SUPPLEMENTARY FIGURE 1 Total effectiveness of the AS04-HPV-16/18 vaccine against cervical infection with HPV-16/18 in young women: vaccination of girls and boys, girls only, or regardless of vaccination strategy (enrolled cohort)

CI: confidence interval; HPV: human papillomavirus; VE: vaccine effectiveness
|                  | Arm A |                  | Arm B |                  | Arm C |                  |
|------------------|-------|------------------|-------|------------------|-------|------------------|
|                  | AS04-HPV-16/18 |                  | AS04-HPV-16/18 |                  | AS04-HPV-16/18 |                  |
|                  | n or mean | %     | n or mean | %     | n or mean | %     | n or mean | %     | n or mean | %     | n or mean | %     |
| Birth cohort     |         |       |          |       |          |       |          |       |          |       |          |       |
| 1992             | 1,382   | 23.8  | 163      | 24.4  | 141      | 23.7  | 1738     | 26.3  | 204      | 26.6  | 171      | 23.4  | 1,754   | 26.2  | 153      | 25.6  |
| 1993             | 1,453   | 25.1  | 168      | 25.1  | 132      | 22.1  | 1656     | 25.1  | 192      | 25.1  | 166      | 22.7  | 1,552   | 23.2  | 143      | 24.0  |
| 1994             | 1,591   | 27.4  | 182      | 27.2  | 191      | 32.0  | 1660     | 25.1  | 191      | 24.9  | 208      | 28.4  | 1,732   | 25.9  | 158      | 26.5  |
| 1995             | 1,373   | 23.7  | 156      | 23.3  | 131      | 22.0  | 1547     | 23.4  | 179      | 23.4  | 187      | 25.5  | 1,646   | 24.6  | 143      | 24.0  |
| Missing or NA    | 0       | 0.0   | 0        | 0.0   | 1        | 0.2   | 0        | 0.0   | 0        | 0.0   | 0        | 0.0   | 0       | 0.0   | 0       | 0.0   |
| Birth quarter    |         |       |          |       |          |       |          |       |          |       |          |       |         |       |         |       |
| Q1−Q2            | 2,986   | 51.5  | 353      | 52.8  | 298      | 50.0  | 3,427    | 51.9  | 382      | 49.9  | 382      | 52.2  | 3,381   | 50.6  | 330      | 55.3  |
| Q3−Q4            | 2,813   | 48.5  | 316      | 47.2  | 297      | 49.8  | 3,174    | 48.1  | 384      | 50.1  | 350      | 47.8  | 3,303   | 49.4  | 267      | 44.7  |
| Missing or NA    | 0       | 0.0   | 0        | 0.0   | 1        | 0.2   | 0        | 0.0   | 0        | 0.0   | 0        | 0.0   | 0       | 0.0   | 0       | 0.0   |
| Area type        |         |       |          |       |          |       |          |       |          |       |          |       |         |       |         |       |
| Urban            | 5,360   | 92.4  | 617      | 92.2  | 578      | 97.0  | 5,304    | 80.4  | 611      | 79.8  | 598      | 81.7  | 5,915   | 88.5  | 544      | 91.1  |
| Semi-urban       | 439     | 7.6   | 52       | 7.8   | 18       | 3.0   | 1,297    | 19.6  | 155      | 20.2  | 134      | 18.3  | 769     | 11.5  | 53       | 8.9   |
| HPV-16/18 seroprevalence stratum |         |       |          |       |          |       |          |       |          |       |          |       |         |       |         |       |
| <20.5%           | 1,739   | 30.0  | 202      | 30.2  | 235      | 39.4  | 1,850    | 28.0  | 218      | 28.5  | 242      | 33.1  | 2,832   | 42.4  | 237      | 39.7  |
| 20.5–24%         | 1,418   | 24.5  | 162      | 24.2  | 153      | 25.7  | 1,344    | 20.4  | 159      | 20.8  | 139      | 19.0  | 1,358   | 20.3  | 106      | 17.8  |
| Arm A | Arm B | Arm C |
|-------|-------|-------|
| **AS04-HPV-16/18** | **Hepatitis B** | **Not vaccinated** | **AS04-HPV-16/18** | **Hepatitis B** | **Not vaccinated** | **Hepatitis B** | **Not vaccinated** |
| n or mean | % | n or mean | % | n or mean | % | n or mean | % | n or mean | % | n or mean | % |
| >24% | 2,642 | 45.6 | 305 | 45.6 | 208 | 34.9 | 3,407 | 51.6 | 389 | 50.8 | 351 | 48.0 | 2,494 | 37.3 | 254 | 42.5 |
| Age at first vaccination, mean (SD), years | 14.1 (0.75) | - | 14.1 (0.76) | - | NA | - | 14.1 (0.75) | - | NA | - | 14.1 (0.75) | - | NA | - |
| Geographic ancestry | | | | | | | | | | | | | | | |
| White European | 5,722 | 98.7 | 660 | 98.7 | 559 | 93.8 | 6,537 | 99.0 | 757 | 98.8 | 690 | 94.3 | 6,631 | 99.2 | 527 | 88.3 |
| Other | 77 | 1.3 | 9 | 1.3 | 12 | 2.0 | 64 | 1.0 | 9 | 1.2 | 5 | 0.7 | 53 | 0.8 | 6 | 1.0 |
| Missing or NA | 0 | 0.0 | 0 | 0.0 | 25 | 4.2 | 0 | 0.0 | 0 | 0.0 | 37 | 5.1 | 0 | 0.0 | 64 | 10.7 |
| **Boys** | N = 2,436 | N = 299 | N = 73 | N = 2 | N = 4,880 | N = 129 | N = 4,040 | N = 109 |
| Birth cohort | | | | | | | | | | | | | | | |
| 1992 | 594 | 24.4 | 72 | 24.1 | 36 | 49.3 | 1 | 50.0 | 1,230 | 25.2 | 51 | 39.5 | 919 | 22.7 | 44 | 40.4 |
| 1993 | 546 | 22.4 | 71 | 23.7 | 17 | 23.3 | 0 | 0.0 | 1,234 | 25.3 | 41 | 31.8 | 948 | 23.5 | 35 | 32.1 |
| 1994 | 648 | 26.6 | 78 | 26.1 | 7 | 9.6 | 1 | 50.0 | 1,194 | 24.5 | 19 | 14.7 | 1,077 | 26.7 | 17 | 15.6 |
| 1995 | 648 | 26.6 | 78 | 26.1 | 13 | 17.8 | 0 | 0.0 | 1,222 | 25.0 | 18 | 14.0 | 1,096 | 27.1 | 13 | 11.9 |
| Birth quarter | | | | | | | | | | | | | | | |
| Q1–Q2 | 1,289 | 52.9 | 151 | 50.5 | 46 | 63.0 | 1 | 50.0 | 2,498 | 51.2 | 62 | 48.1 | 2,057 | 50.9 | 60 | 55.0 |
| Q3–Q4 | 1,147 | 47.1 | 148 | 49.5 | 27 | 37.0 | 1 | 50.0 | 2,382 | 48.8 | 67 | 51.9 | 1,983 | 49.1 | 49 | 45.0 |
| Area type | | | | | | | | | | | | | | | |
| Urban | 2,252 | 92.4 | 276 | 92.3 | 69 | 94.5 | 2 | 100 | 3,761 | 77.1 | 114 | 88.4 | 3,470 | 85.9 | 98 | 89.9 |
| Semi-urban | 184 | 7.6 | 23 | 7.7 | 4 | 5.5 | 0 | 0.0 | 1,119 | 22.9 | 15 | 11.6 | 570 | 14.1 | 11 | 10.1 |
|                  | Arm A |                  |                  | Arm B |                  |                  | Arm C |                  |                  |
|------------------|-------|------------------|------------------|-------|------------------|------------------|-------|------------------|------------------|
|                  | AS04-HPV-16/18 | Hepatitis B | Not vaccinated | AS04-HPV-16/18 | Hepatitis B | Not vaccinated | Hepatitis B | Not vaccinated |
| n or mean        | %     | n or mean        | %               | n or mean | %               | n or mean | %           | n or mean | %           |
| HPV-16/18 seroprevalence stratum |       |                   |                   |       |                   |                   |       |                   |                   |
| <20.5%           | 690   | 28.3             | 88               | 29.4    | 29               | 39.7    | 1            | 50.0    | 1,331       | 27.3           | 43              | 33.3           | 1,737          | 43.0           | 50             | 45.9           |
| 20.5−24%         | 621   | 25.5             | 76               | 25.4    | 10               | 13.7    | 1            | 50.0    | 1,137       | 23.3           | 24              | 18.6           | 880            | 21.8           | 14             | 12.8           |
| >24%             | 1,125 | 46.2             | 135              | 45.2    | 34               | 46.6    | 0            | 0.0     | 2,412       | 49.4           | 62              | 48.1           | 1,423          | 35.2           | 45             | 41.3           |
| Age at first vaccination, mean (SD), years |       |                   |                   |       |                   |                   |       |                   |                   |
| 14.1 (0.78)      | -     | 14.1 (0.76)      | -                | NA     | -                | 14.0 (1.41) | -            | 14.1 (0.77) | -              | NA             | 14.1 (0.76) | -              | NA             |               |
| Geographic ancestry |     |                   |                   |       |                   |                   |       |                   |                   |
| White European   | 2,409 | 98.9             | 296              | 99.0    | 0                | 0.0     | 2            | 100     | 4,832       | 99.0           | 0               | 0.0            | 4,014          | 99.4           | 0              | 0.0            |
| Other            | 27    | 1.1              | 3                | 1.0     | 0                | 0.0     | 0            | 0.0     | 48          | 1.0            | 0               | 0.0            | 26             | 0.6            | 0              | 0.0            |
| Missing or NA    | 0     | 0.0              | 0                | 0.0     | 0                | 73 100  | 0            | 0.0     | 0           | 0.0            | 129             | 100            | 0              | 0.0            | 109           | 100           |

The number of study participants shown is different to previously published data because an interim version of the study database was used formerly (Lehtinen M, Apter D, Baussano I, et al. Characteristics of a cluster-randomized phase IV human papillomavirus vaccination effectiveness trial. *Vaccine*. 2015;33(10):1284-1290)

AS04-HPV-16/18: AS04-adjuvanted HPV-16/18 vaccine; Hepatitis B: Hepatitis B vaccine; HPV: human papillomavirus; N: number of participants; n: number of participants in a given category; NA: not applicable; SD, standard deviation.
**SUPPLEMENTARY TABLE 2** Responses to behavioral questionnaire at Visit 5 (18.5 years of age) (enrolled cohort)

|                        | Arm A          | Arm B          | Arm C          |
|------------------------|----------------|----------------|----------------|
|                        | Girls N = 4,658 | Boys N = 797   | Girls N = 4,905 | Boys N = 637 | Girls N = 4,152 | Boys N = 493 |
| n or mean              | n or mean      | n or mean      | n or mean      | n or mean      | n or mean      | n or mean      |
| Usual residence        |                |                |                |                |                |                |
| Same community as school | 3,961 85.7    | 711 90.5       | 4,258 87.3     | 560 88.7       | 3,500 84.8     | 442 90.4       |
| Occasionally another community | 190 4.1     | 29 3.7         | 174 3.6        | 17 2.7         | 163 3.9        | 15 3.1         |
| Usually another community | 65 1.4       | 5 0.6          | 61 1.3         | 9 1.4          | 63 1.5         | 2 0.4          |
| Another community      | 406 8.8       | 41 5.2         | 387 7.9        | 45 7.1         | 403 9.8        | 30 6.1         |
| Missing                | 36 -          | 11 -           | 25 -           | 6 -            | 23 -           | 4 -            |
| Weekend and holiday residence |             |                |                |                |                |                |
| Same community as school | 3,129 67.4   | 574 72.3       | 3,380 69.1     | 462 72.8       | 2,722 65.7     | 352 72.1       |
| Occasionally another community | 1,431 30.8   | 207 26.1       | 1,426 29.2     | 162 25.5       | 1,351 32.6     | 130 26.6       |
| Usually another community | 85 1.8        | 13 1.6         | 84 1.7         | 11 1.7         | 73 1.8         | 6 1.2          |
| Missing                | 13 -          | 3 -            | 15 -           | 2 -            | 6 -            | 5 -            |
| Age at first menstruation, mean (SD), years | 12.7 (1.3) | NA -          | 12.6 (1.3) | NA -          | 12.6 (1.3) | NA -          |
| Sexual debut at time of study visit |                |                |                |                |                |                |
| Yes                    | 3,648 78.5    | 554 69.8       | 3,892 79.5     | 391 61.6       | 3,258 78.8     | 298 60.7       |
| No                     | 1,000 21.5    | 240 30.2       | 1,005 20.5     | 244 38.4       | 878 21.2       | 193 39.3       |
| Missing                | 10 -          | 3 -            | 8 -            | 2 -            | 16 -           | 2 -            |
| Age at sexual debut, mean (SD), years | 15.9 (1.3) | 16.0 (1.3) | 15.9 (1.3) | 16.1 (1.3) | 15.9 (1.3) | 16.0 (1.4) |
| Number of new partners during the last year | 0         | 1,097 30.2    | 184 33.3       | 1,251 32.3     | 128 32.7       | 1,078 33.2     | 111 37.6 |
|   | 1 | 2 | 3 | 4 | ≥5 | Missing |
|---|---|---|---|---|----|---------|
|   | 1,101 | 563 | 386 | 220 | 270 | 1,021 |
|   | 30.3 | 15.5 | 10.6 | 6.0 | 7.4 | - |
|   | 182 | 86 | 36 | 35 | 29 | 245 |
|   | 33.0 | 15.6 | 6.5 | 6.3 | 5.3 | - |
|   | 1155 | 574 | 371 | 254 | 272 | 1,028 |
|   | 29.8 | 14.8 | 9.6 | 6.6 | 7.0 | - |
|   | 153 | 44 | 22 | 23 | 21 | 246 |
|   | 39.1 | 11.3 | 5.6 | 5.9 | 5.4 | - |
|   | 948 | 491 | 331 | 167 | 230 | 907 |
|   | 29.2 | 15.1 | 10.2 | 5.1 | 7.1 | - |
|   | 105 | 38 | 19 | 10 | 12 | 198 |
|   | 35.6 | 12.9 | 6.4 | 3.4 | 4.1 | - |

**Smoking**

|                  | N | n | NA | SD |
|------------------|---|---|----|----|
| Never smoked     | 2,719 | 58.6 | 489 | 62.0 |
| Former smoker    | 318 | 6.9 | 49 | 6.2 |
| Current cigarette smoker | 1,586 | 34.2 | 228 | 28.9 |
| Current smoker other than cigarettes | 14 | 0.3 | 23 | 2.9 |
| Missing          | 21 | - | 8 | - |

**Alcohol consumption**

|                  | N | n | NA | SD |
|------------------|---|---|----|----|
| None             | 303 | 6.5 | 56 | 7.1 |
| Once a month or less | 1,765 | 38.0 | 257 | 32.4 |
| 2–4 times a month | 2,196 | 47.3 | 364 | 45.9 |
| 1–2 times a week  | 355 | 7.6 | 104 | 13.1 |
| Three times a week or more | 22 | 0.5 | 12 | 1.5 |
| Missing          | 17 | - | 4 | - |

**Drug use**

|                  | N | n | NA | SD |
|------------------|---|---|----|----|
| Never            | 3,858 | 83.2 | 668 | 84.3 |
| Once             | 379 | 8.2 | 52 | 6.6 |
| Twice            | 153 | 3.3 | 30 | 3.8 |
| Three times or more | 248 | 5.3 | 42 | 5.3 |
| Missing          | 20 | - | 5 | - |
**SUPPLEMENTARY TABLE 3** Overall effectiveness of the AS04-HPV-16/18 vaccine against cervical infection with different oncogenic HPV types in young women: vaccination of girls and boys (Arm A), girls only (Arm B), or regardless of vaccination strategy (pooled Arms A and B) (enrolled cohort)

| HPV type | Arm | N invited | Vaccine group | N | n (%) | Vaccine effectiveness, % (95% CI) | P-value |
|----------|-----|-----------|---------------|---|-------|-----------------------------------|---------|
| HPV-31/45 | A   | 12,243    | AS04-HPV-16/18 | 2,784 | 36 (1.3) | 34.5 (-5.1, 59.2) | 0.079 |
|          |     |           | Hepatitis B    | 346  | 31 (9.0) |                     |         |
|          |     |           | Unvaccinated   | 499  | 30 (6.0) |                     |         |
|          |     |           | Total          | 3,629| 97 (4.0) |                     |         |
|          | B   | 14,570    | AS04-HPV-16/18 | 3,069 | 34 (1.1) | 41.3 (6.0, 63.3) | 0.027 |
|          |     |           | Hepatitis B    | 369  | 28 (7.6) |                     |         |
|          |     |           | Unvaccinated   | 591  | 31 (5.2) |                     |         |
|          |     |           | Total          | 4,029| 93 (3.5) |                     |         |
|          |     |           | Pooled A/B     | 5,853| 70 (1.2) | 38.4 (11.2, 57.3) | 0.009 |
|          |     |           | Hepatitis B    | 715  | 59 (8.3) |                     |         |
|          |     |           | Unvaccinated   | 1,090| 61 (5.6) |                     |         |
|          |     |           | Total          | 7,658| 190 (3.7) |                 |         |
|          | C   | 12,607    | Hepatitis B    | 2,711 | 154 (5.7) | -                  | -      |
|          |     |           | Unvaccinated   | 457  | 28 (6.1) |                     |         |
|          |     |           | Total          | 3,168| 182 (5.9) |                     |         |
| HPV-31/33/45 | A   | 12,243    | AS04-HPV-16/18 | 2,784 | 85 (3.1) | 25.2 (-9.9, 49.1) | 0.139 |
|          |     |           | Hepatitis B    | 346  | 42 (12.1) |                     |         |
|          |     |           | Unvaccinated   | 499  | 48 (9.6) |                     |         |
|          |     |           | Total          | 3,629| 175 (6.7) |                     |         |
|          | B   | 14,570    | AS04-HPV-16/18 | 3,069 | 88 (2.9) | 35.0 (5.7, 55.2) | 0.023 |
|          |     |           | Hepatitis B    | 369  | 36 (9.8) |                     |         |
|          |     |           | Unvaccinated   | 591  | 49 (8.3) |                     |         |
|          |     |           | Total          | 4,029| 173 (5.9) |                     |         |
|          |     |           | Pooled A/B     | 5,853| 173 (3.0) | 30.6 (6.6, 48.5) | 0.016 |
|          |     |           | Hepatitis B    | 715  | 78 (10.9) |                     |         |
|          |     |           | Unvaccinated   | 1,090| 97 (8.9) |                     |         |
|          |     |           | Total          | 7,658| 348 (6.3) |                     |         |
|          | C   | 12,607    | Hepatitis B    | 2,711 | 231 (8.5) | -                  | -      |
|          |     |           | Unvaccinated   | 457  | 40 (8.8) |                     |         |
|          |     |           | Total          | 3,168| 271 (8.6) |                     |         |
| HPV-31/33/45/51/52 | A   | 12,243    | AS04-HPV-16/18 | 2,784 | 380 (13.6) | 0.3 (-3.4, 23.7) | 0.985 |
|          |     |           | Hepatitis B    | 346  | 78 (22.5) |                     |         |
|          |     |           | Unvaccinated   | 499  | 105 (21.0) |                 |         |
|          |     |           | Total          | 3,629| 563 (17.6) |                 |         |
|          | B   | 14,570    | AS04-HPV-16/18 | 3,069 | 412 (13.4) | 11.4 (-14.2, 31.2) | 0.351 |
|          |     |           | Hepatitis B    | 369  | 67 (18.2) |                     |         |
|          |     |           | Unvaccinated   | 591  | 106 (17.9) |                 |         |
|          |     |           | Total          | 4,029| 585 (15.9) |                 |         |
| Group       | N invited | N                  | n                  | % of n | CI               | p-value |
|-------------|-----------|--------------------|--------------------|--------|------------------|---------|
| Pooled A/B  | 26,813    | 5,853              | 792 (13.5)         | 6.4 (-14.6, 23.5) | 0.523  |
| Hepatitis B | 715       | 145 (20.3)         |                    |        |                  |         |
| Unvaccinated| 1,090     | 211 (19.4)         |                    |        |                  |         |
| Total       | 7,658     | 1,148 (16.7)       |                    |        |                  |         |
| C           | 12,607    | 2,711              | 445 (16.4)         |        | -                | -       |
| Hepatitis B | 2,711     | 445 (16.4)         |                    |        |                  |         |
| Unvaccinated| 457       | 87 (19.0)          |                    |        |                  |         |
| Total       | 3,168     | 532 (17.7)         |                    |        |                  |         |

| Group       | N invited | N                  | n                  | % of n | CI               | p-value |
|-------------|-----------|--------------------|--------------------|--------|------------------|---------|
| Any oncogenic HPV type† | A | 12,243 | 2,784 | 675 (24.2) | -2.6 (-30.1, 19.1) | 0.833 |
| Hepatitis B | 346 | 117 (33.8) |        |     |                  |         |
| Unvaccinated | 499 | 173 (34.7) |        |     |                  |         |
| Total       | 3,629 | 965 (29.7) |        |     |                  |         |
| B           | 14,570   | 3,069 | 726 (23.7) | 12.0 (-4.5, 25.8) | 0.145 |
| Hepatitis B | 369 | 103 (27.9) |        |     |                  |         |
| Unvaccinated | 591 | 170 (28.8) |        |     |                  |         |
| Total       | 4,029 | 999 (26.4) |        |     |                  |         |
| Pooled A/B  | 26,813   | 5,853 | 1401 (23.9) | 5.8 (-13.0, 21.4) | 0.519 |
| Hepatitis B | 715 | 220 (30.8) |        |     |                  |         |
| Unvaccinated | 1,090 | 343 (31.5) |        |     |                  |         |
| Total       | 7,658 | 1964 (27.9) |        |     |                  |         |
| C           | 12,607   | 2,711 | 737 (27.2) |        | -                | -       |
| Hepatitis B | 2,711 | 737 (27.2) |        |     |                  |         |
| Unvaccinated | 457 | 146 (31.9) |        |     |                  |         |
| Total       | 3,168 | 883 (29.5) |        |     |                  |         |

†HPV-16/18/31/33/35/39/45/51/52/56/58/59/66/68

AS04-HPV-16/18: AS04-adjuvanted HPV-16/18 vaccine; CI: confidence interval; Hepatitis B: Hepatitis B vaccine; HPV: human papillomavirus; N invited: number invited to participate in the study; N: number of participants with available results; n: number of participants with HPV-16/18 cervical infection; %: n/N except for the total, where%

% = (n[AS04-HPV-16/18]+n[hepatitis B]+w*n[not vaccinated])/N[AS04-HPV-16/18]+N[hepatitis B]+w*N[not vaccinated]