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# Distress and mental health care and medication use among survivors of multiple primary cancer diagnoses: Findings from the 2016 National Health Interview Survey

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## ABSTRACT

**Objective:** Over 1 million survivors of multiple primary cancer (MPC) diagnoses reside in the USA. Information regarding their physical and mental health status is limited. This study examined distress and mental health care use among MPC survivors relative to survivors of a single primary cancer (SPC) diagnosis.

**Methods:** Using the 2016 National Health Information Survey, MPC survivors ( $n = 265$ ), SPC survivors ( $n = 2103$ ), and no cancer controls (NCC;  $n = 28,320$ ) were identified. The MPC group was compared to the SPC and NCC groups with regard to multiple distress indices and use of mental health care and anxiety and depression medication.

**Results:** Relative to the SPC group, the MPC group reported more Total Distress ( $M = 9.59$  vs.  $8.84$ ;  $p < .001$ ), and were more likely to report daily or weekly anxiety feelings ( $OR = 2.07$ ;  $p < .001$ ), meet criteria for serious psychological distress ( $OR = 1.49$ ;  $p = .02$ ) and have talked to a mental health professional ( $OR = 1.75$ ;  $p = .01$ ). Comparison of MPC and NweCC groups yielded similar results. The MPC group did not differ from the SPC or NCC groups in severity of anxiety or depression feelings, distress interference, or anxiety and depression medication use.

**Conclusions:** MPC survivors reported greater distress relative to SPC survivors. The clinical significance of this greater distress is unclear, however. While MPC survivors were more likely to have talked to a mental health professional, uptake of mental health care appeared to be suboptimal. MPC and SPC survivors might be considered distinct subgroups and increased attention devoted to potentially unique mental and physical health needs of MPC survivors.

## 1. Introduction

A multiple primary cancer (MPC) is the occurrence of a new cancer in an individual with a prior cancer diagnosis. This new cancer is histologically distinct from a previous cancer diagnosis and is not a recurrence or metastasis of the previous cancer [1]. It is estimated 18.4% of incident cancer diagnoses in the USA are MPC diagnoses [2]. That is, they occurred in individuals with one or more prior cancer diagnoses. Given 1,762,450 incident cancer diagnoses in the USA in 2019 [3], this suggests annually approximately 324,290 individuals experience a MPC diagnosis in the USA. This annual incidence of MPC diagnoses exceeds annual incident diagnoses of any single type of cancer, including cancers of the prostate (174,650), lung/bronchus (228,150), and female breast (268,600) [3]. Furthermore, it is estimated 8% of cancer

survivors in the USA are MPC survivors [4]. Assuming 15.5 million current cancer survivors, this suggests 1.24 million current cancer survivors in the USA are MPC survivors. The total number of cancer survivors in the USA is expected to nearly double to 26.1 million by 2040 [5] and it is anticipated the number of MPC survivors will increase correspondingly. Due to advances in cancer screening and treatment resulting in extended lifespans, many survivors of an initial primary cancer diagnosis will live to experience a later MPC diagnosis.

Distress is a multifactorial unpleasant experience of a psychological, social, spiritual and/or physical nature [6]. Distress is a generic construct that encompasses more specific constructs such as anxiety and depression. Given the many stressors associated with cancer diagnosis and treatment, cancer survivors are at significant distress risk [7,8]. MPC survivors may represent a subgroup at higher distress risk within

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the larger group of all cancer survivors. Stressors associated with diagnosis and treatment of an MPC occur in a survivor likely already physically, psychologically, and/or cognitively compromised due to late or long-term effects. Furthermore, while cancer recurrence differs from an MPC diagnosis, some evidence suggests recurrence is associated with increased distress risk [9–11].

A recent review concluded there is a lack of research examining distress among MPC survivors [12]. Six studies compared distress in MPC and single primary cancer (SPC) survivors [13–18]. Only two included a comparison group with no history of cancer diagnosis, useful for putting differences between MPC and SPC survivors in context [13,14]. Distress indices used to compare MPC and SPC survivors varied including single items assessing suicidal ideation [16] or the number of days when mental health was “not good” [14]. Remaining studies used either a single, multi-item distress measure [13,18] or several multi-item distress measures [15,17]. Results for these six studies consistently found MPC survivors reported more distress compared to SPC survivors. Additionally, one study found no difference between MPC and SPC survivors in extent to which distress interfered with life or activities [13]. Finally, while MPC survivors exhibited greater use of regular medical appointments and cancer screening and monitoring [18], no research has examined utilization of mental health treatment in MPC survivors.

Considerable effort has been devoted to developing methods to screen for and manage distress in cancer survivors [6]. Given the apparent increased risk for distress in MPC survivors, the importance of addressing their distress management needs is likely even greater than SPC survivors. The aim of this study was to compare MPC and SPC survivors with respect to distress, mental health care use, and use of anxiety and depression medication. This study extends prior research in several ways. Specifically, this study includes (a) individuals with no history of cancer diagnosis (i.e., no cancer control (NCC) group); (b) multiple distress indices including measures of generic distress and distress interference and separate indices assessing the frequency and severity of depression and anxiety; and (c) indices assessing utilization of mental health care and anxiety and depression medication. We hypothesize MPC survivors will report greater distress across a variety of distress indices, including indices of generic distress and more specific anxiety and depression indices, compared to SPC and NCC groups. Consistent with their greater distress, we anticipate MPC survivors will report greater use of mental health care and anxiety and depression medication use compared to SPC and NCC groups.

## 2. Methods

### 2.1. Source of data

Data were obtained from the 2016 NHIS survey. The NHIS is an annual cross-sectional household interview survey that tracks health trends in the USA [19]. The target population is the civilian, non-institutionalized population of the USA. For the 2016 NHIS survey, 40,220 households were surveyed and interviews were completed for 33,028 adults. (501 interviews were completed by an adult proxy. These proxy interviews were *excluded*.) The 2016 NHIS survey consisted of a core survey completed by all respondents and several supplements completed only by randomly selected subsets of respondents. Data used in the present study came from the core survey as well as the Adult Functioning and Disability supplement. About one-half of respondents to the core survey were assigned to complete the Adult Functioning and Disability supplement [19]. In the 2016 NHIS survey the household response rate was 67.9%. The conditional response rate for the adult sample was 80.9% while the unconditioned, final response rate was 54.3%. A description of all 2016 NHIS procedures, including wording and response alternatives for all 2016 NHIS questions, can be found at [www.cdc.gov/nchs/nhis/nhisquestionnaires.htm](http://www.cdc.gov/nchs/nhis/nhisquestionnaires.htm).

All study procedures were performed in accordance with ethical

standards contained in the 1964 Declaration of Helsinki. The 2016 NHIS survey was approved by the National Center for Health Statistics Research Ethics Review Board (Protocol #2015–08), including a waiver of the documentation of informed consent. As NHIS data contains no identifiers and is in the public domain, no additional approval from a local institutional ethics board for the analyses reported here was required.

### 2.2. Study sample: identification of SPC, MPC, and NCC groups

Respondents were asked “Have you ever been told by a doctor or other health professional that you had cancer or a malignancy of any kind?” Those answering “yes” were asked “What kind of cancer was it?” and “How old were you when this cancer was first diagnosed?” Identical questions were asked for up to two additional cancer diagnoses. As before, time since cancer diagnosis for survivor groups was defined as the difference between age at survey participation and initial cancer diagnosis [13,14,18].

3529 respondents indicated they had been told by a doctor or health professional they had cancer. Of these, 770 were diagnosed with non-melanoma skin cancer or skin cancer of unknown melanoma status. These individuals were excluded from the sample. Eligibility criteria for the SPC group included: (1) single cancer diagnosis other than non-melanoma skin cancer; (2) age  $\geq 18$  years at diagnosis; (3) time since diagnosis  $\geq 1$  year. Eligibility criteria for the MPC group included: (1)  $\geq 2$  cancer diagnoses other than non-melanoma skin cancers; (2) age  $\geq 18$  years at initial diagnosis; (3) time since initial cancer diagnosis  $\geq 1$  year. Using these criteria, 2103 respondents constituted the SPC group while 265 constituted the MPC group. Within the MPC group, 223 (84%) respondents reported two cancer diagnoses while 42 individuals (16%) reported 3 cancer diagnoses. The remaining 28,320 NHIS respondents had never been told they had cancer and constituted the no cancer control (NCC) group. Of the 31,688 respondents in the current study sample, 14,977 (47.2%) completed the Adult Functioning and Disability Supplement.

### 2.3. Study measures

Demographic information and information on lifetime cigarette and alcohol use were examined as potential covariates to be employed in outcome analyses. Outcome measures included measures of distress (including measures of anxiety and depression) and mental health care and medication use.

### 2.4. Demographic indices

Information regarding age, sex, race, ethnicity, education, and marital status was obtained. Respondents were categorized as either a racial/ethnic nonminority (white, nonhispanic) or minority (all others) and partnered (married or living with partner) or unpartnered (single, never married or divorced, widowed or separated).

### 2.5. Cigarette and alcohol use indices

Lifetime Cigarette and alcohol use were assessed by “have you smoked at least 100 cigarettes in your entire life” (yes vs. no) and “In your entire life, have you had at least 12 drinks of any type of alcoholic beverage” (yes vs. no).

### 2.6. Distress indices

#### 2.6.1. Kessler psychological distress scale (K6) [20]

A six-item (sad, nervous, restless/fidgety, hopeless, everything was an effort, worthless) measure of distress (past 30 days). A Total Distress score is calculated (range 6–30) with higher scores reflecting greater distress. Total Distress scores  $\geq 13$  indicate Serious Psychological

Distress with sensitivity of 0.36 and specificity of 0.96 [20].

### 2.6.2. Distress interference

Respondents endorsing any of the six items in the Kessler Psychological Distress Scale (K6) at least “some of the time” were asked “Altogether, how much did these feelings interfere with your life or activities?” Response options were “a lot,” “some,” “a little,” or “not at all.” This item yielded two distress indices: a continuous measure of distress interference (range 1–4) with higher scores representing greater distress and a categorical measure of distress interference (“a lot” vs remaining 3 response options).

### 2.6.3. Frequency and severity of anxiety feelings

Questions addressing anxiety and depression feelings were asked only of respondents completing the NHIS Adult Functioning and Disability supplement. *Frequency of anxiety feelings* was assessed by a single item “How often do you feel worried, nervous, or anxious? Response options included “daily,” “weekly,” “monthly,” “a few times a year,” and “never.” This item yielded two indices: a continuous measure of frequency of anxiety feelings (range 1–5) with higher scores representing more frequent anxiety feelings and a dichotomous measure of frequency of anxiety feelings (“daily” and “weekly” feelings of anxiety vs. the remaining three response options). Respondents to this item acknowledging feeling worried, nervous or anxious at least “a few times a year” were asked “Thinking about the last time you felt worried, nervous, or anxious, how would you describe the level of those feelings?” Response options included “a little,” “between a little and a lot,” and “a lot.” This item yielded two indices: a continuous measure of *severity of anxiety feelings* (range 1–3) with higher scores representing more severe anxiety feelings and a dichotomous measure of severity of anxiety feelings (“a lot” of feelings of anxiety vs. the remaining two response options).

### 2.6.4. Frequency and severity of depression feelings

Indices of *frequency of depression feelings* and *severity of depression feelings* were derived from a set of questions that paralleled the above-described questions assessing anxiety feelings.

## 2.7. Mental health care and anxiety and depression medication use indices

All respondents were asked “During the past 12 months, have you seen or talked to a mental health professional, such as a psychiatrist, psychologist, psychiatric nurse, or clinical social worker, about your own health?” Response options were “yes” and “no.” Respondents were asked about current use of medication for depression and anxiety. These questions followed questions about frequency of anxiety and depression. Use of anxiety medication was assessed by “Do you take medication for these feelings?” Response options were “yes” and “no.” Use of depression medication was assessed by a similar question.

## 2.8. Statistical analyses

Table 1 shows demographic and clinical characteristics for the three study groups. Chi-square or analysis of variance (ANOVA) compared the MPC, SPC, and NCC groups on age, marital status, racial/ethnic minority status, smoking history (ever smoked 100 cigarettes lifetime vs. not), alcohol history (ever drink 12 alcoholic drinks lifetime vs not) and education. Significant differences ( $p < .05$ ) were found for age, sex, smoking history, and racial/ethnic minority status. The NCC group was younger, less likely to be female and to have smoked 100 cigarettes in their lifetime, and more likely to be a racial/ethnic minority. There was also a trend ( $p = .07$ ) toward differences on education, a variable employed as a covariate in prior research [13,14]. Consequently, age, sex, smoking history, racial/ethnic minority status, and education served as covariates in all subsequent outcome analyses. *t*-tests compared the MPC and SPC groups on age at initial cancer diagnosis and

time since initial diagnosis. The MPC group reported a significantly longer time since initial cancer diagnosis relative to the SPC group. Consequently time since initial diagnosis served as a covariate in all outcome analyses comparing the MPC and SPC groups. Cancer diagnoses reported by the SPC and MPC groups are shown in Appendix A.

Outcome analyses involved two basic sets of comparisons: MPC vs. NCC groups and MPC vs. SPC groups. For continuous outcome indices, analysis of covariance (ANCOVA) was used to compare groups. Cohen's *d* was used to index effect size (ES) [21,22]. For categorical outcome indices, binary logistic regression, including covariates, was used to compare groups. For all MPC vs NCC comparisons, the NCC group was the reference group. For all MPC vs SPC comparisons, the SPC group was the reference group. 95% confidence intervals (CI) were calculated for all Odds Ratios (OR).

As 30 total analyses were conducted for outcome indices (see Tables 2 and 3), the criterion for statistical significance was set at  $p \leq .025$  to reduce Type I error risk.

## 3. Results

### 3.1. Comparison of MPC group to NCC and SPC groups: Distress indices

#### 3.1.1. Generic distress

Tables 2 and 3 compare the MPC, SPC, and NCC groups on distress indices. The MPC group reported greater Total Distress scores relative to the NCC ( $F = 16.71$ ;  $df = 1, 27,962$ ;  $p < .001$ ;  $ES = 0.23$ ) and SPC groups ( $F = 8.47$ ;  $df = 1, 2311$ ;  $p < .001$ ;  $ES = 0.17$ ) (Table 2). The proportion of respondents meeting criteria for Serious Psychological Distress in the MPC, SPC, and NCC groups was 20.2%, 15.3%, and 13.3%, respectively (Table 3). The MPC group was more likely to meet criteria for Serious Psychological Distress relative to the NCC ( $OR = 1.74$ ;  $CI = 1.27$ – $2.39$ ;  $Wald = 11.95$ ;  $df = 1$ ;  $p < .001$ ) and SPC groups ( $OR = 1.49$ ;  $CI = 1.05$ – $2.11$ ;  $Wald = 5.03$ ;  $df = 1$ ;  $p = .02$ ). The MPC group did not differ from the NCC or SPC groups in distress interference with life or activities (Table 2) or the likelihood distress had interfered “a lot” with life or activities (Table 3).

#### 3.1.2. Anxiety

The MPC group reported a greater frequency of anxiety feelings than the NCC group ( $F = 18.35$ ;  $df = 1, 13,876$ ;  $p < .001$ ;  $ES = 0.34$ ) (Table 2). However, there were no differences between the MPC and NCC groups in severity of anxiety feelings. Comparison of the MPC and SPC groups on frequency and severity of anxiety feelings revealed identical results. The MPC group reported greater frequency of anxiety feelings relative to the SPC group ( $F = 11.22$ ;  $df = 1, 1162$ ;  $p < .001$ ;  $ES = 0.28$ ) with no difference in severity of these feelings.

The proportion of respondents reporting daily or weekly anxiety feelings in the MPC, SPC, and NCC groups was 31.5%, 19.6%, and 19.4%, respectively (Table 3). The MPC group was more likely to report daily or weekly anxiety feelings than the NCC ( $OR = 2.39$ ;  $CI = 1.63$ – $2.52$ ;  $Wald = 19.65$ ;  $df = 1$ ;  $p < .001$ ) and SPC ( $OR = 2.07$ ;  $CI = 1.36$ – $3.16$ ;  $Wald = 11.54$ ,  $df = 1$ ;  $p < .001$ ) groups. The proportion of respondents describing the severity of their anxiety feelings as “a lot” in the MPC, SPC, and NCC groups was 11.0%, 10.7%, and 10.4%, respectively. The MPC group did not differ from the NCC or SPC groups in the likelihood of describing severity of their anxiety feelings as “a lot.”

#### 3.1.3. Depression

The MPC group reported more frequent depression feelings than the NCC group ( $F = 7.90$ ;  $df = 1, 13,868$ ;  $p < .01$ ;  $ES = 0.23$ ) (Table 2). However, the MPC and NCC groups did not differ in severity of depression feelings. Comparison of the MPC and SPC groups revealed no significant differences with respect to frequency or severity of depression feelings.

The proportion of respondents reporting daily or weekly depression

**Table 1**  
Demographic and clinical characteristics of MPC, SPC and NCC groups.

	MPC (n = 265)	SPC (n = 2103)	NCC (n = 28,320)	p-value <sup>a</sup>
Racial/Ethnic Minority Status (n, % White, non-Hispanic)	n = 230; 86.8%	n = 1758; 83.6%	n = 19,512; 68.9%	< 0.001
Alcohol History (n, % 12 drinks ever in 1 year)	n = 172; 65.2%	n = 1347; 64.4%	n = 18,690; 66.2%	0.21
Smoking History (n, % ever smoked 100 cigarettes)	n = 152; 57.6%	n = 1103; 52.6%	n = 11,199; 39.6%	< 0.001
Marital Status (n, % Married/Partnered)	n = 120; 45.3%	n = 1061; 50.5%	n = 14,343; 50.8%	0.21
Sex (n, % Female)	n = 145; 54.7%	n = 1275; 60.6%	n = 15,396; 54.4%	< 0.001
Education (yrs)	Mean = 14.0 SD = 3.3	Mean = 15.4 SD = 3.1	Mean = 15.3 SD = 3.1	0.07
Current Age (yrs)	Mean = 69.1 SD = 11.6	Mean = 66.1 SD = 13.3	Mean = 48.7 SD = 18.1	< 0.001
Age at Initial Cancer Dx (yrs)	Mean = 52.3 SD = 15.7	Mean = 54.0 SD = 15.3		0.09
Time Since Initial Cancer Dx (yrs)	Mean = 16.8 SD = 12.7	Mean = 12.0 SD = 10.7		< 0.001

Note: Dx = diagnosis; MPC = Multiple Primary Cancer; SPC=Single Primary Cancer; NCC=No Cancer Comparison; SD = standard deviation; yrs. = years.

<sup>a</sup> For ANOVA, t-test or chi-square, as appropriate.

**Table 2**  
ANCOVA comparison of MPC, SPC and NCC groups with regard to distress indices.

	MPC vs NCC				MPC vs SPC			
	MPC		NCC		MPC		SPC	
	(n = 265)	(n=28320)			(n = 265)	(n = 2103)		
	Mean <sup>a</sup> SD	Mean <sup>a</sup> SD	ES <sup>c</sup>	p-value	Mean <sup>b</sup> SD	Mean <sup>b</sup> SD	ES <sup>c</sup>	p-value
<b>Distress indices</b>								
Total Distress	9.71 4.67	8.71 4.00	0.23	< 0.001	9.59 4.67	8.84 4.04	0.17	< 0.001
Distress Interference with life/activity <sup>d</sup>	2.10 1.02	2.01 1.01	0.09	0.34	2.16 1.02	2.05 1.03	0.11	0.36
<b>Anxiety indices</b>								
Frequency of anxiety feelings <sup>e</sup>	2.63 1.54	2.15 1.30	0.34	< 0.001	2.54 1.54	2.14 1.31	0.28	< 0.001
Severity of anxiety feelings <sup>e,f</sup>	1.53 0.69	1.52 0.68	0.01	0.92	1.51 0.69	1.53 0.68	0.03	0.78
<b>Depression indices</b>								
Frequency of depression feelings <sup>e</sup>	1.91 1.23	1.65 1.05	0.23	0.01	1.93 1.23	1.75 1.15	0.15	0.08
Severity of depression feelings <sup>e,g</sup>	1.57 0.74	1.59 0.72	0.03	0.84	1.55 0.74	1.57 0.70	0.03	0.81

Note: ANCOVA = analysis of covariance; MPC = Multiple Primary Cancer; SPC=Single Primary Cancer; NCC=No Cancer Comparison; ES = effect size; SD = standard deviation.

<sup>a</sup> Adjusted for age, sex, minority status, smoking status.

<sup>b</sup> Adjusted for age, sex, minority, status, smoking status, time since initial cancer diagnosis.

<sup>c</sup> Effect size (Cohen's d).

<sup>d</sup> Asked of respondents acknowledging any of six items on K6 scale(sad, nervous, restless/fidgety, hopeless, everything was an effort, or worthless) at least “some of the time” in past 30 days.

<sup>e</sup> Asked of 14,977 respondents randomly assigned to complete the 2016 NHIS Adult Functioning and Disability Supplement.

<sup>f</sup> Asked of respondents acknowledging feeling worried, nervous, or anxious at least a few times a year.

<sup>g</sup> Asked of respondents acknowledging feelings of depression at least a few times a year.

feelings in the MPC, SPC, and NCC groups was 13.2%, 11.6%, and 8.8%, respectively (Table 3). The proportion of respondents describing the severity of their depression feelings as “a lot” in the MPC, SPC, and NCC groups was 14.5%, 11.8%, and 13.5%, respectively. The MPC group did not differ from the NCC or SPC groups in the likelihood of reporting daily or weekly depression feelings or the likelihood of describing severity of depression feelings as “a lot.”

### 3.1.4. Comparison of MPC group to NCC and SPC groups: Mental health care and medication use indices

Table 3 compares the MPC, SPC, and NCC groups regarding use of mental health care and anxiety and depression medication. The proportion of respondents who reported seeing a mental health professional in the past 12 months in the MPC, SPC, and NCC groups was 12.5%, 9.3%, and 9.0%, respectively. The MPC group was more likely to report seeing a mental health professional relative to the NCC (OR = 1.92; CI = 1.32–2.79; Wald = 11.61; df = 1, p < .001) and SPC (OR = 1.75; CI = 1.16–2.64; Wald = 7.09, df = 1, p = .01)

groups. Among those acknowledging feelings of anxiety within the past month, the proportion who reported current use of anxiety medication in the MPC, SPC, and NCC groups was 15.4%, 14.5%, and 9.4%, respectively. The MPC group did not differ in the use of anxiety medication relative to the NCC or SPC groups. Among those acknowledging feelings of depression within the past month, the proportion who reported current use of depression medication in the MPC, SPC, and NCC groups was 13.2%, 11.6%, and 8.8%, respectively. The MPC group did not differ in the use of depression medication relative to the NCC or SPC groups.

## 4. Discussion

### 4.1. Greater distress risk in MPC survivors

As anticipated, results found MPC survivors reported more distress than MPC survivors. Unlike previous research, this general finding was evidenced across multiple indices of distress, including generic indices



**Table 3**

Logistic regression analyses for indices of distress and mental health care and medication use for MPC, SPC and NCC groups.

	Prevalence			Group comparison					
	MPC	SPC	NCC	MPC vs NCC <sup>a</sup>			MPC vs SPC <sup>b</sup>		
	(n = 265)	(n = 2103)	(n = 28,320)	OR	95% CI	p-value	OR	95% CI	p-value
<b>Distress indices</b>									
Serious Psychological Distress <sup>c</sup>	20.2% (53/282)	15.3% (315/2054)	13.3% (3687/27795)	1.74	1.27-2.39	< .001	1.49	1.05-2.11	0.02
Distress interference with life/activity <sup>d</sup>	11.3% (13/115)	11.7% (90/770)	10.7% (1057/9839)	0.91	0.49-1.69	0.77	1.02	0.53-1.96	0.97
<b>Anxiety indices</b>									
Daily or weekly feelings of anxiety <sup>c</sup>	31.5% (41/130)	19.6% (203/1037)	19.4% (2674/13792)	2.39	1.63-3.52	< .001	2.07	1.36-3.16	< .001
Severity of feelings of anxiety “a lot” <sup>e,f</sup>	11.0% (9/82)	10.7% (66/614)	10.4% (858/8223)	1.02	0.50-2.06	0.97	1.06	0.49-2.28	0.89
<b>Depression indices</b>									
Daily or weekly feelings of depression <sup>e</sup>	13.2% (17/129)	11.6% (120/1037)	8.8% (1215/13786)	1.40	0.83-2.37	0.21	1.13	0.64-1.98	0.68
Severity of feelings of depression “a lot” <sup>e,g</sup>	14.5% (10/69)	11.8% (52/441)	13.5% (726/5364)	1.15	0.57-2.29	0.70	1.44	0.68-3.08	0.35
<b>Mental health care and medication use indices</b>									
Take medication for anxiety <sup>e</sup>	15.4% (20/130)	14.5% (151/1039)	9.4% (1299/13808)	1.43	0.88-2.35	0.15	1.05	0.62-1.76	0.86
Take medication for depression <sup>e</sup>	13.2% (17/129)	11.6% (120/1037)	8.8% (1215/13786)	1.40	0.87-2.28	0.17	1.07	0.64-1.78	0.81
Talked to mental health professional past 12 months	12.5% (33/231)	9.3% (193/2085)	9.0% (2520/28156)	1.92	1.32-2.79	< .001	1.75	1.16-2.64	0.01

Note: MPC = Multiple Primary Cancer; SPC=Single Primary Cancer; NCC=No Cancer Comparison; OR = odds ratio; CI = confidence interval.

<sup>a</sup> NCC reference group; adjusted for age, minority status, sex, smoking status.

<sup>b</sup> SPC reference group; adjusted for age, minority status, sex, smoking status, time since initial cancer diagnosis.

<sup>c</sup> Total Distress Score  $\geq$  13.

<sup>d</sup> Asked of respondents acknowledging any of six items on K6 scale(sad, nervous, restless/fidgety, hopeless, everything was an effort, or worthless) at least “some of the time” in past 30 days.

<sup>e</sup> Asked of approximate 14,977 respondents randomly assigned to complete the 2016 NHIS Adult Functioning and Disability Supplement.

<sup>f</sup> Asked of respondents acknowledging feeling worried, nervous, or anxious at least a few times a year.

<sup>g</sup> Asked of respondents acknowledging feelings of depression at least a few times a year.

of distress and specific indices of anxiety and depression feelings. Our results thus support the general conclusion MPC survivors are at greater risk for distress than SPC survivors [12].

#### 4.2. Clinical importance of greater distress risk in MPC survivors

The clinical importance of this greater risk for distress in MPC survivors is a bit unclear, however. Similar to previous research [13], while the MPC group reported more distress than the SPC and NCC groups, the MPC group did not differ from the SPC or NCC groups in how much distress *interfered* with life or activities. Furthermore, while the MPC group reported more *frequent* feelings of anxiety and depression, relative to both SPC and NCC groups, the three groups did not differ in *severity* of anxiety or depression feelings. Finally, as in prior research [12], when significant differences were found between the MPC and SPC groups, effect sizes were modest. In this study, ES's for continuous measures of distress ranged from 0.17 to 0.28 with odds ratios for dichotomous measures ranging from 1.49 to 2.07. Future research should attempt to clarify the clinical importance of the increased risk for distress consistently evidenced by MPC survivors relative to SPC counterparts.

#### 4.3. Mental health care and medication use in MPC survivors

Despite increased distress risk, no research has examined use of mental health care or anxiety and depression medication in MPC survivors. We found while MPC survivors were at increased distress risk

this did not translate into greater use of anxiety or depression medication relative to SPC or NCC groups. Prescription and use of anxiety and depression medications are based on multiple considerations including frequency and severity of these feelings. As the MPC group did not report more severe anxiety or depression feelings than SPC and NCC groups, it is perhaps not surprising they were no more likely to use anti-anxiety and antidepressant medications. In contrast to the lack of differences in medication use, MPC survivors were more likely to report talking to a mental health professional in the preceding 12 months than either the SPC or NCC groups. Whether those consultations were related to an ongoing concern with distress is unknown, however.

Given their greater risk for distress, it is encouraging MPC survivors were more likely to report talking to a mental health professional. However, the magnitude of this effect was modest, with OR's of 1.75 and 1.92 for comparisons with the SPC and NCC groups, respectively. Furthermore, the 12.5% of MPC survivors who talked to a mental health professional appears low since 20.2% of MPC survivors met criteria for Serious Psychological Distress (Table 3). Our findings suggest mental health care may be underutilized in MPC survivors. This is not surprising. Though recent research suggests an improving situation [23] prior research has documented under-recognition of distress [24,25] and low utilization of mental health care by cancer survivors [26,27]. As uptake of mental health care or anxiety and depression medication use has never been examined in MPC survivors, our results merit replication.

## 5. Study limitations

Study limitations should be acknowledged. We excluded individuals diagnosed with cancer during childhood (< 18 years) from our survivor groups and the NHIS survey includes only non-institutionalized individuals. Thus results may not generalize to all cancer survivors. Additionally, while our use of NHIS data is consistent with the Institute of Medicine's recommendation national household and health care surveys be used to study cancer survivorship [28], there are limitations inherent in this approach. First, variables we could examine were necessarily limited by the questions included in the NHIS. Many of our distress indices were simple ad hoc questions of unknown psychometric quality. Second, lack of information regarding cytotoxic treatment and disease staging precluded analyses of how these factors might be linked to distress risk. Finally, cancer history was assessed by self-report. The validity of these reports varies as a function of many factors, including cancer type and time since diagnosis, resulting potentially in some misclassification [29–33]. In general, a bias toward underreporting prior cancer diagnoses may be present [32]. Self-report of multiple primary cancers might be further compromised by confusion of recurrent and metastatic cancers with additional primary cancers. Future research would benefit from registry-driven recruitment of MPC and SPC survivors for study with assessment of distress by well-validated structured interview and questionnaire methods.

## 6. Conclusions and recommendations for future research

In conclusion, our results suggest additional primary cancer diagnoses are associated with some increased distress risk beyond that associated with an initial cancer diagnosis. Our results are thus consistent with prior studies of distress in MPC survivors [13–18]. However, the clinical importance of this increased distress risk is unclear. Effect sizes in the present study were generally modest as they generally have been in prior studies. Furthermore, increased distress risk was not evident across all distress indices. While our results showed MPC survivors were more likely to meet criteria for Serious Psychological Distress (SPD) and report more frequent feelings of anxiety and, to some degree, depression, MPC and SPC survivors did not differ in reports of severity of anxiety and depression feelings. Similarly, MPC and SPC survivors did not differ in the extent distress interfered with life or activities. Future research should clarify the clinical importance of the increased risk for distress evidenced by MPC survivors in both this as well as prior research. Future research should also further examine use of mental health care and anxiety and depression medication use among MPC survivors. For the moment, it seems reasonable to conclude MPC survivors are at some increased distress risk for distress. Whether this translates into a significantly increased need for supportive care relative to SPC survivors is unclear. The clinically important difference between MPC and SPC survivors may not be the magnitude of distress experienced but rather the nature of specific concerns driving the observed differences in distress between them.

If considered as a separate cancer diagnostic group, individuals diagnosed with a MPC would represent the largest cancer diagnostic group in the USA, exceeding the number of individuals diagnosed with cancers of the prostate, lung/bronchus, or female breast. Each of which has been the focus of a large corpus of cancer survivorship research. Given their numbers, MPC survivors appear to be a highly understudied group of cancer survivors. We suggest it may be useful to consider MPC and SPC survivors as distinct subgroups of cancer survivors with increased attention devoted to the potentially unique needs of MPC survivors. We know cancer survivors are at risk for mental and physical health deficits including fatigue, sleep disturbance, and cognitive deficits. MPC survivors might evidence greater risk for these deficits as well, particularly given their apparent increased risk for distress. There is a need for research detailing the broader mental and physical health status of MPC survivors, identifying subgroups of those potentially at

greatest risk for health deficits, and developing and disseminating strategies for enhancing the survivorship experience of this understudied and potentially unique group of cancer survivors.

## Declaration of Competing interest

All authors have completed the Unified Competing Interest form at [http://www.icmje.org/coi\\_discolosure.pdf](http://www.icmje.org/coi_discolosure.pdf)

The authors have no competing interests to report

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## Appendix A. Supplementary data

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