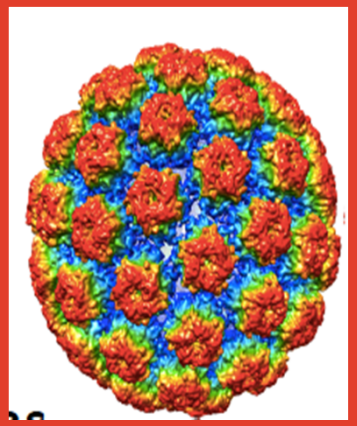
Children's Health Ireland



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

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

Ospidéal Mhuire na Leanaí, Cromghlinn
Our Lady's Children's Hospital, Crumlin

UCD DUBLIN

Temple Street CHILDREN'S UNIVERSITY HOSPITAL

HSE Seirbhíse Sláinte Health Service Executive

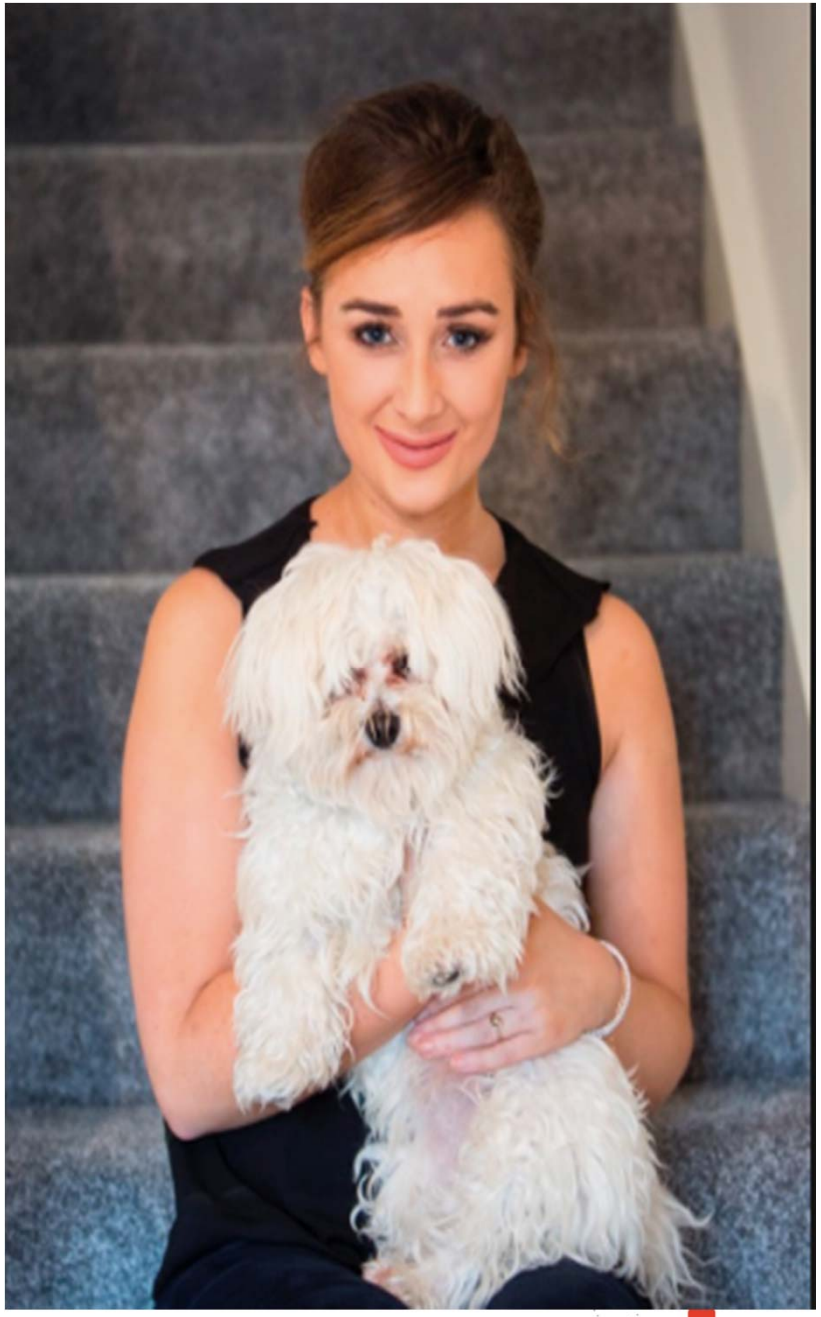
Children's Health Ireland

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, ESPID 2019.

Children's Health Ireland

- 300 women in Ireland develop cervical cancer every year
- 90 women die every year
- 90% can be prevented

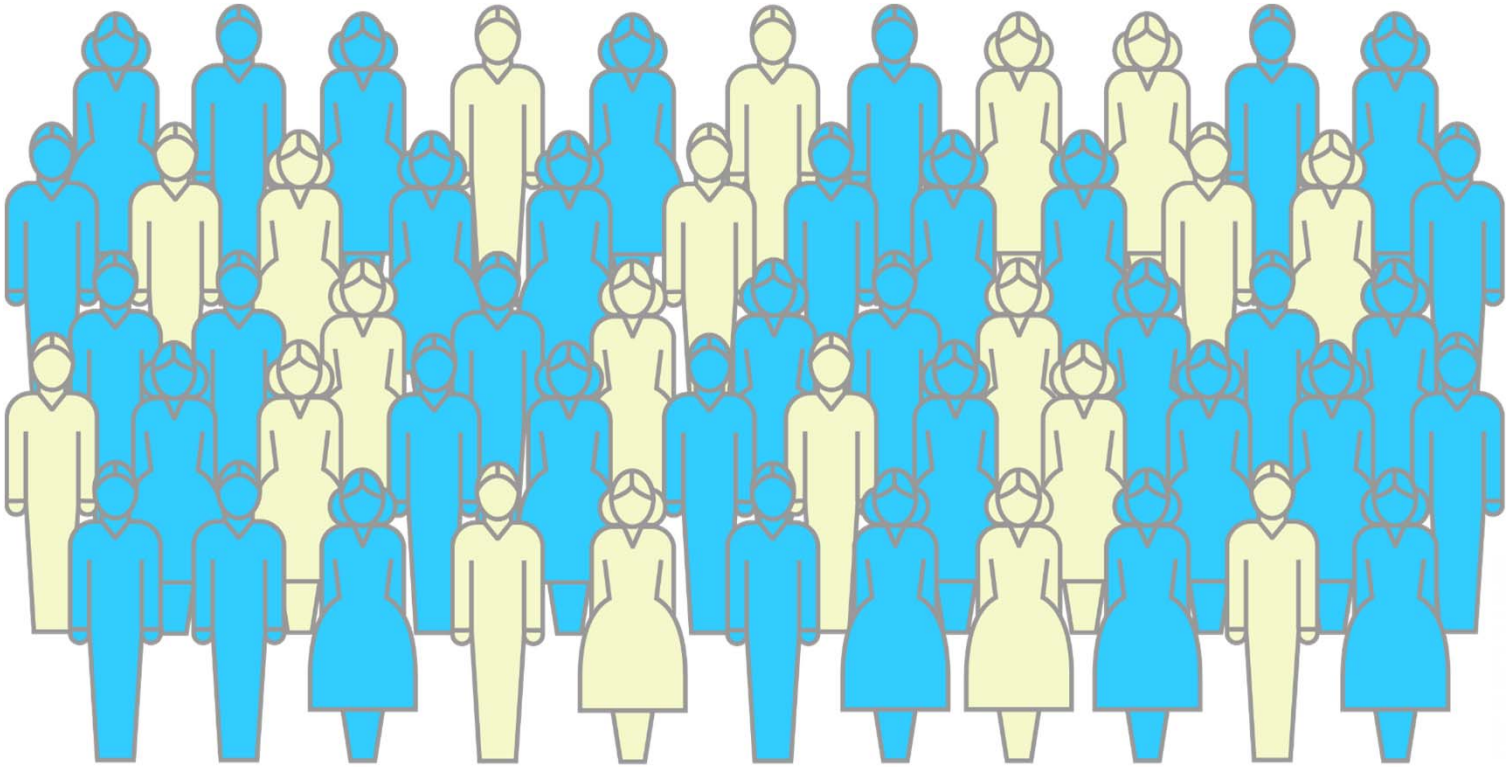


“ No man is an island”…

Equity of Access

Children's Health Ireland

HPV: Common infection
The aim:
Maximun protection for all

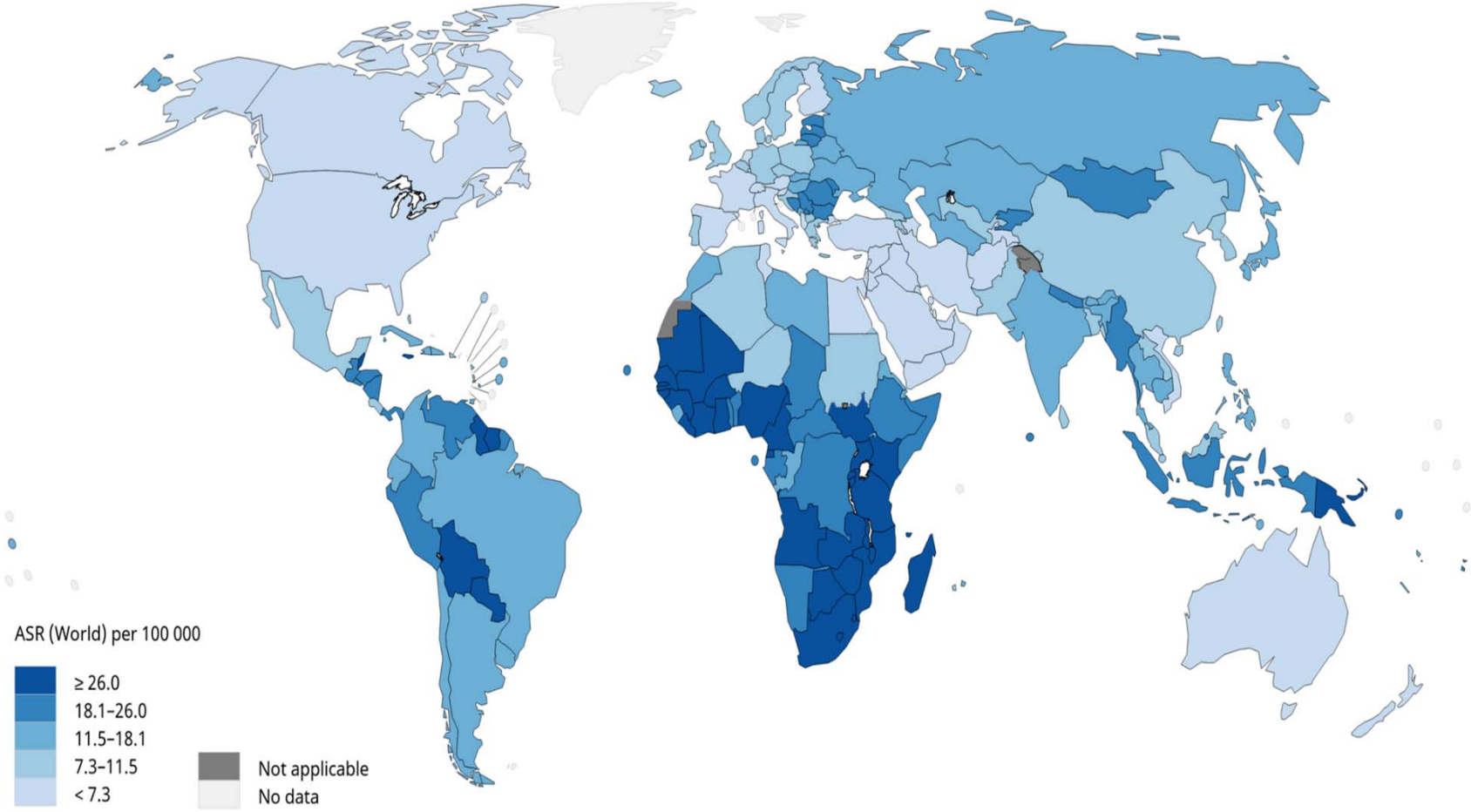


Cervical Cancer 2018

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



Data source: GLOBOCAN 2018
Graph production: IARC
(http://gco.iarc.fr/today)
World Health Organization

World Health Organization

Children's Health Ireland

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

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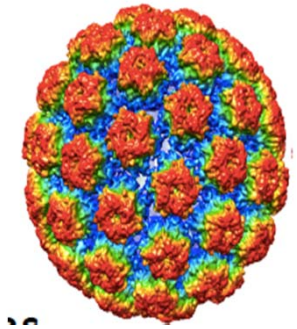
HPV vaccine



- HPV4 will prevent 70% of cervical cancers
- HPV9 will prevent 90% of cervical cancers
- But that's not all…..

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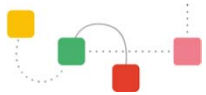
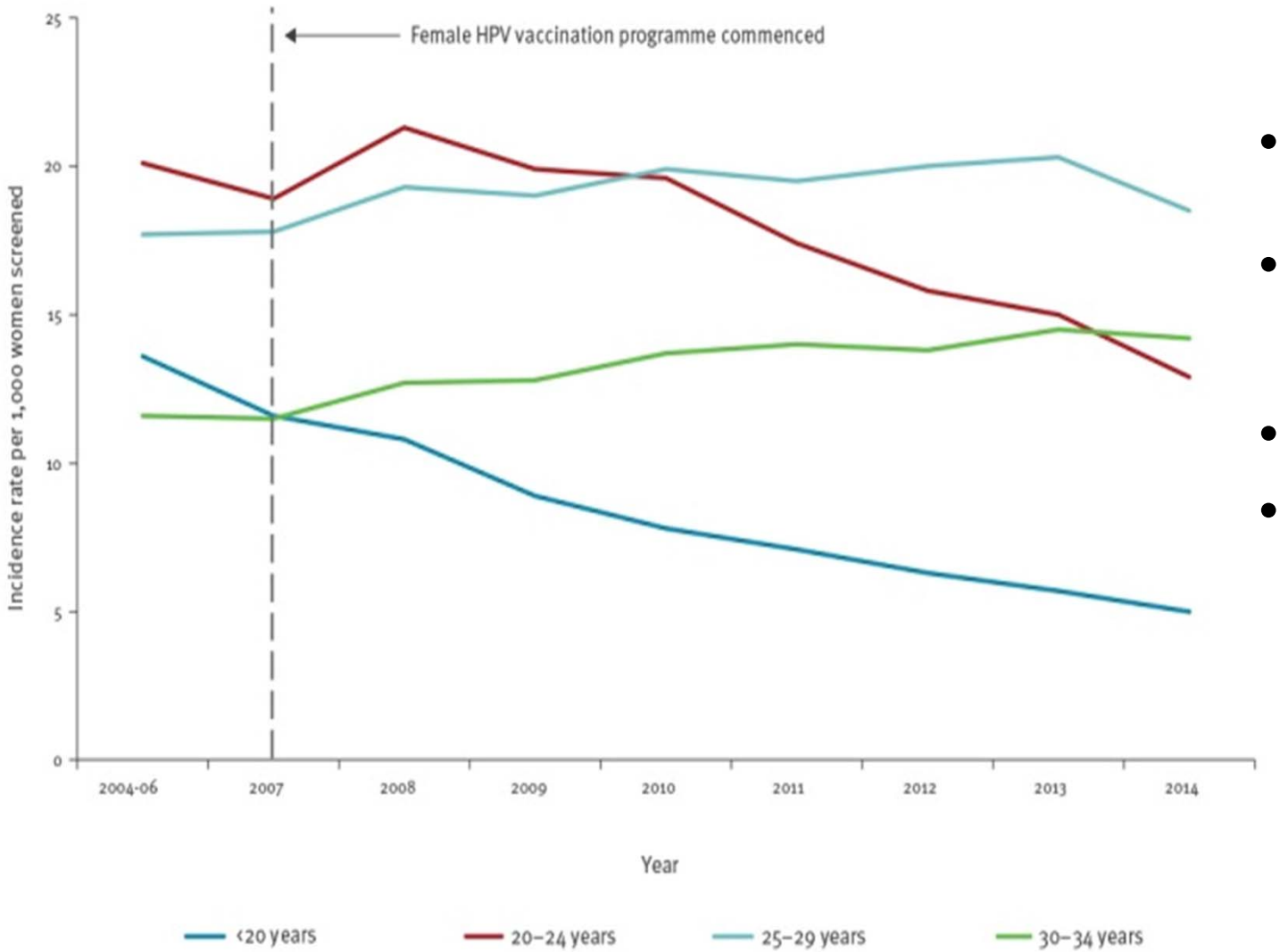
Australia: HPV4 (introduced 2007)

	Pre –Vaccine	Post Vaccine	
HPV type	Population prevalence	Vaccinated	Unvaccinated
6	5.5%	0.2%	2.7%
11	1.5%	0%	1.3%
16*	21.3%	1.5%	12.1%
18*	8.4%	0.6%	7.4%
31*	5.0%	2.7%	8.1%
33*	4.0%	1.4%	2.0%
45*	1.0%	1.7%	6.0%
52*	7.4%	6.9%	9.4%
HPV6/11/16/18	28.7%	2.3%	18.8%

Patel C et al. Euro Surveill 2018;23 (41) pli=1700737



Australia

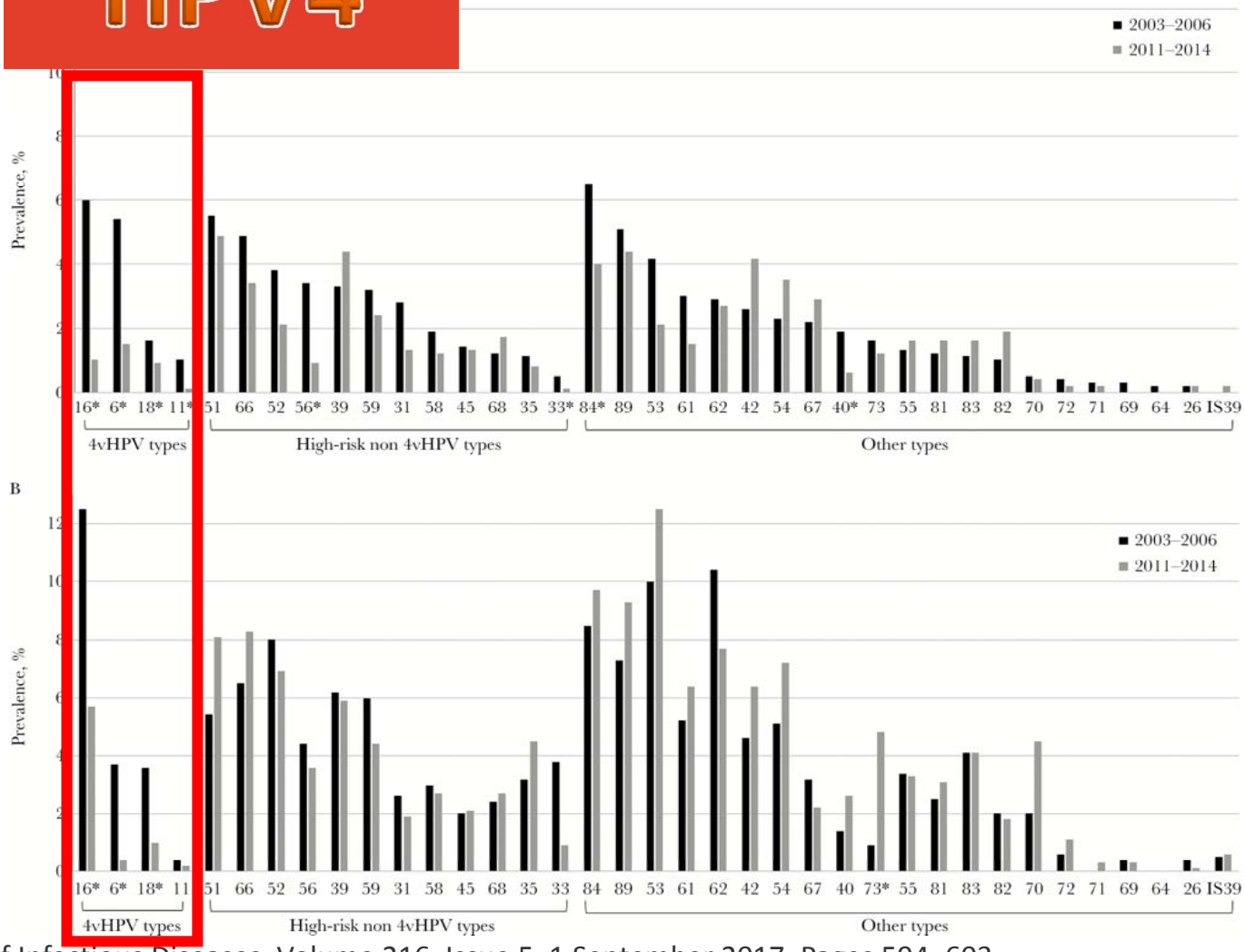


- ↓HPV prevalence
- ↓High grade cervical anomalies
- ↓genital warts
- ↓Juvenile onset recurrent respiratory papillomatosis

Patel C et al. Euro Surveill 2018;23 (41) pli=1700737

USA: HPV4

Prevalence of individual human papillomavirus (HPV) types among females aged 14–19 years (A) and 20–24 years (B)

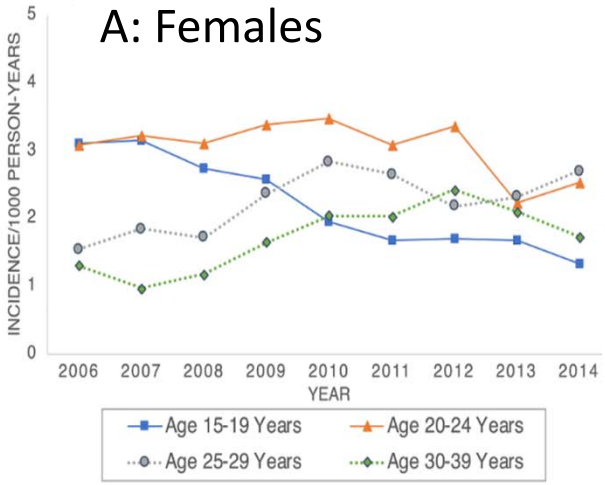


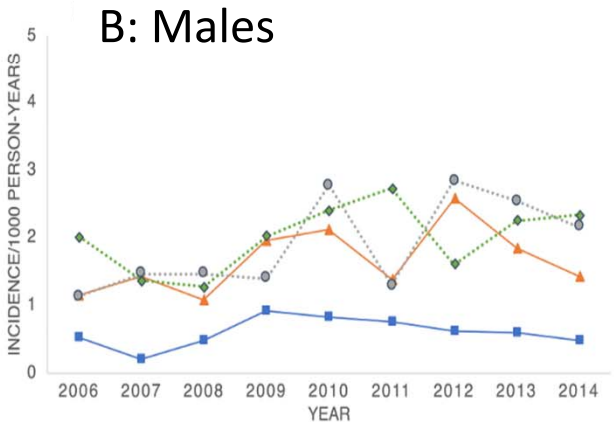
The Journal of Infectious Diseases, Volume 216, Issue 5, 1 September 2017, Pages 594–603, https://doi.org/10.1093/infdis/jix244

ELSEVIER
Papillomavirus Research
Volume 7, June 2019, Pages 141-149

Trends in anogenital wart incidence among Tennessee Medicaid enrollees, 2006–2014: The impact of human papillomavirus vaccination

Jaimie Z. Shing [a], Pamela C. Hull [a], Yuwei Zhu [b], Julia W. Gargano [c], Lauri E. Markowitz [c],

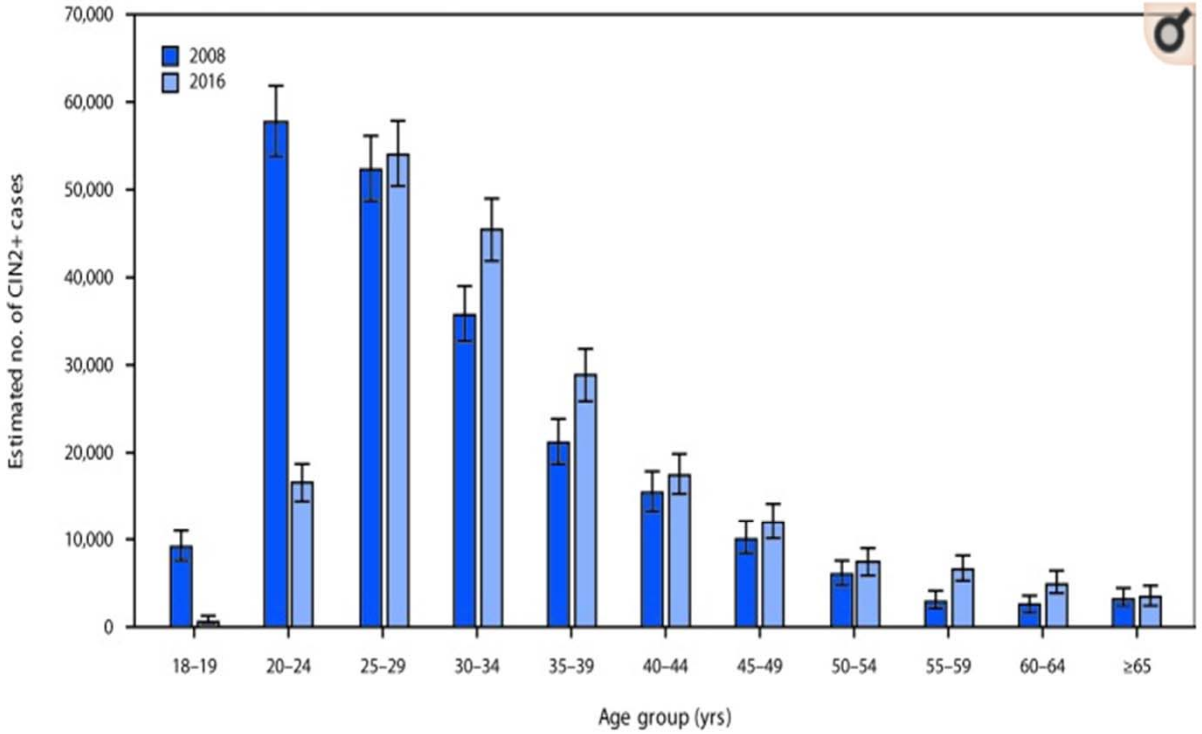




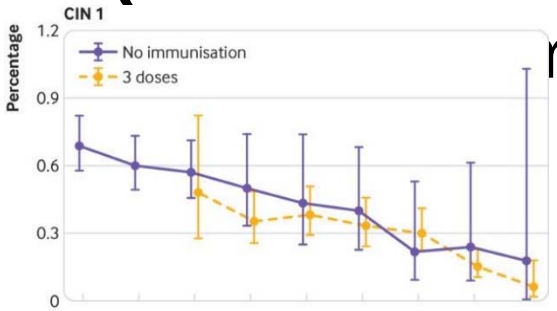
USA

MMWR Morb Mortal Wkly Rep. 2019 Apr 19; 68(15): 337–343.
Published online 2019 Apr 19. doi: 10.15585/mmwr.mm6815a1
PMCID: PMC6476057
PMID: 30998672

Estimated Number of Cases of High-Grade Cervical Lesions Diagnosed Among Women — United States, 2008 and 2016



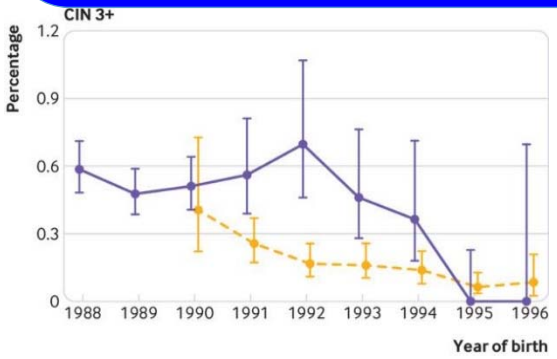
Histological abnormality: (% of women screened) by year of birth and immunisation status



- Compared with unvaccinated women born in 1988, vaccinated women born in '95 and '96

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

- CIN ≥2
- 79% (95% CI 69 – 86) ↓ CIN ≥1



Scotland

Tim Palmer et al. BMJ 2019;365:bmj.l1161

Children's Health Ireland

Dose-related Effectiveness of Quadrivalent Human Papillomavirus Vaccine Against Cervical Intraepithelial Neoplasia: A Danish Nationwide Cohort Study

Freija Verdoodt,[1] Christian Dehlendorff,[2] and Susanne K. Kjaer[1,3]

[1]Virus, Lifestyle and Genes, and [2]Statistics and Pharmacoepidemiology, Danish Cancer Society Research Center, and [3]Department of Gynaecology, Rigshospitalet, University of Copenhagen, Denmark

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

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Does it work?

Costa Rica

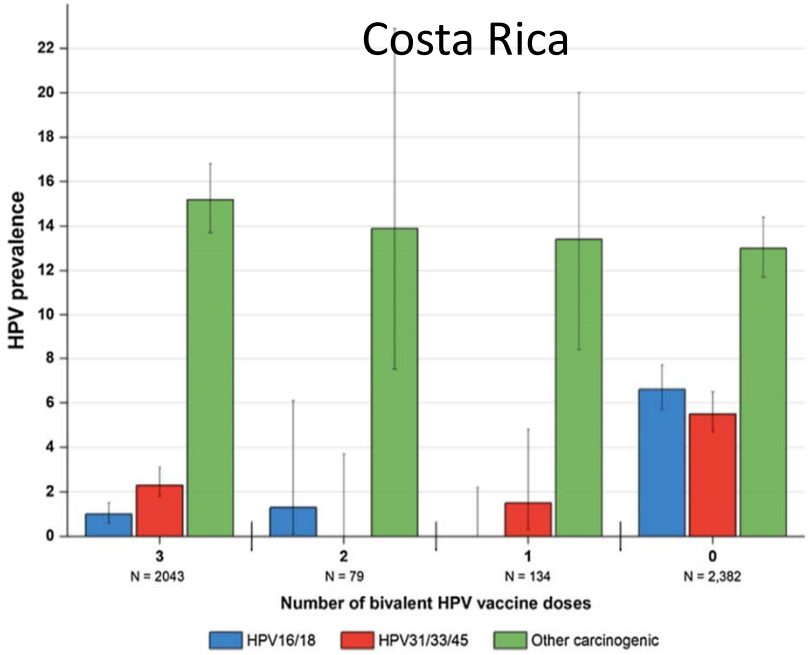

Fig. 2. HPV prevalence measured seven years after initial vaccination among women who received 3, 2, 1, and 0- doses in the Costa Rica HPV Vaccine Trial. Legend. The endpoint was HPV16 or 18 infections detected seven years following enrollment among the HPV vaccine groups and the contemporaneous visit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

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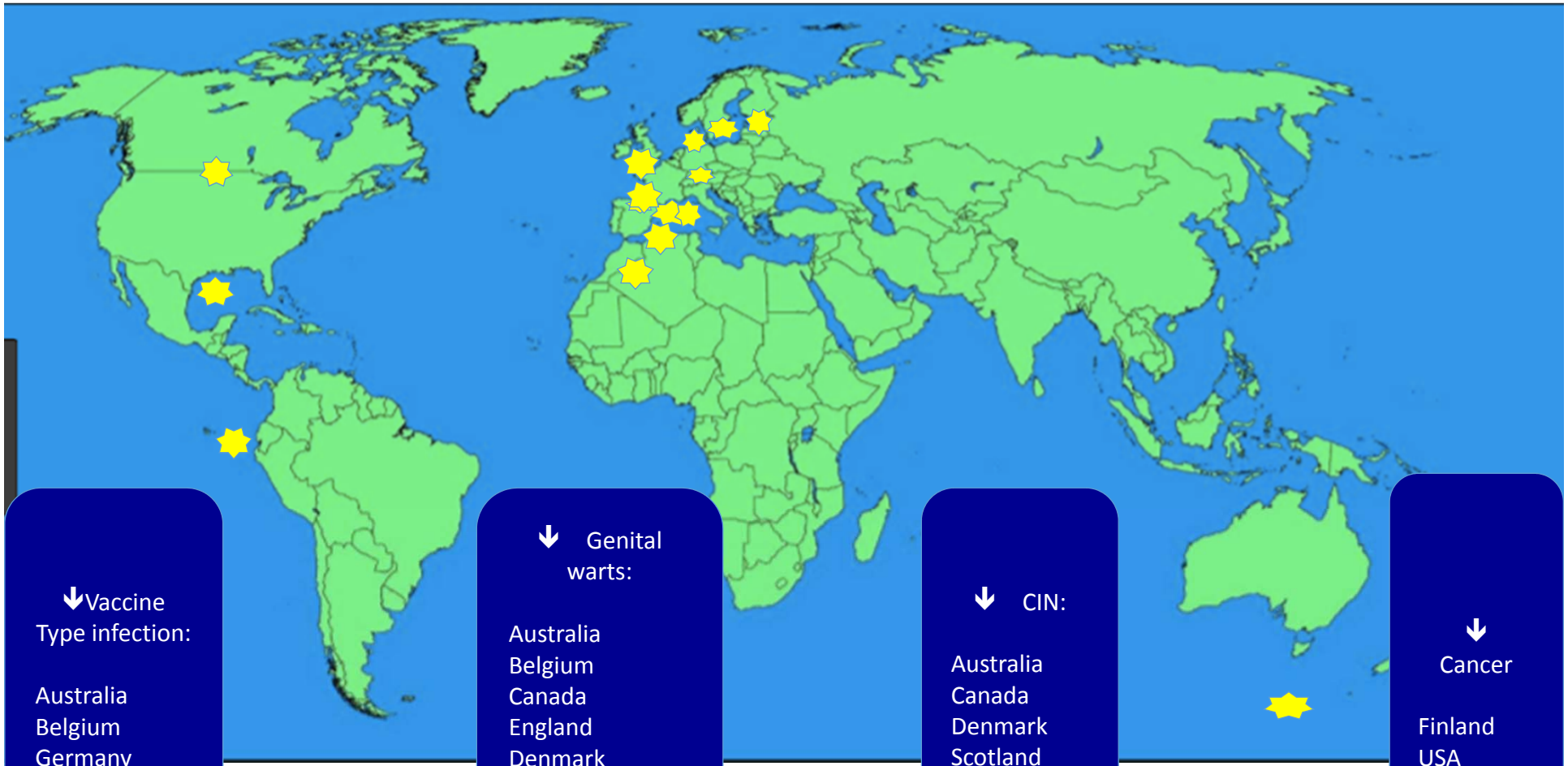
Cervical cancer

HPV rates tumble after routine vaccination

HPV immunisation of 12 and 13-year-old girls has led to 89% decline in disease in Scotland, data reveals

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:

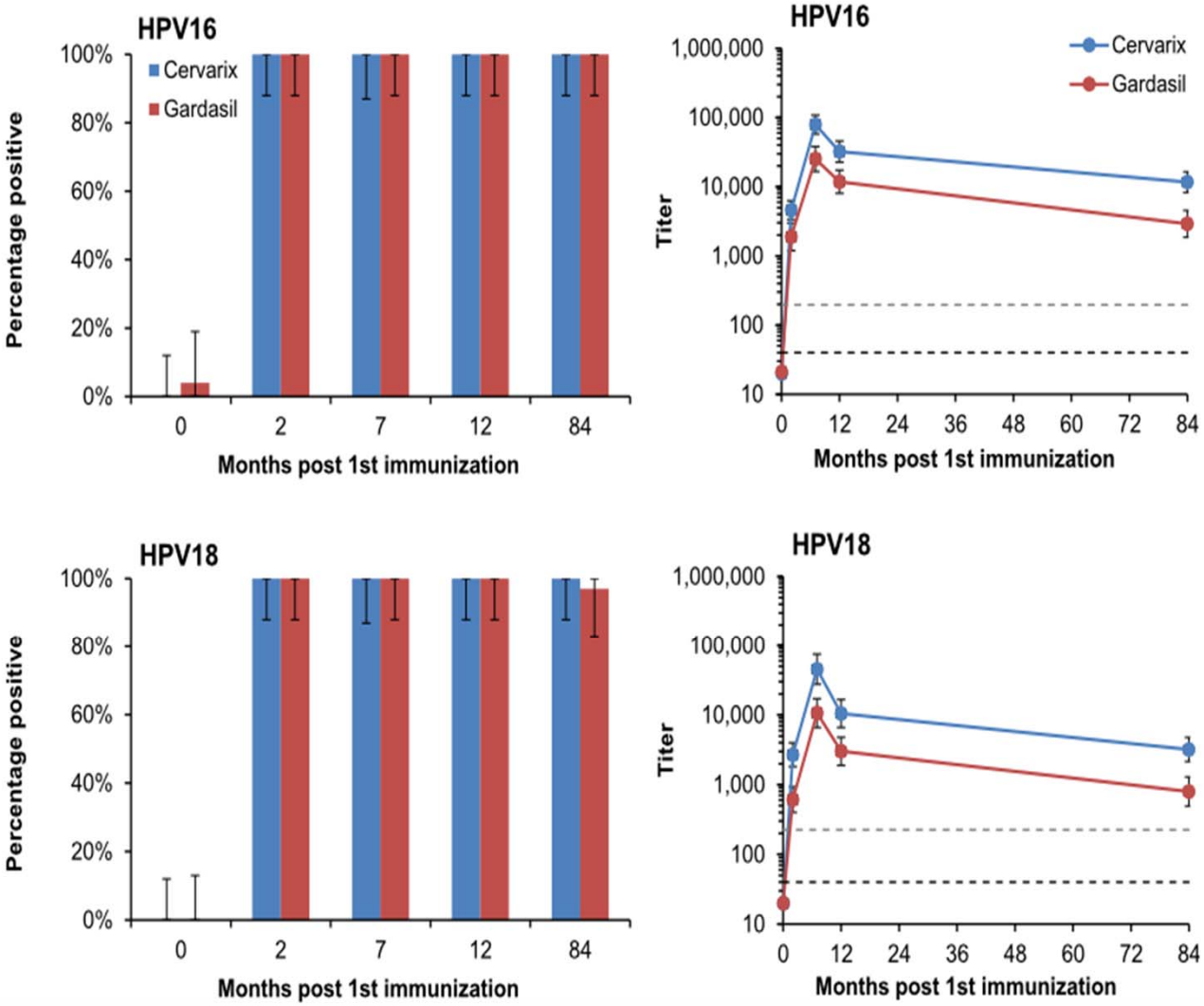
Australia
Canada
Denmark
Scotland
Sweden
USA

↓ Cancer

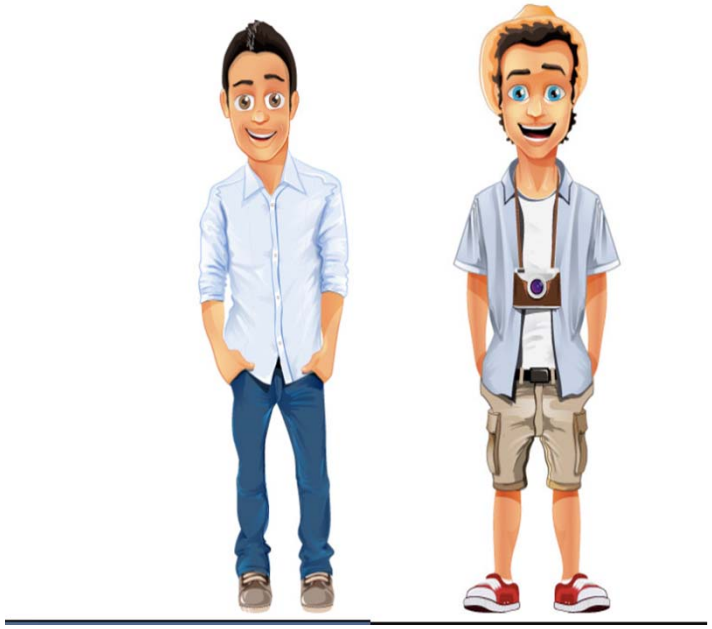
Finland
USA

Durability of antibody response

A. Godi et al./Vaccine 37 (2019) 2455–2462



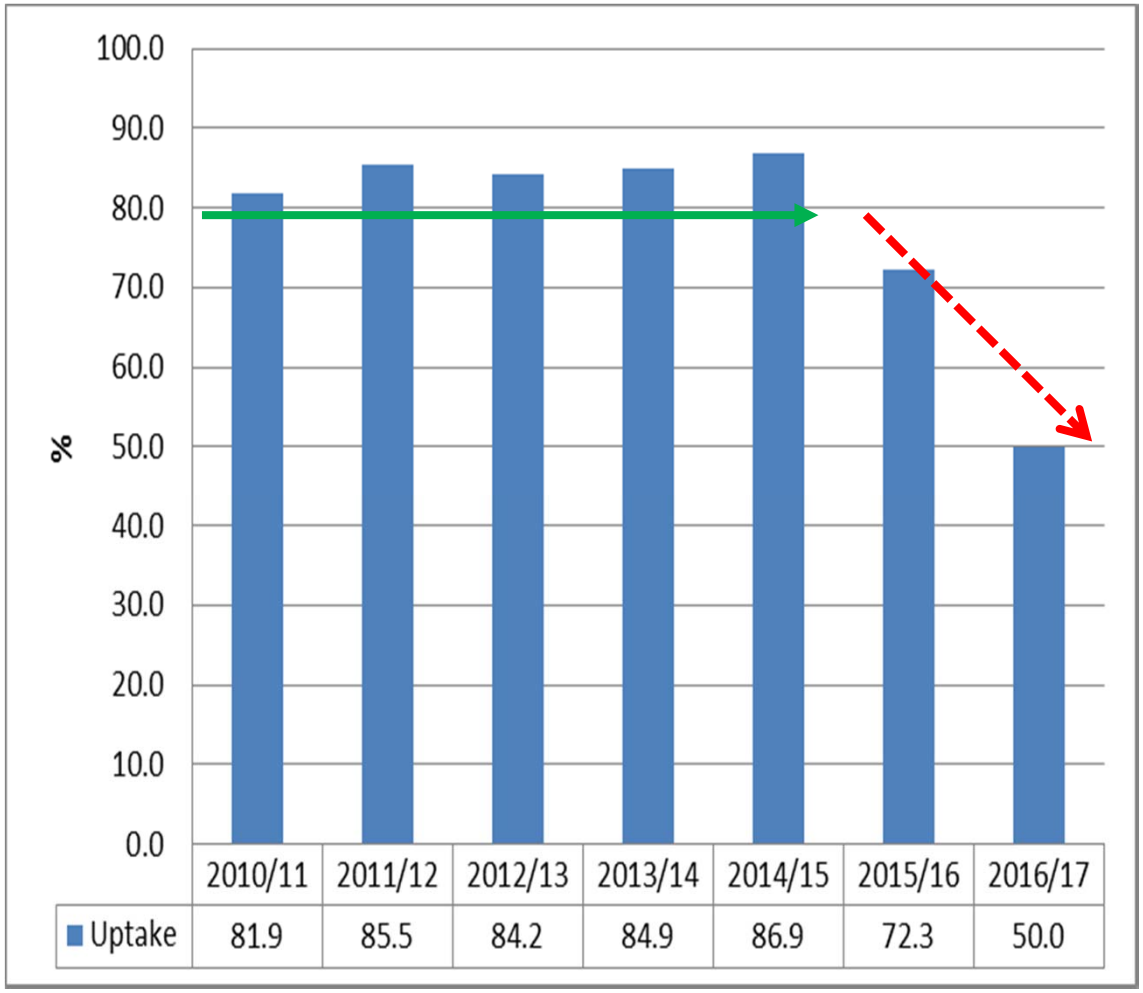
What about the boys?



Direct protection

Increase herd protection

HPV Vaccine Uptake



15,000 girls not vaccinated

www.hpv.ie *slide courtesy Dr. Brenda Corcoran, NIO*

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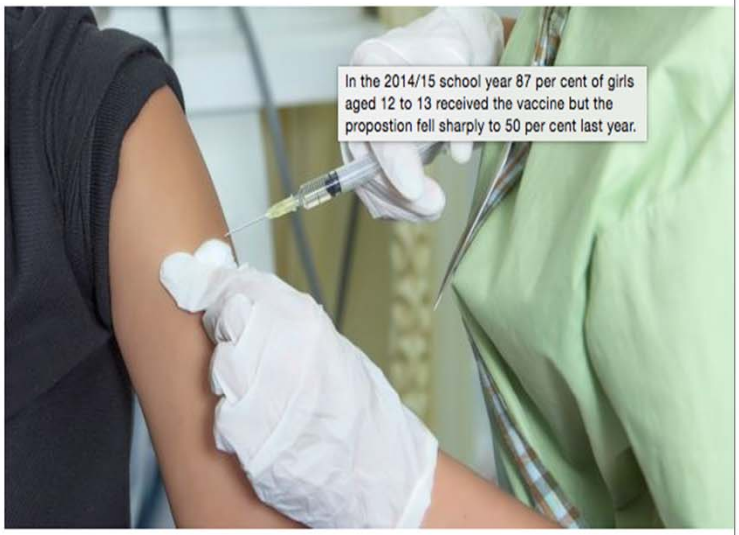
Turning the TIde

HPV vaccine uptake increases following information campaign

HSE say the figures represent success of tackling "misinformation" around vaccine

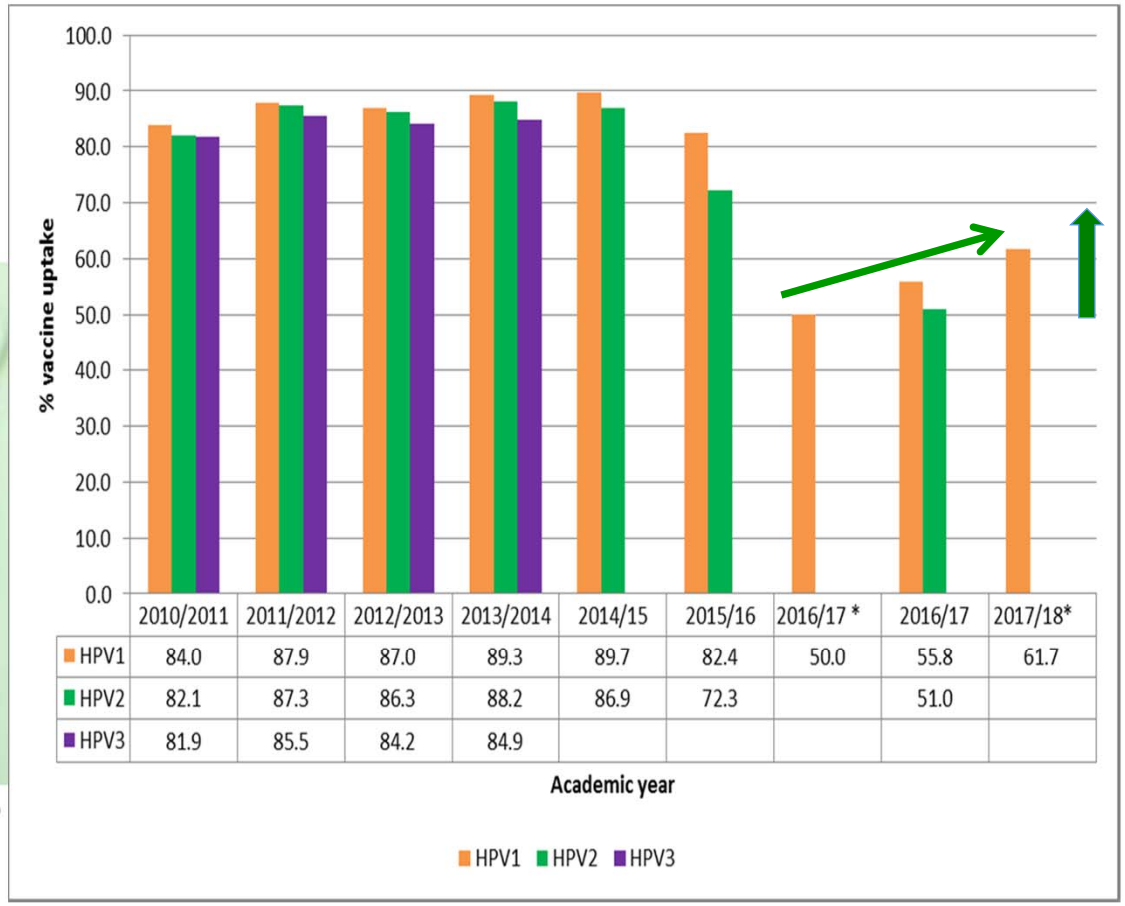
Sun, Dec 3, 2017, 16:32

Jack Power



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

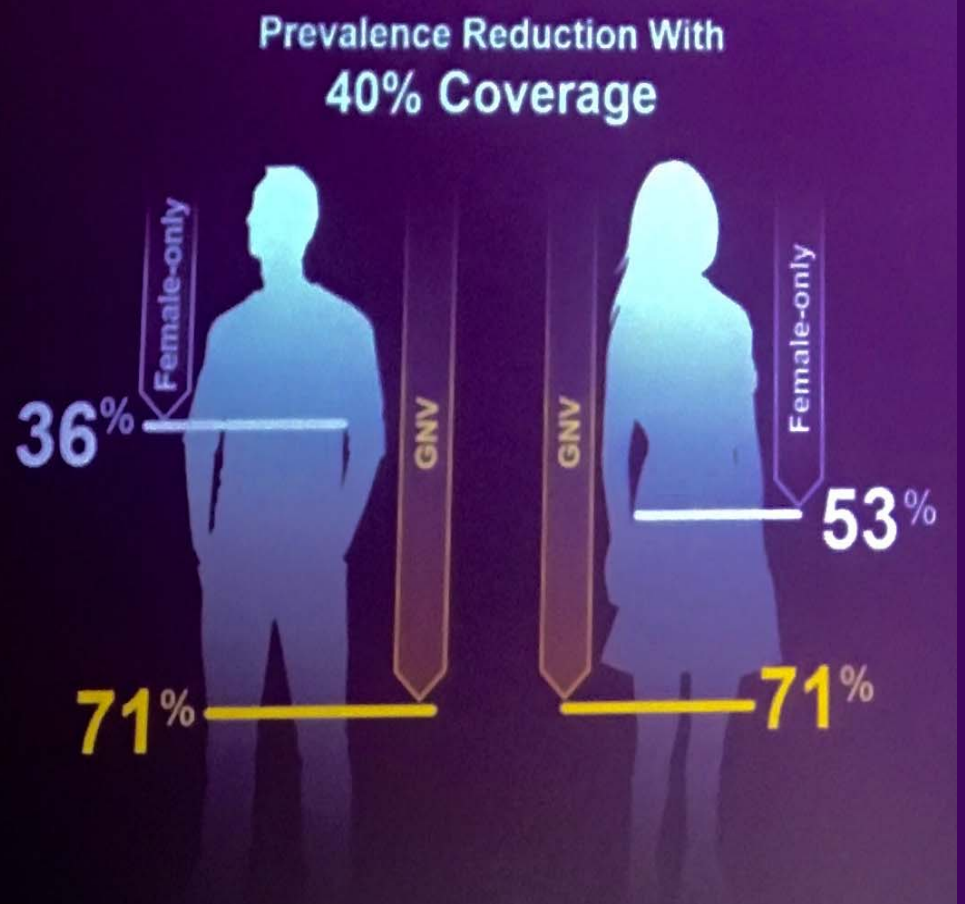
Uptake of the cervical cancer vaccine has increased from 50 to 61 per cent this year following a large drop in the number of young girls availing of it.



	2010/2011	2011/2012	2012/2013	2013/2014	2014/15	2015/16	2016/17 *	2016/17	2017/18*
HPV1	84.0	87.9	87.0	89.3	89.7	82.4	50.0	55.8	61.7
HPV2	82.1	87.3	86.3	88.2	86.9	72.3		51.0	
HPV3	81.9	85.5	84.2	84.9					

Children's Health Ireland

GNV Provides Greater HPV Prevalence Reductions



GNV = gender-neutral vaccination.
Brisson M et al. *Lancet Public Health*. 2016;1:e8–e17.

After 70 yrs with 40% vaccine uptake:-

- Girls only: ↓prevalence by
  - 53% in girls
  - 36% in males.
- **GNV**: ↓prevalence by 71%

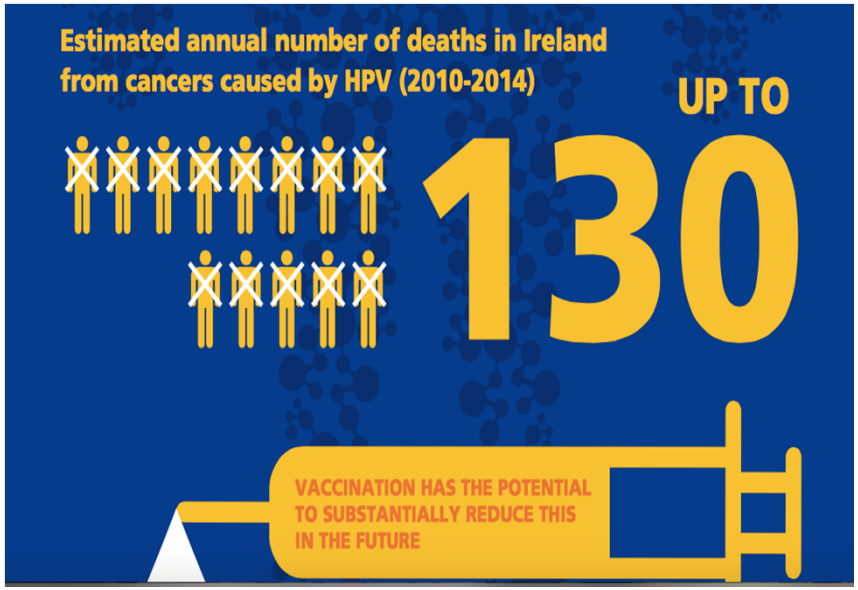
Children's Health Ireland

GNV Provides Greater HPV Prevalence Reductions

GNV = gender-neutral vaccination.
Brisson M et al. *Lancet Public Health*. 2016;1:e8–e17.

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

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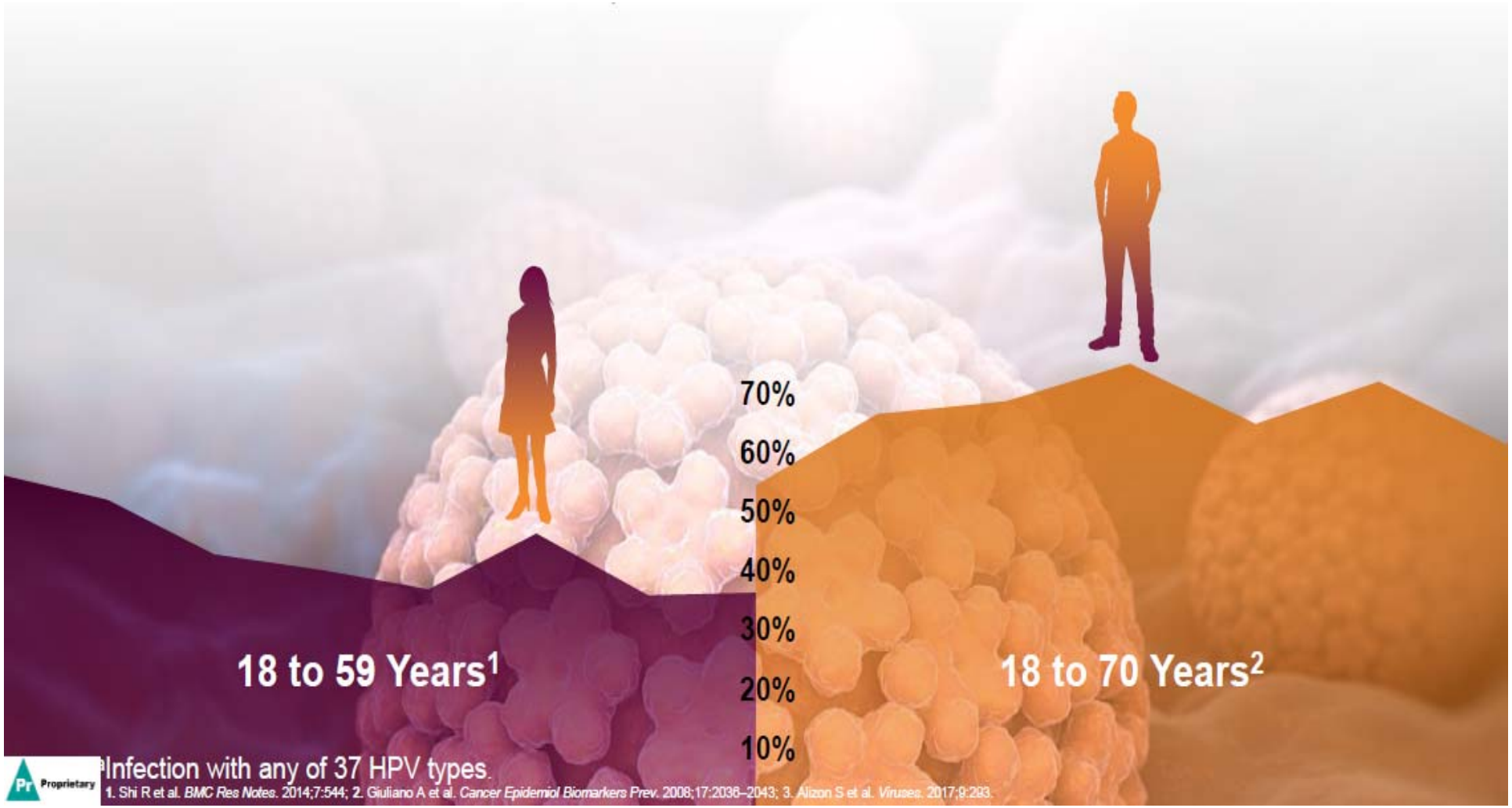
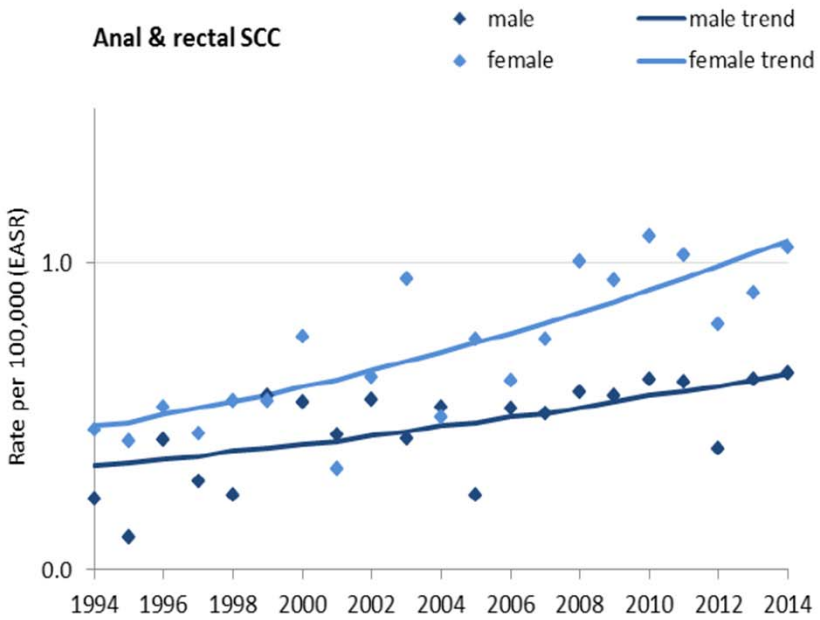
Genital HPV prevalence higher in males than females and does not decrease with age



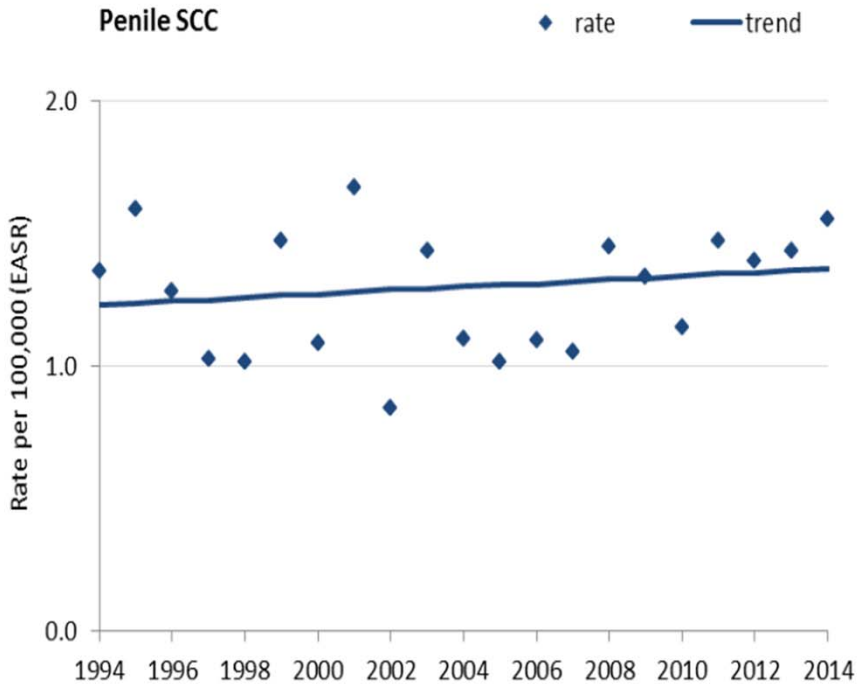
Slide courtesy of MSD

Anal and Penile Cancers 2010-2014



Sex	Period	APC	95% CI	P
Male	1994-2014	**+3.2%**	(+1.1%, +5.5%)	0.005
Female	1994-2014	**+4.3%**	(+2.7%, +5.9%)	<0.001

36 cases/yr
90% HPV related



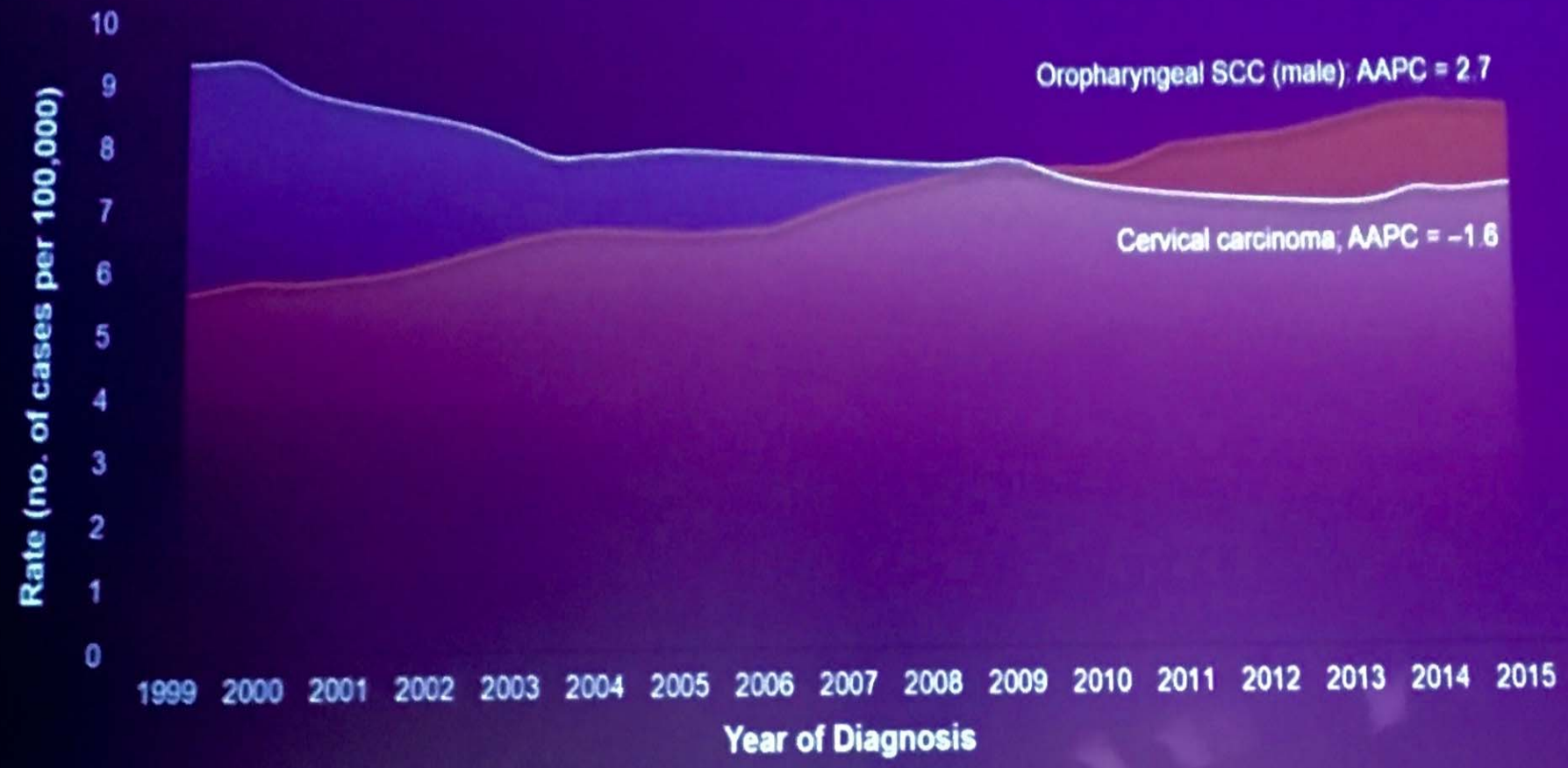
Sex	Period	APC	95% CI	P
Male	1994-2014	+0.5%	(-0.8%, +1.8%)	0.413

32 cases/yr
50% HPV related

National Cancer Registry: Cancer Trends No 33 4th May 2017

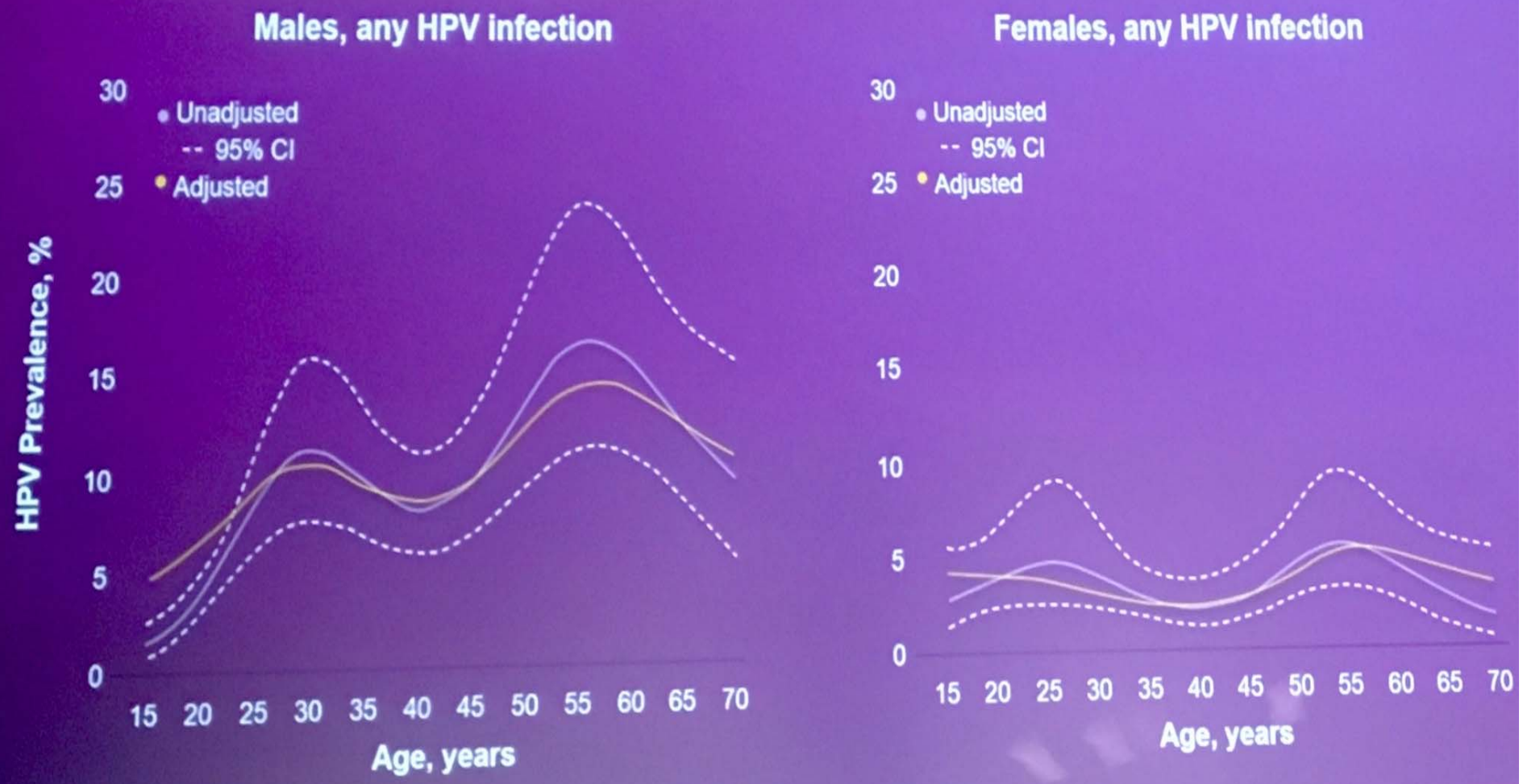
Children's Health Ireland

Rates of Cervical Cancer Are Declining While HPV-Related Oropharyngeal SCC in Males Is Rising (USA)



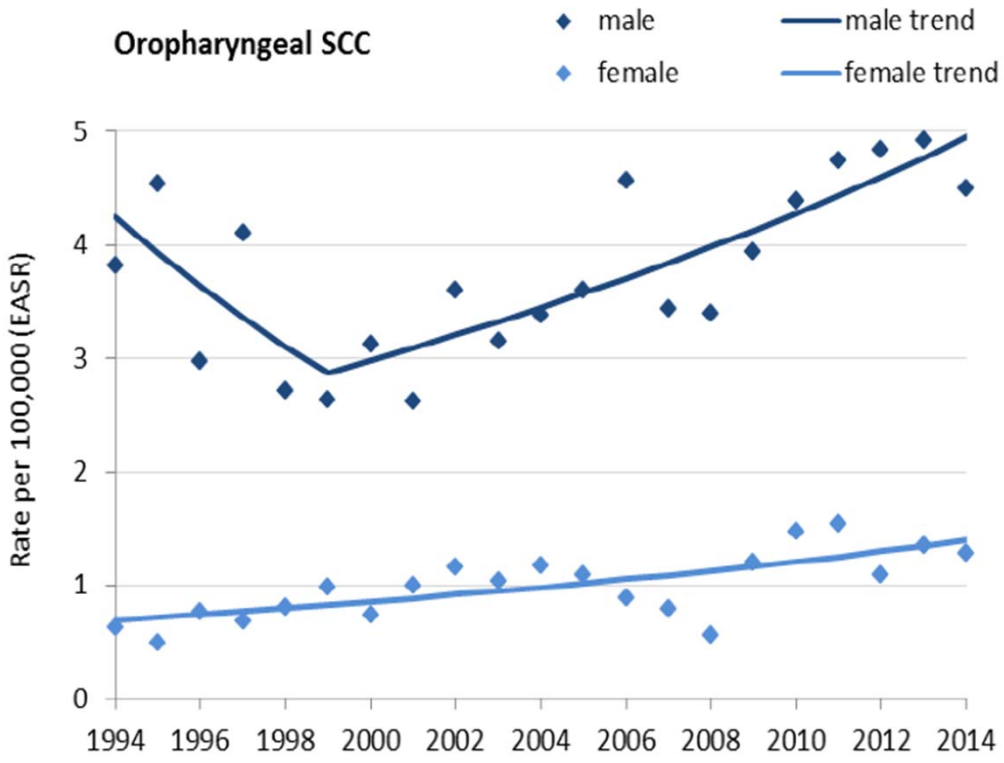
Slide courtesy of MSD

Oral HPV Prevalence Is Significantly Higher in Males Than in Females



Slide courtesy of MSD

Oropharyngeal Cancer: 2010-2014



Sex	*Period*	*APC*	*95% CI*	*P*
Male	1994-1999	-7.5%	(-16.0%, +1.0%)	0.108
	1999-2014	**+3.7%**	(+2.1%, +5.3%)	<0.001
Female	1994-2014	**+3.6%**	(+1.9%, +5.2%)	<0.001

National Cancer Registry: Cancer Trends No 33 4th May 2017

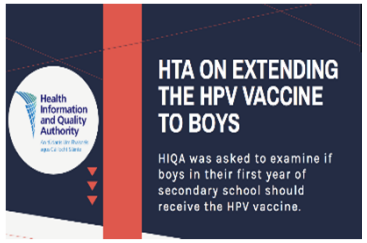
Oropharyngeal cancer (OPC)

Ireland

- 2009 - 2013: 123 cases /yr
- 2014 - 2018: 168 cases/yr

> **37% Increase**

- 33-43%+ are $p16^{INK4a}$ pos



US

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

UK

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

HIQA:HTA of HPV in boys, 4th Dec 2018

Children's Health Ireland

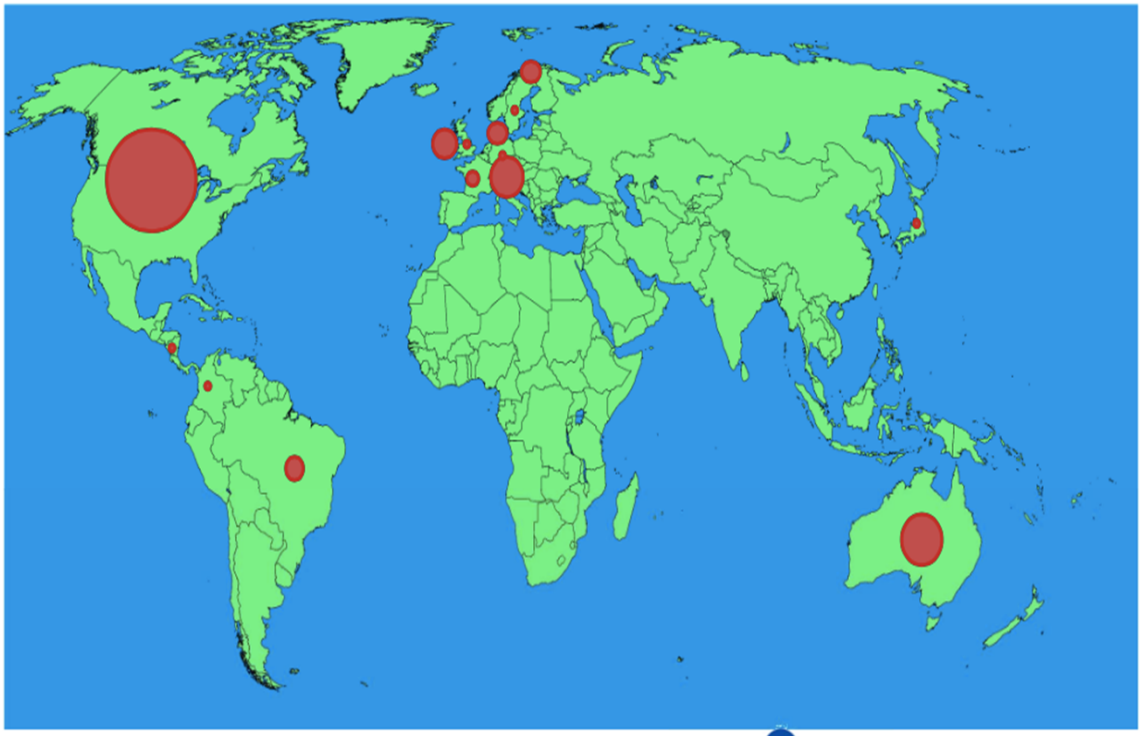
Why Boys?

- ✓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

1. Giuliano A et al. Cancer Epidemiol Biomarkers Prev 2008. 2 De Martel C. Int J Cancer 2017:141,664
3. Giuliano A et al. Papilloma Res2015;1:109.4 Pamani JID 2018;1219. 5 Brotherton Papilloma Res 2016;2:106
6 Elstrom JID 2016;203:199

Is HPV vaccine safe?

HPV Vaccine Safety & Effectiveness 2006 - 2018



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

http//www.who.int/vaccine_safety/vaccrates/en/index.html

Children's Health Ireland

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.

Children's Health Ireland

What can you do:

Be Prepared

Children's Health Ireland

Sources and Perceived Credibility of Vaccine-Safety Information for Parents

AUTHORS: Gary L. Freed, MD, MPH,[a,b,c] Sarah J. Clark, MPH,[a,b] Amy T. Butchart, MPH,[a,b] Dianne C. Singer, MPH,[a,b] and Matthew M. Davis, MD, MAPP[a,b,d,e]

You are so important

TABLE 2 Parental Report of Levels of Trust of Certain People for Vaccine-Safety Information

	A Lot, %	Some, %	Not at All, %
My child(ren)'s doctor	76	22	2
Other health care providers	26	70	4
Government vaccine experts/officials	23	61	16
Family and friends	15	67	18
Parents who believe their child was harmed by a vaccine	8	65	27
Celebrities	2	24	74

www.pediatrics.org/cgi/doi/10.1542/peds.2010-1722P

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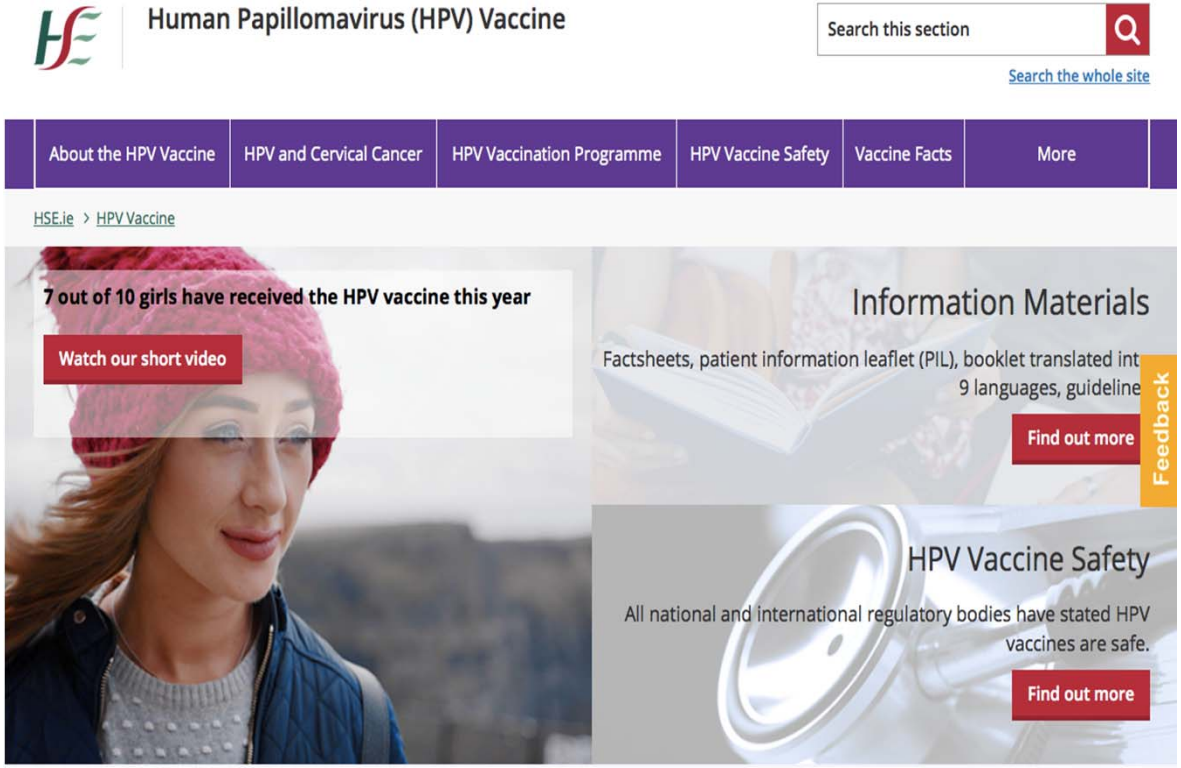
- Be informed
- Reliable information sources



www.hpv.ie

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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

Children's Health Ireland

Together we can…….

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HOW WILL **BUDGET 2018** AFFECT YOU?

Tags # CANCER # CERVICAL CANCER # FACTCHECK # GARDASIL # HPV

FactCheck: No, the reported side effects of the HPV vaccine do NOT outweigh the proven benefits

Following controversy over Super Junior Minister Finian McGrath's comments about the vaccine, TheJournal.ie republishes this Factcheck.

Sep 6th 2017, 5:15 PM 106,485 Views 263 Comme

FACTCHECK
Sifting for truth - so you don't have to

Donal Brennan
@donalb5
Following

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

7:05 PM - 13 Apr 2018

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More than 80% of girls treated over HPV vaccine had only 'transient' effects

Majority of 650 girls requiring treatment were for symptoms like fainting and nausea

about 16 hours ago

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IRISH MEDICAL TIMES

22 September 2017 | Irish Medical Times

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

Advisory Committee, Clinical Professor of Paediatrics, Consultant Paediatrician and Infectious Diseases Specialist at Our Lady's Children's Hospital and the Children's University Hospital, Temple Street, said "More than 230,000 girls in Ireland have safely received the HPV vaccine, along with 227 million people worldwide in countries like the United States, Canada, Australia and New Zealand. Not one of these people anywhere in the world has been medically proven to have had a long-term side effect from

ways a parent can protect their child's health. Ireland's uptake rates for many vaccine in the Primary Childhood Immunisatio Programme are close to the WHO uptake targ of 95 per cent.

Our childhood immunisation programme have had a huge impact in improving the healt of the Irish people.

Diseases that used to be common in thi country and around the world, includin polio, measles, diphtheria, whooping cough

HPV vaccine campaigner Laura Brennan dies aged 26

Updated / Wednesday, 20 Mar 2019 **18:13**

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

Children's Health Ireland