Quantifying the impact of the COVID-19 pandemic on cancer screenings and diagnoses

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Abstract (150/150 words)

COVID-19 impacted hospital systems across the globe. Focus shifted to responding to increased healthcare demand while mitigating COVID-19 spread on their campuses. Mitigation efforts limited medical professional-patient interactions, including patient access to preventive cancer screenings. This study tested five hypotheses: H_1: Cancer screenings significantly decreased during North Carolina's (NC) Stay-At-Home (SAH) orders; H_2: Cancer diagnoses significantly decreased during NC's SAH orders; H_3: Cancer screenings significantly increased after the end of NC's SAH orders; H_4: Cancer diagnoses significantly increased after the end of NC's SAH orders; and H_5: Advanced cancer diagnoses significantly increased after the end of NC's stay-at-home orders. Time series regression analysis was employed to quantify trends. Results suggested strong support of H_1 and H_3, moderate support of H_4, mixed support of H_5, and no support of H_2. Implications of employing robust statistical methods to quantify trends in screenings or diagnoses during periods of health system disruption are discussed.

Keywords: COVID-19; cancer; screening; diagnosis; time series analysis

1. Introduction

The coronavirus 2019 (COVID-19) pandemic influenced all aspects of life beginning in early 2020 with the world's hospital systems at the forefront (1). Nearly immediately, hospitals around the world were required to shift focus, control the numbers of individuals on campuses, and limit interactions between medical professionals and patients (1). In an effort to minimize interactions, one of the major changes in focus involved delaying and limiting elective procedures, including cancer screenings (2). Individuals considered low risk and with a record of normal screenings were recommended to delay screenings for three regularly screened cancers: breast, cervical, and colorectal (2).

Whereas several reports suggest a decrease in screenings during state-issued stay-at-home (SAH) orders, none have employed robust statistical methods to quantify the trends in screenings or diagnoses (3–5). Understanding the impact of COVID-19 on routine cancer screenings and diagnoses is crucial to preparing for the potential short-term implications of this disruption and for improving health care system resilience to avoid such disruptions in the future.

Given the pressures to reduce interactions and limit elective procedures, we anticipate significant disruption in the rates of cancer screenings and diagnoses. We expect to observe reductions in screenings and diagnoses during state-imposed SAH orders, followed by a “catch-up” period with greater than typical cancer screenings and diagnoses after those orders ended. We also expect that the delay in screenings will lead to higher-than-normal levels of advanced cases of cancer during the “catch-up” period. This study tests the following hypotheses:

> *H_1: Cancer screenings significantly decreased during North Carolina’s SAH orders.*
>
> *H_2: Cancer diagnoses significantly decreased during North Carolina’s SAH orders.*
>
> *H_3: Cancer screenings significantly increased after the end of North Carolina’s SAH orders.*

H_4: Cancer diagnoses significantly increased after the end of North Carolina's SAH orders.

H_5: Advanced cancer diagnoses significantly increased after the end of North Carolina's SAH orders.

Time series regression analysis was employed to examine these hypotheses in the following cancers: breast (ICD9: 174, 233, ICD10: C50, D50, Z12.31, Z12.39), cervical (ICD9: 180.0, 180.1, 180.8, 180.9, 233.1; ICD10: C53.0, C53.1, C53.8, C53.9, D06.0, D06.1. D06.7, D06.9, V76.2, Z12.4), colorectal (ICD9: 152-154.9; ICD10: C17-C21.9, Z12.11), leukemia (ICD9: 203.1, 204.00-208.92 but not remissions; ICD10: C91.1, C92.00-C95.90 but not remissions, V76.89, Z12.89), lung and bronchus (ICD9: 162; ICD10: C7A.090, C34, Z212.2 and G0297), and prostate (ICD9: 185, 233.4, 236.5; ICD10: C61, D07.5, V76.44, Z12.5). These cancers were selected for their range in screening regimen, etiology, rarity, and risk factors (6). Data were gleaned from a health information exchange containing records on over 2 million patients in our region. Personal medical records were aggregated and modeled as weekly counts of specific cancer screenings or diagnoses. The relationships between those counts and the following variables were then assessed: an indicator if the week contained a holiday, the number of new patient IDs in the database, and North Carolina state issued stay-at-home orders.

2. Materials and Methods

2.1. Data

Electronic health record data were extracted and compiled from a health information exchange. We limited our sample to records from 2019 and 2020; 2019 records were used to establish a baseline and reference for examining the 2020 data. These data mostly cover the southeastern region of North Carolina.

2.1.1. Obtaining Cancer Outcomes

Entries of cancer screenings or diagnoses were identified by searching for the appropriate ICD9 and ICD10 encounter codes. We used the date associated with each record to determine a weekly count of screenings and diagnoses for each type of cancer. Advanced cases of cancer were identified by searching for codes indicating lymph node involvement or secondary neoplasms (ICD9: 190-199, ICD10: C76-C80) among individuals with one of the cancers of interest. Cases that had lymph node involvement or a secondary neoplasm indicated a stage II-IV diagnosis, thus their cancer diagnoses were coded advanced in our data (7).

2.1.2. Independent Variables

Several independent, time series variables were constructed for model fitting purposes. The main variable of interest involved the North Carolina state issued SAH orders. The mandate initiated on March 30, 2020 and the phased reopening began on May 7, 2020 (8). The variable created to represent this mandate was categorical and coded to indicate whether each week in our data fell before, during, or after the shutdown time frame. As constructed, the variable allowed us to quantify the effects of SAH orders on changes in screenings and diagnoses. Additional variables used for adjustment comprised an indicator for whether the week included a holiday (which would presumably reduce the rate of patient screenings and diagnoses) and the number of new patient IDs in the database (to control for increases in the number of patients in our sample).

2.2. Statistical Methods

Time series regression is a powerful statistical tool for examining relationships between a time-dependent outcome and one or more independent time series variables. A time series regression model is written as follows for temporal unit $t = 1, \ldots, T$:

$$y_t = \beta_0 + \beta_1 x_{1t} + \beta_2 x_{2t} + \cdots + \beta_k x_{kt} + \epsilon_t$$

where y_t is the time series outcome, β_0 is the intercept, $\beta_1, \beta_2, \ldots, \beta_k$ are the parameter estimates associated with independent time series variables $x_{1t}, x_{2t}, \ldots, x_{kt}$, and ϵ_t is the random error term. Time series regression was performed using R statistical software and the R package forecast (9–11).

3. Results

Table 1 presents the counts for screenings, diagnoses, and advanced case diagnoses associated with each cancer. As expected, breast, cervical, colorectal, and prostate had the highest rates of screenings. Incidence of lung cancer was lower than expected and not in the same range as prostate cancer, as national statistics suggest (6). The percent of diagnosed cases indicated as advanced differed in reliability across cancers. For example, the American Cancer Society reports roughly 27% and 6% of breast cancer cases as regional (i.e., cancer spread to nearby lymph nodes) or distant (i.e., cancer spread to distant parts) and we determined 33.5% of ours in those categories (6). However, the American Cancer Society reports roughly 35% and 21% of colorectal cancer cases as regional or distant and we determined only 28.2% from our data (6).

Table 1: Total counts of cancer screenings and diagnoses as well as percent of diagnoses considered advanced

Cancer	Screenings	New Diagnoses	Advanced Cases	Percent Advanced
Breast	101774	5154	1726	33.5
Cervical	10305	3010	297	9.9
Colorectal	28260	2515	709	28.2
Leukemia	25	3094	359	11.6
Lung and bronchus	1193	3018	1324	43.9
Prostate	7572	5301	797	15.0

Figure 1 displays the time series for cancer specific screenings across all cancers considered. The vertical lines in all plots indicate the period when North Carolina was under full SAH orders (March 30, 2020 – May 7, 2020). Figures for new diagnoses and advanced cases can be found in the supplement. The plots in Figure 1 show a clear decrease in screenings and diagnoses across all cancers, particularly for regularly screened cancers (breast, cervical, colorectal, and prostate). Other trends indicate: a potential “catch up” period after the SAH orders that commenced around week 90 (mid-September), a sharp drop at the turn of the new year (the last week in 2019 had 3 days – Sunday December 29, a single work day of Monday December 30, and New Year’s Eve on December 31), and a general increase in screenings over time. As expected, leukemia’s plot is different from the others given the relative infrequency for which it is screened. Supplemental Figures 1 and 2 display cancer diagnoses and advanced case diagnoses over time.

[Figure 1 here]

Figure 1: Cancer screenings over time and by cancer: A) breast cancer, B) cervical cancer, C) colorectal cancer, D) leukemia, E) lung cancer, and F) prostate cancer. The

vertical lines in all plots indicate the period when North Carolina was under full SAH orders (March 30, 2020 – May 7, 2020 or weeks 66-72).

Table 2 includes time series regression results across models and cancers considered. A negative estimate indicates fewer screenings, diagnoses, or advanced case diagnoses during weeks with the given characteristic. Alternatively, a positive estimate indicates more screenings, diagnoses, or advanced case diagnoses during weeks with the given characteristic. Using breast cancer screenings and the SAH orders variable as an example, we observed an average of 662.3 fewer during and 232.5 more after the SAH orders than before the SAH orders were initiated. H_1 was mostly supported as four of the six observed cancers screenings significantly decreased during SAH orders. The null results for leukemia were expected given the relative infrequency for which it is screened. Despite the significant decline in screenings, cancer diagnoses did not significantly decline suggesting H_2 is not supported.

The positive value for the after SAH orders category could represent a “catch up” period, and we observed that trend with breast, cervical, colorectal, lung and bronchus, and prostate cancer screenings as well as breast, cervical, and leukemia diagnoses. These findings indicate that H_3 is mostly supported with cancer screenings increasingly significantly in five of the six observed cancers. H_4 is partially supported as cancer diagnoses increased significantly in three of the six observed cancers but decreased significantly for colorectal diagnoses. We hypothesized that advanced cancer diagnoses would also significantly increase after the end of SAH orders (H_5), but those results are mixed with only three achieving statistical significance. Two of the six observed cancers – cervical and leukemia – had significantly higher rates of advanced diagnoses, while advanced colorectal cancer diagnoses were significantly lower.

Finally, the control variables performed as expected. The holiday variable is negative and significant for breast, cervical, colorectal, lung and bronchus, and prostate cancer screenings, as well as for cervical cancer diagnoses, suggesting fewer observations for weeks with holidays compared to weeks without holidays. The new patient IDs variable was positive and significant for most categories, suggesting as one would expect that having more patients in the dataset increased screenings, total diagnoses, and advanced diagnoses.

Table 2: Time series regression results for screenings, diagnoses, and advanced cases by cancer

	Breast			Cervical			Colorectal		
Model	Screenings	Diagnoses	Advanced	Screenings	Diagnoses	Advanced	Screenings	Diagnoses	Advanced
New Patient IDs	0.02***	0.01***	0.004***	0.002**	0.002***	0.001***	0.01***	0.004***	0.001***
Holiday									
No (Ref)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Yes	-245.6***	-0.3	1.1	-38.2***	-5.5*	-0.3	-87.8***	-1.5	0.7
Stay Home									
Before (Ref)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
During	-662.3***	0.8	3.3	-45.3**	-4.0	0.4	-134.2***	-2.9	1.3
After	232.5***	10.6*	3.2	26.6***	7.6**	1.9***	123.1***	-3.7**	-1.9*

	Leukemia			Lung and Bronchus			Prostate		
Model	Screenings	Diagnoses	Advanced	Screenings	Diagnoses	Advanced	Screenings	Diagnoses	Advanced
New Patient IDs	0.001	0.003***	0.001***	0.001***	0.005***	0.003***	0.004***	0.01***	0.002***
Holiday									
No (Ref)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Yes	-0.06	-4.0	-0.8	-2.9*	-1.7	-0.4	-18.7*	-3.8	-0.9
Stay Home									
Before (Ref)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
During	-0.1	-4.1	0.6	-6.2*	1.7	2.1	-2.5	-2.7	2.1
After	-0.01	24.3***	3.8***	5.5***	-1.5	-0.1	80.7***	-1.1	-1.3

Signif. codes: 0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

4. Discussion

This manuscript displays trends in cancer screenings, diagnoses, and advanced case diagnoses for the years 2019 and 2020. The time series plots and statistical model results offer compelling evidence that the COVID-19 pandemic affected cancer screenings, total diagnoses, and advanced case diagnoses. Notably, we observed a decrease in most cancer screenings during North Carolina's SAH orders for nearly all cancers. Additionally, we observed a potential "catch up" in screenings and diagnoses for many of the cancers under observation after the SAH orders were lifted. Not as evident, but still concerning was the uptick in advanced cervical and leukemia diagnoses after the SAH orders were lifted. Together these observations suggest the potential for delayed or missed cancer diagnoses during the pandemic.

Our hypotheses were largely supported; however, three findings raise additional questions for future inquiry. First, cancer diagnoses did not significantly decrease during North Carolina's SAH orders (H_2), suggesting the disruption to screenings was mitigated for at least a portion of the population. It is possible that doctors and patients with higher risk worked together to ensure screenings were conducted, while lower-risk patients less likely to receive a positive diagnosis opted to pass on screenings. Second, the somewhat counterintuitive findings for advanced cancer diagnoses (H_5) may be influenced by disease etiology. Although we are not able to empirically test it here, it is possible that colorectal diagnoses and advanced case diagnoses remained significantly lower after SAH orders because this disease is largely found in older individuals (median diagnosis age of 68 in men and 72 in women (12)). This older group is more vulnerable to COVID-19 and may not have felt comfortable seeking care once SAH orders were lifted and those diagnoses are yet to be made. Conversely, we observed an increase in advanced case diagnoses for cervical cancer, a disease that is most frequently diagnosed in women between the ages of 35 and 44 (13) – a group that may have been willing to venture out to obtain screenings following the end of the SAH orders. Finally, it is too soon to evaluate the impact of this observed decrease in screenings on cancer survival; however, prior research examining cancer mortality following events that caused a delay in screening suggests a reduction in cancer-specific survival (14–17). Future research might consider these possibilities.

These findings also have implications for health system (or organization) resilience to future natural disasters and infectious disease outbreaks. A strong health system is better positioned to respond to and recover from acute shocks without adverse impact to their ability to perform routine functions. In the context of this article, we considered the impact of the COVID-19 pandemic and associated SAH orders on preventive cancer screenings and diagnoses. Employing robust statistical methods to quantify the changes in screenings and diagnoses during periods of system disruption due to disasters may inform strategies that strengthen “health care system capacity and capability needed to respond to emergencies while also maintaining routine services, that, if neglected, could lead to increased morbidity and mortality” (18).

These methods were not without limitation. First, we were only able to include a single year to represent our baseline. Hurricane Florence greatly impacted our region in

September 2018, which distorted “typical” counts in that year. However, our data indicate that this limitation may not be that consequential. The health information exchange from which we sourced our data experienced a large influx of records for the years under study compared to previous years, presumably given the increase in their number of contributing providers. The more apparent limitation pertains to using aggregated electronic health records for scientific inquiry, as previous literature indicates (19,20). For this research, we reduced the noise to the extent possible by ensuring proper encounter codes and dates, using historical records to identify only new diagnoses, and avoiding possible duplicates by focusing on a single patient ID per patient.

There are several directions for future inquiry that can build on this work by applying different models or exploring other outcomes within these or similar data. For example, one could use change point detection modeling to aid in identifying the time when the effect of the SAH orders ended, since North Carolina (and surely other states) experienced a phased reopening (15,16). Revisiting this research question after more time has passed might also lead to a better picture of the relevant “catch up” period and potential implications of this disruption on cancer mortality.

5. Conclusion

This work quantifies the impact of the COVID-19 pandemic on cancer screenings and diagnoses and suggests the potential for delayed or missed cancer diagnoses, particularly during the state-issued SAH orders. This evident disruption in providing routine medical care also highlights the importance of strengthening health systems (or organizations) and improving resilience to natural disasters and infectious disease outbreaks. Although one should exert caution in generalizing findings beyond this region, we suspect other states that issued SAH orders may have experienced similar trends. We urge other researchers to explore these claims in similar and disparate data sets to improve our understanding of how the global pandemic disrupted health care utilization patterns and the potential downstream consequences of those changes.

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Figures

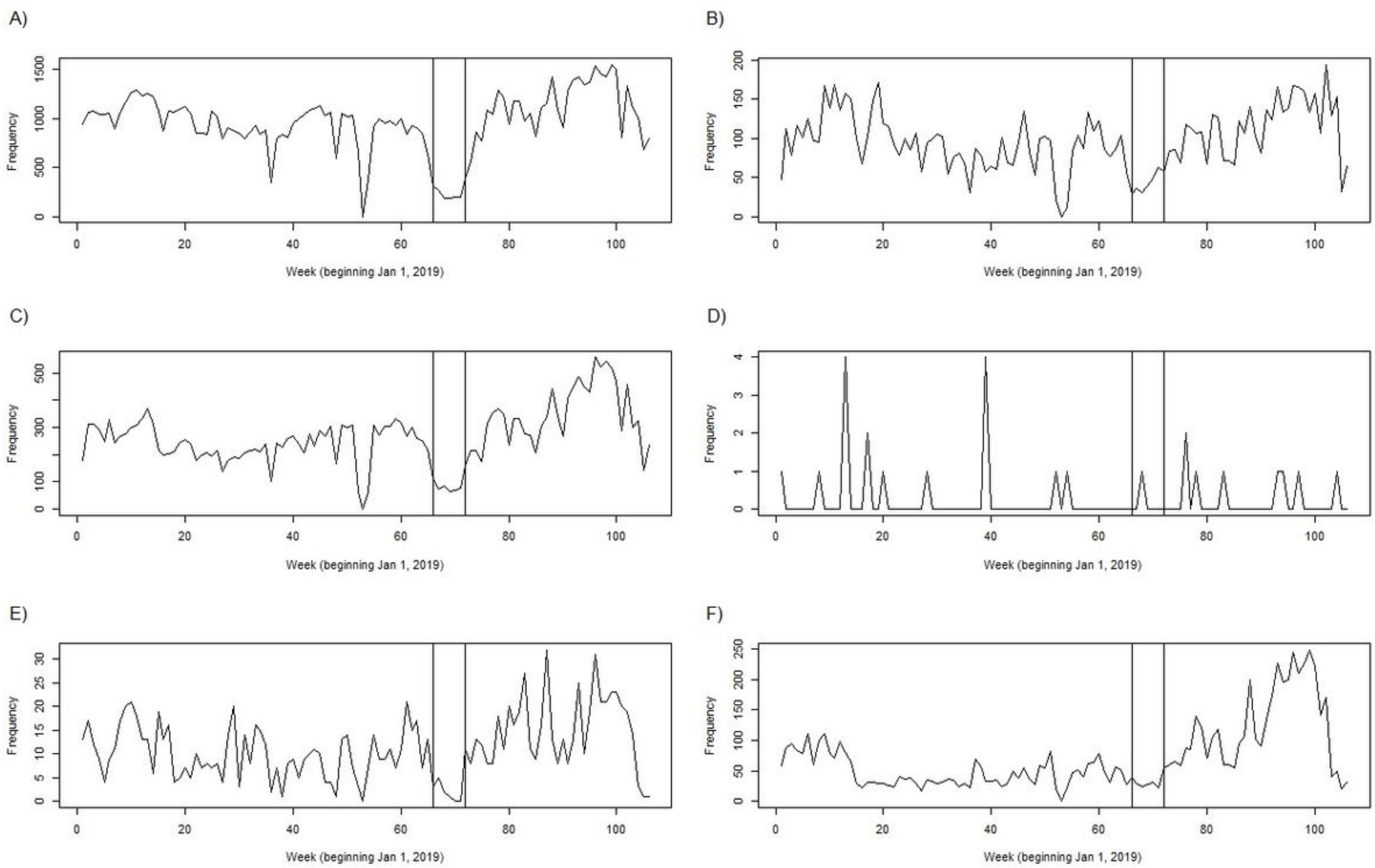

Figure 1

Cancer screenings over time and by cancer: A) breast cancer, B) cervical cancer, C) colorectal cancer, D) leukemia, E) lung cancer, and F) prostate cancer. The vertical lines in all plots indicate the period when North Carolina was under full SAH orders (March 30, 2020 – May 7, 2020 or weeks 66-72).

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