CERVICAL SCREENING PROGRAMME AND COLPOSCOPY UPDATE

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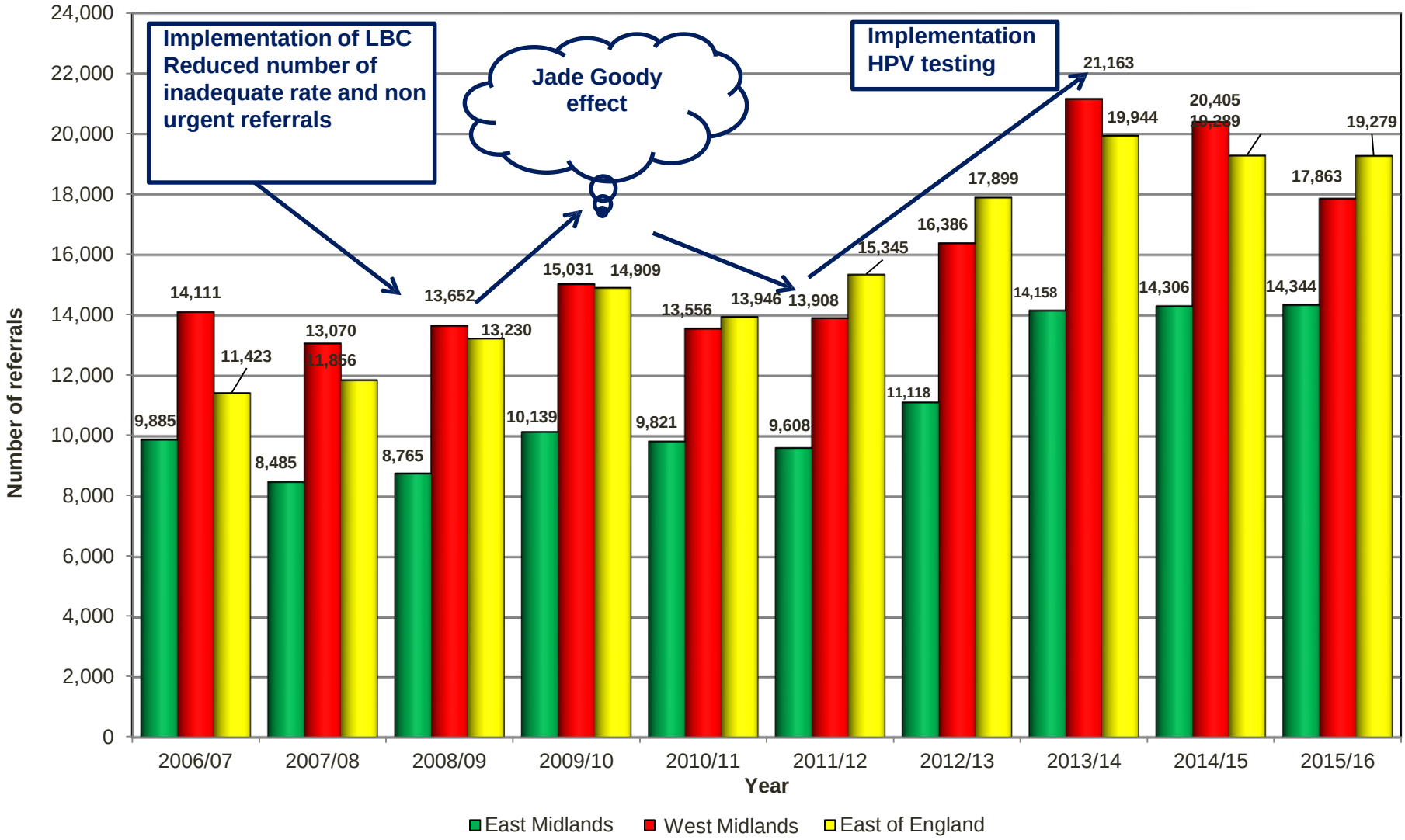
CERVICAL SCREENING

"cervical screening begins with the identification of eligible women and includes sample taking, cytology, colposcopy and histopathology. It ends with the diagnosis of cancer, completion of the screening programme at 65 years of age, or the ending of a surveillance period, whichever is later"

OUTLINE

- Not an overview of cervical screening and colposcopy nor a review of recent colposcopy guidelines!
- Whistle-stop tour of four interesting areas from recent colposcopy update conference
  - Numbers and trends in our Region - for QA purposes East and West Midlands and East of England grouped together as 'Midlands and The East'
  - Early outcomes of the HPV vaccination programme
  - HPV primary screening
  - Cervical Treatment and risk of premature delivery

Referrals – trend



Colposcopy referrals- Midlands and East

- 51,486 women [14,344 East Midlands (27.9%), 17,863 West Midlands (34.7%), 19,279 East of England (37.4%)] were referred to colposcopy in 2015/16
- 4.7% decrease in referrals from 2014/15 (-2,514 referrals)
  - East Midlands 0.3% increase
  - West Midlands 12.5% decrease
  - East of England 0.05% decrease
- Implementation of HPV testing year 4
  - Borderline referrals decrease by 2.2% (-212 referrals)

Treatment at first visit

- Remains wide variation in treatment approaches across the Midlands and East
- Diagnostic biopsy rate at first visit for high grade referrals:
  - Decrease in the East Midlands from 28.9% to 26.6%
  - Increase in the West Midlands from 21.7% to 21.8%
  - Increase in the East of England from 29.9% to 31.1%
- Treatment at First attendance for ‘inadequate’ referrals
  - In total there were 4 cases (3 in the East Midlands, 1 in East of England) where excisional treatment was carried out at first visit on an inadequate referrals
- First attendance for ‘high grade’ referrals
  - 60.0% of women with a high grade referral underwent excisional treatment at their first visit across the Midlands and East (East Midlands 61.3%, West Midlands 59.8%, East of England 60.2%)
  - Low excisional rates need to be audited
- Conservative management of CIN2- need individualized plan

HPV VACCINATION- EARLY OUTCOMES

Background

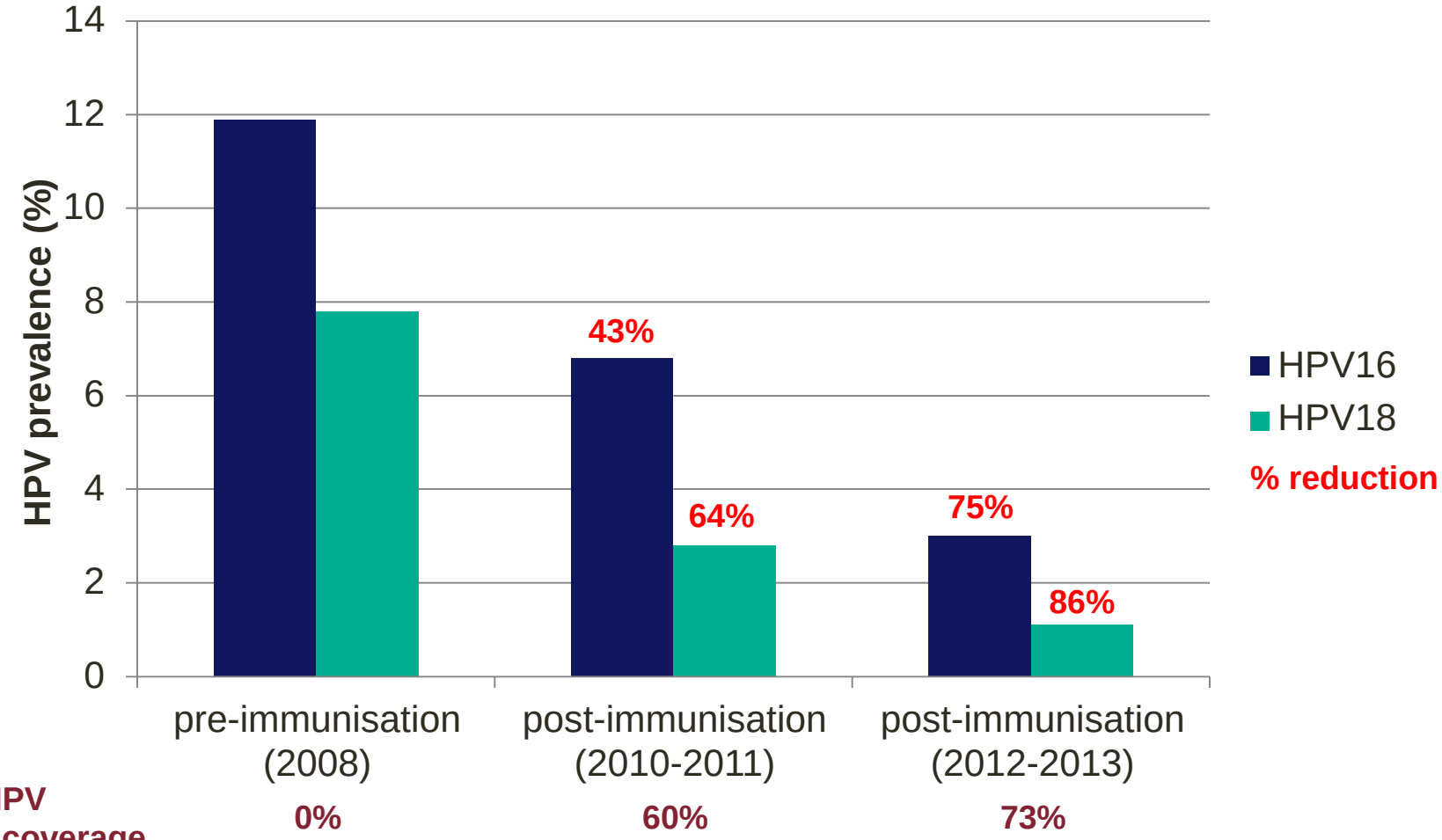
- National HPV Immunisation Programme introduced in September 2008
- The bivalent vaccine (Cervarix) was used initially
  - HPV types 16/18

- From September 2012, the quadrivalent vaccine (Gardasil) has been used in the routine programme
  - HPV types 6/11/16/18

- Vaccine coverage has been high
  - >80% for routine vaccination of 12-13 year olds (~55% for catch-up years)
- Initial impact has been demonstrated with a reduction in the prevalence of HPV infection of the types covered by the vaccine, among 16-24 year old women[1]

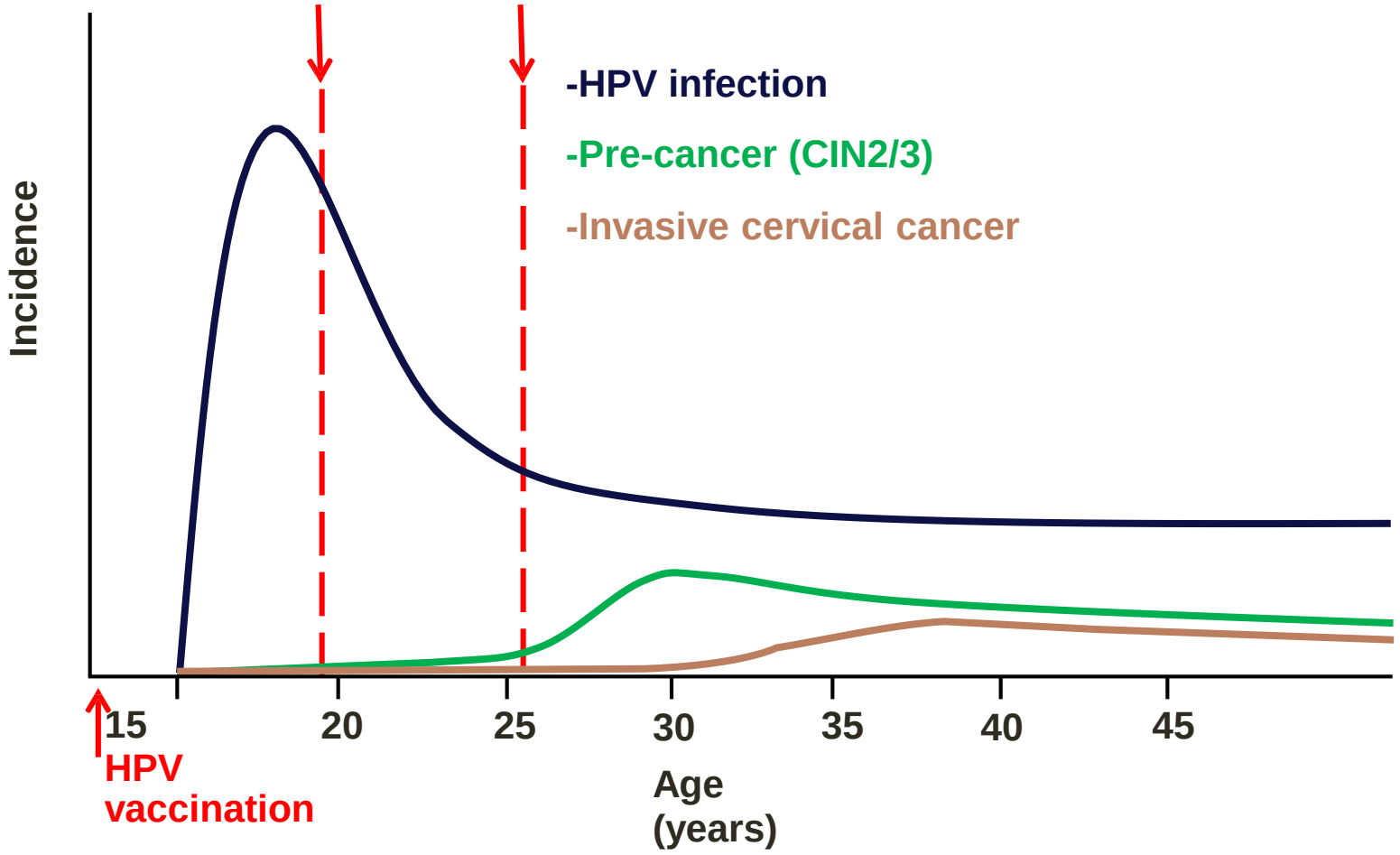
[1]Mesher et al, BMJ Open, 2016

HPV16/18 prevalence among 16 -18 year old females



[1]Mesher et al, BMJ Open, 2016

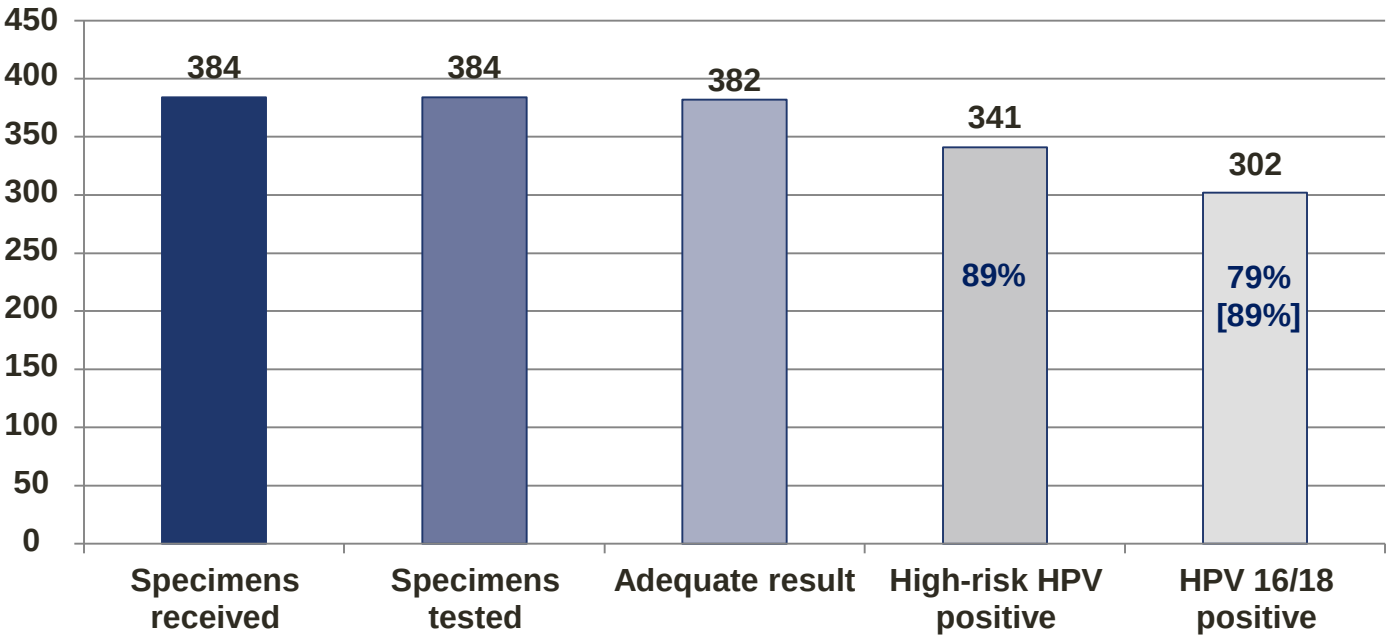
Cervical disease by age



Adapted from Lowry & Schiller, J Clin Invest,116:1167 (2006)

Results: HPV testing

- Results from HPV testing of cases diagnosed in 2013 (collected in 2015):



6 women diagnosed with cervical cancer in 2013 were eligible to receive the HPV vaccine (all of which as part of catch-up). Collection of vaccination history data for these 6 women is pending

Results: HPV type-specific

- Restricted to high-risk HPV positive specimens:

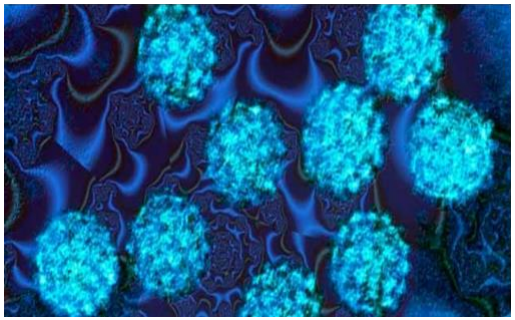
HPV type	Number	% of High-risk HPV positive samples
Multiple infections	**30**	**8.8**
16 + 1 other HR HPV	24	7.0
18 + 1 other HR HPV	2	0.6
33 + 1 other HR HPV	2	0.6
31 + 1 other HR HPV	1	0.3
45 + 1 other HR HPV	1	0.3
Single infection	**311**	**91.2**
16	215	63.0
18	61	17.9
45	15	4.4
33	11	3.2
31	5	1.5
35	1	0.3
39	1	0.3
58	1	0.3
59	1	0.3
Total	***341***	

This is consistent with known HPV distribution in cervical cancers pre-vaccination

Looking ahead

- **Collection of cancer biopsy specimens and vaccination status will continue**
  - **Collection of 2014 diagnoses started in June 2016**
- **In future years, we expect to see:**
  - **Reductions in the incidence of cervical cancer**
  - **Relative reductions in the proportion of cervical cancers positive for HPV16/18**
  - **More women eligible for HPV vaccination among the cervical cancer diagnoses**
- **9valent vaccine recently licenced in Europe (Includes additional 5 high-risk HPV types: 31,33,45,52,58)**

HPV PRIMARY SCREENING



HPV Primary Screening

2013: HPV Primary screening pilot was recommended by the UK NSC

2016: HPV Primary screening recommended by UK NSC

Why?

• the HPV vaccination offered to girls aged 12 to 13 strengthens the rationale for primary HPV screening. The vaccination will offer prevention of HPV and result in a falling number of women who remain at risk of catching HPV and developing cervical cancer

• a primary test for HPV will save more lives by determining a woman's risk earlier. Work to assess extending the screening interval with HPV screening is ongoing. This will follow once confirmatory pilot data and other international evidence is reviewed by the UK NSC

• HPV testing means that if the woman tested does not have high risk HPV, her chances of developing a cancer within five years are very small

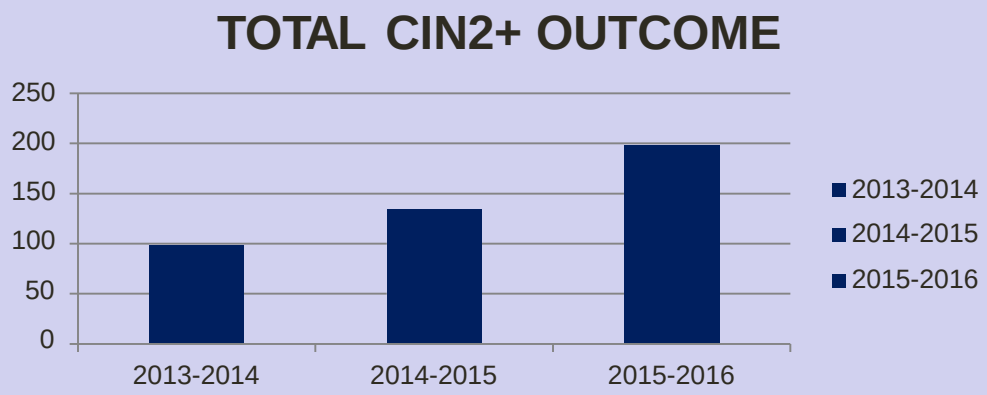
Persistent HPV+ve / Cytology negative

1st screen	HPV +ve Neg cyto R12
2nd @ 12months	HPV +ve Neg cyto R12
3rd @ 24months	HPV +ve Neg cyto **Refer**

Roche Cobas: Genotype 16/18/0 is recorded. (0=other)

Results

YEAR	TOTAL HPV 1°	TOTAL HPVP	% HPVP RATE	HPVP & REFERRED	HPVP & ABNORMAL CYTOLOGY (REFERRED)	% HPVP REFERRAL RATE	% OF HPVP WITH ABNORMAL CYTOLOGY (REFERRED)	HPVP & CYTOLOGY NEGATIVE = R12	% HPVP & CYTOLOGY NEGATIVE = R12	HPVP & CYTOLOGY NEGATIVE (REFERRED)
2013-2014	9078	1046	11.52	288	273	3.01	26.10	749	71.61	15
2014-2015	10512	1414	13.45	391	372	3.54	26.31	1011	71.50	19
2015-2016	10966	1610	14.68	599	469	4.28	29.13	997	61.93	130



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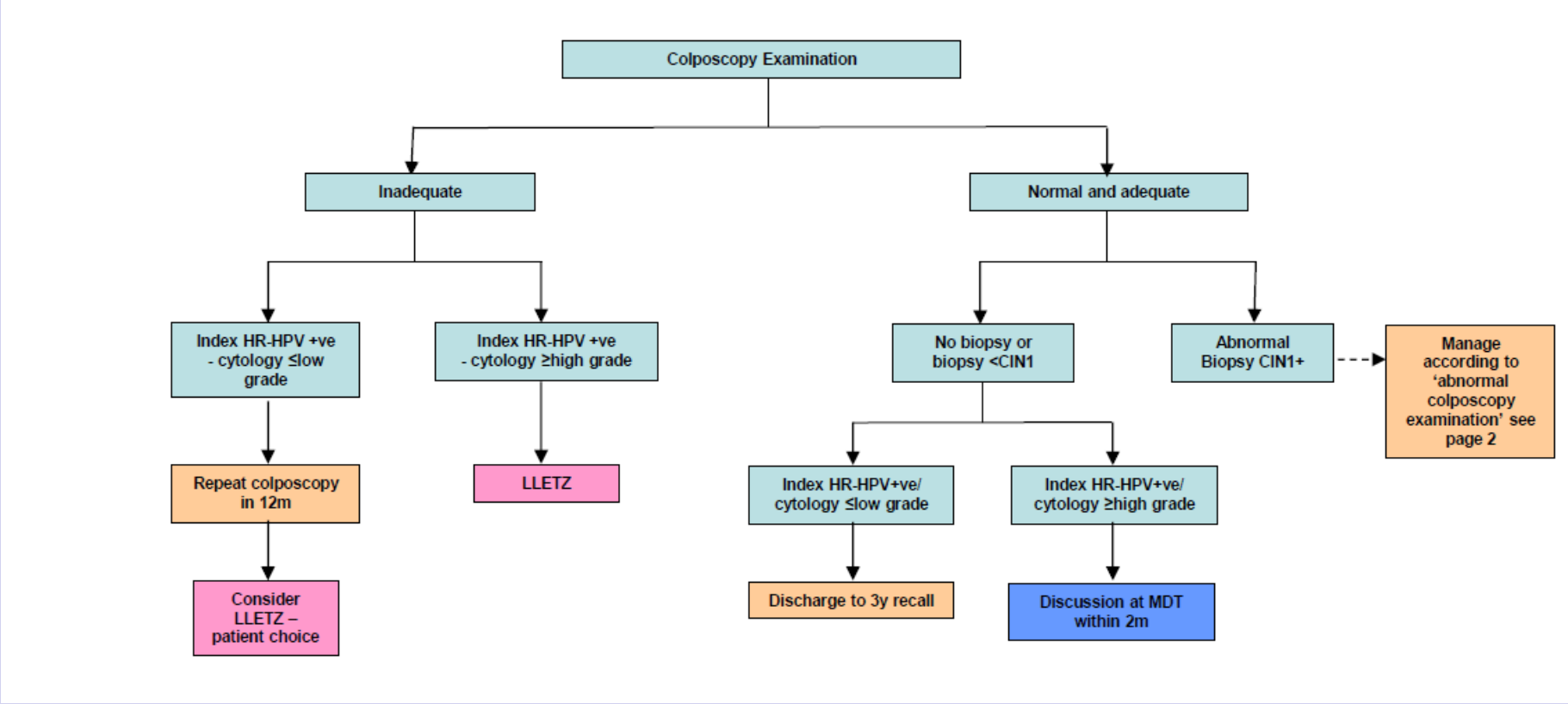
3rd repeat : 130 persistent Neg Cytology HPV+ve cases to colposcopy

7 cases persistent HR HPV+ve with CIN2+ histology

Colposcopy Patient Management Algorithm

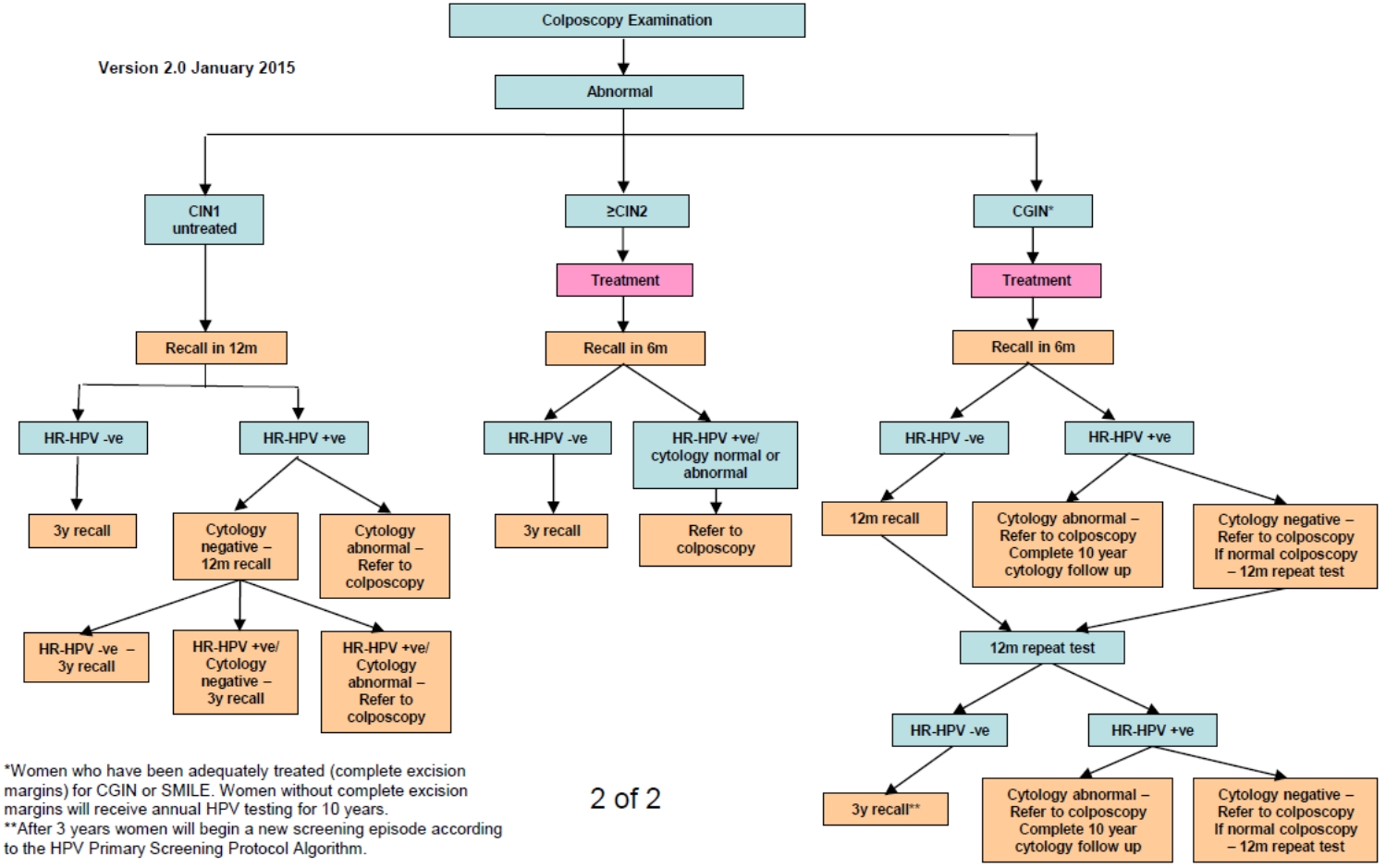


Public Health England

NHS Cancer Screening Programmes

HPV Primary Screening Pilot
Colposcopy Management Recommendations Algorithm

Version 2.0 January 2015



*Women who have been adequately treated (complete excision margins) for CGIN or SMILE. Women without complete excision margins will receive annual HPV testing for 10 years.
**After 3 years women will begin a new screening episode according to the HPV Primary Screening Protocol Algorithm.

Is HPVP acceptable to women?

- Feedback from sample takers and clinicians is consultations take longer

- Patients are particularly anxious when attending colp for persistent HPV+ve/ cytology negative referral.
  -If colp examination appearances normal or biopsy taken and no CIN then discharge

HPV Primary screening is not a perfect test

Women with cervical cancer can test HPV-ve

HPV Primary screening will not identify non HPV related cancers

It is important our sample takers continue to refer women with clinical signs & symptoms for investigation

Queen Mary University of London
Barts and The London School of Medicine and Dentistry
Wolfson Institute of Preventive Medicine

Risk of preterm delivery after excisional treatment for CIN in England (PaCT study)

Castanon A, Landy R, Brocklehurst P, Evans H, Singh N, Walker P, Peebles D, Patnick J, Sasieni P for the PaCT Study Group

PaCT study

North Durham County and Darlington

The James Cook

St James's University Hospital

Royal Preston Hospital

Royal Hallamshire Hospital

Wirral University Hospital

Worcestershire Acute

Barts & London

Hammersmith

St Mary's

Whipps Cross

Royal Devon and Exeter

Royal Cornwall

Results

Case control

- Full colposcopy details for 87% (2284/2626) of selected women
- 80% (1598) of births were after colposcopy
  - 30% (484) diagnostic punch only
  - 63% (1008) single treatment
  - 7% (106) multiple treatment
- Depth available for 87% (974) of treatments

Results by depth
in births post-colposcopy

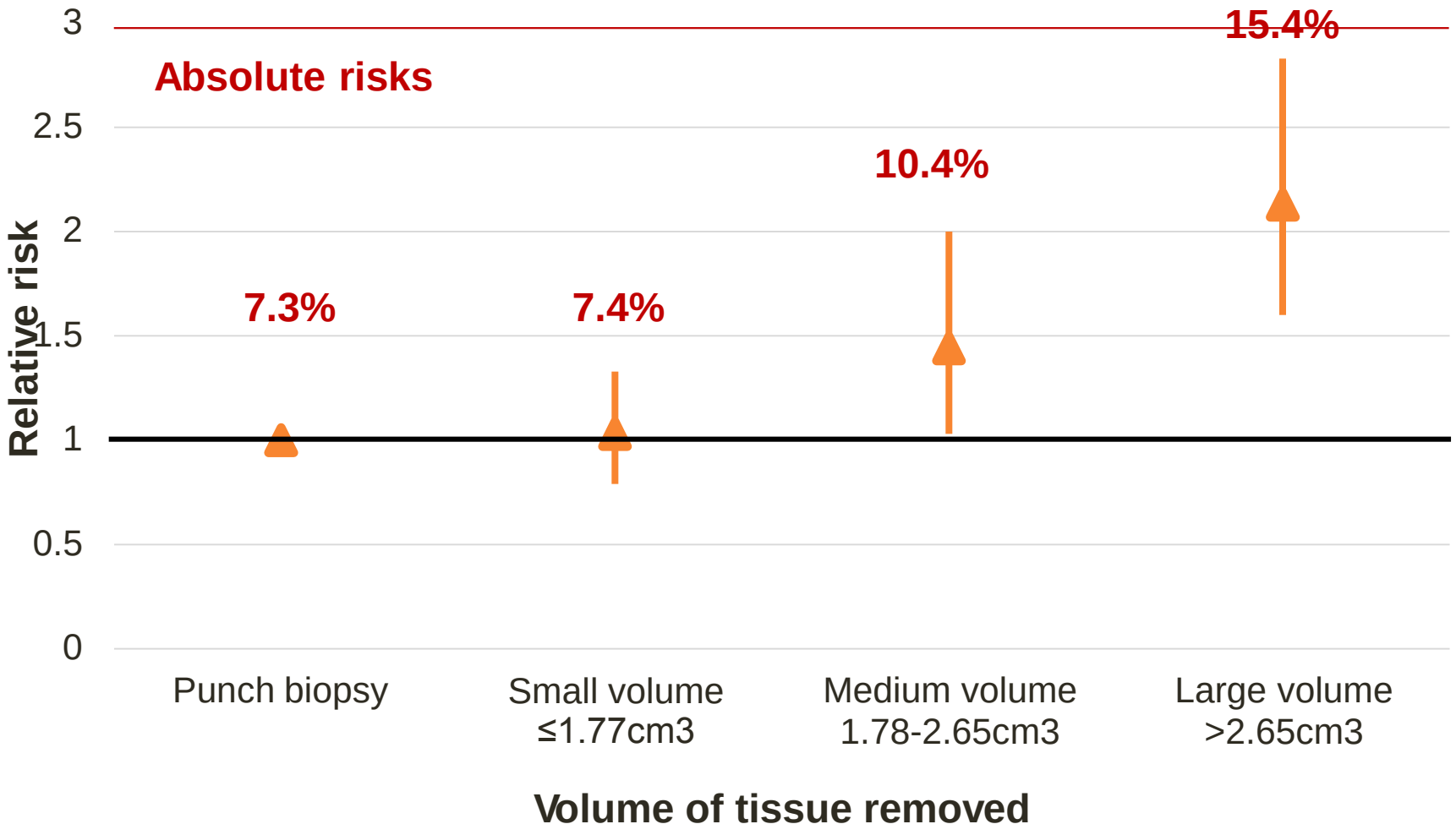
Procedure at colposcopy	Preterm births (N= 768)	RR* (95% CI)	**Absolute risk**
Punch biopsy only	210	0.96 (0.73,1.27)	**7.2%**
1-9mm deep (Small)	173	1 (reference)	**7.5%**
10-14mm deep (Medium)	182	1.28 (0.98, 1.68)	**9.6%**
15-19mm deep(Large)	80	2.04 (1.41, 2.96)	**15.3%**
20+mm deep (Very Large)	54	2.40 (1.53, 3.75)	**18.0%**
Unknown depth	69	1.24 (0.86, 1.79)	**9.3 %**

* The relative and absolute risks are adjusted by study site, parity, deprivation and maternal age at delivery

Castanon et al, BMJ (2014)

Results by volume

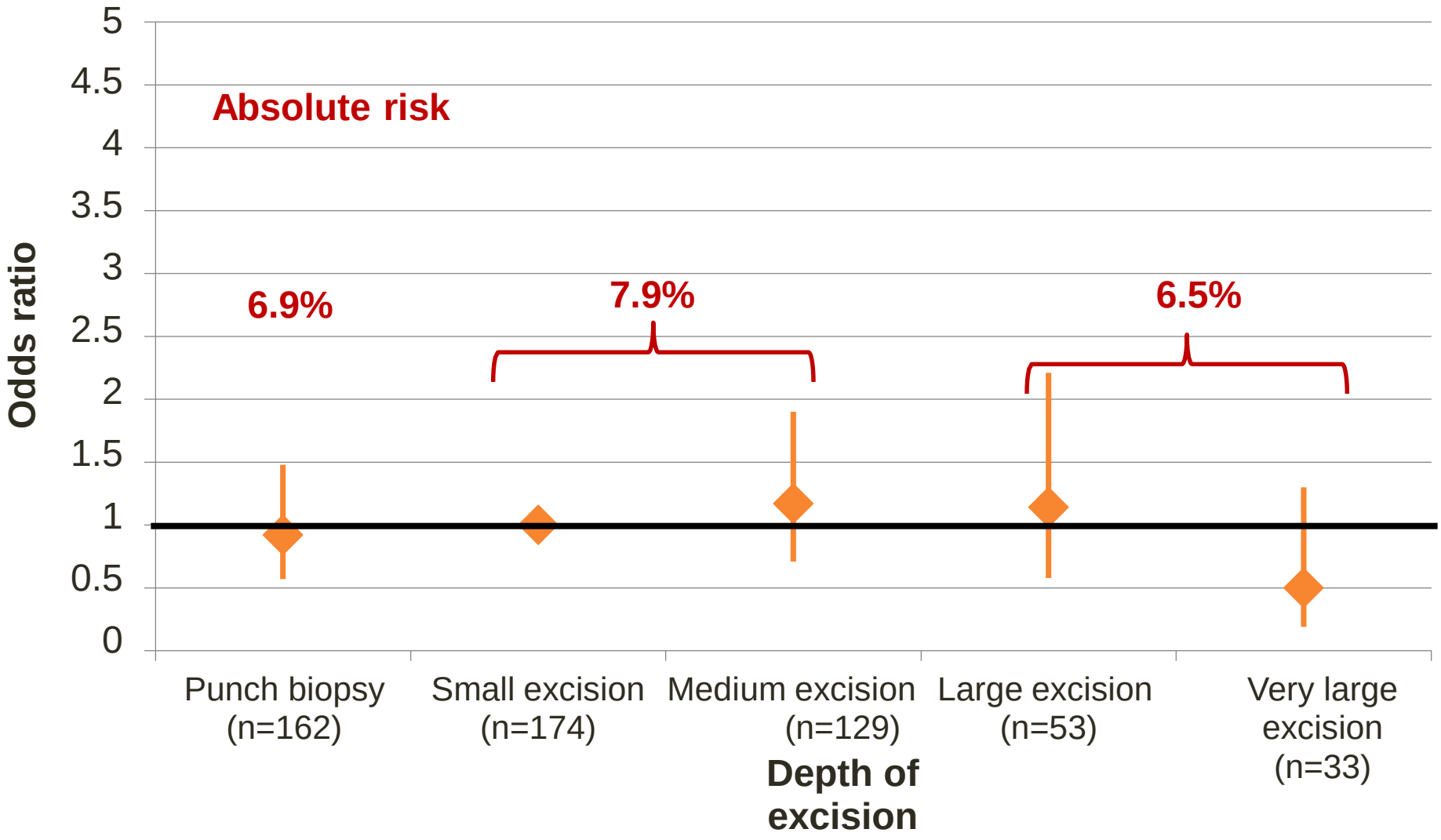
in births post colposcopy



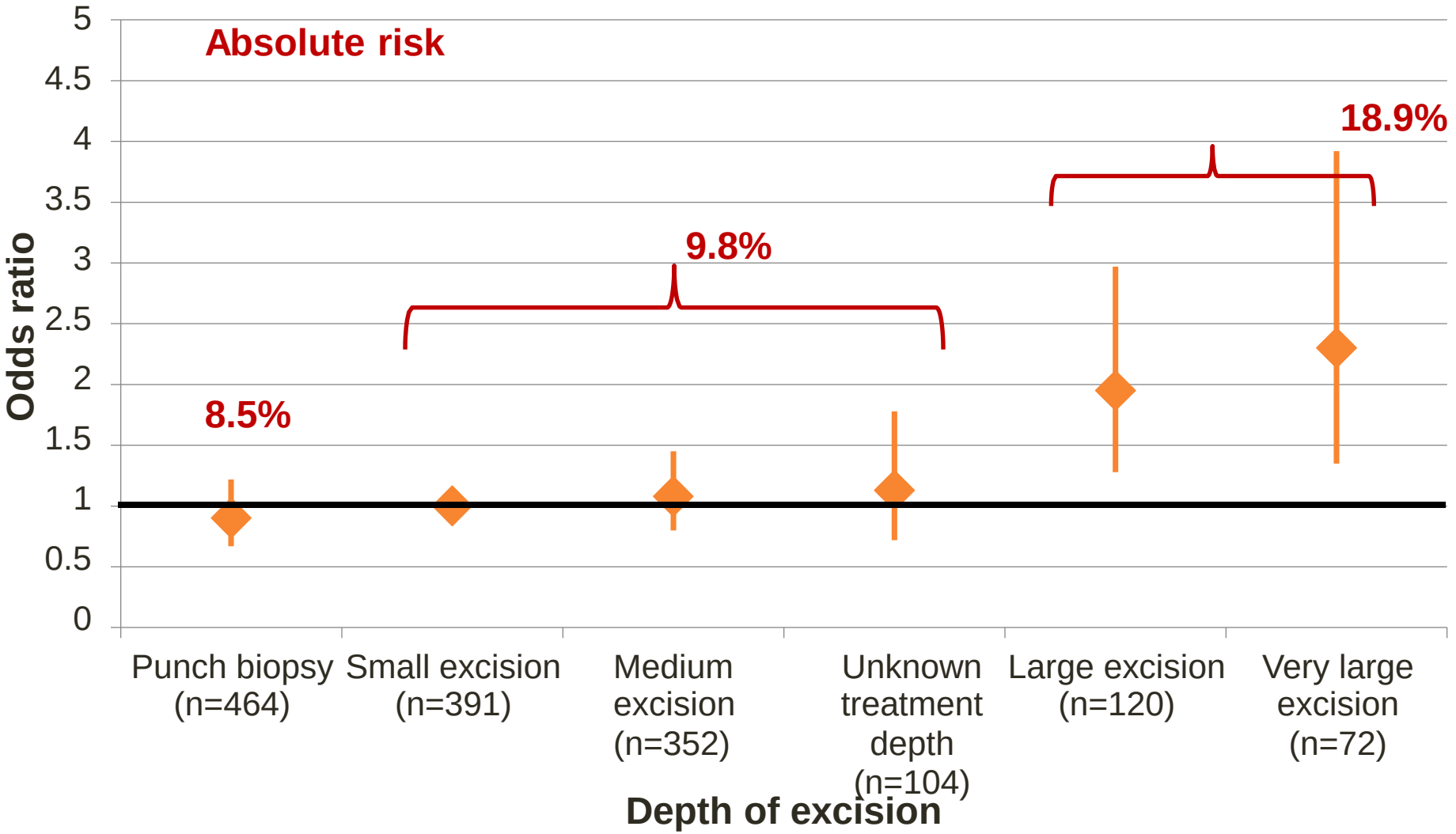
Temporality

- Is the risk of preterm birth only increased with the first birth that occurs after treatment?

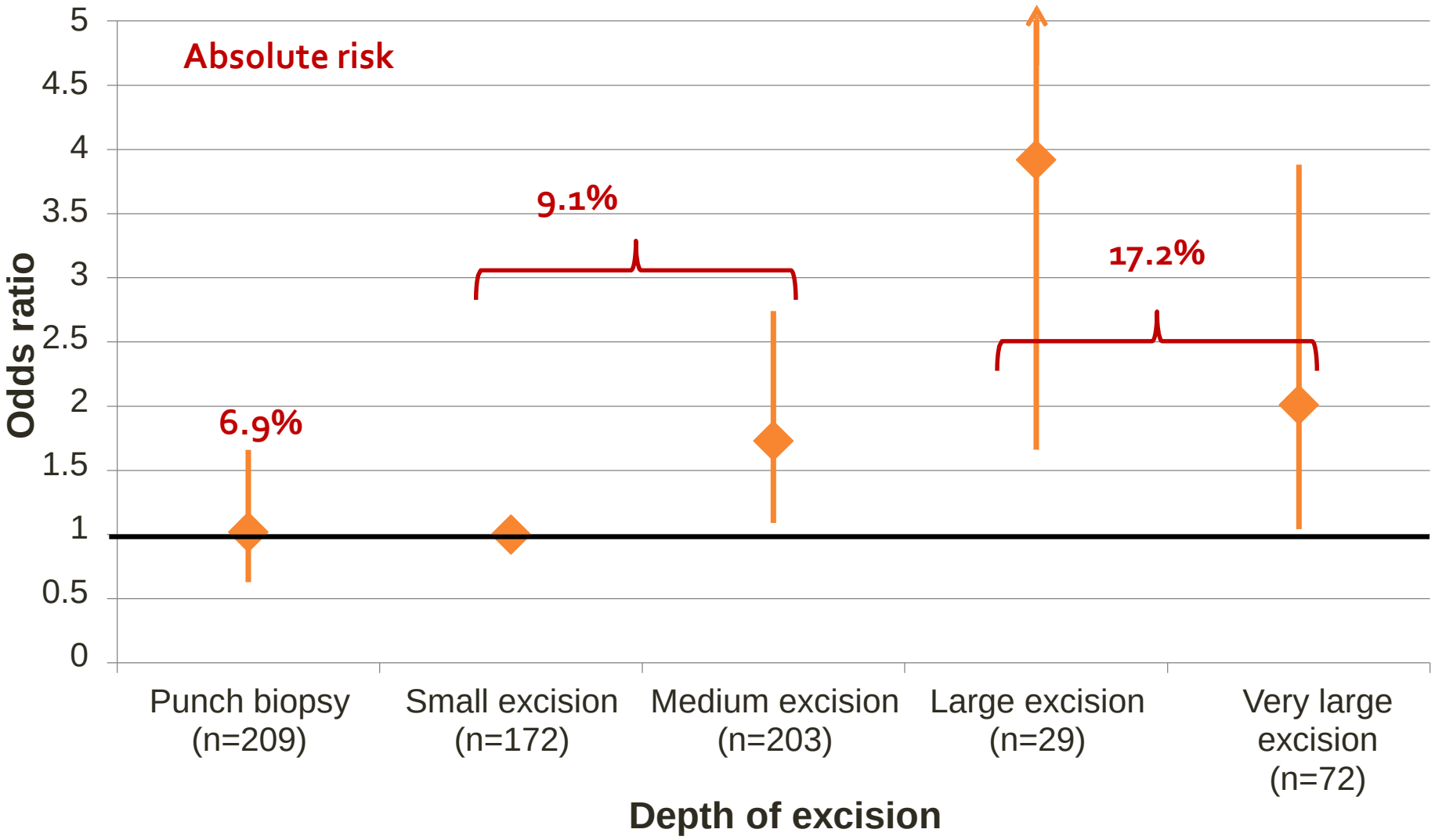
Births before colposcopy



First birth post colposcopy



Second+ births post colposcopy



How are we doing?

- 80% of excisions in England are small- the risk of PTB is at most minimally affected by a small excision; Larger excision over 15mm or 2.66 cubic cm are associated with a doubling of risk of PTL.

- Excisions of ≥10mm are responsible for ≈2.5% of preterm births each year in England

What next?

- Clearly deep excisions will be necessary
- Ensure women are flagged for close obstetric Monitoring

What next?

- Use of biomarkers to stratify risk
  - ? CIN2 (especially if p16-negative)- maybe not automatically treated but discussed at MDT

OTHER INTERESTING FACTS FROM THIS STUDY

In the subgroup analysis for Preterm births under 32 weeks, the risk of preterm labour was 3.6% with excisions greater than 15mm and 6.4% with depth greater than 20mm (small excisions 2% and background population 1.4%)

Time from treatment to conception did not appear to affect risk though data was inadequate

With multiple treatments, the risk was related to the total depth of excised tissue rather than the number of treatments

Therefore overall the risk of preterm labour in general population is 1in 16, rising to 1 in 13 with small excisions (does not reach statistical significance) and 1 in 6 with excisions 15mm or greater

ACKNOWLEDGEMENTS

Public Health England

NHS

Midlands and East Colposcopy Update

Mr Charles Redman and Mr Jullien Brady
QA Colposcopists (Midlands and East)

Public Health England

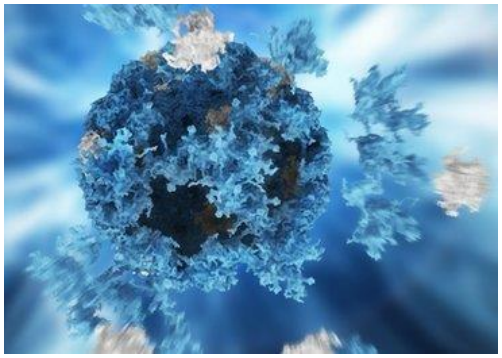
Protecting and improving the nation's health

Monitoring the impact of national HPV vaccination on prevalence among HPV cervical cancers

David Mesher
Marta Checchi, Kavita Panwar, Dipti Devalia, Simon Beddows, Katy Sinka

National Infection Service, Public Health England

Human Papillomavirus (HPV) Primary Screening



Viki Frew

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Any Questions ?

Thank you!