillance from SP-MSD. No personal funding received.

• 6 slides adapted from a MSD sponsored presentation, ESPIID 2019.
• 300 women in Ireland develop cervical cancer every year

• 90 women die every year

• 90% can be prevented
“No man is an island”...

Equity of Access
HPV: Common infection
The aim:
Maximun protection for all
Cervical Cancer 2018

Global: 569,847 new cases, 311,365 deaths
Europe: 61,000 new cases, 25,829 deaths

Estimated age-standardized incidence rates (World) in 2018, cervix uteri, all ages
WHO Director General calls for all countries to take action to end suffering caused by cervical cancer, 2018

“Cervical cancer is one of the most preventable and treatable forms of cancer....”

Call for cervical cancer elimination
1. Increase HPV vaccination coverage
2. Increase screening coverage
3. Reduce mortality from cervical cancer

Need for feasible, global HPV vaccination

Dr Tedros Adhanom Ghebreyesus, WHO Director-General
The Tools

• 3 licensed vaccines
  • HPV2 (Cervarix) 16, 18
  • HPV4 (Gardasil licensed 2006) 6, 11, 16, 18
  • HPV9 (Gardasil 9 licensed 2015) 6, 11, 16, 18, 31, 33, 45, 52 & 58

• Recommended by WHO in 2009
• All girls aged 12-13 years - most effective at this age
  • 2 doses over 6-12 months if initiated < 15yrs
  • 3 doses if initiated at ≥ 15 yrs

• HPV4 protects against 70% cervical cancers and pre cancers
• HPV 9 protects against 90%
• Less common but high oncogenic potential, 35, 39, 51, 56, 59
HPV vaccine

- HPV4 will prevent 70% of cervical cancers
- HPV9 will prevent 90% of cervical cancers
- But that’s not all.....
## Australia: HPV4 (introduced 2007)

<table>
<thead>
<tr>
<th>HPV type</th>
<th>Population prevalence</th>
<th>Vaccinated</th>
<th>Unvaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>5.5%</td>
<td>0.2%</td>
<td>2.7%</td>
</tr>
<tr>
<td>11</td>
<td>1.5%</td>
<td>0%</td>
<td>1.3%</td>
</tr>
<tr>
<td>16*</td>
<td>21.3%</td>
<td>1.5%</td>
<td>12.1%</td>
</tr>
<tr>
<td>18*</td>
<td>8.4%</td>
<td>0.6%</td>
<td>7.4%</td>
</tr>
<tr>
<td>31*</td>
<td>5.0%</td>
<td>2.7%</td>
<td>8.1%</td>
</tr>
<tr>
<td>33*</td>
<td>4.0%</td>
<td>1.4%</td>
<td>2.0%</td>
</tr>
<tr>
<td>45*</td>
<td>1.0%</td>
<td>1.7%</td>
<td>6.0%</td>
</tr>
<tr>
<td>52*</td>
<td>7.4%</td>
<td>6.9%</td>
<td>9.4%</td>
</tr>
<tr>
<td>HPV6/11/16/18</td>
<td>28.7%</td>
<td>2.3%</td>
<td>18.8%</td>
</tr>
</tbody>
</table>

*Pre –Vaccine vs Post Vaccine*  

*Patel C et al. Euro Surveill 2018;23 (41) pli=1700737*
• ↓HPV prevalence
• ↓High grade cervical anomalies
• ↓genital warts
• ↓Juvenile onset recurrent respiratory papillomatosis

Patel C et al. Euro Surveill 2018;23 (41) pli=1700737
Prevalence of individual human papillomavirus (HPV) types among females aged 14–19 years (A) and 20–24 years (B)

The Journal of Infectious Diseases, Volume 216, Issue 5, 1 September 2017, Pages 594–603, https://doi.org/10.1093/infdis/jix244

A: Females

B: Males
Histological abnormality: (% of women screened) by year of birth and immunisation status.

Compared with unvaccinated women born in 1988, vaccinated women born in ‘95 and ‘96 showed:

- 89% (95% CI 81 – 94) CIN ≥ 3
- 88% (95% CI 83 – 92) CIN ≥ 2
- 79% (95% CI 69 – 86) CIN ≥ 1

Routine immunisation of girls 12–13 yrs with the bivalent vaccine has led to a dramatic reduction in pre-invasive cervical disease.

Tim Palmer et al. BMJ 2019;365:bmj.l1161
©2019 by British Medical Journal Publishing Group
Dose-related Effectiveness of Quadrivalent Human Papillomavirus Vaccine Against Cervical Intraepithelial Neoplasia: A Danish Nationwide Cohort Study

Freija Verdoost,1,9 Christian Dehlendorff,3 and Susanne K. Kjaer13

CID 2019, March

• Nationwide cohort 17 – 25 yrs, 2006 -2016
• 590,093 women, 215,309 (36%) vaccinated @ <16yrs, 19% received 3 doses
• Vaccine effectiveness vs CIN3: 63%
  • 1 dose       IRR*0.38 (95%CI 0.14-0.98)
  • 2 doses      IRR 0.38 (95%CI 0.22-0.66)
  • 3 doses      IRR 0.37 (95%CI 0.30-0.45)

*IRR: incidence risk ratio
Does it work?

Costa Rica

Fig. 2. HPV prevalence measured seven years after initial vaccination among women who received 3, 2, 1, and 0 doses in the Costa Rica HPV Vaccine Trial. Legend: The endpoint was HPV16 or 18 infections detected seven years following enrollment among the HPV vaccine groups and the contemporaneous visit among the unvaccinated control group. This was assessed among the total vaccinated cohort and the unvaccinated control group.
Real world benefits of HPV vaccine

- **Vaccine Type infection:**
  - Australia
  - Belgium
  - Germany
  - Sweden
  - USA

- **Genital warts:**
  - Australia
  - Belgium
  - Canada
  - England
  - Denmark
  - France
  - Germany
  - New Zealand
  - Sweden
  - USA

- **CIN:**
  - Australia
  - Canada
  - Denmark
  - Scotland
  - Sweden
  - USA

- **Cancer:**
  - Finland
  - USA
Durability of antibody response
What about the boys?

Direct protection

Increase herd protection
HPV Vaccine Uptake

15,000 girls not vaccinated

www.hpv.ie  slide courtesy Dr. Brenda Corcoran, NIO
Turning the Tide

HPV vaccine uptake increases following information campaign

HSE say the figures represent success of tackling “misinformation” around vaccine

Jack Power

In the 2014/15 school year 87 per cent of girls aged 12 to 13 received the vaccine but the proportion fell sharply to 50 per cent last year.

In the 2014/15 school year 97 per cent of girls aged 12 to 13 received the vaccine but the proportion fell sharply to 50 per cent last year.

Uptake of the cervical cancer vaccine has increased from 50 to 61 per cent this year following a large drop in the number of young girls availing of it.
After 70 yrs with 40% vaccine uptake:-

- Girls only:
  - ↓prevalence by 53% in girls
  - 36% in males.

- **GNV**: ↓prevalence by 71%

GNV = gender-neutral vaccination.
GNV Provides Greater HPV Prevalence Reductions

Prevalence Reduction With 40% Coverage

- GNV: 36%
- Female-only: 71%

Prevalence Reduction With 80% Coverage

- GNV: 53%
- Female-only: 83%

GNV = gender-neutral vaccination.
HPV and Cancer

• HPV cause other cancers:
  - 90% anal
  - 70% vaginal
  - 50% penile
  - 40% vulvar
  - And 13-72% head and neck cancers
HPV and Cancer

- HPV cause other cancers:
  - 90% anal
  - 70% vaginal
  - 50% penile
  - 40% vulvar
  - And 13-72% head and neck cancers
Genital HPV prevalence is higher in males than females and does not decrease with age.
Anal and Penile Cancers 2010-2014

36 cases/yr
90% HPV related

32 cases/yr
50% HPV related

National Cancer Registry: Cancer Trends No 33 4th May 2017
Rates of Cervical Cancer Are Declining While HPV-Related Oropharyngeal SCC in Males Is Rising (USA)

- Oropharyngeal SCC (male): AAPC = 2.7
- Cervical carcinoma; AAPC = -1.6
Oral HPV Prevalence Is Significantly Higher in Males Than in Females

Males, any HPV infection

- Unadjusted
- 95% CI
- Adjusted

Females, any HPV infection

- Unadjusted
- 95% CI
- Adjusted
Oropharyngeal Cancer: 2010-2014

<table>
<thead>
<tr>
<th>Sex</th>
<th>Period</th>
<th>APC</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1994-1999</td>
<td>-7.5%</td>
<td>(-16.0%, +1.0%)</td>
<td>0.108</td>
</tr>
<tr>
<td></td>
<td>1999-2014</td>
<td>+3.7%</td>
<td>(+2.1%, +5.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>1994-2014</td>
<td>+3.6%</td>
<td>(+1.9%, +5.2%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Oropharyngeal cancer (OPC)

Ireland
- 2009 - 2013: 123 cases /yr
- 2014 - 2018: 168 cases/yr
- 33-43%+ are p16\textsuperscript{INK4a} pos

US
- 1988-2004
- HPV \uparrow\ OPC by 225% (0.8 to 2.6/100,00)
  Estimate 70% HPV related

UK
- Doubling of OPC cases 2002-2011, 50% HPV related

\textit{HIQA:HTA of HPV in boys, 4\textsuperscript{th} Dec 2018}
Why Boys?

- High rates of infection across all age groups
- Impacted by certain diseases and cancers
- Remain susceptible throughout life – low rates of seroconversion after natural infection
- No recommended routine screening
- GNV programmes accelerates HPV cancer and disease elimination

2. De Martel C. Int J Cancer 2017:141,664
5. Elstrom JID 2016;203:199
Is HPV vaccine safe?

- > 80 publications
- RCT: 72,835 subjects
- Cohort studies
- Post licensure studies
- Systematic reviews
- Safety reviews

HIQA ADVISES

The following would be an efficient use of resources:

- **Change** to the 9-valent vaccine.
- **Extend** the vaccine to include boys to provide better protection for everyone.
What can you do:

Be Prepared

"Always be prepared."
You are so important.
• Be informed
• Reliable information sources

www.hpv.ie
What we can do:

• Provide a strong, presumptive message for vaccination
• Present it as part of the routine vaccinations
• Emphasize the anti-cancer message
• Focus on disease prevention
• Ask their concerns, Acknowledge their fears, Advise vaccination
• If they decline try again at a later visit
Together we can..........

Donal Brennan
@donaib5

If you don’t want to listen to medics about #HPVvaccine, please listen to @kimmykims31 and @laurabrennan091 - heroes telling their personal stories more powerful than an RCT. #vaccinate #protectourfuture

7:05 PM - 13 Apr 2018

Safeguarding the health of a generation

With the HSE spearheading a new campaign promoting the HPV vaccine, June Shannon reports that the vaccine is safe, effective and saves young lives.
Acknowledgements

• NIAC Committee members, the National Immunisation Office
• The HPSC, and especially......
• All of those parents and adults who choose to get vaccinated to protect themselves and to protect those who cannot be vaccinated

Thank You
My generation saw the end of smallpox.

My generation saw the end of polio.

My generation stopped vaccinating their kids.

My generation will see the return of deadly childhood diseases.