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Rapid Adaptation of Breast Radiotherapy Utilization during the COVID-19 Pandemic at a Large Academic Cancer Centre in Canada

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Abstract:	Background: Mitigation strategies to balance the risk of COVID-19 infection against oncologic risk in breast cancer patients undergoing radiotherapy have been deployed. To this end, shorter hypofractionated regimens have been recommended where appropriate, with prioritization of radiotherapy by oncologic risk and omission or deferral of radiotherapy for lower risk cases. Timely adoption of these measures reduces COVID-19 risk to both patients and health care workers, and preserves resources. Herein we present our early response and adaptation of breast radiotherapy utilization during the COVID-19 pandemic at a large academic cancer centre in Canada. Methods : A state of emergency was announced in Ontario on March 17, 2020 due to the COVID-19 pandemic. Emergency guidelines were instituted. To examine our response, the number of weekly breast RT starts, type of breast RT, and patient age were compared from March 1 to April 30, 2020 to the same period in 2019. Results: Following the declaration of emergency in Ontario, there was a decrease of 39% in radiotherapy starts in 2020 compared to 2019 (79 vs . 129, p<0.001). There was a relative increase in the proportion of patients receiving regional nodal irradiation (RNI) in 2020 compared to 2019 (46% vs . 29%, respectively), with the introduction of hypofractionated RNI in 2020 (27 of 54 cases, 50%). A smaller proportion of patients starting radiotherapy were aged > 50 years in 2020, 66% (78/118) vs . 83% (132/160) in 2019, p=0.0027. Conclusions : A significant reduction in breast radiotherapy starts was noted during the early response to the COVID-19 pandemic, with prioritization of radiotherapy to patients associated with higher oncologic risk requiring RNI. A quick response to a

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Rapid Adaptation of Breast Radiotherapy Utilization during the COVID-19 Pandemic at a Large Academic Cancer Centre in Canada

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Summary

The adaptation of breast radiotherapy utilization during the COVID-19 pandemic at a large academic cancer centre was evaluated. A significant reduction in breast radiotherapy starts was noted during the early response to the pandemic, with prioritization of radiotherapy to patients associated with higher oncologic risk. A rapid response to a health care crisis is critical, and is of particular importance for higher volume cancer sites where the potential impact on resources is greater.

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Abstract

Background: Mitigation strategies to balance the risk of COVID-19 infection against oncologic risk in breast cancer patients undergoing radiotherapy have been deployed. To this end, shorter hypofractionated regimens have been recommended where appropriate, with prioritization of radiotherapy by oncologic risk and omission or deferral of radiotherapy for lower risk cases. Timely adoption of these measures reduces COVID-19 risk to both patients and health care workers, and preserves resources. Herein we present our early response and adaptation of breast radiotherapy utilization during the COVID-19 pandemic at a large academic cancer centre in Canada.

Methods: A state of emergency was announced in Ontario on March 17, 2020 due to the COVID-19 pandemic. Emergency guidelines were instituted. To examine our response, the number of weekly breast RT starts, type of breast RT, and patient age were compared from March 1 to April 30, 2020 to the same period in 2019.

Results: Following the declaration of emergency in Ontario, there was a decrease of 39% in radiotherapy starts in 2020 compared to 2019 (79 *vs*. 129, $p<0.001$). There was a relative increase in the proportion of patients receiving regional nodal irradiation (RNI) in 2020 compared to 2019 (46% *vs*. 29%, respectively), with the introduction of hypofractionated RNI in 2020 (27 of 54 cases, 50%). A smaller proportion of patients starting radiotherapy were aged $\geq$ 50 years in 2020, 66% (78/118) *vs*. 83% (132/160) in 2019, $p=0.0027$.

Conclusions: A significant reduction in breast radiotherapy starts was noted during the early response to the COVID-19 pandemic, with prioritization of radiotherapy to patients associated with higher oncologic risk requiring RNI. A quick response to a health care crisis is critical, and is of particular importance for higher volume cancer sites where the potential impact on resources is greater.

Introduction

In Canada and around the world, healthcare providers are doing extraordinary work to mitigate the transmission of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). Early data suggest that mortality from the virus ranges from 1-4% in the overall population (2), with more severe disease and higher death rates amongst patients with comorbidities and older age (3-5). As well, the risk of infection has been reported to be approximately two-fold higher in cancer patients than the normal population (3,6,7). Therefore, in the management of cancer patients, oncologists must weigh the risk of death and morbidity from COVID-19 against the benefit of cancer therapy when there is the necessity to decrease patient visits to cancer centres, and the potential reduction of health care worker availability due to illnesses (8,9). Consequently, general measures to mitigate COVID-19 transmission to cancer patients receiving radiotherapy have been already described (10).

Breast cancer patients constitute one of the largest groups of patients at most cancer centres, and guidelines for prioritization and multi-disciplinary breast cancer treatment have been developed to assist management decisions during the COVID-19 pandemic (11-13). The majority of breast cancer patients require radiotherapy as part of their overall management, and breast cancer represents approximately 25% of all cases treated with radiotherapy in Ontario (13). Therefore, reducing patient visits to cancer centres at different parts of the COVID-19 pandemic curve is important. Key strategies to mitigate COVID-19 infection in patients requiring breast radiotherapy include the shortening of overall treatment time using hypofractionated (HF) regimens (14), delay of radiotherapy initiation in those with lower oncologic risk, or radiotherapy omission for older lower risk patients, or those with comorbidities, with endocrine therapy (ET) as an alternative (13,15). The effectiveness of these mitigation strategies is dependent on the rapid adoption of these measures. Herein, we describe the experience of early

adoption of such practices during the COVID-19 pandemic in a large academic radiation medicine program.

Methods

This study is an evaluation project of adjuvant breast radiotherapy delivery and utilization at our institution during a 9-week period spanning March 1 to April 30, 2020, compared to the same period in 2019 (Institutional waiver 20-0464). Data collection was performed according to our standard work processes, and included the monitoring of weekly breast radiotherapy starts, type of radiotherapy delivered, and patient age.

In response to the COVID-19 pandemic, a state of emergency was declared in Ontario on March 17, 2020. Our institution followed the principles of the COVID-19 prioritization and breast radiotherapy planning guidelines in accordance with provincial and international guidelines (13,15). Patients were prioritized for breast radiotherapy by higher oncologic risk: the high risk category included patients with locally advanced or pT3-4/pN2-3 disease, and residual nodal after neoadjuvant chemotherapy; intermediate risk included estrogen receptor (ER) positive and pN1a disease, and complete pathologic response after neoadjuvant chemotherapy; and low risk included DCIS and early stage invasive disease.

Consideration of ET only and omission of radiotherapy was made for women aged $\geq$ 70 years with completely excised (minimum margin of 1 mm) low risk invasive disease (pT1/pN0, grades 1 or 2, lymphovascular invasion (LVI) negative, ER positive, HER2 negative, without extensive intraductal component). For patients > 55 years with DCIS measuring < 2.5 cm, grades 1 or 2, and minimum margin of 1 mm, radiotherapy omission was also considered. After breast conserving surgery, radiotherapy delays up to 20 weeks were considered for patients with low-intermediate risk invasive disease (pT1-2/pN0), or DCIS, with systemic therapy, and up to 12 weeks without systemic therapy (16-18). Some low

risk patients eligible for ET, received neoadjuvant ET while waiting for their breast surgery, and adjuvant radiotherapy. Patient comorbidities and performance status were also considered in the decision-making for radiotherapy deferral or omission. Weekly multi-disciplinary case conference, and weekly radiotherapy quality assurance rounds assisted with consensus-building and treatment decisions.

Other key mitigation strategies included adoption of HF regimens to shorten treatment time and minimize visits to the cancer centre. Specifically, preference was given to HF regimens of 40.05 Gy in 15 fractions daily for breast radiotherapy, including regional nodal irradiation (RNI), over conventional fractionation of 50 Gy in 25 fractions (19). In addition, following the publication of the UK FAST-Forward trial (20), 26 Gy in 5 fractions daily for whole breast irradiation (WBI) or partial breast irradiation (PBI) was included as an option to 40.05Gy/15 fractions or 42.40Gy/16 fractions for suitable patients. For patients eligible for a boost (margins less < 1mm, patient age < 40 years, or < 50 years with high risk features of LVI, ER negative or grade 3 disease), the majority received 10Gy/4 fractions. For the purpose of this study, the number of new patients starting radiotherapy was monitored, therefore delivery of a boost was not considered an additional radiotherapy course. To approximate the overall impact on radiotherapy capacity, the total number of treatment visits during this period was also measured and compared to 2019.

For statistical analyses, the exact Poisson test was used to assess equality of two rates, and Pearson's chi-square test for equality of two proportions. All tests were two-sided, and a *p*-value (*p*) less than 0.05 was considered statistically significant.

Results

There was a total of 118 breast radiotherapy starts during the 9-week period following March 1, 2020 compared to 160 starts in the same period in 2019 (Fig. 1). An initial drop in the number of breast

radiotherapy starts was noted within the first 2 weeks after implementation of our emergency guidelines in mid-March (March weeks 3 and 4) compared to 2019, from 43 to 33 (exact Poisson test p = 0.10), representing a 24% decrease (Fig. 1). A significant reduction in radiotherapy starts of 54% (from 34 to 16, 2019 *vs*. 2020, exact Poisson test $p < 0.001$) was observed in the following two weeks (March week 5, April week 1) (Fig. 1). Thereafter in April 2020, the number of radiotherapy starts continued to remain lower than in 2019. There was a total decrease of 39% in radiotherapy starts in 2020 compared to 2019 (79 *vs*. 129, exact Poisson test $p < 0.001$) measured from the beginning of the third week in March (Fig. 1). During the 9-week period in 2020, there were 4 patients with confirmed COVID-19 infection who required a 2-week treatment delay.

When the types of breast radiotherapy plans were evaluated during the 9-week period, a relative increase of 17% in the number of radiotherapy plans that included RNI was noted in 2020 compared to 2019; 46% (54/118) *vs*. 29% (46/160) of all radiotherapy starts, respectively (chi-square test p = 0.005) (Fig. 2A, Table 1). Prior to the COVID-19 pandemic, the standard regimen for RNI used at our centre was 50 Gy in 25 fractions, with HF RNI introduced during the pandemic to shorten RT. We observed a dramatic rise in the use of the 4-field HF RNI regimen during the 9-week period in 2020 (27 of 54 cases, 50%), which corresponded to 270 fewer treatment visits (Table 1). The majority (26 of 27 patients; 96%) receiving HF RNI began radiotherapy from the end of March 2020, approximately 2 weeks after the COVID-19 prioritization guidelines were implemented (Table 1). In comparison, all radiotherapy plans that included RNI in 2019 during the same period used conventional 2 Gy daily fractionation regimen of 50 Gy in 25 fractions (Table 1).

For node negative or breast cancer patients not requiring comprehensive RNI (WBI, PBI, chestwall and high-tangent plans), there was a significant decrease in breast radiotherapy starts during the 9-week period in 2020 compared to 2019; 54% (64/118) *vs*. 71% (114/160) of overall cases, respectively (chi-square test p = 0.005) (Fig. 2B, Table 1). There were only 2 PBI starts after week 3 in March 2020

compared to 13 in the same period in 2019 (Table 1). There was a shift in the use of WBI regimen of 42.40Gy/16 fractions to 40.05Gy/15 fractions observed in early April 2020 (Table 2). The abbreviated 26 Gy in 5 fractions daily regimen for WBI or PBI was introduced after the first week of May, 2020, coinciding with the publication of the FAST-Forward trial (20); no radiotherapy starts with this regimen were noted prior to May 2, 2020. The proportion of boosts delivered in 2020 was 40% (47/118) compared to 48% (77/160) in 2019, corresponding to 120 fewer treatment visits (chi-square test p = 0.21) (Table 3).

In general, older breast cancer patients are more vulnerable to COVID-19 related morbidity and mortality (21). Therefore, the proportion of breast radiotherapy starts for those aged < 50 years *vs*. $\geq$ 50 years during the 9-week period was compared for 2019 and 2020. In 2019, a smaller proportion of patients starting radiotherapy were less than 50 years of age; 18% (28/160) *vs.* 34% (40/118) in 2020 (Fig. 3A). In turn, more patients in 2019 were greater than 50 years; 83% (132/160) *vs.* 66% (78/118) in 2020 (chi-square test $p = 0.0027$) (Fig. 3B). From the beginning of April, there was also a significant difference based on age in 2019 compared to 2020, with breast radiotherapy starts for patients under 50 years at 13% (9/69) in 2019 *vs*. 37% (14/38) in 2020, and for those 50 years or greater, 87% (60/69) in 2019 *vs*. 63% (24/38) in 2020 (chi-square test $p = 0.0087$) (Figs. 3A, 3B).

Based on the number of radiotherapy starts and the total number of fractions per course (inclusive of boost), there was an overall reduction of 45% in the number of visits for breast radiotherapy from 2705 to 1482, measured from mid-March in 2019 and 2020, respectively (Table 3).

Discussion

The COVID-19 pandemic has posed challenges for the delivery of cancer care, with increased risk for vulnerable cancer patients. The safe delivery of care during the pandemic has been guided by

prioritization of oncologic risk and by mitigation strategies to minimize the risk of COVID-19 infection. Rapid deployment of these measures is pivotal to a radiation medicine program, particularly for high volume sites such as breast cancer.

We were able to rapidly implement changes to significantly reduce breast radiotherapy starts, and decrease the overall number of radiotherapy visits to our centre, after the declaration of emergency in Ontario. Patients with higher oncologic risk were prioritized for breast radiotherapy, as judged by the receipt of RNI, which is typically reserved for those with locally advanced or node positive disease. Overall, there was a substantial increase in the proportion of radiotherapy starts that included RNI in 2020 compared to 2019, and a concomitant proportional reduction in the delivery of radiotherapy that excluded comprehensive RNI, usually delivered to patients with node negative or lower risk disease. Collectively, these results suggest that higher risk breast cancer patients were prioritized for breast radiotherapy as a consequence of the adoption of the COVID-19 pandemic guidelines.

There was also a significant decrease in proportion of radiotherapy starts for older patients in 2020 compared to 2019. This finding is consistent with the recommendation to preferentially defer or omit radiotherapy in older women who are eligible for ET. It is also possible that the decrease in radiotherapy starts were at least in part due to patient comorbidities, more likely to be associated with older than younger patients. Very few patients required a treatment delay during the 9-week period due to COVID-19 infection.

The introduction of HF regimens to shorten breast radiotherapy, resulted in a considerable reduction in the number of patient visits during the 9-week period in 2020 compared to 2019. Likely we will continue to see additional gains with the regimen of 26Gy/5 fractions which became available as an option for some patients in May, 2020 at our centre. As a result of decreasing the overall number of treatments, there is less risk to patients and to healthcare workers, reduced pressure on resources, and physical distancing is facilitated. As the availability of breast cancer surgeries and breast cancer screening

programs increase in parallel to a decreased risk of COVID-19, referrals for breast radiotherapy are expected to increase. Therefore, these HF regimens will likely continue to remain an important mitigation strategy for breast radiotherapy in the coming months. With the added possibility of a second wave of COVID-19 (22), there will be a need for flexibility and to nimbly adapt to the pandemic peaks and surges.

This study describes for the first time the experience and adaptation of breast radiotherapy utilization at a large academic centre in North America during the initial response to the COVID-19 pandemic. There have been several reports to date outlining recommendations for the prioritization and treatment of various cancer sites. However, very few reports describe the experience at the cancer centre from a radiation oncology perspective. In a recent retrospective study chronicling the early experience from a large radiation oncology department in New York City during March, 2020, there was a median reduction of 30% for all disease sites for patients on treatment, although the breast site demonstrated a small increase (23). In our study, breast radiotherapy utilization was significantly reduced which facilitated the redistribution of resources to other cancer sites more dependent on primary radiotherapy, such as head and neck.

We acknowledge the limitations of this study which was retrospective and conducted at a single centre. In addition to specific radiotherapy mitigation strategies, the introduction of virtual patient visits, use of personal protective equipment, and physical distancing have been important strategies to minimize COVID-19 risk. Furthermore, during this period we did not specifically capture the number of radiotherapy deferrals, cases with radiotherapy omission, patient comorbidities, patient preference for radiotherapy delay, or surgical delays. However, these factors would have primarily impacted older patients, patients with lower risk disease or patients with clinical comorbidities, and to a lesser extent in those with high risk disease. Indeed, there was a proportional increase in breast radiotherapy starts in 2020 compared to 2019 for higher risk disease requiring RNI.

In conclusion, we describe a rapid response to the COVID-19 prioritization and mitigation strategies for breast radiotherapy at a large academic cancer centre. Understanding the timeliness and effectiveness of the response assists in directing resources and planning during the pandemic. These results and other experiences will further assist in the ongoing management of the COVID-19 pandemic and of possible future health care crises.

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Figure Legends

Figure 1. Number of weekly breast radiotherapy starts comparing the 9-week periods of March 3-May 4, 2019 *vs*. March 1-May 2, 2020. The beginning of March week 3 in 2020 coincided with the declaration of state of emergency in Ontario.

Figure 2. Type of breast radiotherapy starts per week comparing the 9-week periods of March 3-May 4, 2019 *vs*. March 1-May 2, 2020. **A)** Regional nodal irradiation (RNI) starts per week compared for 2019 and 2020. **B)** Radiotherapy starts per week without comprehensive RNI (No RNI), including whole breast irradiation, partial breast irradiation, chestwall or high-tangent plans for 2019 and 2020.

Figure 3. Weekly breast radiotherapy starts comparing the 9-week periods of March 3-May 4, 2019 and March 1-May 2, 2020, for **A)** age < 50 years and **B)** age $\geq$ 50 years.

Breast RT	RNI		WBI/CW/HT		PBI	
2019	CF (25f)	HF (15-16f)	CF (25f)	HF (15-16f)	CF (25f)	HF (15-16f)
March W1	8			8		2
2	1			9		3
3	6			12		2
4	9		1	9		4
5	4		1	10		2
April W1	4			11		2
2	4		1	8		
3	5			7	1	2
4	5		2	14		3
Grand Total	*46*	*0*	*5*	*88*	*1*	*20*
2020						
March W1	7	1		11		
2	5			13		2
3	5			6		3
4	8	1		10		
5		4		3		1
April W1	1	5		2		
2	1	7		1		
3		5		7		1
4		4		4		
Grand Total	*27*	*27*	*0*	*57*	*0*	*7*

Table 1. Type of breast radiotherapy (RT) per week comparing the periods of March 3-May 4, 2019 (top panel) *vs*. March 1-May 2, 2020 (bottom panel). Abbreviations: CF, conventional fractionation; HF, hypofractionation; whole breast irradiation, WBI; chestwall, CW; high-tangent, HT; partial breast irradiation, PBI; regional nodal irradiation (RNI); f, fraction.

WBI/CW/HT Breast RT:	CF	HF		
2019	**50Gy/25f**	**42.56Gy/16f**	**42.4Gy/16f**	**40.05Gy/15f**
March W1		1	6	1
2			8	1
3			12	
4	1	1	7	1
5	1		10	
April W1			11	
2	1		8	
3			7	
4	2		12	2
Grand Total	***5***	***2***	***81***	***5***
2020				
March W1			10	1
2			13	
3			6	
4			10	
5			1	2
April W1				2
2				1
3				7
4		1		3
Grand Total	***0***	***1***	***40***	***16***

Table 2. Weekly breast radiotherapy (RT) regimens compared over the periods of March 3-May 4, 2019 (top panel) *vs*. March 1-May 2, 2020 (bottom panel). Abbreviations: CF, conventional fractionation; HF, hypofractionation; whole breast irradiation, WBI; chestwall, CW; high-tangent, HT; f, fraction.

2019	# Fx (with boost)	# Fx (without Boost)	# of Boost	# of Tx
March W1	398	358	9	18
2	237	213	6	13
3	414	372	10	20
4	513	453	13	23
5	337	315	5	17
April W1	339	306	7	17
2	291	253	9	13
3	323	292	7	15
4	488	442	11	24
Total	***3340***	***3004***	***77***	***160***

2020	# Fx (with boost)	# Fx (without Boost)	# of Boost	# of Tx
March W1	390	366	6	19
2	411	363	10	20
3	286	266	5	14
4	413	375	9	19
5	125	121	1	8
April W1	150	130	5	8
2	149	145	1	9
3	220	195	6	13
4	139	122	4	8
Total	***2283***	***2083***	***47***	***118***

Table 3. Comparison of the total number of fractions (# fx) per week for breast RT initiated during the 9-week period of evaluation, 2019 (left panel) *vs*. 2020 (right panel). Comparisons included the total number of fractions with and without boost, and the total number of RT courses (Tx) and the number of boosts delivered. Abbreviations: Tx, treatment.

Fig 1

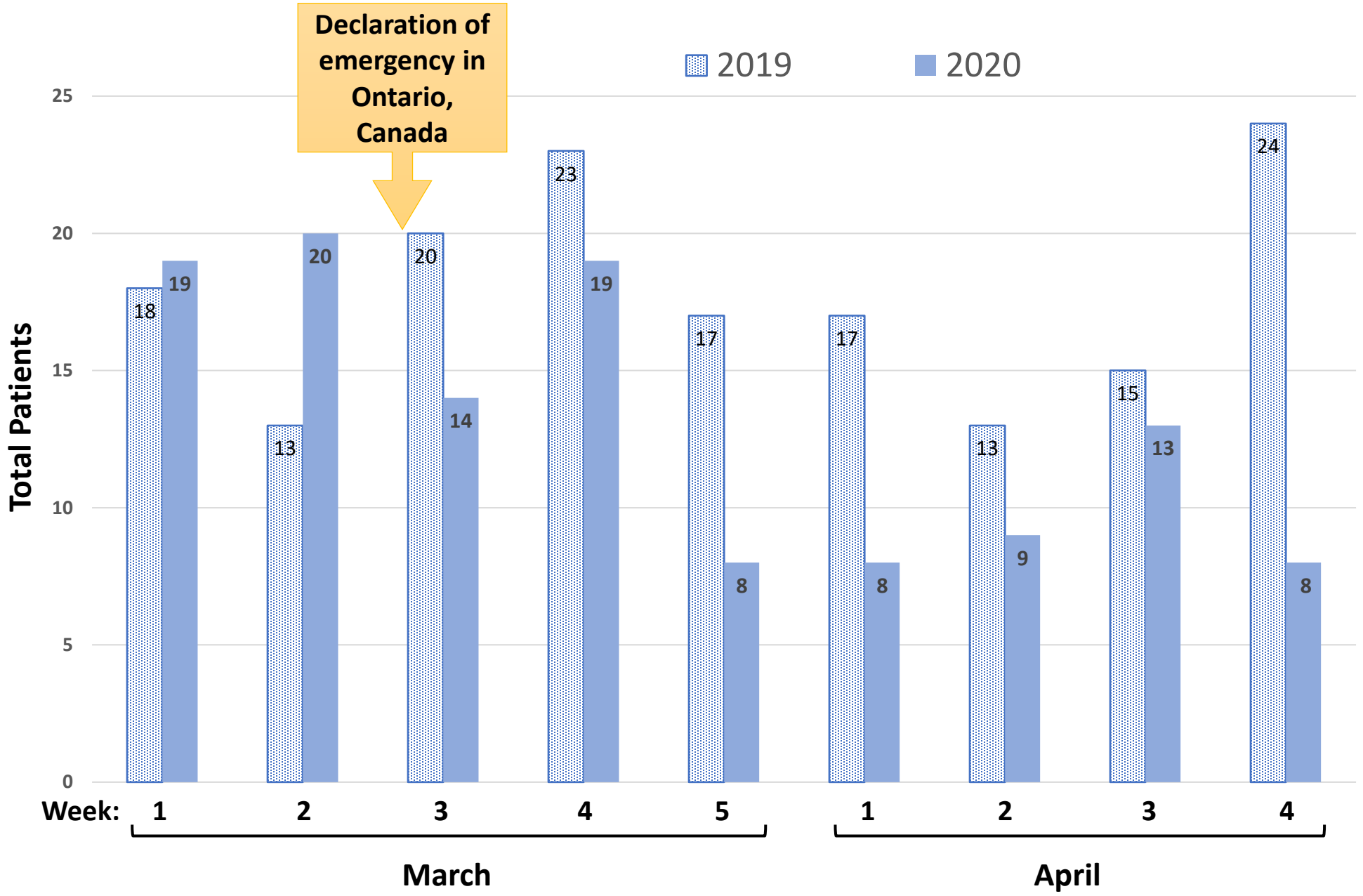

Fig 2A

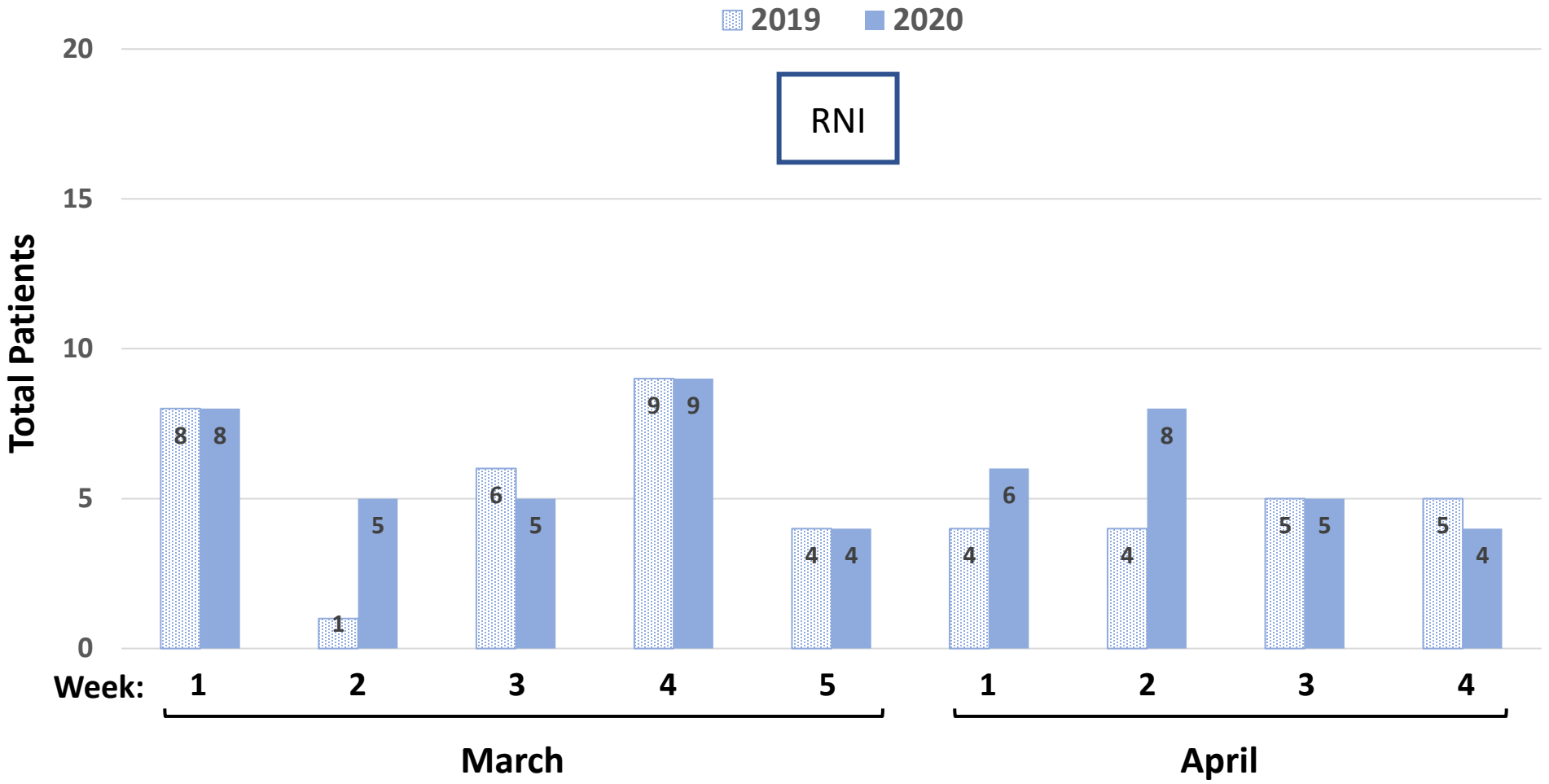

Fig 2B

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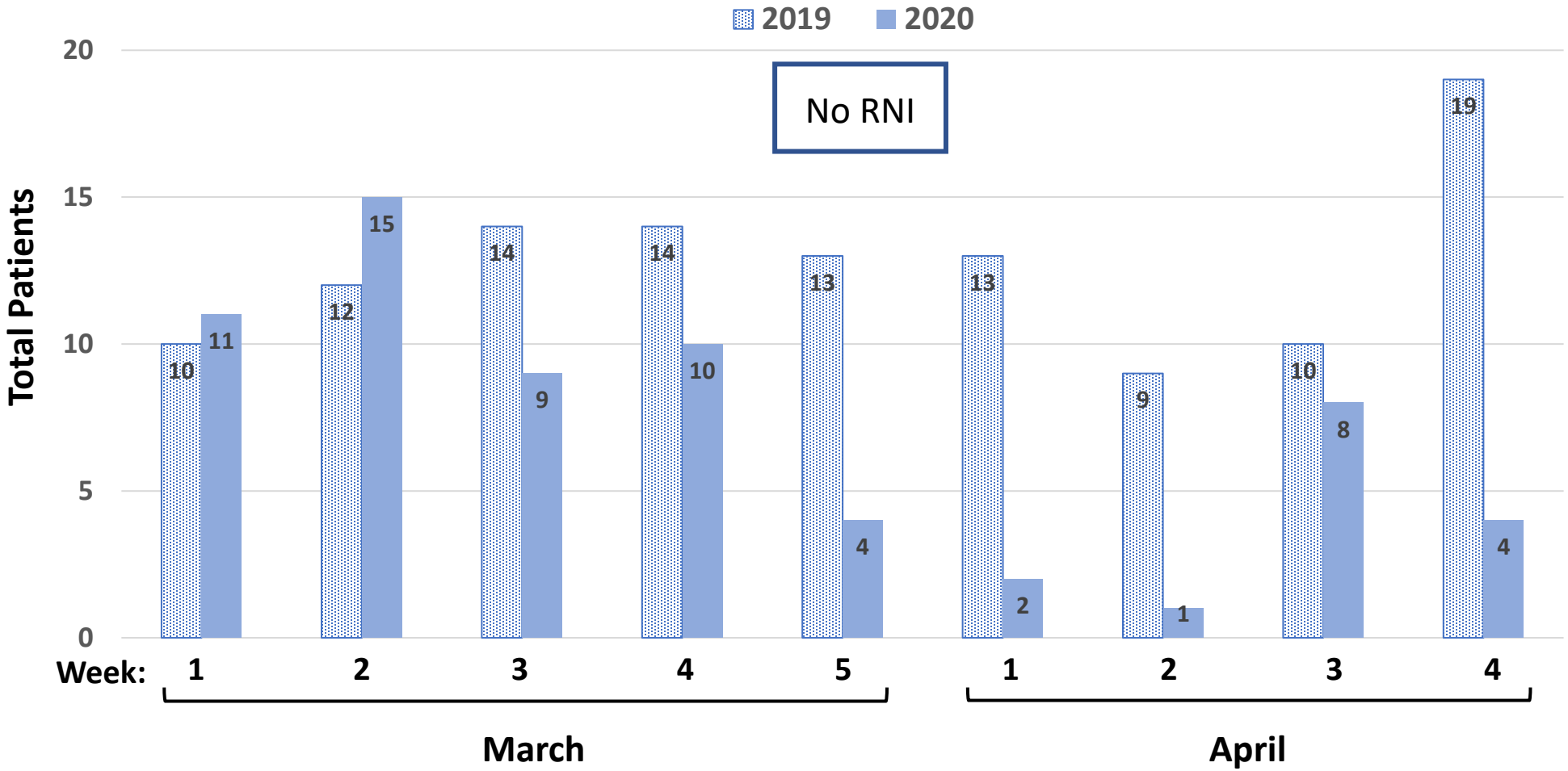

Fig 3A

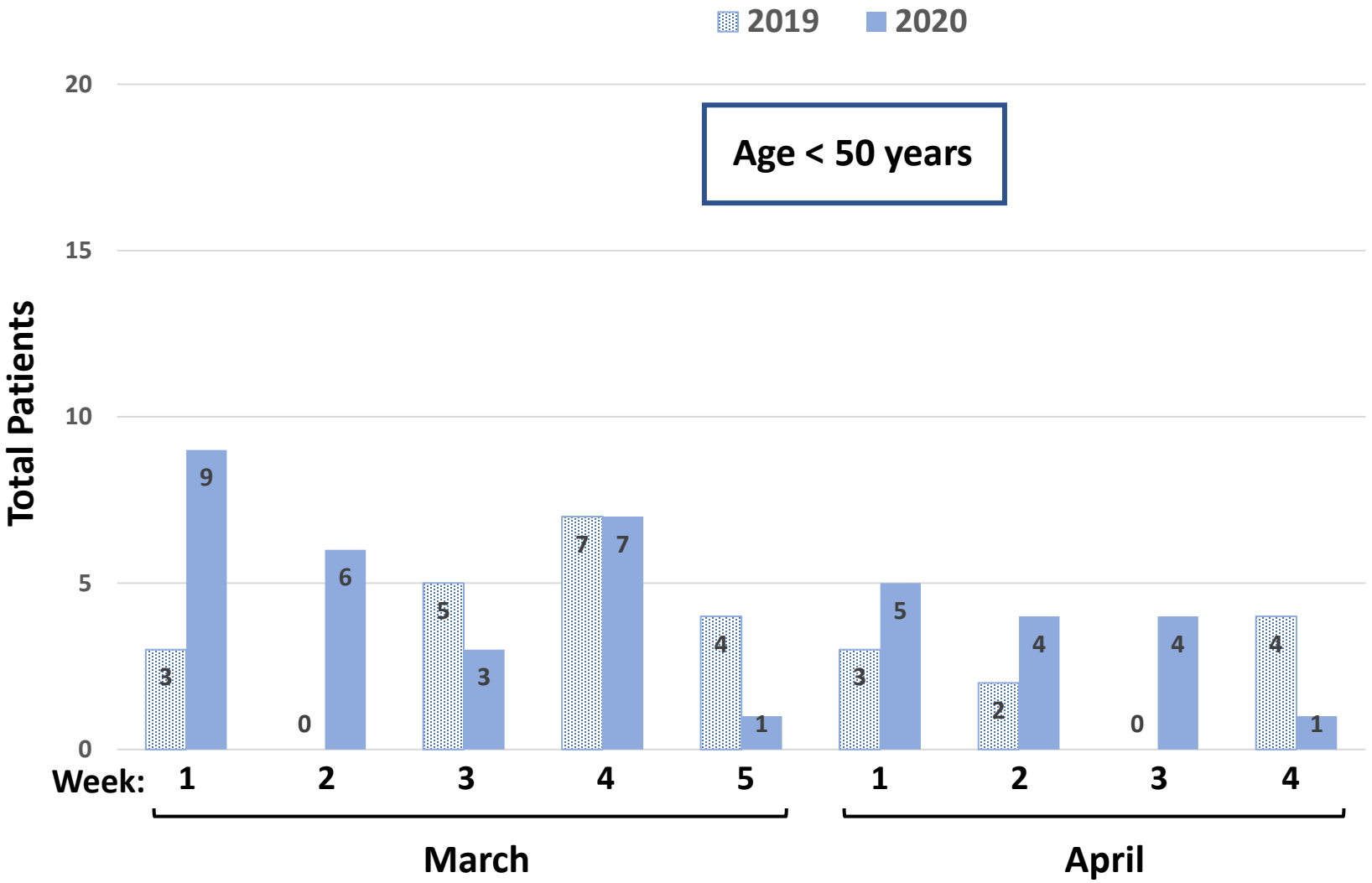

Fig 3B

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