**Supplementary tables:**

**S1 Table. Distribution of cytology results among screen positives in HPV-Screening Arm. by lab and time period since start of the pilot study.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Time period** | **01.02.2015-31.05.2015** | | **01.06.2015-01.10.2015** | | **01.10.2015-01.07.2017** | |
| **Lab 1** | N | % | N | % | N | % |
| **Screen positives** | 179 | 6.2 | 296 | 7.4 | 1325 | 6.6 |
| **Cytology categories** | |  |  |  |  |  |
| NILM | 108 | 60.3 | 183 | 62.0 | 818 | 62.2 |
| ASC-US | 26 | 14.5 | 38 | 12.9 | 170 | 12.9 |
| LSIL | 18 | 10.1 | 18 | 6.1 | 107 | 8.1 |
| ASC-H | 5 | 2.8 | 12 | 4.1 | 51 | 3.9 |
| HSIL. AGC. & AIS | 17 | 9.5 | 22 | 7.5 | 93 | 7.1 |
| Cervical cancer | 0 | 0.0 | 1 | 0.3 | 3 | 0.2 |
| Inadequate\* | 5 | 2.8 | 21 | 7.1 | 74 | 5.6 |
| NA |  | - | 1 | - | 9 | - |
| **Lab 2** |  |  |  |  |  |  |
| **Screen positives** | 213 | 6.7 | 200 | 5.9 | 1003 | 6.4 |
| **Cytology categories** | |  |  |  |  |  |
| NILM | 44 | 20.8 | 104 | 52.0 | 541 | 54.0 |
| ASC-US | 101 | 47.6 | 50 | 25.0 | 226 | 22.6 |
| LSIL | 10 | 4.7 | 11 | 5.5 | 68 | 6.8 |
| ASC-H | 37 | 17.5 | 9 | 4.5 | 85 | 8.5 |
| HSIL. AGC. & AIS | 13 | 6.1 | 22 | 11.0 | 64 | 6.4 |
| Cervical cancer | 1 | 0.5 | 0 | 0.0 | 0 | 0.0 |
| Inadequate | 6 | 2.8 | 4 | 2.0 | 18 | 1.8 |
| NA | 1 | - | 0 | - | 1 | - |
| **Lab 3** |  |  |  |  |  |  |
| **Screen positives** | 129 | 7.5 | 227 | 6.2 | 1114 | 6.5 |
| **Cytology categories** | |  |  |  |  |  |
| NILM | 79 | 61.7 | 129 | 56.8 | 669 | 61.2 |
| ASC-US | 24 | 18.8 | 30 | 13.2 | 135 | 12.3 |
| LSIL | 11 | 8.6 | 34 | 15.0 | 109 | 10.0 |
| ASC-H | 4 | 3.1 | 12 | 5.3 | 58 | 5.3 |
| HSIL. AGC. & AIS | 8 | 6.3 | 17 | 7.5 | 87 | 8.0 |
| Cervical cancer | 0 | 0.0 | 0 | 0.0 | 4 | 0.4 |
| Inadequate | 2 | 1.6 | 5 | 2.2 | 32 | 2.9 |
| NA | 1 | - | 0 | - | 20 | - |

\*One possible explanation for the high proportion of inadequate LBC in Norway could be related to the overall low volume of screening examinations performed by family doctors, who, on average, take only 72 cervical samples annually. The quality of LBC with ThinPrep is indeed dependent on the experience of the smear taker, as blood, mucus, and gynaecological gel can clog the filter during preparation. However, the proportion of inadequate smears in the three labs in our study varied between 1.6% and 7.1% indicating that there are reasons beyond smear collection that may influence the quality of the screening sample, such as preparation and interpretation.

Abbreviations: adenocarcinoma *in situ* (AIS), high-grade squamous intraepithelial lesion (HSIL), atypically squamous cells cannot rule out HSIL (ASC-H), atypical glandular cells (AGC), low-grade squamous intraepithelial lesion (LSIL), atypical squamous cells of undetermined significance (ASC-US), and negative for intraepithelial lesions or malignancy (NILM)

**S2 Table.**  **Comparison of the number of colposcopy referrals and the number, percentage and positive predictive values of CIN2+ and CIN3+ overall and by age among guideline based colposcopy referrals in HPV-screening protocol or LBC-screening protocol.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Age groups (Years)** | | | | | | | **Total** |
|  | **34-39** | **40-44** | **45-49** | **50-54** | **55-59** | **60-64** | **65-69** |
| **HPV-Screening** | N | N | N | N | N | N | N | N |
|  | 14 847 | 12 361 | 12 565 | 11 133 | 10 029 | 8 775 | 7 497 | 77 207 |
| **Number of colposcopies (% of total number of women)** | | | | | | | |  |
| baseline | 595 (4.0) | 461 (3.7) | 305 (2.4) | 206 (1.9) | 126 (1.3) | 95 (1.1) | 68 (0.9) | 1 853 (2.4) |
| increased surveillance | 310 (2.1) | 216 (1.7) | 177 (1.4) | 149 (1.3) | 141 (1.4) | 116 (1.3) | 96 (1.3) | 1 205 (1.6) |
| RR (95%CI) | 1.9 (1.7 to 2.2) | 2.1 (1.8 to 2.5) | 1.7 (1.4 to 2.1) | 1.4 (1.1 to 1.7) | 0.9 (0.7 to 1.1) | 0.8 (0.6 to 1.1) | 0.7 (0.5 to 1.0) | 1.5 (1.4 to 1.7) |
| **Number of CIN2+ (PPV% CIN2+)** | | | | | | | | |
| baseline | 355 (60) | 238 (52) | 149 (49) | 75 (36) | 50 (40) | 33 (35) | 25 (37) | 925 (50) |
| increased surveillance | 103 (33) | 57 (26) | 32 (18) | 19 (13) | 17 (12) | 13 (11) | 10 (10) | 261 (22) |
| RR (95%CI) | 1.8 (1.5 to 2.1) | 2.0 (1.5 to 2.5) | 2.7 (1.9 to 3.8) | 2.9 (1.8 to 4.5) | 3.3 (2.0 to 5.4) | 3.1 (1.7 to 5.5) | 3.5 (1.8 to 6.9) | 2.3 (2.1-2.6) |
| **Number of CIN3+ (PPV % CIN3+)** | | | | | | | | |
| baseline | 299 (50) | 192 (42) | 118 (39) | 61 (30) | 38 (30) | 23 (24) | 22 (32) | 753 (41) |
| increased surveillance | 74 (24) | 45 (21) | 21 (12) | 17 (11) | 12 (9) | 8 (7) | 6 (6) | 183 (15) |
| RR (95%CI) | 2.1 (1.7 to2.6) | 2 (1.5 to 2. 6) | 3.3 (2.1 to 5.0) | 2.6 (1.6 to 4.3) | 3.5 (1.9 to 6.5) | 3.5 (1. 6 to 7.5) | 5.2 (2.2 to 12.1) | 2.7 (2.3 to 3.1) |
|  | | | | | | | | |
| **LBC-Screening** | N | N | N | N | N | N | N | N |
|  | 15 123 | 12 804 | 13 033 | 11 737 | 10 341 | 9 375 | 7 827 | 80 240 |
| **Number of colposcopies (% of total number of women)** | | | | | | | |  |
| baseline | 317 (2.1) | 210 (1.6) | 173 (1.3) | 80 (0.7) | 66 (0.6) | 47 (0.5) | 30 (0.4) | 923 (1.2) |
| increased surveillance | 164 (1.1) | 109 (0.9) | 84 (0.6) | 54 (0.5) | 41 (0.4) | 30 (0.3) | 9 (0.1) | 491 (0.6) |
| RR (95%CI) | 1.9 (1.6 to 2.3) | 1.9 (1.5 to 2.4) | 2.1 (1.6 to 2.7) | 1.5 (1.1 to 2.1) | 1.6 (1.1 t0 2.4) | 1.6 (1.0 to 2.5) | 3.3 (1.6 to 7.0) | 1.9 (1.7 to 2.1) |
| **Number of CIN2+ (PPV% CIN2+)** | | | | | | | | |
| baseline | 211 (67) | 122 (58) | 89 (51) | 34 (43) | 22 (33) | 11 (23) | 12 (40) | 501 (54) |
| increased surveillance | 75 (46) | 56 (51) | 34 (40) | 23 (43) | 9 (22) | 11 (37) | 2 (22) | 210 (43) |
| RR (95%CI) | 1.5 (1.2 to 1.7) | 1.1 (0.9 to 1.4) | 1.3 (0.9 to 1.7) | 1 (0.7 to 1.5) | 1.5 (0.8 to 3.0) | 0.6 (0.3 to 1.3) | 1.8 (0.5 to 6.6) | 1.3 (1.1 to 1.4) |
| **Number of CIN3+ (PPV % CIN3+)** | | | | | | | | |
| baseline | 199 (60) | 115 (55) | 82 (47) | 27 (34) | 20 (30) | 10 (21) | 12 (40) | 465 (50) |
| increased surveillance | 59 (36) | 38 (35) | 26 (31) | 18 (33) | 5 (12) | 8 (27) | 2 (22) | 157 (32) |
| RR (95%CI) | 1.8 (1.4 to 2.2) | 1.6 (1.2 to 2.1) | 1. 5 (1.1 to 2.2) | 1. 0 (0.6 to 1.6) | 2.5 (1.0 to 6.1) | 0.8 (0.4 to 1.8) | 2. 3 (0.5 to 6.6) | 1.6 (1.4 to 1. 8) |

\* Colposcopy examination was always supplemented by tissue sampling which provided a histology diagnose and all women were followed up for the period of 18 months from the baseline exam

Abbreviations: human papillomavirus (HPV), liquid-based cytology (LBC), CIN=cervical intraepithelial neoplasia; CIN1=CIN grade 1; CIN2=CIN grade 2; CIN3=CIN grade 3; ACIS=adenocarcinoma in situ, positive predictive value (PPV) RR= risk ratio; CI=confidence interAA