**Table A.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** |  | **Definition** | **Source registers** |
| PC diagnosis |  | ICD-10 codes: C61 | NPCR. |
| Bone metastasis diagnosis |  | ICD-10 codes: C79.5 | SCR, NPR, NPCR. |
| Androgen deprivation therapy (ADT) |  | ATC codes: L02BB01 (bicalutamide), L02BB02 (Flutamide), L02BB03 (Nilutamide), L02BX01 (Abarelix), L02AE01 (Buserelin), L02BX02 (Degarelix), H01CA01 (Gonadorelin), L02AE03 (Goesrelin), L02AE05 (Histerlin), L02AE02 (Leuprorelin), H01CA02 (Nafarelin), L02AE04 (Triptorelin)  | SPDR. |
| Other ADT |  | ATC codes: G03HA01 (Cyproterone acetate), L02AB02 (Medroxyproge strerone acetate), L02AA02 (Polyestradiol phosphate), L02AB01 (Megestrol), L02AA01 (Diethystilbestrol) | SPDR. |
| Bilateral orchiectomy |  | NCSP codes: KFC10 | NPR. |
| Treatment for CRPC |  | ATC codes: L01DB07 (mitoxantrone), L01XX11 (estramustine), J02AB02 (ketoconazole), L01CD02 (docetaxel), L01CD04 (cabazitaxel) | SPDR. |
| Treatment for mCRPC |  | ATC codes: L02BX03 (abiraterone), L02BB04 (enzalutamide)  | SPDR. |
| Radiopharmaceuticals for bone metastases |  | V10BX02 (samarium), V10BX01 (strontium), V10BX03 (rhenium), V10XX03 (radium) | SPDR. |
| Second primary malignancy (SPM) outcome |  | First record of ICD-10: C00 – C76, C81 – C96, D00 – D09, D37 – D48, excluding C61, or C40 – C41 during follow-up. First record of each ICD-10 code was ensured by verifying that no prior record existed with accuracy of 3 digits (e.g. C16.1 was counted as a first record only if the same person had no history of C16 ICD-10 codes). | SCR,NPR. |
| Solid tumour outcome |  | First record of ICD-10: C00 – C75, excluding C61 or C40 – C41 during follow-up. First record of each ICD-10 code was ensured by verifying that no prior record existed with accuracy of 3 digits (e.g. C16.1 was counted as a first record only if the same person had no history of C16 ICD-10 codes). | SCR,NPR. |
| Bladder cancer outcome |  | First record of ICD-10: C67, D09.0 during follow-up. Verifying that no prior records of the same outcome existed was used to ensure first record. | SCR,NPR. |
| Rectum cancer outcome |  | First record of ICD-10: C20 – C21 during follow-up. Verifying that no prior records of the same outcome existed was used to ensure first record. | SCR,NPR. |
| Colon cancer outcome |  | First record of ICD-10: C18 – C19 during follow-up. Verifying that no prior records of the same outcome existed was used to ensure first record. | SCR,NPR. |
| Lung cancer outcome |  | First record of ICD-10: C33 – C34 during follow-up. Verifying that no prior records of the same outcome existed was used to ensure first record. | SCR,NPR. |
| Myelodysplastic syndrome outcome |  | First record of ICD-10: D46 during follow-up. Verifying that no prior records of the same outcome exist was used to ensure first record. | SCR,NPR. |
| Leukaemia outcome |  | First record of ICD-10: C91 – C95 during follow-up. Verifying that no prior records of the same outcome existed was used to ensure first record. | SCR,NPR. |
| Malignant neoplasm comorbidity |  | ICD-10 codes: C00 – C75, excluding C44 and C61 | SCR,NPR |
| Secondary malignant neoplasm comorbidity |  | ICD-10 codes: C78, C79.0, C79.1, C79.3, C79.4 or C79.7 | SCR,NPR |
| Urinary tract infection comorbidity |  | ICD-10 codes: N39.0 | NPR. |
| Impotence comorbidity |  | ICD-10 codes: N40 | NPR. |
| Retention of urine comorbidity |  | ICD-10 codes: R33 | NPR. |
| Hyperplasia of prostate comorbidity |  | ICD-10 codes: N48.4, F52.2 | NPR. |
| Abnormal serum enzyme levels comorbidity |  | ICD-10 codes: R74 | NPR. |
| Other disorders of urinary system comorbidity |  | ICD-10 codes: N39 | NPR. |
| Renal disease comorbidity |  | ICD-10 codes: N00-N29 | NPR. |
| Hypertension comorbidity |  | ICD-10 codes: I10-I15 | NPR. |
| Liver disease comorbidity |  | ICD-10 codes: K70-K77 | NPR. |
| Angina pectoris comorbidity |  | ICD-10 codes: I20 | NPR. |
| Congestive heart failure comorbidity |  | ICD-10 codes: I50 | NPR. |
| Diabetes mellitus comorbidity |  | ICD-10 codes: E10-E14 | NPR. |
| Hyperlipidaemia comorbidity |  | ICD-10 codes: E78 | NPR. |
| Antineoplastic or immunomodulatory agent |  | ATC codes: L (all) | SPDR. |
| Endocrine therapy |  | ATC codes: L02 (all) | SPDR. |
| Radical prostatectomy |  | NCSP codes: KEC00, KEC01, KEC10, KEC20 | NPR. |
| Radiation therapy |  | NCSP codes: DV069, DV070, DV071, DV072 | NPR. |
| Prednisolone |  | ATC codes: H02AB06 | SPDR. |
| Opioids |  | ATC codes: N02A | SPDR. |

**Table B.**

|  |  |  |
| --- | --- | --- |
| **Medication** | **mPC cohort** | **mCRPC cohort** |
| **First generation antiandrogens** |  |  |
| Bicalutamide | 6,628 (41.55%) | 369 (53.25%) |
| Flutamide | 602 (3.77%) | 47 (6.78%) |
| Nilutamide | 2 (0.01%) | 1 (0.14%) |
| **Luteinizing hormone-releasing hormone (LHRH) - Agonists/Antagonists** |  |  |
| Abarelix | 0 (0.00%) | 0 (0.00%) |
| Buserelin | 1,517 (9.51%) | 88 (12.70%) |
| Degarelix | 6 (0.04%) | 0 (0.00%) |
| Gonadorelin | 0 (0.00%) | 0 (0.00%) |
| Goserelin | 2,129 (13.35%) | 189 (27.27%) |
| Histrelin | 42 (0.26%) | 1 (0.14%) |
| Leuprorelin | 5,508 (34.53%) | 334 (48.20%) |
| Nafarelin | 0 (0.00%) | 0 (0.00%) |
| Triptorelin | 83 (0.52%) | 4 (0.58%) |
| **Other identifiers for castration therapies** |  |  |
| Cyproterone acetate | 325 (2.04%) | 24(3.46%) |
| Medroxyprogesterone acetate | 82 (0.51%) | 13(1.88%) |
| Polyestradiol phosphate | 873 (5.47%) | 65(9.38%) |
| Megestrol | 0 (0.00%) | 0 (0.00%) |
| Diethylstilbestrol | 0 (0.00%) | 0 (0.00%) |
| **Treatments for advanced prostate cancer/CRPC treatments** |  |  |
| Mitoxantrone | 1 (0.01%) | 1 (0.14%) |
| Sipuleucel-T | 0 (0.00%) | 0 (0.00%) |
| Estramustine | 471 (2.95%) | 471 (67.97%) |
| Ketoconazole | 328 (2.06%) | 328 (47.33%) |
| **Chemotherapy** |  |  |
| Docetaxel | 49 (0.31%) | 49 (7.07%) |
| Cabazitaxel | 0 (0.00%) | 0 (0.00%) |
| **mCRPC treatments** |  |  |
| Abiraterone | 47 (0.29%) | 47 (6.78%) |
| Enzalutamide | 0 (0.00%) | 0(0.00%) |

**Table C.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Strata** | **Events** | **Person years** | **Rate per 1000 person years with 95% CI** |  | **Events** | **Person years** | **Rate per 1000 person years with 95% CI** |
| **Solid tumor** |  | **Bladder cancer** |
| **Total** | 1912 | 34,026 | 56.19 (53.19, 58.77) |  | 325 | 36,265 | 8.96 (8.04, 9.99) |
| **Age** |  |  |  |  |  |  |  |
| <65 | 279 | 4,873 | 57.26 (50.92, 64.39) |  | 59 | 5,094 | 11.58 (8.97, 14.95) |
| 65-69 | 282 | 5,095 | 55.35 (49.25, 62.20) |  | 36 | 5,378 | 6.69 (4.83, 9.28) |
| 70-74 | 366 | 6,420 | 57.01 (51.46, 63.16) |  | 63 | 6,817 | 9.24 (7.22, 11.83) |
| 75-79 | 436 | 7,291 | 59.80 (54.44, 65.68) |  | 79 | 7,801 | 10.13 (8.12, 12.63) |
| 80-84 | 334 | 6,251 | 53.44 (48.00, 59.48) |  | 53 | 6,675 | 7.94 (6.07, 10.39) |
| >84 | 215 | 4,097 | 52.48 (45.92, 59.99) |  | 35 | 4,499 | 7.78 (5.59, 10.84) |
| **Rectum cancer** |  | **Colon cancer** |
| **Total** | 86 | 36,670 | 2.35 (1.90, 2.90) |  | 148 | 36,568 | 4.05 (3.44, 4.75) |
| **Age** |  |  |  |  |  |  |  |
| <65 | 7 | 5,155 | 1.36 (0.65, 2.85) |  | 18 | 5,140 | 3.50 (2.21, 5.56) |
| 65-69 | 9 | 5,463 | 1.65 (0.86, 3.17) |  | 12 | 5,443 | 2.20 (1.25, 3.88) |
| 70-74 | 19 | 6,890 | 2.76 (1.76, 4.32) |  | 32 | 6,868 | 4.66 (3.30, 6.59) |
| 75-79 | 20 | 7,889 | 2.54 (1.64, 3.93) |  | 41 | 7,862 | 5.21 (3.84, 7.08) |
| 80-84 | 19 | 6,729 | 2.82 (1.80, 4.43) |  | 26 | 6,714 | 3.87 (2.64, 5.69) |
| >84 | 12 | 4,545 | 2.64 (1.50, 4.65) |  | 19 | 4,542 | 4.18 (2.67, 6.56) |
| **Lung cancer** |  | **Myelodysplastic syndrome** |
| **Total** | 155 | 36,682 | 4.23 (3.61, 4.95) |  | 13 | 36,790 | 0.35 (0.21, 0.61) |
| **Age** |  |  |  |  |  |  |  |
| <65 | 21 | 5,151 | 4.08 (2.66, 6.25) |  | 1 | 5,165 | 0.19 (0.03, 1.37) |
| 65-69 | 33 | 5,459 | 6.05 (4.30, 8.50) |  | 1 | 5,470 | 0.18 (0.03, 1.30) |
| 70-74 | 29 | 6,877 | 4.22 (2.93, 6.07) |  | 4 | 6,906 | 0.58 (0.22, 1.54) |
| 75-79 | 37 | 7,895 | 4.69 (3.40, 6.47) |  | 1 | 7,916 | 0.13 (0.03, 0.90) |
| 80-84 | 24 | 6,741 | 3.56 (2.39, 5.31) |  | 3 | 6,765 | 0.44 (0.14, 1.37) |
| >84 | 11 | 4,560 | 2.41 (1.34, 4.36) |  | 3 | 4,568 | 0.66 (0.21, 2.04) |
| **Leukemia** |  |  |  |  |  |  |  |
| **Total** | 56 | 36,733 | 1.52 (1.17, 1.98) |  |  |  |  |
| **Age** |  |  |  |  |  |  |  |
| <65 | 9 | 5,156 | 1.75 (0.91, 3.35) |  |  |  |  |
| 65-69 | 6 | 5,468 | 1.10 (0.49, 2.44) |  |  |  |  |
| 70-74 | 10 | 6,902 | 1.45 (0.78, 2.69) |  |  |  |  |
| 75-79 | 12 | 7,905 | 1.52 (0.86, 2.67) |  |  |  |  |
| 80-84 | 12 | 6,744 | 1.78 (1.01, 3.13) |  |  |  |  |
| >84 | 7 | 4,558 | 1.54 (0.73, 3.22) |  |  |  |  |

**Table D.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Strata** | **Events** | **Person years** | **Rate per 1000 person years with 95% CI** |  | **Events** | **Person years** | **Rate per 1000 person years with 95% CI** |
| **Solid tumor** |  | **Bladder cancer** |
| **Total** | 73 | 887 | 82.29 (65.42, 103.51) |  | 7 | 938 | 7.46 (3.56, 15.66) |
| **Age** |  |  |  |  |  |  |  |
| <65 | 18 | 196 | 91.74 (57.8, 145.61) |  | 2 | 209 | 9.58 (2.4, 38.32) |
| 65-69 | 12 | 179 | 67.21 (38.17, 118.35) |  | 0 | 182 | NA (NA, NA) |
| 70-74 | 20 | 233 | 85.92 (55.43, 133.18) |  | 2 | 245 | 8.16 (2.04, 32.62) |
| 75-79 | 14 | 167 | 83.99 (49.74, 141.81) |  | 2 | 178 | 11.22 (2.81, 44.87) |
| 80-84 | 7 | 86 | 81.56 (38.88, 171.09) |  | 1 | 89 | 11.2 (1.58, 79.5) |
| >84 | 2 | 27 | 73.86 (18.47, 295.3) |  | 0 | 35 | NA (NA, NA) |
| **Rectum cancer** |  | **Colon cancer** |
| **Total** | 1 | 946 | 1.06 (0.15, 7.5) |  | 4 | 936 | 4.27 (1.6, 11.39) |
| **Age** |  |  |  |  |  |  |  |
| <65 | 0 | 211 | NA (NA, NA) |  | 0 | 211 | NA (NA, NA) |
| 65-69 | 0 | 182 | NA (NA, NA) |  | 0 | 182 | NA (NA, NA) |
| 70-74 | 0 | 246 | NA (NA, NA) |  | 1 | 245 | 4.08 (0.57, 28.96) |
| 75-79 | 1 | 182 | 5.5 (0.77, 39.04) |  | 2 | 180 | 11.12 (2.78, 44.45) |
| 80-84 | 0 | 90 | NA (NA, NA) |  | 0 | 89 | NA (NA, NA) |
| >84 | 0 | 35 | NA (NA, NA) |  | 1 | 29 | 33.98 (4.79, 241.22) |
| **Lung cancer** |  | **Myelodysplastic syndrome** |
| **Total** | 2 | 944 | 2.12 (0.53, 8.47) |  | 0 | 947 | NA (NA, NA) |
| **Age** |  |  |  |  |  |  |  |
| <65 | 0 | 211 | NA (NA, NA) |  | 0 | 211 | NA (NA, NA) |
| 65-69 | 0 | 182 | NA (NA, NA) |  | 0 | 182 | NA (NA, NA) |
| 70-74 | 1 | 245 | 4.08 (0.57, 28.96) |  | 0 | 246 | NA (NA, NA) |
| 75-79 | 1 | 180 | 5.55 (0.78, 39.42) |  | 0 | 182 | NA (NA, NA) |
| 80-84 | 0 | 90 | NA (NA, NA) |  | 0 | 90 | NA (NA, NA) |
| >84 | 0 | 35 | NA (NA, NA) |  | 0 | 35 | NA (NA, NA) |
| **Leukemia** |  |  |  |  |  |  |  |
| **Total** | 3 | 946 | 3.17 (1.02, 9.84) |  |  |  |  |
| **Age** |  |  |  |  |  |  |  |
| <65 | 0 | 211 | NA (NA, NA) |  |  |  |  |
| 65-69 | 0 | 182 | NA (NA, NA) |  |  |  |  |
| 70-74 | 1 | 246 | 4.07 (0.57, 28.88) |  |  |  |  |
| 75-79 | 1 | 182 | 5.5 (0.77, 39.04) |  |  |  |  |
| 80-84 | 1 | 90 | 11.13 (1.57, 79.03) |  |  |  |  |
| >84 | 0 | 35 | NA (NA, NA) |  |  |  |  |