Quantifying the hidden impact of COVID-19 pandemic: The cytology perspective

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BACKGROUND: The burden of the COVID-19 pandemic is often enumerated in lives lost, but the strain on health care resources and mobility limitations contributed to the burden of non–COVID related disease. In this study, we evaluated the impact of the pandemic through a time series review of cytology samples. **METHODS:** Pathology reports for all cytology specimens received from January 2019 through April 2021 at our institution were reviewed. Time series analysis was performed using moving averages, time trend analysis, cross-correlation, and tests of homogeneity. **RESULTS:** During the first peak of the pandemic (March–June 2020), breakpoint analysis showed a downward shift in the number of gynecologic (−89.4%) and non-gynecologic (−70.4%) cytology specimens within a week of declaration of an emergency. Cross-correlation analysis showed a relationship between sample numbers and COVID-19 cases during the initial phase of the pandemic (April–June 2020). During the second surge (October 2020–April 2021), despite the higher incidence of COVID-19, there was a smaller impact on cytology samples (−20.1% and −24.8% for gynecologic and non-gynecologic samples, respectively). During the first 3 months of the pandemic, 154 fewer malignant cases were identified compared with the prior year. Although specimen numbers slowly returned to baseline following the first wave of the pandemic, the earlier decline in malignant diagnoses was not offset during the study period. **CONCLUSIONS:** The deleterious effects of COVID-19 extend beyond direct mortality attributed to the disease. The significant decrease in diagnostic cytology specimens during this period has profound implications including delayed care and missed disease. ***Cancer Cytopathol* 2022;130:824-832**. © *2022 American Cancer Society.*

KEY WORDS: coronavirus disease 2019 (COVID-19); cytopathology; malignancy rate; screening programs; severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

INTRODUCTION

As of the writing of this manuscript, global COVID-19 deaths have exceeded six million.[1,2] Although the burden of the COVID-19 pandemic is often enumerated as lives lost directly to COVID-19, the strain on health care resources and mobility limitations have certainly contributed to the burden of non–COVID related disease. Prior studies have attempted to quantify this impact by comparing all-cause/disease-specific mortality and hospitalization rates to similar time intervals before the pandemic,[3–6] but the excess burden of the pandemic on public health is not limited to the immediate lives lost. The long-term impact of the pandemic may entail an increase in overall mortality, decreased life expectancy, and worsening health care disparities.[7] This is partly caused by reduced capacity of the health care system to deliver timely preventive and screening services to the general population as the focus has shifted toward the unexpected demands of the crisis.[8] The full impact of COVID-19 pandemic is hard to measure and will likely manifest itself in the years to come.

Early in the pandemic, cytology laboratories observed a significant reduction in sample volumes across specimen types attributed to suspension of screening programs, reluctance for in-person health care visits, and concern over the biosafety of procedures for both patients and health care/laboratory workers.[9,10] This reduction

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Received: April 4, 2022; **Revised:** May 16, 2022; **Accepted:** May 31, 2022

Published online June 24, 2022 in Wiley Online Library (wileyonlinelibrary.com)

DOI: 10.1002/cncy.22613, wileyonlinelibrary.com

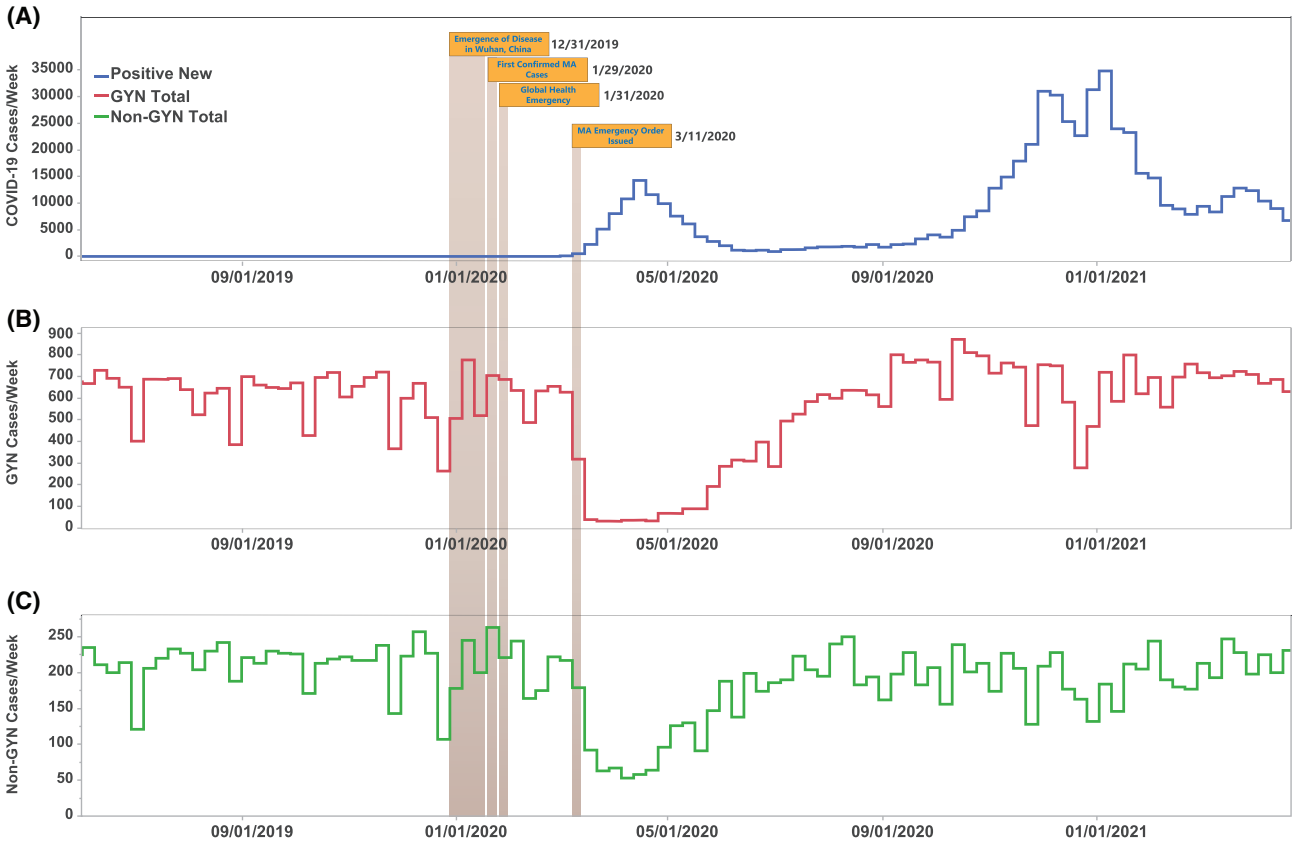

Figure 1. Time-series plots showing (A) the weekly aggregates of new COVID-19 cases in Boston, Massachusetts, and (B) the weekly aggregates of gynecologic and (C) non-gynecologic cytology sample numbers.

was particularly notable with routine Papanicolaou (Pap) test (henceforth GYN) specimens and minimally invasive procedures such as fine-needle aspiration (FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), which were limited to urgent referrals.[9–11] Not surprisingly, the practice of triaging services to patients with a higher preprocedure risk of malignancy resulted in an increase in the overall rate of malignancy in cytology samples.[9–12] The cumulative effect appears to be complex and multifactorial, but concern remains over lingering delays in the diagnosis and treatment of life-threatening malignancies in the general population.[13,14] In this study, we aimed to evaluate the impact of the pandemic on preventive and diagnostic services through a time series review of cytology samples at a single institution.

MATERIALS AND METHODS

Pathology reports for all cytology specimens received from January 2019 through April 2021 at the Brigham and Women's Hospital were reviewed. The data were summarized based on cytology sample type and diagnostic category in daily, weekly, and monthly aggregates. The daily and cumulative reports for Boston, Massachusetts, COVID-19 cases and mortality were extracted from the COVID-19 Interactive Data Dashboard of the Commonwealth of Massachusetts Web site (https://www.mass.gov/info-details/covid-19-response-reporting).

Time series analysis was performed using the "tseries" R package for moving averages, smoothing, and time trend analysis. Testing for homogeneity was performed using the "snht" R package. In this package, the Standard Normal Homogeneity Test (SNHT) is performed on time series data, which searches the data for breakpoints where shifts in values occur. For breakpoint analysis, we set the SNHT to search for periods of 3 weeks' duration, with breakpoint scores of 20 or above considered as significant. Time series visualization was performed using the "ggplot2" R package.

Cross-correlation analysis was performed using the "astsa" R package. In time series analysis, cross-correlation is a measure of similarity between two series as a function of the displacement of one series relative to the other (i.e., cross correlation examines the relationship between two time series).

RESULTS

Effect of COVID-19 pandemic on GYN cytology specimens

Before the pandemic, the average weekly number of GYN cytology specimens at our institution was 634 (over a 1-year period). The average weekly numbers of cases classified as: malignant, high-grade squamous intraepithelial lesion (HSIL), low-grade squamous intraepithelial lesion (LSIL), and atypical squamous cells of uncertain significance (ASCUS) were 0.09, 1.9, 11.8, and 34.1 (over a 1-year-period),r espectively.

During the first peak of the pandemic (March 11, 2020–June 3, 2020), the average weekly GYN cytology volume dropped to 101 (−84.0%, compared with the prior 3-week moving average) (Fig. 1). Breakpoint analysis by SNHT showed a downward shift in the number of weekly accessions occurring during the week of March 4, 2020, whereby a reduction of 89.4% occurred compared with the prior 3-week moving average (Table 1). Accordingly, diagnostic categories including HSIL, LSIL, and ASCUS also showed a marked reduction in the same period (average weekly numbers: 0 [−100%], 1.7 [−90%], and 1 [−95.7%], respectively) (Fig. 2).

Breakpoint analysis showed a return to normal levels after the first peak of the pandemic with phase 1 reopening of the city and resumption of normal health care services (253% increase in volume occurring in the week of May 13, 2020, compared with the prior 3-week moving average). A smaller reduction in volume (−20.1% compared with the prior 3-week moving average) occurred with the second COVID-19 peak (the week of November 4, 2020), corresponding to the issuance of stay-at-home advisory, with this reduction lasting until January 13, 2021, whereby the weekly volume returned to prepandemic levels (Table 1).

Cross-correlation analysis showed a correlation of the reduction in GYN volume with increasing COVID-19 cases during the first peak of the pandemic in Boston, MA, with a zero-week lag (Fig. 3A). This strong correlation was

TABLE 1. Summary of breakpoint analysis

Sample type	BP 1 date	Avg. 3 wk previous BP 1	Avg. 3 wk after BP 1	% Change in avg. BP 1	BP 2 Date	Avg. 3 wk previous BP 2	Avg. 3 wk after BP 2	% Change in avg. BP 2	BP 3 Date	Avg. 3 wk previous BP 3	Avg. 3 wk after BP 3	% Change in avg. BP 3	BP 4 Date	Avg. 3 wk previous BP 4	Avg. 3 wk after BP 4	% Change in avg. BP 4
GYN total	3/4/2020	328	34.7	−89.4	5/13/2020	74.7	263.7	253.0	11/4/2020	825.3	659.3	−20.1	1/13/2021	488.7	704.7	44.2
Non-GYN Total	3/25/2020	206	61	−70.4	5/27/2020	115.7	174	50.4	12/23/2020	204.7	154	−24.8	1/20/2021	154	213	38.3
EBUS-TBNA	3/18/2020	24	6.3	−73.8	6/3/2020	12.3	29	135.8	11/4/2020	36	22	−38.9	N/A		N/A	N/A
Urine	3/11/2020	59	12	−79.7	6/10/2020	33	62.7	90.0	10/7/2020	65.7	49.7	−24.4	1/20/2021	28	53.3	90.4
Thyroid FNA	3/18/2020	22	3	−86.4	5/27/2020	7.7	16.7	116.9	N/A		N/A	N/A	N/A		N/A	N/A
Peritoneal fluid	3/25/2020	28.7	6	−79.1	5/6/2020	8.3	14	68.7	N/A		N/A	N/A	N/A		N/A	N/A
FNA other	3/18/2020	20.7	6.3	−69.6	5/6/2020	9	14.7	63.3	12/23/2020	20.3	12.3	−39.4	1/20/2021	12.3	21.7	76.4
Diagnosis																
Non-GYN: MAL or SUS	3/11/2020	36.3	15	−58.7	4/22/2020	14.3	29.3	104.9	12/23/2020	41	24	−41.5	1/20/2021	29.7	44	48.1
GYN: HSIL	3/11/2020	3.3	0	−100.0	5/13/2020	0.3	2	566.7	N/A		N/A	N/A	N/A		N/A	N/A
GYN: LSIL	3/11/2020	17	1.7	−90.0	5/20/2020	1.7	7	311.8	N/A		N/A	N/A	N/A		N/A	N/A
GYN: ASCUS	3/25/2020	23.3	1	−95.7	6/3/2020	11.7	25	113.7	N/A		N/A	N/A	N/A		N/A	N/A

Abbreviations: ASCUS, atypical squamous cell of uncertain significance; BP, breakpoint; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; FNA, fine-needle aspiration; GYN, gynecologic cytology specimens; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; MAL, malignant; N/A, not applicable; Non-GYN, non-gynecologic cytology specimens; SUS, suspicious for malignancy.

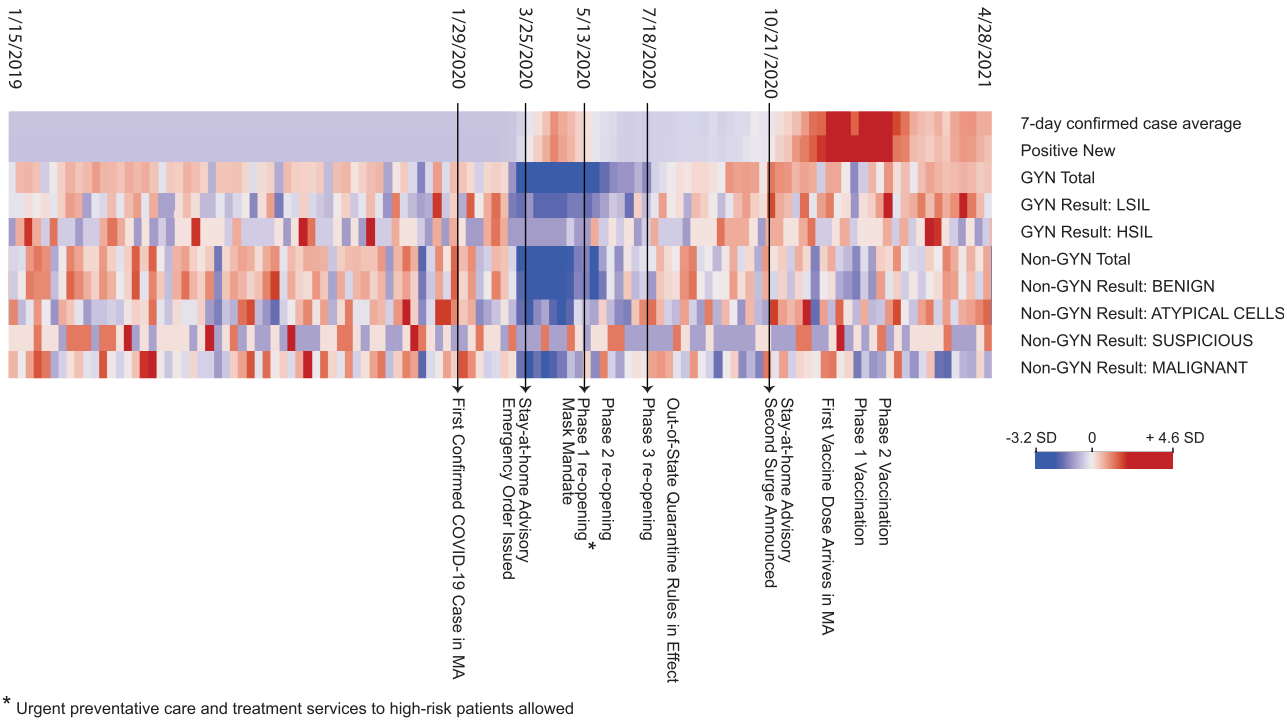

Figure 2. Heatmap showing the normalized and centered values of weekly COVID-19 case numbers in Boston, Massachusetts, along with a breakdown of gynecologic and non-gynecologic sample numbers and diagnostic categories. The color spectrum represents the standard deviation from mean (SD).

not observed during the second peak of the pandemic, likely because of the more modest reduction in specimen numbers compared with the higher number of COVID-19 cases identified during this phase of the pandemic (Fig. 3B).

Effect of COVID-19 pandemic on non-GYN cytology specimens

Before the pandemic, the average weekly volume of non-GYN cytology specimens (body cavity fluids, sputum, brushings, washings, urine, and FNAs) at our institution was 213 (over a 1-year-period). During the first peak of the pandemic (March 11, 2020–June 3, 2020), the average weekly non-GYN cytology specimen numbers dropped to 104 (−51.0%, compared with the prior 3-week moving average) (Figs. 1 and 2). Breakpoint analysis by SNHT showed a downward shift in the number of weekly accessions occurring during the week of March 25, 2020 (corresponding to the first stay-at-home advisory in Massachusetts), whereby a reduction of 70.4% occurred compared with the prior 3-week moving average (Table 1). Breakpoint analysis showed a return to normal levels after the first peak of the pandemic with phase 1 reopening of the city and the resumption of normal health care services (50.4% increase in volume occurring in the week of May 27, 2020, compared with the prior 3-week moving average). Again, a smaller reduction in volume (−24.8% compared with the prior 3-week moving average) occurred with the second COVID-19 peak (the week of December 23, 2020), with this reduction lasting until January 20, 2021, whereby the weekly volumes returned to prepandemic levels (Table 1). Cross-correlation analysis showed correlation of the reduction in non-GYN volumes with increasing COVID-19 cases in the first peak of the pandemic with a 1-week lag (Fig. 3C). A correlation was not observed during the second peak of the pandemic (Fig. 3D).

The reduction in volume was observed for all non-GYN cytology specimen types (Figs. 2 and 4). During the first weeks of the pandemic, thyroid FNA numbers decreased by 86.4% (from a weekly average of 22.0 to a weekly average of 3.0) (Fig. 4A), whereas other FNA samples decreased by 69.6% (from a weekly average of 20.7 to a weekly average of 6.3) (Table 1). Several non-GYN cytology specimen categories also showed a relative reduction during the second peak of the pandemic

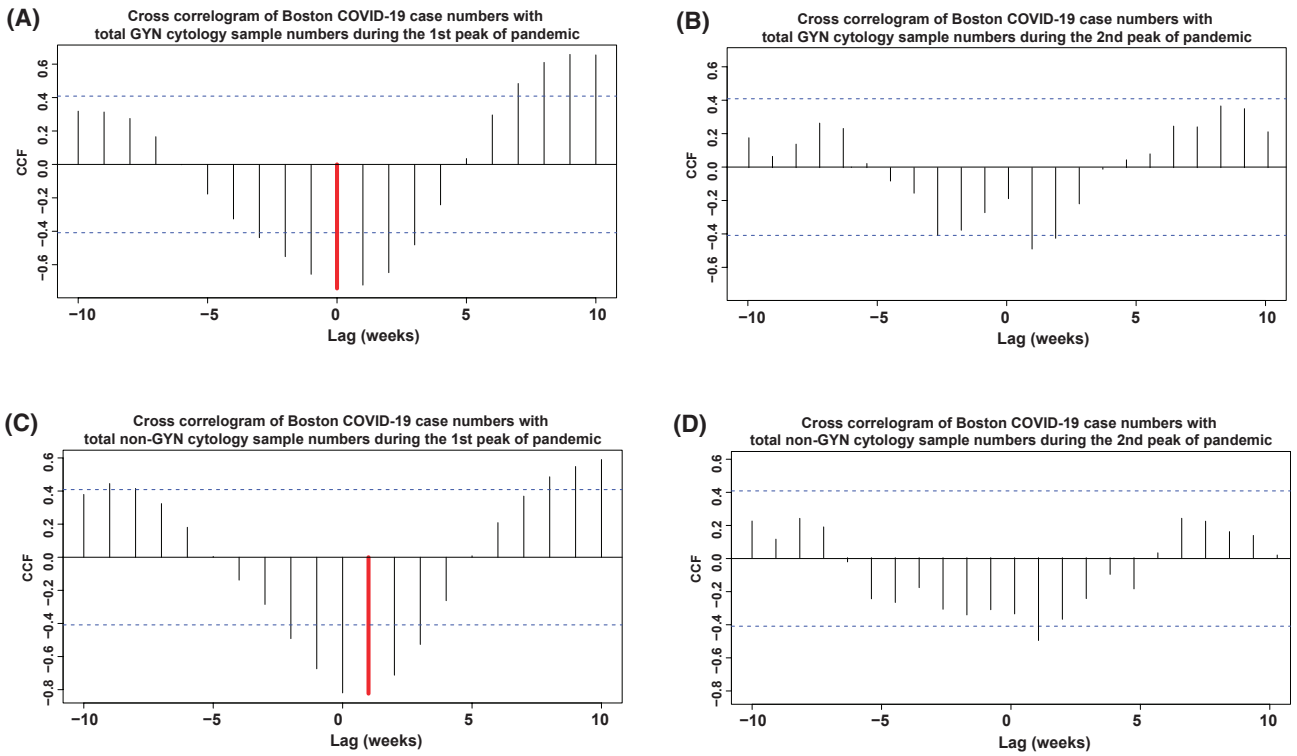

Figure 3. Cross correlogram of Boston COVID-19 case numbers with (A) total gynecologic sample numbers during the first peak of pandemic. The correlations in this time frame are negative with a lag of zero weeks, indicating that an increase in the number of COVID-19 cases led to a below average value of gynecological samples in the same week. (B) Cross correlogram of Boston COVID-19 case numbers sample numbers during the second peak of pandemic. Cross correlogram of (C) non-gynecologic cytology sample numbers during the first peak of pandemic and (D) non-gynecologic cytology sample numbers during the second peak of pandemic. Red bars indicate the point of maximum correlation (between the minima of sample numbers and maxima of COVID-19 case numbers), which occurred in the same week for gynecologic samples and with a 1-week delay for non-gynecologic sample numbers during the first peak of cases. No significant cross correlation was observed between accession numbers and COVID-19 case numbers during the second peak. CCF indicates cross-correlation function.

with FNAs other than thyroid, EBUS-TBNA and urine cytology specimens being the most notable (from weekly averages of 20.3, 36.0, and 65.7 to weekly averages of 12.3 [−39.4%], 22.0 [−38.9%], and 49.7 [−24.4%], respectively) (Fig. 4B-D). Additionally, the weekly urine cytology specimen accession number showed correlation with COVID-19 case numbers during both the first and second peaks of the pandemic (Fig. 4D).

Breakpoint analysis further identified a significant reduction in the absolute number of non-GYN malignant or suspicious diagnoses during the first peak of pandemic (week of March 11, 2020) from a prior 3-week moving average of 36.3 to 15.0 (−58.7%) (Fig. 5; Table 1). During the second peak of the pandemic (week of December 23, 2020), a milder reduction was observed (−41.5%) (Table 1). Cumulatively, during the first 3 months of the pandemic, 154 fewer malignant cases were identified compared with a moving average in the prior year. A similar reduction in the number of malignant cases was not observed during the second surge of the pandemic (Fig. 5). Although specimen numbers slowly returned to baseline following the first wave of the pandemic, there is no evidence that the earlier decline was offset/corrected for the duration of this study.

The total cytology volumes during the first and second surges of the pandemic at our institution showed a correlation with COVID-19–confirmed deaths in Massachusetts. Despite higher overall COVID-19 cases in the second surge of the pandemic, the number of deaths associated with the disease was lower compared with the first surge just as the reduction in the total number of cytology samples was lower during the second surge compared to the first surge (Fig. 6A). Cross correlogram showed that the minima of cytology samples occurred 2 weeks before the peak mortality associated

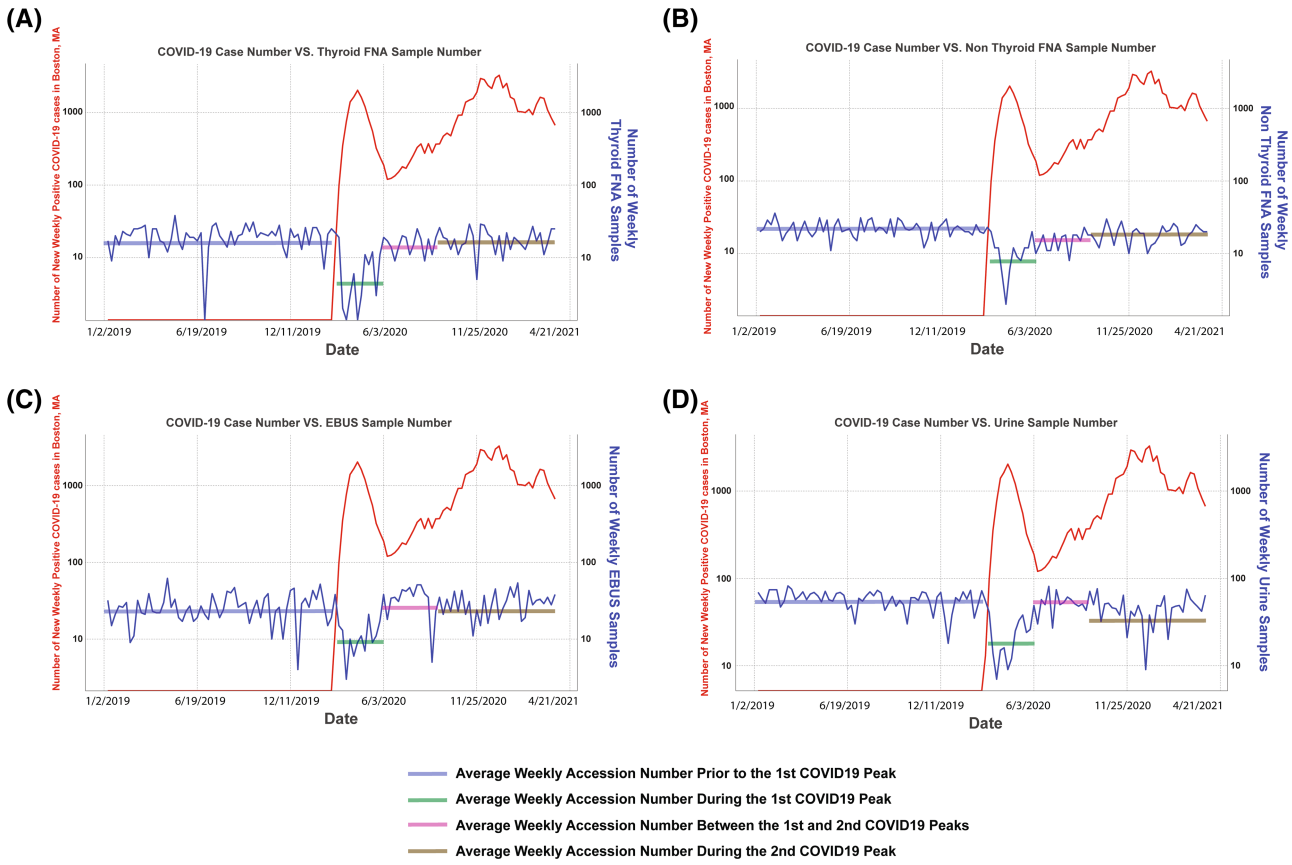

Figure 4. Time series plots showing the weekly aggregates of new COVID-19 cases in Boston, Massachusetts (red line) and the weekly aggregates of selected non-gynecological cytology sample numbers (blue line) for (A) thyroid FNA, (B) non-thyroid FNA, (C) EBUS, and (D) urine cytology samples. The horizontal lines represent weekly sample averages for January 2, 2019–March 10, 2020 (blue), March 11, 2020–June 3, 2020 (green), June 4, 2020–October 7, 2020 (pink), and October 8, 2020–April 21, 2021 (brown).

with COVID-19 during the first and second peaks of the pandemic (Fig. 6B).

DISCUSSION

The deleterious effects of the COVID-19 pandemic on health care goes far beyond the immediate excess mortality, and its magnitude will be elucidated in the years to come. In this study, we attempted to uncover some of the hidden impacts of the pandemic through a time-series review of cytology samples at a single institution.

Globally, cytology laboratories encountered a substantial decrease in sample volumes across specimen types early in the pandemic. Most published studies have focused on the effects of the first surge of COVID-19 cases using a cross-sectional methodology comparing specimen numbers with comparable periods from prior years. Vigliar et al. evaluated the effect of the COVID-19 pandemic on laboratories in 23 countries during the first 4 weeks of peak infection spread in each country. They reported an absolute reduction in the total number of cytology cases and an overall increase in the malignancy rate compared with the corresponding period in 2019. They also reported a higher overall rate of malignancy and concluded that patients with higher oncological risk had been successfully prioritized.[10] Similar observations were made by Rana et al. in a cytology laboratory in India.[15] In another study, Virk et al. showed a considerable reduction in both GYN and non-GYN volumes in their laboratory in New York. Additionally, they observed an increase in the proportions of malignant, suspicious, and atypical diagnoses for non-GYN samples and increased proportions for all the abnormal categories of GYN samples except LSIL.[16] In the Asia-Pacific region, a study of 167 laboratories

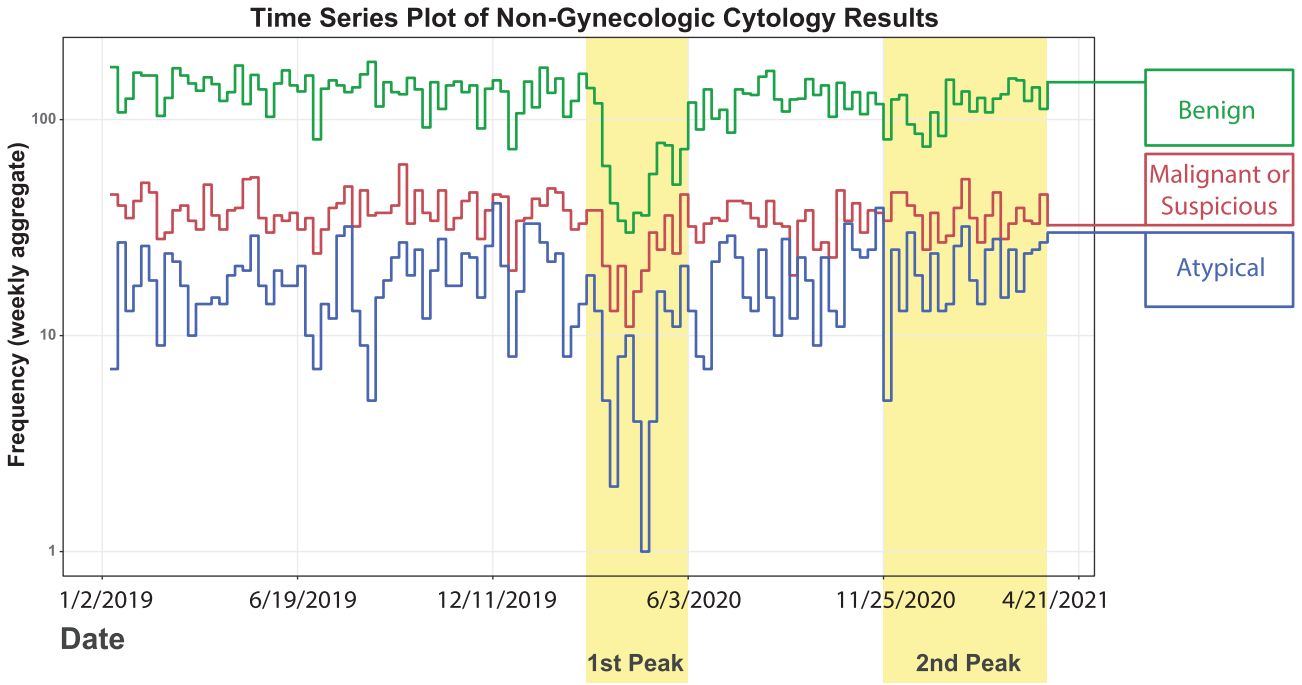

Figure 5. Time-series plots showing the weekly aggregates of non-gynecologic cytology results.

from 24 countries by Wang et al. described a significant reduction in the cytology caseload, most prominent for GYN samples over the 3-month duration of the study (February 1, 2020–April 30, 2020), but the overall rate of malignancy was similar to the corresponding period in 2019.[17] In a follow-up post-lockdown study, Vigliar et al. surveyed 29 respondents in 17 countries for the first 12-week post-lockdown period compared with corresponding periods in 2019. Their results showed an overall increase in the rate of malignancy but an alarming persistence in the reduction of cytology sample volumes (although the rate of reduction had slowed down in the second half of the assessed period).[12,18] Our observations mirror these results, demonstrating that the most significant effect of the pandemic on specimen volume occurred during the first surge (March 11, 2020–June 3, 2020). With the second peak of the pandemic, occurring in late 2020 and early 2021, the effect on sample volume and the number of malignant diagnoses was much less severe compared with the first peak, despite higher COVID-19 case numbers.[19] This is in line with the observation that the second wave of the pandemic in wealthier nations was associated with lower direct mortality.[20] These results suggest that better preparedness and surge capacity planning for the second peak not only reduced the direct mortality of the COVID-19 but also, at least in our institution, appears to have reduced the impact on other aspects of the health care system, including cytology laboratory workload (Fig. 6A).

In practice, cytology functions in some cases as a diagnostic test and in others as a screening tool, and less urgent specimens such as Pap and urine tests tended to be more responsive to rising COVID-19 case numbers and local stay-at-home advisories than other non-GYN specimens (Figs. 2 and 4D). These findings raise concern for delayed care and surveillance of patients. Regardless of the changes in specimen numbers, the relative increase (or decrease) in the malignancy rates during the pandemic may be less meaningful than changes in the absolute number of malignant diagnoses rendered. In our study, we showed an absolute deficit of 154 malignant cases attributed solely to the initial COVID-19 surge period compared with the moving average of the year before the pandemic. Because our data are generated from a referral center, it is possible that some of these cases were still identified as patients sought care closer to home. Still, we saw no evidence of an offsetting of this deficit during the study period, suggesting that a significant number of malignancies were not identified.

Breakpoint analysis showed that during both surges the downward shift in the GYN samples occurred a few

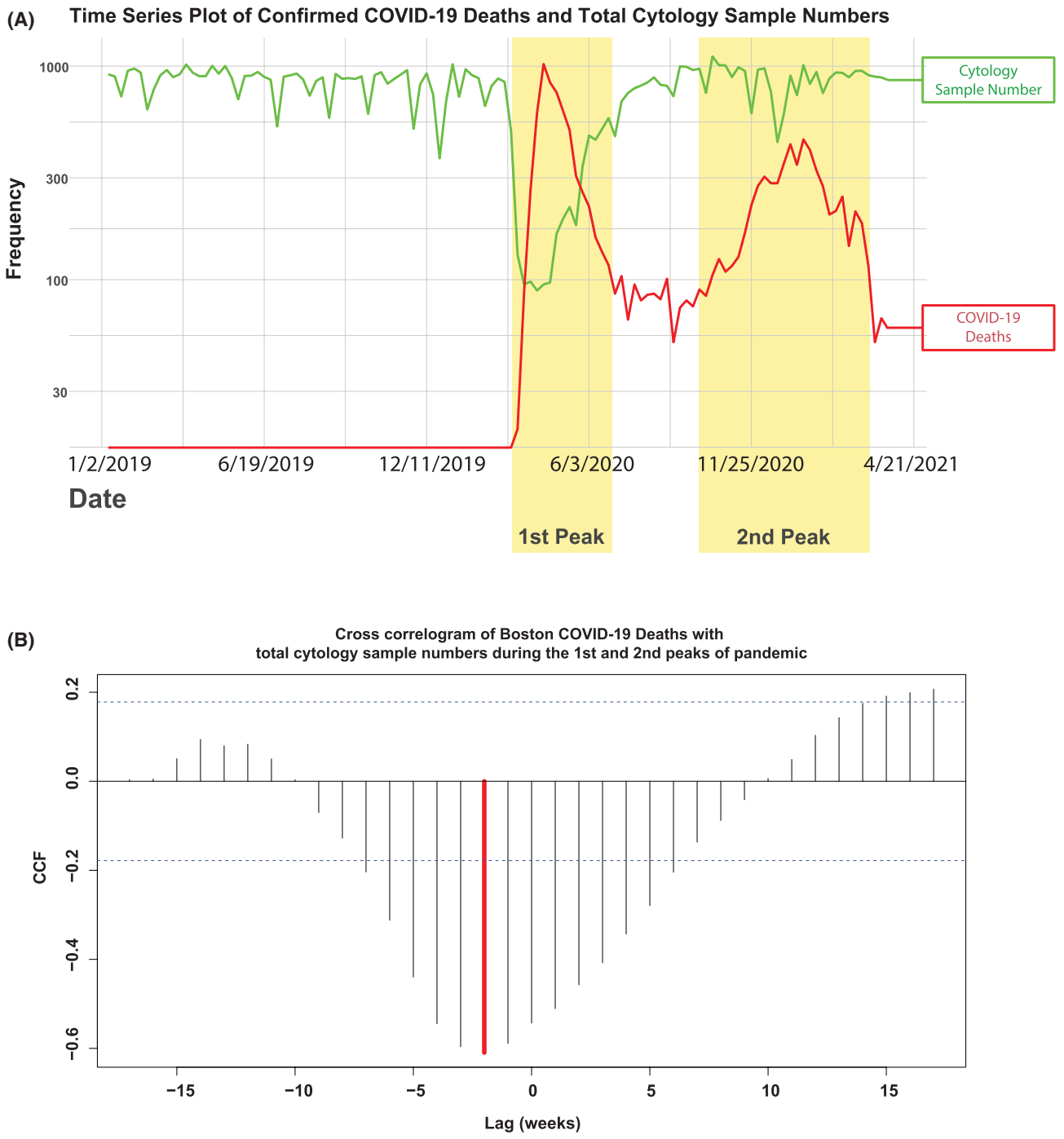

Figure 6. (A) Time-series plots showing the weekly aggregates of new COVID-19 deaths in Boston, Massachusetts (red) and the weekly aggregates of total cytology sample numbers (green). (B) Cross correlogram of Boston COVID-19 deaths with total cytology sample numbers during the first and second peaks of the pandemic. The red bar indicates that the minima of cytology samples occurred 2 weeks before the maxima of COVID-19 deaths. CCF indicates cross-correlation function.

weeks before the downward shift in the non-GYN samples, and mostly coincided (or occurred within 2 weeks) of the issuance of stay-at-home advisories. This is most likely related to the screening nature of Pap tests, which makes patients and providers more willing to postpone testing, whereas many non-GYN samples are diagnostic procedures and thus perceived as more urgent.

The deleterious effects of the COVID-19 pandemic extend beyond any direct mortality attributed to the disease. The significant decrease in cytology specimens

during this period has profound implications. In the best-case scenario, this means delayed care for many patients; in the worst-case scenario, it means missed disease with adverse outcomes that will be measured in the coming years. During the second surge of the disease, despite a higher number of COVID-19 cases, a much less notable effect was observed on cytology sample numbers. This success can be attributed to capacity building in the health care system, allowing for continued routine medical care in addition to caring for COVID-19 patients during this phase of the pandemic. The experience with the COVID-19 pandemic is an invaluable lesson in the vital necessity of contingency planning and capacity building, for the ongoing management of the crisis and any future outbreaks.

AUTHOR CONTRIBUTIONS

Elham Yousefi: Conceptualization, data acquisition, analysis, interpretation of data, and manuscript preparation. **Edmund S. Cibas:** Conceptualization, interpretation of data, and manuscript preparation. **Jeffrey K. Mito:** Conceptualization, analysis, interpretation of data, and manuscript preparation.

FUNDING INFORMATION

This work was performed using departmental funding.

CONFLICT OF INTEREST

The authors made no disclosures.

REFERENCES

1. Johns Hopkins University COVID Resource Center. Accessed May 9, 2022. https://coronavirus.jhu.edu/data/cumulative-cases
2. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet. Infectious diseases.* 2020;20:533–534.
3. Faust JS, Krumholz HM, Du C, et al. All-cause excess mortality and COVID-19–related mortality among US adults aged 25–44 years, March-July 2020. *JAMA.* 2021;325:785–787.
4. Mercier G, Arquizan C, Roubille F. Understanding the effects of COVID-19 on health care and systems. *Lancet Public Health.* 2020;5:e524.
5. Mesnier J, Cottin Y, Coste P, et al. Hospital admissions for acute myocardial infarction before and after lockdown according to regional prevalence of COVID-19 and patient profile in France: a registry study. *Lancet Public Health.* 2020;5:e536–e542.
6. Santi L, Golinelli D, Tampieri A, et al. Non-COVID-19 patients in times of pandemic: Emergency department visits, hospitalizations and cause-specific mortality in Northern Italy. *PLoS One.* 2021;16:e0248995.
7. Aburto JM, Kashyap R, Schöley J, et al. Estimating the burden of the COVID-19 pandemic on mortality, life expectancy and lifespan inequality in England and Wales: a population-level analysis. *J Epidemiol Community Health.* 2021;75:735–740.
8. Devereaux AV, Dichter JR, Christian MD, et al. Definitive care for the critically ill during a disaster: a framework for allocation of scarce resources in mass critical care: from a Task Force for Mass Critical Care summit meeting, January 26–27, 2007, Chicago, *IL. Chest.* 2008;133:51S–66S.
9. Schmitt F. The impact of the COVID-19 pandemic on cytopathology practice. *Cytopathology.* 2021;32:297–298.
10. Vigliar E, Cepurnaite R, Alcaraz-Mateos E, et al. Global impact of the COVID-19 pandemic on cytopathology practice: results from an international survey of laboratories in 23 countries. *Cancer Cytopathol.* 2020;128:885–894.
11. O'Connor E, O'Connor D, Murray D, Quinn AM. Impact of the COVID-19 pandemic on cytopathology services in the West of Ireland. *J Clin Pathol.* 2022;75(5):359–360.
12. Vigliar E, Cepurnaite R, Iaccarino A, et al. Cytopathology practice during the COVID-19 postlockdown: an Italian experience. *Cancer Cytopathol.* 2021;129:548–554.
13. Basu P, Alhomoud S, Taghavi K, Carvalho AL, Lucas E, Baussano I. Cancer screening in the coronavirus pandemic era: adjusting to a new situation. *JCO Glob Oncol.* 2021;7:416–424.
14. Patt D, Gordan L, Diaz M, et al. Impact of COVID-19 on cancer care: how the pandemic is delaying cancer diagnosis and treatment for American seniors. *JCO Clin Cancer Inform.* 2020;4:1059–1071.
15. Rana C, Kumar S, Babu S, et al. Impact of ongoing COVID-19 pandemic on cytology: an institutional experience. *Diagn Cytopathol.* 2021;49:311–315.
16. Virk RK, Wood T, Tiscornia-Wasserman PG. Impact of COVID-19 pandemic on functioning of cytopathology laboratory: experience and perspective from an academic centre in New York. *Cytopathology.* 2021;32:304–311.
17. Wang YH, Bychkov A, Chakrabarti I, et al. Impact of the COVID-19 pandemic on cytology practice: an international survey in the Asia-Pacific region. *Cancer Cytopathol.* 2020;128:895–904.
18. Vigliar E, Pisapia P, Dello Iacovo F, et al. COVID-19 pandemic impact on cytopathology practice in the post-lockdown period: an international, multicenter study. *Cancer Cytopathol.* 2022;130(5):344–351.
19. Miller M. 2019 novel coronavirus COVID-19 (2019-nCoV) data repository. Johns Hopkins University Center for Systems Science and Engineering. *Bulletin - Association of Canadian Map Libraries and Archives (ACMLA).* 2020;47–51.
20. James N, Menzies M, Radchenko P. COVID-19 second wave mortality in Europe and the United States. *Chaos.* 2021;31:031105.