

# Retrospective analysis: 25 to 29 year old females with NILM cytology and a positive high risk HPV test

## Abstract

Co-testing with cytology and a high-risk HPV test is recommended for women 30-65, the same recommendation is not made for women ages 25-29. The guidelines from ACOG, USPSTF, ASCP, ASCCP, and ACS for women 25-29, recommend cytology alone every three years as screening. A retrospective analysis was done at BioReference Laboratories over a 2 year period of time of samples that had NILM cytology with HPV Roche™ co-testing in patients 25 to 29. In addition, biopsy data was analyzed for a subset of these samples. From this analysis, we have concluded that cases of high-grade cervical lesions, including cervical cancers, are missed, when the Pap cytology is normal (NILM). While HPV testing is currently not recommended in 25 to 29 year olds with NILM pap, many of the patients were positive for type 16 and /or type 18 with significant disease detected on biopsy.

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## Introduction

Data from the ATHENA<sup>1</sup> (Addressing the Need for Advanced HPV Diagnostics) study of cervical cancer yielded interesting findings for women ages 25 to 29.

- i. 28% of all the high-grade cervical disease (CIN3 or greater) found in the study was in women 25-29.
- ii. Women 25-29 had more CIN3 or greater than women 40 and older, over 3years (Athena Study).
- iii. More than 50 percent of the CIN3 detected in women 25-29 by a positive HR HPV test was associated with a NILM pap.
- iv. All cancers were in woman 30 or older.

While co-testing with cytology and a high-risk HPV test is recommended for women 30-65, the same recommendation is not made for women ages 25-29. The guidelines from ACOG, USPSTF, ASCP, ASCCP, and ACS for women 25-29, recommend cytology alone every three years as screening. A retrospective analysis was done at BioReference Laboratories over a 2 year period of time of samples that had NILM cytology with HPV Roche™ co-testing in patients 25 to 29. In addition, biopsy data was analyzed for a subset of these samples. From this analysis, we have concluded that cases of high-grade cervical lesions, including cervical cancers, are missed, when the Pap cytology is normal (NILM). While HPV testing is currently not recommended in 25 to 29 year olds with NILM pap, many of the patients were positive for type 16 and /or type 18 with significant disease detected on biopsy.

## Material and methods

Samples were tested using the Roche Cobas® 4800 for HPV non 16/18 High Risk types, Type 16, and Type 18 as per manufacturer's instructions.

<sup>1</sup>The ATHENA HPV trial was a large, prospective clinical study evaluating the performance of the cobas® HPV Test in three relevant populations: women with ASC-US cervical cytology, women with normal cervical cytology, and an overall screening population (25+years) to explore HPV as a first-line test (ongoing longitudinal 3 year study).

## Results

The number of NILM cases for 2014 and 2015 were 144,505 and 172,833 respectively. Of those, 28,177 had a NILM cytology and a positive high risk HPV in 2014 and 30,634 in 2015(19.5% and 17.7% respectively) Figure 1.

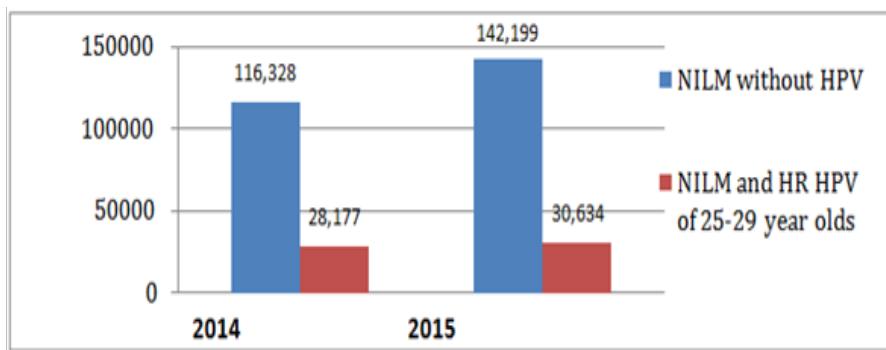
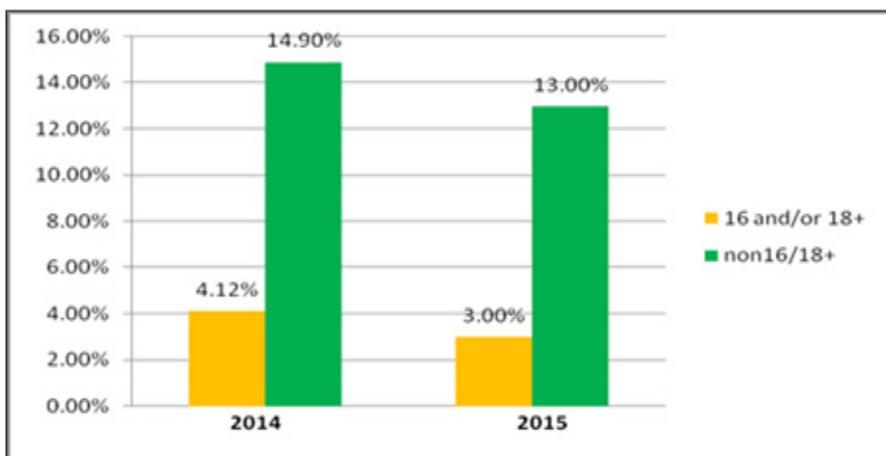
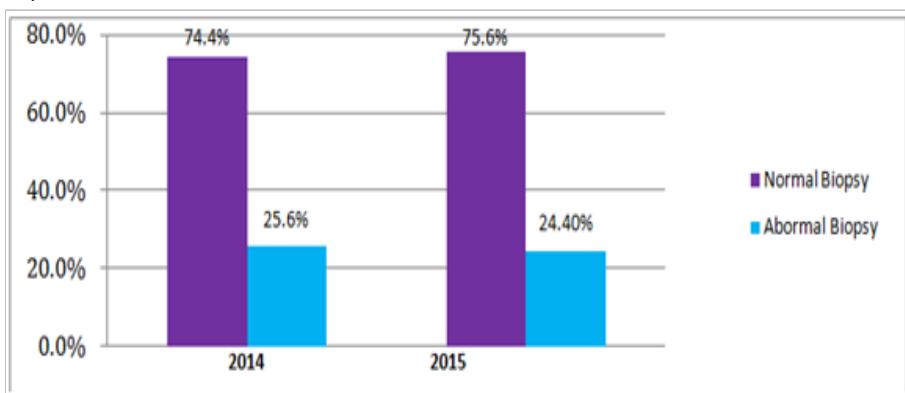
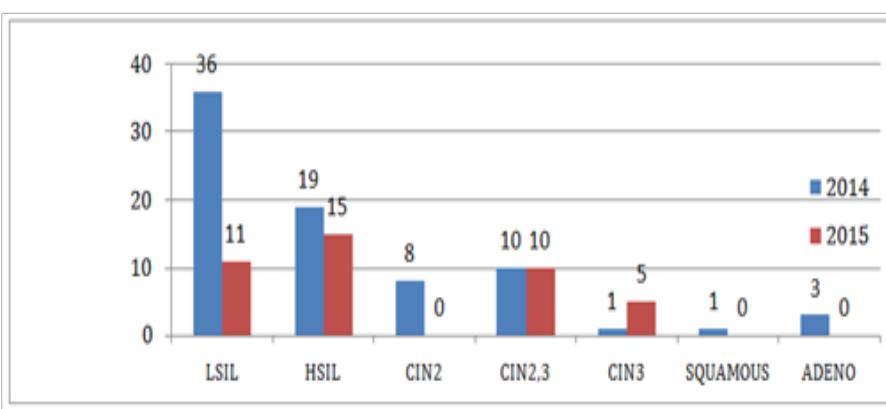
When the positives were analyzed for the type of HPV detected, 1161(4.12%) had type 16 and/or 18 detected in 2014 and 934(3.0%) detected in 2015 Figure 2.

Of the samples that were 16 and/or 18 positive, 304 had a biopsy performed with 78(25.6%) having an abnormal biopsy (LSIL=46.2% and 24.3% HSIL) in 2014 and 213 had a biopsy performed with 52(24.4%) having an abnormal biopsy (LSIL=21.2% and 28.8% HSIL) in 2015 Figure 3.

Analysis of the corresponding abnormal biopsies was in Table 1 & Figure 4.

**Table 1** Abnormal Biopsy Results

Abnormal biopsy results	2014	2015
LSIL	36(46.2%)	11(21.2%)
HSIL	19(24.3%)	15(28.8%)
Of the HSILs:		
CIN2	8	0
CIN2,3	10	10
CIN3	1	5
Squamous Cell Ca (microinvasive)	1	0
Adenocarcinoma-in-situ	3	0

**Figure 1** NILM Pap with HR HPV positive and HR HPV negative.**Figure 2** Analysis of HR HPV positives.**Figure 3** Normal versus abnormal biopsies.**Figure 4** Abnormal biopsy results.

## Conclusion

Based on our findings, cytology alone is insufficient in detecting potential disease in women 25-29 years old. Four (4) cases of cervical cancer were detected of the 304 biopsies tested in 2014 with a NILM pap (1.3%). HPV testing by the Roche Primary screening algorithm would have detected disease in women that were deemed negative by cytology. However, HPV Primary Screening runs the risk of testing negative in women who have HSIL paps and missing high grade lesions and cervical cancer.<sup>1</sup> Therefore, we propose that the recommendations for co-testing of paps and HPV testing be extended to include 25-29 year olds, which would be the best course to detect disease in these women.

## Acknowledgements

None.

## Conflict of interest

The author declares no conflict of interest.

## References

1. Zhou H, Mody R, Luna E, et al. The sensitivity of the cobas HPV test in detecting biopsy-confirmed CIN2/3 cervical lesions: analysis of 33,857 case with cytology and HPV Co-testing. *Journal of the American Society of Cytopathology*. 2014;3(5):S3.