

**Supplementary Table 1.** Estimated ERSPC model parameters\*

| Onset is modeled by<br>a hazard function (5 parameters)†   |          | Transition probability (12 parameters)  |          |             |      |
|--|----------|---|----------|-------------|------|
|  |          | From  | To       | Probability |      |
| Age in years   | Hazard   |   |          |             |      |
| 0  | 0.0000   | T1G6Mx  | T1G7Mx   | 0.27        |      |
| 30   | 0.0000   |   | T2G6Mx   | 0.71        |      |
| 50   | 0.0005   | T1G7Mx  | Clinical | 0.02        |      |
| 70   | 0.0170   |   | T1G8Mx   | 0.19        |      |
| 100  | 0.0503   |   | T2G7Mx   | 0.78        |      |
|  |          | T1G8Mx  | Clinical | 0.03        |      |
| <b>Durations in preclinical states are<br/>modeled by Weibull distributions (13 parameters)</b>  |          | T2G6Mx  | T2G7Mx   | 0.24        |      |
|  | Mean     | Shape   | T3G6Mx   | 0.62        |      |
| T1G6M0   | 2.70868  | 0.90514   | Clinical | 0.15        |      |
| T1G7M0   | 6.49444  | 0.90514   | T2G7Mx   | T2G8Mx      | 0.63 |
| T1G8M0   | 21.6563  | 0.90514   |          | T3G7Mx      | 0.00 |
| T2G6M0   | 4.00188  | 3.84944   |          | Clinical    | 0.36 |
| T2G7M0   | 7.40624  | 3.84944   | T2G8Mx   | T3G8Mx      | 0.00 |
| T2G8M0   | 11.1226  | 3.84944   |          | Clinical    | 1.00 |
| T3G6M0   | 3.53881  | 1.04132   | T3G6Mx   | T3G7Mx      | 0.00 |
| T3G7M0   | 18.9094  | 1.04132   |          | Clinical    | 1.00 |
| T3G8M0   | 23.3957  | 1.04132   | T3G7Mx   | T3G8Mx      | 0.00 |
| TxGxM1 = mean(TxGxM1) × 0.0101638  |          |   | Clinical | 1.00        |      |
|  |          | T3G8Mx  | Clinical | 1.00        |      |
| <b>Correlation between the duration of<br/>preclinical states in an individual (1 parameter)</b> |          | <b>Yearly hazard of additional clinical diagnosis<br/>in different preclinical states (4 parameters)‡</b> |          |             |      |
| Correlation  | 0.866907 | T1GxM0  | 0.056    |             |      |
| <b>Yearly hazard of metastasis in<br/>different preclinical states (9 parameters)</b>            |          | T2GxM0  | 0.001    |             |      |
| T1G6M0   | 0.0003   | T3GxM0  | 0.056    |             |      |
| T1G7M0   | 0.0016   | T1GxM1  | 0.801    |             |      |
| T1G8M0   | 0.0213   | T2GxM1  | 0.014    |             |      |
| T2G6M0   | 0.0045   | T3GxM1  | 0.810    |             |      |
| T2G7M0   | 0.0119   | <b>Sensitivity (4 parameters)</b>   |          |             |      |
| T2G8M0   | 0.0473   | T1GxM0  | 0.936    |             |      |
| T3G6M0   | 0.0017   | T2GxM0  | 0.941    |             |      |
| T3G7M0   | 0.0067   | T3GxM0  | 1.000    |             |      |
| T3G8M0   | 0.1046   | T1GxM1  | 0.962    |             |      |
|  |          | T2GxM1  | 0.965    |             |      |
|  |          | T3GxM1  | 1.000    |             |      |

\*T1, T2, T3 are the three clinical T stages: T1(impalpable), T2 (palpable, confined to the prostate), and T3+ (palpable, with extensions beyond the prostatic capsule), G6 is Gleason score (G) less than 7, G7 is Gleason score of 7, G8 Gleason score more than 7, M0 is the local-regional stage and M1 is the distant stage. Tx, Gx, and Mx imply all clinical T stages, all Gleason scores, and all metastatic stages, respectively.

†Time of tumor onset is generated from a piece-wise linear hazard function.

‡These parameters model a higher incidence in the control arm of the ERSPC trial compared to the population in 1991 (the baseline). The difference in clinical diagnosis between these two populations can for instance be attributed to contamination (screening in the control arm) or to changes in clinical practice leading to earlier diagnosis, eg, to the use of PSA testing for symptomatic disease in a clinical setting.

**Supplementary Table 2.** Observed data in ERSPC–Rotterdam\***Baseline**

| Age group, y   | n        | Incidence per 1000 man-years † |         |        |        |
|--|----------|--------------------------------|---------|--------|--------|
|  |          | T1                             | T2      |        |        |
| 45–49  | 11       | 0.02                           |         |        |        |
| 50–54  | 58       | 0.14                           |         |        |        |
| 55–59  | 131      | 0.36                           |         |        |        |
| 60–64  | 387      | 1.19                           |         |        |        |
| 65–69  | 734      | 2.59                           |         |        |        |
| 70–74  | 950      | 4.50                           |         |        |        |
| 75–79  | 969      | 6.57                           |         |        |        |
| 80–84  | 668      | 7.98                           |         |        |        |
| >85  | 431      | 8.52                           |         |        |        |
| Clinical T stage and metastatic stage distribution, % (n = 1610)‡                |          |                                |         |        |        |
|  | T1       | T2                             | T3      | Total  |        |
| M0   | 12.92    | 47.45                          | 17.76   | 78.14  |        |
| M1   | 1.06     | 11.30                          | 9.50    | 21.86  |        |
| Total  | 13.98    | 58.76                          | 27.27   | 100.00 |        |
| <b>Control arm§</b>  |          |                                |         |        |        |
| Age group, y   | n        | Incidence per 1000 man-years   |         |        |        |
|  |          | T1                             | T2      |        |        |
| 55–59  | 29       | 1.61                           |         |        |        |
| 60–64  | 135      | 3.35                           |         |        |        |
| 65–69  | 192      | 5.13                           |         |        |        |
| 70–74  | 247      | 7.95                           |         |        |        |
| >75  | 146      | 9.85                           |         |        |        |
| Clinical T stage, metastatic stage, and Gleason score distribution, % (n = 472)  |          |                                |         |        |        |
|  | G < 7    | G = 7                          | G > 7   | Total  |        |
| M0   | T1       | 29.87                          | 7.84    | 4.45   | 42.16  |
|  | T2       | 15.47                          | 10.59   | 3.81   | 29.87  |
|  | T3       | 4.24                           | 9.32    | 7.20   | 20.76  |
|  | Subtotal | 49.58                          | 27.75   | 15.47  | 92.80  |
| M1   | T1       | 0.00                           | 0.00    | 0.00   | 0.00   |
|  | T2       | 0.21                           | 0.85    | 1.69   | 2.75   |
|  | T3       | 0.00                           | 1.27    | 3.18   | 4.45   |
|  | Subtotal | 0.21                           | 2.12    | 4.87   | 7.20   |
| Total  |          | 49.79                          | 29.87   | 20.34  | 100.00 |
| <b>Screen arm§</b>   |          |                                |         |        |        |
| Detection rate per 1000 men screened by round of screening                       |          |                                |         |        |        |
|  | Round 1  | Round 2                        | Round 3 |        |        |
| Age group, y   | n        | rate                           | n       | rate   |        |
| 55–59  | 176      | 27.64                          | 20      | 20.77  |        |
| 60–64  | 239      | 44.81                          | 171     | 35.14  |        |
| 65–69  | 366      | 76.81                          | 189     | 49.74  |        |
| 70–74  | 287      | 86.73                          | 170     | 59.30  |        |
| Clinical T stage, metastatic stage, and Gleason score distribution, % (n = 1815) |          |                                |         |        |        |
| Round 1  | G < 7    | G = 7                          | G > 7   | Total  |        |
| M0   | T1       | 28.23                          | 6.61    | 1.04   | 35.88  |
|  | T2       | 29.84                          | 12.75   | 3.59   | 46.18  |
|  | T3       | 6.89                           | 7.84    | 2.64   | 17.37  |
|  | Subtotal | 64.97                          | 27.20   | 7.27   | 99.43  |
| M1   | T1       | 0.00                           | 0.00    | 0.00   | 0.00   |
|  | T2       | 0.00                           | 0.00    | 0.00   | 0.00   |
|  | T3       | 0.00                           | 0.09    | 0.47   | 0.57   |

|         |          |       |       |       |        |
|---------|----------|-------|-------|-------|--------|
|         | Subtotal | 0.00  | 0.09  | 0.47  | 0.57   |
| Total   |          | 64.97 | 27.29 | 7.74  | 100.00 |
| Round 2 | G < 7    | G = 7 | G > 7 | Total |        |
| M0      | T1       | 52.00 | 9.09  | 0.73  | 61.82  |
|         | T2       | 24.73 | 7.64  | 1.82  | 34.18  |
|         | T3       | 2.00  | 1.27  | 0.36  | 3.64   |
|         | Subtotal | 78.73 | 18.00 | 2.91  | 99.64  |
| M1      | T1       | 0.00  | 0.00  | 0.00  | 0.00   |
|         | T2       | 0.18  | 0.00  | 0.18  | 0.36   |
|         | T3       | 0.00  | 0.00  | 0.00  | 0.00   |
|         | Subtotal | 0.18  | 0.00  | 0.18  | 0.36   |
|         | Total    | 78.91 | 18.00 | 3.09  | 100.00 |
| Round 3 | G < 7    | G = 7 | G > 7 | Total |        |
| M0      | T1       | 56.41 | 7.18  | 0.00  | 63.59  |
|         | T2       | 27.69 | 4.62  | 2.56  | 34.87  |
|         | T3       | 0.51  | 0.00  | 1.03  | 1.54   |
|         | Subtotal | 84.62 | 11.79 | 3.59  | 100.00 |
| M1      | T1       | 0.00  | 0.00  | 0.00  | 0.00   |
|         | T2       | 0.00  | 0.00  | 0.00  | 0.00   |
|         | T3       | 0.00  | 0.00  | 0.00  | 0.00   |
|         | Subtotal | 0.00  | 0.00  | 0.00  | 0.00   |
|         | Total    | 84.62 | 11.79 | 3.59  | 100.00 |

Incidence of interval cancers per 1000 man-years by time since last screening

| Time (t)<br>since last<br>screening, y | n  | Incidence |
|--|----|-----------|
| 0 ≤ t < 1                              | 8  | 0.50      |
| 1 ≤ t < 2                              | 7  | 0.48      |
| 2 ≤ t < 3                              | 12 | 0.84      |
| 3 ≤ t < 4                              | 18 | 1.46      |
| t ≥ 4                                  | 52 | 4.21      |

\*T1, T2, T3 are the three clinical T stages: T1(impalpable), T2 (palpable, confined to the prostate), and T3+ (palpable, with extensions beyond the prostatic capsule), G < 7 is Gleason score (G) less than 7, G = 7 is Gleason score of 7, G > 7 Gleason score more than 7 , M0 is the local or regional stage and M1 is the distant stage. For clinical T stage, metastatic stage, and Gleason score distribution, only completed cases (cases for which the clinical T stage, Gleason score and metastatic stage are known) are shown.

†Data from the Netherlands Cancer Registry for 1991.

‡Data from the Rotterdam Cancer Registry for 1992 and 1993.

§ For the screen arm, data for cases diagnosed up to December 31, 2006, are presented. For the control arm, data for cases diagnosed up to July 4, 2004, are presented. Data for the control arm were collected from the Rotterdam cancer registry. Because there is a delay of 1–2 years in the reporting of tumors, the cutoff date for the control arm is different from that of the screen arm.

**Supplementary Table 3.** Observed incidence and stage distribution in the US population\*

| Year  | Age group (years) |       |       |       |       |       |       |
|---|-------------------|-------|-------|-------|-------|-------|-------|
|   | 50–54             | 55–59 | 60–64 | 65–69 | 70–74 | 75–79 | 80–84 |
| <b>Observed incidence per 1000 man-years</b>  |                   |       |       |       |       |       |       |
| 1985  | 0.27              | 0.94  | 2.26  | 4.48  | 6.81  | 9.15  | 11.09 |
| 1986  | 0.32              | 0.93  | 2.34  | 4.79  | 7.09  | 9.47  | 11.60 |
| 1987  | 0.37              | 1.16  | 2.61  | 5.29  | 8.25  | 10.90 | 12.14 |
| 1988  | 0.37              | 1.11  | 2.81  | 5.43  | 8.86  | 10.91 | 12.81 |
| 1989  | 0.36              | 1.21  | 3.16  | 6.15  | 9.19  | 11.58 | 12.82 |
| 1990  | 0.49              | 1.42  | 3.66  | 7.24  | 10.76 | 13.39 | 14.79 |
| 1991  | 0.70              | 1.93  | 4.93  | 9.36  | 14.47 | 16.78 | 17.47 |
| 1992  | 0.90              | 2.57  | 6.04  | 11.31 | 15.80 | 18.14 | 17.75 |
| 1993  | 0.95              | 2.71  | 5.97  | 10.66 | 13.92 | 14.45 | 13.99 |
| 1994  | 0.99              | 2.60  | 5.54  | 9.33  | 12.16 | 11.76 | 10.65 |
| 1995  | 1.04              | 2.85  | 5.39  | 8.71  | 11.14 | 10.55 | 9.65  |
| 1996  | 1.19              | 2.85  | 5.78  | 8.34  | 10.65 | 10.44 | 9.00  |
| 1997  | 1.27              | 3.04  | 5.72  | 9.00  | 10.80 | 10.47 | 9.38  |
| 1998  | 1.27              | 3.15  | 5.49  | 8.69  | 10.36 | 10.79 | 9.16  |
| 1999  | 1.40              | 3.29  | 6.28  | 9.41  | 11.37 | 10.96 | 9.12  |
| 2000  | 1.39              | 3.55  | 6.17  | 9.35  | 10.75 | 10.70 | 9.25  |
| <b>Observed percentage of distant disease</b> |                   |       |       |       |       |       |       |
| 1985  | 18.85             | 18.84 | 17.51 | 19.00 | 19.41 | 21.04 | 24.34 |
| 1986  | 18.75             | 19.86 | 16.78 | 15.77 | 19.89 | 20.04 | 23.93 |
| 1987  | 21.30             | 15.71 | 14.31 | 14.86 | 15.50 | 17.48 | 22.33 |
| 1988  | 23.84             | 15.29 | 14.83 | 14.87 | 15.20 | 17.56 | 21.11 |
| 1989  | 15.88             | 15.41 | 13.79 | 14.12 | 13.51 | 17.41 | 22.55 |
| 1990  | 11.59             | 13.39 | 12.10 | 11.44 | 12.28 | 14.94 | 19.45 |
| 1991  | 7.62              | 8.01  | 8.45  | 8.36  | 9.44  | 11.71 | 19.17 |
| 1992  | 5.69              | 6.47  | 6.23  | 5.78  | 7.12  | 9.53  | 12.99 |
| 1993  | 4.52              | 5.36  | 5.98  | 5.30  | 6.04  | 8.92  | 14.49 |
| 1994  | 2.27              | 4.81  | 4.53  | 5.38  | 5.27  | 8.26  | 13.70 |
| 1995  | 4.01              | 3.62  | 5.13  | 4.66  | 6.22  | 8.31  | 12.95 |
| 1996  | 4.18              | 3.82  | 3.69  | 3.71  | 5.29  | 7.49  | 13.18 |
| 1997  | 3.65              | 2.91  | 3.35  | 4.13  | 4.87  | 6.39  | 11.52 |
| 1998  | 2.33              | 3.30  | 3.70  | 3.31  | 4.75  | 6.62  | 11.31 |
| 1999  | 3.16              | 2.62  | 2.67  | 3.65  | 3.99  | 5.21  | 9.59  |
| 2000  | 2.00              | 2.58  | 2.14  | 3.23  | 3.84  | 5.60  | 8.89  |

\*Data from the National Cancer Institute's Surveillance, Epidemiology, and End Results database. The data are based on nine catchment areas of the United States: San Francisco–Oakland, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta.