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Article

Risk Factors of Health-Related Quality of Life among Gastrointestinal Cancer Survivors in the U.S: With a Focus on Social and Behavioral Determinants of Health (SBDH)

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Abstract: **Background:** Increasing number of long-term gastrointestinal (GI) cancer survivors highlights the importance of understanding factors that contribute to their health-related quality of life (HRQoL). We investigated the risk factors of HRQoL, including demographics, clinical characteristics, and social and behavioral determinants of health (SBDH). **Methods:** Adult GI cancer survivors (n = 3,201) in the BRFSS surveys from 2014-2021 (except for 2015) were analyzed. Unadjusted/adjusted logistic regression was used. **Results:** The majority were female (54%) and White (78%), with a median age of 67. Survivors who were 65 years or older, diagnosed with colorectal cancer, or who had fewer comorbidities were more likely to report significantly better HRQoL. Significant social factors of poor HRQoL were being unmarried, racial and ethnic minorities, low socioeconomic status, and poor health care access. Significant behavioral factors of poor HRQoL were lack of physical activity, heavy alcohol consumption, and current smoking, with lack of physical activity being the most significant factor. **Conclusions:** The SBDH have a critical role in HRQoL. Future studies are warranted to develop a tailored survivorship intervention, such as physical rehabilitation and to explore machine learning/artificial intelligence predictive models to identify cancer survivors at a high risk of developing poor HRQoL.

Keywords: Gastrointestinal; Cancer survivor; Social and behavioral determinants of health; Health-related quality of life

1. Introduction

Gastrointestinal (GI) cancer is a group of cancers that can affect any part of the GI tract, such as esophageal, gastric, colorectal, anal, gall bladder, pancreatic, and liver [1]. GI cancer is among the leading cause of death in the United States (U.S.) [2]. GI cancer in the U.S. is projected to account for 34% of cancer incidence [1]. The 5-year overall age-standardized relative GI cancer survival rate is rising due to improvements in early identification and treatment (42% between 1975 and 1990 to 94% between 2012 and 2018) in the U.S. in all combined cancer stages and GI cancer types [2]. It is predicted that by 2050, there will be 350,000 GI cancer survivors living in the U.S. [1,2,3].

As more GI cancer survivors live longer, health-related quality of life (HRQoL)[3] becomes increasingly significant among this group. Many GI cancer survivors experience poor HRQoL [4-6]. Indeed, a growing number of GI cancer survivors, not only are living longer, but also are burdened with the risk of cancer recurrence, financial distress, the long-term symptom consequences of cancer per se, and its treatment [6-8]. The multiple burdens (e.g., physical challenges) in GI cancer survivors can significantly impact their HRQoL [2, 4-7, 9].

Of note, significant cancer survivorship disparities were observed across various social and behavioral determinants of health (SBDH) factors such as race, income status, or education levels, and health risk behaviors [10, 11]. Therefore, understanding the associations of SBDH factors with HRQoL of GI cancer survivors can inform targeted interventions to improve their overall well-being. However, identifying GI cancer survivors at a high risk of developing poor HRQoL is under-investigated [12].

To our knowledge, while numerous studies have shown that SBDH have a significant impact on cancer survival and mortality rates [11, 13, 14], very few studies have examined SBDH risk factors of HRQoL in cancer survivors in the U.S. [15]. For example, higher income was associated with better HRQoL, whereas lower educational status negatively impacted HRQoL among Hispanic/Latino-American cancer survivors in mixed cancer types [16] or in breast cancer survivors [17, 18]. Burse et al. (2022) [15] also examined the association between SBDH and HRQoL in cancer survivors with mixed cancer types in the U.S. Burse et al. found that current smoking was positively and significantly associated with poor physical HRQoL, but healthy eating (e.g., fruit and vegetable consumption), heavy alcohol consumption, and health care coverage were not associated with HRQoL after covariate adjustment. However, these studies [15-18] were limited in identifying the most significant SBDH risk factors of poor HRQoL, specific to GI cancer survivors.

Understanding the roles of SBDH on HRQoL among GI cancer survivors is crucial to gain insight into the specific social challenges and needs of this population. Lower socioeconomic status and poor lifestyle, including health risk behaviors, are associated with a higher risk of GI cancer, as well as higher mortality and recurrence rates in GI cancers [17]. Poor diet (e.g., red meat, fast food consumption), sedentary lifestyles, and smoking status contribute to GI cancer development as well as poor disease prognosis [19]. SBDH may play a role in not only the risk for GI cancer development but also hastening symptoms and poor HRQoL. Researchers have identified that poor SBDH were associated with severe and frequent GI and psychological symptoms [4-7], which contribute to the risk of poor physical and mental HRQoL in GI cancer survivors.

Marco et al. (2019)[20] reported that cancer survivors with prostate, melanoma, gynecological, and urological cancers had higher HRQoL scores than those with colorectal cancer. Thus, HRQoL can differ by cancer type, thus, it is important to identify SBDH risk factors of HRQoL specific to GI cancer survivors instead of examining these relations in all combined cancer types [20].

Therefore, the purpose of this study is to examine the associations of SBDH with HRQoL among GI cancer survivors in the U.S. Our aims are to: (1) identify the most influential or significant risk factors of poor HRQoL outcomes (general, physical, and mental) including demographic and clinical characteristics, and SBDH (e.g., race, health risk behaviors, income, education, health care access, homeownership); and (2) to quantify the associations of SBDH with HRQoL after covariate adjustment among GI cancer survivors. Our focused SBDH as primary risk factors of poor HRQoL.

Significant demographic and clinical characteristics related to HRQoL in Aim 1 were adjusted as covariates in Aim 2.

2. Materials and Methods

2.1. Data Source and Study Population

A nationwide telephone survey known as the Behavioral Risk Factors Surveillance System (BRFSS) was launched by the CDC in 1984 [21]. In all 50 U.S. states, the District of Columbia, and three U.S. territories, BRFSS interviewers gather information on health-related behaviors, sociodemographic factors, the top preventable causes of death, and preventive health practices among non-institutionalized residents (18 years of age or older). The BRFSS conducts surveys over landlines or cellular telephones using a random digit dialing sampling technique. The validity and reliability of BRFSS data have been demonstrated [21]. We conducted a secondary data analysis using publicly available BRFSS survey data. The institutional review board (IRB) waived approval for this study.

A cross-sectional study was conducted by combining BRFSS data in GI cancer survivors from 2014 to 2021 except for 2015 (due to no GI cancer data availability).

Survey questions about diet were asked only in the survey for the years 2017, 2019, and 2021. We merged surveys to examine diet (the surveys 2017, 2019, and 2021) as a risk factor for HRQoL. Individuals ≥ 18 years old who self-reported a personal history of esophageal, stomach, colon, rectal, liver, and pancreatic cancers were included as adult GI cancer survivors in this study. We excluded individuals if they refused to respond to any of the survey questions or had missing responses or values of any of the included variables used in this study.

2.2. Measures

2.2.1. Primary Outcomes of Interest

CDC's HRQoL-4 measure was used in this study. The CDC HRQoL-4 measure included self-reported general, physical, and mental health status and usual activity limitations by physical or mental health status [16]. Our primary outcomes include all three items of the HRQoL-4 measure - general, physical, and mental health items. The following survey questions were used to measure each health status [21]: for general health, *“Would you say that in general, your health is excellent, very good, good, fair or poor?”*; for physical health, *“Now thinking about your physical health, which includes physical illness and injury, for how many days during the past 30 days was your physical health not good?”*; and for mental health, *“Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?”* We used the cutoff for categorizing the primary outcomes validated by CDC [22]. General health was dichotomized as “better” if answered as excellent, very good, or good versus “poor” if answered as fair or poor. Physical and mental health status were also dichotomized as “better” versus “poor.” Better physical health was defined as having 0 to 13 physically unhealthy days, while poor physical health was defined as having 14 or more such days. Similarly, mental health was defined as having 0 to 13 mentally unhealthy days, while poor mental health was defined as having 14 or more such days.

2.2.2. Correlates of HRQoL: Demographic and Clinical Characteristics

In the BRFSS data, we included age, sex, GI cancer types, and comorbidities as demographic and clinical characteristics as potential covariates.

2.2.3. Social and Behavioral Determinants of Health (SBDH)

In our study, SBDH was measured as a risk factor for poor HRQoL, including social determinants of health (SDOH) and health risk behaviors. Healthy People 2030, a national health

initiative [23], sorts social determinants of health (SDOH) into five key areas of economic status, education, social and community context, healthcare access and quality, and neighborhood and built environment. To correspond BRFSS data to the SDOH in accordance with Healthy People 2030, we included social community context (race, ethnicity, and marital status), education, economic status (annual household income, employment status, homeownership – rent versus own home), and healthcare access (health care insurance coverage, time since the last health checkup, and concerns of medical costs limited the number of doctor visits). There were no available variables of BRFSS data that matched up with neighborhood and built environment area of the Healthy People 2030. In our study, we further included behavioral risk factors including diet, physical activity, alcohol consumption, and smoking status (Figure 1). The diet variable (fruit and vegetable consumption per day) was grouped into two categories: "Less than one time per day" and "One or more times per day." The BRFSS physical activity questions, "Adults who reported doing overall routine physical activity or exercise during the past 30 days other than their regular jobs? and no physical activity or exercise during the past 30 days," were used for the current study. The BRFSS defined heavy drinking as having more than seven drinks per week for women and more than 14 drinks per week for men. Current smoking was considered a binary variable (either "yes" or "no") [24]. None of the variables related to social and community context, quality of care, or environmental factors (e.g., zip code, pervert index, environmental safety, transportation) were available in the BRFSS dataset of GI cancer survivors.

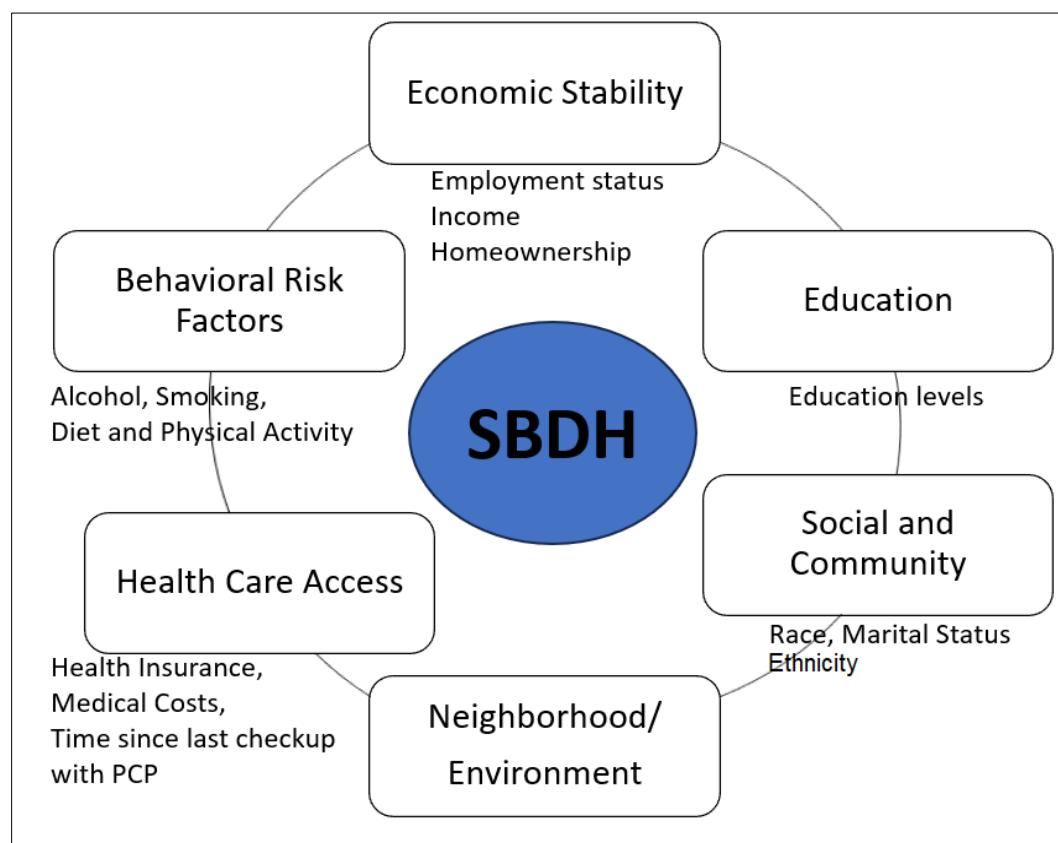


Figure 1. Healthy People 2030 Framework's 5 domains of SDOH, and Behavioral risk factors, which are corresponding Social and Behavioral Determinants of Health (SBDH) for the current study.

2.3. Statistical Analysis

The BRFSS is designed to obtain health-related information on the population of interest. i.e., the adult U.S. population residing in different states [23]. Data weighting helps make sample data more representative of the population from which the data were collected. BRFSS data weights incorporate both population characteristics and BRFSS survey design. BRFSS weighting methodology consists of

1) design weight or factors, and 2) some method of adjusting the population's demographics, such as ranking or interactive proportional fitting. The design weight accounts for the probability of selection and adjusts for nonresponse bias and non-coverage errors [25]. Complex survey procedures with appropriate stratification and weighting of the data were applied to the study sample in our study.

The statistical analysis for this study involves a combination of descriptive statistics, univariate analysis, and logistic regression. Descriptive statistics were used to summarize the main outcomes and participants' characteristics. To examine the unadjusted correlated with HRQoL outcomes, the Chi-square test was used to analyze categorical independent variables, and the Analysis of Variance (ANOVA) was used for continuous independent variables. Logistic regression was then used to estimate the odds ratios (O.R.s) and 95% confidence intervals (C.I.s) for the association between each HRQoL outcome and SBDH. We only included SBDH factors in the regression models if they were significantly associated with HRQoL outcomes. Correlation analyses between the independent variables and variance inflation factors (VIF) were calculated to assess multi-collinearity, if the VIF is greater than 5 for the current study [26]. Stepwise eliminations were performed in multivariate regression models to select a parsimonious model while minimizing collinearity among variables [27]. The survey years, demographic and clinical characteristics significantly associated with HRQoL were adjusted as covariates for the final regression model. Unadjusted and adjusted O.R.s and 95% C.I.s were reported for the final models. All statistical analyses are performed using R statistical software program. The level of significance for all analyses was set at $p < 0.05$ (two-sided).

3. Results

3.1. Demographic and Clinical Characteristics

The unweighted population consisted of 3,201 GI cancer survivors (Table 1). Weighting to the respective state populations, cancer survivors represented 229,428 adult GI cancer survivors in the combined dataset from 2014 to 2021 except for 2015 (Table 1). The demographic and clinical characteristics are described in Table 1.

Table 1. Demographic and Clinical Characteristics among GI Cancer Survivors.

A. Main dataset (2014 to 2021, except for 2015)		B. Subset of main dataset (2017, 2019, & 2021 with diet variables)	
	Total Weighted Study N =229,428 unweighted n = 3,201		Total Weighted Study N =123,261 unweighted n = 835
Year, n (%)	229,428	Years, n (%)	123,261
2014	12,576 (5.5)	2014	not included
2016	20,718(9.0)	2016	not included
2017	16,870(7.4)	2017	51,236 (47)
2018	14,128(6.2)	2018	not included
2019	196(<0.1)	2019	70(3.8)
2020	141,212(62)	2020	not included
2021	23,729(10)	2021	4 11(49)
Demographics (% otherwise specified)			
Age, median (Interquartile range, IQR)		67 (58, 76)	
Age group	18-64	43%	67 (58, 77)
	65 or older	57%	32% 68%
Sex	Male	46%	48%
	Female	54%	52%
Clinical Characteristics, n (%)			
Types of GI Cancer	Colorectal (intestine)	72.3%	77.1%
	Esophageal	5.2%	6%
	Liver	10%	7.4%
	Pancreatic	5.1%	4.6%
	Stomach	7.2%	4.9%
Comorbidities			

The participants self-reported if they had ever been told by a health professional that they had ("yes"/"no")

Heart Attack (Yes)	12%	9.2%
Coronary Heart Disease (Yes)	12%	11%
Asthma (Yes)	17%	14%
Stroke (Yes)	8.3%	8.3%
Chronic Obstructive Pulmonary Disease (Yes)	14.5%	13.2%
Diabetes (Yes)	51.3%	54.9%
Chronic Arthritis (Yes)	48.9%	45.6%
Chronic Kidney Disease (Yes)	8.4%	11%
Overweight or obese per Body Mass Index (Yes)	29.5%	14%

Note. Interquartile range, IQR.

In main dataset, about half of the GI cancer survivors were 65 years or older (57%) with a median age of 67 years old, and female (54%) (Table 1A). Among GI cancer survivors, colorectal cancer was the most common cancer (72.3%), followed by liver cancer (10%), and stomach cancer (7.2%). In terms of comorbidities, diabetes (51.3%) was the most common chronic condition, followed by chronic arthritis (48.9%) among GI cancer survivors. In the subset of the main dataset combining 2017, 2019, and 2021 surveys with available diet variables (Table 1B), similar results were found: Majority of GI cancer survivors were 65 years or older (68%), female (52%), and ever having been diagnosed with colorectal cancer (77.1%). Diabetes and chronic arthritis were the most common chronic conditions.

3.2. HRQoL Outcomes and SBDH

The HRQOL and SBDH factors are described in Table 2. In the main BRFSS dataset, over half of GI cancer survivors reported better general (62%) and mental (56%) HRQoL, while 43% reported better physical HRQoL (Table 2A). In main dataset, approximately half of GI cancer survivors were married or partnered (49%) and had at least a college education (50%). 78% of GI cancer survivors were non-Hispanic White. About 57.3% of the cancer survivors had an annual household income of at least \$35,000, and 93% had healthcare coverage. Most of the cancer survivors were on retirement benefits (55.3%), homeowners (79%), not heavy drinkers (91%), and not current smokers (83%). About 65% of GI cancer survivors reported routine physical activity or exercise over the last month. Similar results were found in the subset of BRFSS data combining 2017, 2019, and 2021. In this subset of BRFSS data (Table 2B), the majority of participants have consumed fruits (68%) and vegetables (80%) one or more times per day.

Table 2. HRQoL Outcomes and SBDH among GI Cancer Survivors (%).

A. Main dataset (2014 to 2021, except for 2015)		B. Subset of main dataset (2017, 2019, & 2021 with diet variables)
Total Weighted Study N =229,428 <i>unweighted n = 3,201</i>		Total Weighted Study N =123,261 <i>unweighted n = 835</i>
HRQoL Outcomes (%)		
General Health	Poor	38%
	Better	62%
Mental Health	Poor	44%
	Better	56%
Physical Health	Poor	57%
	Better	43%
Social and Community Context		
Race/Ethnicity	Non-Hispanic White	78%
	Non-Hispanic Black	12%
	Non-Hispanic Other	5.5%
	Hispanic	4.5%
Marital status	Married/Partnered	49%
	Divorced/Widowed/Single	48%
Education		

High school or less	50%	34%
Attended College or technical school	31%	32%
Graduated from College or technical school	19%	33%
Economic Stability		
Employment Status	Employed	28%
	Unemployed	11.7%
	Retirement Benefits	55.3%
	Homemaker	5%
Household Income (annual)		
Less than \$15,000		9.4%
\$15,000 to <\$25,000		18%
\$25,000 to <\$35,000		15.3%
\$35,000 to <\$50,000		22.7%
\$50,000 to <\$100,000		33.1%
\$100,000 or more		1.5%
Homeownership	Own	79%
	Rent	18%
	Other arrangement	3%
Health Care Access		
Health Insurance	Yes	93%
	No	6.2%
	Don't know/Not sure	0.8%
Medical Costs:		
In the past 12 months, could not see doctor due to medical costs (Yes or No)	Yes	Yes
	(8%)	(6.9%)
Health Care Access: Time since last checkup with primary care providers		
Within past years	87%	86%
1 but <2 years ago	7.8%	8%
2 but < 5 years ago	3.3%	3%
5 or more years ago	1.6%	2%
Never	0.1%	1%
Behavioral Risk Factors		
At least one alcohol in the past 30 days	Yes	40%
	No	60%
Heavy drinking per week	Yes	9%
	No	91%
Smoking Status	Current	17%
	Former	40%
	Never	43%
Physical Activity	Yes	65%
	No	35%
Diet (Fruits)	Less than one time per day	no data
	One or more times per day	available
Diet (Vegetables)	Less than one time per day	no data
	One or more times per day	available

3.3. Correlates of HRQoL: Demographic and Clinical Characteristics

We examined demographic and clinical characteristics with HRQoL to identify potential covariates for our primary analyses (i.e., SBDH and HRQoL) (Table 3). Older age group, married/partnered, and no diagnosis of asthma were significantly associated with better general and mental HRQoL ($P < .001$). Several chronic conditions were associated with poor HRQoL in all three HRQoL outcomes. Ever having been diagnosed with colorectal cancer (compared to other types of GI cancer such as liver and pancreatic cancers), no past medical history of coronary heart disease and chronic kidney disease were significantly associated with better general and physical HRQoL ($P < .05$).

Table 3. Correlates of HRQoL: Demographic and Clinical Characteristics.

Main dataset (2014 to 2021, except for 2015), Total Weighted Study N =229,428, unweighted n = 3,201										
Variables	General HRQoL			Mental HRQoL			Physical HRQoL			
	Poor	Better	p	Poor	Better	p	Poor	Better	p	
Demographics (% otherwise specified)										
Age, Median (IQR)	64(13)	65(14)	.367	57(15)	60(15)	.314	63(13)	61(16)	.840	
Age group	18-64	37.5	29.0	<.001	56.5	42.6	<.001	40.5	37.3	.440
	65 or older	61.5	70.0		42.5	57.0		58.8	61.9	
Sex	Male	46.7	46.0	.674	38.8	39.5	.822	45.5	42.3	.237
	Female	53.3	54.0		61.2	60.5		54.5	57.7	
Clinical Characteristics (%)										
Types of GI cancer		<.001			.710			<.001		
Colorectal		71.0	83.8		71.9	73.1		68.0	78.3	
Esophageal		6.0	4.2		6.5	5.5		7.3	4.4	
Liver		10.2	4.5		10.0	8.4		10.6	5.8	
Pancreatic		6.3	3.9		4.5	6.6		7.3	5.3	
Stomach		6.6	4.6		7.2	7.5		6.8	6.2	
Comorbidities										
Heart Attack	Yes	18.7	7.5	<.001	16.4	10.4	.023	18.8	12.2	.003
	No	80.2	91.9		82.3	88.2		80.4	86.7	
Coronary Heart Disease		<.001			.380			<.001		
	Yes	18.8	8.0		15.7	12.2		20.3	11.5	
	No	79.3	90.4		82.8	86.0		78.4	86.5	
Asthma	Yes	20.2	11.3	<.001	25.6	15.5	<.001	20.5	18.8	.576
	No	79.5	88.4		74.4	84.3		79.3	80.7	
Stroke	Yes	13.3	5.2	<.001	14.2	8.0	.001	11.3	8.4	.002
	No	85.9	94.6		84.1	91.6		87.9	91.2	
COPD	Yes	23.5	9.0	<.001	26.4	16.4	.001	24.9	15.7	<.001
	No	75.4	90.6		71.9	61.0		74.1	83.5	
Diabetes	Yes	33.3	21.4	<.001	31.3	25.2	.043	31.6	26.9	.023
	No	63.4	76.8		65.4	71.8		65.4	70.5	
Chronic Arthritis	Yes	59.2	42.9	<.001	66.4	51.4	<.001	62.2	54.3	.011
	No	40.5	56.5		33.7	48.1		37.4	45.2	
Chronic Kidney Disease		<.001			.556			.012		
	Yes	13.0	5.6		11.7	10.1		13.8	8.4	
	No	86.0	94.0		87.1	88.9		85.2	90.9	
Overweight/Obese		.886			.123			.323		
	Yes	31.5	31.8		30.6	36.4		31.9	32.9	
	No	64.3	64.3		66.4	59.9		64.5	62.1	

Note. Interquartile range, IQR; Significant findings (p <.05) were highlighted in bold.

3.4. Potential Impact of SBDH on HRQoL

The associations of SBDH with HRQoL are described in Table 4.

Table 4. Associations of SBDH with HRQoL (%).

Main dataset (2014 to 2021, except for 2015) Total Weighted Study N =229,428, unweighted n = 3,201										
SBDH risk factors	General HRQoL			Mental HRQoL			Physical HRQoL			
	Poor	Better	p	Poor	Better	p	Poor	Better	p	
Social and Community Context										
Race/Ethnicity			<.001				.230		.398	
Non-Hispanic White	77.3	83.0		77.4	79.6		80.6	78.3		
Non-Hispanic Black	8.9	6.2		6.2	7.1		6.8	8.9		
Non-Hispanic Other	6.7	4.6		6.2	8.4		3.5	4.1		
Hispanic	4.4	2.4		4.0	3.3		3.9	4.0		
							3.4	2.9		
Marital Status	44.0	52.2	<.001	41.0	49.7	.002	49.3	46.3	.096	
Married/Partnered	56.0	47.8		59.0	50.3		50.7	53.7		
Divorced/Widowed/Single										
Education										
High school or less	47.2	35.8	<.001	41.3	38.4	.014	12.5	9.9	<.001	
Attended College or technical school	30.9	29.4		33.4	32.4		33.1	28.7		
Bachelor's degree or graduate or more	21.6	34.5		24.9	67.5		54.5	60.9		
Economic Stability										
Employment Status			<.001			<.001			<.001	
Employed	17.0	29.0		17.4	27.3		16.0	25.3		
Unemployed	20.1	17.1		45.3	33.0		32.5	18.5		
Retirement Benefits	58.9	48.9		31.1	47.0		45.7	51.7		
Homemaker	4.0	5.0		6.2	2.7		5.8	4.5		
Household Income/year	36.4		<.001	42.8	27.1	<.001	38.7	29.3	.002	
Less than \$25,000	12.0	20.7		8.7	10.4		10.6	8.9		
\$25,000 to <\$35,000	12.6	10.9		11.7	15.1		12.4	12.6		
\$35,000 to <\$50,000	21.9	12.8		22.6	29.1		23.1	30.8		
\$50,000 to <\$100,000	0.8	35.2		0.2	2.8		0.7	1.8		
\$100,000 or more				2.2						
Homeownership	Own	72.7	81.8	<.001	66.9	75.2	.012	71.2	75.9	.234
	Rent	22.9	15.1		26.1	21.9		24.0	19.9	
Health Care Access										
Health Insurance	Yes	94.2	94.7	.580	91.0	93.3	.289	93.9	94.2	.786

No		5.1	4.3	7.5	6.3	5.3	5.3	
Medical Costs: In the past 12 months, could not see a doctor due to medical costs. (Yes/No)	Yes	Yes	.101	Yes	Yes	.108	Yes	.050
	(10.3)	(6.6)		(15.1)	(8.9)		(11.9)	(8.1)
Time since last checkup with PCP -Within the past year -More than 1 year ago/never		87.5	.021	85.4	80.8	.060	84.3	88.3
	84.6	12.5		14.6	19.2		15.7	11.7
		15.4						
Behavioral Risk Factors								
At least one alcoholic drink in the past 30 days	Yes	28.1	42.3	<.001	32.6	39.9	.050	28.5
	No	71.3	57.0		67.4	59.6		70.8
Heavy drinking per wk.	Yes	94.7	92.3	.022	92.8	92.9	.184	94.2
	No	4.4	6.7		7.0	5.8		4.9
								5.7
Smoking Status	Current	17.9	8.8	<.001	28.0	13.3	<.001	18.8
	Former	41.9	38.8		37.3	36.6		41.0
	Never	39.4	51.9		33.8	49.4		39.4
Physical Activity	Yes	50.5	73.1	<.001	49.3	65.4	<.001	46.5
	No	52.8	26.7		50.2	34.6		53.0
								34.7
Subset of the main dataset (2017, 2019, & 2021 with diet variables)								
Weighted Study N =123,261, unweighted n= 835								
Diet (Fruits)		69.7	64.9	.290	65.6	59.5	.574	72.0
-Less than one time per day		27.0	31.7		31.8	37.9		26.9
-One or more times per day								31.5
Diet (Vegetables)		80.5	74.4	.004	84.4	71.6	.025	82.8
- Less than one time per day		15.2	23.3		12.3	25.0		15.6
-One or more times per day								23.6

Note. Significant findings (p <.05) were highlighted in bold. PCP, Primary Care Provider.

Given the significant correlates of SBDH with HRQoL (Table 4), we further quantify the potential impact of SBDH on HRQoL using regression models. Unadjusted and adjusted odds ratios (O.R.s) of each HRQoL outcome in relation to the SBDH are shown in Table 5. In the unadjusted models, many SBDH factors significantly increased the risk of poor general, mental, and physical HRQoL (e.g., racial and ethnic minorities, non-married or partnered status, lower education and income levels, unemployment, home renters, more time since the last checkup, poor health behaviors- heavy alcohol drinking, current smoking, and lack of physical activity). However, daily fruit and vegetable consumption, health insurance, and medical costs were not significantly associated with HRQoL.

In the adjusted multivariate logistic models adjusting covariates (survey years, age, GI cancer types, and comorbidities) (Table 5), among social determinants of health, non-Hispanic Whites (OR = 1.05, 95% CI: 1.01 to 1.10) and married/partnered status (OR = 1.10, 95% CI= 1.05 to 1.16), higher education levels (OR = 1.33, 95% CI = 1.11, 1.52), being employed (OR = 1.12, 95% CI = 1.06, 1.13), higher income (OR = 1.08, 95% CI= 1.05, 1.32), and health care access within the past year since the

last checkup with primary care provider (OR = 1.41, 95% CI = 1.13, 1.77), were associated with better general health HRQoL. Similar results were found for mental and physical HRQoL. Regarding behavioral determinants of health, lack of physical activity, alcohol consumption, and current smoking were significantly associated with poor HRQoL (all three outcomes). Among all SBDH in our study, physical activity participation was the most significant risk factor for better HRQoL (OR = 1.98 for general, OR = 1.74 for mental, and OR = 1.94 for physical HRQOL), followed by better health care access (frequent health checkup) (OR = 1.41 for general, OR = 1.46, for mental, and OR = 1.49 for physical HRQOL).

4. Discussion

The current study marks the initial exploration of SBDH risk factors of HRQoL among U.S. adults with various GI cancer types, encompassing social and behavioral factors of SBDH. Our findings underscore the significant associations of poor HRQoL with many individual-level demographic and clinical characteristics, and SBDH in poor status, such as low economic stability, poor health care access, non-Hispanic Blacks, poor health risk behaviors, were significantly associated with poor general, mental, or physical HRQOL. Lack of physical activity and less health care access (i.e., less frequent health checkups) were the major SBDH factors of poor HRQoL in all three outcomes among GI cancer survivors.

Table 5. Potential Impact of SBDH on HRQoL among GI Cancer Survivors.

OR/Adjusted OR 95% CI	Main dataset (2014 to 2021, except for 2015)					
	Total Weighted Study N =229,428, unweighted n = 3,201					
	Better General HRQoL (62%, Weighted n =137,905)		Better Mental HRQoL (56%. Weighted n = 124,559)		Better Physical HRQoL (43%, Weighted n = 98,654)	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Social and Community Context						
Race	Non-Hispanic Whites	1.05** (1.01, 1.10)	1.02* (1.01., 1.12)	not applicable	not applicable	not applicable
Racial/ethnic minorities (ref) ^a						
Marital status	Married/Partnered	1.10** (1.05, 1.16)	1.06* (0.99, 1.12)	1.13* (1.03, 1.24)	1.01 (0.98, 1.20)	not applicable
Divorced/Widowed/Single(ref)						
Education						
High school or less/College(ref)	Bachelor's/graduate or more	1.27* (1.22, 1.32)	1.33* (1.11, 1.52)	1.18** (1.07, 1.28)	1.06 (0.98,1.19)	1.18** (1.1, 1.26)
						1.11* (1.01,1.21)
Employment Status						
Unemployed/ homemakers/ Retired benefits (ref)	Employed	1.14** (1.12, 1.7)	1.12** (1.06, 1.13)	1.13** (1.07, 1.19)	1.13** (1.06,1.19)	1.11** (1.06, 1.15)
						1.09** (1.03,1.14)
Household Income/year						
Less than <\$35,000 (ref)	Equal to more than \$35,000	1.11** (1.08, 1.14)	1.08** (1.05, 1.32)	1.10** (1.05, 1.16)	1.07* (1.01,1.12)	1.07** (1.03, 1.10)
						0.96 (0.92,1.01)

Homeownership	Rent (ref)	1.25** (1.12, 1.40)	1.11 (0.91, 1.25)	1.37** (1.11,1.69)	1.11 (0.90, 1.36)	0.84 (0.63, 1.02)	1.10 (0.85,1.13)
Health Care Access							
Time since the last checkup with PCP		1.41** 1.27* (1.13, 1.77)	1.38 (0.99, 1.96)	1.46* (1.01,2.11)	1.41* (1.02, 1.92)	1.49* (1.07,2.08)	
Within the past year		(1.03, 1.56)					
More than one year ago/never(ref)							
Health Risk Behaviors							
At least one alcoholic drink in the past 30 days	Yes (ref)	1.21** (1.21, 1.43)	1.39** (1.22, 1.56)	0.98 (0.6, 1.10)	1.21 (0.93,1.56)	1.32** (1.09, 1.59)	1.21 (0.99,1.48)
	No						
Heavy drinking per/week	Yes (ref)	1.05 (0.99, 1.13)	1.16** (0.92. 1.26)	1.14 (0.94, 1.3)	1.06 (0.94,1.34)	0.98 (0.82, 1.16)	1.05 (0.87,1.20)
	No						
Smoking Status Current (ref)		1.25** (1.29, 1.30)	1.21** (1.14, 1.27)	1.28** (1.19, 1.36)	1.21** (1.01,1.31)	1.12* (1.02, 1.20)	1.02 (0.9,1.12)
	Former/Never						
Physical Activity	Yes	2.34** (2.01, 2.73)	1.98** (1.71, 2.32)	1.93** (1.45, 2.51)	1.74** (1.33,2.28)	2.15** (1.73, 2.71)	1.94** (1.55,2.43)
	No (ref)						
Subset of the main dataset (2017, 2019, & 2021 with diet variables)							
Weighted Study N =123,261, unweighted n= 835							
		Better General HRQoL (63%, Weighted n =75,717)	Better Mental HRQoL (87%, Weighted n = 104,880)	Better Physical HRQoL (76%, Weighted n = 90,251)			
Diet (Vegetables)		1.11 (0.90, 1.23)	0.91 (0.78 1.06)	1.11 (0.90, 1.26)	1.32 (0.91,1.53)	0.96 (0.87, 1.06)	0.99 (0.85,1.11)
- Less than one time per day(ref)							
-One or more times per day							

Note. * p<.05, ** p<.01. ^aRacial/ethnic minorities include Hispanic, Non-Hispanic Blacks and Others; other GI. Cancers include liver, esophageal, pancreatic, stomach cancers. We adjusted for survey years, age, types of GI. cancers, and comorbidities in adjusted regression models. PCP, Primary Care Provider.

Our study is one of the few studies examining the HRQoL in different GI cancer types. Our analyses showed significant evidence of GI cancer-type differences in HRQoL (general, and physical outcomes). Notably, GI cancer survivors diagnosed with esophageal, liver, pancreatic, and stomach cancers more likely reported poor general and physical HRQoL, compared to colorectal cancer survivors. One possibility is a higher cancer burden in certain GI cancer types compared to colorectal cancer. For example, liver and pancreatic cancers generally have a poor prognosis and are often diagnosed at advanced stages with high mortality rates [11]. Furthermore, this can be due to the better prognosis of colorectal cancer compared to live or pancreatic cancer as the early screening and diagnosis of colorectal cancer are well established [28]. Interestingly, the older adults (65 years or older) reported better general and mental HRQoL, but not physical HRQoL in our study. This could be due to the fact that older adults are capable of higher resilience and more capable of managing or resolving conflicts, despite socioeconomic status, and personal health conditions; or older adults in the retirement stage might have fewer responsibilities, dealing with more major life events, compared to those of younger adults (18-64 years old) [29]. It is important to identify different risk factors that

contribute to HRQoL between younger and older age groups, which can provide age-tailored cancer survivorship interventions.

In our study, non-Hispanic Black and other racial and ethnic groups (e.g., Asian, Native Hawaiian, and other Pacific Islander, Multiracial) had a higher prevalence of reporting poor general HRQoL at 22.7%, compared to 17% who reported better general HRQoL ($p < .001$). Similarly, in a large sample case-control, population-based study from the Surveillance, Epidemiology, and End Results (SEER) study, non-Hispanic White cancer survivors had better HRQoL scores than Black cancer survivors and Hispanics in the U.S. [30]. This might be due to the structural racism that exists in the U.S. including in the healthcare system, which could result in poor health care access, low health literacy, disparities in cancer survivorship care, disparities in treatment options and quality of care, disparities in cancer stages, comorbidity burden, socioeconomic status, insurance coverage, and lack of community resources and policy support [30]. Consistent with previous research [15, 30], we observed that married/partnered, high-income status, high educational levels, owning a home, frequent health care access, and optimal health behaviors were associated with better HRQoL outcomes. Marital status, which is often used as a proxy of social support, was significantly related to better general and mental HRQoL [31]. Future studies should explore the influence of structural racism and social support on HRQoL outcomes [32].

In GI cancer survivors, we also showed that current engagement in physical activity was the most impactful factor related to better HRQoL outcomes after analyzing various risk factors in our study. Numerous studies have demonstrated significant associations between physical activity and better mental and physical HRQoL among cancer survivors [33, 34]. The mechanisms through which physical activity improves the HRQoL are unknown. One explanation could be symptoms such as fatigue and psychological distress acting as a mediator between physical activity and HRQoL in cancer survivors [5, 35, 36]. Other potential mechanisms that could explain the link between P.A. and HRQoL are systemic inflammation, the release of endorphins, or by blocking or diminishing external or internal forces that cause stress in cancer survivors [37-39]. We did not find a significant association between daily fruit and vegetable consumption and HRQoL in the adjusted models. It is possible that daily fruit and vegetable consumption may not be a sufficient measure for diet, or fully reflect the nutritional status (including diet quality and food groups), which is significantly associated with the risk of GI cancers and cancer survivorship [40]. Other health risk behaviors including smoking status and alcohol habits were also associated with HRQoL. These health risk behaviors increase the risk of cancer recurrence, and poor disease progress in cancer survivors in the long term [41].

These findings have important implications for clinical practice and public health interventions. Our findings suggest that lifestyle interventions (specifically targeting physical activity) and the screening and, prevention of health risk behaviors as well as the promotion of healthy behaviors must be an integral part of cancer survivorship care. For example, healthcare providers should emphasize the importance of physical activity and smoking cessation for GI cancer survivors and consider referral to functional or mental health rehabilitation for those with poor mental or physical HRQoL. Policymakers should consider supporting a community-based cancer survivorship program. The findings of our study could be leveraged to develop a machine learning (ML) and artificial intelligence (A.I.)-based predictive model of HRQoL. These models could incorporate data on demographics, clinical characteristics, and SBDH risk factors to identify patients at risk of poor HRQoL and inform personalized interventions to improve their HRQoL. Furthermore, these models could help identify factors most strongly associated with HRQoL, which could inform the development of more effective interventions.

The study strengths include utilizing the BRFSS data as a reliable data source, with national representation to increase the generalizability of the research findings [25]. The BRFSS survey also used reliable and validated instruments within samples, which increases the consistency of the measures and generalizability and reduces data collection bias. Our study adds to the body of literature by identifying risk factors of poor HRQoL in three HRQoL outcomes with a primary focus on the roles of SBDH, specific to GI cancer survivors. There are limitations to our study. Our study is limited by the cross-sectional nature of the data, which limits our ability to establish causality. For

example, whether poor SDOH status mediates the relationships between racial and ethnic minorities and poor HRQoL, or whether poor SDOH status increases the likelihood of developing chronic conditions, which, in turn, can negatively impact HRQoL. Self-reported HRQoL data may be subject to reporting bias. Symptoms (particularly fatigue, psychological distress, and GI symptoms), as well as dietary factors like, red meat consumption and the amount of fruits and vegetables consumed, have been found to be associated with HRQoL in GI cancer survivors. However, these variables were not examined in the current study. Additionally, other SBDH factors such as poverty level, neighborhood and environmental factors, and social support level data were not available in our study. This lack of inclusion limits the comprehensive understanding of the impact of these factors on the HRQoL of GI cancer survivors. We also could not adjust for cancer stages, or types of cancer treatments (e.g., radiation, chemotherapy, or surgery) associated with HRQoL in GI cancer survivors [20].

5. Conclusions

Our findings provide valuable insights into the SBDH as well as demographic and clinical characteristics that may influence HRQoL among GI cancer survivors in the U.S. The results of our study highlight the important role of age, comorbidities, and type of GI cancers (non-colorectal cancer) on HRQoL. In addition, multiple SBDH including low economic stability, unemployment, poor health care access, smoking and alcohol health risk behaviors, and lack of physical activity contribute to poor HRQoL among GI cancer survivors. Thus, future studies are warranted to consider the comprehensive assessment of HRQoL and to develop and test tailored cancer survivorship interventions for GI cancer survivors at a high risk of developing poor HRQoL, particularly for underserved and racial and ethnic minority populations with social or economic disadvantages, and ML/AI approaches could be one strategy to help improve the HRQoL of this group of GI cancer survivors.

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