Incident Cancer Detection During the COVID-19 Pandemic

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ABSTRACT

Background: Resource restrictions were established in many jurisdictions to maintain health system capacity during the COVID-19 pandemic. Disrupted healthcare access likely impacted early cancer detection. The objective of this study was to assess the impact of the pandemic on weekly reported cancer incidence. Patients and Methods: This was a population-based study involving individuals diagnosed with cancer from September 25, 2016, to September 26, 2020, in Ontario, Canada. Weekly cancer incidence counts were examined using segmented negative binomial regression models. The weekly estimated backlog during the pandemic was calculated by subtracting the observed volume from the projected/expected volume in that week. Results: The cohort consisted of 358,487 adult patients with cancer. At the start of the pandemic, there was an immediate 34.3% decline in the estimated mean cancer incidence volume (relative rate, 0.66; 95% CI, 0.57–0.75), followed by a 1% increase in cancer incidence volume in each subsequent week (relative rate, 1.009; 95% CI, 1.001–1.017). Similar trends were found for both screening and nonscreening cancers. The largest immediate declines were seen for melanoma and cervical, endocrinologic, and prostate cancers. For hepatobiliary and lung cancers, there continued to be a weekly decline in incidence during the COVID-19 period. Between March 15 and September 26, 2020, 12,601 fewer individuals were diagnosed with cancer, with an estimated weekly backlog of 450. Conclusions: We estimate that there is a large volume of undetected cancer cases related to the COVID-19 pandemic. Incidence rates have not yet returned to prepandemic levels.

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Background
Cancer survival rates have improved over the past decade, in part because of earlier detection of disease.1,2 However, screening programs with accessible in-person care have been impacted by the emergency health measures put in place during the COVID-19 pandemic.3–8 Disruption to healthcare access may negatively impact early detection of cancers and lead to a spurious decline in observed cancer incidence. Some countries observed a decrease in incidence rates during the first 1 to 2 months of the pandemic,9–12 although few studies provide a longitudinal population-based perspective. In many databases, reported incidence undercounts true population incidence. In Ontario, Canada, reported incidence rates approximate the true population incidence, thanks to a comprehensive cancer data reporting system. The objective of this study was to assess the impact of the COVID-19 pandemic on weekly reported cancer incidence rates, by cancer type, from September 2016 to September 2020.

Patients and Methods
Study Design and Population
This was a population-based cohort study in Ontario, Canada. The analysis is presented in accordance with the STROBE guidelines.13 All individuals diagnosed with cancer in Ontario from September 25, 2016, to September 26, 2020, were identified using the Ontario Cancer Registry (OCR); this database consists of all cancers diagnosed in the province since 1964 and has a >95% capture of incident cancers.14–15 All pathology reports with a cancer diagnosis are required to be submitted to the OCR, in addition to any death certificates with cancer included on the form.16 All reporting must occur within 30 days. Therefore, the OCR is a robust registry of cancer cases in the Ontario jurisdiction. At the time of analysis, the OCR was updated up to and including September 26, 2020. Individuals included in our study had to have a valid
Data Sources
The analysis was performed using data held at the ICES (previously known as the Institute for Clinical Evaluative Sciences). Demographic characteristics, vital status, and date of death for all individuals covered under the Ontario Health Insurance Plan were obtained from the Registered Persons Database. The OCR was used to capture information on date of diagnosis and cancer type. Immigration status was retrieved from the Immigration, Refugees and Citizenship Canada Permanent Resident database. The Ontario Marginalization Index quantifies the degree of marginalization across the province with respect to deprivation, residential instability, dependency, and ethnic concentration. The Canadian Institute for Health Information (CIHI) Discharge Abstract Database contains information on hospitalizations. These datasets were linked using unique encoded identifiers and analyzed at the ICES. Use of the data in this project is authorized under section 45 of Ontario’s Personal Health Information Protection Act and does not require review by a research ethics board.

Outcome and Exposure
The period from September 25, 2016, to September 26, 2020, was divided into weekly intervals. With the population of Ontario being stable over these years, our study outcome was the number of new cancers diagnosed in each week. The exposure of interest was the COVID-19 versus pre–COVID-19 periods, where weeks before March 15, 2020, were considered part of the pre–COVID-19 period and weeks on or after March 15, 2020, were considered part of the COVID-19 period. In Ontario, many family physicians’ offices abruptly stopped seeing patients in person on March 15, 2020. Screening programs formally closed until May 1, 2020, and elective surgery was canceled as part of a health directive to decrease the spread of COVID-19. Cancers with organized screening programs in Ontario include breast, cervical, colorectal, and lung; screening cancers) were compared with those without one (nonscreening cancers). All other cancers were considered nonscreening cancers. Lung cancer screening for high-risk patients using low-dose CT of the thorax has existed in Ontario since 2017 but is currently only available at select sites.

Statistical Trend Analyses
The distributions of baseline characteristics were compared for patients diagnosed during the pre–COVID-19 versus COVID-19 periods. Characteristics included age, sex, rurality (based on RIO23 [Rurality Index for Ontario]), neighborhood income quintile, area of residence, type of cancer diagnosis, immigration status, deprivation quintiles via marginalization indices, and comorbidity via Elixhauser score. Each of these characteristics was abstracted from one of our linked data sources and measured at the time of cancer diagnosis. Because of the large cohort size, standardized differences (rather than P values) were used to establish whether baseline characteristics were similar between the pre–COVID-19 and COVID-19 groups; a standardized difference <0.1 indicated balance between groups.

To quantify changes in cancer incidence volume trends due to the COVID-19 pandemic, the weekly cancer incidence counts were examined using segmented negative binomial regression models. These models were used to estimate the cancer incidence volume trend before COVID-19 (September 25, 2016, through March 14, 2020; preperiod intercept and preperiod slope), the immediate drop in cancer incidence volume at the start of the first week of the pandemic (March 15, 2020; COVID-19-period relative change in intercept), and the cancer incidence volume trend during the COVID-19 period (COVID-19 period slope). Results from this segmented regression model were then plotted to illustrate changes in cancer incidence volume before and during the pandemic period. Secondarily, the estimated backlog in diagnosing cancers in each week after the start of the pandemic was calculated by subtracting the observed volume from the projected/expected volume in that week (if there had been no pandemic). Trend analyses were conducted overall (for all cancer types) and then separately for each type of cancer. A planned subgroup analysis stratified the results based on the existence of a provincial screening program, whereby cancers with an organized provincial screening program (breast, cervix, colorectal, and lung; screening cancers) were compared with those without one (nonscreening cancers). Sensitivity analyses were performed comparing mid-March to September in 2016 through 2019 with the same period in 2020 to ensure that seasonality did not impact our findings. We reported rate ratios using 95% confidence intervals. Analyses were conducted using SAS Enterprise Guide 7.1 (SAS Institute Inc).

Results
The cohort consisted of 358,487 adult patients diagnosed with cancer between September 25, 2016, and September 26, 2020, in Ontario, Canada, of whom 37,479 were diagnosed during the COVID-19 period. The distributions of baseline characteristics for patients diagnosed in the pre–COVID-19 period compared with the COVID-19 period can be seen in Table 1. All standardized differences were <0.1, indicating that care has been equitable based on our measured characteristics and that no group was disproportionally impacted by COVID-19–related disruptions.
Results from the segmented negative binomial regression model, overall and stratified by screening cancers and nonscreening cancers, are seen in Table 2. Regarding overall trends in incidence of all cancers, the calculated mean volume at the initial week of the observation period was 1,761 (preperiod intercept; 95% CI, 1,678–1,847). In the following weeks (still before the pandemic), there was no significant relative change in cancer incidence volume (preperiod slope; relative rate, 1.0001; 95% CI, 0.9996–1.0005) (Figure 1). At the start of the pandemic (week of March 15, 2020), there was an immediate 34.3% drop in the mean cancer incidence volume (COVID-19 period relative change in intercept; relative rate, 0.66; 95% CI, 0.57–0.75) compared with prepandemic values, followed by a 1% increase in cancer incidence volume in each subsequent week (COVID-19 period slope; relative rate, 1.009; 95% CI, 1.001–1.017) until September 26, 2020. Similar trends (with respect to immediate drop in incidence once the pandemic began and slow increase afterward) were found for both screening and nonscreening cancers, and these were not statistically different.

When examining incidence trends for each type of cancer separately, the largest immediate drops (by ≥50%) in the volume at the start of the pandemic were seen for melanoma and cervical, endocrine (predominantly thyroid), and...
prostate cancers. These results are further illustrated in Figures 1 and 2, which show that the volumes of cancer incidence in the most recent weeks have not yet returned to those observed before the pandemic. This is seen overall (Figure 1) and for both screening and nonscreening cancers (Figure 2). Immediate drops in incidence were observed for all cancers at the start of the pandemic. For hepatobiliary and lung cancers, there continued to be a weekly decline in incidence during the COVID-19 period (Figures 3 and 4). Overall, this has resulted in 12,601 fewer individuals diagnosed with cancer than expected (had there been no pandemic) from March 15 to September 26, 2020, with an estimated weekly undetected case count of 450 (Table 3).

Discussion
In this population-based cohort study, there was a 34% immediate decline in mean weekly cancer incidence with only a slow recovery (1% per week) from March 15 to September 26, 2020. Baseline sociodemographic and clinical characteristics of patients who were diagnosed with cancer before and during the COVID-19 period did not differ, indicating that access to diagnostic care during the pandemic was equitable. Overall, screening and nonscreening cancers were equally affected, although there was variability between individual cancer types. The largest declines (>50%) in cancer incidence were noted for melanoma and cervical, endocrine, and prostate cancers. Hepatobiliary and lung cancers not only had a decline in initial incidence (4.0% and 13.5%, respectively) but also had a continued decline in cases even up to September 2020. Weekly mean cancer incidence rates did not return to prepandemic levels. We estimate the presence of 12,601 undetected cancer cases in this period.

These potentially missed cancer cases, along with the continued decline in cancer incidence in some cancers, raise grave concerns regarding real-world diagnostic delays. Several modeling studies have demonstrated a negative impact on survival outcomes for patients with cancer in cases of a large surgical case backlog.\textsuperscript{7,25-27} These studies were used in the early pandemic period to demonstrate the potential negative effect of diagnostic and surgical delays on population health outcomes. Although modeling

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated Mean Weekly Pre–COVID-19 Cancer Incidence\textsuperscript{a} (n, 95% CI)</th>
<th>Decline in Weekly Cancer Incidence, March 15, 2020 (Change in Intercept, %)\textsuperscript{b}</th>
<th>COVID-19 Cancer Incidence Weekly Change in Volume (Slope) RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers</td>
<td>1,761 (1,678–1,847)</td>
<td>34.3%</td>
<td>1.009 (1.001–1.017)</td>
</tr>
<tr>
<td>Screening program available</td>
<td>744 (710–779)</td>
<td>35.0%</td>
<td>1.008 (1.001–1.016)</td>
</tr>
<tr>
<td>Breast</td>
<td>212 (202–222)</td>
<td>30.5%</td>
<td>1.0005 (0.993–1.008)</td>
</tr>
<tr>
<td>Cervical</td>
<td>146 (134–159)</td>
<td>68.1%</td>
<td>1.036 (1.022–1.050)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>181 (173–190)</td>
<td>33.1%</td>
<td>1.014 (1.006–1.022)</td>
</tr>
<tr>
<td>Lung</td>
<td>205 (198–213)</td>
<td>13.5%</td>
<td>0.997 (0.991–1.004)</td>
</tr>
<tr>
<td>Screening program not available</td>
<td>1,016 (967–1,069)</td>
<td>33.7%</td>
<td>1.009 (1.001–1.017)</td>
</tr>
<tr>
<td>CNS</td>
<td>18 (17–19)</td>
<td>6.5%</td>
<td>0.995 (0.984–1.006)</td>
</tr>
<tr>
<td>Endocrine</td>
<td>55 (50–60)</td>
<td>63.1%</td>
<td>1.037 (1.022–1.053)</td>
</tr>
<tr>
<td>Genitourinary (excluding prostate)</td>
<td>160 (150–170)</td>
<td>22.7%</td>
<td>1.0001 (0.999–1.011)</td>
</tr>
<tr>
<td>Gynecologic (excluding cervical)</td>
<td>80 (76–85)</td>
<td>29.9%</td>
<td>1.006 (0.996–1.016)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>50 (47–53)</td>
<td>32.3%</td>
<td>1.0112 (1.001–1.022)</td>
</tr>
<tr>
<td>Hepatobiliary</td>
<td>80 (76–83)</td>
<td>4.0%</td>
<td>0.997 (0.990–1.004)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>84 (80–88)</td>
<td>7.9%</td>
<td>0.986 (0.977–0.995)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>71 (65–76)</td>
<td>54.6%</td>
<td>1.020 (1.007–1.032)</td>
</tr>
<tr>
<td>Prostate</td>
<td>178 (166–191)</td>
<td>54.7%</td>
<td>1.025 (1.013–1.037)</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>25 (23–27)</td>
<td>29.0%</td>
<td>1.006 (0.994–1.019)</td>
</tr>
<tr>
<td>Stomach</td>
<td>27 (25–29)</td>
<td>33.1%</td>
<td>1.011 (0.999–1.022)</td>
</tr>
</tbody>
</table>

Abbreviations: CNS, central nervous system; RR, rate ratio.

\textsuperscript{a}Three estimates are provided: (1) estimated mean weekly pre–COVID-19 cancer incidence, (2) estimated immediate change in weekly cancer incidence at the start of the pandemic (ie, change in intercept), and (3) estimated weekly change in cancer incidence during COVID-19 (ie, slope difference of the pre–COVID-19 and COVID-19 periods expressed as a rate ratio).

\textsuperscript{b}Weekly incidence based on >3 years of data from September 25, 2016, through March 14, 2020.

\textsuperscript{c}Decline in weekly cancer cases compared the prior mean weekly volume at week 0 with the first week of the pandemic (March 15, 2020); the cancer sites that had a >50% decline in incidence are shown in bold.
studies can provide evidence of what might occur, data on the real-world effects of such delays were lacking. Our study helps quantify the problem and confirms widespread diagnostic delay.\textsuperscript{7,28} This analysis should be replicated in other jurisdictions that may have had different public health policies and COVID-19 infection rates.

**Figure 1.** Overall weekly cancer incidence segmented regression from September 25, 2016, through September 26, 2020. The vertical solid line represents the start of the pandemic (March 15, 2020). The lighter shade represents pre-COVID-19, and the darker shade represents the COVID-19 period.

**Figure 2.** Weekly screening and nonscreening cancer incidence segmented regression from September 25, 2016, through September 26, 2020. The vertical solid line represents the start of the pandemic (March 15, 2020). The lighter shade represents pre-COVID-19, and the darker shade represents the COVID-19 period.
Our data suggest some level of prioritization of cases (biopsy, imaging, and surgical resection), given some of the largest declines in cancer incidence among some of the most indolent cancers. Local guidelines help shape the narrative around this prioritization, particularly regarding surgical case prioritization.\textsuperscript{29–33} Fortunately, cancer

**Figure 3.** Weekly hepatobiliary cancer incidence segmented regression from September 25, 2016, through September 26, 2020. The vertical solid line represents the start of the pandemic (March 15, 2020). The lighter shade represents pre-COVID-19, and the darker shade represents the COVID-19 period.

**Figure 4.** Weekly lung cancer incidence segmented regression from September 25, 2016, through September 26, 2020. The vertical solid line represents the start of the pandemic (March 15, 2020). The lighter shade represents pre-COVID-19, and the darker shade represents the COVID-19 period.
COVID-19. Some of these cases may have presented as the low absolute number of deaths in Ontario caused by they would be accounted for by COVID-19 deaths, given cases missing as a result of diagnostic delays.

Future granular work looking at staging data, which are not yet curated in the OCR, may identify more subtle health equity gaps.

An explanation for the decline in reported incidence may be related to delays in seeking care, given the public messaging on avoiding an already overburdened health system. A study by Lou et al\textsuperscript{15} demonstrated that patients want early detection and treatment even in the midst of a pandemic peak. A concerted public health campaign to ensure patients attend appointments for medical concerns during a pandemic will require more than messaging and advertisements. Providers in the system, especially in primary care, will need to quell patient and caregiver concerns regarding ongoing risk of COVID-19 transmission and to reinforce the value of early detection and treatment of cancers.

Although this study elucidates the number of cancer cases that have yet to be detected, we still do not know exactly where the “missing” cases are. It is unlikely that they would be accounted for by COVID-19 deaths, given the low absolute number of deaths in Ontario caused by COVID-19. Some of these cases may have presented as advanced cancers that were palliated without a biopsy, but these would ultimately appear on death certificates and still be captured. Our study only covers 6.5 months since the start of the pandemic, so missed cancer diagnoses would, in most cases, not yet have progressed to death, because many cancers would not experience a mortality event within 6 months of diagnosis. Our concern is that many cancers will present in a delayed fashion and that many will be unresectable or incurable at presentation. Clear public health messaging is required, even during subsequent pandemic waves, to ensure that patients are seeing physicians when they have new symptoms and have reasonable access to diagnostic imaging and biopsy when appropriate. Screening programs should remain open, and access to surgery should be prioritized for cancer cases.

One limitation of our study is related to data access. The OCR data are transferred to the ICES annually in February. We historically reviewed the files transferred over the past several years (and compared them with the updates provided the next year). Using this approach, we were able to determine that the data were comprehensive, as they relate to cancer incidence, up to and including September 2020. Fortunately, the pandemic did not impact our data acquisition processes. The OCR staff were working remotely and were not redeployed. They had full access to the usual incoming pathology reports and death certificates. Hospital-level data have not been delayed, with robust reporting throughout the pandemic. These processes were not disrupted and therefore were not likely to change cancer ascertainment at the registry level. Some patients with undiagnosed cancers may have died of other causes (such as COVID-19 or other comorbidities), whereas others may have died of their cancers, which may have presented at a very advanced stage. In the OCR, patients who die of cancer (even if it has not been biopsied, but when it is included on the death certificate) are captured. Therefore, we believe that the estimates provided are quite robust, and it is unlikely that deaths related to COVID-19 (low absolute number in Ontario) would significantly change our estimates.

**Conclusions**

We estimate that there is a large volume of undetected cancer cases related to the pandemic, with incidence rates not yet having returned to prepandemic levels and with some cancers more impacted than others. The population profile of those diagnosed with cancer was not different during the pandemic compared with before. Public health messaging and advisories are required to highlight the importance of early presentation with new symptoms to physicians. Ongoing urgent vaccination of the population to achieve herd immunity will allow safe cancer care. Although this pandemic is ongoing, a cancer recovery plan needs to be initiated. Physicians should

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Total Missing Cases\textsuperscript{a}</th>
<th>Weekly Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers</td>
<td>12,601</td>
<td>450</td>
</tr>
<tr>
<td>Screening program available</td>
<td>5,528</td>
<td>197</td>
</tr>
<tr>
<td>Breast</td>
<td>1,964</td>
<td>70</td>
</tr>
<tr>
<td>Cervical</td>
<td>1,808</td>
<td>65</td>
</tr>
<tr>
<td>Colorectal</td>
<td>898</td>
<td>32</td>
</tr>
<tr>
<td>Lung</td>
<td>869</td>
<td>31</td>
</tr>
<tr>
<td>Screening program not available</td>
<td>7,074</td>
<td>253</td>
</tr>
<tr>
<td>CNS</td>
<td>76</td>
<td>3</td>
</tr>
<tr>
<td>Endocrine</td>
<td>600</td>
<td>21</td>
</tr>
<tr>
<td>Genitourinary\textsuperscript{b}</td>
<td>937</td>
<td>33</td>
</tr>
<tr>
<td>Gynecologic\textsuperscript{c}</td>
<td>666</td>
<td>24</td>
</tr>
<tr>
<td>Head and neck</td>
<td>294</td>
<td>11</td>
</tr>
<tr>
<td>Hepatobiliary</td>
<td>180</td>
<td>6</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>561</td>
<td>20</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1,056</td>
<td>38</td>
</tr>
<tr>
<td>Prostate</td>
<td>1,597</td>
<td>57</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>191</td>
<td>7</td>
</tr>
<tr>
<td>Stomach</td>
<td>185</td>
<td>7</td>
</tr>
</tbody>
</table>

Abbreviation: CNS, central nervous system.

\textsuperscript{a}Potentially missed cancer cases measured compared the period from March 15–September 26, 2020, with the average incidence of the 3 prior years over the same period of weeks. This is the number of expected cases missing as a result of diagnostic delays.

\textsuperscript{b}Excluding cervical.

\textsuperscript{c}Excluding prostate.
encourage continued screening and early biopsy for suspected cancers despite the ongoing pandemic.

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Data availability statement: The dataset from this study is held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS. The full dataset creation plan and underlying analytic code are available from the authors upon request, with the understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification. The use of the data in this project is authorized under section 45 of Ontario’s Personal Health Information Protection Act and did not require review by a research ethics board. The lead author affirms that the article is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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