Received: 10 May 2021 | Revised: 15 September 2021 | Accepted: 28 September 2021
DOI: 10.1002/ijc.33838

CANCER EPIDEMIOLOGY

IJC International Journal of Cancer

Mobility as a driver of severe acute respiratory syndrome coronavirus 2 in cancer patients during the second coronavirus disease 2019 pandemic wave

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Funding information
Südtiroler Sanitätsbetrieb

Abstract
We retrospectively analyzed the epidemiological characteristics of cancer patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and their correlations with publicly available mobility data. Between 19 October 2020 and 28 February 2021, 4754 patient visits were carried out, and 1454 treatments have been applied at the Haemato-Oncology Day Hospital Merano. Additional measures to prevent local SARS-CoV-2 transmission included a specific questionnaire for coronavirus disease 2019 (COVID-19) symptoms as well as a SARS-CoV-2 real-time polymerase-chain reaction (RT-PCR) 2 days prior to any intravenous or subcutaneous therapy. Community mobility was assessed through publicly available mobile phone tracking data from Google; 106/719 (14.7%) cancer patients have been tested positive for SARS-CoV-2 by PCR during the second wave compared to 5/640 (0.8%) within the first wave ($P < .001$); 66/106 (62%) had solid tumors, and 40/106 (38%) had hematological malignancies; 90/106 (85%) patients received ongoing antitumor therapies. Mortality rate of COVID-19 positive cancer patients (7/106; 6.6%) was higher compared to the overall population (731/46 421; 1.6%; $P < .001$). Strict control measures at our department led to a significantly lower test positivity rate compared to the general population, resulting in a reduction of 58.5% of new SARS-CoV-2 cases. Over time, infection rates and community mobility correlated in the first and second wave after initiating and lifting restrictions. Our findings underscore the importance of strict preventive control measures including testing and contact tracing in vulnerable subpopulations such as cancer patients, particularly if social restriction policies are being lifted. Smartphone-based mobility data may help to guide policy makers to prevent a vulnerable population like cancer patients from virus transmission.

KEYWORDS
cancer, COVID-19, lockdown, mobility, SARS-CoV-2

Abbreviations: COVID-19, coronavirus disease 2019; i.v./s.c., intravenous or subcutaneous; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Dominic Fong and Maximilian J. Mair contributed equally to this work.

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What's new?
Patients with cancer constitute a vulnerable population to severe COVID-19 disease, and the effects of social restrictions on this risk group remain unclear. Here, despite maintenance of strict local mitigation strategies including testing, the authors report a >20-fold increase in the number of confirmed SARS-CoV-2-positive cancer patients in an outpatient department during the second wave compared to the first wave. Early relaxation of movement restrictions was associated with SARS-CoV-2 spread in cancer patients, even though to a lower extent than in the general population. The findings highlight the importance of strict preventive control measures and testing strategies in cancer patients.

1 | INTRODUCTION

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a single-stranded RNA virus, characterized by human-to-human transmission that causes the coronavirus disease 2019 (COVID-19).[1] The COVID-19 outbreak, declared a pandemic on 11 March 2020 by the World Health Organization (WHO), has resulted in more than 129 million confirmed cases and over 2.8 million deaths all over the world by 31 March 2021.[2] Northern Italy, one of the epicenters during the first COVID-19 wave, was affected early and severely before spreading SARS-CoV-2 across surrounding regions. As a consequence, the Italian government implemented a nationwide strict lockdown in March 2020 to contain the spread of the epidemic.[3] Restrictions on mobility, closure of school, university and nonessential workplaces and a national stay-at-home order in conjunction with proactive testing and contact tracing have emerged drastically, leading to a reduction of the growth rate of confirmed cases and deaths.

In early May, as the incidence of cases declined after more than 2 months of nationwide lockdown measures, Italy lifted restrictions cautiously in phases followed by the complete re-opening implemented on 3 June 2020.[4] Despite the acute situation in spring 2020, the COVID-19 epidemic was largely mitigated during the summer.[5] However, as other countries, Italy experienced a resurgence of COVID-19 in autumn with a rise in daily infections. As a consequence, the Italian government has enacted again decrees that gradually introduced containment measures to reduce the pandemic.

During the second wave of the pandemic, several countries resorted to targeted measures, in an attempt to protect the health care system from being overwhelmed while preserving the economy as much as possible. The Italian government enforced a zone system on 3 November 2020, entailing different levels of restriction based on the severity of the epidemic in each region.[6] South Tyrol is a province (autonomous province of Bolzano) in northern Italy with a total population of more than 530 000 inhabitants as of 2019. As of 28 February 2021, a total of 53 804 SARS-CoV-2 cases and 1031 COVID-19-associated deaths were reported in South Tyrol.[2] Based on South Tyrol's autonomy, the province may exercise varying degrees of self-government. Therefore, the local authorities decided for less stringent restrictions than those recommended at national level during the second COVID-19 pandemic wave.

Mobile phone data can provide relevant information about how people move and how these patterns change or take effect after implementation of mobility restrictions in a state of emergency such as a pandemic.[7] Recent studies have investigated the impact of human mobility and control measures on the SARS-CoV-2 spread in different countries.[8-14] However, these effects may differ in particularly vulnerable population groups such as cancer patients. Due to disease and treatment-related immune deficiency, cancer patients who are infected by SARS-CoV-2 may experience more difficult outcomes than other nonvulnerable populations.[15] There is still no information available on the effects of large-scale social restrictions policy on COVID-19 epidemic in cancer patients, and the impact of less severe measures remains unclear. The aim of our study is to investigate the region-specific spread of COVID-19 in South Tyrol during the second epidemic wave after local restrictions were relaxed and its impact on cancer patients.

2 | MATERIALS AND METHODS

2.1 | Patient cohort

All patients treated at the outpatient department of the "Franz Tappeiner" Hospital Merano between 19 October 2020 and 28 February 2021 were included in our retrospective study. Specific infection prevention and control measures were maintained by the hospital as well as our outpatient clinic as described previously.[16,17] In addition, the healthcare team was separated by Home Office to reduce the risk of infection, and medical care was provided by telemedicine on a case-by-case basis. Testing for SARS-CoV-2 RNA 2 days prior to any intravenous or subcutaneous (i.v./s.c.) treatment was performed using a real-time polymerase-chain reaction (RT-PCR) on respiratory samples obtained from nasopharyngeal swabs. Test results were required before patients entered our department, and treatment was deferred for all patients with positive tests until they had been tested negative. Our approach was to recognize symptomatic as well as asymptomatic SARS-CoV-2 infection in patients before entering our outpatient clinic, to protect both patients and healthcare workers. These additional local preventive measures facilitated our continued provision of oncological treatment throughout the pandemic. The reported, daily RT-PCR-confirmed SARS-CoV-2 cases, COVID-19-related mortalities as well as number of hospitalized patients during the observation period were acquired from the Italian Civil Protection Department.[2]

2.2 | Local mobility restrictions

Since October 2020, the Italian Government has started to implement a series of travel restrictions and lockdown policies at the national level, which was then followed by a second Italian lockdown on 3 November 2020.[6] In particular, the Italian government tightened the coronavirus rules over the festive season including New Year and Epiphany. Travel between the regions was only allowed for work, health, and emergency reasons with the need to hold a completed self-certification.

Despite national restrictions, in response to the decrease of the number of daily new cases in South Tyrol, a series of local lifting policies were announced by the local government. On 30 November, the provincial government of the Autonomous Province of Bolzano announced to reopen commercial activities as well as intermediate schools.[18] In addition, from 4 December until 23 December, bars and restaurants were allowed to open between 5 AM until 6 PM daily, and hotels and other guest accommodation reopened in compliance with the distancing rules. From 7 December, trading activity in public areas in the form of markets was allowed.[19] On 21 December, the coronavirus rules over the festive season have been relaxed again, and traveling during the day within the region South Tyrol was not limited over Christmas, New Year and Epiphany.[20] Furthermore, bars and restaurants reopened on 7 January 2021.[21] However, general rules on physical spacing, wearing of face masks, social distancing and hygiene were recommended throughout the observation period.

2.3 | Mobility data

Considering the different lockdown policies of the Italian government and the autonomous province of Bolzano, we examined the relationship of temporal variation of SARS-CoV-2 rates, policy implementation and mobility levels in South Tyrol during the second wave (19 October 2020 to 28 February 2021). We used open access cellphone mobility data for the autonomous province of Bolzano, since they show movement trends across different categories of places to a reference period before the implementation of any measures.[22] The data show how visits to places, such as residential, workplaces or groceries and pharmacy, change compared to a pre-pandemic baseline value for that day of the week. The baseline was defined as the median value, for the corresponding day of the week, during the 5-week period 3 January until 6 February 2020. Average mobility was taken as the average reduction in mobility across the five Google mobility categories (retail and recreation, grocery and pharmacy, parks, transit stations and workplace).

2.4 | Statistical analyses

Independence of categorical variables was tested using the chi-square and Fisher's exact tests as appropriate. Means of continuous variables were compared using the Mann-Whitney *U* test. Correlations between mobility and infection/hospitalization rates as well as fatalities per week were evaluated using Spearman's rho, where a $|r| > .7$ was interpreted as strong correlation, $.5 < |r| \le .7$ as medium correlation and $.3 < |r| \le .5$ as weak correlation. Each processed Google category was analyzed independently. Test positivity rates were calculated as the ratio between positive tests and performed tests. The estimated number of SARS-CoV-2 positive cancer patients was calculated by the test positivity rate in the general population multiplied by the number of performed tests at our department. Due to the hypothesis-generating design of the study, no correction for multiple testing was applied.[23] Statistical analysis was performed using GraphPad Prism 9 (La Jolla, CA) as well as R 4.0.1 (The R Foundation for Statistical Computing, Vienna, Austria) and RStudio 1.3.1056 (Boston, MA) using the package "corrplot" (v0.84).

3 | RESULTS

3.1 | Demographic characteristics and clinical outcomes in SARS-CoV-2 infected cancer patients

Demographic and clinical characteristics of cancer patients tested positive for SARS-CoV-2 are summarized in Table 1. From 19 October 2020 to 28 February 2021, 719 consecutive cancer patients treated at our hemato-oncological outpatient department were included in our retrospective study; 4754 patient visits were carried out, and 1454 treatments have been applied intravenously or subcutaneously. During the observation period, 106 cancer patients with RT-PCR-confirmed SARS-CoV-2 infection were detected. Based on the history of a cancer diagnosis, patients have been categorized into two groups with hematological malignancies and solid tumors. Median age for SARS-CoV-2 positive patients with malignant hematologic disorders ($N = 40$) was 62 years (range: 31-88), and for SARS-CoV-2 positive patients with solid tumors ($N = 66$) was 67 years (range: 28-85), respectively.

Ninety out of 106 (85.0%) SARS-CoV-2 positive patients received active anticancer treatment. Among those patients not receiving active treatment, 5/66 (7.6%) oncological patients were cancer survivors in routine follow-up, whereas 1/66 (1.5%) patients received best supportive care (BSC). In the subgroup of patients with hematological malignancies, routine follow-up was performed in 2/40 (5.0%) patients, whereas 8/40 (20%) patients were treated with BSC. Among all positive patients, SARS-CoV-2 infection was community-acquired while no in-hospital infection was observed according to contact tracing procedures, which were performed by local authorities.

TABLE 1 Characteristics and clinical outcomes in SARS-CoV-2 infected cancer patients (N = 106) during the second COVID-19 pandemic wave

	Solid tumors (N = 66)	Hematological malignancies (N = 40)
Demographics		
Median age, years (range)	67 (28-85)	62 (31-88)
Male, no. of patients (%)	31 (46.9%)	25 (62.5%)
Baseline clinical characteristics		
Current smoker	19 (28.8%)	7 (17.5%)
Comorbidity		
Cardiovascular disease	20 (30.3%)	16 (40.0%)
Endocrine disorders	17 (25.8%)	11 (27.5%)
Chronic renal failure	4 (6.1%)	5 (12.5%)
Chronic lung disease	7 (10.6%)	2 (5.0%)
Obesity (BMI ≥ 30)	9 (13.6%)	4 (10.0%)
No comorbidity	9 (13.6%)	2 (5.0%)
Cancer diagnosis		
Breast cancer	18 (27.3%)	
Lung cancer	11 (16.7%)	
Colorectal cancer	9 (13.6%)	
Renal cancer	6 (9.1%)	
Prostate cancer	6 (9.1%)	
Ovarian cancer	4 (6.1%)	
Melanoma	2 (3.0%)	
Gastric cancer	2 (3.0%)	
Pancreatic cancer	2 (3.0%)	
Mesothelioma	1 (1.5%)	
Biliary tract cancer	1 (1.5%)	
Cancer of unknown primary	1 (1.5%)	
Bladder cancer	1 (1.5%)	
Appendix cancer	1 (1.5%)	
Brain cancer	1 (1.5%)	
Indolent lymphoma		14 (35.0%)
Chronic myeloproliferative disease		12 (30.0%)
Aggressive lymphoma		5 (12.5%)
Multiple myeloma		5 (12.5%)
Myelodysplastic syndrome		2 (5.0%)
Hodgkin lymphoma		2 (5.0%)
Cancer treatment		
Chemotherapy	13 (19.7%)	14 (35.0%)
Chemoimmunotherapy	9 (13.6%)	1 (2.5%)
Immunotherapy	20 (30.3%)	7 (17.5%)
Targeted therapy	12 (18.2%)	8 (20.0%)
Antihormonal therapy	5 (7.6%)	—
Follow-up	5 (7.6%)	2 (5.0%)
Best supportive care	1 (1.5%)	8 (20.0%)
Radiotherapy	1 (1.5%)	—
COVID-19 disease		
SARS-CoV-2 transmission		
Outside hospital	66 (100%)	40 (100%)
COVID-19 disease course		
COVID-19 home care	53 (80.3%)	29 (72.5%)
COVID-19 ward	12 (18.2%)	8 (20.0%)
ICU	1 (1.5%)	3 (7.5%)
Median hospitalized days (range)	25 (8–31)	29 (16–49)
Median days to negative SARS-CoV-2 PCR (range)	18.5 (7-64)	21.5 (8-63)
Clinical outcome		
Recovered from COVID-19	62 (93.9%)	37 (92.5%)
COVID-19-related death	4 (6.1%)	3 (7.5%)

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; ICU, intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

3.2 | Significant increase of SARS-CoV-2 infections in cancer patients during the second COVID-19 pandemic wave

Compared to the first wave, we observed a significant increase of SARS-CoV-2 infections within our outpatient department (Figure 1). During the first wave between 15 March and 30 June 2020 (peaked on 12 April 2020), 5/640 (0.8%) cancer patients have been tested positive for SARS-CoV-2 by RT-PCR compared to 106/719 (14.7%) cases during the second wave (from 19 October 2020 to 28 February 2021; peaked on 13 November 2020), respectively ($P < .001$, Fisher's exact test). Therefore, the overall infection rate within our department was ~20 times higher during the second wave. Considering the second COVID-19 pandemic wave, 82/106 (77.4%) patients reported mild symptoms or were asymptomatic, whereas 20/106 (18.9%) were hospitalized and 4/106 (3.7%) were admitted to intensive care units (ICUs; Table 1). The median in-hospital stay was 25 days (range: 8-31) for patients with solid tumors, and 29 days (range: 16-49) for patients with hematological malignancies, respectively. The median time to SARS-CoV-2 negative RT-PCR from nasopharyngeal swab was

18.5 days (range: 7-64) for patients with solid tumors, and 21.5 days (range: 8-63) for patients with hematological malignancies, respectively. Overall, 7/106 (6.6%) patients died (four with solid tumors and three with hematological malignancies) due to COVID-19, resulting in a significantly higher lethality as compared to the general population (1.6%; 731/46 421; $P < .001$, chi-square test) in South Tyrol.

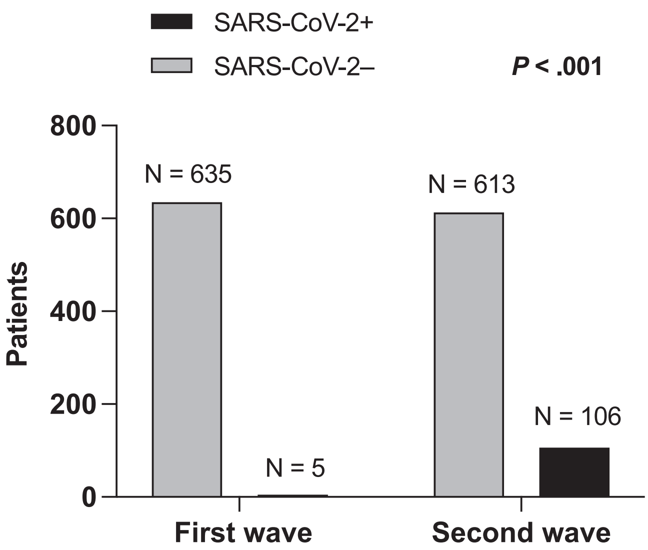

FIGURE 1 Absolute number of RT-PCR-confirmed SARS-CoV-2 infections at our hemato-oncological outpatient department during the first and second waves of the COVID-19 pandemic. *P*-value as determined by chi-square test

3.3 | Early relaxation of movement restrictions is associated with a significant increase of SARS-CoV-2 infection rates

In November 2020, the province of South Tyrol experienced a surge of daily notification rates for SARS-CoV-2 cases with a 7-day moving average of 103.4/100 000 inhabitants, prompting local authorities to implement a large-scale screening campaign based on rapid antigen diagnostic tests for SARS-CoV-2.[24] However, after the 7-day average of daily notification rates significantly dropped to 31.5/100 000, local authorities decided to lift restrictions gradually before Christmas holidays. Of note, as pointed out in the patients and methods section, we only used RT-PCR-confirmed SARS-CoV-2 cases for our analyses.

Although a decrease in mobility could also be observed in the second wave, mobility measures declined to a much lesser extent as compared to the first wave. Figure 2 shows the week-specific mobility trend during the first (Figure 2A) and second (Figure 2B) waves for the mean value of the five categories retail and recreation, grocery and pharmacy, parks, transit stations and workplace with respect to a baseline, which is defined as the median value for the corresponding day of the week, during the pre-pandemic 5-week period from 3 January until 6 February 2020. We found a temporal variation in mobility across all five categories during the second wave, with the median mobility reached its minimum in the week starting on 16 November 2020, with a reduction of −47.7% (mean of all categories) from baseline. Shortly thereafter, mobility recovered with an estimated reduction in mobility in the week starting on 14 December 2020 reaching −27.8% from baseline. Of note, we observed a considerable increase in weekly case numbers of SARS-CoV-2 infections,

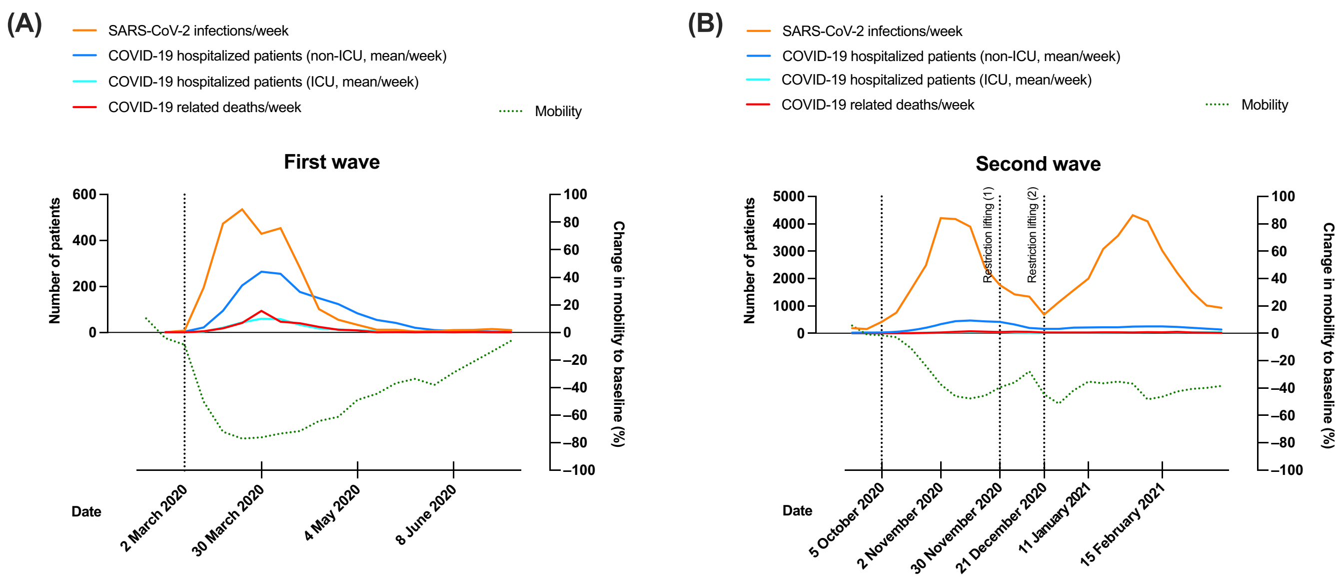

FIGURE 2 Numbers of SARS-CoV-2 cases, hospitalizations and deaths related to COVID-19 and mobility data in South Tyrol during the first (A) and second (B) pandemic waves. Mobility data from South Tyrol (Autonomous Province Bolzano/Bozen) as retrieved from Google Inc, representing the percentual change from pre-pandemic baseline mobility. Mobility is depicted as the mean value from the categories retail and recreation, grocery and pharmacy, parks, transit stations and workplace (green spotted line) and was overlaid with weekly COVID-19-associated deaths (red line), SARS-CoV-2 infection rates (orange line), hospitalized patients (dark blue line) and patients in ICU (light blue line) related to COVID-19 during the respective lockdown period. The dotted vertical lines indicate two important points in time when restrictions were lifted in South Tyrol [Color figure can be viewed at wileyonlinelibrary.com]

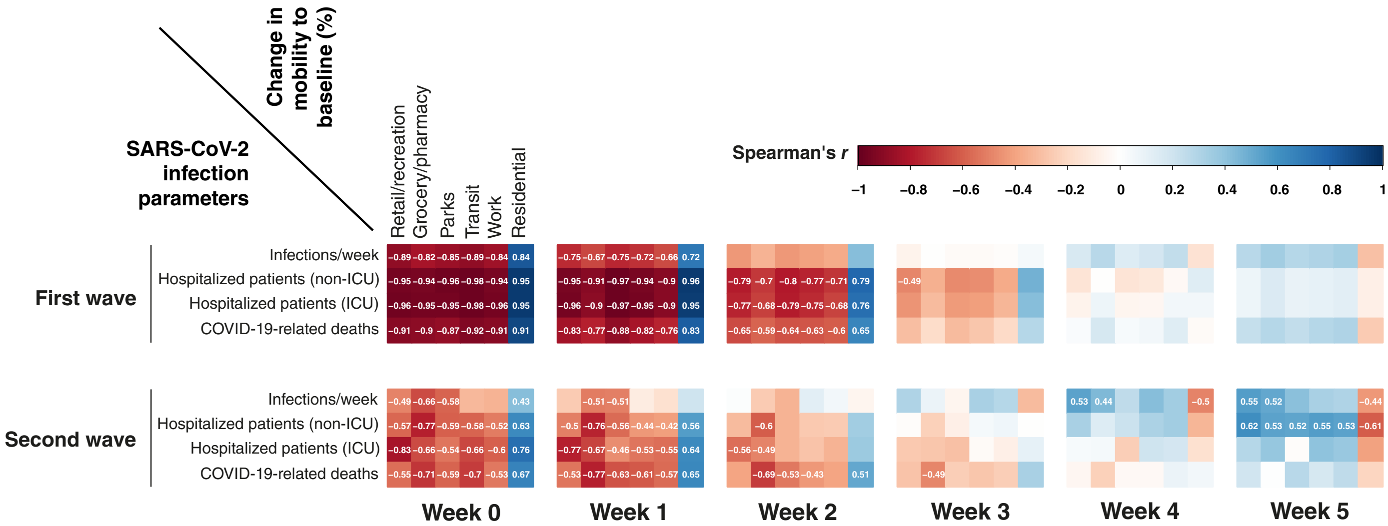

FIGURE 3 Correlation heatmaps between SARS-CoV-2 infection parameters and mobility in South Tyrol over time. Spearman correlation coefficients (r) of the number of new SARS-CoV-2 cases per week, COVID-19-related (non)-ICU admissions and COVID-19-associated deaths with each place category from Google Mobility Report. Weeks −1 to −5 represent correlations of new SARS-CoV-2 cases, COVID-19 associated hospitalizations and deaths with mobility data of the preceding 1 to 5 weeks. Spearman correlation coefficient was omitted for insignificant values (P > .05) [Color figure can be viewed at wileyonlinelibrary.com]

with a lag time of few weeks during the second wave, after two different points in time when the provincial government announced to reopen commercial activity (30 November 2020) and further easement of restrictions over the holiday season (21 December 2020; dotted vertical lines; Figure 2B).

More specifically, Figure 3 shows Spearman correlation coefficients between weekly epidemiological and mobility parameters for both pandemic waves. Overall, changes in mobility parameters significantly correlated with new SARS-CoV-2 cases/week, hospital admissions (both non-ICU and ICU wards) and deaths associated with COVID-19 in the general population. In both pandemic waves, a decrease in mobility was significantly associated with still increasing numbers of infections, admissions including ICUs and deaths in the same week where mobility changes took place ("week 0"), albeit at a lesser extent in the second wave (first wave: $|r|$ = .82-98; second wave: $|r|$ = .43-.83). However, cases, admissions and deaths were positively correlated with mobility parameters that changed in the preceding 4 to 5 weeks ("week −4/week −5") in the second pandemic wave ($|r|$ = .44-.62, P < .05), suggesting a latency of up to 5 weeks between changes in mobility restrictions and alterations in epidemiological parameters.

3.4 | Effectiveness of additional local interventions on SARS-CoV-2 transmission in cancer patients

Figure 4A shows the positivity rates of SARS-CoV-2 PCR tests per week from our outpatient department compared to the general population in South Tyrol, with significant differences in 7/19 weeks (P-values as given in Figure 4A, chi-square test). Our findings demonstrate that the test positivity rate in the general population as well as

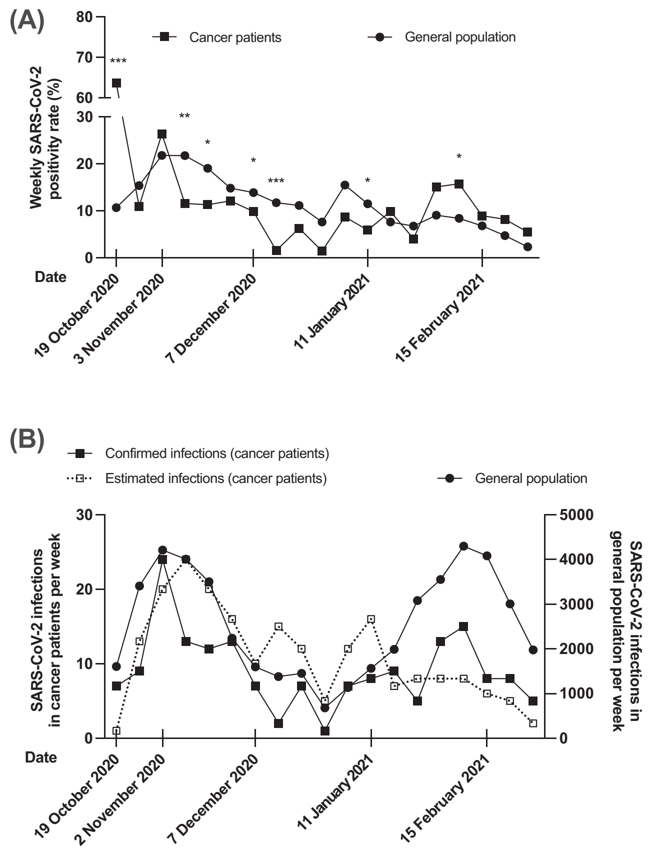

FIGURE 4 (A) Weekly test positivity rates and (B) new SARS-CoV-2 infections in the general population and patients with cancer at our department. In patients with cancer, confirmed SARS-CoV-2 infections (as determined by RT-PCR) were compared to estimated cases as calculated by positivity rates of the general population multiplied by the number of performed PCR tests at our department. *P < .05, **P < .01 and ***P < .001 as determined by chi-square test

our cancer patients continued to decline (remain comparable) over the given period. The disconnection to the rise in infection rates in the same period (Figure 4B) appears to be driven by a significant increase in testing over time. As most of that screening involved people who had no exposure or symptoms, numerous negative results were generated, possibly explaining that the positivity rates may stay relatively flat or decrease even as infection rates and case counts climbed. Of note, an estimated number of 62 SARS-CoV-2 cases were prevented at out outpatient department within the first 14 weeks of the 19-week observation period. In total, this means a reduction of 58.5% (62/106) of cases, which can be attributed to additional specific precautions and continued patient education against COVID-19 at our department.

4 | DISCUSSION

In light of the ongoing global COVID-19 pandemic, there is a growing body of evidence regarding the clinical and epidemiological characteristics of SARS-CoV-2 infected patients. However, patients with cancer constitute a vulnerable population at higher risk of contracting severe COVID-19 disease, and data from the second pandemic wave are still limited for this risk group.[25-27] Our findings demonstrate that despite maintenance of strict local mitigation strategies, compared to the first wave, we observed a >20-fold increase in the number of confirmed SARS-CoV-2 positive cancer patients at our outpatient department during the second wave. Local easement of restrictions, and in particular relaxation of mobility, probably helped accelerated transmission of coronavirus in the general population, although the impact was much lesser within our clinic due to strict targeted containment measures.

Since the onset of COVID-19, a surge of interest has been noted in the use of cellphone mobility data to map epidemiologically relevant population movement, as mobile phone data can be collected in near real time from broad levels of the population and seems to be a reliable source of information.[28-31] Several studies have shown that mobility correlates with SARS-CoV-2 in terms of transmissibility, reproduction number or infection rate in different countries.[8-14] As these rapidly available data can also help to better understand the effect of movement restrictions or their ease and can be used to identify new hotspots for community transmission, mobility reports provide a useful tool for authorities for timing and modification of social distancing measures. In addition, modeling studies have already pointed out that resuming economic activities and social life is likely to lead to a resurgence of COVID-19.[11,32,33] However, while these studies examined the reduction of SARS-CoV-2 infections in the general population, available data on the effects in cancer patients are limited. Furthermore, the majority of studies analyzed the variation in human mobility after implementation of social distancing measures and its impact on transmission, while data on the effect of post-relaxation mobility on SARS-CoV-2 are limited.

Vinceti et al described the effect of two successive lockdowns with different intensity in Northern Italy.[34] They found that mobility restriction inversely correlated with the daily number of newly diagnosed SARS-CoV-2 cases only after the second, more rigid lockdown. Similar to the study by Badr et al[35] who reported a lag time of 11 days since the beginning of social distancing to the onset of COVID-19 case growth reduction, they noted a peak in new cases occurring about 14 to 18 days after the implementation of tight measures. In contrast, less stringent measures led to an insufficient reduction in mobility without affecting the infection curve.

To the best of our knowledge, this is the first report to take into account the effect of changes in mobility and its impact on SARS-CoV-2 infections in cancer patients after interventions have been relaxed. Compared to the first COVID-19 pandemic wave, when Italy imposed a national lockdown, we observed a significant increase of SARS-CoV-2 infections in South Tyrol during the second wave, after the provincial government enacted less strict restrictions and early relaxation of interventions. To obtain a quantitative estimate of the infection patterns for the general population compared to cancer patients, while taking into account the reinforced test strategy, we also compared the positivity rate of both subgroups. Despite a more aggressive testing strategy at our department, the number of confirmed SARS-CoV-2 positive cases was significantly lower throughout the second pandemic wave compared to the general population. Our results indicate that adherence to strict preventive measures can reduce the risk of potential additional infection rates in specific risk groups like cancer patients, if social-distancing interventions are being lifted.

In a recent comparative analysis including nine countries and regions from Europe and the Asia Pacific region, Han et al presented important lessons that can be learnt about the complex and challenging task of easing COVID-19 restrictions.[36] Among others, they pointed out the importance of protecting most vulnerable populations to reopen safely. Therefore, despite strict adherence to measures to prevent and control transmission, a resurgence of infection is likely when restrictions are lifted prematurely, particularly if additional risk factors such as the spread of more contagious virus variants occur. As treatment delay in oncological patients may have a potential negative effect on the outcome,[37] close monitoring and continuation of mitigation strategies are necessary to reduce the risk for SARS-CoV-2 infection in cancer patients exposed to a hospital environment considered at risk for transmission. Thus, policy makers should also take into account additional localized and temporal preventive efforts, which result in lower number of infection rates in these vulnerable subpopulations. Under the pressure of the reopening of economic activities, more detailed studies are needed to assess targeted implementation of mobility restrictions for specific risk groups such as patients with cancer.

Another important issue related to lockdown and mobility restrictions might be their effects on physical activity and mental health support. Several studies have reported a positive influence of physical activity and exercise on the reduction of recurrence and mortality in cancer patients as well as a favorable impact on cancer- and treatment-related side effects.[38] As the pandemic increased the unhealthy behaviors in the population, maintenance and adherence to an active lifestyle are crucial. In order to optimize daily physical activity and reach as many patients, the use of personalized telehealth tools may be helpful.[39] In addition, COVID-19 amplifies the health risks of hot weather particularly in people with underlying medical conditions.[40] Therefore, authorities and communities should be prepared for hot weather and heat waves to reduce heat-related illness.

Important limitations of our study include the retrospective study design within a single institution as well as not considering here the potential impact to infection rates due to population-based interventions including social distancing and personal protective equipment that may also lead to a reduction of the transmissibility. In addition, mobile phone data may not be generalizable and applicable to the overall population, as some demographic groups like children or elderly may be under-represented.[31] Furthermore, as noticed in other countries, emergence of novel SARS-CoV-2 variants, which is a natural event due to mutations in the RNA virus genome, was also detected in South Tyrol. The new variants, which have rapidly become dominant in United Kingdom (B.1.1.7; also known as 501Y.V1/VOC-202012/01), South Africa (501Y.V2/B.1.351/20H) or Brazil (P.1/B1.1.28.1/20J/501YV3), have aroused concern in different countries through their effects on virus transmissibility, disease severity, reinfection rates and the effectiveness of vaccines.[41] As on 28 February 2021, we could detect four mutant strains of SARS-CoV-2 (three B.1.1.7 variants and one 501Y.V2 variant) within our patient cohort. Further genomic surveillance is necessary to clarify if spread of these variants in cancer patients may lead to greater hospitalizations and mortality.

In conclusion, our findings underscore the importance of maintaining additional strict preventive control measures as well as testing and contact tracing in vulnerable subpopulations such as cancer patients, particularly if social restriction policies are being lifted. Considering the uncertainty about the impact of new virus variants as well as the probability that COVID-19 will further persist or become a recurrent seasonal disease, strategies to modify protection of at-risk individuals are an urgent need. Further studies may evaluate the effect of these measures to reduce morbidity and mortality in cancer patients during COVID-19 pandemic.

ACKNOWLEDGMENTS

The authors thank all the staffs of the Outpatient Clinic for their efforts and dedication to the study and acknowledge all the participants whose contributions made our study possible. This work has been supported by the budget of the Südtiroler Sanitätsbetrieb.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The datasets used and analyzed during our study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

The study was approved by the local ethics committee of the "Südtiroler Sanitätsbetrieb" (amended protocol number 35-2020) and was performed in accordance with national regulations and the Declaration of Helsinki and all its amendments. Informed consent was obtained from all individual participants included in the study.

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How to cite this article: Fong D, Mair MJ, Lanthaler F, Alber M, Mitterer M. Mobility as a driver of severe acute respiratory syndrome coronavirus 2 in cancer patients during the second coronavirus disease 2019 pandemic wave. *Int. J. Cancer*. 2022;150(3):431-439. doi:10.1002/ijc.33838