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Understanding the prevalence of prediabetes and diabetes in patients with cancer in clinical practice. A real-world cohort study

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Abstract

BACKGROUND: This study aimed to understand the prevalence of prediabetes and diabetes in patients with cancer overall, by tumor site, by cancer treatment, and by time point in the cancer continuum.

METHODS: This cohort study has been conducted at the Huntsman Cancer Institute, Salt Lake City, Utah. Patients with a first primary invasive cancer enrolled in the Total Cancer Care protocol between July 2016 and July 2018 were eligible for this analysis. The prevalence of prediabetes and diabetes is based on ICD code, laboratory tests for HbA1c (%), fasting plasma glucose (mg/dl), non-fasting blood glucose (mg/dl), or insulin prescription.

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Author Contributions

Dr Ose had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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RESULTS: The final cohort comprised 3,512 patients with cancer, with a mean age of 57.8 years at cancer diagnosis. Of all patients, 49.1% (n=1,724) were female. At cancer diagnosis, the prevalence of prediabetes was 6.0% (95% CI: 5.3–6.8) and of diabetes 12.2% (95% CI: 11.2–13.3). One year after diagnosis the prevalences were 16.6% for prediabetes (95% CI: 15.4–17.9) and 25.0% for diabetes (95% CI: 23.6–26.4). At the end of the observation period, the prevalence of prediabetes was 21.2% (95% CI: 20.4–23.0) and of diabetes was 32.6% (95% CI: 29.2–32.1). Patients with myeloma (39.2%; 95% CI: 32.6–46.2) had the highest prevalence of prediabetes and patients with pancreatic cancer the highest prevalence of diabetes (65.1%; 95% CI: 57.0–72.3). In patients who underwent chemotherapy (prediabetes: 29.1% vs 15.6%; diabetes: 37.6% vs 29.0%), radiation therapy (prediabetes: 24.3% vs. 19.9%; diabetes: 33.7% vs 32.1%), or immunotherapy (diabetes: 29.2% vs 20.4; prediabetes: 36.0% vs 32.2%), the prevalence of prediabetes and diabetes was higher compared to patients not undergoing those therapies.

CONCLUSIONS: Every second patient with cancer suffers from prediabetes or diabetes. It is essential to foster interprofessional collaboration and to develop evidence-based practice guidelines. A better understanding of the impact of cancer treatment on the development of prediabetes and diabetes remains critical.

Background

Cancer and diabetes are challenging health systems worldwide. In the United States (US), it is estimated that 5% of the population (16.9 million people) have cancer.[1] At the same time, 9.4% of the US population (30.3 million people) suffer from diabetes mellitus (DM). Additionally, 33.9% of American adults (84.1 million people) are living with prediabetes (preDM), raising their chances of developing DM.[2] Overall, cancer and diabetes are often diagnosed simultaneously, independent of age, suggesting a possible common underlying mechanism.[3]

The co-occurrence of cancer and DM raises significant health challenges. In patients with cancer, DM is associated with higher rates of complications,[4,5] a higher risk for hospitalization,[6,7] increased mortality,[8–10] increased psychological distress,[11] and decreased Health Related Quality of Life (HRQoL).[12–14] In fact, DM is a common cause of non-cancer mortality in patients with cancer.[15]

Research on the relationship between cancer and DM has long been focused on DM and its role as a risk factor in the development of several different types of cancer.[16–19] However, a recent study by Hwangbo et al. has suggested that this relationship may be bi-directional as the diagnosis of diabetes not uncommonly occurs after cancer diagnoses.[20] Still, the entire extent of the problem is not well understood. Just a few studies address the prevalence of DM in patients with cancer world-wide[21–23], or the US.[24–27] Evidence for the prevalence of preDM in patients with cancer remains scarce.[21]

Moreover, most studies addressing the prevalence of preDM or DM in patients with cancer are either retrospective analyses which did not include clinical data (e.g., HbA1c, glucose measures)[24,26] or clinical studies with a small number of patients and a focus on one specific cancer. For both types of studies, the lack of cancer specifics (e.g., first primary

cancer), timing of diabetes onset, and/or treatment characteristics limits the comparability and clinical utility of their results.

The aim of this study is to examine the prevalence of preDM and DM in patients with cancer, by utilizing a large, prospective cancer cohort. We incorporated clinical data to determine the prevalence of preDM and DM in patients with cancer overall, by tumor site, by cancer treatment, and by time point in the cancer continuum.

Methods

Design and population

This cohort study utilized the Total Cancer Care (TCC) protocol at the University of Utah (UofU) Huntsman Cancer Institute (HCI). TCC is the primary biobanking research protocol which serves as a large centralized clinical data and tissue repository. Participants enrolled under this protocol agree to be followed throughout their lifetime and release medical data for research, including cancer occurring before enrollment. The study population at the time of this project includes 5,865 individuals, men and women, who enrolled in TCC between July 1, 2016 and July 31, 2018. Participants were recruited at local sites in Salt Lake City, Utah, including the HCI as well as UofU hospitals and clinics. All patients provided informed consent. The HCI-TCC protocol was approved by the University of Utah (UofU) Institutional Review Board (IRB #89989).

Cancer characteristics

All patients included in this analysis have an ICD-O (International Classification of Diseases for Oncology) diagnosis.[28] The determination of the tumor behavior is based on ICD-O morphology codes. Only patients with a tumor behavior code “3” (malignant, primary site) were included in this analysis. The determination of whether a tumor was the first tumor was based on the sequence number, coded in the cancer registry. In this analysis, we included patients with the sequence number “0” (first and only tumor) and “1” (first of more than one tumor). The onset of cancer was defined as the date of the first ICD-O diagnosis documented in the Huntsman Cancer Registry (HCR), even if this date is prior to TCC enrollment. The definition of tumor sites was based on the SEER Site Recode of ICD-O codes (ICD-O-3/WHO 2008 Definition).[55]

Determination of prediabetes and diabetes

The criteria for the determination of preDM and DM (Table 1) were based on the guidelines of the American Diabetes Association (ADA).[29] The onset of preDM/DM was defined as the date of the first qualifying ICD code (preDM: ICD-9 790.xx, ICD-10 R73.xx; DM: ICD-9 250.xx, ICD-10 E8-E13), and/or laboratory results (preDM: HbA1c 5.7%−6.4%, fasting plasma glucose (FPG) 100–125 mg/dl, blood glucose (BG) 140–199 mg/dl; DM; HbA1c >6.4%, FPG >125 mg/dl, BG >199), and/or prescription for insulin. If the determination of DM or preDM was based solely on a laboratory result, a second test in the respective range (preDM or DM), at least three days after, was required to confirm the diagnosis.

Data collection

Patients in this study were identified through the TCC Cancer Clinical Research (CCR) database. The CCR contains study information and is linked with related research- and clinical information systems. For this analysis we included data form the Huntsman Cancer Registry and the University of Utah Health Enterprise Data Warehouse. Data from both sources (eTable 1) were available for the time between January 2000 to July 2019 (for patients recruited between July 2016 and July 2018), allowing at least one year of follow-up for each patient.

Exclusion criteria

Participants were excluded from analysis if they did not have a documented ICD-O diagnosis in the HCR, were not treated in the UofU Health system (HCR 'class of case' numbers: 30, 31, 33, 35, 37, 38, 40–43, 49, 99), were not diagnosed between January 2000 and December 2018, were not between 18 and 90 years old at cancer diagnosis or the cancer was not primary or not invasive (Figure 1).

Statistical analysis

Clinicodemographic characteristics were examined by diabetes status (preDM, DM, and neither). Total counts and percentages among the diabetes status groups are displayed for categorical variables as well as means and standard deviations (SD) for quantitative variables. Differences in clinicodemographics by diabetes status were examined by chi-squared tests for categorical variables and one-way ANOVA for continuous variables. Pairwise comparisons for characteristics by diabetes status (pre-DM vs. neither, DM vs. neither, DM vs. pre-DM) were examined by chi-squared tests for categorical variables and t-tests for continuous variables. The p-values from these pairwise comparisons were adjusted for multiplicity using Hommel's multiple comparison procedure. All statistical tests were two-sided, and p-values< 0.05 considered statistically significant.

The prevalence of preDM and DM with 95% confidence intervals is presented by clinicodemographics, tumor site, therapy (surgery, chemotherapy, radiation therapy, hormone therapy, immunotherapy, glucocorticoids), diagnostic indicator (ICD-code, laboratory test results, insulin prescription), as well as by the time point within the cancer continuum (at or before cancer diagnosis, after cancer diagnosis). A patient was considered as having DM or pre-DM at or before cancer diagnosis if they met DM or pre-DM criteria up to two weeks after cancer diagnosis. Complementarily, the time point 'after cancer diagnosis' started two weeks after cancer diagnosis and was subdivided in 'One month after' (up to 30 days), 'Six month after' (up to 182 days), 'One year after' (up to 365 days) and 'End of the observation period' (>365 days).

The length of follow-up was defined as the number of days between cancer diagnosis and the last documented date from data sources in the EDW (e.g. encounter, ICD-code, laboratory test). The median follow-up in months is provided. 95% CIs are constructed by the Wilson score confidence interval for binomial proportions.[30] Analyses are conducted in R (R Foundation for Statistical Computation, Vienna, Austria), version 3.5.3.

Results

Description of the cohort

The HCI-TCC©-DM cohort (Figure 1) comprises 3,512 patients with cancer (median follow-up 28 months), with a mean age of 57.8 years at cancer diagnosis. Of all patients, 49.1% (n=1,724) were female, 90.5% (n=3,177) were non-Hispanic white, 60.4% (n=2,122) were overweight or obese, and 70.2% (n=2,464) were Utah residents (Table 2).

Cancers of the breast (13.8%; n=484) and prostate (14.1%; n=494) were the most common in this cohort (Table 3). Regarding cancer severity and treatment, 31.2% (n=1,096) of all patients were stage III/IV, 84.2% (n=2,957) had undergone surgery and 41.5% (n=1,458) had undergone chemotherapy. 83.7% (n=2,938) of patients were treated with glucocorticoids (Table 2).

Compared to patients with neither preDM nor DM, patients with preDM or DM were older (preDM: P=0.04; DM: P<0.001), more often underwent chemotherapy (PreDM/DM: P<0.001), or immune-therapy (PreDM/DM: P<0.001), were more often treated with glucocorticoids (preDM: P<0.001; DM: P=0.01) and less frequently underwent surgery (PreDM/DM: P<0.001). Compared to patients with neither preDM nor DM, patients with DM were more often male (P=0.02) and more often Hispanic (DM: P=0.001); patients with preDM more frequently received radiation therapy (P<0.01) (Table 2; eTable 2).

Prevalence by clinicodemographics

Compared to female patients (30.7%; 95% CI: 28.6–32.9), the prevalence of DM was higher in male patients (34.5%; 95% CI: 32.3–36.7). Across BMI categories, the prevalence of DM for patients with normal weight was 22.7% (95% CI: 20.0–25.7), the prevalence of diabetes for patients who were overweight was 28.0% (95% CI: 25.3–30.8) and the prevalence of diabetes for obese patients was 43.1% (95% CI: 40.2–46.0) (eTable 3).

Prevalence by time point

At cancer diagnosis, the prevalence of preDM was 6.0% (95% CI: 5.3–6.8) and of DM was 12.2% (95% CI: 11.2–13.3). One year after diagnosis, the prevalence of preDM was 16.6% (95% CI: 15.4–17.9) and of diabetes was 25.0% (95% CI: 23.6–26.4). At the end of the observation period, the prevalence of prediabetes was 21.2% (95% CI: 19.9–22.6) and of diabetes was 32.6% (95% CI: 31.1–34.2) (Table 3).

Prevalence by diagnostic indicator

Solely based on ICD codes, the prevalence of preDM was 4.2% (95% CI: 3.6–4.9) and of DM 21.1% (95% CI: 19.8–22.5) at the end of the observation period. Based lab values, the prevalence of preDM was 20.6% (95% CI: 19.3–22.0) and the prevalence of DM was 22.2% (95% CI: 20.9–23.6). With respect to insulin prescription, we observed a prevalence of 21.9% (95% CI: 20.5–23.3) for DM (Table 3).

Prevalence by cancer treatment

Patients undergoing chemotherapy had a higher prevalence of preDM (29.1% vs 15.6%) and DM (37.6% vs 29.0%) compared to patients who did not receive chemotherapy. The same was true in patients undergoing radiation therapy for preDM (24.3% vs 19.9%) and DM (33.7% vs 32.1%), patients undergoing immunotherapy for preDM (29.2% vs 20.4%) and DM (36.0% vs 32.2%), as well as patients receiving glucocorticoids for preDM (22.3% vs 15.5%) and DM (33.1% vs 30.1%).

Prevalence by tumor site

There were vast differences in the prevalence of preDM and DM between tumor sites (Table 4), with the highest prevalence for preDM in patients with myeloma (39.2%) and DM in patients with pancreatic cancer (65.1%), respectively. The lowest prevalence of preDM and DM was observed among patients with melanoma of the skin (preDM: 11.0%; DM: 20.1%) (Table 4; Figure 2).

Discussion

Our analysis has three major findings: First, in patients with cancer, preDM/DM are highly prevalent, and every second patient is affected. Second, the prevalence of preDM/DM varies widely with respect to the tumor site and cancer treatment. For example, in patients with pancreas cancer as well as in patients undergoing chemotherapy, the prevalence of DM is markedly higher than in the whole population. Third, the prevalence of preDM/DM increases substantially following cancer diagnosis. Consequently, there may be the potential to prevent the new onset of preDM/DM, as well as the transition from preDM to DM.

At the time of cancer diagnosis, the prevalence of DM in our cohort (mean age 58 years) was 12.2%, a value very similar to the 12.7% DM prevalence reported by the CDC for adults age 45–64.[2] However, the 2.5-fold increase in DM prevalence up to 32.6% by the end of the observation period suggests very strongly that the cancer treatment markedly, and pathologically, increased the risk for the development of diabetes. This prevalence rate of 32.6% was much higher than previously reported DM prevalences in patients with cancer.[24] Interestingly, the prevalence of preDM in our cohort at the time of cancer diagnosis was 6.0%, a value much lower than the expected preDM prevalence of 40.9% reported by the CDC for adults age 45–64.[2] Reasons for our likely underestimation of the prevalence of prediabetes are listed below. However, consistent with finding that the prevalence of DM increased substantially following cancer diagnosis, the 2.6-fold increase in prediabetes prevalence up to 21.2% by the end of the observation period is also consistent with the notion that cancer treatment markedly raises blood sugar levels and increases the risk for the development of preDM.

Regarding specific cancer types, we observed a high prevalence of DM in patients with pancreatic cancer, bladder cancer, as well as cancer of the respiratory system. Patients with breast cancer, melanoma of the skin, and prostate cancer had the lowest prevalence of DM in our sample. Previous studies have pointed in the same direction.[21,27,31,32] In contrast to earlier studies, our results provide a systematic overview of the prevalence of preDM and

DM for various cancer types.[33] For most of these cancer types the prevalence of preDM has never been reported before.

Cancer and diabetes are closely linked and share several risk factors. For example, common risk factors are male sex, older age, and obesity.[34,35] Also in our study, patients with DM tend to be older, more often men and more often obese compared to patients with cancer without DM. However, shared risk factors alone cannot explain the rapid rise of DM after cancer diagnosis. For example, in the study of Hwangbo et al., the risk of developing DM after cancer diagnosis was similar in women and men and younger patients were at higher risk compared to older patients.[36,20]

Instead, increasing evidence supports the impact of cancer treatment on the development of DM. In our study, patients undergoing chemotherapy, radiation therapy, immunotherapy, or treated with glucocorticoids had a higher prevalence of DM compared to patients not receiving those treatments. Previous research has indicated that treatment with antineoplastics is linked to hyperglycemia and DM, by interfering with insulin production and secretion (e.g., L-Asparaginase,[37,38] immune checkpoint inhibitors[39–41]), reducing insulin sensitivity (e.g., nucleoside metabolic inhibitors,[42,43] mTOR inhibitors[44,45]) or both (e.g., selective estrogen receptor modulators[46]). Glucocorticoids, as part of the cancer treatment or used to treat cancer treatment side effects,[47,48] are also related to hyperglycemia in patients with cancer.[49–51]

Still, diagnosing and managing DM in patients with cancer remains a challenge. Glycemic control is frequently insufficient[26] and preDM as well as DM is frequently undiagnosed in patients with cancer.[21] Often, providers and patients prioritize treatment of cancer over managing DM.[52,53] In the absence of specific guidelines, specific roles, and responsibilities of managing DM and other chronic diseases remain unclear.[54]

Strengths and limitations

This study has several strengths. The basis for this analysis is the HCI-TCC-DM cohort, a large real-world patient with cancer population from the Western US. Our population was restricted to patients diagnosed with a pathologically-confirmed first primary invasive cancer. Through the linkage of the HCI-TCC clinical data repository, the Huntsman Cancer Registry, and the University of Utah Health Enterprise Data Warehouse (EDW) a wealth of clinical and study-related data was available for this analysis. To the best of our knowledge, this is the first study to systematically analyze the prevalence of preDM and DM across cancer types.

This study also has several limitations. The prevalence of preDM and DM was based on clinical data and had been assessed based on ADA guidelines.[29] However, even if glucose is measured several times during cancer treatment (e.g., before surgery), systematic glucose monitoring is neither standard of care nor part of the HCI-TCC protocol. Therefore, the measurement of fasting or fed blood glucose levels alone may underestimate the true prevalence of preDM and DM.

Also, since pre-DM as a formal diagnosis is often not coded (and certainly under-reported), and the fact that glucose tolerance tests were not performed, the prevalence of pre-DM may have been underestimated. Additionally, since pre-DM and DM are often treated with various glucose lowering drugs, restricting the diagnosis criteria to only one drug (insulin) may have also led to an underestimation of the prevalence of preDM and DM. Also, the ADA guidelines have not been specifically developed for patients with cancer. Whether elevated lab results, even if they are two days apart, are actually diagnostic for DM, perhaps only stress-induced hyperglycemia, reflect the impact of cancer treatment (e.g., glucocorticoid-induced preDM or DM), or other factors, cannot be determined conclusively.

However, the diagnosis of DM was determined solely by lab values only in 8.9% (n=102) of all patients with DM (n=1,145). In all other cases, patients had at least an insulin prescription or a DM-related ICD code. Moreover, only 2,5% (n=29) of all DM patients received glucocorticoids on the same both days as their elevated glucose levels (in the DM range) were measured.

Because coding for preDM is often omitted, the portion of patients in which preDM was determined solely based on lab values was higher. In 80.3% (n=598) of all patients with preDM (n=745), the definition of preDM was based solely on lab values. Out of all patients with preDM, 27,2% (n=203) patients received glucocorticoids on the same days as when their elevated glucose levels (in the preDM range) were measured. Overall, more detailed analyses, examining the impact of glucocorticoids and chemotherapeutic agents on the development of new-onset DM and preDM after a cancer diagnosis, are needed.

Conclusions

In patients with cancer, prediabetes and diabetes are highly prevalent and this prevalence increases markedly after diagnosis. In order to enable strategies for the prevention and management of diabetes during and after cancer treatment, it is essential, (1) to recognize that patients with cancer are at high risk for developing diabetes and related complications (e.g., hyperglycemia), (2) to foster interprofessional collaboration between cancer treatment, endocrinology, and primary care, and (3) to develop and implement evidence-based practice guidelines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflict of Interest Disclosures

Dr. Ulrich has as cancer center director oversight over research funded by several pharmaceutical companies but has not received funding directly herself.

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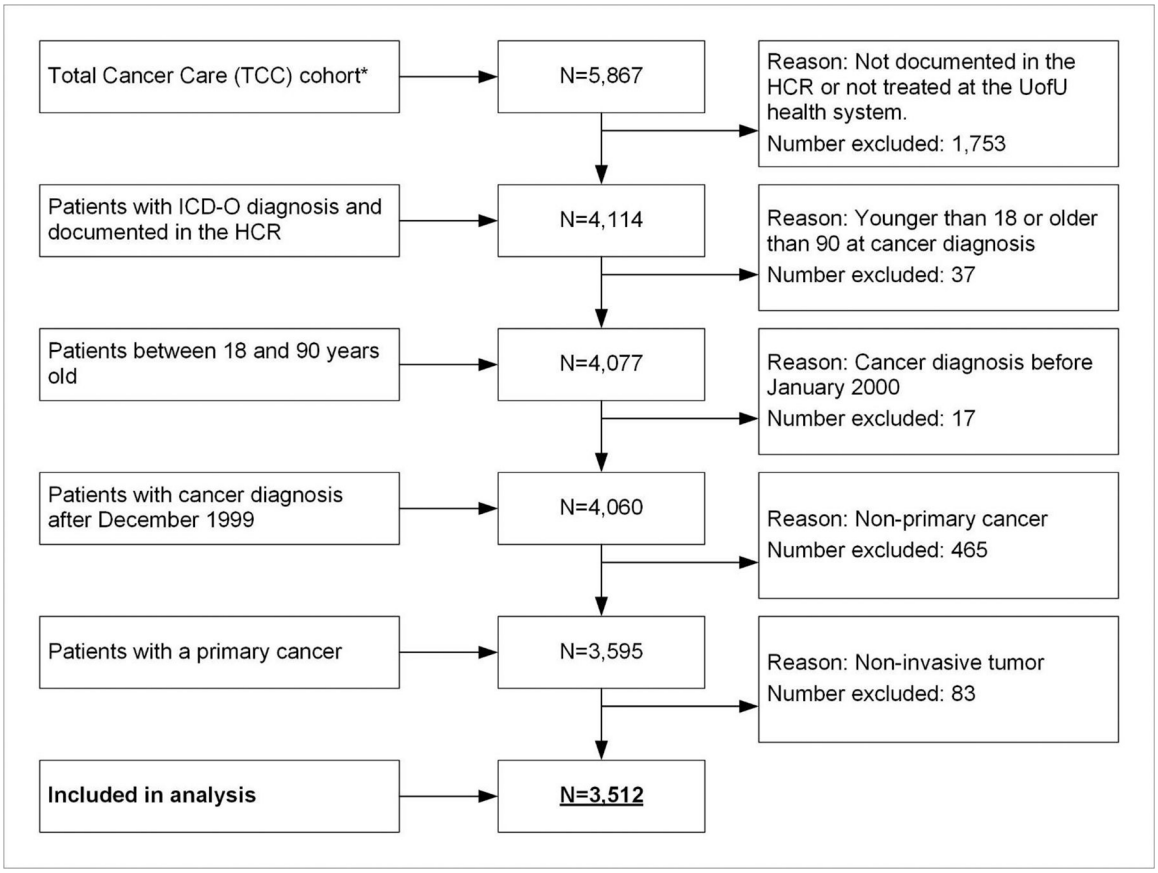

Figure 1:

Flowchart with exclusion criteria

* Participants in the TCC cohort as of July 31, 2018

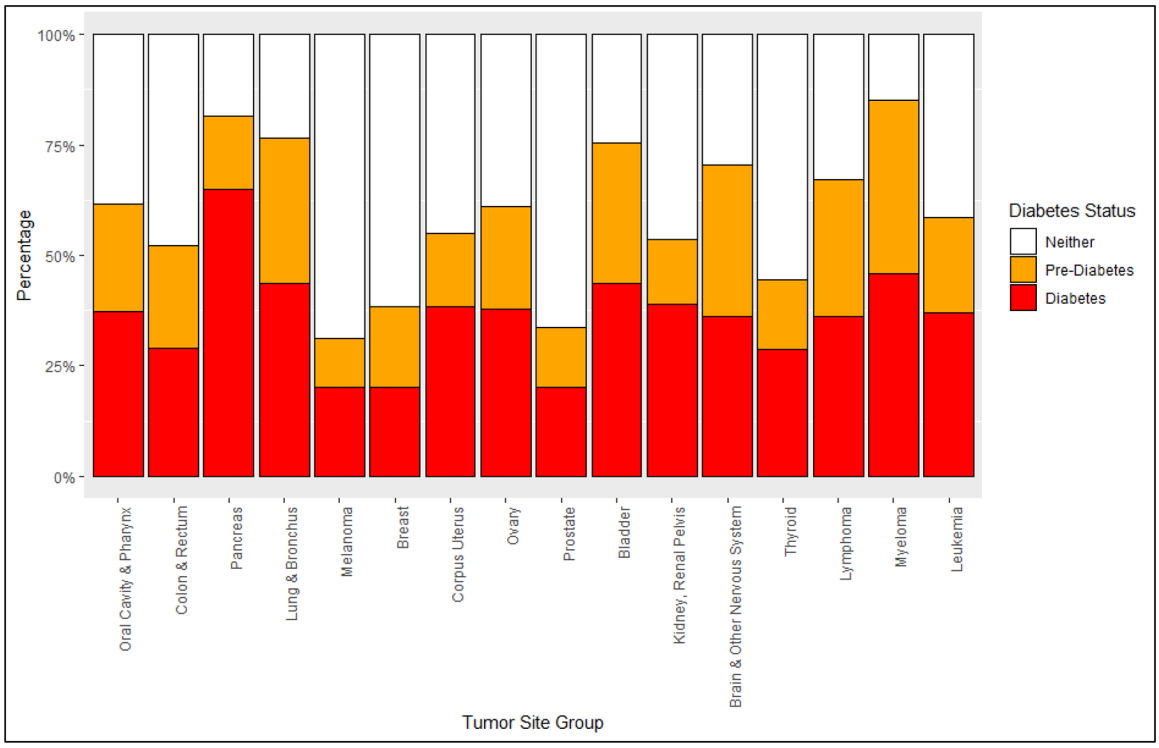

Figure 2:
Patterns of diabetes and pre-diabetes among selected cancer types

Table 1:

Diagnostic indicators for prediabetes and diabetes

Indicator	Prediabetes	Diabetes
ICD 9	790.xx	250.XX
ICD 10	R73.xx	E8 to E13
HbA1c (%) *	5.7–6.4	≥ 6.5
Fasting plasma glucose (mg/dl) *	100–125	≥ 126
Blood glucose (mg/dl) *	140–199	≥ 200
Prescriptions	-	Insulin

* To confirm diagnosis, 2+ laboratory test results more than two days apart were required if no other indication of diagnosis was given (ICD code, insulin prescription)

Table 2:

Clinicodemographic characteristics by diabetes status among patients with cancer (n=3,512)

	Total[a]	Prediabetes	Diabetes	Neither	p-value
Study Population n (%)	3,512 (100)	745 (21.2)	1,145 (32.6)	1,622 (46.2)	
Age (years) mean (SD)[b]	57.8 (14.0)	57.4 (14.1)	60.4 (13.1)	56.2 (14.2)	<0.001
Age categorized n (%)[b]					<0.001
<50 years	854 (24.3)	194 (26.0)	206 (18.0)	454 (28.0)	
50 to 64 years	1,440 (41.0)	293 (39.3)	463 (40.4)	684 (42.2)	
65 to 79 years	1,091 (31.1)	238 (31.9)	423 (36.9)	430 (26.5)	
80+ years	127 (3.6)	20 (2.7)	53 (4.6)	54 (3.3)	
Sex n (%)					0.02
Female	1,724 (49.1)	360 (48.3)	529 (46.2)	835 (51.5)	
Male	1,788 (50.9)	385 (51.7)	616 (53.8)	787 (48.5)	
Race and Ethnicity n (%)					<0.001
Non-Hispanic White	3,177 (90.5)	678 (91.0)	1,006 (87.9)	1,493 (92.0)	
Non-Hispanic Black	18 (0.5)	10 (1.3)	2 (0.2)	6 (0.4)	
Non-Hispanic Asian	38 (1.1)	7 (0.9)	15 (1.3)	16 (1.0)	
Non-Hispanic Other[c]	142 (4.0)	26 (3.5)	54 (4.7)	62 (3.8)	
Hispanic	137 (3.9)	24 (3.2)	68 (5.9)	45 (2.8)	
BMI kg/m^2 mean (SD)[d]	29.1 (6.6)	28.1 (5.8)	31.3 (7.7)	28.0 (5.8)	<0.001
BMI kg/m^2 category n (%)[d]					<0.001
Underweight (<18.5)	33 (0.9)	7 (0.9)	9 (0.8)	17 (1.0)	
Normal (18.5 – 24.99)	814 (23.2)	198 (26.6)	185 (16.2)	431 (26.6)	
Overweight (25.0 – 29.99)	1,004 (28.6)	222 (29.8)	281 (24.5)	501 (30.9)	
Obese (>=30)	1,118 (31.8)	210 (28.2)	482 (42.1)	426 (26.3)	
Unknown	543 (15.5)	108 (14.5)	188 (16.4)	247 (15.2)	
Population n (%)[e]					0.31
Rural	1,125 (32)	223 (29.9)	362 (31.6)	540 (33.3)	
Non-Rural	2,357 (67.1)	515 (69.1)	770 (67.2)	1,072 (66.1)	
Unknown	30 (0.9)	7 (0.9)	13 (1.1)	10 (0.6)	
State of Residence n (%)[f]					<0.001
Utah	2,464 (70.2)	557 (74.8)	818 (71.4)	1,089 (67.1)	
Idaho	425 (12.1)	65 (8.7)	146 (12.8)	214 (13.2)	
Wyoming	274 (7.8)	45 (6.0)	86 (7.5)	143 (8.8)	
Nevada	168 (4.8)	39 (5.2)	54 (4.7)	75 (4.6)	
Other	181 (5.2)	39 (5.2)	41 (3.6)	101 (6.2)	
Cancer Stage n (%)					<0.001

	Total[a]	Prediabetes	Diabetes	Neither	p-value
Stage 0-I	872 (24.8)	137 (18.4)	226 (19.7)	509 (31.4)	
Stage II	638 (18.2)	107 (14.4)	208 (18.2)	323 (19.9)	
Stage III	553 (15.7)	94 (12.6)	167 (14.6)	292 (18.0)	
Stage IV	543 (15.5)	153 (20.5)	199 (17.4)	191 (11.8)	
Unknown/ Not Applicable[g]	906 (25.8)	254 (34.1)	345 (30.1)	307 (18.9)	
Cancer treatment n (%)					
Surgery	2,957 (84.2)	594 (79.7)	945 (82.5)	1,418 (87.4)	<0.001
Chemotherapy	1,458 (41.5)	425 (57.0)	548 (48.0)	485 (29.9)	<0.001
Radiation	1,035 (29.5)	251 (33.7)	349 (30.5)	435 (26.8)	0.002
Hormone therapy	731 (20.8)	169 (22.7)	204 (17.8)	358 (22.1)	0.01
Immunotherapy	339 (9.7)	99 (13.3)	122 (10.7)	118 (7.3)	<0.001
Glucocorticoids	2,938 (83.7)	656 (88.1)	972 (84.9)	1,310 (80.8) 1.5)	<0.001
Cancer Sequence Number n (%)					<0.001
00 – only one primary cancer	3,084 (87.8)	632 (84.8)	977 (85.3)	1,475 (90.9)	
01 – multiple primary cancer	428 (12.2)	113 (15.2)	168 (14.7)	147 (9.1)	

[a] Not all %s add up to 100 because of rounding decimal places;

[b] At cancer diagnosis;

[c] American Indian/Alaska Native, Hawaiian/Other Pacific Islander, Other, or Unknown;

[d] Body Mass Index, at cancer diagnosis (90 days window before and after cancer diagnosis);

[e] Determined from RUCA score on zip code;

[f] Determined from last known residence;

[g] Brain and nervous system cancers are not routinely staged; n=number; SD=standard deviation; BMI=body mass index

Table 3:

Prevalence of prediabetes and diabetes among patients with cancer by diabetes indicator, time frame and treatment (n=3,512)

	Total	Prediabetes		Diabetes	
	No	**No**	**% (95% CI)**	**No**	**% (95% CI)**
Study Population	3,512	745	21.2 (19.9–22.6)	1,145	32.6 (31.1–34.2)
By time point [c]	3,512				
At cancer diagnosis[d]		211	6.0 (5.3–6.8)	429	12.2 (11.2–13.3)
After cancer diagnosis					
One month after		306	8.7 (7.8–9.7)	590	16.8 (15.6–18.1)
Six months after		536	15.3 (14.1–16.5)	824	23.5 (22.1–24.9)
One year after		584	16.6 (15.4–17.9)	877	25.0 (23.6–26.4)
End of OP (>365 days)		745	21.2 (19.9–22.6)	1,145	32.6 (31.1–34.2)
By diagnostic indicator [a,e]	3,512				
Based on ICD codes		147	4.2 (3.6–4.9)	742	21.1 (19.8–22.5)
DM Type 1		-	-	56	1.6 (1.2–2.1)
DM Type 2		-	-	700	19.9 (18.6–21.3)
DM secondary		-	-	36	1.0 (0.7–1.4)
DM other		-	-	232	6.6 (5.8–7.5)
Based on lab values[b]		725	20.6 (19.3–22.0)	781	22.2 (20.9–23.6)
HbA1c (%)		184	5.2 (4.5–6.0)	314	8.9 (8.0–9.9)
Fasting plasma glucose (mg/dl)		25	0.7 (0.5–0.1.0)	42	1.2 (0.9–1.6)
Blood glucose (mg/dl)		745	21.2 (19.9–22.6)	732	20.8 (19.5–22.2)
Based on insulin prescription		-	-	768	21.9 (20.5–23.3)
By cancer treatment [e]					
Chemotherapy					
Yes	1,458	425	29.1 (26.9–31.5)	548	37.6 (35.1–40.1)
No	2,050	320	15.6 (14.1–17.2)	594	29.0 (27.1–31.0)
Surgery					
Yes	2,957	594	20.1 (18.7–21.6)	945	32.0 (30.3–33.7)
No	555	151	27.2 (23.7–31.1)	200	36.0 (32.2–40.1)
Radiation					
Yes	1,035	251	24.3 (21.7–27.0)	349	33.7 (30.9–36.7)
No	2,477	494	19.9 (18.4–21.6)	796	32.1 (30.3–34.0)
Hormone therapy					
Yes	731	169	23.1 (20.2–26.3)	204	27.9 (24.8–31.3)
No	2,777	576	20.7 (19.3–22.3)	939	33.8 (32.1–35.6)
Immunotherapy					

	Total	Prediabetes		Diabetes	
	No	No	% (95% CI)	No	% (95% CI)
Yes	339	99	29.2 (24.6–34.3)	122	36.0 (31.1–41.2)
No	3,172	646	20.4 (19.0–21.8)	1,022	32.2 (30.6–33.9)
Glucocorticoids					
Yes	2,938	656	22.3 (20.9–23.9)	972	33.1 (31.4–34.8)
No	574	89	15.5 (12.8–18.7)	173	30.1 (26.5–34.0)

OP=Observation period;

[a] Numbers are not mutually exclusive. For example, a patient can have an ICD code for DM and a HbA1c in the DM range;

[b] preDM and DM diagnoses based solely on lab values were valid only if a patient had at least 2 lab values greater than 2 days apart to more fully establish robust diagnosis;

[c] Sum of patients with preDM by 'time frame' is 1,343. This number reflects the number of all patients who had pre-DM over time ('Lifetime' prevalence'). Because 598 patients transitioned to DM, at end of the observation period 745 patients have preDM;

[d] Prevalence as of two weeks after cancer diagnosis including all cases before cancer diagnosis;

[e] At the end of the observation period

Table 4:

Prevalence of prediabetes and diabetes by tumor site at the end of the observation period (n=3,512)[a]

	Total	Prediabetes		Diabetes	
	No (%)	No	% (95% CI)	No	% (95% CI)
Study Population	3,512 (100)	745	21.2 (19.9–22.6)	1,145	32.6 (31.1–34.2)
Oral Cavity and Pharynx	116 (3.3)	28	24.1 (17.3–32.7)	44	37.9 (29.6–47.0)
Digestive System	397 (11.3)	81	20.4 (16.7–24.6)	184	46.3 (41.5–51.3)
Colon and Rectum	186 (5.3)	43	23.1 (17.6–29.7)	54	29.0 (23.0–35.9)
Pancreas	146 (4.2)	24	16.4 (11.3–23.3)	95	65.1 (57.0–72.3)
Other[b]	65 (1.9)	14	21.5 (13.3–33)	35	53.8 (41.9–65.4)
Respiratory System	235 (6.7)	75	31.9 (26.3–38.1)	101	43.0 (36.8–49.4)
Lung and Bronchus	209 (6.0)	69	33.0 (27.0–39.6)	91	43.5 (37.0–50.3)
Other[c]	26 (0.7)	6	23.1 (11.0–42.1)	10	38.5 (22.4–57.5)
Skin[d]	295 (8.4)	32	10.8 (7.8–14.9)	60	20.3 (16.1–25.3)
Melanoma of the skin	283 (8.1)	31	11.0 (7.8–15.1)	57	20.1 (15.9–25.2)
Other[e]	12 (0.3)	1	8.3 (0.4–35.4)	3	25.0 (8.9–53.2)
Breast	484 (13.8)	88	18.2 (15–21.9)	98	20.2 (16.9–24.1)
Female Genital System	278 (7.9)	47	16.9 (13–21.8)	104	37.4 (31.9–43.2)
Corpus and Uterus	162 (4.6)	27	16.7 (11.7–23.2)	62	38.3 (31.1–45.9)
Ovary	82 (2.3)	19	23.2 (15.4–33.4)	31	37.8 (28.1–48.6)
Other[f]	34 (1.0)	1	2.9 (0.2–14.9)	11	32.4 (19.1–49.2)
Male Genital System	518 (14.7)	69	13.3 (10.7–16.5)	105	20.3 (17.0–23.9)
Prostate	494 (14.1)	66	13.4 (10.6–16.6)	100	20.2 (16.9–24.0)
Other[g]	24 (0.7)	3	12.5 (4.3–31.0)	5	20.8 (9.2–40.5)
Urinary system	194 (5.5)	46	23.7 (18.3–30.2)	79	40.7 (34.1–47.8)
Bladder	94 (2.7)	30	31.9 (23.4–41.9)	41	43.6 (34.0–53.7)
Kidney and Renal Pelvis	95 (2.7)	14	14.7 (9.0–23.2)	37	38.9 (29.8–49.0)
Other[h]	5 (0.1)	2	40.0 (11.8–76.9)	1	20.0 (1.0–62.4)
Brain-nervous system	244 (6.9)	84	34.4 (28.7–40.6)	88	36.1 (30.3–42.3)
Endocrine system	114 (3.2)	18	15.8 (10.2–23.6)	33	28.9 (21.4–37.9)
Thyroid	108 (3.1)	17	15.7 (10.1–23.8)	31	28.7 (21.0–37.9)
Other[i]	6 (0.2)	1	16.7 (0.9–56.4)	2	33.3 (9.7–70.0)
Lymphoma	61 (1.7)	19	31.1 (20.9–43.6)	22	36.1 (25.2–48.6)
Myeloma	194 (5.5)	76	39.2 (32.6–46.2)	89	45.9 (39.0–52.9)
Leukemia	246 (7.0)	53	21.5 (16.9–27.1)	91	37.0 (31.2–43.2)
Miscellaneous[j]	136 (3.9)	29	21.3 (15.3–28.9)	47	34.6 (27.1–42.9)

[a]Using row percentages;

[b] Esophagus, Stomach, Small Intestine, Liver, Intra Bile Duct, Anus, Gallbladder Other Biliary, Retroperitoneum, Peritoneum, Other Digestive Organs;

[c] Nose, Larynx, Pleura, Trachea, Other;

[d] excluding Basal and Squamous;

[e] Other Non-Epithelial, Squamous Cell Carcinoma;

[f] Cervix Uteri, Vagina, Vulva, Other Genital Organs;

[g] Testis, Penis, Other Genital Organs;

[h] Ureter, Other Urinary Organs;

[i] Other Endocrine System Organs;

[j] Kaposi Sarcoma, Mesothelioma, Eye Orbit, Soft tissue, Bone Joints, Other Miscellaneous