

Original Research Article

A Cross-Sectional Study of Depressive Symptoms among Women with Gynecological Cancer Before and During the COVID-19 Pandemic.

Abstract

Objective

Cancer patients are at a high risk of exhibiting depressive symptoms. However, little is known whether gynecological cancer (GC) worsens this risk. This study seeks to compare depressive symptoms amongst women diagnosed with GC and women diagnosed with other cancer types before COVID-19 pandemic and during the COVID-19 pandemic. It also seeks to compare both study periods to confirm if COVID-19 influenced depressive symptoms of women with GC.

Method

A retrospective cross-sectional study was conducted to find an association between depressive symptoms and gynecological cancers using other cancer diagnosis in females as a reference. We utilized the sample adult file of NHIS (National Health Interview Survey) data from 2019 (Pre-Pandemic data) and data from 2020 (Pandemic data). We also utilized the PHQ-8 scale to quantify major depressive disorder. Each of the 8 items were scored from 0-3. All statistical analysis were performed using SAS v9.4 ((SAS Institute Inc, Cary, NC), and statistical significance was set at $\alpha = 0.05$.

Results

A weighted population of women with GC vs other cancer types was obtained. Women with GC tend to have lesser Age, Educational status, Health status, Income. They also tend to be more obese and smokers. Women with GC tend to have had hysterectomy (68.03% vs 35.43%) and access to care during COVID-19 (71.63% vs 68.01%). Severe depressive symptoms were higher before pandemic and among women with GC OR 2.89 (95% CI 1.64 - 5.12). Moderate depressive symptoms were higher during the pandemic and among women with GC OR 2.19 (95% CI 1.35 – 3.57). Among women with GC, depressive symptoms were less likely in 2020 than 2019 with an OR 0.57 (95% CI 0.36 – 0.91)

Conclusion

Based on the data available, women with gynecologic cancer are more prone to having depressive symptoms than women with other cancer types. Therefore, policies should be implemented to improve wellness of women with gynecologic cancer.

Comment [DE1]: It is not in line with title and objective. No covid related conclusion whereas title and objective states that

Introduction

Cancer patients are at a high risk of psychiatric disorders including depression¹. Depressive symptoms often decrease the quality of life of cancer patients and could decrease survival of these patients². Depressive symptoms could also affect the patient's ability to cope with cancer³. According to the meta-analysis done by Krebber et al., the prevalence rate of depression among cancer survivors in the U.S ranges between 8% to 24%⁴. Depressive symptoms could increase suicidality in cancer patients⁵ and also decrease medication adherence⁶. Depression is the most commonly studied psychological variable with respect to cancer progression and mortality in cancer patients⁷. A previous study conducted by Klapheke et al. showed that depressive symptoms among Medicare beneficiaries were higher among older women with gynecological cancer (31.9%, 32.2%, 25.3% for cervical, ovarian and uterine cancer, respectively) when compared to cancer free older women⁸. Another study showed that younger women within the age of 30-49 years are at a higher risk of having depressive symptoms after undergoing hysterectomy due to gynecological cancer⁹. Even those who had undergone unilateral or bilateral oophorectomy tend to exhibit an increased degree of depression following hysterectomy¹⁰. Also, depressive symptoms were noticeable among individuals with cancer during the COVID-19 pandemic⁴⁰.

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This study seeks to compare depression amongst women diagnosed with gynecological cancers and women diagnosed with other cancer types before COVID-19 pandemic and during the COVID-19 pandemic. It also seeks to compare both study periods to confirm if COVID-19 influenced depressive symptoms of women with gynecological cancers.

Methods

1. Study design and data source

A retrospective cross-sectional study was conducted to find an association between depressive symptoms and gynecological cancers using other cancer diagnosis in females as a reference. We utilized the sample adult file of NHIS (National Health Interview Survey) data from 2019 (Pre-Pandemic data) and data from 2020 (Pandemic data). NHIS is the principal source of information on the health of the civilian noninstitutionalized population of the United States. It is one of the major data collection programs of the National Center for Health Statistics (NCHS) which is part of the Centers for Disease Control and Prevention (CDC). The main objective of NHIS is to monitor the health of the United States population through the collection and analysis of data on a broad range of health topics¹¹.

2. Study Sample

We identified women who reported having a diagnosis of either of the following: Cervical, Ovarian or Uterine cancer. A few women in the cohort had more than one GC. Also, women who had cancer but did not respond positively to having GC were also identified. A separate sample was obtained for the 2019 respondents and 2020 respondents.

3. Demographic and Patient Characteristics

We hypothesized that differences in age group of cancer survivors should be accounted for in this study due to the association of age with depression and cancer¹²¹³, Marital status was also accounted for because people who are partnered tend to have more support thus decreasing risk of depression¹⁴, educational level and income group tend to have a strong association with increased socioeconomic status¹⁵¹⁶. We also included race, region, health status, BMI, lifestyle choices like smoking and type of insurance owned by people in the cohort¹⁷¹⁸¹⁹²⁰.

We searched literatures of top comorbid conditions and surgical procedures associated with psychological symptoms, we resolved to include hypertension, diabetes, hysterectomy, arthritis, pain, stroke, mobility (defined as difficulty in walking or taking steps) and COVID-19²¹²²²³.

4. Patient Health Questionnaire (PHQ-8)

We utilized the self-report scale comprising of eight items that directly relate to eight symptoms of major depressive disorder as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth edition*²⁴²⁵. According to the data collected by NHIS, patients were asked how often they had these symptoms in the past 2 weeks:

- i. Little interest in things that normally interest them (Anhedonia)
- ii. Feeling down (Sadness)
- iii. Trouble with sleeping (Insomnia)
- iv. Feeling tired (Lethargy)
- v. Undereating (Anorexia)
- vi. Feeling bad about oneself (Melancholia)
- vii. Trouble concentrating/forgetfulness (Amnesia)
- viii. Moving or speaking slow or fast (Psychomotor retardation)

Each of the eight items were scored from 0-3, which results in a maximum score of 24. The PHQ-8 scale was classified into four categories: patients having none-minimal symptoms (values 0-4), mild (values 5-9), moderate (values 10-14) and severe (values 15-24)²⁴.

5. Statistical Analyses

Descriptive statistics were used to describe the baseline characteristics and outcome measures of nationally representative sample of the cohort. All baseline demographics were treated as a categorical variable. We reported count and column percentage for the categorical variables. The covariates were Age, Marital status, Educational level, Race, Health status, Income group, Census region, BMI (Body Mass Index), Smoking status, Type of Insurance. Selected co-morbid conditions and surgeries include Hypertension, Diabetes, Hysterectomy, Arthritis, Pain, Stroke, Mobility, COVID-19. Also, access to care during COVID-19 pandemic was also recorded. Pearson's chi square (χ^2) test was used to evaluate differences in demographic and patient characteristics of women diagnosed with gynecological cancer and women with other types of cancer across two distinct period of time: 2019 (Pre-Pandemic) and 2020 (Pandemic).

A hierarchical multiple logistics regression analysis was performed to find the likelihood of depressive symptoms in women who reported having gynecological cancers in comparison to women who reported having other cancer types. Also, multiple logistics regression was used to find the likelihood of having a higher level of depressive symptoms during COVID-19 pandemic as compared to the pre-pandemic period. . First, the outcome to be determined was the likelihood

of depressive symptoms in gynecological cancer patient as compared to women with other cancer types. The PHQ-8 categories were used as the predictor. Adjustments were made in a stepwise format with predictors hypothesized to be confounders. Baseline characteristics with $p < 0.05$ were utilized to make adjustments for sensitivity analysis. The final model had all the above covariates plus patient characteristics with $p < 0.05$.

All statistical analysis were performed using SAS v9.4 ((SAS Institute Inc, Cary, NC), and statistical significance was set at $\alpha = 0.05$).

Comment [DE3]: Statistician to please check

Results

A total number of 2246 women were included in the cohort who reported to have had cancer diagnosis in 2019. Out of this numbers, 405 women reported having a diagnosis of gynecological cancer with a weighted population of 2694991 and 1841 women reported having a diagnosis of other cancer types with a weighted population of 10601324. For 2020, We identified 2398 women who reported having a diagnosis for cancer. Out of this number, 393 women reported having a diagnosis of gynecological cancer with a weighted population of 2607996 and 2005 women reported having a diagnosis of other cancer types with a weighted frequency of 11051152.

Age distribution was similar in 2019 and 2020 for people with GC with a weighted proportion of 43.79% and 42.6% respectively for people aged 46-65 years. The Other cancer group tend to have more people with age > 65 years with a weighted proportion of 53.97% and 54.65% across 2019 and 2020 respectively. More people in the cohort tend to be partnered especially people in the other cancer category. It is interesting to note that people in the GC category tend to be less educated with most of them attaining less than a bachelor's degree. There was no statistical significance for race in both groups. Those with GC tend to report having 'bad or worse' health status. Income group was significantly lower for people with GC maybe because they are less educated than those with other types of cancer. In both years, GC and other cancers were evenly spread across the four regions of the United States. Women with GC tend to be more obese than women who have other cancer types. Based on the data, smoking tends to be prevalent among women with GC than women with other cancer types across 2019 (55.37% vs 41.81%) and in 2020 (54.41% vs 41.32%). Women in both cohorts have a similar distribution of insurance coverage with most women having private insurance.

The selected comorbidities that could be predictors of depression in cancer patients did not vary across GC and other cancer types. Hypertension, Diabetes, Arthritis, Mobility, Pain, COVID-19, and Stroke were not statistically significant at $p < 0.05$. However, surgical procedure like Hysterectomy was significantly greater among women with gynecological cancer with a weighted proportion of 68.03% versus 35.43% for women with GC versus other cancer types respectively. Also, a significant proportion of women in the cohort were able to access care without delays during the pandemic period (71.63% vs 68.01% respectively for GC vs other cancer types respectively). However, access to cancer care wasn't statistically significant across women with GC vs other cancer types.

Table 1: Baseline Characters of Women with Gynecological Cancer Compared to Women with Other Cancer Types in 2019 and 2020

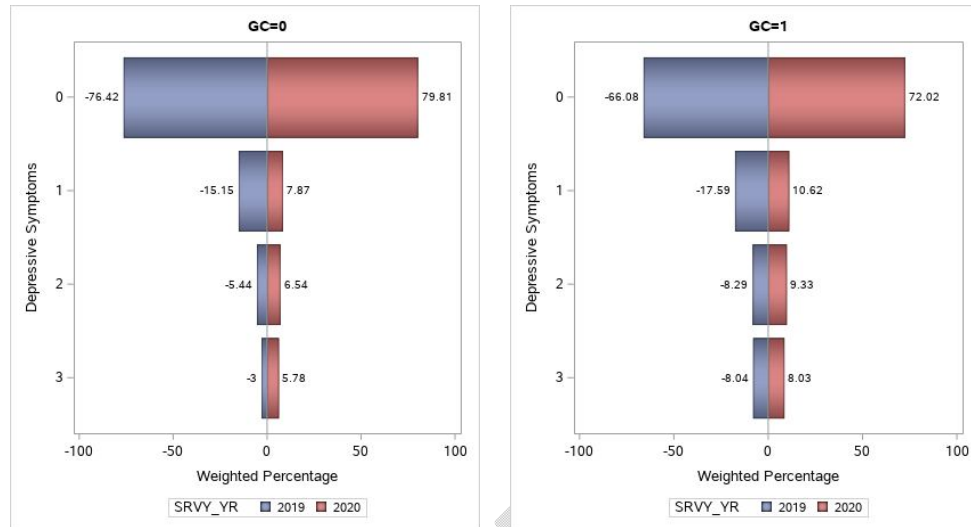
		2019 (Pre-Pandemic Period)			2020 (Pandemic Period)		
		GC n=2.69*10 ⁶	Other cancer n=10.6*10 ⁶	p-value	GC n=2.61*10 ⁶	Other cancer n=11.05*10 ⁶	p-value
Age n(%)	18-45	0.65 (24.21)	1.12 (10.58)	<0.001	0.58 (22.39)	1.02 (9.19)	<0.001
	46-65	1.18 (43.79)	3.75 (35.45)		1.11 (42.6)	3.99 (36.15)	
	>65	0.86 (31.99)	5.72 (53.97)		0.91 (35.01)	6.04 (54.65)	
Marital status n(%)	Partnered	1.46 (54.45)	5.91 (55.77)	0.6921	1.37 (52.69)	6.6 (59.76)	0.0415
	Not Partnered	1.22 (45.55)	4.69 (44.22)		1.23 (47.31)	4.45 (40.24)	
Educational level n(%)	≥ Bachelors	0.58 (21.68)	3.37 (31.76)	<0.001	0.5 (19.24)	3.47 (31.42)	<0.001
	< Bachelors	2.11 (78.31)	7.23 (68.24)		2.11 (80.75)	7.58 (68.58)	
Race n(%)	White only	2.23 (82.8)	9.05 (85.36)	0.3025	2.11 (80.95)	9.56 (86.54)	0.0312
	Non-white	0.46 (17.2)	1.55 (14.64)		0.49 (19.05)	1.49 (13.46)	
Health n(%)	Good or better	1.8 (66.95)	7.91 (74.62)	0.0148	1.83 (70.15)	8.39 (75.92)	0.0588
	Bad or worse	0.89 (33.05)	2.69 (25.38)		0.78 (29.84)	2.66 (24.08)	
Income group n(%)	<35000	1 (37.36)	3.23 (30.49)	0.0984	1.11 (42.42)	2.97 (26.85)	<0.001
	35000 - 49999	0.42 (15.73)	1.44 (13.59)		0.39 (14.98)	1.53 (13.81)	
	50000 - 74999	0.43 (15.93)	1.94 (18.33)		0.43 (16.54)	1.79 (16.27)	
	75000 - 99999	0.32 (11.83)	1.32 (12.4)		0.21 (8.05)	1.47 (13.31)	
	≥ 100000	0.52 (19.14)	2.67 (25.14)		0.47 (18)	3.29 (29.75)	
Region n(%)	Northeast	0.37 (13.8)	1.97 (18.61)	0.1875	0.37 (14.25)	2.07 (18.71)	0.3573
	Midwest	0.61 (22.79)	2.28 (21.46)		0.59 (22.99)	2.48 (22.44)	
	South	1.13 (42.11)	3.96 (37.35)		1.08 (41.79)	4.13 (37.36)	
	West	0.57	2.39 (22.57)		0.55	2.37 (21.49)	

		(21.27)			(20.97)		
BMI n(%)	Obese	1.02 (37.77)	3.09 (29.22)	0.0059	0.96 (36.92)	3.38 (30.62)	0.0594
	Not Obese	1.67 (62.23)	7.5 (70.78)		1.65 (63.08)	7.66 (69.38)	
Smoke n(%)	Smoker	1.49 (55.37)	4.43 (41.81)	<0.001	1.42 (54.41)	4.57 (41.32)	<0.001
	Non-Smoker	1.2 (44.63)	6.17 (58.19)		1.19 (45.59)	6.48 (58.67)	
Insurance n(%)	Private	1.41 (62.6)	6.07 (65.52)	0.4123	1.29 (61.96)	6.24 (64.1)	0.5676
	Non-Private	0.84 (37.39)	3.19 (34.48)		0.79 (38.03)	3.5 (35.93)	

Table 2: Comparison of Certain Factors Associated with Depression Across Women Diagnosed with Gynecological Cancer and Women with Other Cancer Types Within 2019 and 2020

	2019 (Pre-Pandemic Period)			2020 (Pandemic Period)		
	GC n=2.69*10 ⁶	Other cancer n=10.6*10 ⁶	p-value	GC n=2.61*10 ⁶	Other cancer n=11.05*10 ⁶	p-value
Hypertension n(%)	1.17 (43.45)	4.97 (46.89)	0.3014	1.19 (45.46)	5.08 (45.97)	0.8852
Diabetes n(%)	0.47 (17.48)	1.54 (14.54)	0.2362	0.5 (19.19)	1.49 (13.44)	0.0184
Hysterectomy n(%)	1.83 (68.03)	3.75 (35.43)	<0.001	-	-	-
Arthritis n(%)	1.03 (38.21)	3.99 (37.65)	0.854	1.21 (46.25)	5.11 (46.23)	0.9955
Mobility n(%)	0.98 (37.25)	3.94 (38.28)	0.75	0.99 (38.49)	4.11 (37.94)	0.8669
Pain n(%)	1.06 (39.27)	3.55 (33.45)	0.0529	1.03 (39.45)	3.89 (35.21)	0.2009
Stroke n(%)	0.14 (5.27)	0.8 (7.57)	0.1723	0.18 (7)	0.69 (6.29)	0.6561
Covid n(%)	-	-	-	0.04 (1.66)	0.16 (1.46)	0.8062
Access to care during COVID-19 n(%)	-	-	-	0.96 (71.63)	3.83 (68.01)	0.3886

Figure A-B: Pyramid Plot Comparing Depressive Symptoms Across 2019 (Pre-Pandemic) vs 2020(Pandemic) Period



Key:
 0 – none/minimal depressive symptoms, 1 – mild depressive symptoms, 2 – moderate depressive symptoms, 3 – severe depressive symptoms.
 GC=0 (women with other cancer types) GC=1 (women with gynecological cancer)
 SRVY_YR – Survey Year

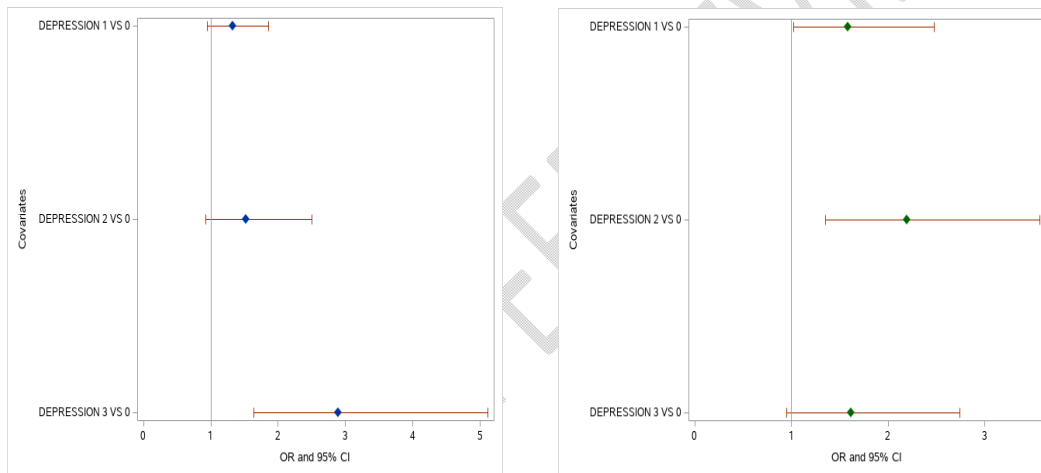
Figure A and B illustrates the comparison of depressive symptoms in 2019 vs 2020 time period which defines the pre-pandemic and pandemic period respectively. Women with PHQ-8 score ranging from 0-4 were classified as having none/minimal depressive symptoms. Considering both time periods, A weighted percentage of 66.08% vs 72.02% was obtained for women with GC while 76.42% vs 79.81% was obtained for women with other cancer types. This shows that women with GC tend to have higher degrees of depressive symptoms although this lessened during the pandemic. Another striking result is the increased weighted percentage for severe depressive symptoms for women with gynecological cancer. 8.04% vs 3% in 2019 and 8.03% vs 5.78% in 2020 was obtained for women with gynecological cancer when compared to women with other cancer types.

Table 3: OR Comparing Different Levels of Depressive Symptoms Among Women with Gynecological Cancer and Women with Other Cancer Types.

	2019 (Pre-Pandemic)		2020 (Pandemic)	
	OR (95% CI)	adj OR (95% CI)	OR (95% CI)	adj OR (95% CI)
None/Minimal	-	-	-	-
Mild	1.32 (0.94 - 1.85)	1.13 (0.79 - 1.61)	1.59 (1.02 - 2.48)	1.35 (0.84 - 2.16)
Moderate	1.52 (0.92 - 2.5)	0.9 (0.48 - 1.68)	2.19 (1.35 - 3.57)	1.96 (1.16 - 3.29)
Severe	2.89 (1.64 - 5.12)	1.93 (1.01 - 3.71)	1.62 (0.95 - 2.74)	1.28 (0.73 - 2.22)

N/B: Women with other cancer type are the reference group.
OR: Odds ratio, CI: Confidence Interval, adj: Adjusted

Figure C-D: Forest Plots Illustrating OR with 95%CI of Various Levels of Depressive Symptoms Comparing Women with Gynecological Cancer vs Other Cancer type in 2019 and 2020 respectively.



Key: 0 – none/minimal depressive symptoms, 1 – mild depressive symptoms, 2 – moderate depressive symptoms, 3 – severe depressive symptoms

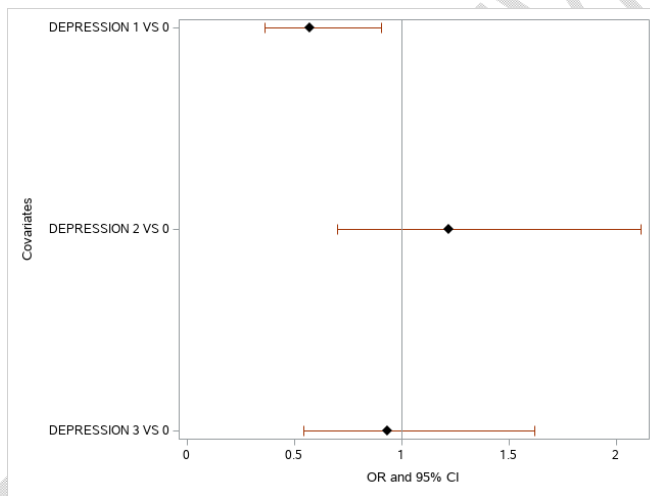
Table 3 illustrates the logistic regression model built for four categories of depressive symptoms for people in the cohort. The 'None/Minimal' group was used as the reference group. Also, comparison was made between women with GC vs women with other cancer types(reference group). In 2019, Mild depressive symptoms were consistent with an OR of 1.32 (95% CI of 0.94 -1.85), Moderate depressive symptoms were consistent with an OR of 1.52 (95% CI of 0.92 – 2.5), Severe depressive symptoms were seen to be strongly associated with women who have GC with an OR of 2.89 (95% CI of 1.64-5.12). In 2020, Mild depressive symptoms were consistent with an OR of 1.59 (95% CI of 1.02 -2.48), Moderate depressive symptoms were seen to be strongly associated with women who have GC with an OR of 2.19 (95% CI of 1.35 – 3.57), Severe depressive symptoms were consistent with an OR of 1.62 (95% CI of 0.95-2.74). Figure C and D illustrates the point estimates of the odds ratios including the upper and lower limits at different levels of depressive symptoms.

Table 4: OR Comparing Different Levels of Depressive Symptoms Among Women with Gynecological Cancer in 2020 vs 2019.

	2020 vs 2019	
	OR (95% CI)	adj OR (95%CI)
None/Minimal	-	-
Mild	0.57 (0.36 - 0.91)	0.56 (0.35 - 0.89)
Moderate	1.22 (0.7 - 2.12)	1.15 (0.67 - 1.97)
Severe	0.94 (0.54 - 1.62)	0.87 (0.5 - 1.51)

Key: Global reference group was 2019. Internal reference group was none/minimal depressive symptoms.
OR: Odds ratio, CI: Confidence Interval, adj: Adjusted

Figure E: Forest Plot Illustrating OR with 95% CI of Various Levels of Depressive Symptoms Comparing Women with Gynecological Cancer in 2020 vs 2019



Key: 0 – none/minimal depressive symptoms, 1 – mild depressive symptoms, 2 – moderate depressive symptoms, 3 – severe depressive symptoms

Table 4 compared depressive symptoms in 2019 and 2020 for only women in the cohort who had GC. The reference group are women who were categorized as having ‘None/Minimal’ symptoms based on the PHQ-8 guideline. Also, 2019 was used as the global reference group. The result obtained showed that women with GC were less likely to show mild depressive symptoms in 2020 than in 2019 with an OR of 0.57 (0.36 – 0.91). moderate depressive symptoms were consistent with an OR of 1.22 (0.7 – 2.12), severe depressive symptoms were consistent with an OR of 0.94 (0.54 – 1.62). Sensitivity analysis was done by adjusting for potential confounders in the cohort selected. Figure E was also essential to graphically illustrate the point estimates of the odds ratios at various levels of depressive symptoms including the upper and lower limits.

Comment [DE4]: Statistician to please check are the results explained according to objective

Discussion

This retrospective cross-sectional study used NHIS data for two distinct year periods: 2019 (pre-pandemic) and 2020 (pandemic) period to assess depressive symptoms among women who have GC compared to women who have other cancer types. This study also compared depressive symptoms among women with GC in 2020 vs 2019. In this study, GC refers to women who have at least one diagnosis of cervical, uterine, and ovarian cancer.

From our baseline statistics, we compared women with GC versus women with other cancer types. In 2019, the weighted proportion for GC survivors tilted towards people who are 46-65 years but in 2020, most of the study population were >65 years. The age distribution is in accordance with the statistics presented by the CDC on prevalence of GC²⁶. Also, there was a statistically significant difference between the age distribution of women in the population who have GC versus other cancer types this is similar to a previous study conducted with NHIS data³⁶. Most women across both study period was partnered and in 2020, women with other cancer types tend to have partners than women with GC. Previous studies have attributed this to decreased sexual functions, body dysmorphism and lesser social functioning due to chemotherapy and radiotherapy²⁷. Women across both study population tend to have less than a bachelor's degree. However, the impact of lesser education tends to tilt towards women with GC. There was a strong correlation between lesser education and income group of women in the cohort. An outcome consistent with a previous study²⁸. Women with GC tend to have lesser income than women with other cancer types. 4 out of 5 women in this study are non-hispanic white women. This is uniform across cancer type and study period. Most women in the cohort reported having good or better health status. However, women with GC tend to report having bad or worse health status similar to this web based study by Shirali et al.²⁹. Body Mass Index of women in this cohort explains that they were mostly not obese. However, in comparison to women with other cancer types, women with GC tend to be more obese¹⁷³⁰. Women with GC tend to be smokers than women with other cancer types despite smoking being a prevalent risk factor across people diagnosed with cancer^{31 36}. Although most women in this cohort tend to have more private insurance, there was no statistically significance difference between the insurance type utilized by women with GC versus women with other cancer types.

From past literatures, certain conditions have been found to be associated with depression²¹²²²³³². We selected a few to find out if there was any difference between GC and other cancer types. Hypertension wasn't statistically different between both groups. However, less people in the study population have been diagnosed with it. Also, most people in the study population have never had a diagnosis of diabetes. Fewer women reported having arthritis, chronic pain, and difficulty with mobility. Also, a very small number, about 1:20 reported having stroke. We only got data for those who have had hysterectomy in 2019. It is not surprising to see that a significant number of women with GC have had hysterectomy and this number was two times more than women with other cancer types. In 2020, we discovered that only about 2% of women with GC and other cancer types reported testing positive to COVID-19. We also found out that a significant number also reported having access to care during the COVID-19 pandemic. This result is surprising because previous studies shows that there was a decline in access to care for cancer patients during COVID-19 pandemic leading to increased mortality³³³⁴.

We sought to understand the likelihood of having different hierarchies of depressive symptoms given when a patient report having GC versus when a patient report having other cancer types (reference group). To do this, a logistic regression model was built. None/minimal depressive symptom used as the reference group. Women with GC were seen to have more likelihood of having mild, moderate, and severe depressive symptoms when compared to women with other cancer types. In 2019, women with GC were seen to be more likely to have severe depressive symptoms ranging from an odds ratio of 1.64 to 5.12. In 2020, moderate depressive symptoms were the most statistically significant depressive symptom. Ranging from an odds ratio of 1.35-3.57. In 2019, a sensitivity analysis was done by adjusting for age, educational status, smoking and if the woman has undergone a hysterectomy. In 2020, depressive symptoms were adjusted for age, educational status, and smoking. The odds ratios obtained were comparable to the initial values. However, a narrower confidence interval was obtained.

The second aim of this study was to compare depressive symptoms in 2020 versus 2019 among women who reported having a diagnosis of GC. The logistic regression model built had 2019 as the global reference group. None/minimal depressive symptoms was used as the reference group for the other depressive symptoms. Based on our result, In 2020, women with GC were less likely to have mild depressive symptoms when compared to the women in 2019. This result was surprising given the expectation of the pandemic to have influenced depressive symptoms. Conversely, In 2020, women with GC were more likely to have moderate depressive symptoms but this result wasn't statistically significant.

Clinical Implications of this Study

This study demonstrates that gynecological cancer patients are more likely to have severe depressive symptoms than women with other cancer types and by extension, the larger population of healthy women. Measures should be taken to include mental health evaluation as part of therapy for women diagnosed with gynecological cancers. They should also be monitored over time to ensure adherence to medications and eventual remission of depressive symptoms.

Comment [DE5]: COVID?

Strengths

Some strength of this study lies on the fact that we utilized the NHIS (National Health Interview Survey) data which is the principal source of information on the health of civilian noninstitutionalized population in the United States. Secondly, weighting the sample makes it more nationally representative and closely captures many demographic and socioeconomic characteristics of women living with cancer³⁵. Also, this study sets a precedent on comparison of depressive symptoms gynecological cancer survivors versus women with other cancer types before and during the widespread COVID-19 pandemic. This research is highly scalable and can be built upon.

Limitations

Despite trying to minimize bias in this study, we still had limitations. The most important being that hysterectomy was not accounted for in the 2020 data. It is our belief that this might have affected our sensitivity analysis for 2020. Also, the pattern of coding for depressive symptoms in 2020 was different from 2019. Thirdly, data for this study were largely obtained via patient-reported questionnaire. This is subject to non-response and reporting bias. Also, the style of reporting may

also be biased. However, there is some agreement between patient-reported questionnaires and medical records according to Rosenman et al³⁷. lastly, due to the seemingly short time for survival in gynecological cancer patients³⁸ and the fact that minority groups are less likely to seek medical help due to being uninsured³⁹, the population-based survey may have underestimated the prevalence.

Conclusion

This study showed that women with gynecological cancer were more likely to exhibit depressive symptoms when compared to women diagnosed with other cancer type. By extension, this means that they are more likely to be depressed than the healthy population. As such, more programs should be set up to evaluate the mental health of women living with gynecological cancer. They should also get support that could alleviate their depressive symptoms to improve their health outcomes and overall quality of life.

Comment [DE 6]: Title objective and conclusion need to be in line please

Ethical Approval

The data utilized is deidentified and publicly available to researchers. As such, it is exempted from an IRB review.

References

1. Mitchell, A. J., Chan, M., Bhatti, H., Halton, M., Grassi, L., Johansen, C., & Meader, N. (2011). Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: A meta-analysis of 94 interview-based studies. *The Lancet Oncology*, *12*(2), 160–174. [https://doi.org/10.1016/s1470-2045\(11\)70002-x](https://doi.org/10.1016/s1470-2045(11)70002-x)
2. Piquart, M., & Duberstein, P. R. (2010). Depression and cancer mortality: A meta-analysis. *Psychological Medicine*, *40*(11), 1797–1810. <https://doi.org/10.1017/s0033291709992285>
3. Sotelo, J. L., Musselman, D., & Nemeroff, C. (2014). The biology of depression in cancer and the relationship between depression and cancer progression. *International Review of Psychiatry*, *26*(1), 16–30. <https://doi.org/10.3109/09540261.2013.875891>
4. Krebber, A. M., Buffart, L. M., Kleijn, G., Riepma, I. C., Bree, R., Leemans, C. R., Becker, A., Brug, J., Straten, A., Cuijpers, P., & Verdonck-de Leeuw, I. M. (2013). Prevalence of depression in cancer patients: A meta-analysis of diagnostic interviews and self-report instruments. *Psycho-Oncology*, *23*(2), 121–130. <https://doi.org/10.1002/pon.3409>
5. Walker, J., Waters, R. A., Murray, G., Swanson, H., Hibberd, C. J., Rush, R. W., Storey, D. J., Strong, V. A., Fallon, M. T., Wall, L. R., & Sharpe, M. (2008). Better Off Dead: Suicidal Thoughts in Cancer Patients. *Journal of Clinical Oncology*, *26*(29), 4725–4730. <https://doi.org/10.1200/jco.2007.11.8844>
6. Krebber, A. M., Buffart, L. M., Kleijn, G., Riepma, I. C., Bree, R., Leemans, C. R., Becker, A., Brug, J., Straten, A., Cuijpers, P., & Verdonck-de Leeuw, I. M. (2013). Prevalence of depression in cancer patients: A meta-analysis of diagnostic interviews and self-report instruments. *Psycho-Oncology*, *23*(2), 121–130. <https://doi.org/10.1002/pon.3409>
7. Satin, J. R., Linden, W., & Phillips, M. J. (2009). Depression as a predictor of disease progression and mortality in cancer patients. *Cancer*, *115*(22), 5349–5361. <https://doi.org/10.1002/cncr.24561>
8. Klapheke, A. K., Keegan, T. H. M., Ruskin, R., & Cress, R. D. (2020). Depressive symptoms and health-related quality of life in older women with gynecologic cancers. *Journal of Geriatric Oncology*, *11*(5), 820–827. <https://doi.org/10.1016/j.jgo.2019.10.001>
9. Harnod, T., Chen, W., Wang, J.-H., Lin, S.-Z., & Ding, D.-C. (2018). Hysterectomies are associated with an increased risk of depression: A population-based Cohort Study. *Journal of Clinical Medicine*, *7*(10), 366. <https://doi.org/10.3390/jcm7100366>
10. Wilson L., Pandeya N., Byles J., Mishra G. Hysterectomy and incidence of depressive symptoms in midlife women: The Australian Longitudinal Study on Women's Health. *Epidemiol. Psychiatr. Sci.* 2017;1–12. doi: 10.1017/S2045796016001220.
11. Centers for Disease Control and Prevention. (2022, February 8). NHIS - 2021 NHIS. Centers for Disease Control and Prevention. Retrieved August 6, 2022, from <https://www.cdc.gov/nchs/nhis/2021nhis.htm>
12. Stordal, E., Mykletun, A., & Dahl, A. A. (2003). The association between age and depression in the general population: A multivariate examination. *Acta Psychiatrica Scandinavica*, *107*(2), 132–141. <https://doi.org/10.1034/j.1600-0447.2003.02056.x>
13. Gong, T.-T., Wu, Q.-J., Vogtmann, E., Lin, B., & Wang, Y.-L. (2012). Age at menarche and risk of ovarian cancer: A meta-analysis of epidemiological studies. *International Journal of Cancer*, *132*(12), 2894–2900. <https://doi.org/10.1002/ijc.27952>
14. Marital satisfaction and marital status as a protective factor of depression and anxiety. (2017). *REVISTA ARGENTINA DE CLINICA PSICOLOGICA*. <https://doi.org/10.24205/03276716.2017.1008>

15. Lorant, V., Croux, C., Weich, S., Deliège, D., Mackenbach, J., & Anseau, M. (2007). Depression and socio-economic risk factors: 7-year longitudinal population study. *British Journal of Psychiatry*, 190(4), 293–298. <https://doi.org/10.1192/bjp.bp.105.020040>
16. Zare, H., Meyerson, N. S., Nwankwo, C. A., & Thorpe, R. J. (2022). How income and income inequality drive depressive symptoms in U.S. adults, does sex matter: 2005–2016. *International Journal of Environmental Research and Public Health*, 19(10), 6227. <https://doi.org/10.3390/ijerph19106227>
17. Polanka, B. M., Vransy, E. A., Patel, J., & Stewart, J. C. (2017). Depressive disorder subtypes as predictors of incident obesity in US adults: Moderation by race/ethnicity. *American Journal of Epidemiology*, 185(9), 734–742. <https://doi.org/10.1093/aje/kwx030>
18. Erving, C. L., & Frazier, C. (2021). The association between multiple chronic conditions and depressive symptoms: Intersectional distinctions by race, nativity, and gender. *Journal of Health and Social Behavior*, 62(4), 599–617. <https://doi.org/10.1177/00221465211040174>
19. Eitle, D., & Eitle, T. M. N. (2018). Obesity, overweightness, and depressive symptomology among American Indian Youth. *Journal of Racial and Ethnic Health Disparities*, 5(6), 1305–1314. <https://doi.org/10.1007/s40615-018-0479-9>
20. Byeon, H. (2015). Association among smoking, depression, and anxiety: Findings from a representative sample of Korean adolescents. *PeerJ*, 3. <https://doi.org/10.7717/peerj.1288>
21. Kang, H.-J., Kim, S.-Y., Bae, K.-Y., Kim, S.-W., Shin, I.-S., Yoon, J.-S., & Kim, J.-M. (2015). Comorbidity of depression with physical disorders: Research and clinical implications. *Chonnam Medical Journal*, 51(1), 8. <https://doi.org/10.4068/cmj.2015.51.1.8>
22. Smith, E., & Kneebone, I. (2016). Assessment and psychological interventions for depression comorbid with cardiovascular disease. *Cardiovascular Diseases and Depression*, 351–364. https://doi.org/10.1007/978-3-319-32480-7_20
23. Whooley, M. A. (2012). Diagnosis and treatment of depression in adults with comorbid medical conditions. *JAMA*, 307(17), 1848. <https://doi.org/10.1001/jama.2012.3466>
24. Kroenke, K., Strine, T. W., Spitzer, R. L., Williams, J. B. W., Berry, J. T., & Mokdad, A. H. (2009). The PHQ-8 as a measure of current depression in the general population. *Journal of Affective Disorders*, 114(1-3), 163–173. <https://doi.org/10.1016/j.jad.2008.06.026>
25. Dhingra, S. S., Kroenke, K., Zack, M. M., Strine, T. W., & Balluz, L. S. (2011). PHQ-8 Days: A measurement option for DSM-5 Major Depressive Disorder (MDD) severity. *Population Health Metrics*, 9(1). <https://doi.org/10.1186/1478-7954-9-11>
26. Centers for Disease Control and Prevention. (2019, September 13). Gynecologic cancer incidence, United States-2012–2016. Centers for Disease Control and Prevention. Retrieved August 7, 2022, from [https://www.cdc.gov/cancer/uscs/about/data-briefs/no11-gynecologic-cancer-incidence-UnitedStates-2012-2016.htm#:~:text=The%20most%20common%20gynecologic%20cancer,women%20\(9.60%20per%20100%2C000\).](https://www.cdc.gov/cancer/uscs/about/data-briefs/no11-gynecologic-cancer-incidence-UnitedStates-2012-2016.htm#:~:text=The%20most%20common%20gynecologic%20cancer,women%20(9.60%20per%20100%2C000).)
27. Iżycki, D., Woźniak, K., & Iżycka, N. (2016). Consequences of gynecological cancer in patients and their partners from the sexual and psychological perspective. *Menopausal Review*, 2, 112–116. <https://doi.org/10.5114/pm.2016.61194>
28. The time and timing of work: Unique challenges facing low-income families. (2014). *Work-Family Challenges for Low-Income Parents and Their Children*, 119–128. <https://doi.org/10.4324/9781410609755-13>
29. Shirali, E., Yarandi, F., Ghaemi, M., & Montazeri, A. (2020). Quality of life in patients with gynecological cancers: A web-based study. *Asian Pacific Journal of Cancer Prevention*, 21(7), 1969–1975. <https://doi.org/10.31557/apjcp.2020.21.7.1969>

30. Wichmann, I. A., & Cuello, M. A. (2021). Obesity and gynecological cancers: A toxic relationship. *International Journal of Gynecology & Obstetrics*, 155(S1), 123–134. <https://doi.org/10.1002/ijgo.13870>
31. Jacob, L., Freyn, M., Kalder, M., Dinas, K., & Kostev, K. (2018). Impact of tobacco smoking on the risk of developing 25 different cancers in the UK: A retrospective study of 422,010 patients followed for up to 30 Years. *Oncotarget*, 9(25), 17420–17429. <https://doi.org/10.18632/oncotarget.24724>
32. Rubio-Guerra, A. F., Rodriguez-Lopez, L., Vargas-Ayala, G., Huerta-Ramirez, S., Serna, D. C., & Lozano-Nuevo, J. J. (2013). Depression increases the risk for uncontrolled hypertension. *Experimental and clinical cardiology*, 18(1), 10–12.
33. Thomson, C. A., Overholser, L. S., Hébert, J. R., Risendal, B. C., Morrato, E. H., & Wheeler, S. B. (2021). Addressing cancer survivorship care under covid-19: Perspectives from the cancer prevention and control research network. *American Journal of Preventive Medicine*, 60(5), 732–736. <https://doi.org/10.1016/j.amepre.2020.12.007>
34. Nekhlyudov, L., Duijts, S., Hudson, S. V., Jones, J. M., Keogh, J., Love, B., Lustberg, M., Smith, K. C., Tevaarwerk, A., Yu, X., & Feuerstein, M. (2020). Addressing the needs of cancer survivors during the COVID-19 pandemic. *Journal of Cancer Survivorship*, 14(5), 601–606. <https://doi.org/10.1007/s11764-020-00884-w>
35. Bell, B. A., Onwuegbuzie, A. J., Ferron, J. M., Jiao, Q. G., Hibbard, S. T., & Kromrey, J. D. (2012). Use of design effects and sample weights in complex health survey data: A review of published articles using data from 3 commonly used adolescent health surveys. *American Journal of Public Health*, 102(7), 1399–1405. <https://doi.org/10.2105/ajph.2011.300398>
36. Okoye, G., H. Antwi, K. C. Ben-Umeh, and R. Vincent. “Comparison of Healthcare Resource Utilization (HcRU) Between Age Groups of Women Diagnosed With Gynecological Cancers in the United States”. *International Journal of Research and Reports in Gynaecology*, Vol. 5, no. 3, Aug. 2022, pp. 106-14, <https://journalijrrgy.com/index.php/IJRRGY/article/view/67>.
37. Rosenman, R., Tennekoon, V., & Hill, L. G. (2011). Measuring bias in self-reported data. *International Journal of Behavioural and Healthcare Research*, 2(4), 320. <https://doi.org/10.1504/ijbhr.2011.043414>
38. Sehouli, J., Chekerov, R., Keller, M., Oskay-Oezcelik, G., Braicu, E. I., & Richter, R. (2018). The impact of health related quality of life (hrqol) on short term survival of recurrent ovarian cancer patients: Analysis of pooled data from the north-eastern German Society of Gynecological Oncology (NOGGO) meta data base. *Journal of Clinical Oncology*, 36(15_suppl), 5539–5539. https://doi.org/10.1200/jco.2018.36.15_suppl.5539
39. Collins, Y., Holcomb, K., Chapman-Davis, E., Khabele, D., & Farley, J. H. (2014). Gynecologic cancer disparities: A report from the Health Disparities Taskforce of the Society of Gynecologic Oncology. *Gynecologic Oncology*, 133(2), 353–361. <https://doi.org/10.1016/j.ygyno.2013.12.039>
40. Gallagher, S., Bennett, K. M., & Roper, L. (2021). Loneliness and depression in patients with cancer during COVID-19. *Journal of psychosocial oncology*, 39(3), 445–451. <https://doi.org/10.1080/07347332.2020.1853653>

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