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Association of mental health diagnosis with race and all-cause mortality after a cancer diagnosis: large-scale analysis of electronic health record data

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Abstract

Background: Disparity in mental health care among cancer patients remains understudied.

Methods: We conducted a large, retrospective, single tertiary-care institution cohort study based on de-identified electronic health record data of 54,852 adult cancer patients without prior mental health diagnosis (MHD) diagnosed at the University of California, San Francisco between 1/2012 and 9/2019. The exposure of interest was early onset MHD with or without psychotropic medication (PM) within 12 months of cancer diagnosis and primary outcome was all-cause mortality.

Results: 8.2% of patients received a new MHD at a median of 197 days (interquartile-range [IQR] 61-553) after incident cancer diagnosis, 31.0% received a PM prescription, and 3.7% a MHRV. 62.6% of patients were non-Hispanic white (NHW), 10.8% Asian, 9.8% Hispanic, and 3.8% Black. Compared to NHWs, minority cancer patients had reduced adjusted odds of MHDs, PM prescriptions, and MHRVs, particularly for generalized anxiety (Asian: odds ratio [OR] 0.66, 95% confidence interval 0.55-0.78; Black: OR 0.60, 0.45-0.79; Hispanic: OR 0.72, 0.61-0.85) and selective-serotonin-reuptake-inhibitors (SSRI; Asian: OR 0.43, 0.37-0.50; Black: OR 0.51,

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Author Contributions

Conceived and designed the overall study: WCC, JCH, LB, OM. Obtained data access and IRB approval: JCH, WCC. Patient selection and data curation: WCC, JCH. Data analysis: WCC, JCH. Interpreted the data: WCC, LB, SEB, MWR, LEK, JDT, OM, CCP, JCH. Writing – original draft: WCC, JCH. Writing – review and editing: WCC, LB, SEB, MWR, LEK, JDT, OM, CCP, JCH.

Conflict of Interest Notification: JCH and JDT, are coinventors on a pending patent related to machine learning algorithms for acute care episodes during radiation treatment, unrelated to the present study.

0.40-0.61; Hispanic: OR 0.79, 0.70-0.89). New early MHD with PM was associated with elevated all-cause mortality (12-24 months: hazard ratio [HR] 1.43, 1.25-1.64) that waned by 24-36 months (HR 1.18, 0.95-1.45).

Conclusions and Relevance: New mental health diagnosis with psychotropic medication was a marker of early mortality among cancer patients. Minority cancer patients were less likely to receive documentation of mental health diagnoses or treatment, which may represent missed opportunities to identify and treat cancer related mental health conditions.

Precis:

In this large-scale retrospective electronic health record analysis, minority patients were less likely to receive documentation of mental health diagnosis or treatment after a cancer diagnosis, which may represent missed opportunities to identify and treat cancer related mental health conditions.

Keywords

Mental health; distress; electronic health record; psychotropic medication; psycho-oncology

Introduction

A cancer diagnosis can be associated with significant mental and emotional distress[1,2], and the incidence of new mental health diagnoses and psychotropic medications is significantly elevated in the months immediately before and after a cancer diagnosis[3]. Both pre-existing and new-onset mental health conditions among cancer patients have been associated with higher overall and cancer-specific mortality[4–13,14]. In the primary psychiatric literature, disparity in the identification of mental health conditions, access to and utilization of mental health services[15–21], and decreased prescription of SSRI and other psychotropic medications[16,22–24,25], among minorities in the United States is well documented, but this disparity in the context of cancer patients is less well studied[25].

The aim of this study was to characterize the temporal dynamics and racial differences of the onset of new mental health diagnoses, psychotropic medications and mental-health related visits after a cancer diagnosis, and to examine the association of these exposures with all-cause mortality among a diverse cohort of cancer patients in the United States. To this end, we interrogated a novel, comprehensive institutional corporate data warehouse (CDW) containing de-identified electronic health records of all patients engaging with a single health system[26]. This system serves approximately 8% of all cancer patients within a geographic catchment area spanning most of Northern California[27], an ethnically diverse region with an estimated population of over 15 million.

Methods

Study Population

We identified a cohort of all adult patients (18 years and older) with an incident cancer diagnosis at the University of California, San Francisco (UCSF) between January 2012 and September 2019. Patients were identified using an institutional CDW populated with

a de-identified copy of the electronic health record (EHR). Patients included in this study were required to have at least two or more visits with at least 30 days between the first and last visit. Incident malignant cancer diagnoses were identified using available diagnosis codes associated with outpatient or inpatient encounters (Supplemental Methods). Incident mental health diagnoses (MHD) were similarly identified: psychotic disorders, mood disorders, and anxiety disorders were included (Supplemental Methods). Finally, a cohort of patients without an MHD preceding an incident cancer diagnosis was identified (Figure 1, N=54,852). This retrospective cohort study was performed according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Institutional review board approval was waived due to the de-identified nature of the dataset.

Clinical Variables

In addition to cancer and MHD, other clinical covariates were collected including age at time of cancer diagnosis, sex, smoking status, marital status, race, and baseline modified Charlson comorbidity score excluding malignancy[28]. Cancer diagnoses were subcategorized based on common disease sites (eTable 1); patients with metastatic disease at diagnosis were included in a separate category. More details on extraction and encoding of these variables are described in the supplemental methods (Supplemental Methods). First prescription and total number of prescriptions of an oral psychotropic medication was extracted from provider medication orders (Supplemental Methods). Psychotropic medications included were: selective serotonin receptor inhibitors (SSRI), tricyclic antidepressants (TCA), non-SSRI antidepressants, antipsychotics, anxiolytics (non-benzodiazepine), benzodiazepines, and lithium (Supplemental methods, eTable 2). First mental health encounter was extracted based on text-matching of encounters associated with a department or provider type with the prefix “psych” (Supplemental methods).

Exposures and Outcomes

The exposures of interest were early MHD after an incident cancer diagnosis, defined as onset of a new MHD within 12 months after a cancer diagnosis, and early MHD requiring medication, defined as onset of a new early MHD with onset of a new psychotropic medication prescription within 12 months. The outcome of interest was all-cause mortality. Time to death was determined based on available dates of death within the California Death Certificate Registry[29], and calculated from the date of appearance of the incident cancer diagnosis code. Median follow up was estimated using the reverse Kaplan-Meier method[30].

Statistical Analysis

Multivariable adjusted time-partitioned mortality hazard ratios were constructed using epochs of 12-24, 24-36, and 36-60 months; to corroborate these estimates, time-varying adjusted hazard ratios were also estimated using the Loess fit of Schoenfeld residuals[31], as well as via a flexible parametric survival model with the exposure modeled as a time-varying coefficient with 5 degrees-of-freedom (Supplemental methods). Unless otherwise specified, multivariable models were adjusted for age, sex, baseline smoking status, marital status, race, cancer subsite, and modified Charlson comorbidity score. Sensitivity analyses were undertaken using a subset of patients with complete data (N=49,901), patients with metastatic cancer at diagnosis (N=1,971), and with a subset of patients with at least one

EHR encounter 6 months or more prior to cancer diagnosis (N=18,928), to allow sufficient lead-in time to uncover prior MHD or cancer diagnoses (eTable 3, eTable 5). Unless specified, hazard and odds ratios in the main text are from multivariate adjusted models. All hazard ratios (HR) and odds ratios (OR) are reported with a 95% confidence interval (CI), and all statistical tests were 2-tailed, with P-values ≤0.05 considered significant.

Results

Cohort characteristics

A total of 54,852 cancer patients with 96,064 person-years of EHR follow-up were included (Table 1). Patients continued to have EHR documentation up to a median of 20.4 months after an incident cancer diagnosis (IQR 5.3-44.7). 62.6% of patients were non-Hispanic white (NHW), 10.8% Asian, 9.8% Hispanic, and 3.8% Black. 10,333 patients died (18.8%, 5-year overall survival: 63.1%); overall survival (OS) curves by cancer subsite can be found in the supplement (eFigure 1), and 5-year OS ranged from 11.3% for pancreatic cancer to 84.7% for prostate cancer.

Prevalence of mental health diagnoses, psychotropic medications, and mental-health related visits after a cancer diagnosis

4,476 patients (8.2%) experienced a new MHD after an incident cancer diagnosis, 2,007 (3.7%) received one or more mental health related visits (MHRV), and 17,027 (31.0%) received one or more oral psychotropic medication prescriptions. The most common new MHDs were generalized anxiety disorder (Table 1, 39.5%), depression (29.1%), and reactive/adjustment disorder (21.6%). New onset of psychotic disorder was rare (1.4%). 24.8% of cancer patients received an oral benzodiazepine prescription after diagnosis, 8.9% received a non-SSRI antidepressant, and 5.7% received an SSRI prescription.

Timing of onset of mental health diagnoses, psychotropic medications, and mental-health related visits after a cancer diagnosis

After a cancer diagnosis, median time to onset of a new MHD was 197 days (IQR 61-553), and median time of onset of a psychotropic medication prescription was 224 days (IQR 72-652). The probability of a new MHD, new psychotropic medication order, and new psych-related visit began to rise in the 3 months preceding a cancer diagnosis and was markedly elevated in the first 6 months after a cancer diagnosis (Figure 1), with an early peak shortly after diagnosis. Cancers associated with worse survival appeared to be correlated with a greater probability of new MHD: together, patients with lung, pancreatic, and liver cancers (N=5,984) experienced a 9.27-fold (95% confidence interval [CI] 3.63-14.90) increase in MHD in the first 6 months after cancer diagnosis over baseline (−2 to −1 years), compared to 2.96-fold (1.82-4.11) for prostate cancer (N=7,780), and 2.25-fold (1.16-3.33) for non-melanoma skin cancer (N=7,198, Figure 1, eFigures 2–4).

Variation in cancer type, mental health diagnosis, psychotropic medications, and MHRV by race

There was significant variation in race by cancer disease site (χ^2=5035.9, P<0.0001). Cancers with lowest proportion of NHW (eFigure 5) included liver and bile duct

(41.8%), non-colorectal gastrointestinal (other GI, 50.1%), lung (50.4%), and gynecologic malignancies (51.7%). Cancers with greatest NHW proportion included non-melanoma skin (83.7%), melanoma (82.5%), and prostate (69.7%). After adjusting for disease site, demographics, smoking, and Charlson comorbidity score, minority race was associated with significantly lower adjusted odds of receiving a MHD, psychotropic medication prescription, and MHRV (eTable 4). There was variation in the magnitude of this association depending on the specific type of MHD or psychotropic medication, and also by disease site (eTable 5). For example, compared to NHW, all minorities appeared to have the lowest odds of receiving a generalized anxiety diagnosis (Asian: OR 0.66, 0.55-0.78; Black: OR 0.60, 0.45-0.79; Hispanic: OR 0.72, 0.61-0.85), but only Asian patients had statistically significantly lower odds of receiving a depression diagnosis (Asian: 0.77, 0.63-0.92; Black: 0.84, 0.63-1.09; Hispanic: 0.94, 0.78-1.12), and only Hispanic patients had statistically significantly lower odds of receiving an adjustment disorder diagnosis (Asian: 1.04, 0.85-1.25; Black: 0.72, 0.49-1.01; Hispanic: 0.73, 0.58-0.91). In other words, MHDs were less frequent overall among minorities, and were shifted towards adjustment disorder among Asians, towards depression among Black and Hispanic patients, and away from generalized anxiety disorder among all minorities, as compared to NHW. Among disease sites, decreased odds of MHD was most consistent across minorities with metastatic and hematologic malignancies (eTable 5), and most pronounced among Asian liver/bile duct cancer patients (OR 0.41, 0.25-0.66), Black prostate cancer patients (0.53, 0.29-0.88), and Hispanic gynecologic (0.56, 0.36-0.84) and pancreatic cancer (0.37, 0.11-0.95) patients.

Similarly, minorities appeared to have significantly lower adjusted odds of receiving an oral psychotropic medication prescription, and this effect was most striking for SSRIs (Asian: OR 0.43, 0.37-0.50; Black: OR 0.51, 0.40-0.61; Hispanic: OR 0.79, 0.70-0.89).

Mortality over time associated with new onset mental health diagnoses

Because the increased probability of MHD was greatest in the first 12 months after a cancer diagnosis, and in order to limit the effect of immortal time bias[32], we next examined the impact of a new early MHD in this time period with or without a new psychotropic medication on all-cause mortality. Tests of interaction between MHD with or without medication and minority status (NHW vs non-NHW) were non-significant for the primary endpoint, so a single multivariable model was used, adjusting for covariates as described in the methods. In this analysis, early MHD was associated with elevated all-cause mortality in the first 12-24 months after cancer diagnosis (Table 2, adjusted HR 1.43, 1.25-1.64), but this effect waned by 24-36 months (HR 1.18, 0.95-1.45).

There appeared to be variation in this mortality association based upon receipt of a psychotropic medication prescription, the type of medication prescribed, and the type of MHD. Early MHD without a psychotropic medication prescription (N=481), for example, was not associated with elevated mortality at any timepoint, whereas early MHD with a psychotropic medication (N=1,521) was associated with significantly greater mortality 12-24 months after diagnosis (HR 2.61, 2.22-3.06).

Among MHD subtypes, the mortality association was of greatest magnitude for adjustment disorder (12-24 months: HR 1.80, 1.41-2.30), while generalized anxiety disorder did not appear to be associated with elevated mortality at any timepoint (Table 2).

Among medication subtypes, the mortality association was of greatest magnitude for antipsychotic medications (12-24 months: HR 2.78, 2.38-3.26), and lowest for SSRIs (12-24 months: HR 1.34, 1.16-1.56) and TCAs (12-24 months: HR 1.00, 0.77-1.29).

Finally, in a non-time-partitioned multivariable Cox model, minority race was associated with elevated all-cause mortality with a hazard ratio ranging from 1.16 (1.09-1.23) among Asian patients, 1.32 (1.20-1.45) among Black patients, and 1.20 (1.12-1.28) among Hispanic patients (eTable 6, eFigure 6).

Discussion

Key findings

We find a clear rise in new mental health diagnoses and psychotropic medications preceding a cancer diagnosis and peaking in the ensuing 12 months. Minority cancer patients were less likely to receive a new mental health diagnosis, a psychotropic medication prescription, or a mental-health visit, as documented in the EHR; in particular, minorities were less likely to receive a generalized anxiety disorder diagnosis or to receive an SSRI prescription. Finally, we find that the appearance of a MHD and a psychotropic medication prescription within 12 months of a cancer diagnosis was associated with elevated all-cause mortality in the short term (12-24 months after cancer diagnosis), but not in the longer term. These decreased odds of MHD and treatment may represent missed opportunities for the identification and amelioration of cancer related distress and mental health conditions among minority patients.

Interpretation in the context of prior work

We use the appearance of a MHD in the EHR as a proxy for diagnosis of a mental health condition, with the understanding that the conditions leading up to the coding of a MHD in the EHR are complex and involve not only the psychological distress and mental health of the patient, but multiple factors of the healthcare system which make it more or less likely for a MHD to be identified and coded. Decreased identification of depression and anxiety conditions, decreased access to and utilization of mental health services[15–21], and decreased prescription of SSRI and other psychotropic medications[16,22–24,25], among minorities in the United States is well documented in the psychiatric literature, but this disparity in the context of cancer patients is less well studied[25]. One prior study by Alcala et al[33] utilized a cross-sectional phone survey in California to examine the impact of a history of cancer diagnosis on psychological distress as measured by the Kessler 6 score, and found that Black and Hispanic respondents were disproportionately more adversely impacted by a cancer diagnosis than NHWs. Furthermore, the preponderance of data indicates that, when studied systematically via interview-based or other direct forms of measurement, psychological distress and mental health conditions among cancer patients are at least similar across ethnic and racial lines, if not more common among minorities[25,34–36]. Thus, our findings may be

more likely to reflect differences in the detection and coding of MHD rather than underlying differences in the true prevalence of distress and mental health conditions among minority cancer patients.

Our finding of elevated all-cause mortality in the early-term among patients receiving a new MHD with a psychotropic medication prescription is consistent with the results of the prior Swedish national database analysis[13], among others[6,9,12,37,38], although prior studies did not distinguish between receipt of psychotropic medication, and did not examine the temporal dynamics of the mortality association. Our data appears to suggest that a new MHD with psychotropic medication may be a correlative marker of greater burden of cancer disease and treatment, given the positive correlation between MHD and psychotropic medication prescriptions with disease sites known to have poorer outcome, and the limitation of the mortality association to an early timepoint of between 12-24 months, during which time mortality from cancer would presumably be dominant. Others have also postulated a role for physiologic effects of stress and mental health disorders leading to elevated mortality from both cancer progression[39] and intercurrent disease[40–43].

Significance of findings

The National Comprehensive Cancer Network's (NCCN's) most recent guidelines for cancer related distress[44] (v1.2021) provides a set of standards of care that include the recognition, monitoring, and treatment of distress throughout the timespan of a cancer patient's care.

Our analysis demonstrates the usefulness of utilizing EHR data to probe systemwide patterns of cancer and mental health related care. Our findings of statistically significantly decreased odds of coding of MHDs, prescription of psychotropic medications, and mental-health related visits, among minority cancer patients appear to reflect larger patterns in the general psychiatric literature, and require further study. These decreased odds do not appear to be explained by more favorable cancer characteristics among minorities, who were in fact more likely to have cancers associated with poorer prognosis; moreover, when considered as a whole as well as within disease-site strata, minorities experienced at least equal and often higher mortality than NHWs (eFigure 6, eTable 6).

In addition, the patterns of disparity identified here may be revealing. For example, odds of MHD appeared to be approximately more equal among minorities and NHWs in breast cancer patients, who were at the same time more likely in general to receive a MHD, and appeared more likely to be engaged with treatment through mental-health related visits or psychotropic medication (eFigure 2–4), compared to disease sites with similar prognosis such as prostate and non-melanoma skin. This may reflect a pattern of care in breast oncology involving greater awareness of cancer related MHD, and perhaps a greater availability and organization of resources at our institution to engage breast patients in screening and treatment. This increased awareness and allocation of resources may be due in part to the history of psycho-oncology, in which many trials have been performed in the field of breast oncology[45–49]. It is possible that similar efforts in other disease sites may ultimately result in greater parity in the aforementioned endpoints.

Strengths and limitations

Major strengths of our study include the large sample size encompassing ostensibly all cancer patients engaging with a single institution, which was possible due to the use of a novel comprehensive de-identified EHR corporate data warehouse. Our direct analysis of EHR data could serve as a platform for future efforts to develop predictive models for identifying cancer patients at risk for mental health conditions, and to design and evaluate interventions.

Limitations of our study include the lack of cancer stage and treatment data, the limited availability of medication prescription indication and confirmation of administration, and the lack of more granular cause of death data. We further attempt to mitigate these limitations by adjusting for cancer site, as there are significant variations in general prognosis, for example between lung and prostate cancer. Moreover, sensitivity analysis using a subset of patients with metastatic disease at diagnosis, identified similar association of early MHD+PMD with mortality, as well as similar disparities in MHDs, PMs, and MHRVs.

We chose not to exclude patients with incomplete clinical/demographic data and not to impute data, as both actions can introduce bias[50,51]; instead, we show that our findings are robust to sensitivity analyses, including complete case analysis. Our mortality endpoint was collected from an independent data source, for which prior validation studies have shown completeness rates of greater than 95%[29]. Out-migration bias was unlikely to be significant; on average, out-migration from California between 2012 and 2018 was approximately 600,000 per year, or ~1.5% of the state population[52].

It is likely that the rate of new MHD reported here is an underestimate of the true prevalence of distress and mental health conditions in a cancer patient population, which has previously been estimated in interview-based and direct measurement studies to be between 20 and 50%. Nevertheless, the appearance of a MHD in the EHR may better estimate the degree to which providers are identifying and addressing psychological distress and mental health symptoms in a real world cancer treatment setting. Finally, the generalizability of our study is limited, as other institutions are likely to serve populations with differing demographics; however, the analysis approach we outline could be generalized to other settings.

Conclusions

Cancer patients who experience an onset of a mental health condition and psychotropic medication prescription after diagnosis are at elevated risk of all-cause mortality in the short-term. Minority cancer patients were less likely to receive a mental health diagnosis, psychotropic medication prescription, or mental-health related visit, as documented in the electronic health record, which may represent missed opportunities to identify and ameliorate cancer related distress. These results support and underline current guidelines calling for timely and equitable screening and treatment of cancer related distress and mental health conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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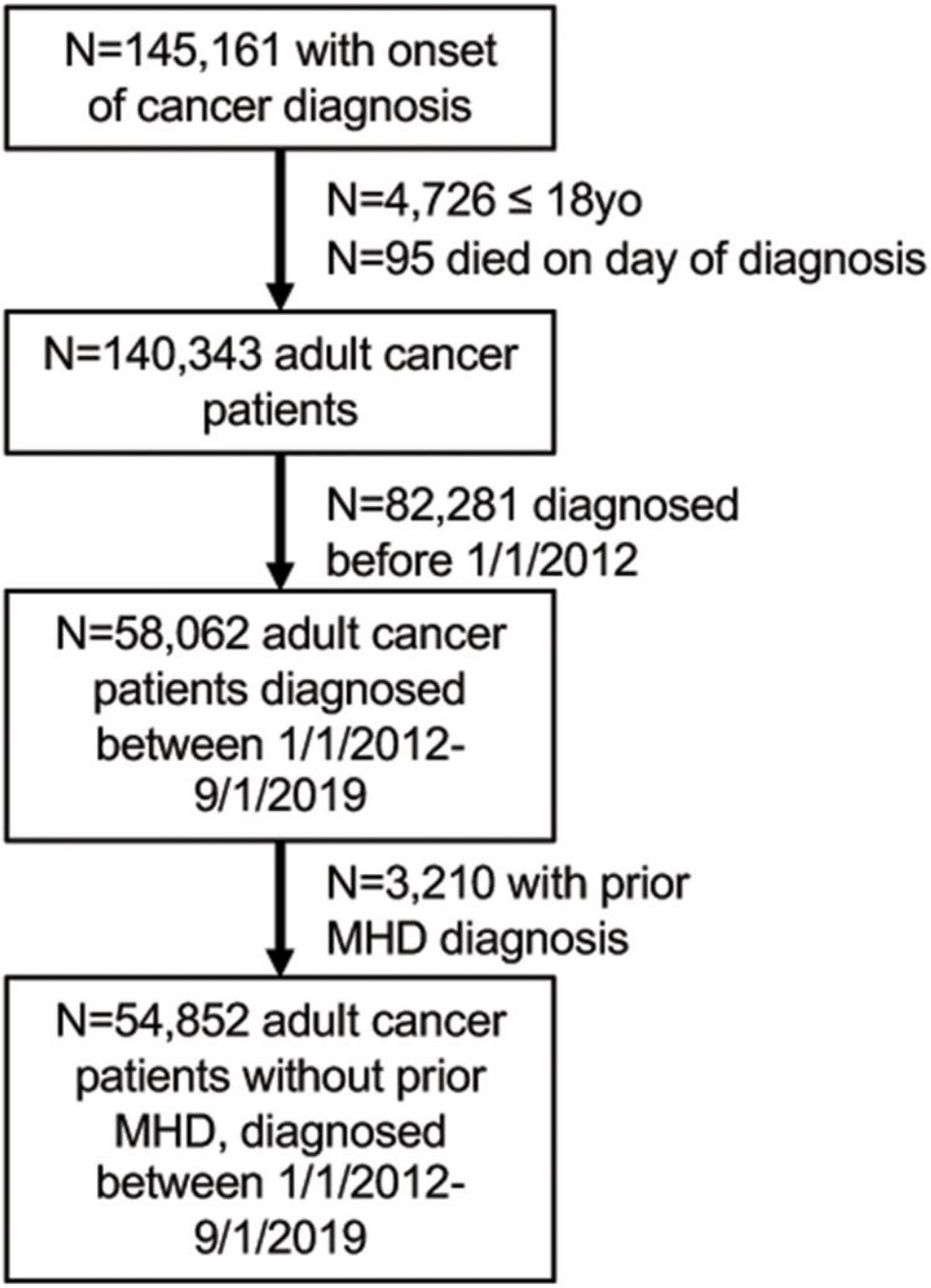
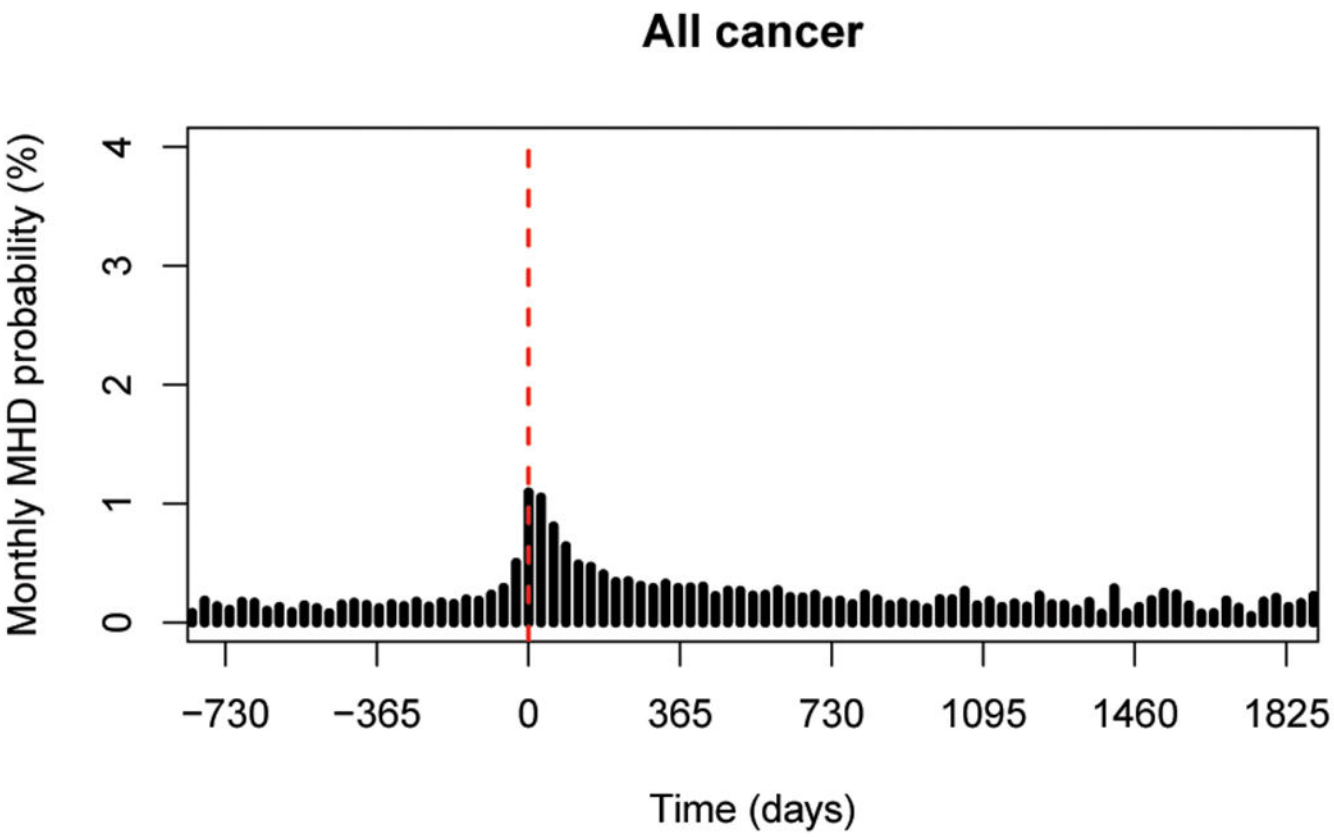
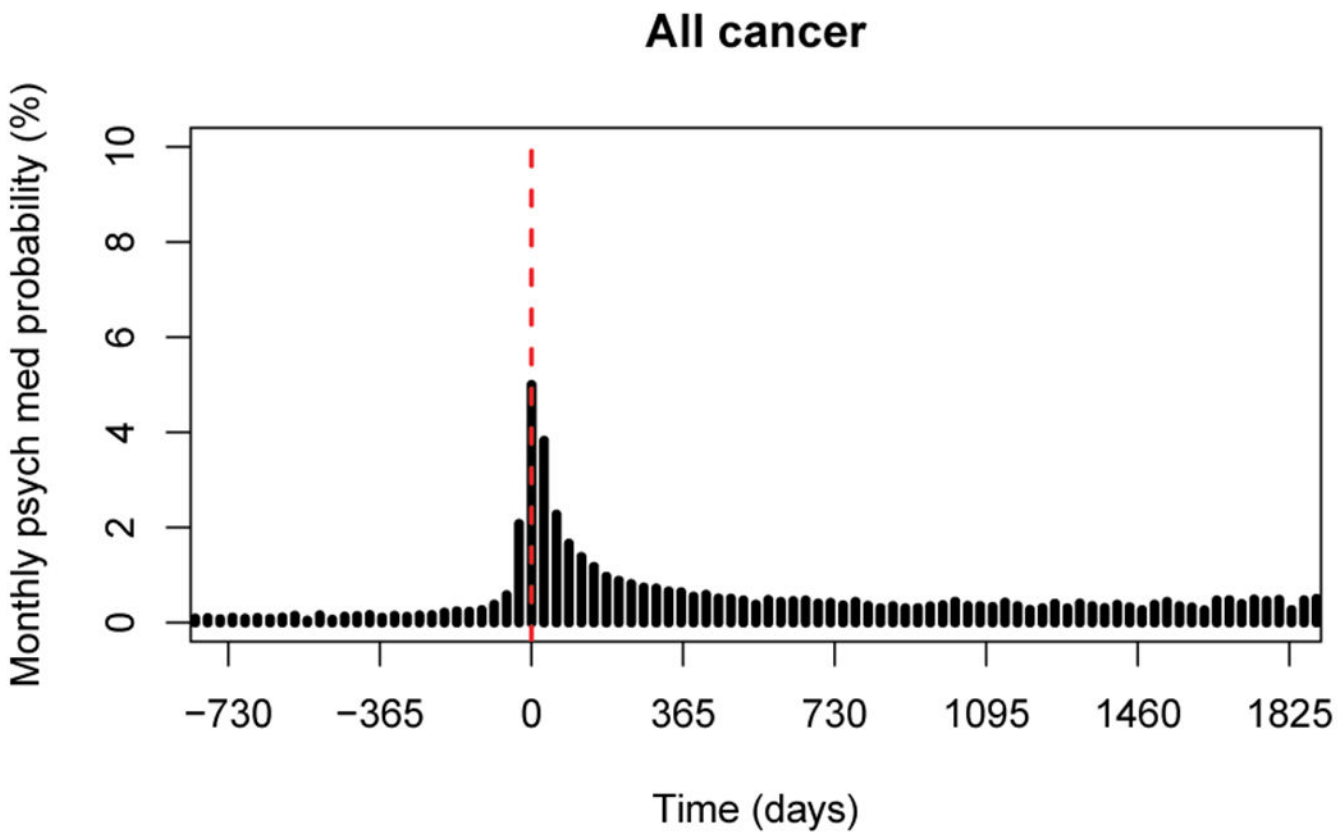
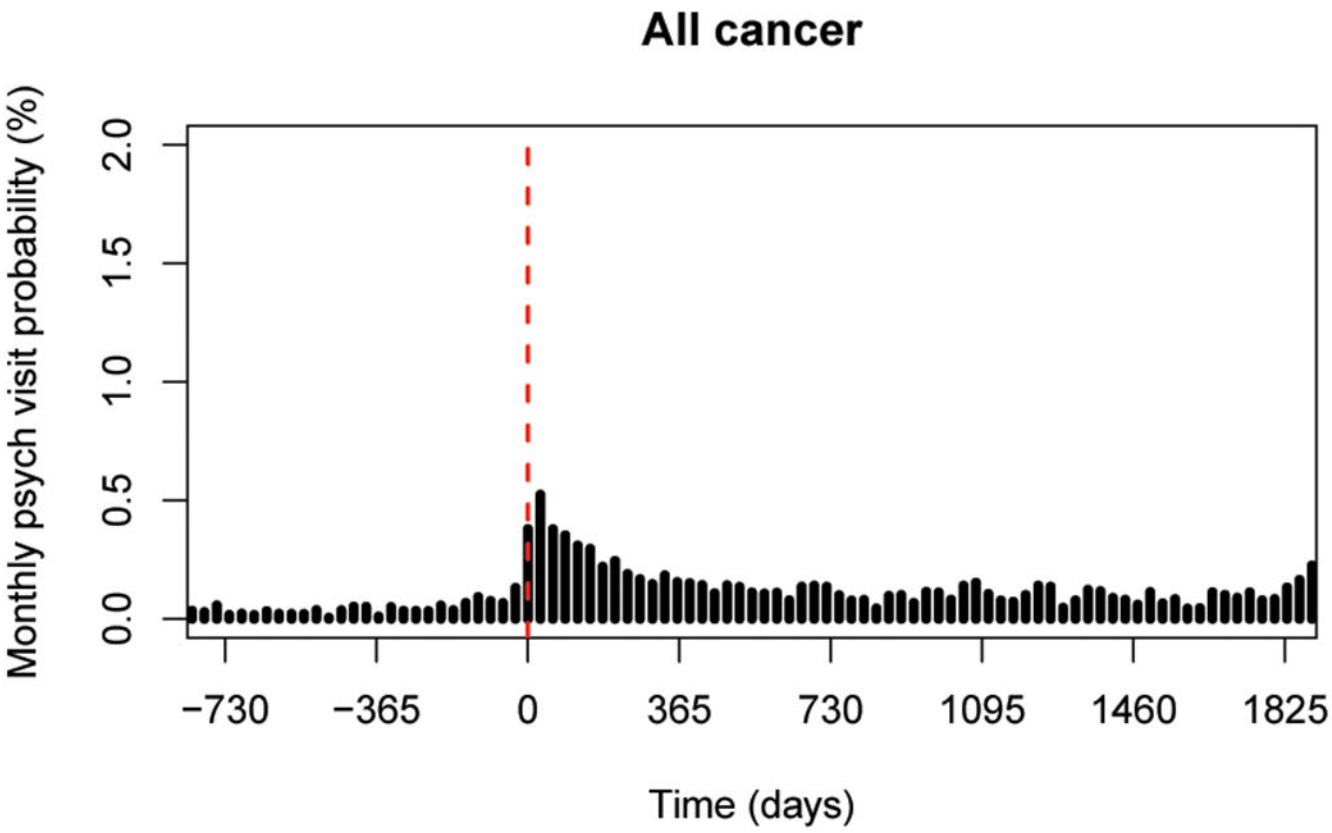
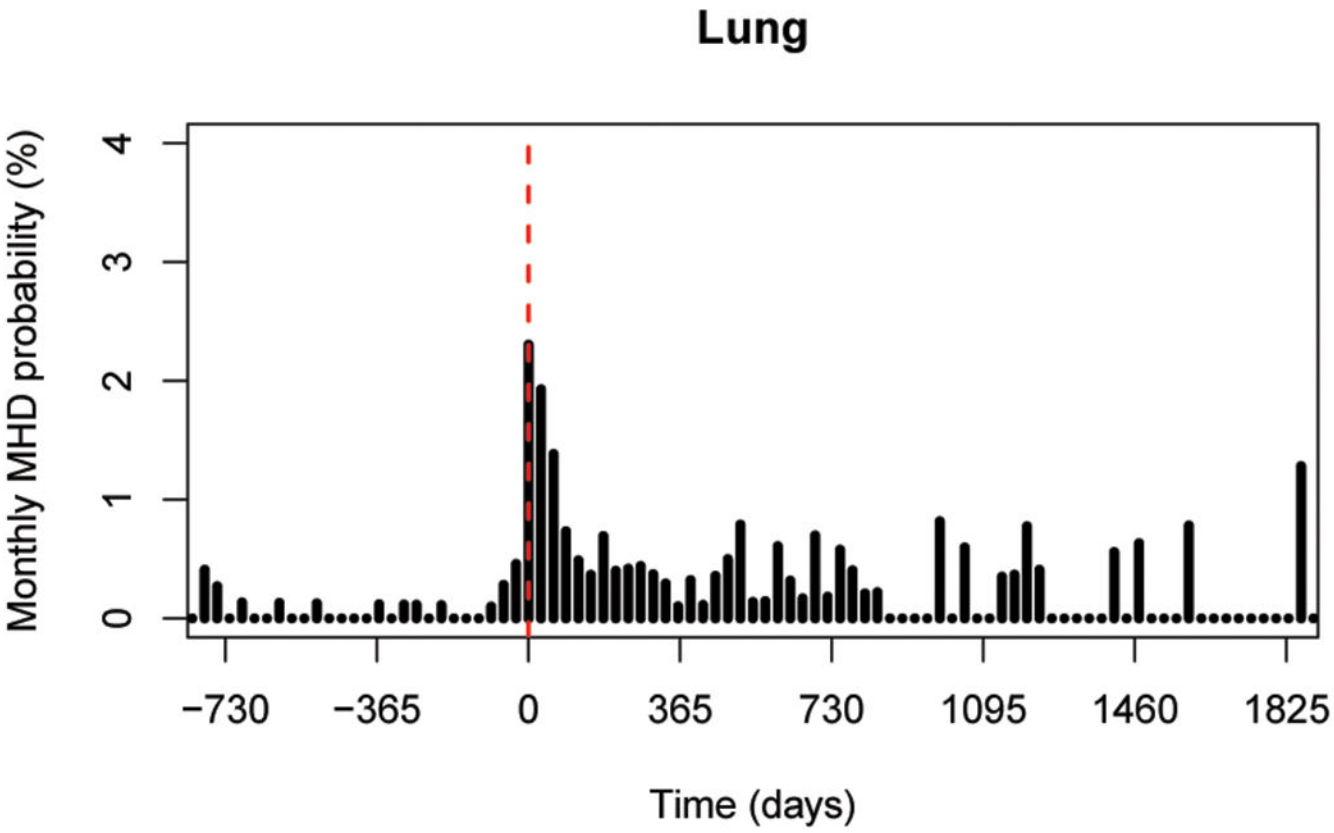


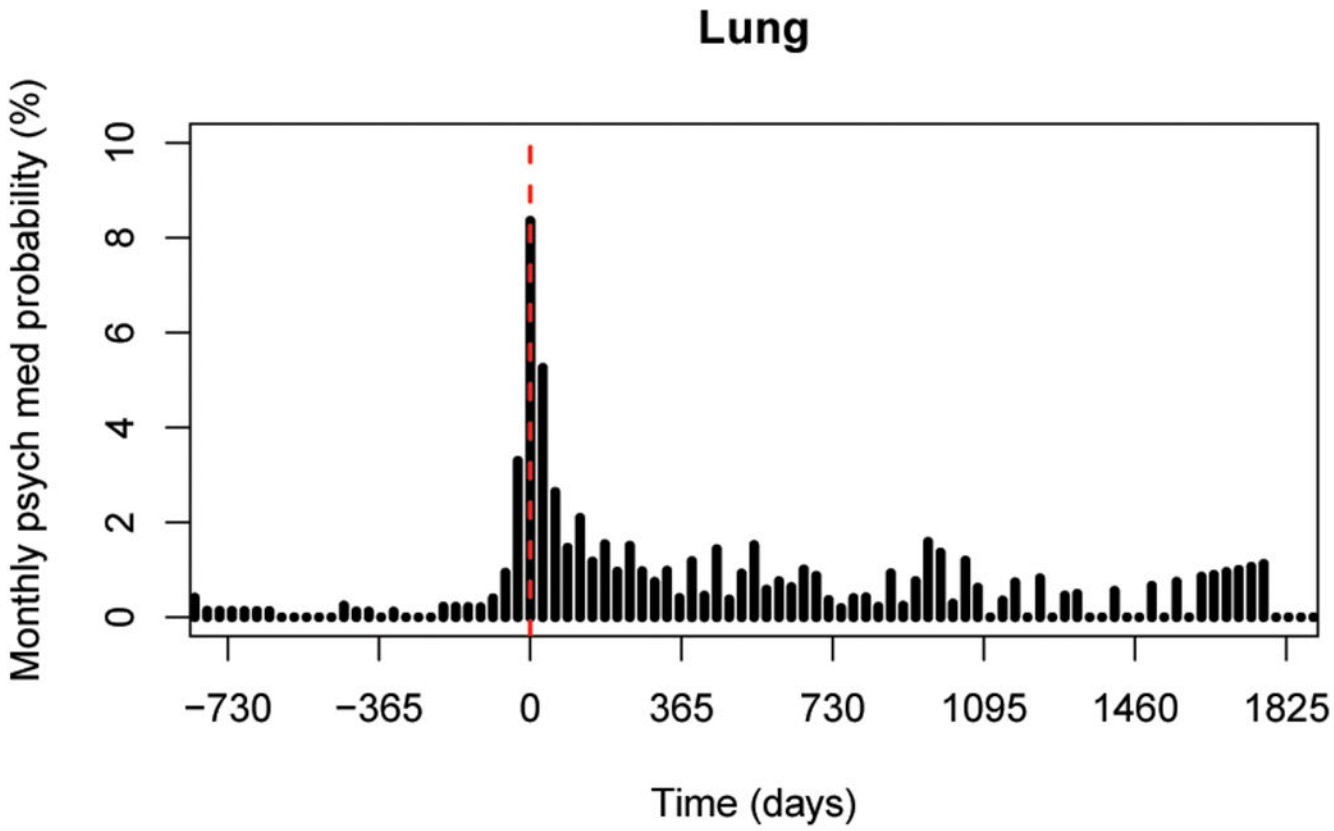
Figure 1.
Consort diagram.

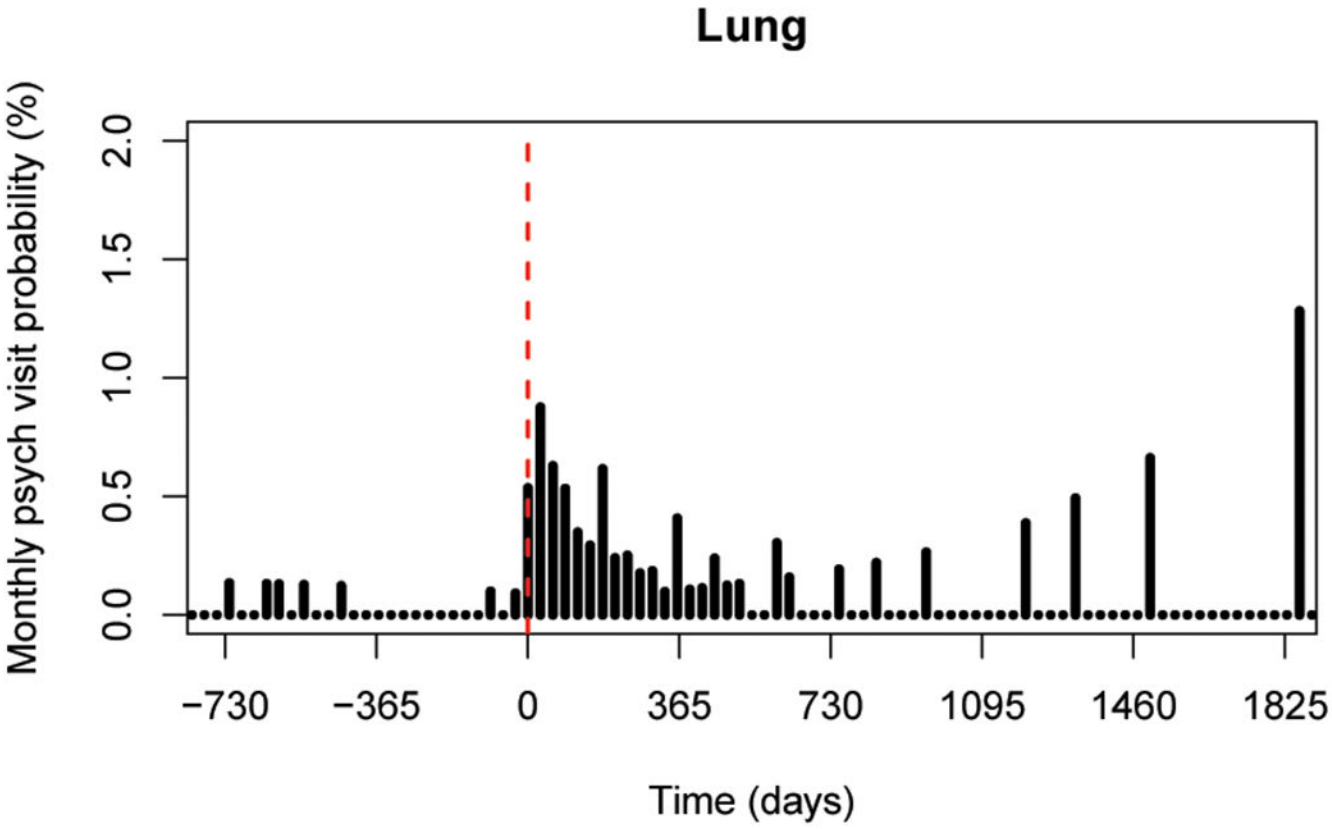


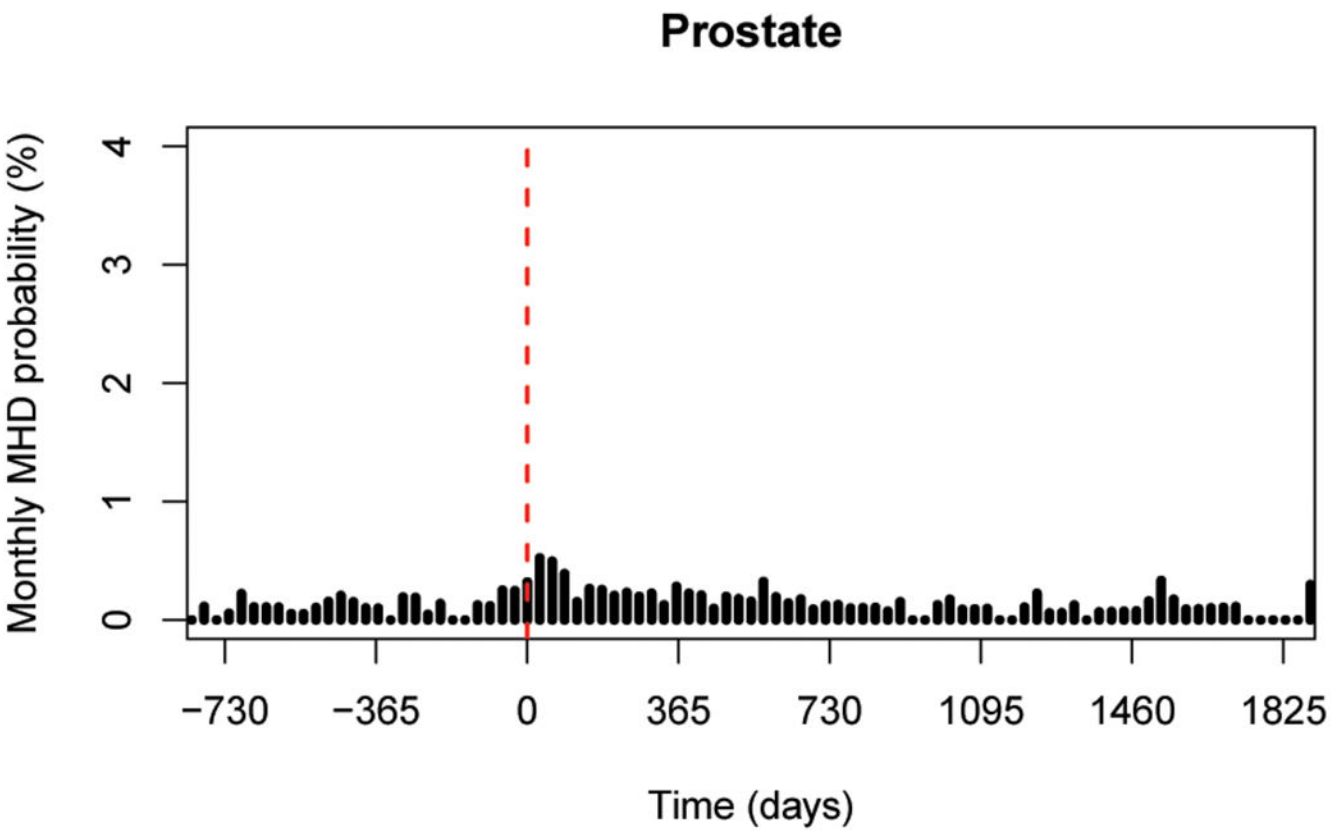


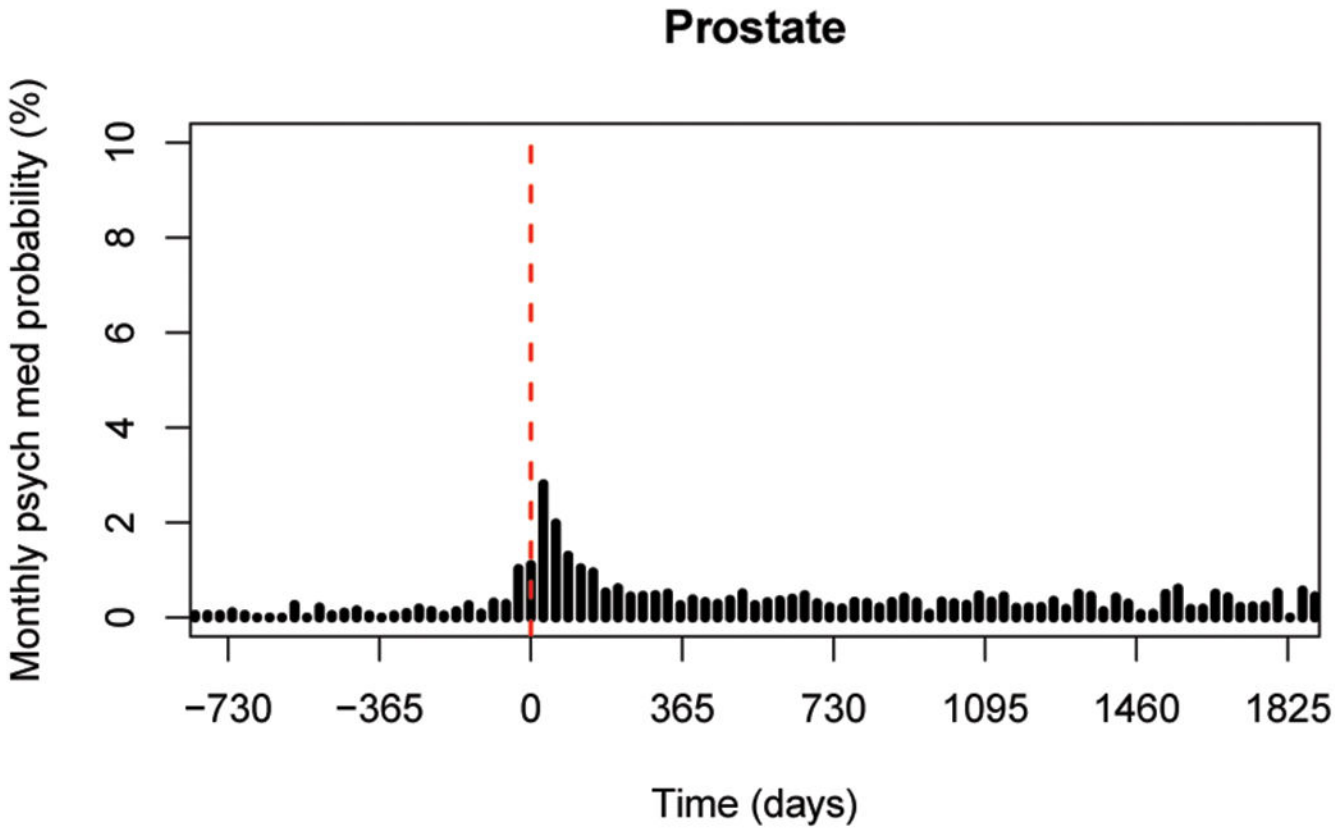












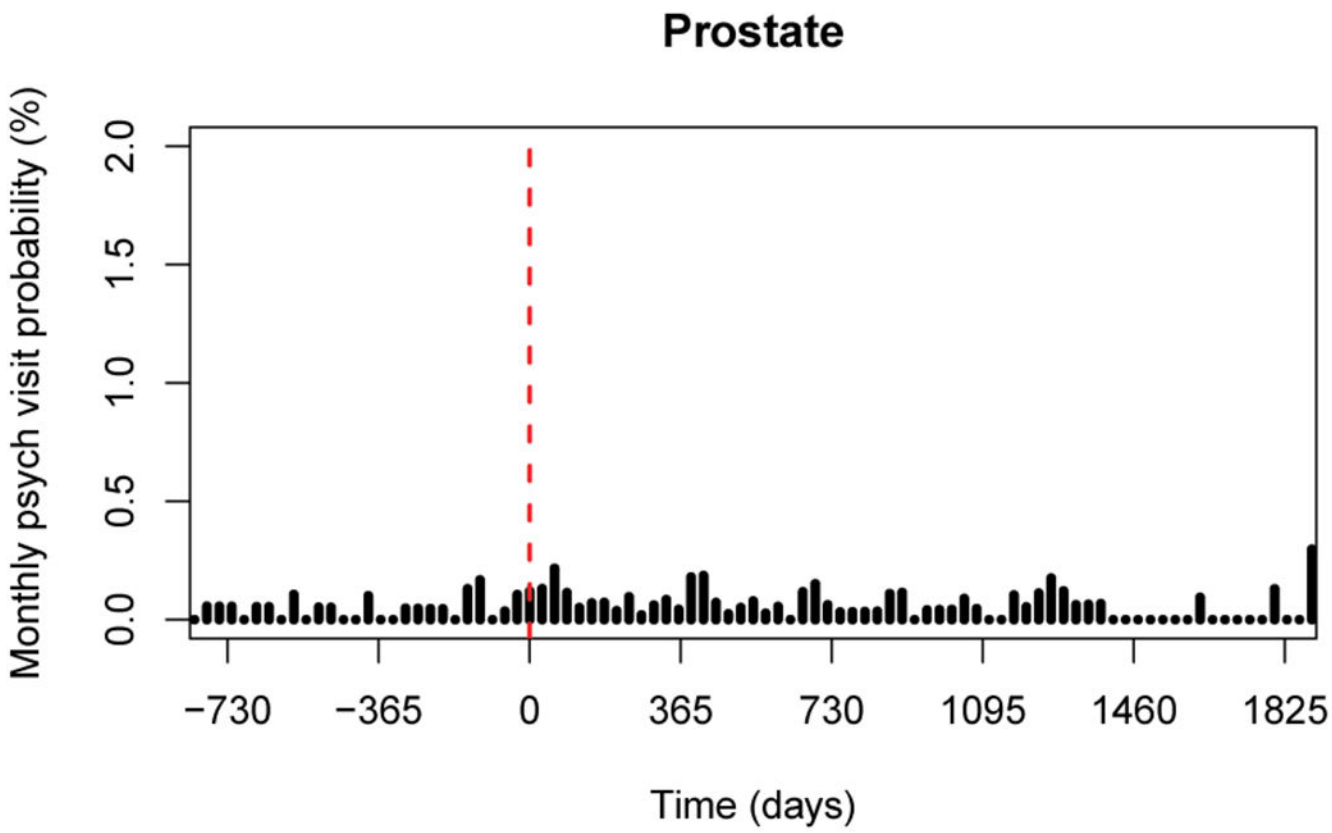


Figure 2. Temporal onset of mental health diagnoses, psychotropic medications, and mental-health related visits among cancer patients.

Histograms are shown of the monthly probability of a new onset mental health diagnosis, psychotropic medication, or psych-related visit between 2 years pre-cancer diagnosis and 5 years post-diagnosis, for: A) all cancer patients, B) lung cancer patients, and C), prostate cancer patients. The red dashed line denotes the time of cancer diagnosis. Each vertical bar represents a single month. The monthly risk was calculated as the number of events within a given month, divided by the number of patients at risk, which is the number of patients with pre-cancer and post-cancer follow up encompassing the given time period.

Table 1.

Clinical and Demographic Characteristics

	All patients	MHD
Patients	54852	4476
Median age (IQR)	62.1 (51.9-70.2)	57.7 (46.4-66.2)
Female	25152 (45.9%)	2568 (57.4%)
Cancer subsite		
Bladder and ureter	1453 (2.6%)	108 (2.4%)
Bone, soft tissue and sarcoma	1471 (2.7%)	145 (3.2%)
Breast	4878 (8.9%)	750 (16.8%)
Central nervous system	2941 (5.4%)	216 (4.8%)
Colorectal	2443 (4.5%)	204 (4.6%)
GI, other	877 (1.6%)	61 (1.4%)
Gynecologic	2922 (5.3%)	251 (5.6%)
Head and neck	1655 (3%)	189 (4.2%)
Hematologic	4888 (8.9%)	495 (11.1%)
Kidney	1487 (2.7%)	81 (1.8%)
Liver and bile duct	2672 (4.9%)	202 (4.5%)
Lung	1981 (3.6%)	207 (4.6%)
Melanoma	2177 (4%)	158 (3.5%)
Metastatic	1971 (3.6%)	173 (3.9%)
Other	4727 (8.6%)	377 (8.4%)
Pancreatic	1331 (2.4%)	85 (1.9%)
Prostate	7780 (14.2%)	371 (8.3%)
Skin, other	7198 (13.1%)	403 (9%)
Modified Charlson Score		
0	44390 (80.9%)	3101 (69.3%)
1	5873 (10.7%)	753 (16.8%)
2-3	3143 (5.7%)	436 (9.7%)
4	827 (1.5%)	101 (2.3%)
5-7	587 (1.1%)	79 (1.8%)
8+	32 (0.1%)	6 (0.1%)
Smoking status		
Never smoker	30853 (56.2%)	2498 (55.8%)
Former smoker	18324 (33.4%)	1671 (37.3%)
Current light smoker	716 (1.3%)	65 (1.5%)
Current heavy smoker	2186 (4%)	182 (4.1%)
Other or unknown	2773 (5.1%)	60 (1.3%)
Marital status		
Married	31481 (57.4%)	2416 (54%)

	All patients	MHD
Single	12162 (22.2%)	1238 (27.7%)
Widowed	2747 (5%)	201 (4.5%)
Divorced or separated	3587 (6.5%)	360 (8%)
Significant other	789 (1.4%)	111 (2.5%)
Other or unknown	4086 (7.4%)	150 (3.4%)
Race		
White or Caucasian	34316 (62.6%)	2931 (65.5%)
Asian	5948 (10.8%)	505 (11.3%)
Hispanic	5365 (9.8%)	479 (10.7%)
Black	2110 (3.8%)	182 (4.1%)
Hawaiian or Pacific Islander	515 (0.9%)	33 (0.7%)
Native American	203 (0.4%)	21 (0.5%)
Other or unknown	6395 (11.7%)	325 (7.3%)
MHD and PM		
New onset MHD	4476 (8.2%)	-
New onset MHD+PM	3634 (6.6%)	-
New onset early MHD	2867 (5.2%)	-
New onset early MHD+PM	1521 (2.8%)	-
New onset MHD by type (N=4476)		
Deression	1303 (29.1%)	-
Bipolar disorder	55 (1.2%)	-
Manic episode	3 (0.1%)	-
Other mood disorder	81 (1.8%)	-
Psychotic disorder	63 (1.4%)	-
Generalized anxiety	1767 (39.5%)	-
Reactive or adjustment	968 (21.6%)	-
Panic disorder	31 (0.7%)	-
Other stress related	205 (4.6%)	-
New onset PM by type		
SSRI	3109 (5.7%)	1166 (26.1%)
Tricyclic antidepressant	1022 (1.9%)	272 (6.1%)
Non-SSRI antidepressant	4888 (8.9%)	1626 (36.3%)
Non-benzodiazepine axiolytic	42 (0.1%)	16 (0.4%)
Antipsychotic	1490 (2.7%)	486 (10.9%)
Lithium	171 (0.3%)	60 (1.3%)
Benzodiazepine	13613 (24.8%)	3004 (67.1%)
Any PM	17027 (31%)	3634 (81.2%)
Number of PM		
0	37825 (69%)	842 (18.8%)

	All patients	MHD
1	11444 (20.9%)	1593 (35.6%)
2	4120 (7.5%)	1268 (28.3%)
3	1220 (2.2%)	605 (13.5%)
4+	243 (0.4%)	168 (3.8%)

Table 2.

Time Stratified Hazard Ratios for Exposures of Interest

Time Stratified Hazard Ratios			
	12-24 months	**24-36 months**	**36-60 months**
Primary exposures *			
Early MHD (N=2867)	1.43 (1.25-1.64)	1.18 (0.95-1.45)	1.00 (0.80-1.25)
Early MHD+PM (N=1521)	2.61 (2.22-3.06)	1.10 (0.75-1.63)	0.60 (0.35-1.04
Early MHD without PM (N=481)	0.94 (0.60-1.46)	0.78 (0.39-1.56)	0.92 (0.49-1.71)
Early MHD subtypes *			
Depression (N=785)	1.48 (1.17-1.87)	1.23 (0.88-1.74)	0.96 (0.67-1.38)
Generalized anxiety (N=1199)	1.13 (0.90-1.43)	0.82 (0.56-1.21)	1.08 (0.78-1.50)
Adjustment disorder (N=629)	1.80 (1.41-2.30)	1.68 (1.14-2.45)	0.83 (0.46-1.50)
Early MHD+PM subtypes *			
MHD+Antipsychotic (N=194)	2.78 (2.38-3.26)	2.49 (1.92-3.23)	2.19 (1.63-2.94)
MHD+SSRI (N=395)	1.34 (1.16-1.56)	1.29 (1.03-1.61)	1.15 (0.90-1.47)
MHD+Non-SSRI-ADP (N=567)	1.75 (1.57-1.95)	1.84 (1.57-2.16)	1.33 (1.11-1.61)
MHD+Benzo (N=1263)	1.50 (1.38-1.62)	1.40 (1.24-1.58)	1.16 (1.02-1.32)
MHD+TCA (N=61)	1.00 (0.77-1.29)	1.17 (0.84-1.64)	0.85 (0.57-1.27)

Models adjusted for age, sex, smoking status, marital status, race, cancer subsite, and modified Charlson comorbidity score. Whole model P-values were <0.01 for all models (Likelihood ratio and Wald's test). Values shown are hazard ratios with 95% confidence interval in parentheses.

* Reference population was patients without a new MHD after a cancer diagnosis at any time.

Abbreviations used: ADP, antidepressant; MHD, mental health diagnosis; PM, psychotropic medication; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.