

## **Impact of Covid-19 on Tuberculosis Prevention and Treatment in Canada: a multicentre analysis of 10,833 patients**

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**Summary:** At three TB centres in Montreal and Toronto, analysis of programmatic data reveal that cornerstone measures for maintaining TB control— treatment of latent and active tuberculosis— fell after Covid-19 public health emergencies were declared.

## **Footnote Page**

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## Abstract

We assessed the Covid-19 pandemic's impact on treatment of latent tuberculosis, and of active tuberculosis, at three centres in Montreal and Toronto, using data from 10,833 patients (8685 with latent tuberculosis infection, 2148 with active tuberculosis). Observation periods prior to declarations of Covid-19 public health emergencies ranged from 219 to 744 weeks, and post-declarations, from 28 to 33 weeks. In the latter period, reductions in latent tuberculosis infection treatment initiation rates ranged from 30% to 66%. At two centres, active tuberculosis treatment rates fell by 16% and 29%. In Canada, cornerstone measures for tuberculosis elimination weakened during the Covid-19 pandemic.

**Key words:** tuberculosis, latent tuberculosis, Covid-19, cascade of care, diagnosis, treatment

## 1 **Background**

2 Tuberculosis (TB) preventive therapy, along with prompt diagnosis and treatment of  
3 active TB, are cornerstones of TB control. In Canada, most TB prevention and care  
4 occurs in outpatient settings. Thus, we sought to determine if reductions in non-urgent  
5 clinical activities mandated in response to the Covid-19 pandemic resulted in fewer  
6 individuals initiating treatment for latent TB infection (LTBI) or active TB, in Canada's  
7 two most populous cities: Montreal and Toronto. Data from high TB burden, low and  
8 middle-income countries demonstrate an impact on various aspects of TB care in a  
9 variety of settings [1]. By contrast, few data have been published, on the impact of  
10 Covid-19 on LTBI treatment — a fundamental aspect of the World Health Organization's  
11 Global End TB Strategy in low TB incidence countries [2]. Such data are of value for  
12 understanding how Covid-19 mitigation policies might affect TB elimination efforts in low  
13 TB incidence countries.

14 Canada is a low TB burden country, with a national TB incidence of 4.8 per 100,000 in  
15 2017 [3]. However, TB incidence in certain Canadian subpopulations is considerably  
16 higher than the national average. In 2017, Montreal and Toronto saw TB rates of 6.0  
17 and 9.8 per 100,000, respectively [4, 5].

18 The cities of Montreal (in the province of Quebec) and Toronto (Ontario) have been the  
19 epicentres of Covid-19 in Canada. As of August 26, 2021, Canada had accumulated  
20 1,482,664 Covid-19 cases [6], of which 9% (136,960) in Montreal and 11% (168,864) in  
21 Toronto; and 26,864 Covid-19 deaths, of which 18% (4,775) and 13% (3,586) in  
22 Montreal and Toronto, respectively [7-9].

## 23 **Methods**

24 On March 14 and March 17, 2020, the provincial governments of Quebec and Ontario  
25 respectively declared public health emergencies due to the Covid-19 pandemic. In both  
26 provinces, public health emergency measures, enacted at different timepoints, included:  
27 mandated reductions in non-Covid-19 health care services such as halting non-urgent  
28 ambulatory medical visits; closure of non-essential businesses; limits on indoor and  
29 outdoor gatherings; cessation of in-person school attendance; and physical distancing  
30 and mandatory mask wearing in indoor public places. Stay-at-home orders were not  
31 enacted during the period under study. Using data from electronic medical record  
32 systems, we compared treatment starts for LTBI and active TB pre- and post-public  
33 health emergency declarations in three TB clinics in Montreal and Toronto: the Montreal  
34 Chest Institute (MCI), Toronto Western Hospital (TWH), and St. Michael's Hospital  
35 (SMH, Toronto). All three are tertiary centres specialized in TB care, receiving referrals  
36 for LTBI and active TB diagnosis and treatment from large networks of general  
37 practitioners, specialists, public health departments, and Canada's federal immigration  
38 programme. We used treatment initiation as a metric of evaluation because in all three  
39 clinics, every patient prescribed LTBI or active TB treatment is registered in the clinic  
40 database.

41 Data were available from November 26, 2005 to November 3, 2020 and January 1,  
42 2006 to October 27, 2020 at the MCI and TWH, respectively. At SMH, data were  
43 available from January 1, 2016 to September 29, 2020 for LTBI, and from April 2, 2011  
44 to September 29, 2020 for active TB. For each clinic, we counted the number of patients  
45 starting treatment each week, for LTBI and for active TB, separately. We classified each

46 week as falling either in the “Covid era” or the “pre-Covid era”. The Covid era started  
47 Week 12 of 2020, the week after the provincial governments declared public health  
48 emergencies. The pre-Covid era included all weeks up to Week 12 of 2020. We used  
49 Poisson regression to estimate rate ratios and 95% confidence intervals (CI) comparing  
50 weekly rates of treatment initiation (number of patients starting treatment per week) in  
51 the Covid and pre-Covid eras. In order to account for confounding from variations in  
52 weekly and yearly treatment initiations, the model adjusted for the year and the week of  
53 the year. All analyses were performed using R statistical software (RStudio, version  
54 1.3.1073) [10]. Each site either had research ethics board approval or waiver of review  
55 requirement due to use of aggregate data for quality improvement.

## 56 **Results**

57 **Table 1** compares the pre-Covid and Covid eras with respect to the number of weeks of  
58 observation available, number of patients starting therapy, and weekly rates of  
59 treatment initiation. A total of 8685 patients initiated LTBI treatment during the study  
60 period: 6842 at the MCI, 1534 at TWH, and 309 at SMH. At each site, the adjusted rate  
61 ratio comparing the number of LTBI treatment initiations per week between Covid and  
62 pre-Covid eras demonstrated significant reductions ranging from 30% at the MCI to  
63 66% at SMH. **Figure 1** shows the average number of weekly LTBI registrations in each  
64 year.

65 A total of 2148 patients initiated treatment for active TB: 869 at the MCI, 927 at TWH,  
66 and 352 at SMH. The adjusted rate ratio for per week for active TB treatment initiation  
67 was lower in the Covid era by 16% at the MCI and by 29% at TWH. At SMH, the

68 adjusted rate ratio showed a 2% higher rate of active TB treatment initiation during the  
69 Covid era. The observed differences in active TB treatment initiation rates between  
70 Covid and pre-Covid eras were not significant at any of the three sites.

71 We did three sensitivity analyses. First, for both LTBI and active TB, we fit an  
72 autoregressive model to account for potential correlation between weeks. Results were  
73 very similar, with little to no difference in the rate ratios and corresponding 95% CIs. The  
74 degree of correlation between two consecutive weeks were minimal, ranging from -0.05  
75 to 0.05 for all but one model. The only exception was LTBI treatment initiations at the  
76 MCI, with a correlation of 0.28, and accounting for correlation the adjusted rate ratio  
77 was 0.69 (95%CI: 0.51, 0.94).

78 The second sensitivity analysis focused on latent TB treatment. We divided the Covid  
79 era into two time periods: first wave, and post-first wave, defining the latter period as the  
80 time from when clinical services were permitted to start increasing again (approximately  
81 mid-June in all sites) until the date that data were extracted at each site. Overall,  
82 150/225 Covid-era LTBI treatment initiations occurred post-first wave. At the MCI and  
83 TWH, the rate of LTBI treatment initiation were significantly higher post-first wave vs  
84 during the first wave (rate ratios: MCI, 1.7, 95%CI: 1.2-2.3; TWH, 2.1, 95%CI: 1.0-5.1)  
85 but did not exceed the pre-Covid era (i.e. there was no evidence of catching up in  
86 diagnoses, comparing post-first wave to pre-Covid era: MCI, 0.9, 95%CI: 0.7-1.1; TWH,  
87 0.9, 95%CI: 0.6-1.4). At SMH, LTBI treatment initiation rates post-first wave were nearly  
88 identical to during the first wave (comparing post-first wave to first wave: 1.0, 95%CI:  
89 0.4, 2.8) and significantly lower than pre-Covid era rates.

90 The third sensitivity analysis restricted the analysis for latent TB infection to individuals  
91 who were at high risk of re-activation: close contacts or immunosuppressed individuals.  
92 The observed associations were similar as in our primary analyses for the two sites  
93 where data on re-activation risk were available (MCI: 0.80 [95%CI: 0.64-0.98]; SMH:  
94 0.61 [95%CI: 0.29-1.19]).

## 95 **Discussion**

96 To assess the impact of Covid-19 on latent and active tuberculosis treatment initiation,  
97 we used data from three tuberculosis clinics in Canada: the Montreal Chest Institute,  
98 Toronto Western Hospital, and St. Michael's Hospital. We found that during and  
99 immediately after the first wave of Covid-19 in Quebec and Ontario, all three centres  
100 experienced major reductions in the initiation of treatment for LTBI, and at two centers  
101 there were signs of reduced treatment initiation for active TB as well. For both latent TB  
102 and active TB, we interpret decreased treatment initiations as reflecting reduced access  
103 to non-Covid-19 related health services, rather than indicative of true reductions in the  
104 incidence of TB transmission or disease. At our centers, all individuals with active TB  
105 diagnosis initiate treatment very shortly; hence, our observed reductions for active TB  
106 treatment indicate reduced diagnoses—likely from fewer people accessing medical  
107 care. For latent TB infection, our databases only track individuals prescribed treatment  
108 rather than all individuals referred for evaluation of newly diagnosed latent TB. Because  
109 indications to treat latent TB did not change, we interpret reductions in treatment  
110 initiations are because fewer people were being evaluated.



111 There is a paucity of published data available on the impact of Covid-19 on TB  
112 programmes in low TB incidence, high income countries. McQuaid et al. reviewed the  
113 literature on disruptions to TB preventative therapy and diagnostics across numerous  
114 high TB burden populations [1]. To add to the generalizability of current data, it is  
115 important to consider the affects of Covid-19 in well-developed, low TB incidence  
116 countries. TB prevention and control in low burden countries remains an essential  
117 aspect of tuberculosis elimination, with a particular need to maintain adequate TB care  
118 for individuals with LTBI and at high risk of developing active TB. A consortium including  
119 the Stop TB Partnership and the World Health Organization spoke to the negative  
120 impact of Covid-19 on global TB care [11, 12], surveying subjective impressions of  
121 individuals working in TB programmes. While such pragmatic studies are important for  
122 advocacy, analysis of programmatic data provide objective observations with a  
123 quantitative assessment of the magnitude of the impact. Two studies have reported the  
124 adverse affects of Covid-19 on TB care in low TB incidence countries using registry or  
125 programmatic data [13, 14], and while observations were consistent with ours, the  
126 analyses were limited to descriptive statistics, and only one study had data on LTBI [13].  
127 Our study thus provides an important contribution to the current literature, through the  
128 use of registry data, adjusted analyses, and granular information for the impacts on  
129 LTBI.

130 Some limitations should be considered. First, we were underpowered to identify  
131 significant reductions for active TB. Second, we did not consider the impact of the  
132 second and third waves of Covid-19 in Canada, as they occurred after data extraction.

133 A major strength of our study is the availability of several years of programmatic data  
134 from multiple centres. That all three sites observed significant reductions in LTBI  
135 treatment initiation speaks to the generalizability of our results. Given reductions in  
136 outpatient services were part of public health emergency measures across Canada, it is  
137 likely that TB care in other provinces was similarly affected.

138 In summary, since the enactment of public health emergency measures against Covid-  
139 19 in Canada, there has been a weakening of one of the cornerstone measures for  
140 maintaining TB control, treatment of LTBI. The other cornerstone — early detection and  
141 treatment of active TB — may also have been adversely affected. To avoid resurgence  
142 of an ancient pathogen in the wake of measures to mitigate the spread of a novel one,  
143 we call on federal and provincial governments to mobilize resources to ensure TB  
144 clinics across Canada can continue to operate at full capacity regardless of the local  
145 epidemiology of Covid-19.

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158 **Potential conflicts of interest**

159 All authors report no potential conflicts of interest.

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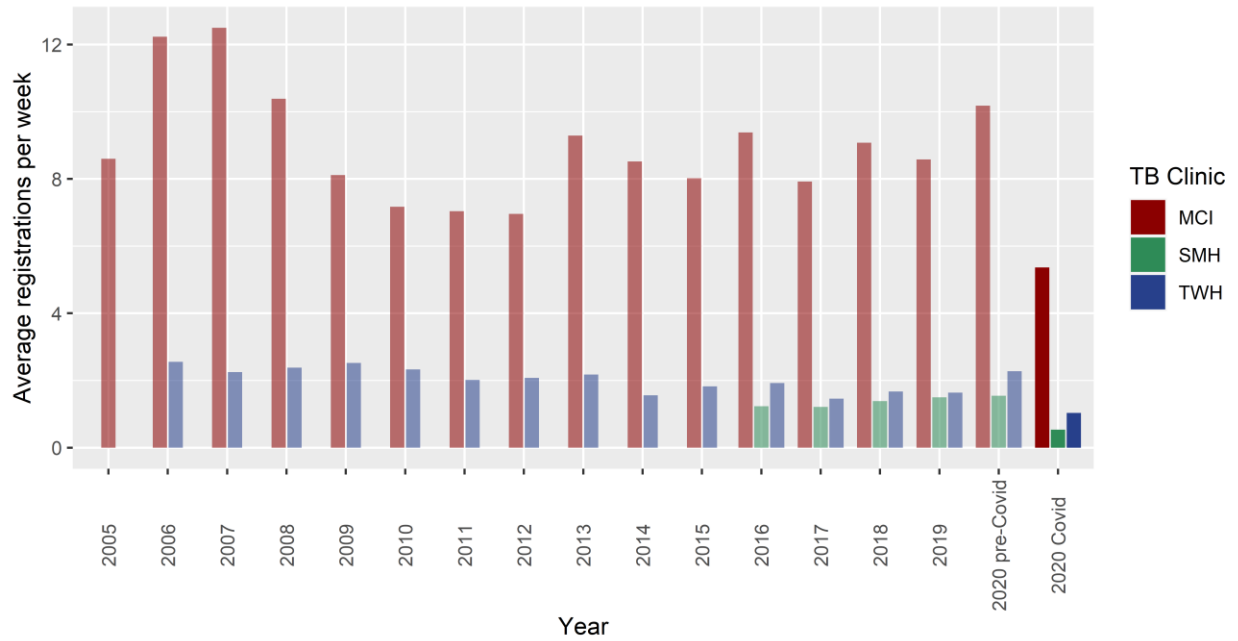
**Table 1. Treatment initiations per week at tuberculosis clinics in Montreal and Toronto before and after declaration of public health emergencies due to Covid-19**

	Montreal Chest Institute		Toronto Western Hospital		St. Michael's Hospital	
	Pre-Covid	Covid	Pre-Covid	Covid	Pre-Covid	Covid
<b>Latent TB infection</b>						
Number of weeks in clinical database	744	33	739	32	219	28
Number of patients starting therapy	6665	177	1501	33	294	15
Rate (per week)	9.0	5.4	2.0	1.0	1.3	0.5
Adjusted rate ratio (95% CI) <sup>a</sup>	0.70 (0.60, 0.82)		0.68 (0.47, 0.96)		0.34 (0.18, 0.57)	
<b>Active TB</b>						
Total weeks	744	33	739	32	466	28
Total patients	839	30	904	23	330	22
Rate (per week)	1.1	0.9	1.2	0.7	0.7	0.8
Adjusted rate ratio (95% CI) <sup>a</sup>	0.84 (0.56, 1.21)		0.71 (0.45, 1.07)		1.02 (0.62, 1.60)	

<sup>a</sup>Adjusted rate ratios and 95% confidence intervals (CI) were estimated using Poisson regression.

**Figure 1. Annual average number of patients starting treatment for latent tuberculosis infection per week before and after declarations of Covid-19 public health emergencies at three tuberculosis clinics in Montreal and Toronto.**

Legend: MCI, Montreal Chest Institute; SMH, Saint-Michael's Hospital; TWH, Toronto Western Hospital



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