Author’s response to reviews

Title: Why Acute Ischemic Stroke Patients in the United States Use or Do Not Use Emergency Medical Services Transport? Findings of an Inpatient Survey

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Author’s response to reviews:

ITEM-WISE RESPONSES TO REVIEW COMMENTS

Jane Brice (Reviewer 1):
Thank you for the opportunity to review this interesting manuscript. I hope my comments will be useful to you.

Abstract
1. Please mention in the methods that patents were surveyed while hospitalized for their stroke event.
Response: This is now mentioned in the closing sentence of the Introduction section and the Methods section, p. 7 and 8 of the manuscript.

Introduction
1. The first paragraph is a bit overstated. Yes, patients who arrive by EMS have faster initiation of reperfusion. Yes, quicker reperfusion leads to better outcomes. But, relatively few patients receive reperfusion treatments. The relative benefit of arriving by EMS is not large and likely
does not "critically determine survival and long-term outcomes. Many, many, many factors play into survival and long-term benefits of which EMS is but one.
Response: Thank you for bringing this to our attention. We have made appropriate changes in the first paragraph of the Introduction section. Further, in response to a similar comment by Reviewer 2, we have added related information with additional references. This section now reads as follows (p. 6): “Evidence is clear that AIS patients who receive quick reperfusion treatments with alteplase and endovascular thrombectomy have better survival and disability mitigation. Emergency medical services (EMS) transport is associated with greater likelihood of hospital arrival within the intravenous alteplase treatment window, 4.5 hours since stroke onset.5 Among patients arriving within the alteplase window, neuroimaging initiation and reperfusion treatments gets initiated more rapidly for EMS arrivals.6,7 These effects are mediated by various events triggered by EMS. EMS arrival itself attracts immediate attention of the hospital emergency medical team bypassing ED triage and wait times.8-9 Further, if advance notification of a brain attack (stroke) patient en-route is communicated by the EMS staff (BAT prenotification) the hospital stroke team is activated and in place ahead of the patient’s arrival.10, 11 Prenotification also triggers a clearing the neuroimaging suite of non-emergent patients to attend to the anticipated stroke patient immediately. Nationally, about 59% of AIS patients arrive by EMS.12 However only about 30% of AIS patients arrive within the treatment window, with EMS patients being much more likely than personal transport users to arrive within the treatment window.13 Patients’ knowledge about stroke symptoms and a decision to promptly call EMS at symptom onset may be critical for survival and mitigating long-term disability for some patients.”

Methods
1. I like your conceptual framework. Please tell us how it was developed. Was it based entirely upon the Schroeder and Sen studies cited? There are quite a few other studies that have also examined reasons for EMS activation by stroke patients.
Response: Thanks again for drawing our attention to the fact that we cited only two studies in the Methods section describing conceptual framework development. In restricting word count typically imposed by most journals, we reserved maximum space for reporting the findings.

We had cited Kothari et al in the Introduction section but overlooked to include it in the Methods section. This is now included. Additionally, we have added Moseley et al who reported on a study from Australia that interviewed stroke patients. We did not include it earlier as we focused on American studies given that the US health care system is quite different from most other developed countries. We could not find other studies that interviewed stroke survivors who had a completed EMS decision (in contrast to studies that asked for responses to a hypothetical stroke scenario). We are happy to add references if recommended. The remaining conceptual framework items not found in documented studies were compiled from expert consultations - medical and paramedical personnel engaged in the care of AIS patients.

In response to this comment and the next one we have included in the paper, the process of survey development, pretesting and survey deployment including staff training. All persons who contributed ideas to survey development who are not co-authors were acknowledged in the Acknowledgements section of the paper. The new material on survey development and deployment is as follows (p. 8-9):
“Survey development, pretesting and administration
A survey was developed, starting with a draft conceptual framework of the potential decision drivers of EMS decisions based on the documented literature. Because of paucity of documented data on EMS decision-making, we added substantial new content based on brainstorming with experts: the neurologist (study coinvestigator and manuscript coauthor), hospital stroke unit nurse coordinator, stroke unit floor nurse, Stroke Rehabilitation and Physical Therapy unit Director(a physical therapist by training), and the hospital’s GWTG-Stroke registry staff who track patients until discharge using an intranet-enabled patient tracking tool through the various unit/ward transfers. To add the perspectives of field EMS staff and to adapt the survey wording to the general population reading level, the resulting draft survey was discussed with the Chief of the South Carolina Emergency Medical Services Bureau, a trained EMS technician with field EMT experience who supervises EMS operations in South Carolina (also a co-author of this study). The final draft survey was finalized to be consistent with a 5th grade reading level. The Patient Consent form was adapted from the study hospital’s IRB-cleared consent template used for consenting patients for clinical trials and interventional studies.

After finalization, the PI trained the pilot survey administrator (a stroke unit nurse experienced in consenting patients for clinical trials). The PI and the stroke nurse reviewed the survey jointly item by item and developed consensus on responding to potential patient questions and concerns. Following training, the survey (programmed into a touchscreen computer) was pretested by the stroke nurse with 10 patients wherein ambiguities in question wording, language above patient comprehension level, and question order glitches were discovered and rectified. Following pretesting, the graduate student assistant and stroke registry staff were trained (the latter performed survey work after-hours when able and to ensure continuity of survey activity during university breaks in summer and winter). Because the wording and survey progression issues during pretesting were minor with no relevance to data integrity, these 10 surveys were included in the final data for analysis.

The programmed survey was set to default to the next applicable question as each question was answered. In almost all cases, patients completed the survey on their own, occasionally seeking clarification from the survey staff who stood by. We chose computer-based self-administration to enable patients to freely answer socially sensitive questions (alcohol, drug use, medical mistrust, etc.). Graduate student assistants (2 graduate students over the course of the study) who administered the survey were additionally trained in determining patient eligibility for survey from the online (intranet) Patient Tracking tool updated each day by the Registry staff, and to contact the floor nursing staff to obtain clinical fitness clearance to interview the patient.”

In addition to the above change in the Methods section, we have added information from the new references in the Introduction section as follows (p. 7): “Two studies including one from Australia reported symptom characteristics, family history of stroke, presence of family member or friend/associate at the time of stroke, and cues received from a relative/bystander were associated with the decision to call for an ambulance.15,18 “

2. Who were the research assistants? How were they trained?
Response: The survey research assistants were of three types, a) stroke unit nurse with experience in clinical trial consent and participation (pretested the survey and conducted some subsequent surveys; b) graduate student research assistants working part time during their working hours and during fall and spring semester times, supplemented by c) Stroke Unit Registry staff who undertook to interview patients during their free time and after-hours, particularly to maintain survey activities during university breaks when graduate students were not available on campus.

The training is now described in the paper shown above under Methods Comment 1. We may add that the PI and/or stroke nurse trained the survey administrators except the replacement graduate assistant (after the original graduate assistant graduated) who was trained by the stroke registry staff that gained experience in administering the survey.

3. 108 subjects in 18 months seems pretty small. To what do you attribute this?
Response: We had key structural barriers to completion and it was not for lack of attempts to contact all patients. We have provided greater detail on this in the Discussion section as follows (P. 14-15): “One study limitation is the small fraction of all AIS discharges surveyed, 9.8% of eligible patients. Two structural barriers interacted to impede survey coverage: a) limited availability of survey staff time (graduate research assistants available for 20 hours a week and patchy survey staff coverage during university breaks between major semesters (stroke unit/stroke registry staff working after-hours), b) limited patient availability primarily due to short inpatient stay (with patients getting discharged to skilled nursing facilities after acute care needs were met). Median length of stay during the study period was 5 days (45% of all patients discharged on the 4th day or earlier). Stroke patients typically experience intensive medical care in the first 2-3 days (unavailable for survey) or they are medically unfit, being in the acute recovery phase. Consistent with these conditions, survey staff found 34% of patients were already discharged at their first attempt to contact the patient. Other reasons for not contacting the patient were: not contacted (weekends, university breaks), patient not available for survey due to being asleep, ICU transfer, expired or assigned to hospice care. The distribution of survey-eligible patients by survey completion status and reasons for non-completion is presented in Appendix 7. Given survey comprehensiveness and the transient availability of this acute care population, the distribution of reasons shows that it will require far more intensive resource expenditures to achieve a significantly better completion rate. Nevertheless, given the observed minimal differences between surveyed and not-surveyed patients on most demographic and stroke characteristics, and the similarity of stroke severity of surveyed patients to recent nationwide AIS cohorts (median admission NIHSS score nationwide, 4.0). 13 it appears reasonable to use the evidence produced to initiate public health and medical care facility-level initiatives to improve EMS use by stroke-symptomatic patients.”

4. When discussing the random identification, please spell out identification rather than use id. Unless you are Freud.
Response: We have carried out this correction wherever the term ID appears.

Results
1. When you say "surveyed patients were not substantially different from non-respondents despite some statistically significant differences in age, sex, race, and stroke severity", what do
you mean? There were differences, what do you mean when you say patients were not substantially different.
Response: We wanted this sentence to convey that the statistically significant differences are of small magnitude and do not justify concerns about using the survey findings for actions. We have changed the sentence to read as follows: “Surveyed patients were slightly more likely than those not surveyed to be female, younger, White/Other race, slightly less likely to have severe stroke, and to have received alteplase reperfusion treatment.”

2. I find it interesting that 46% of subjects recommended full insurance coverage of EMS when so few subjects identified that as a concern in calling EMS.
Response: We have provided the potential reason for this apparent contradiction in the Discussion section, their previous EMS use experience which may have prompted them to make this recommendation. The section in the Discussion section reads: “Interestingly, although a fifth of respondents considered the financial burden of EMS costs before making their decision, it was not reported as a priority reason for their decision. Regression analyses also showed that it was not a barrier for EMS use, similar to a North Carolina study.14 However, almost 50% of surveyed patients, recommended insurance mandates for full coverage of EMS when used by stroke-symptomatic patients. Their recommendation may reflect the prior experience of 58% of surveyed patients who had used EMS in the past, with one-third of them incurring most or all EMS costs out-of-pocket.”

Discussion

1. Nationally, only 53% of stroke patients use EMS. Why do you think you had a much higher EMS utilization rate (69%)? Is this the rate of EMS use in your GWTG database? Or is there some selection bias here?
Response: In responding to another comment we present more recent EMS use data from nationwide GWTG registry data which shows 59% using EMS in a 2015 publication. The surveyed cohort rate of EMS use is 69%. This is because our survey data captures all EMS use regardless of whether it was used to reach the study hospital or the hospital that they were taken to before transferring to the study hospital. GWTG data on EMS arrival rate exclude transfer patients from other hospitals. When we apply the same exclusion, our surveyed cohort EMS use rate drops to 49.5%. It appears that our survey cohort has a somewhat lower EMS use rate than national cohorts.

2. You cite similarity of respondents and non-respondents as a mitigating factor for small sample size and then add "as well as documented nationwide AIS cohorts". What does that mean?
Response: The surveyed cohort, the entire AIS discharged cohort during the study period, and national cohorts all have a median NIHSS stroke severity score of 4. On this metric they are similar. The confusing sentence noted above is reworded as follows: “Nevertheless, given the observed minimal differences between surveyed and not-surveyed patients on most demographic and stroke characteristics, and the similarity of stroke severity of surveyed patients to recent nationwide AIS cohorts (median admission NIHSS score nation-wide, 4.0). 13 it appears reasonable to use the evidence produced to initiate public health and medical care facility-level initiatives to improve EMS use by stroke-symptomatic patients.”
Alison Porter (Reviewer 2): This article is interesting in that it takes a very different stance to most work on decision making about use of pre-hospital care - while much of the literature concentrates on why people call for an ambulance when it's not appropriate, this paper explores why people don't call for one when it would probably be a good idea. It's a well-written piece of work, but I do have some concerns about it.

It is a weakness of the paper that the sample is a very small proportion of the total number of patients admitted (108/1179), and small in terms of absolute numbers - Table 2 reports figures as low as two people, which is really too small to be meaningful. The authors describe a convenience sampling approach, but it's not entirely clear what they did - did they approach all 1179 patients? If not, how were patients selected? How many were approached but did not complete the survey? If a patient was not available, did they try contacting them again later?
Response: We have explained this issue in response to a comment by Reviewer 1, see above.

In the introductory section, the authors correctly point out that, on average, it's good to use EMS as it can get you to reperfusion faster. It would be useful to have more discussion of this - is it because of shorter transit times, or because patients brought in by ambulance get priority attention in the ED? It would also be useful to flag up at the beginning that, for some patients, it may not be to their advantage to wait for an ambulance - as respondents living in rural areas pointed out in the survey. And can we be confident that all patients would have received an immediate response if they had contact EMS, or might some have been triaged to wait?
Response: Thank you for raising this point. In response to this comment and an allied comment by Reviewer 1, we have added this information with additional references in the Introduction section. This section now reads as follows (p. 6): “Emergency medical services (EMS) transport is associated with greater likelihood of hospital arrival within the intravenous alteplase treatment window, 4.5 hours since stroke onset. Among patients arriving within the alteplase window, neuroimaging initiation and reperfusion treatments gets initiated more rapidly for EMS arrivals. These effects are mediated by various events triggered by EMS. EMS arrival itself attracts immediate attention of the hospital emergency medical team bypassing ED triage and wait times. Further, if advance notification of a brain attack (stroke) patient en-route is communicated by the EMS staff (BAT prenotification) the hospital stroke team is activated and in place ahead of the patient’s arrival. Prenotification also triggers a clearing the neuroimaging suite of non-emergent patients to attend to the anticipated stroke patient immediately.”

From the beginning (and in the title) it's worth pointing out that this work was conducted in the US, which has particular contextual issues.
Response: This is carried out in the title and Introduction section

P6, line 24 states that 53% of patients arrive by EMS - where? And this reference is ten years old, so should not be presented as current data.
Response: We thank the reviewer for drawing our attention to the dated information. We have now replaced it with data from the most recent study available on this matter, Mochari-
Greenberger et al 2015 which reports a rate of 59% based on GWTG data. These changes are carried out in the Abstract, Summary box and Introduction sections.

On p7 the authors state that the survey was informed by the conceptual framework given in Fig 1. The list of factors given in Fig 1 is very comprehensive, but I'm not sure it can be described as a conceptual framework - there's no sense of the sequence in which factors operate, or how they might interact; it would also be useful to see some grouping into, say, intrinsic and extrinsic factors, or predisposing/immediate.

Response: We use the term conceptual framework defined as: “A conceptual framework is an analytical tool with several variations and contexts. It can be applied in different categories of work where an overall picture is needed. It is used to make conceptual distinctions and organize ideas. Strong conceptual frameworks capture something real and do this in a way that is easy to remember and apply.” Second, “The use of the term conceptual framework crosses both scale (large and small theories)[4][5] and contexts (social science,[6][7] marketing,[8] applied science,[9] art[10] etc.). Its explicit definition and application can therefore vary. Conceptual frameworks are particularly useful as organizing devices in empirical research. (Ref: https://en.wikipedia.org/wiki/Conceptual-framework accessed Oct 17,2019). We are not intending our framework to represent a theoretical framework which is a more advanced conceptual framework positing sequence of constructs and directions of effects. Also, our groupings used are meant to be intuitively understandable to a general interest reader, to comprehend how EMS decision-making may occur (symptom-related factors, cues to action, financial factors, etc). While theoretically many items may fit into some theoretical groupings such as pre-disposing factors or intrinsic/extrinsic factors, from an intuitive perspective, given the number of factors we have represented, esoteric grouping would make it counter-intuitive and dense for a general reader not specialized in social behavior theories. We present this conceptual frameworks to create a mental map of a construct and its parts (in this case EMS decision-making). As such we have not changed the conceptual framework as currently shown. Both the scale of our data and the current state of art remain far from positing and testing sequence of effects among the factors. As such we have retained the conceptual framework in its present form.

I am confused by the data presented in Table 2, which reports people's priority reasons for their choice - I would expect the numbers to add up 108, but they are way over - but below 108x3, which you would expect if all 'top 3' reasons reported. Needs explanation of how the data were handled.

Response: Up to 3 priority responses were all counted. Some patients gave less than 3 priority reasons. This is clarified in the Results section as follows: “Patients reported their priority reasons for using or not using EMS, shown in descending order of frequency in Table 2 (multiple reasons per patient, total add up to more than 108).” The table also shows corresponding edits to make this point.

Gerard Fitzgerald, MD (Reviewer 3): Thank you for asking me to review this paper. It is a relatively straightforward survey seeking to identify the factors that appear to influence EMS use by patients with acute ischaemic stroke. The survey respondents were patients who had been
diagnosed with an AIS and was conducted 2-7 days after admission to hospital (interquartile range 2-5).
The methods and analytical techniques are clearly outlined, and the findings expressed clearly. My only significant observation is that the calls to action are predicated largely on these patients being described as having chronic disease. This may well be true. However, AIS may be the first presentation of atherosclerotic vascular disease and thus recommendations focused on the primary care advice to patients with chronic disease may be limited. It may be more useful to include patients with adverse risk factors (smoking, hypertension, Diabetes etc).
Response: Thank you for bringing up this point. Out of 15 GWTG stroke-relevant risk factors, 13 are chronic medical conditions including hypertension, diabetes, etc. Two of the 15 are risk factors, smoking and alcohol/drug abuse. We have listed the risk factors also in the Discussion section on page 16. To also defuse this confusion in Table 1, we added a footnote indicating the GWTG comorbidities/risk factors. We have also corrected this language in the text, from co-morbidities to risk factors. To explore your point about some patients first showing up with a stroke without a previously-diagnosed medical condition, we analyzed the data and found that of 108 patients, 10 had no co-morbidities, only smoking or alcohol/drug abuse history. Thank you for bringing that up.

The concerned text in the Discussion section is reworded to state: “Regardless, the persisting knowledge gaps reinforce the need for major public health and medical community efforts to develop effective communications and outreach strategies to educate patients with stroke-relevant co-morbidities and risk factors (smoking, alcohol/drug abuse) as well as the general population. Innovative communication strategies including technology-assisted approaches may help address this challenge. Another approach could be to include stroke education as a standard of care in chronic disease management and the management of patients with lifestyle risk factors.

May I make a number of relatively minor observations for consideration by the authors:

1. Financial concerns are often lowly cited as a significant factor in emergency medicine even in jurisdictions that do not have universal (fee free) access. However, this should be treated with caution. At the macro systems level there is mixed evidence. ED utilisation rates are higher in the US than in jurisdictions such as the UK and Australia that provide free (at the point of delivery) ED access. Other evidence suggests that bystanders and family members may influence such decisions; in either direction. Perhaps a brief discussion on the US context may be helpful for an international readership.
Response: We agree with the concern of the reviewer. Which is why we emphasize that insurers should be required to cover EMS use at no out of pocket costs for stroke symptomatic patients.

2. Was the survey pilot tested prior to its use?
Response: It was pilot tested with 10 patients. The section on survey development is now revised in response to this comment and other comments by reviewers and shown earlier.

3. On page 9 you mention the survey was self-administered. Please include here how (by touchscreen mentioned in the abstract)
Response: The revised survey related section referred to above has this information.
4. The survey included less than 10% of the patient population. I realise comparisons between the survey population and the patient population were done to test representativeness but it may be worth commenting a little more on this relatively low response rate for a survey administered by research staff. Additionally, comparisons between the sample and population include do show substantial differences in age gender, race and stroke severity. In particular, stroke severity would appear to be a major factor in determining EMS use. It would be worth discussing how the findings of this survey may inform the management of the other 90% who did not respond.

Response: We have run additional analysis to quantify the impact of the various factors affecting survey completion. We now describe the reasons for low survey completion rate and provided greater detail on comparison of the surveyed vs. not surveyed cohort as follows which should address the multiple concerns expressed in this paragraph:

Comparisons between the sample and population: We have changed the narrative in the Results section, which now reads as follows (p. 12):

“Surveyed patients were slightly more likely than those not surveyed to be female, younger, White/Other race, slightly less likely to have severe stroke, and to have received alteplase reperfusion treatment. (Appendix 2) “

We describe the reasons for low survey completion (p. 14-15):
Discussion section: “One study limitation is the small fraction of all AIS discharges surveyed, 9.8% of eligible patients. Two structural barriers interacted to impede survey coverage: a) limited availability of survey staff time (graduate research assistants available for 20 hours a week and patchy survey staff coverage during university breaks between major semesters (stroke unit/stroke registry staff working after-hours), b) limited patient availability primarily due to short inpatient stay (with patients getting discharged to skilled nursing facilities after acute care needs were met). Median length of stay during the study period was 5 days (45% of all patients discharged on the 4th day or earlier). Stroke patients typically experience intensive medical care in the first 2-3 days (unavailable for survey) or they are medically unfit, being in the acute recovery phase. Consistent with these conditions, survey staff found 34% of patients were already discharged at their first attempt to contact the patient. Other reasons for not contacting the patient were: not contacted (weekends, university breaks), patient not available for survey due to being asleep, ICU transfer, expired or assigned to hospice care. The distribution of survey-eligible patients by survey completion status and reasons for non-completion is presented in Appendix 7. Given survey comprehensiveness and the transient availability of this acute care population, the distribution of reasons shows that it will require far more intensive resource expenditures to achieve a significantly better completion rate.

Nevertheless, given the observed minimal differences between surveyed and not-surveyed patients on most demographic and stroke characteristics, and the similarity of stroke severity of surveyed patients to recent nationwide AIS cohorts (median admission NIHSS score nationwide, 4.0). 13 it appears reasonable to use the evidence produced to initiate public health and medical care facility-level initiatives to improve EMS use by stroke-symptomatic patients”

We have added Appendix 7 (shown in red font in the Appendices document) to show the results of analysis.
5. The recommendations include public awareness of stroke and the value of EMS use. The authors may be aware that there is considerable concern for increasing EMS demand in publicly funded jurisdictions and so balanced messages are important for an international readership. The design of those messages however, could be informed by the findings of research such as this. Messages may need to deal with the perceptions of severity, costs and remoteness.
Response: We agree about the concern. Balanced messages should be developed to ensure that EMS use does not get out of control.

6. The paper did identify a group of patients who contacted their physician's office to be told not to call EMS. The authors may consider additional research to find out why this is so and to recommend more strongly including this element into the professional awareness programs.
Response: We agree. We are seeking support for such a study. In addition we have added the following to the Conclusion section (p. 19): “It may be beneficial to initiate care guideline reviews by medical, nursing and physician assistant professional organizations to include stroke education as a standard of care for patient populations with stroke risk factors including lifestyle factors such as smoking and alcohol/drug use. The finding of vague/incorrect phone guidance provided by some physician office staff when patients contacted them at stroke onset indicates the need for medical professional organizations to institute standardized training of physician office staff in phone guidance protocols for stroke and other emergent medical symptoms.”