FIVE YEARLY HPV TESTS ARE SAFER & MORE EFFECTIVE THAN TWO YEARLY PAP TESTS

VCS Pathology

RENEWAL READY SET·GO! 2017

"At longer intervals HPV-based screening provides 60—70% greater protection against invasive cervical carcinomas compared with cytology" – Ronco et al, Lancet 2014[1]

FACT

HPV testing is more effective than Pap tests even at longer intervals

As shown in the figure below, an analysis of HPV testing (blue line) compared to cytology (red line) from four European randomised controlled trials in 176,000 women demonstrated that HPV testing prevents more cervical cancer than cytology based screening.[1]

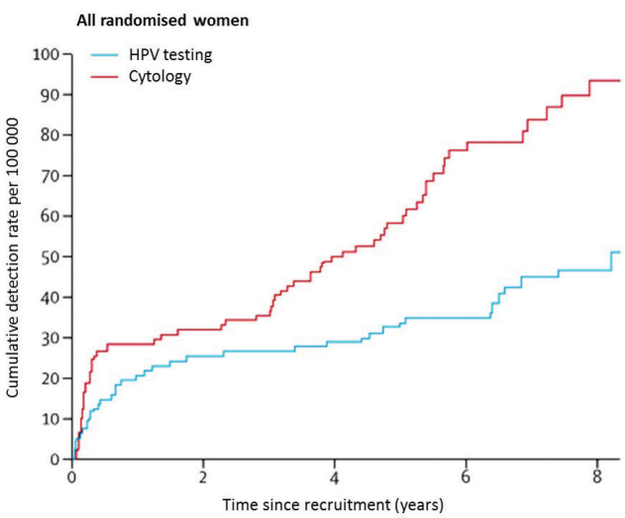

FIGURE 1: Cumulative detection of invasive cervical carcinoma

FACT

HPV testing is safer than Pap tests even at longer intervals

The long term negative predictive value (how long does a negative test indicate a low risk of disease) is the main determinant of the safe screening interval to use. Figure 2 is taken from a large European cohort analysis of many thousands of women with similar demographic background to Australia. All women are negative at time zero. The three lines represent women who had cytology alone (upper blue line), HPV testing alone (red middle line) and both cytology and HPV testing (lower green line).

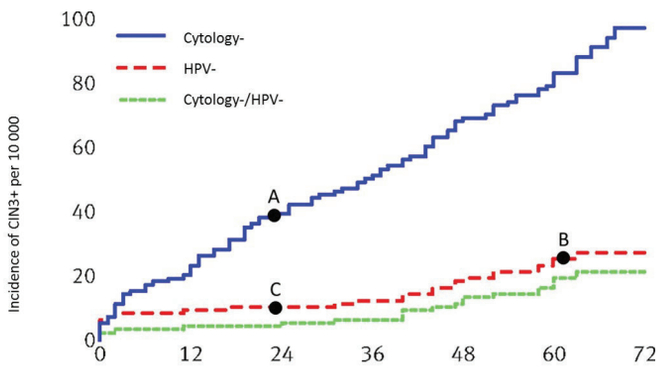

FIGURE 2: Kaplan-Meier plots of cumulative incidence rate for CIN3+ for women according to baseline test results in first 72 months of follow-up, excluding Denmark and Tübingen[2]

As can be seen at point A, two years after their negative Pap test, women have a cumulative incidence of CIN3+ of 4 per 1000 women. Notably the rate in women who were HPV negative at 2 years (red line) is only 1 per 1000 women (Point C). By 5 years (point B) the initially HPV negative women have a cumulative CIN3+ rate of 2.5 per 1000 women which is *still substantially lower than the rate at two years in the Pap test group.* **These data thus clearly demonstrate that women are safer 5 years after a negative HPV test than they are two years after a negative Pap test.** Shorter HPV testing intervals are not necessary or recommended because recently acquired HPV infections are mostly transient, so more frequent testing would result in an unnecessary increase in referral to colposcopy.

Co-testing strategies demonstrate very minimal additional sensitivity compared with HPV testing alone as seen Figure 2 (green line compared to red line). This very small gain in protection against the development of pre-cancerous lesions after a single screening test, does not result in significantly improved cervical cancer prevention but co-testing would result in many more women being referral for colposcopy, and additional treatment, in the absence of pre-cancerous changes.

FACT

HPV testing is more sensitive than cytology

HPV tests are more sensitive for the detection of pre-cancerous change (CIN2+/ AIS) than Pap tests. HPV infection is necessary but not sufficient for the development of almost all cervical cancer and occurs before the development of pre-cancerous changes (see Figure 3). HPV tests used for screening are calibrated to detect the presence of oncogenic HPV at levels associated with high grade lesions. Randomised controlled trial results show that HPV based screening detects persistent high grade CIN before cytology, thus increasing the probability of treatment before invasion.[1] This is the explanation for HPV testing showing greater prevention of cervical cancer and a lower risk of high grade CIN/cancer after a negative test over time.

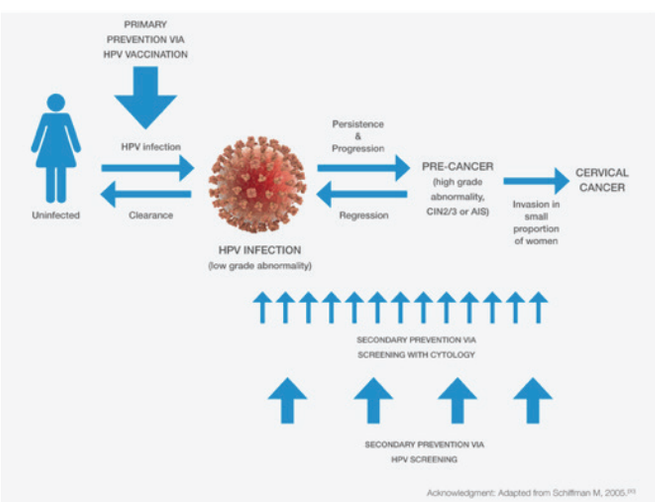

FIGURE 3: HPV to cervical cancer [3]

REFERENCES

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FACT

Both HPV tests and Pap tests are less sensitive for the detection of cancer than they are for the detection of pre-cancerous abnormalities

This is probably explained by the presence of blood and debris, that can obscure the presence of abnormal cells in LBC and can cause inhibition of the amplification step in HPV testing, crucial to accurate nucleic acid testing. Regular screening is recommended to prevent cervical cancer from developing rather than to detect cervical cancer that is already present.

Whilst some people say that Pap tests are more sensitive for the detection of cervical cancer than HPV tests, studies that support this view have significant biases favouring the performance of cytology over HPV tests.[4,5] These "look back" studies included available paired testing episodes (HPV tests and Pap tests) for which subsequent biopsy material was available. Because the laboratories undertook cytology on all samples, but only undertook HPV testing on samples that had abnormal findings on cytology, cases that were HPV positive but cytology negative were missed in the analysis. So false negative cytology cases could not be identified. Even under these biased conditions, the studies both reported improved performance of HPV testing, compared with LBC, for the detection of pre-cancerous abnormalities.

Any women with possible symptoms of cervical cancer (pain, bleeding or discharge) should have diagnostic cytology and HPV testing and appropriate referral regardless of age. This is not screening.[14]

The 2016 Guidelines recommend that 'Women at any age who have signs or symptoms suggestive of cervical cancer should have a co-test, and referral for appropriate investigation to exclude genital tract malignancy should be considered.'

CONCLUSION:

The renewed NCSP will be more effective than the current highly successful program and reductions in cervical cancer incidence and mortality of 20 to 30% are predicted with Australian specific modelling.