

Supplementary Materials

Supplementary Methods

- Cancer-free Cohort Inclusion Criteria
 - 1) male, 2) non-cancer patients. and 3) birth year must be within a range of plus or minus two years from the corresponding case. Furthermore, they must meet one of two residency criteria: having lived in Utah since 1966, when the Utah Cancer Registry was statewide, or having lived in Utah since they were adults and more likely to get cancer, which in this case means controls who moved to Utah when they were at least 35 years of age. Individuals from the general population were excluded if they had been diagnosed with any type of cancer during the follow-up period from 2004 to 2017. Individuals from the general population were excluded if they had been diagnosed with any type of cancer during the follow-up period from 2004 to 2017.
- Validation data
 - As part of a pilot study on cancer patients (R21 CA185811), we sent a 24-page questionnaire to 423 eligible cancer patients and received questionnaires from 221 patients (52.2% response rate; 1). To validate our methods for using the EMR and statewide facility data to identify incident disease diagnoses, we obtained self-reported disease diagnoses from the questionnaire to compare the concordance between self-report vs. EMR/statewide data. For depression, the sensitivity was 82.6% and specificity was 95.7%.
- Clinical Classification and Mental Health Disorder Outcomes
 - The Clinical Classification Software codes were used to categorize ICD-9/10 codes into three levels of specificity (Levels 1-3), with level 1 being the broadest (e.g., mental illness (5)) down to level 2 (e.g., mood disorders (5.8)) and level 3 being the most specific (e.g., depressive disorders (5.8.2)). Level 3 outcomes diagnosed after cancer diagnosis were considered incident cases. Level 3 outcome diagnoses prior to the start of each analysis period were considered prevalent cases of those outcomes, and individuals were excluded from the relevant models. Level 2 outcomes were broader and contained multiple disparate conditions; thus, we did not exclude prevalent diagnoses. Mental health disorders that only can be developed or diagnosed in childhood were excluded, including Attention deficit conduct and disruptive behavior disorder (5.3), Developmental disorder (5.5) and its related disorders, Disorders usually diagnosed in infancy childhood or adolescence (5.6) and its related disorders. Moreover, some outcomes that had limited observations were excluded from this table: Personality disorder (5.9), Screening and history of mental health and substance abuse codes (5.14), Miscellaneous mental disorder (5.15) and its related disorders.
- Follow up time
 - Follow-up time for incident cases of each outcome was calculated from the prostate cancer survivor's diagnosis to the date of mental health diagnosis, last date of follow-up, or date of death. The last date of follow up was determined by the most recent date that the patient or individual was observed in the data sources within the UPDB. The first date of follow-up of the general population was established as the date of diagnosis of their matched prostate cancer survivors. Individuals who did not have any mental health outcome were censored at the date of last follow-up if that date fell within the analysis period.

- Person-time at Risk Calculation
 - Prevalent level 1 and 2 outcomes were excluded due to their pre-existing diagnostic status. Prevalent outcomes, or conditions diagnosed prior to the onset of cancer, were thus taken into account. In the 0-2 year timeframe, individuals with a mental health diagnosis preceding their cancer diagnosis were omitted from the analysis. In cases where participants experienced an incident event within the 0-2 year period, the subsequent follow-up duration was employed to calculate the person-time at risk. Conversely, for participants without any incident event during this period, the person-time at risk was designated as 2 years.
 - For the 2-5 year risk assessment, a 5-year span was employed as the endpoint. Similarly, the 10-year timeframe was utilized as the endpoint for calculating risks spanning 5-10 years. Subsequent to these delineated periods, the entire cohort contributed follow-up time for the calculation of person-time at risk.

- CCI Calculation
 - To calculate the CCI score, as described by Charlson et al. (2), all medical record data prior to the cancer diagnosis were used to identify 17 comorbidities. Different weights were then assigned to each of these comorbidities, and a total score was calculated by summing the weighted scores for all comorbidities present in the patient. The resulting CCI score can range from 0 to 37, with higher scores indicating a greater burden of comorbidities and a worse prognosis.

- Radiotherapy Dose and Androgen Deprivation Therapy Duration Calculation
 - The cancer treatment drug prescription and radiotherapy data were obtained from the UPDB (2013-2017), including the Utah All Payer Claims data. Healthcare Common Procedure Coding System (HCPCS) and the Current Procedural Terminology (CPT) Code were utilized to identify detailed treatment information (Supplemental Table1). For patients receiving radiotherapy (n=1,455), we reviewed patterns of radiotherapy with claims codes to confirm actual patient treatment regimen, with the NCCN prostate cancer guideline, version 2006 to version 2020. Radiotherapy dosage was categorized into five categories based on dose distribution, especially 6.5-27.5 Gy representing the incompleteness status of RT regimen. ADT duration was categorized into five most common ADT plans based on distributions used in previous clinical trials.
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- Proportional Hazard Ratio Assumption
 - The PH assumption was checked for each model using a test for nonzero slope of the Schoenfeld residuals vs time. Models that were in violation of the PH assumption were then fit with flexible parametric survival models with restricted cubic splines. HRs from the Cox PH models were reported where there were no substantive differences.

- Confounder Evaluation
 - We identified potential confounders based on the three properties of confounding variables (3). Demographic and clinical factors were considered as potential confounders in this study since they are risk factors for the outcome of mental health disorders

(property 1). For property 2 of confounders, there are associations between PSA values and race/ethnicity and age at diagnosis. Race/ethnicity and age at diagnosis are not on the causal pathway between the exposure and outcome (property 3), thus they were selected as potential confounders and adjusted for in the analysis.

- Missing data
 - The missing values for variables were imputed using fully conditional specification discriminant function methods. For example, BMI was imputed by considering covariates such as cancer diagnosis, baseline CCI, and age at prostate cancer diagnosis. As a sensitivity analysis, models were run both with and without imputed values to ensure that the inferences remained unchanged despite the imputation of missing variables.

References

1. Soisson S, Ganz PA, Gaffney D, et al. Long-term Cardiovascular Outcomes Among Endometrial Cancer Survivors in a Large, Population-Based Cohort Study. *J Natl Cancer Inst.* 2018 Dec 1;110(12):1342-1351.
2. Charlson ME, Carrozzino D, Guidi J, et al. Charlson Comorbidity Index: A Critical Review of Clinimetric Properties. *Psychother Psychosom.* 2022;91(1):8-35.
3. Rothman K, Greenland S, & Lash TL. *Modern Epidemiology*. 3rd ed. Philadelphia, PA; Lippincott Williams & Wilkins; 2008.

Supplementary Table 1. Side-effect Codes, Mental Health Outcomes ICD 9/10 Codes, and Treatment Codes (Mental illness is a level 1 disease, 5.x is level 2 (e.g., mood disorders), 5.x.x is level 3(e.g., depressive disorders))

| | ICD-9 Code | ICD-10 Code |
|----------------------------------|---|--|
| Sexual Dysfunction | 60784, 30270, 30271, 30272, 30273, 30274, 30275, 30276, 30279, 79981, 60889 | N529, R6882, N5311, N5312, N5313, N5314, N5319 |
| Genitourinary Dysfunction | 7883, 78830, 78831, 78832, 78833, 78834, 78835, 78836, 78837, 78838, 78839 | N3642, R32, N393, N3941, N3942, N3943, N3944, N3945, N3946, N39490, N39491, N39492, N39498, R350, R310, R311, R312, R3121, R3129, R319, N35111, N37, N35014, N99110, N358, N35811, N35812, N35813, N35814, N35816, N35819, N3582, N359, N35911, N35912, N35913, N35914, N35916, N35919, N3592, R338, R339, R3911, R3912, R3914, R3916, N139, N3000, N3001, N3090, N3091, R34, R350, R351, R358 |
| Bowel Dysfunction | 56949, 5581, 5589, 56941, 56981, 5693, 5789 | K6289, K529, K626, K632, K625, K922 |

Supplementary Table 1 continued.

| | ICD-9 Code | ICD-10 Code |
|--|---|--|
| Mental Illness(5) | | |
| Adjustment disorder(5.1) | 3090,3091, 30922, 30923, 30924, 30928, 30929, 3093, 3094, 30982, 30983, 30989, 3099 | F4320, F4321, F4322, F4323, F4324, F4325, F4329, F438, F439 F064, F4000, F4001, F4002, F4010, F4011, F40210, F40218, F40220, F40228, F40230, F40231, F40232, F40233, F40240, F40241, F40242, F40243, F40248, F40290, F40291, F40298, F408, F409, F410, F411, F413, F418, F419, F42, F422, F423, F424, F428, F429, F430, F4310, F4311, F4312, F488, F489, R452, R453, R454, R455, R456, R457, R4581, R4582, R4583, R4584 |
| Anxiety disorder(5.2) | 29384, 30000, 30001, 30002, 30009, 30010, 30020, 30021, 30022, 30023, 30029, 3003, 3005, 30089, 3009, 3080, 3081, 3082, 3083, 3084, 3089, 30981, 3130, 3131, 31321, 31322, 3133, 31382, 31383 2900, 29010, 29011, 29012, 29013, 29020, 29021, 2903, 29040, 29041, 29042, 29043, 2908, 2909, 2930, 2931, 2940, 2941, 29410, 29411, 29420, 29421, 2948, 2949, 3100, 3102, 3108, 31081, 31089, 3109, 3310, 3311, 33111, 33119, 3312, 33182, 797 | F0150, F0151, F0280, F0281, F0390, F0391, F04, F05, F070, F0781, F0789, F079, F09, F482, G300, G301, G308, G309, G3101, G3109, G311, G3183, R4181, R54 |
| Delirium dementia and cognitive disorders(5.4) | 29600, 29601, 29602, 29603, 29604, 29605, 29606, 29610, 29611, 29612, 29613, 29614, 29615, 29616, 29640, 29641, 29642, 29643, 29644, 29645, 29646, 29650, 29651, 29652, 29653, 29654, 29655, 29656, 29660, 29661, 29662, 29663, 29664, 29665, 29666, 2967, 29680, 29681, 29682, 29689, 29690, 29699, 29383, 29620, 29621, 29622, 29623, 29624, 29625, 29626, 29630, 29631, 29632, 29633, 29634, 29635, 29636, 3004, 311 | F0630, F0631, F0632, F0633, F0634, F3010, F3011, F3012, F3013, F302, F303, F304, F308, F309, F310, F3110, F3111, F3112, F3113, F312, F3130, F3131, F3132, F314, F315, F3160, F3161, F3162, F3163, F3164, F3170, F3171, F3172, F3173, F3174, F3175, F3176, F3177, F3178, F3181, F3189, F319, F320, F321, F322, F323, F324, F325, F328, F3281, F3289, F329, F330, F331, F332, F333, F3340, F3341, F3342, F338, F339, F340, F341, F348, F3481, F3489, F349, F39, R4586 |
| Mood disorders(5.8) | 29600, 29601, 29602, 29603, 29604, 29605, 29606, 29610, 29611, 29612, 29613, 29614, 29615, 29616, 29640, 29641, 29642, 29643, 29644, 29645, 29646, 29650, 29651, 29652, 29653, 29654, 29655, 29656, 29660, 29661, 29662, 29663, 29664, 29665, 29666, 2967, 29680, 29681, 29682, 29689, 29690, 29699 | F0630, F0631, F0632, F0633, F0634, F3010, F3011, F3012, F3013, F302, F303, F304, F308, F309, F310, F3110, F3111, F3112, F3113, F312, F3130, F3131, F3132, F314, F315, F3160, F3161, F3162, F3163, F3164, F3170, F3171, F3172, F3173, F3174, F3175, F3176, F3177, F3178, F3181, F3189, F319, F320, F321, F322, F323, F324, F325, F328, F3281, F3289, F329, F330, F331, F332, F333, F3340, F3341, F3342, F338, F339, F340, F341, F348, F3481, F3489, F349, F39, R4586 |
| Bipolar disorders (5.8.1) | 29383, 29620, 29621, 29622, 29623, 29624, 29625, 29626, 29630, 29631, 29632, 29633, 29634, 29635, 29636, 3004, 311 | F320, F321, F322, F323, F324, F325, F328, F3281, F3289, F329, F330, F331, F332, F333, F3340, F3341, F3342, F338, F339, F340, F341, F348, F3481, F3489, F349, F39, R4586 |
| Depressive disorder (5.8.2) | 29381, 29382, 29500, 29501, 29502, 29503, 29504, 29505, 29510, 29511, 29512, 29513, 29514, 29515, 29520, 29521, 29522, 29523, 29524, 29525, 29530, 29531, 29532, 29533, 29534, 29535, 29540, 29541, 29542, 29543, 29544, 29545, 29550, 29551, 29552, 29553, 29554, 29555, 29560, 29561, 29562, 29563, 29564, 29565, 29570, 29571, 29572, 29573, 29574, 29575, 29580, 29581, 29582, 29583, 29584, 29585, 29590, 29591, 29592, 29593, 29594, 29595, 2970, 2971, 2972, 2973, 2978, 2979, 2980, 2981, 2982, 2983, 2984, 2988, 2989 | F060, F062, F200, F201, F202, F203, F205, F2081, F2089, F209, F21, F22, F23, F24, F250, F251, F258, F259, F28, F29 F1010, F1011, F10120, F10121, F10129, F1014, F10150, F10151, F10159, F10180, F10181, F10182, F10188, F1019, F1020, F1021, F10220, F10221, F10229, F10230, F10231, F10232, F10239, F1024, F10250, F10251, F10259, F1026, F1027, F10280, F10281, F10282, F10288, F1029, F10920, F10921, F10929, F1094, F10950, F10951, F10959, F1096, F1097, F10980, F10981, F10982, F10988, F1099, G621, I426, K2920, K2921, K700, K7010, K7011, K702, K7030, K7031, K7040, K709, O99310, O99311, O99312, O99313, O99314, O99315, P043, Q860 |
| Schizophrenia and other psychotic disorders (5.10) | 2910, 2911, 2912, 2913, 2914, 2915, 2918, 29181, 29182, 29189, 2919, 30300, 30301, 30302, 30303, 30390, 30391, 30392, 30393, 30500, 30501, 30502, 30503, 3575, 4255, 5353, 53530, 53531, 5710, 5711, 5712, 5713, 76071, 9800 | V6542, F1110, F1111, F11120, F11121, F11122, F11129, F1114, F11150, F11151, F11159, F11181, F11182, F11188, F1119, F1120, F1121, F11220, F11221, F11222, F11229, F1123, F1124, F11250, F11251, F11259, F11281, F11282, F11288, F1129, F1190, F11920, F11921, F11922, F11929, F1193, F1194, F11950, F11951, F11959, F11981, F11982, F11988, F1199, F1210, F1211, F12120, F12121, F12122, F12129, F12150, F12151, F12159, F12180, F12188, F1219, F1220, F1221, F12220, F12221, F12222, F12229, F1223, F12250, F12251, F12259, F12280, F12288, F1229, F1290, F12920, F12921, F12922, F12929, F1293, F12950, F12951, F12959, F12980, F12988, F1299, F1310, F1311, F13120, F13121, F13129, F1314, F13150, F13151, F13159, F13180, F13181, F13182, F13188, F1319, F1320, F1321, F13220, F13221, F13229, F13230, F13231, F13232, F13239, F1324, F13250, F13251, F13259, F1326, F1327, F13280, F13281, F13282, F13288, F1329, F1390, F13920, F13921, F13929, F13930, F13931, F13932, F13939, F1394, F13950, F13951, F13959, F1396, F1397, F13980, F13981, F13982, F13988, F1399, F1410, F1411, F14120, F14121, |
| Alcohol-related disorders (5.11) | 2920, 29211, 29212, 2922, 29281, 29282, 29283, 29284, 29285, 29289, 2929, 30400, 30401, 30402, 30403, 30410, 30411, 30412, 30413, 30420, 30421, 30422, 30423, 30430, 30431, 30432, 30433, 30440, 30441, 30442, 30443, 30450, 30451, 30452, 30453, 30460, 30461, 30462, 30463, 30470, 30471, 30472, 30473, 30480, 30481, 30482, 30483, 30490, 30491, 30492, 30493, 30520, 30521, 30522, 30523, 30530, 30531, 30532, 30533, 30540, 30541, 30542, 30543, 30550, 30551, 30552, 30553, 30560, 30561, 30562, 30563, 30570, 30571, 30572, 30573, 30580, 30581, 30582, 30583, 30590, 30591, 30592, 30593, 64830, 64831, 64832, 64833, 64834, 65550, 65551, 65553, 76072, 76073, 76075, 7795, 96500, 96501, 96502, 96509 | |
| Substance-related disorders (5.12) | | |

F14122, F14129, F1414, F14150, F14151, F14159, F14180, F14181, F14182, F14188, F1419, F1420, F1421, F14220, F14221, F14222, F14229, F1423, F1424, F14250, F14251, F14259, F14280, F14281, F14282, F14288, F1429, F1490, F14920, F14921, F14922, F14929, F1494, F14950, F14951, F14959, F14980, F14981, F14982, F14988, F1499, F1510, F1511, F15120, F15121, F15122, F15129, F1514, F15150, F15151, F15159, F15180, F15181, F15182, F15188, F1519, F1520, F1521, F15220, F15221, F15222, F15229, F1523, F1524, F15250, F15251, F15259, F15280, F15281, F15282, F15288, F1529, F1590, F15920, F15921, F15922, F15929, F1593, F1594, F15950, F15951, F15959, F15980, F15981, F15982, F15988, F1599, F1610, F1611, F16120, F16121, F16122, F16129, F1614, F16150, F16151, F16159, F16180, F16183, F16188, F1619, F1620, F1621, F16220, F16221, F16229, F1624, F16250, F16251, F16259, F16280, F16283, F16288, F1629, F1690, F16920, F16921, F16929, F1694, F16950, F16951, F16959, F16980, F16983, F16988, F1699, F17200, F17201, F17203, F17208, F17209, F17210, F17211, F17213, F17218, F17219, F17220, F17221, F17223, F17228, F17229, F17290, F17291, F17293, F17298, F17299, F1810, F1811, F18120, F18121, F18129, F1814, F18150, F18151, F18159, F1817, F18180, F18188, F1819, F1820, F1821, F18220, F18221, F18229, F1824, F18250, F18251, F18259, F1827, F18280, F18288, F1829, F1890, F18920, F18921, F18929, F1894, F18950, F18951, F18959, F1897, F18980, F18988, F1899, F1910, F1911, F19120, F19121, F19122, F19129, F1914, F19150, F19151, F19159, F1916, F1917, F19180, F19181, F19182, F19188, F1919, F1920, F1921, F19220, F19221, F19222, F19229, F19230, F19231, F19232, F19239, F1924, F19250, F19251, F19259, F1926, F1927, F19280, F19281, F19282, F19288, F1929, F1990, F19920, F19921, F19922, F19930, F19931, F19932, F19939, F1994, F19950, F19951, F19959, F1996, F1997, F19980, F19981, F19982, F19988, F1999, F550, F551, F552, F553, F554, F558, O355XX0, O355XX1, O355XX2, O355XX3, O355XX4, O355XX5, O355XX9, O99320, O99321, O99322, O99323, O99324, O99325, P0441, P0449, P961, P962, T400X1A, T400X1D, T400X1S, T400X3A, T400X3D, T400X3S, T400X4A, T400X4D, T400X4S, T400X5A, T400X5D, T400X5S, T400X6A, T400X6D, T400X6S, T401X1A, T401X1D, T401X1S, T401X3A, T401X3D, T401X3S, T401X4A, T401X4D, T401X4S, T401X5A, T401X5D, T401X5S, T405X1A, T405X1D, T405X1S, T405X3A, T405X3D, T405X3S, T405X4A, T405X4D, T405X4S, T405X5A, T405X5D, T405X5S, T405X6A, T405X6D, T405X6S, T407X1A, T407X1D, T407X1S, T407X3A, T407X3D, T407X3S, T407X4A, T407X4D, T407X4S, T407X5A, T407X5D, T407X5S, T407X6A, T407X6D, T407X6S, T408X1A, T408X1D, T408X1S, T408X3A, T408X3D, T408X3S, T408X4A, T408X4D, T408X4S, T408X5A, T408X5D, T408X5S, T40901A, T40901D, T40901S, T40903A, T40903D, T40903S, T40904A, T40904D, T40904S, T40905A, T40905D, T40905S, T40906A, T40906D, T40906S, T40991A, T40991D, T40991S, T40993A, T40993D, T40993S, T40994A, T40994D, T40994S, T40995A, T40995D, T40995S, T40996A, T40996D, T40996S

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Suicide and intentional self-inflicted injury (5.13)

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Supplementary Table 1 continued.

| Treatment codes | Type | CPT code | HCPCS code | ICD procedure code |
|-------------------------------------|----------------|---|---|---|
| | | 52601, 52630, 52647, 52648, 52649, 53850, 53852, 53854, 55801, 55810, 55812, 55815, 55821, 55831, 55840, 55842, 55845, 55866, 55873, 55880, 55899 | | 60.21, 60.29, 60.3, 60.4, 60.5, 60.6, 60.62, 60.69 |
| Surgery | | | 77014, 77385, 77386, 77387, 77402, 77407, 77412 | |
| Radiotherapy | | G6001- G6017 | | |
| Androgen-deprivation therapy | Leuprolide | | C9430, J1950, J9217, J9218, J9219, J1952, J1951, S9560 | |
| | Goserelin | | J9202 | |
| | Triptorelin | | J3315, C9016, J3316 | |
| | Histrelin | | J9155 | |
| | Flutamide | | J9202, J8999, S0175 | |
| | Other medicine | | National Drug Code Dictionary | |

Supplementary Table 2. The Event Frequency of Mental Illness among Prostate Cancer Survivors Compared to the General Population

| Diagnosis (CCS Code) | 0-2 y After Cancer Diagnosis | | 2-5 y After Cancer Diagnosis | | 5-10 y After Cancer Diagnosis | | 10+ y After Cancer Diagnosis | |
|--|--------------------------------|-----------------------------|-------------------------------|----------------------------|-------------------------------|-----------------------|------------------------------|-----------------------|
| | Cancer Cases(n[%]) N=18,134 | Gen. Pop (n[%]) N=73,470 | Cancer Cases(n[%]) N=16757 | Gen. Pop (n[%]) N=66811 | Cancer Cases(n[%]) N=12264 | Gen.(n[%]) N=47344 | Cancer Cases(n[%]) N=5439 | Gen.(n[%]) N=19945 |
| Mental illness(5) | 5433 (30.0) | 14638 (19.9) | 4502 (26.9) | 17199 (25.7) | 4455 (36.3) | 16362 (34.6) | 2013 (37.0) | 6862 (34.4) |
| Adjustment disorder(5.1) | 77 (0.4) | 196 (0.3) | 76 (0.5) | 256 (0.4) | 112 (0.9) | 304 (0.6) | 44 (0.8) | 125 (0.6) |
| Anxiety disorder(5.2) | 1260 (7.0) | 3602 (4.9) | 1233 (7.4) | 4284 (6.4) | 1209 (9.9) | 3965 (8.4) | 464 (8.5) | 1368 (6.9) |
| Delirium dementia and cognitive disorders(5.4) | | | | | | | | |
| Mood disorders(5.8) | 469 (2.6) | 2329 (3.2) | 650 (3.9) | 2760 (4.1) | 886 (7.2) | 2995 (6.3) | 416 (7.7) | 1274 (6.4) |
| Bipolar disorders (5.8.1) | 1748 (9.6) | 5100 (6.9) | 1673 (10.0) | 5903 (8.8) | 1627 (13.3) | 5232 (11.1) | 652 (12.0) | 1958 (9.8) |
| Depressive disorder (5.8.2) | 139 (0.8) | 461 (0.6) | 113 (0.7) | 434 (0.7) | 67 (0.6) | 280 (0.6) | 7 (0.1) | 32 (0.2) |
| Schizophrenia and other psychotic disorders (5.10) | 1330 (7.3) | 3658 (5.0) | 1064 (6.4) | 3584 (5.4) | 781 (6.4) | 2438 (5.2) | 78 (1.4) | 254 (1.3) |
| Alcohol-related disorders (5.11) | 171 (0.9) | 833 (1.1) | 209 (1.3) | 970 (1.5) | 238 (1.9) | 855 (1.8) | 43 (0.8) | 140 (0.7) |
| Substance-related disorders (5.12) | 277 (1.5) | 1325 (1.8) | 265 (1.6) | 1341 (2.0) | 287 (2.3) | 1119 (2.4) | 82 (1.5) | 324 (1.6) |
| Suicide and intentional self-inflicted injury (5.13) | 359 (2.0) | 1484 (2.0) | 331 (2.0) | 1797 (2.7) | 337 (2.8) | 2120 (4.5) | 158 (2.9) | 803 (4.0) |
| | 55 (0.3) | 265 (0.4) | 72 (0.4) | 306 (0.5) | 66 (0.5) | 305 (0.6) | 25 (0.5) | 81 (0.4) |

Supplementary Table 3a. Comparison of Pre- and Post- Cancer Diagnosis Clinic Visit Frequencies among Prostate Cancer Patients and the General Population

| Clinic Visit Frequency | Pre-diagnosis | | | Post-diagnosis | | |
|------------------------|----------------------------------|-----------------------------|-----------------------|----------------------------------|-----------------------------|-----------------------|
| | Prostate Cancer Patient [N (n%)] | General Population [N (n%)] | P for Chi-Square Test | Prostate Cancer Patient [N (n%)] | General Population [N (n%)] | P for Chi-Square Test |
| 1-15 | 8172 (45.1) | 35075 (47.7) | <.0001 | 4958 (27.3) | 32106 (43.7) | <.0001 |
| 16-30 | 3605 (19.9) | 13289 (18.1) | | 3186 (17.6) | 12102 (16.5) | |
| 31-45 | 1955 (10.8) | 7062 (9.6) | | 2283 (12.6) | 7041 (9.6) | |
| 46-60 | 1159 (6.4) | 4187 (5.7) | | 1737 (9.6) | 4461 (6.1) | |
| 61-120 | 1823 (10.1) | 6830 (9.3) | | 3641 (20.1) | 7522 (10.2) | |
| 120+ | 702 (3.9) | 2888 (3.9) | | 2125 (11.7) | 3777 (5.1) | |

Supplementary Table 3b. Risks of Mental Illness among prostate cancer survivors compared to the general population, adjusted for Pre-diagnosis Clinical Visit Frequency

| Diagnosis(CCS Code) | 0-2 y After Cancer Diagnosis | | | 2-5 y After Cancer Diagnosis | | | 5-10 y After Cancer Diagnosis | | | 10+ y After Cancer Diagnosis | | |
|--|------------------------------|---------------------|-------------|------------------------------|---------------------|-------------|-------------------------------|---------------------|-------------|------------------------------|---------------------|-------------|
| | Adj.HR(95% CI) | | | Adj.HR(95% CI) | | | Adj.HR(95% CI) | | | Adj.HR(95% CI) | | |
| | HR | Lower Limit | Upper Limit | HR | Lower Limit | Upper Limit | HR | Lower Limit | Upper Limit | HR | Lower Limit | Upper Limit |
| Mental illness(5) | 1.74 | (1.68 -1.80) | | 1.02 | (0.98 -1.05) | | 0.99 | (0.95 -1.03) | | 0.95 | (0.88 -1.01) | |
| Adjustment disorder(5.1) | 2.07 | (1.39 -3.07) | | 1.19 | (0.82 -1.74) | | 1.70 | (1.23 -2.34) | | 1.22 | (0.79 -1.88) | |
| Anxiety disorder(5.2) | 1.52 | (1.41 -1.64) | | 1.10 | (1.02 -1.19) | | 1.12 | (1.03 -1.21) | | 1.18 | (1.03 -1.34) | |
| Delirium dementia and cognitive disorders(5.4) | 0.69 | (0.62 -0.77) | | 0.77 | (0.70 -0.85) | | 0.91 | (0.83 -1.00) | | 1.00 | (0.87 -1.16) | |
| Mood disorders(5.8) | 1.49 | (1.40 -1.59) | | 1.12 | (1.05 -1.19) | | 1.13 | (1.06 -1.21) | | 1.18 | (1.06 -1.32) | |
| Bipolar disorders (5.8.1) | 1.61 | (1.09 -2.38) | | 1.15 | (0.76 -1.72) | | 1.08 | (0.92 -1.28) | | | NA | |
| Depressive disorder (5.8.2) | 2.16 | (1.92 -2.43) | | 1.13 | (0.98 -1.29) | | 1.02 | (0.58 -1.81) | | 1.39 | (0.73 -2.63) | |
| Schizophrenia and other psychotic disorders (5.10) | 0.78 | (0.64 -0.95) | | 0.74 | (0.61 -0.88) | | 0.93 | (0.78 -1.11) | | 1.19 | (0.77 -1.83) | |
| Alcohol-related disorders (5.11) | 0.92 | (0.79 -1.07) | | 0.78 | (0.67 -0.91) | | 1.07 | (0.91 -1.25) | | 0.98 | (0.73 -1.32) | |
| Substance-related disorders (5.12) | 1.12 | (0.98 -1.28) | | 0.76 | (0.67 -0.88) | | 0.60 | (0.53 -0.69) | | 0.69 | (0.56 -0.84) | |
| Suicide and intentional self-inflicted injury (5.13) | 0.77 | (0.52 -1.15) | | 1.07 | (0.75 -1.53) | | 0.78 | (0.55 -1.10) | | 1.32 | (0.77 -2.29) | |
| Miscellaneous mental disorders (5.15) | 1.28 | (1.10 -1.50) | | 1.20 | (1.04 -1.39) | | 0.94 | (0.80 -1.09) | | 1.24 | (0.97 -1.58) | |
| Sexual and gender identity disorders (5.15.5) | 2.03 | (1.46 -2.84) | | 1.54 | (0.99 -2.38) | | 0.44 | (0.19 -1.02) | | | NA | |
| Sleep disorders (5.15.6) | | - | | | | | | | | | | |
| Somatoform disorders (5.15.7) | 3.71 | (0.38 -36.65) | | 2.32 | (1.11 -4.86) | | 0.85 | (0.36 -2.04) | | | NA | |
| | 2.05 | (0.87 -4.83) | | 1.00 | (0.38 -2.61) | | 0.46 | (0.15 -1.42) | | | NA | |

Bold value indicates statistical significance (P<0.05).

All hazard ratios adjusted for baseline BMI, baseline CCI, pre-diagnosis clinic visits frequency, and ethnicity/race. CI, confidence interval.

* Proportional hazard assumption not met; flexible spline model used.

b. Some outcomes that developed or diagnosed before adulthood were excluded from this table: Attention deficit conduct and disruptive behavior disorder (5.3), Developmental disorder (5.5) and its related disorders, Disorders usually diagnosed in infancy childhood or adolescence (5.6) and its related disorders,

c. Some outcomes that had limited observations were excluded from this table: Personality disorder (5.9), Screening and history of mental health and substance abuse codes (5.14), Miscellaneous mental disorder (5.15) and its related disorders.

Supplementary Table 4. Risks of Mental Illness among Prostate Cancer Survivors compared to the General Population Stratified by Risk Group

| Diagnosis(CCS Code) | Low-risk Group | | | Intermediate-risk Group | | | High-risk Group | | |
|--|----------------|--------------------|-------------|-------------------------|--------------------|-------------|-----------------|--------------------|-------------|
| | Adj.HR(95% CI) | | | Adj.HR(95% CI) | | | Adj.HR(95% CI) | | |
| | HR | Lower Limit | Upper Limit | HR | Lower Limit | Upper Limit | HR | Lower Limit | Upper Limit |
| Mental illness(5) | 1.16 | (1.10 1.22) | | 1.27 | (1.23 1.32) | | 1.62 | (1.54 1.71) | |
| Adjustment disorder(5.1) | 1.16 | (0.85 1.57) | | 1.18 | (0.94 1.50) | | 3.11 | (2.37 4.07) | |
| Anxiety disorder(5.2) | 1.28 | (1.17 1.39) | | 1.26 | (1.18 1.35) | | 1.62 | (1.48 1.77) | |
| Delirium dementia and cognitive disorders(5.4) | 0.89 | (0.79 0.99) | | 0.83 | (0.76 0.91) | | 0.93 | (0.83 1.04) | |
| Mood disorders(5.8) | 1.20 | (1.11 1.30) | | 1.27 | (1.19 1.35) | | 1.61 | (1.48 1.74) | |
| Bipolar disorders (5.8.1) | 1.42 | (1.01 1.99) | | 0.91 | (0.68 1.22) | | 1.84 | (1.26 2.70) | |
| Depressive disorder (5.8.2) | 1.34 | (1.17 1.53) | | 1.47 | (1.32 1.62) | | 1.79 | (1.55 2.05) | |
| Schizophrenia and other psychotic disorders (5.10) | 0.89 | (0.74 1.07) | | 0.80 | (0.68 0.93) | | 1.22 | (1.01 1.47) | |
| Alcohol-related disorders (5.11) | 0.79 | (0.67 0.94) | | 0.92 | (0.81 1.05) | | 1.32 | (1.11 1.56) | |
| Substance-related disorders (5.12) | 0.66 | (0.57 0.77) | | 0.73 | (0.65 0.81) | | 1.36 | (1.19 1.55) | |
| Suicide and intentional self-inflicted injury (5.13) | 0.95 | (0.69 1.30) | | 0.91 | (0.71 1.17) | | 1.37 | (0.98 1.91) | |

Bold value indicates statistical significance (P<0.05).

All hazard ratios adjusted for baseline BMI, baseline CCI, and ethnicity/race. CI, confidence interval.

Supplementary Table 5. Demographic Risk Factors for Specific Types of Mental Illness Among Prostate Cancer Survivors

| | Prostate Cancer Patients(n[%]) | | Mood Disorder | | Prostate Cancer Patients(n[%]) | | Anxiety | | Prostate Cancer Patients(n[%]) | | Depression | |
|---|--------------------------------|--------|---------------|---------------------|--------------------------------|--------|-------------|---------------------|--------------------------------|--------|-------------|---------------------|
| | | | HR | 95% CI | | | HR | 95% CI | | | HR | 95% CI |
| Ethnicity | | | | | | | | | | | | |
| Non-Hispanic | 3190 | (90.6) | | Reference | 2615 | (90.3) | | Reference | 1221 | (89.2) | | Reference |
| Hispanic | 335 | (9.5) | 1.15 | (1.03 -1.29) | 280 | (9.7) | 1.18 | (1.05 -1.34) | 148 | (10.8) | 1.30 | (1.10 -1.54) |
| Race | | | | | | | | | | | | |
| White | 3351 | (94.6) | | Reference | 2733 | (94.4) | | Reference | 1288 | (94.1) | | Reference |
| Black | 20 | (0.6) | 0.89 | (0.57 -1.38) | 19 | (0.7) | 1.05 | (0.67 -1.65) | 8 | (0.6) | 0.93 | (0.46 -1.86) |
| Asian | 9 | (0.3) | 0.41 | (0.21 -0.79) | 3 | (0.1) | 0.17 | (0.06 -0.53) | 5 | (0.4) | 0.56 | (0.23 -1.35) |
| Multiple Races | 140 | (4.0) | 1.14 | (0.97 -1.35) | 125 | (4.3) | 1.28 | (1.07 -1.53) | 55 | (4.0) | 1.15 | (0.88 -1.51) |
| Other\$ | 5 | (0.1) | 2.12 | (0.88 -5.09) | 3 | (0.1) | 1.38 | (0.45 -4.28) | 3 | (0.2) | 3.05 | (0.98 -9.47) |
| Baseline BMI(kg/m2) ^a | | | | | | | | | | | | |
| <18.5 | 17 | (0.5) | 2.08 | (1.28 -3.38) | 12 | (0.4) | 1.64 | (0.92 -2.90) | 9 | (0.7) | 2.39 | (1.22 -4.68) |
| 18.5-24.9 | 761 | (21.5) | | Reference | 685 | (23.7) | | Reference | 324 | (23.7) | | Reference |
| 25-29.9 | 1798 | (50.7) | 1.14 | (1.05 -1.24) | 1461 | (50.5) | 1.00 | (0.91 -1.09) | 702 | (51.3) | 1.05 | (0.92 -1.20) |
| 30+ | 968 | (27.3) | 1.39 | (1.26 -1.53) | 737 | (25.5) | 1.11 | (1.00 -1.23) | 334 | (24.4) | 1.15 | (0.99 -1.35) |
| Baseline CCI ^a | | | | | | | | | | | | |
| 0 | 1378 | (38.9) | | Reference | 1232 | (42.6) | | Reference | 638 | (46.6) | | Reference |
| ≥1 | 2166 | (61.1) | 2.00 | (1.87 -2.15) | 1663 | (57.4) | 1.77 | (1.64 -1.91) | 731 | (53.4) | 1.53 | (1.37 -1.71) |
| Education ^b | | | | | | | | | | | | |
| High school or less | 1616 | (45.6) | | Reference | 1320 | (45.6) | | Reference | 602 | (44.0) | | Reference |
| College | 986 | (27.8) | 1.02 | (0.94 -1.10) | 778 | (26.9) | 1.01 | (0.92 -1.10) | 409 | (29.9) | 1.11 | (0.98 -1.26) |
| Post College | 942 | (26.6) | 1.01 | (0.94 -1.10) | 797 | (27.5) | 1.05 | (0.97 -1.15) | 358 | (26.2) | 1.02 | (0.90 -1.17) |
| Baseline Marital Status ^b | | | | | | | | | | | | |
| Married | 3089 | (87.2) | | Reference | 2533 | (87.5) | | Reference | 1175 | (85.8) | | Reference |
| Widowed | 275 | (7.8) | 1.06 | (0.94 -1.21) | 209 | (7.2) | 1.06 | (0.91 -1.22) | 114 | (8.3) | 1.10 | (0.90 -1.34) |
| Unmarried | 180 | (5.1) | 1.47 | (1.25 -1.71) | 153 | (5.3) | 1.52 | (1.28 -1.80) | 80 | (5.8) | 1.67 | (1.32 -2.12) |
| Residency | | | | | | | | | | | | |
| Urban | 3030 | (85.5) | | Reference | 2485 | (85.8) | | Reference | 1154 | (84.3) | | Reference |
| Rural | 514 | (14.5) | 0.94 | (0.86 -1.04) | 410 | (14.2) | 0.92 | (0.83 -1.03) | 215 | (15.7) | 1.03 | (0.89 -1.19) |
| Census Tract Level Median Household Income | | | | | | | | | | | | |
| \$32,048 or less | 90 | (2.5) | | Reference | 82 | (2.8) | | Reference | 36 | (2.6) | | Reference |
| \$32,048 - \$53,413 | 1234 | (34.8) | 0.99 | (0.80 -1.23) | 1001 | (34.6) | 0.89 | (0.71 -1.12) | 497 | (36.3) | 0.99 | (0.71 -1.40) |
| \$53,413 - \$106,827 | 2093 | (59.1) | 0.94 | (0.76 -1.16) | 1708 | (59.0) | 0.84 | (0.67 -1.04) | 809 | (59.1) | 0.93 | (0.67 -1.31) |
| \$106,827 - \$373,894 | 124 | (3.5) | 1.12 | (0.85 -1.48) | 102 | (3.5) | 0.96 | (0.71 -1.28) | 24 | (1.8) | 0.75 | (0.45 -1.27) |
| Yost Socioeconomic (SES) Index ^g | | | | | | | | | | | | |
| Quintile 1 | 618 | (17.4) | | Reference | 519 | (17.9) | | Reference | 248 | (18.1) | | Reference |
| Quintile 2 | 611 | (17.2) | 0.89 | (0.80 -1.00) | 478 | (16.5) | 0.84 | (0.74 -0.95) | 275 | (20.1) | 0.94 | (0.79 -1.12) |
| Quintile 3 | 750 | (21.2) | 1.04 | (0.93 -1.16) | 592 | (20.5) | 0.97 | (0.86 -1.09) | 270 | (19.7) | 0.93 | (0.78 -1.11) |
| Quintile 4 | 662 | (18.7) | 0.97 | (0.87 -1.09) | 542 | (18.7) | 0.94 | (0.83 -1.06) | 254 | (18.6) | 0.91 | (0.77 -1.09) |
| Quintile 5 | 870 | (24.6) | 0.95 | (0.86 -1.06) | 743 | (25.7) | 0.95 | (0.85 -1.07) | 301 | (22.0) | 0.84 | (0.71 -0.99) |
| Baseline Health Insurance Status | | | | | | | | | | | | |
| Medicare | 1376 | (38.8) | | Reference | 1031 | (35.6) | | Reference | 519 | (37.9) | | Reference |
| Other Government Support ^e | 107 | (3.0) | 1.27 | (1.03 -1.57) | 94 | (3.3) | 1.28 | (1.02 -1.61) | 33 | (2.4) | 1.19 | (0.82 -1.72) |

| | | | | | | | | | | | | |
|--------------------------|------|--------|-------------|---------------------|------|--------|-------------|---------------------|-----|--------|-------------|---------------------|
| Private Health Insurance | 1365 | (38.5) | 0.81 | (0.74 -0.90) | 1155 | (39.9) | 0.80 | (0.72 -0.89) | 497 | (36.3) | 0.81 | (0.69 -0.96) |
| Blue Cross/Blue Shield | 280 | (7.9) | 0.73 | (0.63 -0.84) | 274 | (9.5) | 0.83 | (0.71 -0.96) | 102 | (7.5) | 0.73 | (0.58 -0.93) |
| Other ^f | 124 | (3.5) | 0.90 | (0.74 -1.09) | 100 | (3.5) | 0.84 | (0.67 -1.04) | 51 | (3.7) | 0.98 | (0.72 -1.33) |

a. Adjusted for race/ethnicity, diagnosis age, and education.

b. Adjusted for race/ethnicity, and diagnosis age

c. Adjusted for baseline BMI and baseline CCI.

d. Adjusted for race/ethnicity and AJCC staging

e. Adjusted for race/ethnicity, baseline BMI, diagnosis year, age at diagnosis, and education.

f. Adjusted for race/ethnicity, baseline BMI, baseline CCI, risk group, age at diagnosis, and education.

Bold value indicates statistical significance (P<0.05).

Abbreviation: HR, hazard ratio; CI, confidence interval; BMI, body mass index, CCI, Charlson Comorbidity Index

Supplementary Table 6. Clinical Risk Factors for Specific Types of Mental Illness Among Prostate Cancer Survivors

| | Prostate Cancer Patients(n[%]) | | Mood Disorder | | Prostate Cancer Patients(n[%]) | | Anxiety | | Prostate Cancer Patients(n[%]) | | Depression | |
|---|--------------------------------|--------|---------------|---------------------|--------------------------------|--------|-------------|---------------------|--------------------------------|--------|-------------|---------------------|
| | | | HR | 95% CI | | | HR | 95% CI | | | HR | 95% CI |
| Diagnosis year ^c | | | | | | | | | | | | |
| 2004-2008 | 1544 | (43.6) | | Reference | 1221 | (42.2) | | Reference | 854 | (62.4) | | Reference |
| 2009-2012 | 1152 | (32.5) | 1.12 | (1.04 -1.22) | 952 | (32.9) | 1.25 | (1.14 -1.36) | 426 | (31.1) | 0.66 | (0.59 -0.74) |
| 2013-2017 | 848 | (23.9) | 1.20 | (1.09 -1.31) | 722 | (24.9) | 1.51 | (1.36 -1.67) | 89 | (6.5) | 0.20 | (0.16 -0.25) |
| Age at diagnosis ^d | | | | | | | | | | | | |
| <50 | 115 | (3.2) | 1.39 | (1.15 -1.69) | 102 | (3.5) | 1.48 | (1.21 -1.81) | 55 | (4.0) | 1.85 | (1.40 -2.44) |
| 50-59 | 792 | (22.4) | 1.07 | (0.98 -1.17) | 723 | (25.0) | 1.19 | (1.08 -1.30) | 288 | (21.0) | 1.05 | (0.91 -1.21) |
| 60-69 | 1450 | (40.9) | | Reference | 1191 | (41.1) | | Reference | 537 | (39.2) | | Reference |
| 70-79 | 960 | (27.1) | 0.98 | (0.91 -1.07) | 738 | (25.5) | 0.92 | (0.84 -1.01) | 381 | (27.8) | 1.04 | (0.91 -1.18) |
| 80+ | 227 | (6.4) | 0.97 | (0.84 -1.12) | 141 | (4.9) | 0.76 | (0.64 -0.91) | 108 | (7.9) | 1.25 | (1.01 -1.54) |
| PSA value, ng/ml ^b | | | | | | | | | | | | |
| <4 | 508 | (14.3) | | Reference | 400 | (13.8) | | Reference | 198 | (14.5) | | Reference |
| 4-6.9 | 1501 | (42.4) | 0.86 | (0.78 -0.96) | 1242 | (42.9) | 0.92 | (0.82 -1.03) | 586 | (42.8) | 0.89 | (0.76 -1.04) |
| 7-10 | 687 | (19.4) | 0.86 | (0.77 -0.97) | 550 | (19.0) | 0.91 | (0.80 -1.03) | 271 | (19.8) | 0.89 | (0.74 -1.07) |
| 10.1-20 | 508 | (14.3) | 0.87 | (0.77 -0.98) | 415 | (14.3) | 0.96 | (0.84 -1.10) | 191 | (14.0) | 0.84 | (0.69 -1.03) |
| >20 | 340 | (9.6) | 1.01 | (0.88 -1.16) | 288 | (10.0) | 1.18 | (1.01 -1.38) | 123 | (9.0) | 1.03 | (0.82 -1.30) |
| Gleason Grade Group ^b | | | | | | | | | | | | |
| 3+3 or less | 1470 | (41.5) | | Reference | 1240 | (42.8) | | Reference | 600 | (43.8) | | Reference |
| 3+4 | 1037 | (29.3) | 1.07 | (0.99 -1.16) | 839 | (29.0) | 1.02 | (0.93 -1.11) | 405 | (29.6) | 1.10 | (0.97 -1.25) |
| 4+3 | 438 | (12.4) | 1.08 | (0.97 -1.20) | 352 | (12.2) | 1.04 | (0.92 -1.17) | 149 | (10.9) | 1.04 | (0.87 -1.25) |
| 4+4 | 288 | (8.1) | 1.19 | (1.05 -1.36) | 243 | (8.4) | 1.24 | (1.08 -1.43) | 106 | (7.7) | 1.22 | (0.99 -1.50) |
| 9 or 10 | 311 | (8.8) | 1.49 | (1.31 -1.68) | 221 | (7.6) | 1.30 | (1.12 -1.51) | 109 | (8.0) | 1.66 | (1.35 -2.04) |
| Modified Risk group ^b | | | | | | | | | | | | |
| Very low | 365 | (10.3) | | Reference | 318 | (11.0) | | Reference | 146 | (10.7) | | Reference |
| Low | 601 | (17.0) | 1.08 | (0.95 -1.24) | 503 | (17.4) | 1.04 | (0.90 -1.19) | 231 | (16.9) | 0.95 | (0.77 -1.17) |
| Favorable intermediate | 1013 | (28.6) | 1.11 | (0.99 -1.25) | 809 | (27.9) | 1.02 | (0.89 -1.16) | 425 | (31.0) | 1.09 | (0.90 -1.32) |
| Unfavorable intermediate | 593 | (16.7) | 1.04 | (0.91 -1.18) | 490 | (16.9) | 0.98 | (0.85 -1.13) | 213 | (15.6) | 0.92 | (0.75 -1.14) |
| High | 462 | (13.0) | 1.23 | (1.07 -1.41) | 376 | (13.0) | 1.15 | (0.99 -1.34) | 176 | (12.9) | 1.15 | (0.92 -1.44) |
| Very high | 510 | (14.4) | 1.40 | (1.22 -1.60) | 399 | (13.8) | 1.30 | (1.12 -1.50) | 178 | (13.0) | 1.38 | (1.11 -1.72) |
| AJCC staging ^c | | | | | | | | | | | | |
| I | 966 | (27.3) | | Reference | 821 | (28.4) | | Reference | 377 | (27.5) | | Reference |
| II | 1763 | (49.8) | 1.04 | (0.96 -1.13) | 1422 | (49.1) | 0.99 | (0.91 -1.08) | 701 | (51.2) | 1.08 | (0.95 -1.22) |
| III | 620 | (17.5) | 1.18 | (1.06 -1.30) | 480 | (16.6) | 1.08 | (0.97 -1.21) | 221 | (16.1) | 1.17 | (0.99 -1.38) |
| IV | 195 | (5.5) | 1.68 | (1.43 -1.96) | 172 | (5.9) | 1.84 | (1.55 -2.17) | 70 | (5.1) | 1.97 | (1.52 -2.55) |
| First Course of Treatment ^f | | | | | | | | | | | | |
| Surgery Only | 1474 | (41.6) | | Reference | 1245 | (43.0) | | Reference | 555 | (40.5) | | Reference |
| Radiation Only | 640 | (18.1) | 0.90 | (0.81 -0.99) | 522 | (18.0) | 0.92 | (0.82 -1.02) | 269 | (19.7) | 0.94 | (0.80 -1.10) |
| Hormone Only | 166 | (4.7) | 1.26 | (1.06 -1.50) | 121 | (4.2) | 1.28 | (1.05 -1.56) | 62 | (4.5) | 1.23 | (0.93 -1.63) |
| surgery + radiation | 46 | (1.3) | 1.23 | (0.92 -1.66) | 32 | (1.1) | 0.97 | (0.68 -1.38) | 12 | (0.9) | 0.92 | (0.52 -1.64) |
| surgery + hormone | 76 | (2.1) | 1.34 | (1.06 -1.69) | 64 | (2.2) | 1.42 | (1.10 -1.83) | 31 | (2.3) | 1.45 | (1.00 -2.09) |
| Radiation+Hormone | 392 | (11.1) | 1.10 | (0.98 -1.24) | 274 | (9.5) | 0.97 | (0.85 -1.12) | 166 | (12.1) | 1.24 | (1.03 -1.49) |
| Chemo+Other# | 80 | (2.3) | 1.27 | (1.01 -1.61) | 74 | (2.6) | 1.45 | (1.13 -1.85) | 23 | (1.7) | 1.06 | (0.69 -1.62) |
| None | 670 | (18.9) | 0.94 | (0.84 -1.04) | 563 | (19.5) | 1.03 | (0.92 -1.15) | 251 | (18.3) | 0.88 | (0.74 -1.04) |
| Short-term Side Effect ^h | | | | | | | | | | | | |
| Sexual Dysfunction ^g | 780 | (22.0) | 1.51 | (1.39 -1.64) | 681 | (23.5) | 1.57 | (1.44 -1.72) | 248 | (18.1) | 1.38 | (1.20 -1.59) |
| Urinary dysfunction | 1637 | (46.2) | 1.88 | (1.76 -2.01) | 1309 | (45.2) | 1.80 | (1.67 -1.94) | 582 | (42.5) | 1.78 | (1.59 -1.98) |
| Bowel Dysfunction and Gastrointestinal Bleeding | 542 | (15.3) | 1.65 | (1.50 -1.81) | 445 | (15.4) | 1.68 | (1.51 -1.86) | 232 | (17.0) | 1.74 | (1.51 -2.00) |
| None | | | | Reference | | | | Reference | | | | Reference |

a. Adjusted for race/ethnicity, diagnosis age, and education.

- b. Adjusted for race/ethnicity, and diagnosis age
- c. Adjusted for baseline BMI and baseline CCI.
- d. Adjusted for race/ethnicity and AJCC staging
- e. Adjusted for race/ethnicity, baseline BMI, diagnosis year, age at diagnosis, and education.
- f. Adjusted for race/ethnicity, baseline BMI, baseline CCI, risk group, age at diagnosis, and education.
- g. Sexual bothersome is excluded in sexual dysfunction due to the overlapping issue with mental illness.
- h Adjusted for race/ethnicity, first course of treatment, baseline BMI, baseline CCI, risk group, age at diagnosis, and education.

Bold value indicates statistical significance ($P < 0.05$).

Abbreviation: HR, hazard ratio; CI, confidence interval; BMI, body mass index, CCI, Charlson Comorbidity Index

Other: included surgery+RT+chemo, surgery+chemo, RT+chemo, RT+ ADT+chemo

Supplementary Table 7. Risk Factors related to Radiotherapy and Androgen Deprivation Therapy for Mental Illness Among Prostate Cancer Survivors with Adjustment for Clinical and Socioeconomic Factors, 2013-2017

| | Patient Number (n [%]) | | Mental Illness | | Depression | | Mood Disorder | | Anxiety | |
|--|------------------------|--------|----------------|----------------------|-------------|-----------------------|---------------|-----------------------|-------------|----------------------|
| | | | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| Radiation Type ^a | | | | | | | | | | |
| EBRT | 764 | (52.5) | | Reference | | Reference | | Reference | | Reference |
| Brachytherapy | 462 | (31.8) | 0.80 | (0.65 - 0.99) | 1.54 | (0.41 - 5.72) | 0.65 | (0.46 - 0.92) | 0.84 | (0.57 - 1.24) |
| EBRT+ Brachytherapy | 229 | (15.7) | 0.89 | (0.70 - 1.13) | | NA | 0.73 | (0.48 - 1.10) | 0.75 | (0.45 - 1.23) |
| Radiation Dose, Gy (categorical) ^b | | | | | | | | | | |
| 6.5-27.5 (incomplete RT regimen) | 365 | (25.1) | 1.23 | (1.00 - 1.52) | 3.137 | (0.84 - 11.74) | 1.37 | (0.94 - 1.93) | 1.09 | (0.74 - 1.60) |
| 27.6-80.9 | 608 | (41.8) | | Reference | | Reference | | Reference | | Reference |
| 81.0-124.9 | 241 | (16.6) | 1.94 | (1.40 - 2.69) | 9.46 | (1.76 - 50.84) | 3.02 | (1.74 - 5.24) | 2.41 | (1.33 - 4.36) |
| 125.0+ | 241 | (16.6) | 2.28 | (1.15 - 4.54) | 36.31 | (2.76 - 478.46) | 4.46 | (1.82 - 10.96) | 1.44 | (0.34 - 6.05) |
| P for trend ^c | | | | 0.0056 | | 0.1025 | | 0.0012 | | 0.2976 |
| Radiation dose ^b , 10Gy (continuous) | | | 1.00 | (1.00 - 1.01) | 1.14 | (1.00 - 1.30) | 1.00 | (0.99 - 1.01) | 1.001 | (0.99 - 1.01) |
| ADT type ^a | | | | | | | | | | |
| Orchiectomy | 11 | (1.0) | 0.91 | (0.40 - 2.05) | | NA | 1.29 | (0.41 - 4.10) | 0.98 | (0.24 - 4.04) |
| Medical Castration | 1077 | (97.8) | | Reference | | | | Reference | | Reference |
| Surgical and Medical Castration | 13 | (1.2) | 0.77 | (0.36 - 1.64) | 2.04 | (0.26 - 15.91) | 0.91 | (0.29 - 2.89) | 0.88 | (0.22 - 3.60) |
| Medical Castration ^a | 1101 | | | | | | | | | |
| LHRH agonists/antagonists alone | 344 | (31.6) | | Reference | | Reference | | Reference | | Reference |
| LHRH agonists/antagonists+ Antiandrogens | 370 | (33.9) | 1.21 | (0.98 - 1.49) | 1.73 | (0.62 - 4.79) | 1.35 | (0.95 - 1.91) | 1.05 | (0.70 - 1.58) |
| Antiandrogens alone | 278 | (25.5) | 1.30 | (1.03 - 1.63) | 1.39 | (0.38 - 5.06) | 1.22 | (0.82 - 1.81) | 1.18 | (0.77 - 1.82) |
| Abiraterone or Enzalutamide ^d | 98 | (9.0) | 1.25 | (1.06 - 1.48) | 1.70 | (0.45 - 6.40) | 1.77 | (1.10 - 2.86) | 2.52 | (1.53 - 4.14) |
| ADT administration ^e _ metastatic prostate cancer patients only | | | | | | | | | | |
| Intermittent | 41 | (22.0) | | Reference | | Reference | | Reference | | Reference |
| Continuous | 145 | (78.0) | 1.94 | (1.11 - 3.38) | 1.83 | (0.34 - 9.93) | 0.96 | (0.45 - 2.05) | 1.14 | (0.49 - 2.62) |
| ADT duration ^e , month (categorical) | | | | | | | | | | |
| 1-3 | 208 | (19.1) | 1.00 | (0.78 - 1.29) | 1.34 | (0.39 - 4.61) | 1.43 | (0.96 - 2.14) | 1.32 | (0.85 - 2.06) |
| 4-6 | 400 | (36.7) | | Reference | | Reference | | Reference | | Reference |
| 7-17 | 242 | (22.2) | 1.13 | (0.89 - 1.42) | 1.11 | (0.30 - 4.04) | 1.22 | (0.81 - 1.84) | 1.25 | (0.80 - 1.95) |
| 18-28 | 118 | (10.8) | 0.99 | (0.74 - 1.34) | 3.55 | (1.16 - 10.89) | 1.49 | (0.94 - 2.36) | 1.41 | (0.84 - 2.39) |
| 29+ | 122 | (11.2) | 1.15 | (0.87 - 1.51) | 0.45 | (0.11 - 1.93) | 1.34 | (0.86 - 2.09) | 1.33 | (0.79 - 2.23) |
| P for trend | | | | 0.3844 | | 0.6238 | | 0.5509 | | 0.5209 |
| ADT duration ^e , 6 months (continuous) | | | 1.04 | (1.00 - 1.08) | 1.00 | (0.87 - 1.15) | 1.05 | (1.00 - 1.11) | 1.04 | (0.97 - 1.11) |
| P value | | | | 0.0348 | | 0.9557 | | 0.0610 | | 0.2455 |

a. Adjusted for race/ethnicity, baseline BMI, baseline CCI, risk group, age at diagnosis, diagnosis year, PSA value, Gleason grade group, socioeconomic status, and AJCC staging.

b. Adjusted for race/ethnicity, radiotherapy type, baseline BMI, baseline CCI, risk group, age at diagnosis, diagnosis year, PSA value, Gleason grade group, socioeconomic status, and AJCC staging.

c. Adjusted for race/ethnicity, ADT type, baseline BMI, baseline CCI, risk group, age at diagnosis, and diagnosis year.

d. Including LHRH agonists/antagonists + abiraterone, orchiectomy+ abiraterone, LHRH agonists/antagonists+ enzalutamide, orchiectomy+ enzalutamide, abiraterone alone, enzalutamide alone, and Other Complicated ADT combination

e. P for trend was tested for trend and did not include incomplete RT regimen category (6.5-27.5 Gy).

Bold value indicates statistical significance (P<0.05).

Abbreviation: HR, hazard ratio; CI, confidence interval; BMI, body mass index, CCI, Charlson Comorbidity Index

Supplementary Table 8A. Risk Factors related to Radiotherapy and Androgen Deprivation Therapy for Anti-Depressant Use Among Prostate Cancer Survivors, 2013-2017

| | Patient Number(n[%]) | | Anti-Depressant Use | | |
|--|-------------------------|-------|---------------------|----------------------|--|
| | | | HR | 95% CI | |
| Radiation Type ^a | | | | | |
| EBRT | 764 | 52.51 | | Reference | |
| Brachytherapy | 462 | 31.75 | 1.46 | (1.03 - 2.08) | |
| EBRT+Brachy | 229 | 15.74 | 1.01 | (0.71 - 1.45) | |
| Radiation Dose, Gy ^b | 1455 | | | | |
| 6.5-27.5 (incomplete) | 365 | 25.09 | | Reference | |
| 27.6-81.0 | 608 | 41.79 | 0.85 | (0.60 - 1.19) | |
| 81.0-125 | 241 | 16.56 | 1.27 | (0.81 - 1.99) | |
| 125+ | 241 | 16.56 | 1.76 | (0.22 - 14.18) | |
| P for trend | | | | 0.4920 | |
| Radiation dose, 10Gy ^b | | | 1.00 | (1.00 - 1.01) | |
| ADT type ^a | | | | | |
| Orchiectomy | 11 | 1.00 | 1.23 | (0.16 - 9.25) | |
| Medical Castration | 1077 | 97.82 | | Reference | |
| Surgical and Medical Castration | 13 | 1.18 | 1.17 | (0.51 - 2.66) | |
| Medical Castration ^a | 1101 | | | | |
| LHRH agonists/antagonists alone | 344 | 31.56 | | Reference | |
| LHRH agonists/antagonists+ | 370 | 33.94 | 2.16 | (1.61 - 2.91) | |
| Antiandrogens | | | | | |
| Antiandrogens alone | 278 | 25.50 | 1.82 | (1.32 - 2.53) | |
| CYP17 Inhibitor or New Generation of | | | | | |
| Antiandrogens ^d | 98 | 8.99 | 1.45 | (1.13 - 1.87) | |
| Intermittent_ metastatic only, ADT only ^c | | | | | |
| Yes | 41 | 22.04 | | Reference | |
| No | 145 | 77.96 | 1.00 | (0.49 - 2.04) | |
| ADT duration, month ^c | | | | | |
| 1-3 | 208 | 19.08 | 1.79 | (1.27 - 2.52) | |
| 4-6 | 400 | 36.70 | | Reference | |
| 7-18 | 242 | 22.20 | 1.06 | (0.77 - 1.46) | |
| 18-28 | 118 | 10.83 | 1.47 | (1.00 - 2.16) | |
| 28+ | 122 | 11.19 | 0.61 | (0.41 - 0.92) | |
| P for trend | | | | 0.0029 | |
| ADT duration, 6 months | | | 0.95 | (0.90 - 1.01) | |

a. Adjusted for race/ethnicity, baseline BMI, baseline CCI, AJCC stage, age at diagnosis, and diagnosis year . b. Adjusted for race/ethnicity, radiotherapy type, baseline BMI, baseline CCI, AJCC stage, age at diagnosis, and diagnosis year .c. Adjusted for race/ethnicity, ADT type, baseline BMI, baseline CCI, AJCC stage, age at diagnosis, and diagnosis year .d. Including LHRH agonists/antagonists + CYP17 inhibitors, Orchiectomy+CYP17 inhibitors, LHRH agonists/antagonists+ New Generation of Antiandrogens, Orchiectomy+New Generation of Antiandrogens, CYP17 Inhibitors alone, New Generation of Antiandrogens alone, and Other Complicated ADT combination.

Bold value indicates statistical significance (P<0.05). Abbreviation: HR, hazard ratio; CI, confidence interval; BMI, body mass index, CCI, Charlson Comorbidity Index

Supplementary Table 9. Risks of Mental Health Disorders among Prostate Cancer Survivors compared to the General Population, Identified by Psychiatry/Psychological Consultation

| Follow-up Period | Prostate Cancer Patients [N(%)] | | General Population [N(%)] | | Adj.HR(95% CI) | | |
|------------------|---------------------------------|-------------|---------------------------|--------------|----------------|--|--|
| | Hazard Ratio | Lower Limit | Upper Limit | | | | |
| 0-2 year | 2036 (2.2) | 4459 (4.9) | 1.88 | (1.77 | -1.98) | | |
| 2-5 year | 792 (0.9) | 4926 (5.8) | 0.63 | (0.58 | -0.68) | | |
| 5-10 year | 545 (0.6) | 4491 (4.9) | 0.51 | (0.46 | -0.56) | | |

Bold value indicates statistical significance (P<0.05).

All hazard ratios adjusted for baseline BMI, baseline CCI, and ethnicity/race. CI, confidence interval. HR, Hazard Ratio.

Supplementary Table 10. Risks of Mental Illness among Prostate Cancer Survivors Compared to the Prostate-cancer-free General Population

| Diagnosis(CCS Code) | 0-2 y After Cancer Diagnosis | | | 2-5 y After Cancer Diagnosis | | | 5-10 y After Cancer Diagnosis | | | 10+ y After Cancer Diagnosis | | |
|--|------------------------------|---------------------|-------------|------------------------------|---------------------|-------------|-------------------------------|---------------------|-------------|------------------------------|---------------------|-------------|
| | Adj.HR(95% CI) | | | Adj.HR(95% CI) | | | Adj.HR(95% CI) | | | Adj.HR(95% CI) | | |
| | HR | Lower Limit | Upper Limit | HR | Lower Limit | Upper Limit | HR | Lower Limit | Upper Limit | HR | Lower Limit | Upper Limit |
| Mental illness (5) | 1.75 | (1.69 -1.81) | | 1.01 | (0.98 -1.05) | | 0.98 | (0.94 -1.02) | | 0.94 | (0.88 -1.01) | |
| Adjustment disorder (5.1) | 1.68 | (1.26 -2.23) | | 1.20 | (0.91 -1.58) | | 1.34 | (1.04 -1.73) | | 1.16 | (0.76 -1.76) | |
| Anxiety disorder (5.2) | 1.54 | (1.44 -1.65) | | 1.18 | (1.10 -1.26) | | 1.17 | (1.09 -1.26) | | 1.20 | (1.06 -1.36) | |
| Delirium dementia and cognitive disorders(5.4) | 0.72 | (0.64 -0.80) | | 0.84 | (0.76 -0.92) | | 0.97 | (0.89 -1.06) | | 0.99 | (0.85 -1.14) | |
| Mood disorders (5.8) | 1.55 | (1.46 -1.64) | | 1.18 | (1.11 -1.25) | | 1.18 | (1.11 -1.25) | | 1.21 | (1.08 -1.35) | |
| Bipolar disorders (5.8.1) | 1.32 | (0.97 -1.79) | | 1.19 | (0.86 -1.65) | | 0.97 | (0.64 -1.48) | | | NA | |
| Depressive disorder (5.8.2) | 2.07 | (1.85 -2.30) | | 1.12 | (0.99 -1.27) | | 1.14 | (0.98 -1.33) | | 1.24 | (0.61 -2.50) | |
| Schizophrenia and other psychotic disorders (5.10) | 0.83 | (0.69 -0.99) | | 0.83 | (0.70 -0.98) | | 0.98 | (0.83 -1.16) | | 1.08 | (0.72 -1.64) | |
| Alcohol-related disorders (5.11) | 0.84 | (0.73 -0.97) | | 0.72 | (0.63 -0.84) | | 0.98 | (0.85 -1.13) | | 0.86 | (0.65 -1.15) | |
| Substance-related disorders (5.12) | 1.08 | (0.96 -1.23) | | 0.77 | (0.68 -0.88) | | 0.59 | (0.52 -0.67) | | 0.68 | (0.55 -0.82) | |
| Suicide and intentional self-inflicted injury (5.13) | 0.81 | (0.58 -1.12) | | 1.05 | (0.79 -1.39) | | 0.81 | (0.60 -1.09) | | 1.53 | (0.89 -2.62) | |
| Miscellaneous mental disorders (5.15) | 1.35 | (1.18 -1.55) | | 1.25 | (1.09 -1.42) | | 1.07 | (0.94 -1.23) | | 1.27 | (0.99 -1.61) | |
| Sexual and gender identity disorders (5.15.5) | 1.73 | (1.33 -2.24) | | 1.38 | (0.98 -1.93) | | 0.52 | (0.30 -0.91) | | 1.02 | (0.13 -8.06) | |
| Sleep disorders (5.15.6) | 1.18 | (0.72 -1.91) | | 1.39 | (0.93 -2.09) | | 1.68 | (1.10 -2.59) | | 1.80 | (0.25 -13.25) | |
| Somatoform disorders (5.15.7) | 1.57 | (0.97 -2.55) | | 1.03 | (0.63 -1.69) | | 0.81 | (0.45 -1.46) | | 1.00 | (0.06 -15.99) | |

Bold value indicates statistical significance (P<0.05).

All hazard ratios adjusted for baseline BMI, baseline CCI, and ethnicity/race. CI, confidence interval.

* Proportional hazard assumption not met; flexible spline model used.

b. Some outcomes that developed or diagnosed before adulthood were excluded from this table: Attention deficit conduct and disruptive behavior disorder (5.3),

Developmental disorder (5.5) and its related disorders, Disorders usually diagnosed in infancy childhood or adolescence (5.6) and its related disorders,

c. Some outcomes that had limited observations were excluded from this table: Personality disorder (5.9), Screening and history of mental health and substance abuse codes (5.14), Miscellaneous mental disorder (5.15) and its related disorders.

Supplementary Figure 1. The Dose Distribution of Radiotherapy and ADT among Prostate Cancer Patients

