# HPV PRIMARY SCREENING PILOTS: EVALUATION REPORT TO THE NATIONAL SCREENING COMMITTEE . FEBRUARY 2015

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## SUMMARY

HPV testing as a primary screening method is expected to be more sensitive than cytology, resulting in increased detection of CIN2 or worse, and may enable the screening interval to be extended for HPV negative women. A pilot of HPV testing as primary screening is now under way in the six sites in England that previously acted as pilot and sentinel sites for HPV triage.

This paper reports on the results of baseline testing in the first 18 months of the pilot, together with colposcopy outcomes for these baseline tests, and limited results on retesting in those women HPV positive /cytology negative at baseline and recalled at 12 months. Sites have only partially converted to primary HPV screening, and results for primary HPV testing are compared to those for primary cytology screening in the same sites.

Positive rates and referral rates fall in all sites with increasing age up to ages 60-64 as expected. There is variation between sites in HPV positive rates and referral rates, but the positive predictive value (PPV) of HPV positivity for referral does not appear to be associated with positive or referral rates. Overall referral rates are slightly but significantly higher for HPV primary screening than for primary cytology for all ages combined and in the younger age group (25-49), but slightly lower in the age group 50-64.

Overall 8.6% of women tested were HPV positive /cytology negative and scheduled for recall at 12 months. Of those due for retesting so far, 72% have been tested. Of these 40% had become HPV negative, 21% were referred (either due to abnormal cytology or persistent HPV 16 or 18) and 38% remain on non-routine recall.

Attendance at colposcopy did not differ significantly between women referred following HPV primary testing and those referred following primary cytology (70.8% vs 69.5%).

If the HPV primary screening results are restricted to those sites for which colposcopy outcomes are available for primary cytology, the detection rate of CIN2+ for all ages is significantly higher with HPV primary screening (1.25 vs 1.09, $p< 0.001$), as is the detection rate of CIN3+ (0.82% vs 0.72%, $p<0.01$).

In conclusion, baseline screening by HPV primary testing achieves a higher detection rate of CIN2 or worse, with a small increase also in the number of referrals to colposcopy. Further data on the outcomes of repeat testing at 12 and 24 months, and on routine recall screens at 3 and 5 years, will be required to determine the full impact of introduction HPV primary testing and to inform the optimum protocol including the potential for extending the screening interval.

**BACKGROUND**

The causative role of human papilloma virus (HPV) in the development of cervical cancer has led to the inclusion of HPV testing in routine cervical screening, and HPV triage of women with borderline/mild cytology is now policy throughout the NHS Cervical Screening Programme (NHSCSP). Triage allows approximately a third of all women with borderline cytology or mild dyskaryosis to be returned immediately to routine recall, thus reducing the burden on cytology services.

However results from other studies have shown that HPV testing as a primary screening method is expected to be more sensitive than cytology, resulting in increased detection of CIN2 or worse, and may enable the screening interval to be extended for HPV negative women. The effect of HPV vaccination as a primary prevention measure will be to markedly reduce the prevalence of HR HPV infection, and will begin to be detectable from 2015 onwards.

A pilot of HPV testing as primary screening is now under way in the six sites in England that previously acted as pilot and sentinel sites for HPV triage. The flowchart for the first year of the pilot is included in the Appendix.

The main aims of this phase the evaluation of the pilot are to study the effect of the introduction of HPV primary screening on the uptake/coverage of cervical screening, rates of referral to and attendance at colposcopy, numbers of women place on non-routine recall and rates of compliance with 1 year recall (HPV positive/cytology negative women), and the detection rates of CIN2 or worse and CIN3 or worse, together with the positive predictive value (PPV) of referral to colposcopy.

This paper reports on the results of baseline testing in the first 18 months of the pilot, together with colposcopy outcomes for these baseline tests; there are limited results so far on retesting in women HPV positive / cytology negative at baseline and recalled at 12 months.

Comparison will be made between laboratories, with different populations and using different assays, as well as variation in reporting of cytological abnormalities. Considerable variation between sites in referral rates and PPVs was observed in the previous pilots of HPV triage.

The higher HPV positive rate in the 25-29 age group has in the past led to some discussion as to whether younger women should be included HPV primary screening, and key results are presented for this age group.

**DATA COLLECTION**

The pilot sites provide individual data for HPV sample/cytology records, including NHS number to enable subsequent linkage to further HPV or cytology tests and/or colposcopy results. In order for sites to be able to provide these data to the evaluators, an Information Sharing Agreement was drawn up between the Cancer Screening Programmes and the Centre for Cancer Prevention, QMUL. This agreement was approved in July 2014.

Data have been received from all sites on HPV primary screening and for 5 sites on primary cytology screening for samples received up to 31.10 2014. The data include a total of 167,919 primary HPV tests and 331,955 primary cytology samples.

Women with a HPV positive/cytology negative result are recalled at 12 months. Data for women due for 12 months recall are restricted to those due for recall up to 31 July 2014 (i.e. those tested up to 31.07.2013). The results for colposcopy outcomes included in this report have been restricted to referrals following primary HPV or cytology tests reported up to 31.07.2014 (18.06.2014 for Liverpool). Data on colposcopy outcomes for primary cytology samples are only available for four sites.

**Uptake of invitations**

It is not possible to link individual tests to date of invitation. As a result it is difficult to compare the uptake of HPV primary testing and primary cytology, as a number of primary cytology tests will result from earlier invitations, and both HPV and cytology testing may include opportunistic testing.

Data on the numbers of women invited by month in primary HPV and primary cytology districts in each site have been received from the Health and Social Care Information Centre (HSCIC), but further work is required to identify the appropriate denominators to be used to estimate uptake. Other means of comparing uptake and coverage are being explored.

## RESULTS

### HPY primary testing results

Table 1A presents the results of primary HPV testing by age group, and Table 1B the results by site, including details of the assays used in each site.

The overall HPV positive rate is 12.9%, and the overall referral rates 4.3% of those tested. Positive rates and referral rates fall in all sites with increasing age up to ages 60-64 as expected.

Overall, HPV positive rates are somewhat higher in Bristol and Sheffield (14.6% and 15.7% respectively) than in the other sites (10.9-11.7%). Referral rates range from 2.8 % to 5.4 %, and PPVs of HPV positivity for referral range from 25.8% to 46.3%, but do not appear to be associated with positive/referral rates. Overall 8.5% of women tested would be scheduled for recall at 12 months, falling from 17.3% at ages 25-29 to less than 4% at ages 60-64.

Figure 1 shows HPV positive rates over time for each site, and Figure 2 by 5 year age group.

### HPV typing results

HPV typing data have been received from 4 sites; overall 31.9% of those samples typed are HPV 16 and/or 18, and the PPV for referral was 43.5% (Table 2), compared with 32.6% for that in the same sites for any HPV positivity.

### Comparison with primary cytology results

Comparing referral rates with those for primary cytology screening (Table 3) there is a slightly higher referral rate following HPV primary screening (4.31% vs 4.05%), This difference remains significant if data from Liverpool (which are not included in the primary cytology results) are excluded from the HPV primary testing results. The referral rate in the age group 25-49 is significantly higher for HPV primary testing than for primary cytology (5.12% vs 4.68% with the exclusion of the one site for which primary cytology data are not available). By contrast the referral rate at ages 50-64 is significantly lower following primary HPV testing (1.37% vs 1.61%).

### Repeat tests

Of 380 women with invalid primary HPV tests up to 31.7.2014, 250 (65.8%) have been retested, of which 9.2% were HPV positive, and 2.0% referred. Of 207 women with positive HPV/inadequate cytology results, 146 (70.5%) have been retested, of which 80.2% were HPV positive and 23.3% referred.

Of the 1051 women with HPV +ve/ cytology negative results at initial testing (up to 31.7.2013), 72.0% (757) had had a repeat test reported (Table 4). Of those retested, 59.8% remained HPV positive, and 35.8% of these (162/453) were referred to colposcopy (either due to abnormal cytology or due to persistent HPV 16 or 18 (a policy now adopted in four of the pilot sites). Overall therefore 38% (291/757) of those retested would remain on non-routine recall. This proportion is similar in different age groups.

Of those 258 women HPV 16 or 18 positive at baseline due for retesting at 12 months, 182 have been retested; of these 56% and 48% respectively remained positive for the same type at retesting, and 27% of these had abnormal cytology.

**Attendance at colposcopy**

Data are available for all six sites for HPV primary testing and for four sites for primary cytology. Of the 5936 women referred to colposcopy up to 31 July 2014 following a positive primary HPV test, 70.8 % had attended (Table 6). This compares to the 69.5% of 8744 women referred following positive primary cytology (Table 8).

The PPV of colposcopy (the percentage of lesions detected among those attending) for CIN2+ is 38.1% following primary HPV testing and 35.4% for primary cytology, (24.5% and 23.4% respectively for CIN3+). If the data for HPV testing are restricted to those sites for which primary cytology results are available, the PPV for CIN2+ is 36.7%, and that for CIN3+ is 24.0%.

Tables 7 & 9 show the detection rates of CIN1, CIN2 + and CIN3+ for baseline samples reported in the period up to 31 July 2014, Detection rates of CIN2+ are 1.13% for HPV and 1.06% for cytology (0.71and 0.68% for CIN3+). Again, if the data for HPV testing are restricted to those sites for which primary cytology results are available, the detection rates are 1.25% for CIN2+ and 0.82% for CIN3+.

**Summary results by age group**

Tables 10 and 11 summarise the key results for the age groups 24-29 and 30-64, and 24-49 and 50-64.

If the HPV results are restricted to those sites for which colposcopy outcomes are available for primary cytology, the PPV of colposcopy for CIN2 is significantly lower for HPV primary screening (40.9% vs 44.2%, p=0.048) for ages 24-29, but significantly higher for ages 30 to 64 (32.8 vs 28.8%, p <0.01). With the same restriction, the detection rate of CIN2+ for all ages is significantly higher with HPV primary screening (1.25 vs 1.09, p< 0.001), as is the detection rate of CIN3+ (0.82% vs 0.72%, p<0.01).

**DISCUSSION**

These results reflect the first 18 months of screening in the HPV pilot sites. They suggest that the introduction of primary HPV testing would lead to an initial small increase in referrals to colposcopy of around 2 per 1000 women tested, equivalent to an increase of around 5-6% in the number of referrals. This is accompanied by an increase in detection of CIN2 or worse of around 1 to 1.5 per 1000 women tested at baseline screening. However it should be emphasised that these figures do not included the impact of referrals following repeat testing at 12 or 24 months under the current protocol. Preliminary results suggest that retesting at 12 months may lead to a further 16 women per 1000 initially tested being referred (if 20 % of those retested are referred). There are insufficient

data at present to study the effect on detection of CIN. The attendance at 12 month repeat testing of 72% in women due for recall up to 31 July is encouraging; it is hoped that 80% can be achievable.

There continues to be variation in both HPV positive rates and referral rates between sites, but it is not clear whether this is due to use of different assays or other differences including cytological reporting. This variation has implications for future differences in the performance of the screening programme, and reasons for this variation will be explored further.

Women in the 25-29 year age group have high HPV positive rates, and a high proportion of these will be scheduled for retesting at 12 months. However the HPV positivity in this age group will reduce considerably once the vaccinated cohort reach age 25 from 2016 onwards, so that these high rates will become less of a problem in future years.

In conclusion, baseline screening by HPV primary testing achieves a higher detection rate of CIN2 or worse, with a small increase also in the number of referrals to colposcopy. Further data on the outcomes of repeat testing at 12 and 24 months, and on routine recall screens at 3 and 5 years, will be required to determine the full impact of the introduction of HPV primary testing and to inform the optimum protocol including the potential for extending the screening interval.

**Table 1A HPV primary screening results May 2013 – October 2014 by age group**

| Age group | Total tested | HPV positive | (% of tested) | Borderline/ Mild | (% of tested) | Moderate or worse | (% of tested) | Total referred | (% of tested) | HPV positive referred | (PPV of HPV +ve for referral) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 15-19 | 7 | 3 | (42.9) | 1 | (14.3) | 0 | (0.0) | 1 | (14.3) | 1 | (33.3) |
| 20-23 | 158 | 71 | 44.9) | 26 | (16.5) | 5 | (3.2) | 33 | (20.9) | 33 | (46.5) |
| 24 | 2620 | 877 | (33.5) | 219 | (8.4) | 106 | (4.0) | 326 | (12.4) | 326 | (37.2) |
| 25-29 | 29046 | 8231 | (28.3) | 2019 | (7.0) | 1104 | (3.8) | 3193 | (11.0) | 3192 | (38.8) |
| 30-34 | 23297 | 3700 | (15.9) | 842 | (3.6) | 403 | (1.7) | 1272 | (5.5) | 1268 | (34.3) |
| 35-39 | 21591 | 2427 | (11.2) | 488 | (2.3) | 224 | (1.0) | 732 | (3.4) | 732 | (30.2) |
| 40-44 | 24457 | 2124 | (8.7) | 440 | (1.8) | 154 | (0.6) | 609 | (2.5) | 608 | (28.6) |
| 45-49 | 26012 | 1900 | (7.3) | 382 | (1.5) | 97 | (0.4) | 501 | (1.9) | 500 | (26.3) |
| 50-54 | 18650 | 1190 | (6.4) | 227 | (1.2) | 67 | (0.4) | 295 | (1.6) | 295 | (24.8) |
| 55-59 | 13858 | 747 | (5.4) | 138 | (1.0) | 52 | (0.4) | 192 | (1.4) | 192 | (25.7) |
| 60-64 | 7041 | 333 | (4.7) | 42 | (0.6) | 18 | (0.3) | 61 | (0.9) | 61 | (18.3) |
| 65-69 | 1093 | 60 | (5.5) | 12 | (1.1) | 2 | (0.2) | 15 | (1.4) | 15 | (25.0) |
| 70-74 | 72 | 17 | (23.6) | 5 | (6.9) | 0 | (0.0) | 5 | (6.9) | 5 | (29.4) |
| 75-79 | 14 | 2 | (14.3) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| 80-84 | 2 | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | N/A |
| 85-89 | 1 | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | N/A |
| **Total** | **167919** | **21682** | **(12.9)** | **4841** | **(2.9)** | **2232** | **(1.3)** | **7235** | **(4.3)** | **7228** | **(33.3)** |

**Table 1B HPV primary screening results May 2013 – October 2014 by site**

| Site | Assay | Total tested | HPV positive | (% of tested) | Borderline/ Mild | (% of tested) | Moderate or worse | (% of tested) | Total referred | (% of tested) | HPV positive referred | (PPV of HPV +ve for referral) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bristol | TP/Genprobe | 19608 | 2868 | (14.6) | 690 | (3.5) | 199 | (1.0) | 913 | (4.7) | 912 | (31.8) |
| Liverpool | SP/Genprobe | 15926 | 1861 | (11.7) | 440 | (2.8) | 342 | (2.1) | 796 | (5.0) | 796 | (42.8) |
| London | TP/Abbott | 18629 | 2171 | (11.7) | 826 | (4.4) | 180 | (1.0) | 1006 | (5.4) | 1006 | (46.3) |
| Manchester | SP/Abbott | 56525 | 6485 | (11.5) | 1447 | (2.6) | 760 | (1.3) | 2267 | (4.0) | 2264 | (34.9) |
| Norfolk and Norwich | TP/Roche | 14734 | 1610 | (10.9) | 275 | (1.9) | 127 | (0.9) | 415 | (2.8) | 415 | (25.8) |
| Sheffield | SP/Roche | 42497 | 6687 | (15.7) | 1163 | (2.7) | 624 | (1.5) | 1838 | (4.3) | 1835 | (27.4) |
| **Total** | | **167919** | **21682** | **(12.9)** | **4841** | **(2.9)** | **2232** | **(1.3)** | **7235** | **(4.3)** | **7228** | **(33.3)** |

**Table 2 HPV primary screening : HPV typing results from 4 sites**

| Age group | Total HPV typed | HPV 16 | (% of typed) | HPV 18 | (% of typed) | HPV 16 or 18 | (% of typed) | HPV 16 or 18 referred | (% HPV 16/18 referred) |
|---|---|---|---|---|---|---|---|---|---|
| 15-19 | 3 | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | N/A |
| 20-23 | 59 | 13 | (22.0) | 4 | (6.8) | 17 | (28.8) | 12 | (70.6) |
| 24 | 371 | 110 | (29.6) | 32 | (8.6) | 133 | (35.8) | 61 | (45.9) |
| 25-29 | 6548 | 2030 | (31.0) | 635 | (9.7) | 2540 | (38.8) | 1259 | (49.6) |
| 30-34 | 2831 | 685 | (24.2) | 229 | (8.1) | 892 | (31.5) | 406 | (45.5) |
| 35-39 | 1884 | 360 | (19.1) | 140 | (7.4) | 489 | (26.0) | 186 | (38.0) |
| 40-44 | 1704 | 295 | (17.3) | 129 | (7.6) | 416 | (24.4) | 148 | (35.6) |
| 45-49 | 1484 | 267 | (18.0) | 101 | (6.8) | 364 | (24.5) | 114 | (31.3) |
| 50-54 | 965 | 166 | (17.2) | 62 | (6.4) | 226 | (23.4) | 59 | (26.1) |
| 55-59 | 590 | 128 | (21.7) | 43 | (7.3) | 168 | (28.5) | 54 | (32.1) |
| 60-64 | 284 | 67 | (23.6) | 16 | (5.6) | 80 | (28.2) | 16 | (20.0) |
| 65-69 | 56 | 21 | (37.5) | 3 | (5.4) | 24 | (42.9) | 9 | (37.5) |
| 70-74 | 16 | 1 | (6.3) | 1 | (6.3) | 2 | (12.5) | 1 | (50.0) |
| 75-79 | 2 | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | N/A |
| **Total** | **16797** | **4143** | **(24.7)** | **1395** | **(8.3)** | **5351** | **(31.9)** | **2325** | **(43.4)** |

**Table 3A Primary cytology, all sites, May 2013 – October 2014 by age group**

| Age group | Total tested | Borderline/ Mild | (% of tested) | Moderate or worse | (% of tested) | HPV tested | HPV positive | (% of tested) | Referral | (% of tested) | Borderline/ mild referred | (PPV of borderline mild for referral) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 15-19 | 64 | 8 | (12.5) | 0 | (0.0) | 5 | 3 | (60.0) | 4 | (6.3) | 4 | (50.0) |
| 20-23 | 703 | 98 | (13.9) | 16 | (2.3) | 82 | 45 | (54.9) | 80 | (11.4) | 56 | (57.1) |
| 24 | 5552 | 487 | (8.8) | 195 | (3.5) | 489 | 402 | (82.2) | 604 | (10.9) | 411 | (84.4) |
| 25-29 | 55619 | 4281 | (7.7) | 1918 | (3.4) | 5446 | 3263 | (59.9) | 5159 | (9.3) | 3074 | (71.8) |
| 30-34 | 48020 | 2541 | (5.3) | 803 | (1.7) | 3549 | 1639 | (46.2) | 2496 | (5.2) | 1531 | (60.3) |
| 35-39 | 43850 | 1791 | (4.1) | 474 | (1.1) | 2456 | 1039 | (42.3) | 1572 | (3.6) | 985 | (55.0) |
| 40-44 | 47723 | 1590 | (3.3) | 332 | (0.7) | 2050 | 813 | (39.7) | 1191 | (2.5) | 788 | (49.6) |
| 45-49 | 49366 | 1516 | (3.1) | 252 | (0.5) | 1820 | 715 | (39.3) | 1015 | (2.1) | 710 | (46.8) |
| 50-54 | 35481 | 1047 | (3.0) | 175 | (0.5) | 1212 | 450 | (37.1) | 621 | (1.8) | 437 | (41.7) |
| 55-59 | 27482 | 663 | (2.4) | 116 | (0.4) | 726 | 290 | (39.9) | 417 | (1.5) | 282 | (42.5) |
| 60-64 | 15267 | 344 | (2.3) | 82 | (0.5) | 381 | 140 | (36.7) | 223 | (1.5) | 138 | (40.1) |
| 65-69 | 2398 | 87 | (3.6) | 19 | (0.8) | 78 | 27 | (34.6) | 48 | (2.0) | 34 | (39.1) |
| 70-74 | 284 | 28 | (9.9) | 4 | (1.4) | 15 | 6 | (40.0) | 12 | (4.2) | 8 | (28.6) |
| 75-79 | 92 | 9 | (9.8) | 2 | (2.2) | 5 | 2 | (40.0) | 2 | (2.2) | 2 | (22.2) |
| 80-84 | 42 | 2 | (4.8) | 5 | (11.9) | 1 | 0 | (0.0) | 2 | (4.8) | 2 | (100.0) |
| 85-89 | 8 | 2 | (25.0) | 1 | (12.5) | 0 | 0 | N/A | 1 | (12.5) | 1 | 50.0) |
| 90-94 | 3 | 0 | (0.0) | 1 | (33.3) | 0 | 0 | N/A | 0 | (0.0) | 0 | N/A |
| 95-99 | 1 | 0 | (0.0) | 0 | (0.0) | 0 | 0 | N/A | 0 | (0.0) | 0 | N/A |
| **Total** | **331955** | **14494** | **(4.4)** | **4395** | **(1.3)** | **18315** | **8834** | **(48.2)** | **13447** | **(4.1)** | **8463** | **(58.4)** |

**Table 3B Primary cytology, all sites, May 2013 – October 2014 : ages 24-49**

| Site | Total tested | Borderline/ Mild | (% of tested) | Moderate or worse | (% of tested) | HPV tested | HPV positive | (% of tested) | Referral | (% of tested) | Borderline/ mild referred | (PPV of borderline mild for referral) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bristol | 37640 | 1679 | (4.5) | 442 | (1.2) | 2096 | 1289 | (61.5) | 1911 | (5.1) | 1365 | (81.3) |
| London | 46041 | 3590 | (7.8) | 453 | (1.0) | 4004 | 1767 | (44.1) | 2597 | (5.6) | 1882 | (52.4) |
| Manchester | 67664 | 3304 | (4.9) | 1296 | (1.9) | 4593 | 1969 | (42.9) | 2779 | (4.1) | 1631 | (49.4) |
| Norfolk & Norwich | 44076 | 1615 | (3.7) | 682 | (1.5) | 2097 | 1213 | (57.8) | 1899 | (4.3) | 1127 | (69.8) |
| Sheffield | 54709 | 2018 | (3.7) | 1101 | (2.0) | 3020 | 1633 | (54.1) | 2851 | (5.2) | 1494 | (74.0) |
| **Total** | **250130** | **12206** | **(4.9)** | **3974** | **(1.6)** | **15810** | **7871** | **(49.8)** | **12037** | **(4.8)** | **7499** | **(61.4)** |

**Table 3C Primary cytology, all sites, May 2013 – October 2014 : ages 50-64**

| Site | Total tested | Borderline/ Mild | (% of tested) | Moderate or worse | (% of tested) | HPV tested | HPV positive | (% of tested) | Referral | (% of tested) | Borderline/ mild referred | (PPV of borderline mild for referral) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bristol | 10284 | 150 | (1.5) | 25 | (0.2) | 169 | 88 | (52.1) | 146 | (1.4) | 105 | (70.0) |
| London | 12248 | 798 | (6.5) | 87 | (0.7) | 872 | 316 | (36.2) | 466 | (3.8) | 337 | (42.2) |
| Manchester | 22787 | 536 | (2.4) | 125 | (0.5) | 560 | 192 | (34.3) | 213 | (0.9) | 146 | (27.2) |
| Norfolk & Norwich | 14738 | 231 | (1.6) | 46 | (0.3) | 262 | 111 | (42.4) | 161 | (1.1) | 104 | (45.0) |
| Sheffield | 18173 | 339 | (1.9) | 90 | (0.5) | 456 | 173 | (37.9) | 275 | (1.5) | 165 | (48.7) |
| **Total** | **78230** | **2054** | **(2.6)** | **373** | **(0.5)** | **2319** | **880** | **(38.0)** | **1261** | **(1.6)** | **857** | **(41.7)** |

**Table 3C Primary cytology, all sites, May 2013 – October 2014 by site**

| Site | Total tested | Borderline/ Mild | % of tested | Moderate or worse | % of tested | HPV tested | HPV positive | % of tested | Referral | % of tested | Borderline/ mild referred | PPV of borderline mild for referral |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bristol | 48159 | 1847 | 3.8% | 470 | 1.0% | 2280 | 1387 | 60.8% | 2080 | 4.3% | 1487 | 80.5% |
| London | 59238 | 4468 | 7.5% | 552 | 0.9% | 4936 | 2102 | 42.6% | 3127 | 5.3% | 2265 | 50.7% |
| Manchester | 91901 | 3934 | 4.3% | 1448 | 1.6% | 5213 | 2191 | 42.0% | 3024 | 3.3% | 1800 | 45.8% |
| Norfolk & Norwich | 59090 | 1863 | 3.2% | 729 | 1.2% | 2376 | 1332 | 56.1% | 2069 | 3.5% | 1238 | 66.5% |
| Sheffield | 73567 | 2382 | 3.2% | 1196 | 1.6% | 3510 | 1822 | 51.9% | 3147 | 4.3% | 1673 | 70.2% |
| **Total** | **331955** | **14494** | **4.4%** | **4395** | **1.3%** | **18315** | **8834** | **48.2%** | **13447** | **4.1%** | **8463** | **58.4%** |

**Table 4. HPV primary screening, HPV positive, cytology negative tests, by age group (first test up to 31st July 2013)**

| Age | Total HPV + Cytology Neg | Retested | % | Still HPV+ | (% of retested) | Borderline/ mild | (% of retested) | Moderate + | (% of retested) | Referred | (HPV 16/18 persistent, Cyt neg) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 - 23 | 6 | 4 | (66.7) | 4 | (100.0) | 1 | (25.0) | 0 | (0.0) | 1 | (0) |
| 24 | 14 | 13 | (92.9) | 9 | (69.2) | 1 | (7.7) | 0 | (0.0) | 1 | (0) |
| 25-29 | 351 | 234 | (66.7) | 148 | (63.2) | 28 | (12.0) | 11 | (4.7) | 65 | (21) |
| 30-34 | 199 | 136 | (68.3) | 87 | (64.0) | 18 | (13.2) | 4 | (2.9) | 31 | (5) |
| 35-39 | 133 | 96 | (72.2) | 60 | (62.5) | 8 | (8.3) | 6 | (6.3) | 14 | (1) |
| 40-44 | 116 | 94 | (81.0) | 41 | (43.6) | 8 | (8.5) | 2 | (2.1) | 14 | (4) |
| 45-49 | 106 | 81 | (76.4) | 45 | (55.6) | 7 | (8.6) | 1 | (1.2) | 15 | (6) |
| 50-54 | 68 | 52 | (76.5) | 31 | (59.6) | 7 | (13.5) | 1 | (1.9) | 10 | (2) |
| 55-59 | 39 | 34 | (87.2) | 23 | (67.6) | 2 | (5.9) | 0 | (0.0) | 8 | (6) |
| 60-64 | 17 | 12 | (70.6) | 4 | (33.3) | 1 | (8.3) | 1 | (8.3) | 2 | (0) |
| 65-69 | 2 | 1 | (50.0) | 1 | (100.0) | 0 | (0.0) | 0 | (0.0) | 1 | (1) |
| **Total** | **1051** | **757** | **(72.0)** | **453** | **(59.8)** | **81** | **(10.7)** | **26** | **(3.4)** | **162** | **(46)** |

**Table 5. HPV primary screening, HPV positive, cytology negative tests in age groups 24-29, 30 -64 (first test up to 31st July 2013)**

| Age | Total HPV + Cytology Neg | Retested | (%) | Still HPV+ | (% of retested) | Borderline/ mild | (% of retested) | Moderate + | (% of retested) | Referred | (HPV 16/18 persistent, Cyt neg) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 24-29 | 365 | 247 | (67.7) | 157 | (63.6) | 29 | (11.7) | 11 | (4.5) | 66 | (21) |
| 30-64 | 678 | 505 | (74.5) | 291 | (57.6) | 51 | (10.1) | 15 | (3.0) | 94 | (24) |
| **Total** | **1043** | **751** | **(72.1)** | **448** | **(59.6)** | **80** | **(10.6)** | **26** | **(3.5)** | **160** | **(45)** |

**Table 6. HPV primary testing: Colposcopy outcomes (PPV of colposcopy attendance) (women referred up to 31st July 2014/ 18th June 2014 for Liverpool)**

| Site | Total referred | Total attended | (% of referred) | CIN1 | ( % of attended) | CIN2 + | (% of attended) | CIN3 + | (% of attended) | Cervical Cancer | (% of attended) | Outcome not known | (% of attended) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bristol | 727 | 347 | (47.7) | 81 | (23.3) | 93 | (26.8) | 41 | (11.8) | 1 | (0.3) | 16 | (4.6) |
| Liverpool | 654 | 581 | (88.8) | 59 | (10.2) | 227 | (39.1) | 142 | (24.4) | 3 | (0.5) | 0 | (0.0) |
| London | 833 | 548 | 65.8% | 147 | 26.8% | 190 | 34.7% | 83 | 15.1% | 2 | 0.4% | 0 | 0.0% |
| Manchester | 1832 | 935 | 51.0% | 207 | 22.1% | 388 | 41.5% | 242 | 25.9% | 18 | 1.9% | 25 | 2.7% |
| Norfolk and Norwich | 352 | 349 | 99.1% | 83 | 23.8% | 115 | 33.0% | 77 | 22.1% | 6 | 1.7% | 1 | 0.3% |
| Sheffield | 1538 | 1444 | 93.9% | 131 | 9.1% | 589 | 40.8% | 445 | 30.8% | 14 | 1.0% | 11 | 0.8% |
| **Total** | **5936** | **4204** | **70.8** | **708** | **16.8%** | **1602** | **38.1%** | **1030** | **24.5%** | **44** | **1.0%** | **53** | **1.3%** |

**Table 7. HPV primary screening: detection rate of CIN following referral to colposcopy at 1st test (up to 31st July 2014 / 18th June 2014 for Liverpool)**

| Site | Total tested | CIN 1 | (% of tested) | CIN 2 + | (% of tested) | CIN 3 + | (% of tested) | Cervical Cancer | (% of tested) | Outcome not known | (% of tested) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Bristol | 15538 | 81 | (0.52) | 93 | (0.60) | 41 | (0.26) | 1 | (0.01) | 16 | (0.10) |
| Liverpool | 12898 | 59 | (0.46) | 227 | (1.76) | 142 | (1.10) | 3 | (0.02) | 0 | (0.00) |
| London | 15230 | 147 | (0.97) | 190 | (1.25) | 83 | (0.54) | 2 | (0.01) | 0 | (0.00) |
| Manchester | 45316 | 207 | (0.46) | 388 | (0.86) | 242 | (0.53) | 18 | (0.04) | 25 | (0.06) |
| Norfolk and Norwich | 12404 | 83 | (0.67) | 115 | (0.93) | 77 | (0.62) | 6 | (0.05) | 1 | (0.01) |
| Sheffield | 35728 | 131 | (0.37) | 589 | (1.65) | 445 | (1.25) | 14 | (0.04) | 11 | (0.03) |
| **Total** | **137114** | **708** | **(0.52)** | **1602** | **(1.17)** | **1030** | **(0.75)** | **44** | **(0.03)** | **53** | **(0.04)** |

**Table 8A. Primary cytology : Colposcopy outcomes, (PPV of colposcopy attendance) (women referred at their 1st test, up to 31st July 2014) by site**

| Site | Total referred | Total attended | (% of referred) | CIN1 | (% of attended) | CIN 2 + | (% of attended) | CIN 3 + | (% of attended) | Cervical Cancer | (% of attended) | Outcome not known | (% of attended) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bristol | **1709** | **718** | **(42.0)** | **140** | **(19.5)** | **166** | (23.1) | **70** | (9.7) | **4** | **(0.6)** | **36** | **(5.0)** |
| London | **2656** | **1335** | **(50.3)** | **391** | **(29.3)** | **280** | (21.0) | **155** | (11.6) | **10** | **(0.7)** | **0** | **(0.0)** |
| Norfolk and Norwich | **1713** | **1707** | **(99.6)** | **340** | **(19.9)** | **698** | (40.9) | **521** | (30.5) | **24** | **(1.4)** | **14** | **(0.8)** |
| Sheffield | **2666** | **2320** | **87.0%** | **387** | **(16.7)** | **1011** | 43.6% | **675** | 29.1% | **21** | **0.9%** | **42** | **(1.8)** |
| **Total** | **8744** | **6080** | **69.5%** | **1258** | **(20.7)** | **2155** | 35.4% | **1421** | 23.4% | **59** | **1.0%** | **92** | **1.5%** |

**Table 8B. Primary cytology : Colposcopy outcomes, (PPV of colposcopy attendance) by cytology (women referred at their 1st test, up to 31st July 2014) by site**

| Cytology grade | Total referred | Total attended | % of referred | CIN 1 | ( % of attended) | CIN 2 + | ( % of attended) | CIN 3 + | ( % of attended) | Cervical Cancer | ( % of attended) | Outcome not known | (% of attended) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Borderline/Mild | 5674 | 3755 | (66.2) | 1021 | (27.2) | 598 | (15.9) | 225 | (6.0) | 2 | | 64 | (1.7) |
| Moderate + | 2382 | 1956 | (82.1) | 203 | (10.4) | 1524 | (77.9) | 1188 | (60.7) | 56 | (2.9) | 14 | (0.7) |
| Negative | 729 | 353 | (48.4) | 34 | (9.6) | 14 | (4.0) | 7 | (2.0) | 0 | (0.0) | 14 | (4.0) |
| Inadequate | 59 | 16 | (27.1) | 0 | (0.0) | 1 | (6.2) | 1 | (6.2) | 1 | (6.2) | 0 | (0.0) |
| **Total** | **8744** | **6080** | **69.5%** | **1258** | **(20.7)** | **2155** | 35.4% | **1421** | 23.4% | **59** | **1.0%** | **92** | **1.5%** |

**Table 9. Primary cytology testing: detection rate of CIN following referral to colposcopy at 1st test (up to 31st July 2014)**

| Site | Total tested | CIN 1 | (% of tested) | CIN 2 + | (% of tested) | CIN 3 + | (% of tested) | Cervical Cancer | (% of tested) | Outcome not known | (% of tested) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Bristol | 38675 | 140 | (0.36) | 166 | (0.43) | 70 | (0.18) | 4 | (0.01) | 36 | (0.09) |
| London | 47920 | 391 | (0.82) | 280 | (0.58) | 155 | (0.32) | 10 | (0.02) | 0 | (0.00) |
| Norfolk and Norwich | 49185 | 340 | (0.69) | 698 | (1.42) | 521 | (1.06) | 24 | (0.05) | 14 | (0.03) |
| Sheffield | 61618 | 387 | (0.63) | 1011 | (1.64) | 675 | (1.10) | 21 | (0.03) | 42 | (0.07) |
| **Total** | **197318** | **1258** | **(0.64)** | **2155** | **(1.09)** | **1421** | **(0.72)** | **59** | **(0.03)** | **92** | **(0.05)** |

**Table 10. HPV primary screening summary table**

| | 24 - 29 | | 30 - 64 | | 24 - 49 | | 50 - 64 | | All ages | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Total tested** | 31666 | | 134906 | | 127023 | | 39549 | | 167919 | |
| **HPV Positive (% of tested)** | 9108 | (28.8) | 12421 | (9.2) | 19259 | (15.2) | 2270 | (5.7) | 21682 | (12.9) |
| **(95%CI)** | | (28.2-29.3) | | (9.1-9.4) | | (15.0-15.4) | | (5.5-6.0) | | (12.8-13.1) |
| **Referred (% of tested)** | 3519 | (11.1) | 3662 | (2.7) | 6633 | (5.2) | 548 | (1.4) | 7235 | (4.3) |
| **(95% CI)** | | (10.8-11.5) | | (2.6-2.8) | | (5.1-5.3) | | (1.3-1.5) | | (4.2-4.4) |
| **PPV of HPV for referral** | 3518 | (38.6) | 3656 | (29.4) | 6626 | (34.4) | 548 | (24.1) | 7228 | (33.3) |
| **(95% CI)** | | (37.6-39.6) | | (28.6-30.2) | | (33.7-35.1) | | (22.4-25.9) | | (32.7-24.0) |
| **HPV + Cytology neg (12 mth repeats)** | 5484 | (17.3) | 8619 | (6.4) | 12408 | (9.8) | 1695 | (4.3) | 14199 | (8.5) |
| **n (%) retested[1]** | 247 | (67.7) | 505 | (74.5) | 654 | (71.1) | 98 | (79.0) | 757 | (72.0) |
| **HPV + 12 months later n (% of tested)** | 157 | (63.6) | 291 | (57.6) | 390 | (59.6) | 58 | (59.2) | 59.8 | |
| **Attended Colp [2] (% of referred)** | 2045 | (70.6) | 2128 | (71.1) | 3872 | (71.1) | 301 | (67.6) | 4204 | (70.8) |
| **CIN 2+ (PPV of colposcopy)** | 888 | (43.4) | 706 | (34.5) | 1521 | (39.3) | 73 | (24.3) | 1602 | (38.1) |
| | | (41.3-45.6) | | (31.2-35.2) | | (37.7-40.8) | | (19.4-29.1) | | (36.6-39.6) |
| **CIN 3+ (PPV) of colposcopy)** | 587 | (28.7) | 441 | (21.6) | 986 | (25.5) | 42 | (14.0) | 1030 | (24.5) |
| **Detection CIN 2+ (% of tested to 31.07.2014)** | | (3.41) | | (0.64) | | (1.47) | | (0.23) | | (1.17) |
| **(95% CI)** | | (3.20-3.64) | | (0.60-0.69) | | (1.40-1.54) | | (1.77-2.89) | | (1.11-1.23) |
| **Detection CIN 3+ (% of tested to 31.07.2014)** | | (2.26) | | (0.40) | | (0.95) | | (0.13) | | (0.75) |

**1. due for retesting by 31.7.2014**

**2. Referrals to 31.7.2014**

**Table 11. Primary cytology summary table**

| | 24 - 29 | | 30 - 64 | | 24 - 49 | | 50 - 64 | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Total tested** | 61171 | | 267189 | | 250130 | | 78230 | | 331955 | |
| **HPV Positive (% of tested)** | 3665 | (61.8) | 5086 | (41.7) | 7871 | (49.8) | 880 | (38.0) | 8834 | (48.2) |
| **Referred (% of tested)** | 5763 | (9.4) | 7535 | (2.8) | 12037 | (4.8) | 1261 | (1.6) | 13447 | (4.1) |
| **(95% CI)** | | (9.2-9.7) | | (2.76-2.88) | | (4.7-4.9) | | (1.5-1.7) | | (3.98-4.11) |
| **PPV, of Borderline/ Mild for referral** | 3485 | (73.1) | 4871 | (51.3) | 7499 | (61.4) | 857 | (41.7) | 8463 | (58.4) |
| **Attended Colp[2] (% of referred)** | 2623 | (73.2) | 3422 | (67.5) | 5455 | (71.1) | 590 | (65.2) | 6080 | (69.5) |
| **CIN 2+ (PPV of colposcopy)** | 1160 | (44.2) | 987 | (28.8) | 2033 | (37.3) | 114 | (19.3) | 2155 | (35.4) |
| **(95% CI)** | | (42.3-46.1) | | (27.3-30.4) | | | | | | |
| **CIN 3+ (PPV of colposcopy)** | 755 | (28.8) | 663 | (19.4) | 1342 | (24.6) | 76 | (12.9) | 1421 | (23.4) |
| **Detection CIN 2+ (% of tested to 31.07.2014)** | | (3.10) | | (0.62) | | (1.36) | | (0.25) | | (1.09) |
| **(95% CI)** | | (3.02-3.39) | | (0.59-0.66) | | (1.30-1.42) | | (0.21-0.30) | | (1.05-1.14) |
| **Detection CIN 3+ (% of tested to 31.07.2014)** | | (2.02) | | (0.42) | | (0.89) | | (0.17) | | (0.72) |

**2. Referrals to 31.7.2014**

**Table 12. Referral rates by site**

| | HPV primary | | | Primary cytology | | |
|---|---|---|---|---|---|---|
| **Site** | **Tested** | **Referred** | **(% of tested)** | **Tested** | **Referred** | **(% of tested)** |
| Bristol | 19608 | 913 | (4.7%) | 48159 | 2080 | (4.3%) |
| Liverpool | 15926 | 796 | (5.0%) | - | - | - |
| London | 18629 | 1006 | (5.4%) | 59238 | 3127 | (5.3%) |
| Manchester | 56525 | 2267 | (4.0%) | 91901 | 3024 | (3.3%) |
| Norfolk and Norwich | 14734 | 415 | (2.8%) | 59090 | 2069 | (3.5%) |
| Sheffield | 42497 | 1838 | (4.3%) | 73567 | 3147 | (4.3%) |
| **Total** | **167919** | **7235** | **(4.3%)** | **331955** | **13447** | **(4.1%)** |

**Figure 1. HPV positive rates by month**

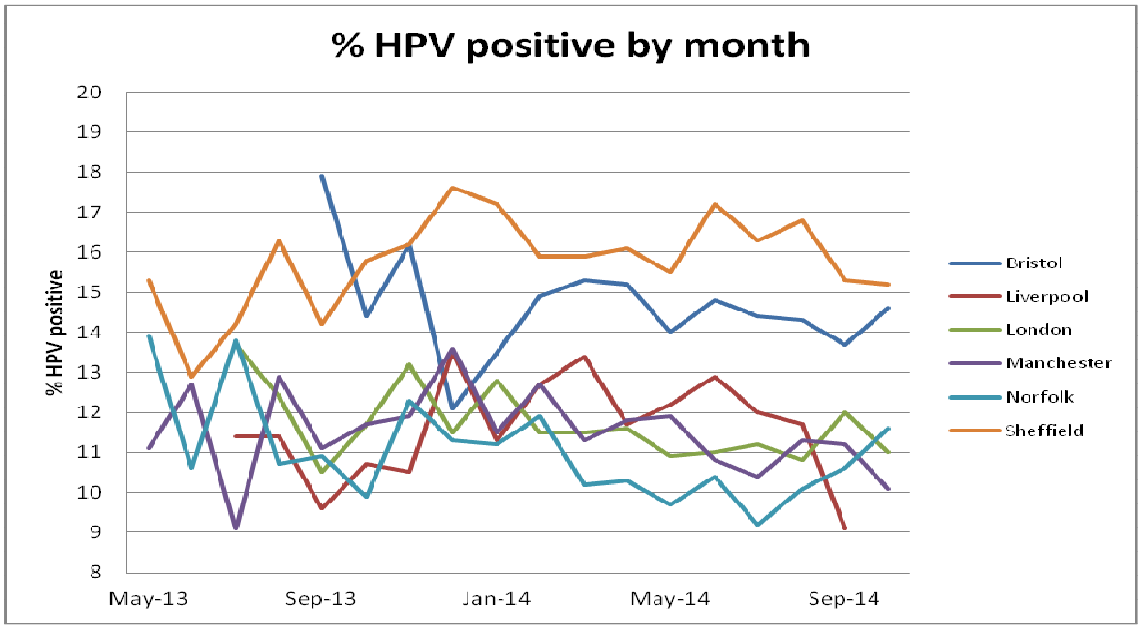
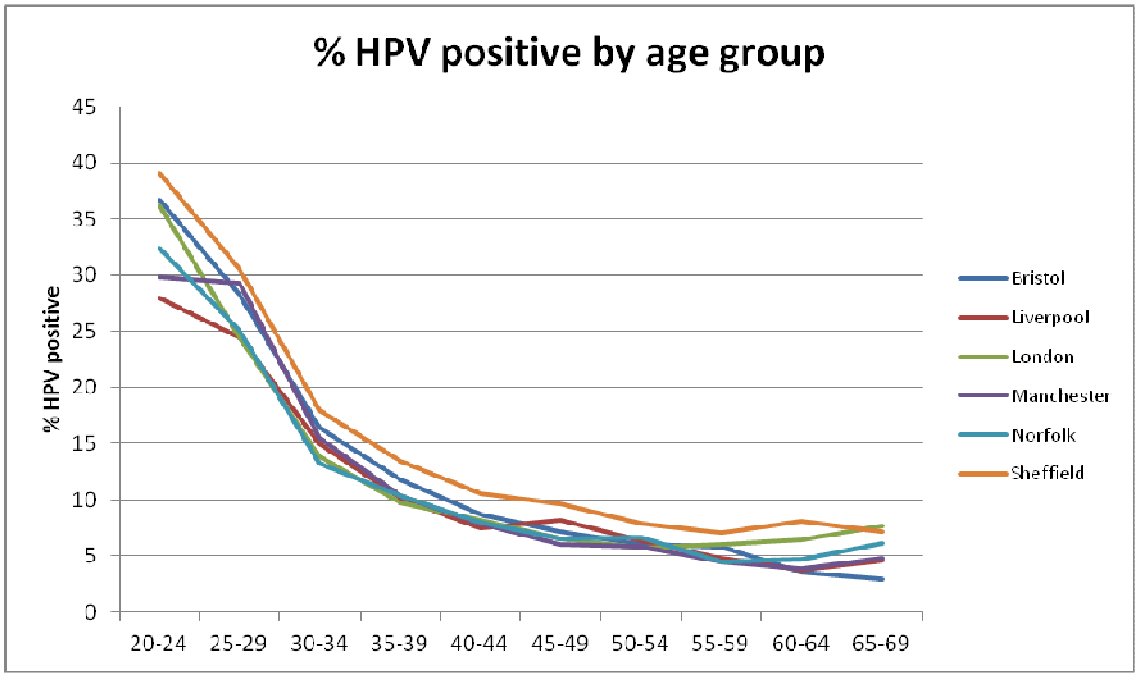
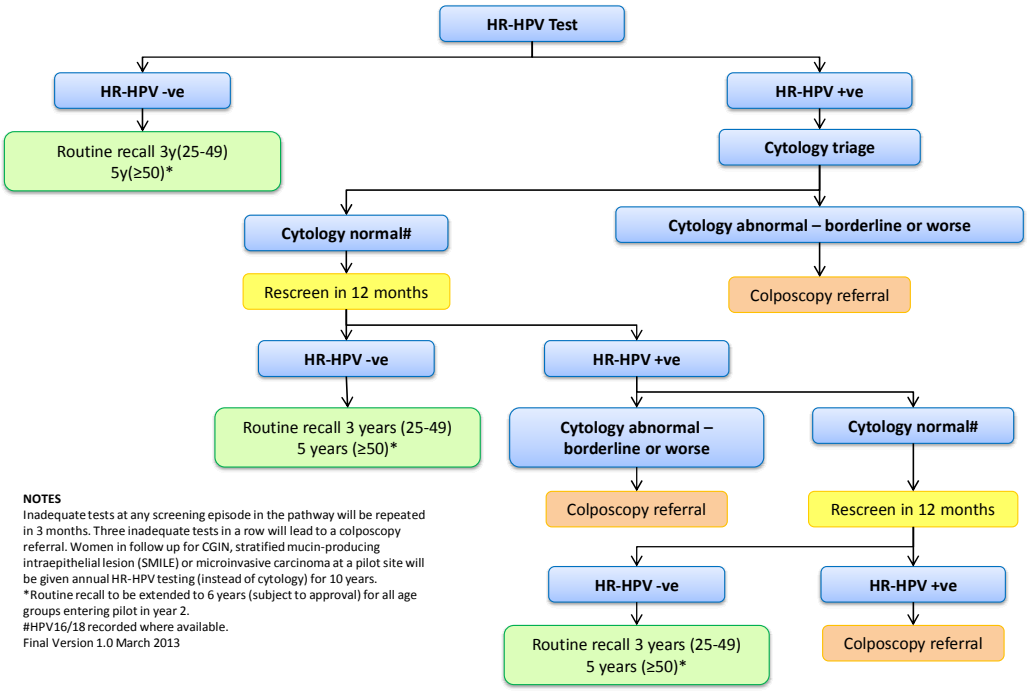


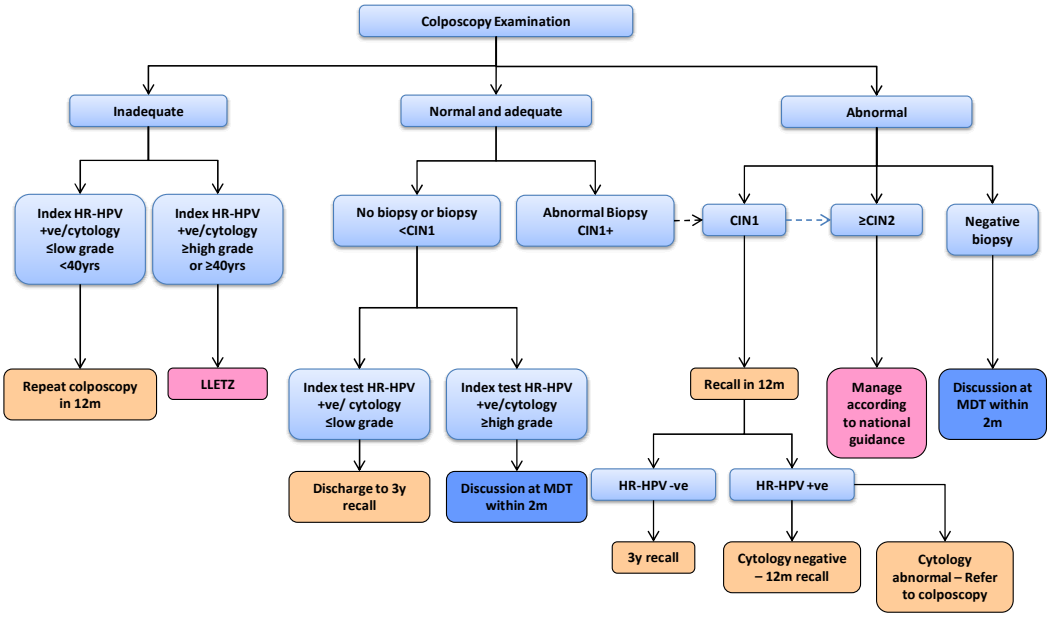

**Figure 2. HPV positive rates by age groups**



APPENDIX




HPV Primary Screening Algorithm – Pilot Year 1:
All women aged 25-64 on routine call/recall and early recall




HPV Primary Screening Pilot: Colposcopy Management Recommendations