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Age, hrHPV genotype and ZedScan impact on the prevalence and detection of CIN2+ in hrHPV positive cytology negative samples

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Introduction

Primary screening with hrHPV has been demonstrated an increased sensitivity to detect CIN2+. Evaluation of the NHSCSP hrHPV screening pilot confirmed an increased detection of CIN2+ in the prevalent round with a reduction in CIN2+ in the subsequent incident round [1]. While all women with any abnormal cytology were referred, those who tested positive for persistent hrHPV but had negative cytology were triaged to colposcopy. hrHPV genotyping was used at three study sites including Sheffield [2]. Women who tested positive for persistent HPV16 or 18 were referred after a second positive test at 12 months, while those who tested positive for persistent HPVO were referred at 24 months.

Objective

To establish the prevalence of CIN2+ in women referred to colposcopy with persistent hrHPV but negative cytology, according to hrHPV genotype, age at referral and colposcopic performance with and without electrical impedance spectroscopy (ZedScan) [3].

Methods

A prospective cohort study of all women referred to the Jessop Wing Colposcopy Clinic, Sheffield with persistent hrHPV infection and negative cytology as per the HPV primary screening algorithm over a five year period between 1st June 2014 and 31st July 2019. Data was collected prospectively. Roche Cobas 4800 was used for HPV detection and genotyping (HPV16/18/O). Surepath LBC was used for cytology. Women underwent routine colposcopy with or without adjuvant ZedScan examination.

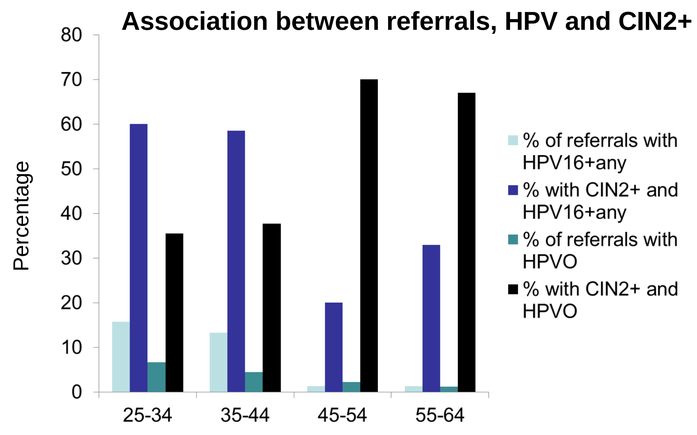
ZedScan™ /

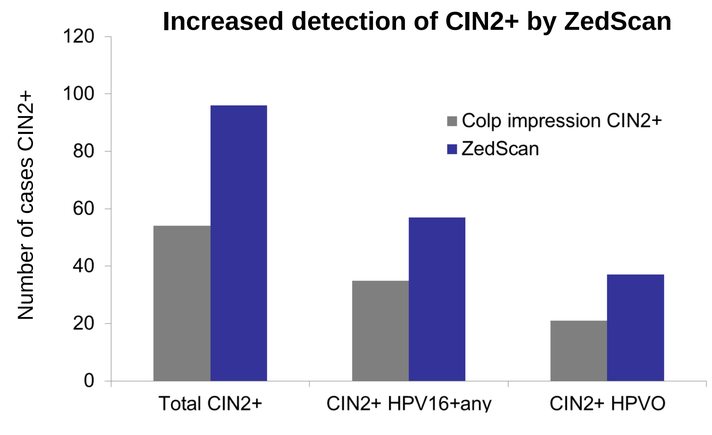
Results

3107 women were referred to colposcopy representing 31.3% of all screening referrals.

Referrals increased from 273 in year 1 to 668 year 2, 740 year 3, 734 year 4 and 692 year 5. Referral to colposcopy increased by 70% by year 2 with over 50% associated with HPVO infections.

- 1530 women were aged 25-34, 726 aged 35-44, 508 aged 45-54, 271 aged 55-64 and 65 over 65yrs.
- hrHPV genotyping was available for 3104 women. HPVO was the most prevalent (56.6%) followed by HPV16 (25.1%). 12% had multiple infections.
- 6.8% had an inadequate colposcopy, 0.9% in women aged 25-34, 29.5% in those aged 55-64 and 44.6% over 65yrs.
- 67% had a normal colposcopic impression, 24% low grade, 9% high grade.
- 33.1% underwent biopsy, 97.2% had a single biopsy.
- 7% (218) had CIN2+ of which 114 had CIN3+ with one adenocarcinoma.
- The PPV for a colposcopic impression of CIN2+ was 43.6%.
- Women who were HPV16 positive were more likely to have a colposcopic impression of CIN2+ (10.9% vs 6.9%) and had a higher PPV (57.3%) when compared to HPVO (32.1%).
- The prevalence of CIN2+ was 10.7% for HPV16, 3.6% for HPV18 and 4.7% for HPVO.





- 1168 women underwent a ZedScan examination.
- ZedScan detected an extra 42 cases of CIN2+ including 9 cases when the colposcopic impression was normal.
- Increased detection was independent of HPV genotype ($p<0.0005$).
- More women in the ZedScan group underwent biopsy but the PPV for CIN2+ was the same as the non ZedScan group.
- The PPV for a ZedScan directed biopsy was significantly higher when compared to a biopsy taken with a colposcopic impression of CIN1 or less (21.4% vs 13.7%, $p<0.001$).

Conclusions

Women who have persistent HPV16 infection have a higher prevalence of CIN2+. Colposcopy performs better in this group with a higher PPV, however most cases referred to colposcopy have HPVO. Older women have more inadequate colposcopic examinations.

The PPV for a directed biopsy is low for women with low grade colposcopic impression.

Routine use of ZedScan increases the detection of CIN2+, which is not dependent on genotype, so confirming previous studies within a primary HPV screening setting [4,5]. This study demonstrates the poor performance of colposcopy when the prevalence of CIN2+ is low.

References

1. *Rebolj et al 2019 BMJ 364:I240*
2. *Rebolj 2019 Br J Cancer 121:455-63*
3. *Tidy et al 2020 BJOG 127:1260-7*
4. *MacDonald et al 2017 E J Obstet Gynecol Repro Biol 211:194-7*
5. *Tidy et al 2018 E J Gynaecol Oncol 48:* doi:10.12892/ejgo3882.2018