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Title: Telemedicine use and outcomes after transient ischemic attack and minor stroke during the COVID-19 pandemic
Authors: Amy Y.X. Yu MD MSc, Jeremy Penn BSc, Peter C. Austin PhD, Douglas S. Lee MD PhD, Joan Porter MSc, Jiming Fang PhD, Donald A. Redelmeier MD MSHSR, Moira K. Kapral MD MSc

Reviewer 1: Dr. Muzakkir Amir
Institution: Hasanuddin University School of Medicine, RSUP Dr Wahidin Sudirohusodo
General comments (author response in bold)

Dear author, I have no specific comment regarding your excellent work. This study will provide an alternative way to provide health care in this pandemic era.
Thank you for reviewing our work.

Reviewer 2: Dr. Emily Ramage
Institution: University of Newcastle
General comments (author response in bold)

Thank you very much for the opportunity to review the article which tackles an important area in telemedicine and stroke research. The article is well written and clearly highlights some important priorities for stroke care and the potential value of telemedicine. Please see below my comments for consideration.
We thank the reviewer for their positive and constructive comments.

The study looked at 90-day follow-up, therefore conclusions regarding can only be drawn on the short-term (90-day) impact of telemedicine care. Please amend the wording in the article to reflect this. Furthermore, a limitation that should be discussed is the lack of long-term follow-up, and future research might be needed to determine if lack of in-person appointments impacts admissions or adverse events beyond the 90-day period.
We agree that the paper lacks longer-term outcomes. We have amended our conclusions in the abstract (page 3) and in the main article (page 11) to reflect this: "Care and short-term outcomes after TIA or minor stroke remained stable…"

We also now acknowledge this limitation (page 11): "The current study focused on the first 90 days after TIA because patients are at highest risk for stroke recurrence during that period,3,4 and future studies on telemedicine and longer-term outcomes after TIA are needed."

Another potential limitation that is not addressed is non-medical secondary prevention strategies such as lifestyle interventions which form part of national (and international guidelines). The impact of COVID-19 on these strategies also warrants investigation as it has the potential to impact future cardiovascular events and hospital re-admission.
We agree that data on lifestyle interventions are not available in administrative data and have now added this limitation on page 11: "… we could not evaluate renewal of acetylsalicylic acid as this medication is available over the counter nor lifestyle interventions for stroke prevention (e.g., diet, exercise) as this information is not available in administrative data."

The cohort of people with stroke or TIA had consistently small but higher risks for secondary stroke, particularly hypertension the leading risk factor for stroke was approximately 4% higher in the pre-telemedicine cohort. Could the authors please discuss the potential impact on this on results.
We agree with the reviewer that there were numerical differences in vascular risk factors in the pre-pandemic group compared to the group during the pandemic, but these differences were small, with standard differences below 0.1. In addition, we adjusted for baseline risk factors in our analyses. Nevertheless, we acknowledge in our limitations that given the observational nature of our study, residual confounding remains possible (page 11): "Residual confounding from the effects of the pandemic, stroke severity, admission thresholds, patient health-seeking behavior, or other unmeasured confounders is possible."

The authors may also wish to elaborate on future research to examine potential additional benefits of telemedicine such as cost saving via an economic evaluation.
Thank you for this comment. We agree that an economic evaluation of the use of telemedicine is an interesting topic for future research. This question is likely applicable to health conditions beyond TIA or minor stroke. We added this point to the Limitations (page 12): "We did not evaluate the economic implications of telemedicine for either patients or the health care system, and this is a relevant area for future study."

Reviewer 3: Dr. Rizwana Shahid
General comments (author response in bold)

the title needs to be reconsidered as the study is about comparing telemedicine services before and after the COVID 19 pandemic, but title doesn't support it.
Thank you for this suggestion. We have now changed the title as follows: "Telemedicine use and outcomes after transient ischemic attack and minor stroke during the COVID-19 pandemic."

The comparison before and after is significantly different (5 years vs one year), which makes the comparison invalid as the variables should be roughly same to make head to head comparison.
Comparing the pandemic year (2020/21) to the previous five years (2015/2020) is a strength of the paper. We show medians and proportions to compare patient characteristics and the main clinical outcomes are shown as rates using time-to-event analyses. Thus, we trust our comparisons are valid.

The outcome measure did not consider the completed stroke after a TIA and the factors leading to it.
We evaluated re-hospitalization for stroke within 90 days after the emergency department visit for TIA as a marker for stroke after TIA. We agree that given the limitations of administrative data, we do not have the details on the specific factors leading to stroke and we discuss the potential of residual confounding on page 11: "Residual confounding from the effects of the pandemic, stroke severity, admission thresholds, patient health-seeking behavior, or other unmeasured confounders is possible."

Reviewer 4: Mr. Mišo Gostimir

Institution: University of Ottawa
General comments (author response in bold)

The authors have presented a very interesting, timely, and well-planned study that captures a "hot topic" and provides meaningful information for healthcare providers (both specialized and non-specialized) and policymakers. This manuscript would be highly beneficial to the widespread CMAJ audience.
We thank the reviewer for the detailed review and constructive comments.

While this manuscript is very deserving of publication, there are some matters which should be addressed before acceptance: Page 5, Line 52-54, Setting a 100-day cutoff to define pre-telemedicine medications seems as though it may not be capturing all pre-existing prescriptions because some patients may have longer intervals between refills. While it may not be possible to change this at this point, it should be cited as a potential limitation.
We agree with the reviewer. We chose a 100-day cut-off for baseline medications in an effort to exclude medications the patients may not be actively taking (a single course of antibiotics, a PRN medication) and to exclude any discontinued medication. We have now added an explanation for this choice on page 6: "We defined baseline medication as any prescription filled between 100 days prior to the ED visit and up to 7 days after the visit. We chose this definition to capture active medications, but we acknowledge that we may have missed some medications with longer intervals between dispensations."

Page 8, Line 3-6 "Supplemental Table 3" should be in parentheses.
We have added the parentheses.

Page 8, Line 38-45. This comment should be repositioned to the discussion section rather than the results section.
Thank you for this suggestion. The sentence now reads: "There was an overall increase in vascular imaging use and a shift from using carotid Dopplers in favor of CT-angiography (Supplemental Figure 1)."

The authors' interpretation of the changes in the use of vascular imaging is quite relevant and would be interesting to the audience, so this deserves its own paragraph(s) in the "Discussion" section. There are also several questions/clarifications related to this result, which may be answered in the Discussion, as noted above. Presumably, CDUS would play more of a role in assessments for carotid endarterectomy, whereas CTA might serve other roles in addition to assessing the carotids. Adding to the confusion are the "in ED" vs. "within 14 days" time periods, which can lead to many different interpretations of which investigations are being ordered when and which investigations increased with the introduction of telemedicine.

Figure 3 The choice of wording for stroke investigations is confusing and deserves clarification in the legend, or a change in wording altogether. At first glance, "vascular imaging" might not intuitively encompass CTA and/or MRA and/or CDUS (based on the definition in Supp Table 1). Similarly, readers might not conclude that "brain imaging" means only MR head and/or CT head without having to reference the Supplemental Table 1. This creates a somewhat misleading presentation of the data and might lead to different interpretations based on which definitions of each category are considered.

Grouping together of CDUS, MRA, and CTA as "Vascular Imaging" Stemming from the comment above, the grouping of these 3 modalities is somewhat confusing (i.e. CDUS has a more specific use than MRA/CTA; many readers might confuse whether MRA/CTA falls under "neuroimaging" or "vascular imaging". Is it possible to separate the neurovascular imaging from the ultrasound to determine which one increased in the telemedicine era (both in the immediate ED visit and in the 14-day post-visit period)? If so, this would be relevant to perform and include in the updated manuscript. Supplemental Figure 1 does not provide enough information to answer these questions, and many readers are unlikely to take the time to review supplemental figures/tables.

We thank the reviewer for this important comment. We agree that our definition of neuroimaging and vascular imaging was unclear, and this should be in the main paper in addition to being in Supplemental Table 1. Thus, we have added the following in the methods on page 6: "Neuroimaging is defined as imaging with computed tomography (CT) or magnetic resonance imaging (MRI) of the head. Vascular imaging is defined as vessel imaging with carotid Dopplers, CT-angiography, or MR-angiography."

The Canadian Stroke Best Practice Guidelines make the distinction between neuroimaging and vascular imaging and recommend urgent vascular imaging, with carotid Dopplers, CT-angiogram, or MR-angiogram as soon as possible in the assessment of acute TIA or stroke (most recent guidelines are referenced in Ref #14, but this has been in the guidelines since at least 2015 by Casaubon et al.). Thus, we differentiated neuroimaging from vascular imaging and grouped carotid Dopplers, CT-angiogram, and MR-angiogram under vascular imaging.

The Canadian Stroke Best Practice Guidelines also state that where possible, a CT or MR-angiogram should be performed instead of carotid Dopplers. Carotid Dopplers do not have any more specific utility in the evaluation of TIA or stroke than CT or MR-angiogram. The main difference is that CT or MR-angiogram allows for the additional visualization of the posterior circulation and intracranial circulation, whereas carotid Dopplers are largely limited to the cervical carotid arteries. That is our rationale for showing in Supplemental Figure 1 the change in the use of carotid Dopplers vs CT or MR-angiogram.

Finally, we differentiate vascular imaging performed in the ED versus within 14 days because the guidelines recommend that patients with TIA with the highest risk of stroke recurrence undergo neuroimaging and vascular imaging before discharge from ED. We acknowledge in the limitations that administrative data do not have information on the severity of the TIA, but we thought it is nevertheless relevant to show readers vascular imaging in the ED versus within 14 days before and after 2020. We have further clarified this point in the methods (page 6): "We show neuroimaging and vascular imaging performed in the ED and within 14 days of the ED visit separately because the timing of neurovascular imaging is highly relevant in the management of TIA." And we have referenced the guidelines Ref #14.

To summarize, we distinguish neuroimaging vs vascular imaging, carotid Dopplers vs CT- or MR-angiogram, and timing of vascular imaging (ED vs within 14 days) because these are clinically relevant and based on guideline recommendations. We have added this to the discussion (page 9):

"We found an increase in the use of neurovascular imaging after April 1, 2020, but this was likely due to a change in clinical practice because neurovascular imaging increased throughout the study period (Supplemental Figure 1). This observation, along with the shift from carotid Dopplers to CT-angiography, are consistent with

the Canadian Stroke Best Practice Recommendations,14 and it is reassuring that these gains appear to have been maintained despite the implementation of telemedicine during the pandemic."

Differences in Specialist vs. GP Follow-up This is a topic that deserves more attention in the Results and Discussion. While it is alluded to at various points in the manuscript, it deserves a row in Table 1 and the authors should spend more space on this topic in the Discussion. There are several possible explanations to explore beyond the difference in billing code availability and presence/absence of infrastructure—telemedicine visits for stroke/TIA follow-up visits might differ between GPs and specialists for other reasons (e.g. comfort with medium of assessment for given condition from the perspective of the patient and/or physician, safety, etc.).
We agree this is an interesting observation and we have dedicated a paragraph to discuss this on page 10. This information is not in Table 1 because these are outcomes, not patient baseline characteristics. Instead, this is presented in the results section and shown in Supplemental Table 2. We do not have any direct data in the current study on why follow-up visits might differ between family doctors versus specialists. We want to avoid commenting on the comfort with the medium of assessment as it is not clear that the pattern we observed for care after TIA can be generalized to the use of telemedicine for other health conditions. We now acknowledge this uncertainty on page 10: "We do not know if other factors, such as familiarity with the use of telemedicine or comfort with virtual assessments for neurological disorders, affected uptake in different physician groups."

The study has determined that telemedicine appears to be a safe option for TIA and minor stroke follow-ups. However, the CMAJ audience would likely be very interested to know whether this is specific to follow-ups with specialists, family physicians, or both. If this question cannot be answered, the choice of wording in the concluding statements should be made more specific and this should perhaps be listed as a limitation.
We agree with the reviewer that it is difficult to determine causality between a specific exposure variable and an outcome in an observational study. For instance, a patient with many physician visits may have a better outcome from having closer follow-up. On the other hand, another patient may have many visits to evaluate new symptoms and clinical deterioration and therefore experience a worse outcome. We discuss residual confounding in the limitations section (page 11): "Residual confounding from the effects of the pandemic, stroke severity, admission thresholds, patient health-seeking behavior, or other unmeasured confounders is possible." We have also softened our conclusions to (page 12): "Our findings suggest that care via telemedicine can be complementary to in-person assessments without negatively affecting care and outcomes."

Difference in outcomes based on age groups A major question that readers might be left with is whether telemedicine is safe in all age groups (i.e. is the barrier of technology use a factor to consider for more elderly patients?). The standardized differences used in the Results section and Table 1 do not capture this detail and instead only compare the mean age between the two cohorts. Conversely, Supplemental Table 3 analyzes age as an ordinal variable, which is more appropriate but still does not answer this question because only an ANOVA test was used (pairwise comparisons are also needed to determine which groups have differences between each other).

One may be left with the question of whether follow-up via telemedicine was suboptimal or more efficacious in certain age groups in terms of both outcomes (as defined by the authors) and access to follow-up. Based on the submitted manuscript, it seems that this data is available but has simply not been presented or analyzed in such a way to answer this highly relevant question.
We agree that further dedicated work to evaluate whether there are certain groups of patients who are more vulnerable to poor outcomes when telemedicine is used is needed. As shown in Supplemental Table 3, the sample sizes were very small when stratified by certain patient characteristics (e.g., age groups) and thus we are underpowered to answer the question of whether telemedicine is suboptimal or more effective in certain subgroups of patients.

Methods- Should include which statistical software was used in the analysis.
We have now added this information on page 7: "All data analyses were performed using SAS Enterprise Guide version 9.4 (SAS Institute Inc., Cary, North Carolina).