Risk of high grade CIN (CIN2+) in women with persistent high risk HPV genotypes and negative cytology

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Disclosures

Zilico Ltd
- Shareholder, Consultancy, Patent holder

Qiagen
- Speaker fee

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- Speaker fee

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- Travel and conference fees

Primary HPV Screening

Increased sensitivity to detect CIN2+

Increase screening intervals

- 3yrs to 5yrs, 5yrs to 10yrs

Post HPV vaccination population

To be implemented in several countries

- Australia, Germany, Italy, Netherlands and UK
- USA – co-testing with cytology and hrHPV

Primary HPV screening

Evaluated in England in six large cytology laboratories

Partial conversion to primary HPV screening

Age range 25-64yrs

Different HPV platforms

Different LBC platforms

Agreed algorithms for screening and colposcopy

Little international consensus on management of women who have persistent hrHPV infection and negative cytology

Primary HPV Screening

First test – call or recall

- Age range 25 to 65
- hr-HPV primary test
- If negative – routine recall
- If positive – reflex cytology
- If cytology positive (any grade) referral to colposcopy
- If cytology negative repeat hr-HPV test at 12 months

Primary HPV Screening

12 month recall

- hr-HPV primary test
- If negative – routine recall
- If positive – reflex cytology
- If cytology positive (any grade) referral to colposcopy
- If cytology negative but still positive for HPV 16 and or HPV 18 referral to colposcopy
- If cytology negative but still positive for HPV O repeat hrHPV test at 12 months

Primary HPV Screening

24 month recall

- hr-HPV primary test
- If negative – routine recall
- If positive – reflex cytology
- If cytology positive (any grade) referral to colposcopy
- If cytology negative but still positive for HPV O referral to colposcopy

Primary HPV Screening

All women aged 25 - 65

Commenced April 2013

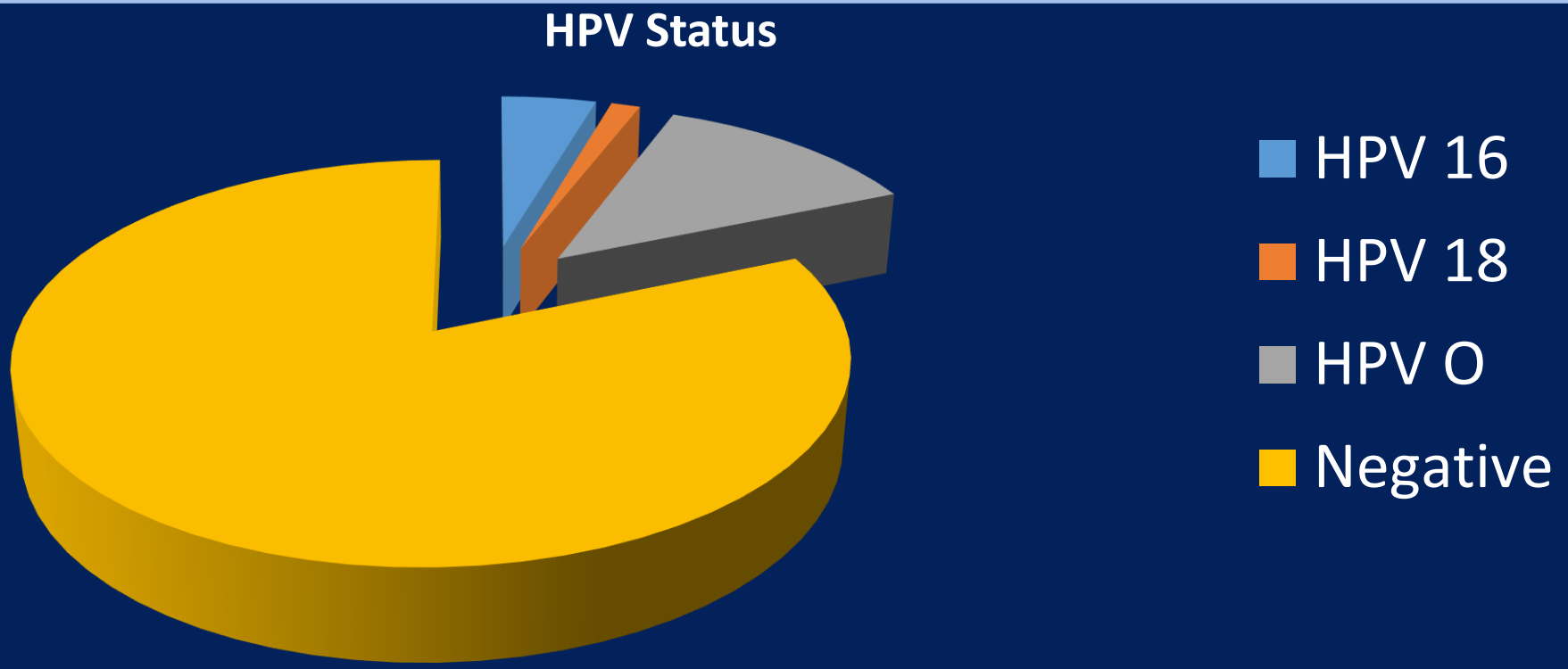
314,244 women underwent primary HPV testing to Dec 2015

651,307 women underwent primary cytology testing to July 2015

hr-HPV positive rates

- Average 12.7%, range 10.5 – 15.0%
- HPV 16/18 4.0%
- Age 24-29 – 27.6%
- Age 50-64 – 5.5%

hr-HPV status at Sheffield



15.0% of the screened population are hr-HPV positive

68.4% of hr-HPV positive women are positive for only HPV O

N=88,924

Persistent hr HPV infection cytology negative

1076 women referred to the colposcopy clinic in Sheffield

318 year one, 758 year two

hrHPV infections

HPV O	41%	HPV16	33%
HPV 18	8%	Multiple	18%

22% had an abnormal colposcopic examination (LG+HG colp impression)

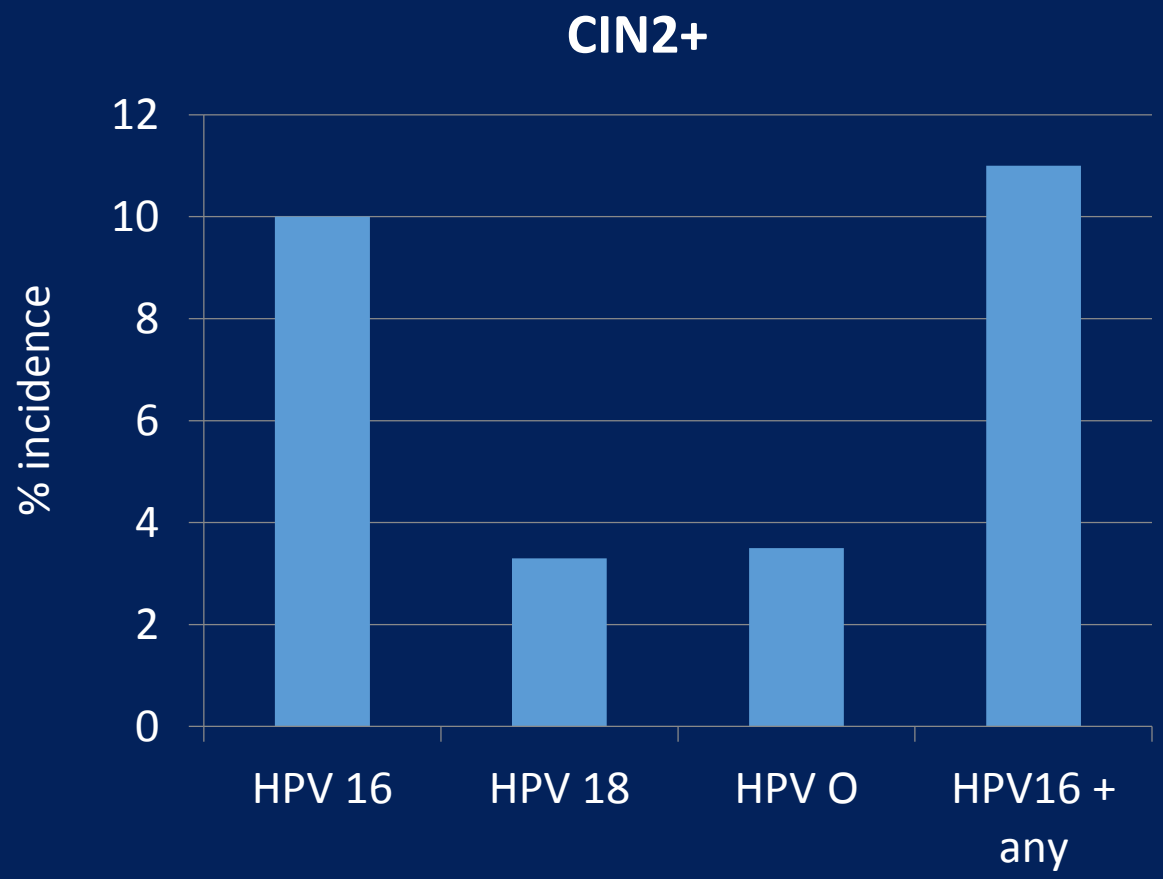
6% had an inadequate examination

31% had a biopsy (no ECC), 5% underwent LLETZ (LEEP)

Risk of CIN2+

- HPV 16 1 in 10
- HPV 18 1 in 30
- HPV O 1 in 28
- HPV 16 + any 1 in 9

- PPV for Colposcopic impression of CIN2+ was 47.4%
- Risk of LG-CIN 1 in 30 for all hrHPV genotypes



Primary HPV Screening - Conclusions

15% of women are hrHPV positive at first screen and 4% will be positive for HPV 16. Of those who are hrHPV positive 68% will be for HPV O genotypes

Primary hrHPV testing with reflex cytology is more sensitive in detection of CIN2+ compared with cytology, 1.52% *vs* 1.48%

Over 66% of women with a persistent hrHPV will have negative cytology

The incidence of CIN2+ in women with persistent HPV infection cytology negative results varies by hrHPV genotype

HPV 16 10%, HPV 18 3.3%, HPV O 3.5%, HPV 16 + any 11%

Primary HPV Screening - Conclusions

Follow up of women with persistent hrHPV infection increases referrals to colposcopy by 67%

83% of women referred to colposcopy with persistent hrHPV infection cytology negative results were discharged to routine recall

Can we triage these women before colposcopy?

Evaluated p16/Ki67 dual staining – poor sensitivity and specificity

Potential role of methylation markers – host, HPV

Adjunctive technologies in colposcopy to exclude disease