

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Incidence of delirium in the Canadian Emergency Department and its consequences on hospital length of stay : a prospective observational multicentre cohort study
AUTHORS	Emond, Marcel; Boucher, Valérie; Carmichael, Pierre-Hugues; Voyer, Philippe; Pelletier, Mathieu; Gouin, Émilie; Daoust, Raoul; Berthelot, Simon; Lamontagne, Marie-Ève; Morin, Michèle; Lemire, Stéphane; Thien Tuong, Minh Vu; Nadeau, Alexandra; Rheault, Marcel; Juneau, Lucille; Le Sage, Natalie; Lee, Jacques

VERSION 1 – REVIEW

REVIEWER	Rakesh C. Arora University of Manitoba, Winnipeg, Canada
REVIEW RETURNED	15-Jul-2017

GENERAL COMMENTS	<p>Summary: This is a multicentre, prospective observational cohort examining the impact of delirium in 338 patients initially presenting in the ED on ED and hospital LOS.</p> <p>Study Strengths:</p> <ol style="list-style-type: none">1. Multicentre data using a systematic screening tool.2. Delirium assessments were performed within the first 8 hours to attempt to ensure that only incident delirium was captured in the analysis.3. Follows STROBE reporting guidelines (checklist included) <p>Comments/Concerns:</p> <p>The following comments/questions are seeking clarification on a few issues (separated by section) to further strengthen the manuscript.</p> <p>GENERAL COMMENTS: Research Question Novelty: This is an important, multicentre study. There have been, however, other recent studies that have examining the impact of delirium in patients in the ED and long-term functional outcomes (i.e. PMID: 28263444; PMID:21521405, PMID:20363527). Furthermore, a recent study (PMID: 28675451) has indicated that delirium screening in the ED with a paired intervention does not appear to lead to modification of outcomes. These previous investigations limit the impact of this study. While the Authors have provided multicentre data, it would be of benefit for the Authors to provide additional information to further articulate the novelty of their initiative.</p> <p>METHODS: Can the Authors provide further discussion on why they</p>
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chose to use of CAM vs. Brief Confusion Assessment Method (a.k.a. bCAM (i.e. PMID: 28263444)) in this study?

METHODS: Please clarify how the Clinical Frailty Scale was used to assess cognition in the enrolled patients.

METHODS: Can the Authors please clarify (and why) that the inter-rater kappa was only tested at the coordinating centre (pg 9, ln 33-35).

METHODS: Please provide further details on the process of obtaining a "sample analysis of missing patients".

RESULTS: It would be helpful to have some information on chief complaint of the patient presenting to the ED. In addition, for patients presenting with a surgical (or surgical-like) illness, did the Authors capture any information on adequacy of pain control and/or use of narcotics?

RESULTS: Do the Authors have any information on the time of day of presentation (i.e. day vs. night)? In addition, do they have any information on the length of time patients waited in the waiting room of their ED prior to first assessment by the MD?

RESULTS: Table 1 indicates the variable of "proper lighting". Please define what this means and how this was controlled at different times of the day both in the ED and the ward.

RESULTS: Table 1 indicates a variable use of physical restraints between the 4 sites. Was the use of restraints standardized or protocolized between sites. Was this in the ED or the ward?

RESULTS: Were data on the use of both benzodiazepines, anti-psychotic medications captured?

RESULTS: Was preoperative alcohol use assessed in this patient population?

RESULTS: ED LOS (Figure 4) was adjusted for site, age, Charlson, APACHE, OARS and TICS-m scores, however there are many other factors impact ED LOS. For example, length of time of response of consulting services and ward bed availability are likely not fully explained by the stratification by site. Can the Authors provide further details/description on how these pragmatic variables were addressed in their study design and analysis?

RESULTS: Can the Authors provide any information on visitation policies in their EDs and wards? How many of the older adults had regular bedside presence of an accompanying family member/friend?

RESULTS: Please clarify if the first episode of delirium occurred in the ED or on the ward in the studied population.

RESULTS: Please provide information on the time of admission to the ward as well as the admitting service. In addition, it would be helpful to know if any of the admitting service routine engage in delirium screening and/or management practices.

Minor Concerns:

	<ol style="list-style-type: none"> 1. Suggest to use the term older adult instead of “elderly, elders, seniors etc...” 2. The statement “Our study experts suggested... (pg 6, ln 24)” is odd and should be revised. 3. Pg 10, Ln 46 “RASSS” should be revised to “RASS”. 4. There are other grammatical and typographical errors that require additional refinement.
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REVIEWER	Jin Han Vanderbilt University Medical Center USA
REVIEW RETURNED	30-Jul-2017

GENERAL COMMENTS	<p>This manuscript sought to determine the incidence of delirium and how it incident delirium affects hospital length of stay (LOS). The study would have been more informative if it had evaluated how incident delirium impacts hospital LOS differently than prevalent delirium in the ED. Defining incident delirium in the ED is also challenging; at what point during the ED stay is delirium truly an incident case. One of the key features of delirium is that it fluctuates. In patients who were classified with incident delirium, is it possible that some of these patients actually had prevalent delirium, but were lucid at the initial assessment? Below are my specific comments:</p> <p>Abstract: The abstract objectives state you were looking at both ED LOS and hospital LOS outcomes, while the manuscript’s outcome is just hospital LOS. Please keep this consistence. I would consider just focusing on hospital LOS. The problem with the ED LOS outcome is that it is difficult to know if the incident delirium caused prolonged ED LOS or the ED LOS caused the incident delirium.</p> <p>Introduction Overall: One thing that is missing from the introduction why we readers care about the distinction between incident and prevalent delirium? Do they effect outcomes differently?</p> <p>Page 6, lines 7-11, Methods: It seems like your hospitals have a significant boarding problem. Is it possible to give the readers a sense of how significant this boarding problem is? What is the average RF and boarding LOS of stay? Also, did you screen 7 days a week, 24 hours a day?</p> <p>Page 6, lines 12-14, Methods: Why did you only include patients who were fully or semi-independent. Patients who are functionally impaired are likely the most vulnerable to developing delirium and adverse outcomes. As a result, their exclusion hampers the external validity of your study.</p> <p>Page 6, lines 16-17, Methods: You also excluded patients who were unable to consent. Did you attempt to contact their authorized surrogates to obtain consent? If not, excluding patients who are non-consentable would be excluding a vulnerable, but important patient population.</p> <p>Page 6, lines 56-57, Methods: The CAM’s lowest sensitivity based upon Wei et al’s systematic review was 46%. I would consider using a slightly more contemporary systematic review published by Wong et al.[1].</p>
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Page 7, line 14-22, Methods: What was the clinical and educational backgrounds of the research assistants?

Page 7, lines 25-27, Methods: Please state if you defined incident delirium if it only occurred in the ED or if you included incident delirium that occurred during first 24 hours of the hospital stay.

Page 7, lines 30-42, Methods: I thought that the specific method of the CAM required you to have both altered mental status and a fluctuating course. Also, I would mention that you used the SENS method to ascertain delirium for your study.

Page 7, lines 51-57, Methods: You stated that you adjusted for age, Charlson, and APACHE. Why didn't you also adjust for the TICS-m as well as pre-delirium cognition or frailty as they may be potential confounders? Some would also argue that ED LOS is a potential confounder as well.

Page 9, lines 32-36, Results: I would think that reporting the Kappa for the CAM would be sufficient. Also consider reporting the CAM's kappa in the preceding paragraph as this was not one of your primary study objectives.

Page 8, lines 38-55, Results: I think reporting data at the site level may be too much detail. Personally, I would just report the overall results from all 4 sites combined.

Discussion Overall: The discussion is too long and not very well organized. The goal of the discussion is provide context of how your findings add to the literature and what clinicians should do about your findings. I would considering reading Horton et al.'s paper about how to write a discussion section [2]. I would consider organizing your discussion into the following paragraphs: (a) Summarize your results, (b) Discuss the importance of incident delirium and how it differentially affects outcomes compared with prevalent delirium, (c) Discuss the potential mechanisms for incident delirium and what EDs should do to prevent it from happening. (d) Limitations. (e) Conclusions.

Page 10, lines 10-13, Discussion: I would consider deleting any mention of ED LOS as this was not the primary objective of your study.

Page 10, lines 15-30, Discussion: I would avoid providing too much detail on each study. Also, Bo et al's study looked at ED LOS as a risk factor for incident delirium and seems out of place. The second paragraph should focus on what other studies have done with regard to evaluating incident delirium and outcomes.

Page 10, lines 33-39, Discussion: Han et al's study reported prevalent delirium rather than incident delirium. I would also consider deleting this paragraph since I am unclear how this is relevant to your discussion.

References

1. Wong CL, Holroyd-Leduc J, Simel DL, Straus SE: Does this patient have delirium?: value of bedside instruments. JAMA 2010, 304(7):779-786.
2. Horton R: The hidden research paper. JAMA 2002, 287(21):2775-2778.

VERSION 1 – AUTHOR RESPONSE

Manuscript : 2017-018190

Journal: BMJ Open

Title: Incidence of delirium in the Emergency Department and its consequences on hospital length of stay : a prospective observational multicentre cohort study in Canadian EDs

Editorial requests	
Questions	Answers
Please revise your title so that it includes your study design and setting. This is the preferred format for the journal.	Done, p. 1
Please change the “INTERPRETATION” heading to “DISCUSSION” on page 10.	Done, p. 10

The authors would like to thank the editor and reviewers for their comments that helped improve the manuscript. For details, please refer to the responses in the following tables.

Reviewer 1	
Questions	Answers
Research Question Novelty: This is an important, multicentre study. There have been, however, other recent studies that have examined the impact of delirium in patients in the ED and long-term functional outcomes (i.e. PMID: 28263444; PMID:21521405, PMID:20363527). Furthermore, a recent study (PMID: 28675451) has indicated that delirium screening in the ED with a paired intervention does not appear to lead to modification of outcomes. These previous investigations limit the impact of this study. While the Authors have provided multicentre data, it would be of benefit for the Authors to provide additional information to further articulate the novelty of their initiative.	Population in these articles was different from our population. People included in the present study was independent and semi-dependent while the previous cited studies included people from nursing homes and people functionally dependent. We added this information in the objective of the study to point out more this difference.
Can the Authors provide further discussion on why they chose to use of CAM vs. Brief Confusion Assessment Method (a.k.a. bCAM	We chose to use the CAM because it is the gold standard to screen for delirium. In addition, to date, the bCAM has not been

(i.e. PMID: 28263444)) in this study?	validated in French, which make it less useful in our context.
Please clarify how the Clinical Frailty Scale was used to assess cognition in the enrolled patients.	The clinical frailty scale was used to assess patients' frailty, not cognitive status. It has been changed in the text in order to be clearer (measures, p. 6).
Can the Authors please clarify (and why) that the inter-rater kappa was only tested at the coordinating centre (pg 9, ln 33-35).	Due to some budget limitations, we could only test the inter-rater kappa at our centre.
Please provide further details on the process of obtaining a "sample analysis of missing patients".	Details had been added to the text (measures, p.7).
It would be helpful to have some information on chief complaint of the patient presenting to the ED. In addition, for patients presenting with a surgical (or surgical-like) illness, did the Authors capture any information on adequacy of pain control and/or use of narcotics?	The information relative to the diagnostic of consultation was added to the table 1. Concerning the information relative to medications, data are being analyzed actually for a future article.
Do the Authors have any information on the time of day of presentation (i.e. day vs. night)? In addition, do they have any information on the length of time patients waited in the waiting room of their ED prior to first assessment by the MD?	The information relative to the time of day of presentation to ED was added to the table 1. The information on the length of time patients waited in the waiting room is not available, because the capture was unreliable among the 4 sites.
Table 1 indicates the variable of "proper lighting". Please define what this means and how this was controlled at different times of the day both in the ED and the ward.	The proper lighting was defined as "is the patient able to read, according to the RAs?". It was controlled at each follow-up.
Table 1 indicates a variable use of physical restraints between the 4 sites. Was the use of restraints standardized or protocolized between sites. Was this in the ED or the ward?	Table 1 is about initial interview, so it present information about ED. The use of physical restraints was not standardized between the 4 sites. It was left to the decision of ED professionals.
Were data on the use of both benzodiazepines, anti-psychotic medications captured?	Concerning the information relative to medications, data are being analyzed actually for a future article. However, for your information, here is what we got (all sites together), before/during hospitalization, for the use of benzodiazepines (n=113/n=160), of anti-psychotics (n=23, n=26) and narcotics (n=53, n=125).
Was preoperative alcohol use assessed in this patient population?	No, it wasn't assessed in this study.

ED LOS (Figure 4) was adjusted for site, age, Charlson, APACHE, OARS and TICS-m scores, however there are many other factors impact ED LOS. For example, length of time of response of consulting services and ward bed availability are likely not fully explained by the stratification by site. Can the Authors provide further details/description on how these pragmatic variables were addressed in their study design and analysis?	Information relative to length of time of responses of consulting services and ward bed availability were not available.
Can the Authors provide any information on visitation policies in their EDs and wards? How many of the older adults had regular bedside presence of an accompanying family member/friend?	The rules governing visits are different among sites, and both in the ED and on the ward in the same hospital. For this reason, we don't have the information about regular bedside presence.
Please clarify if the first episode of delirium occurred in the ED or on the ward in the studied population.	Information was added in the text.
Please provide information on the time of admission to the ward as well as the admitting service. In addition, it would be helpful to know if any of the admitting service routine engage in delirium screening and/or management practices.	The information about the admitting service was not available, because the capture was unreliable among the four sites. In fact, it varies a lot across different hospitals. ED does not have a routine for delirium.
1. Suggest to use the term older adult instead of "elderly, elders, seniors etc..."	The change has been made in the text.
2. The statement "Our study experts suggested... (pg 6, ln 24)" is odd and should be revised.	This statement has been reworded in order to be clearer.
4. There are other grammatical and typographical errors that require additional refinement.	Particular attention has been given to correct any grammatical or typographical errors.

Reviewer 2	
Questions	Answers
This manuscript sought to determine the incidence of delirium and how it incident delirium affects hospital length of stay (LOS). The study would have been more informative if it had evaluated how incident delirium impacts hospital LOS differently than prevalent delirium in the ED. Defining incident delirium in the ED is also challenging; at what point during the ED stay is delirium truly an	This is an interesting question, and could be answered in a supplementary study.

<p>incident case. One of the key features of delirium is that it fluctuates. In patients who were classified with incident delirium, is it possible that some of these patients actually had prevalent delirium, but were lucid at the initial assessment?</p>	
<p>The abstract objectives state you were looking at both ED LOS and hospital LOS outcomes, while the manuscript's outcome is just hospital LOS. Please keep this consistence. I would consider just focusing on hospital LOS. The problem with the ED LOS outcome is that it is difficult to know if the incident delirium caused prolonged ED LOS or the ED LOS caused the incident delirium.</p>	<p>In fact, we looked at both ED LOS and hospital LOS. This information has been added to the abstract objectives and to the title.</p>
<p>One thing that is missing from the introduction why we readers care about the distinction between incident and prevalent delirium? Do they effect outcomes differently?</p>	<p>Those explications has been added to the introduction (p. 5)</p>
<p>It seems like your hospitals have a significant boarding problem. Is it possible to give the readers a sense of how significant this boarding problem is? What is the average RF and boarding LOS of stay? Also, did you screen 7 days a week, 24 hours a day?</p>	<p>Information relative to ward bed availability was not recorded.</p> <p>The frequency of the screening was added in methods (p. 6)</p>
<p>Why did you only include patients who were fully or semi-independent. Patients who are functionally impaired are likely the most vulnerable to developing delirium and adverse outcomes. As a result, their exclusion hampers the external validity of your study.</p>	<p>Explications had been added in the methods (p. 6)</p>
<p>You also excluded patients who were unable to consent. Did you attempt to contact their authorized surrogates to obtain consent? If not, excluding patients who are non-consentable would be excluding a vulnerable, but important patient population.</p>	<p>Explications had been added in the methods (p. 6)</p>
<p>The CAM's lowest sensitivity based upon Wei et al's systematic review was 46%. I would consider using a slightly more contemporary systematic review published by Wong et al.[1].</p>	<p>This has been changed in the text.</p>
<p>What was the clinical and educational backgrounds of the research assistants?</p>	<p>The clinical and educational backgrounds of the RAs were quite large. There was an experimented research nurse, and the other were students in different study fields related</p>

	to health. Except for the research nurse, none of the RAs had a clinical experience with screening tests like the CAM or the DI.
Please state if you defined incident delirium if it only occurred in the ED or if you included incident delirium that occurred during first 24 hours of the hospital stay.	This information has been added in outcomes (p. 7)
I thought that the specific method of the CAM required you to have both altered mental status and a fluctuating course. Also, I would mention that you used the SENS method to ascertain delirium for your study.	This information has been added in outcomes (p.8)
You stated that you adjusted for age, Charlson, and APACHE. Why didn't you also adjust for the TICS-m as well as pre-delirium cognition or frailty as they may be potential confounders? Some would also argue that ED LOS is a potential confounder as well.	In fact, we also adjust for the TICS-m and frailty. This information had been added to statistical analyses (p.8).
I would think that reporting the Kappa for the CAM would be sufficient. Also consider reporting the CAM's kappa in the preceding paragraph as this was not one of your primary study objectives.	The section on CAM's kappa has been changed to the corresponding paragraph.
I think reporting data at the site level may be too much detail. Personally, I would just report the overall results from all 4 sites combined.	Data from each sites has been removed in the text. However, we let them in tables and figures.
The discussion is too long and not very well organized. The goal of the discussion is provide context of how your findings add to the literature and what clinicians should do about your findings. I would considering reading Horton et al.'s paper about how to write a discussion section [2]. I would consider organizing your discussion into the following paragraphs: (a) Summarize your results, (b) Discuss the importance of incident delirium and how it differentially affects outcomes compared with prevalent delirium, (c) Discuss the potential mechanisms for incident delirium and what EDs should do to prevent it from happening. (d) Limitations. (e) Conclusions.	We worked on the discussion to make it shorter and better organized.
Discussion: I would consider deleting any mention of ED LOS as this was not the	ED LOS has been added to the primary objective of the study.

primary objective of your study.	
Discussion: Han et al's study reported prevalent delirium rather than incident delirium. I would also consider deleting this paragraph since I am unclear how this is relevant to your discussion.	We deleted the paragraph concerning the prevalent delirium.

VERSION 2 – REVIEW

REVIEWER	Jin Han Vanderbilt University Medical Center, USA
REVIEW RETURNED	27-Oct-2017

GENERAL COMMENTS	<p>Incident Delirium Review</p> <p>This manuscript sought to determine the incidence of delirium in the ED and how it effects ED LOS and hospital LOS. While the data presented in this manuscript is of great interest, I still have significant concerns. I am still not fully convinced that ED LOS is a relevant outcome. It is far more likely that prolonged ED LOS is the significant driver of incident delirium. Your multivariable model as constructed implies that incident delirium (independent variable) is driving longer ED LOS (dependent variable) which seems mechanistically implausible. In my opinion, treating ED LOS as an outcome distracts from the primary message of the manuscript.</p> <p>An alternative approach may be to: (1) Describe the incidence of delirium in the ED, (2) Describe how incident delirium impacts hospital LOS, and (3) determine if ED LOS is associated with incident delirium (ED LOS becomes the independent variable and incident delirium is the dependent variable) as exploratory objective to identify modifiable risk factors. This approach actually better aligns with how your discussion is currently structured. Below are my additional comments:</p> <p>MAJOR</p> <p>Page 4, lines 24 – 43, Introduction: Personally, I agree that it is important prevalent and incident delirium may be important to distinguish from one another. However, I'm not sure if the introduction does enough to make the reader care why we should care about making the distinction between incident and prevalent delirium? It may also be worth pointing out that McCusker et al. observed that incident delirium, but not prevalent delirium increased hospital LOS [1]. I would also make it clearer that incident delirium is a preventable event and preventing delirium is a far more cost-effective method to improve the outcomes of older patients.</p> <p>Page 6, lines 30 – 32, Methods: What was the rationale for assessing for incident delirium up to 24 hours after hospital admission, especially since this is an ED-focused study?</p> <p>Page 6, lines 32 – 33, Methods: Please specify what time the RAs screened for patients. What happened in patients who were enrolled</p>
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at the end of the enrollment window (11th hour) with regard to the second assessment?

Page 10, lines 38 – 40, Limitation: I would state that because you excluded patients with moderate to severe dementia, your findings may not be generalizable to a more vulnerable patient population since they were excluded.

Page 10, lines 41 to 42, Limitation: You state that the CAM's sensitivity when used by research assistants is "34% and 58%". While I agree that multiple CAM assessments increases its sensitivity, exclusion of delirious patients from your study was based upon the initial and single CAM assessment. It is very possible that patients who were actually delirious were misclassified as non-delirious, and erroneously enrolled in the study. This should be mentioned as a limitation.

Discussion Overall: Conventionally, the conclusions should follow the limitations section. The two paragraphs after the limitations (page 11, lines 4 – 8, and 9 – 13) should be integrated into the discussion paragraphs before the limitations. What is also missing from the discussion is what EDs can potentially do to reduce the risk of incident delirium? Should we start implementing delirium prevention protocols in the ED?

Table and Figures Overall Comment: I feel that there is too much data being presented in the table and figures. My primary concern is that this will negatively impact the manuscript's readability and distract from your primary message. Providing site level data is also unconventional for multi-center studies. What should the reader supposed to take away from the fact that incident delirium was significantly associated with ED LOS in one site only?

Table 1. Instead of presenting the site-level data, consider placing the data for the entire cohort in one column and the missed patients in the other.

Figure 2. I'm not sure you have to present delirium incidence of the SPEC method. I would label each bar with delirium incidence rather than the difference in incidence between the SENS and SPEC method.

MINOR

Page 2, lines 8-9, Abstract participants: You may want to mention that you included ED patients who were non-delirious after the first 8 hours.

Page 2, lines 22-25, Abstract conclusions: What about the relationship between incident delirium and ED LOS?

Page 7, lines 3 – 5, Methods: Please add the reference for the CAM's sensitivity and specificity.

Page 7, lines 32- 40, Methods: Consider moving the SENS/SPEC description to the previous section where you are describing the CAM.

Page 8, lines 7 – 8, Methods: Consider changing "Cumulative incidence rates are estimated using Kaplan-Meier curves" to

	<p>“Cumulative incidence rates for delirium were estimated using Kaplan-Meier curves.”</p> <p>I’m not sure if Figures 4 and 5 are really needed.</p> <p>REFERENCES 1. McCusker J, Cole MG, Dendukuri N, Belzile E: Does delirium increase hospital stay? Journal of the American Geriatrics Society 2003, 51(11):1539-1546.</p>
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VERSION 2 – AUTHOR RESPONSE

Editorial requests :

		Authors ‘response
1	<p>“The study focused on the incident delirium, because in opposite to prevalent delirium, ED services can act in a way to prevent it.” Suggest revising to: “The study focused on the incident delirium because, as opposed to prevalent delirium, ED services can act in a way to prevent it.”</p>	Done
2	<p>“As well, the incidence of delirium was collected for those patients” Suggest revising to: “The incidence of delirium was also collected for those patients”</p>	Done
3	<p>Can you elaborate on your response to the following comment from reviewer 1? “ED LOS (Figure 4) was adjusted for site, age, Charlson, APACHE, OARS and TICS-m scores, however there are many other factors impact ED LOS. For example, length of time of response of consulting services and ward bed availability are likely not fully explained by the stratification by site. Can the Authors provide further details/description on how these pragmatic variables were addressed in their study design and analysis?” You say that this information was not available. Have you discussed this as a limitation in the discussion section?</p>	<p>We know from experience that our data about consultant timing to be unreliable in our system. We choose not to include this variable with high variability.</p>

		Authors 'response
1	<p>This manuscript sought to determine the incidence of delirium in the ED and how it affects ED LOS and hospital LOS. While the data presented in this manuscript is of great interest, I still have significant concerns. I am still not fully convinced that ED LOS is a relevant outcome. It is far more likely that prolonged ED LOS is the significant driver of incident delirium. Your multivariable model as constructed implies that incident delirium (independent variable) is driving longer ED LOS (dependent variable) which seems mechanistically implausible. In my opinion, treating ED LOS as an outcome distracts from the primary message of the manuscript.</p> <p>An alternative approach may be to: (1) Describe the incidence of delirium in the ED, (2) Describe how incident delirium impacts hospital LOS, and (3) determine if ED LOS is associated with incident delirium (ED LOS becomes the independent variable and incident delirium is the dependent variable) as exploratory objective to identify modifiable risk factors. This approach actually better aligns with how your discussion is currently structured.</p>	<p>This was address in the objective and clarified. The first outcome is incidence of delirium, the second outcome is the impact on hospital LOS. ED LOS is described as a co-variable, not an outcome.</p>
2	<p>Page 4, lines 24 – 43, Introduction: Personally, I agree that it is important prevalent and incident delirium may be important to distinguish from one another. However, I'm not sure if the introduction does enough to make the reader care why we should care about making the distinction between incident and prevalent delirium? It may also be worth pointing out that McCusker et al. observed that incident delirium, but not prevalent delirium increased hospital LOS [1]. I would also make it clearer that incident delirium is a preventable event and preventing delirium is a far more cost-effective method to improve the outcomes of older patients.</p>	<p>The item concerning the reference of McCusker was right, modification was done in the text.</p>
3	<p>Page 6, lines 30 – 32, Methods: What was the rationale for assessing for incident</p>	<p>We assessed the patient up to 24h on the basis that a patient who develop a delirium</p>

	delirium up to 24 hours after hospital admission, especially since this is an ED-focused study?	let say an hour after arrival on the ward is most likely due to the 48 hours in the ED than the first hour on the ward. We kept this evaluation for possible causality purposes.
4	Page 6, lines 32 – 33, Methods: Please specify what time the RAs screened for patients. What happened in patients who were enrolled at the end of the enrollment window (11th hour) with regard to the second assessment?	The patient were screen on a 12h basis, mid-morning and mid-evening.
5	Page 10, lines 38 – 40, Limitation: I would state that because you excluded patients with moderate to severe dementia, your findings may not be generalizable to a more vulnerable patient population since they were excluded.	Addressed in the discussion
6	Page 10, lines 41 to 42, Limitation: You state that the CAM's sensitivity when used by research assistants is "34% and 58%". While I agree that multiple CAM assessments increases its sensitivity, exclusion of delirious patients from your study was based upon the initial and single CAM assessment. It is very possible that patients who were actually delirious were misclassified as non-delirious, and erroneously enrolled in the study. This should be mentioned as a limitation.	A line was added in the limitation section about misclassification.
7	Discussion Overall: Conventionally, the conclusions should follow the limitations section. The two paragraphs after the limitations (page 11, lines 4 – 8, and 9 – 13) should be integrated into the discussion paragraphs before the limitations. What is also missing from the discussion is what EDs can potentially do to reduce the risk of incident delirium? Should we start implementing delirium prevention protocols in the ED?	Adjusted
8	Table and Figures Overall Comment: I feel that there is too much data being presented in the table and figures. My primary concern is that this will negatively impact the manuscript's readability and distract from your primary message. Providing site level data is also unconventional for multi-center	We choose to keep this information in the actual manuscript

	studies. What should the reader supposed to take away from the fact that incident delirium was significantly associated with ED LOS in one site only?	
9	Table 1. Instead of presenting the site-level data, consider placing the data for the entire cohort in one column and the missed patients in the other.	Delirium is a fluctuating disease per se, we believe that evidence of disparities among site will be useful to readers. Data about missed and included patients are presented in the text.
10	Figure 2. I'm not sure you have to present delirium incidence of the SPEC method. I would label each bar with delirium incidence rather than the difference in incidence between the SENS and SPEC method.	We choose to keep this information in the actual manuscript
11	Page 2, lines 8-9, Abstract participants: You may want to mention that you included ED patients who were non-delirious after the first 8 hours.	Addressed
12	Page 2, lines 22-25, Abstract conclusions: What about the relationship between incident delirium and ED LOS?	Adjusted: ED LOS is a co-variable and this was made clearer in the text.
13	Page 7, lines 3 – 5, Methods: Please add the reference for the CAM's sensitivity and specificity.	Reference for CAM's sensitivity and specificity was already there (Inouye et al. 1990)
14	Page 7, lines 32- 40, Methods: Consider moving the SENS/SPEC description to the previous section where you are describing the CAM.	Done, as suggested.
15	Page 8, lines 7 – 8, Methods: Consider changing "Cumulative incidence rates are estimated using Kaplan-Meier curves" to "Cumulative incidence rates for delirium were estimated using Kaplan-Meier curves."	Done, as suggested.
16	I'm not sure if Figures 4 and 5 are really needed.	We choose to keep this information in the actual manuscript

VERSION 3 – REVIEW

REVIEWER	Jin Han Vanderbilt University Medical Center, USA
REVIEW RETURNED	15-Dec-2017

GENERAL COMMENTS

Overall Comments: Your most recent revision states that ED LOS is now a co-variable and no longer an outcome interest. If that is the case, I would consider removing:

1) The adjusted mean ED LOS from the abstract.

2) Page 9, lines 22 to 27, Methods - You mention ED LOS as one of the outcomes of your multivariable models.

3) Page 9, lines 22 to 27, Results: You mention the results of the ED LOS linear model.

4) Figure 4 also references the ED LOS linear model. Removing this figure will also bring you under 5 table/illustration limit as specified in the author instructions:

http://bmjopenrespres.bmj.com/pages/authors/#original_research

Page 6, lines 30 – 32, Methods: In my previous review, I inquired about the rationale for assessing for incident delirium up to 24 hours after hospital admission, especially since this is an ED-focused study. You replied, "We assessed the patient up to 24h on the basis that a patient who develop a delirium let say an hour after arrival on the ward is most likely due to the 48 hours in the ED than the first hour on the ward. We kept this evaluation for possible causality purposes." Please add this text to the manuscript body.

Page 7, lines 34 to 35, Methods: How did you determine delirium incidence in patients who were missed?

Page 8, lines 9 to 18, Methods: You mentioned that ED LOS is now a co-variable rather than an outcome. If you did adjust for ED LOS in your hospital LOS model, then please mention this.

Page 10, lines 39 – 39, Discussion: You stated that "Our cohort represents only a portion of the older adult population usually seen in the ED and may not be generalizable to all elders". Can you please be more specific to how your cohort represented a portion of seniors and how this may have impacted your findings? For example, you could state that you only included independent and semi-independent seniors limiting the generalizability of your findings to dependent seniors. This, however, would likely under estimate your delirium incidence.

Page 11, line 11, Discussion: Please add a conclusion at the end of the discussion that briefly summarizes your findings.

Figure 2: I still think it is unnecessary to report delirium incidence with both the SENS and SPEC CAM methods. I just think it will just bring confusion to the readers especially since you state that you chose to use the SENS method to report delirium incidence in the methods. If you choose to report both, you should provide justification for this in methods. At least to me, the only reason that makes any sense to present both methods is that one (SPEC) served as a sensitivity analysis to ensure that both methods had similar delirium incidences. If you choose to perform a sensitivity analysis, you should consider rerunning the hospital LOS models with the SPEC definition of delirium incidence.

VERSION 3 – AUTHOR RESPONSE

Comments	Answer
Comment from the editor	
Please avoid using acronyms in the title. We suggest amending to: "Incidence of delirium in the Canadian Emergency Department and its consequences on hospital length of stay : a prospective observational multicentre cohort study."	We made the modification as suggested.
Comments from the reviewer 2	
<p>1. Overall Comments: Your most recent revision states that ED LOS is now a co-variable and no longer an outcome interest. If that is the case, I would consider removing:</p> <p>1) The adjusted mean ED LOS from the abstract. 2) Page 9, lines 22 to 27, Methods - You mention ED LOS as one of the outcomes of your multivariable models. 3) Page 9, lines 22 to 27, Results: You mention the results of the ED LOS linear model. 4) Figure 4 also references the ED LOS linear model. Removing this figure will also bring you under 5 table/illustration limit as specified in the author instructions: http://bmjopenrespres.bmj.com/pages/authors/#original research</p>	The four items were removed from the article.
<p>2. Page 6, lines 30 – 32, Methods: In my previous review, I inquired about the rationale for assessing for incident delirium up to 24 hours after hospital admission, especially since this is an ED-focused study. You replied, "We assessed the patient up to 24h on the basis that a patient who develop a delirium let say an hour after arrival on the ward is most likely due to the 48 hours in the ED than the first hour on the ward. We kept this evaluation for possible causality purposes." Please add this text to the manuscript body.</p>	The item was added to the text.
<p>3. Page 7, lines 34 to 35, Methods: How did you determine delirium incidence in patients who were missed?</p>	The precision has been brought to the text.
<p>4. Page 8, lines 9 to 18, Methods: You mentioned that ED LOS is now a co-variable rather than an outcome. If you did adjust for ED LOS in your hospital LOS model, then please mention this.</p>	The modification was made.
<p>5. Page 10, lines 39 – 39, Discussion: You stated that "Our cohort represents only a portion of the older adult population usually seen in the ED and may not be generalizable to all elders". Can you please be more specific to how your cohort represented a portion of seniors and how this may have impacted your findings? For example, you could state that you only included independent and semi-independent seniors limiting the generalizability of your findings to dependent seniors. This, however, would likely under estimate your delirium incidence.</p>	We made changes to better reflect the reason why our cohort represents only a portion of the older adults population.

6. Page 11, line 11, Discussion: Please add a conclusion at the end of the discussion that briefly summarizes your findings.	A conclusion was added at the end of the discussion.
7. Figure 2: I still think it is unnecessary to report delirium incidence with both the SENS and SPEC CAM methods. I just think it will just bring confusion to the readers especially since you state that you chose to use the SENS method to report delirium incidence in the methods. If you choose to report both, you should provide justification for this in methods. At least to me, the only reason that makes any sense to present both methods is that one (SPEC) served as a sensitivity analysis to ensure that both methods had similar delirium incidences. If you choose to perform a sensitivity analysis, you should consider rerunning the hospital LOS models with the SPEC definition of delirium incidence.	We removed delirium with SPEC method from the figure 2.

VERSION 4 – REVIEW

REVIEWER	Jin Han Vanderbilt University Medical Center, USA
REVIEW RETURNED	17-Jan-2018

GENERAL COMMENTS	<p>In the discussion first paragraph, consider removing the following sentence: "A statistically non-significant increase of 5.0 hours was also found in the average ED LOS between those 2 groups, but this increase is of clinical importance for patient care."</p> <p>Conventionally, the limitations are placed right before the conclusions.</p> <p>Page 11, lines 12 to 16, Discussion: I would add a sentence or two of what we should do when we identify patients at high risk for delirium. A sentence stating that patients at high risk for developing delirium may be appropriate for delirium prevention protocols and cite the following: http://www.ncbi.nlm.nih.gov/pubmed/26062023.</p> <p>Page 11, lines 17 to 18, Conclusion: Please consider expanding the conclusion. You can just use the abstract conclusions or alternatively, use the following: "In conclusion, the incidence of delirium was 12.1% in community dwelling older adults enrolled from 4 Canadian EDs. Incident delirium was significantly increased hospital length of stay by 4 days negatively affecting the patient and healthcare system."</p> <p>and therefore has important implications for patients and could contribute to ED overcrowding through a deleterious feedback loop. Developing delirium increases hospital stay by 4.4, with the impact it can have on our health system.</p> <p>Figure 2. Please add the incidence of delirium for each of the sites above each bar.</p>
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VERSION 4 – AUTHOR RESPONSE

Comments	Answer
Comments from the editor	
<p>There are still some grammatical/ typographical errors in the manuscript. Can you please thoroughly proofread the paper one more time?</p> <p>Some examples are included below from the 'Authors' contribution' section (page 1):</p> <p>“He was responsible of design..” should be “He was responsible FOR design..”</p> <p>“..were responsible for all four site recruitment.” Should be something like: “..were responsible for recruitment at all four sites.”</p> <p>“are all collaborator of INDEED project” should be “are all collaborators of the INDEED project”</p> <p>“reviewed, and approved the manuscript.” Should be “reviewed and approved the manuscript.”</p>	<p>We made the modifications as suggested.</p>
Comments from the reviewer 2	
<p>In the abstract objective, please change "non-delirious community older adults" to "non-delirious community dwelling older adults."</p>	<p>We made the modification as suggested.</p>
<p>In the discussion first paragraph, consider removing the following sentence: "A statistically non-significant increase of 5.0 hours was also found in the average ED LOS between those 2 groups, but this increase is of clinical importance for patient care."</p>	<p>The item was removed from the text.</p>
<p>Conventionally, the limitations are placed right before the conclusions.</p>	<p>We made the modification as suggested.</p>
<p>Page 11, lines 12 to 16, Discussion: I would add a sentence or two of what we should do when we identify patients at high risk for delirium. A sentence stating that patients at high risk for developing delirium may be appropriate for delirium prevention protocols and cite the following: http://www.ncbi.nlm.nih.gov/pubmed/26062023.</p>	<p>We added a sentence as suggested.</p>
<p>Page 11, lines 17 to 18, Conclusion: Please consider expanding the conclusion. You can just use the abstract conclusions or alternatively, use the following: "In conclusion, the incidence of delirium was 12.1% in community dwelling older adults enrolled from 4 Canadian EDs. Incident delirium was significantly increased hospital length of stay by 4 days negatively affecting the patient and healthcare system."</p> <p>and therefore has important implications for patients and could contribute to ED overcrowding through a deleterious feedback loop. Developing delirium increases hospital stay by 4.4, with the impact it can have on our health system.</p>	<p>We made the modifications as suggested.</p>
<p>Figure 2. Please add the incidence of delirium for each of the sites</p>	<p>The incidence for each site</p>

above each bar.

was added to the figure.