PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Between-hospital and between-neighborhood variance in trauma outcomes: Cross-sectional observational evidence from the Detroit metropolitan area
AUTHORS	Sall, Lauren; Hayward, R. David; Fessler, Mary; Edhayan, Elango

VERSION 1 – REVIEW

REVIEWER	PD Dr. Claas Buschmann Institute of Legal Medicine and Forensic Sciences, Charité, Berlin / Germany
REVIEW RETURNED	08-Feb-2018

GENERAL COMMENTS	Thank you for the opportunity to review this interesting article. The article is well written and structured, and the literature list is up-to-date. I generally recommend publication. Nonetheless, I have some small amendments that should be addressed before publication: • Please give mean ages of the populations studied. Were younger people poorer or poorer people younger, i. e. do they live in “dangerous” neighborhoods? The lack of co-existent morbidities in younger ages might cover poorer trauma outcome from lower socioeconomic status and vice versa. Please discuss. • Pre-hospital trauma mortality is a significant issue that was not addressed in this study. Please discuss this topic and add "Kleber C, Giesecke MT, Tsokos M, Haas NP, Schaser KD, Poloczek S, Buschmann C (2012) Overall Distribution of Trauma-related Deaths in Berlin 2010: Advancement or Stagnation of German Trauma Management? World J Surg 36:2125-2130." to the reference list. • Please give some information about the emergency medical infrastructure in your area and possibly differences with regard to different neighborhoods. After the suggested changes have been made, I recommend publication. I do not have to see the article again.

REVIEWER	Lynne Moore Laval University, Québec, Canada
REVIEW RETURNED	07-May-2018

GENERAL COMMENTS	This study aims to advance knowledge on the relative influence of neighborhood factors and hospital-based factors (referred to here as quality of care) on outcome disparities for trauma admissions. An interesting questions but this study has many limitations. In particular, authors only present one table in their results section which is insufficient for a full-length article. They also do not

	demonstrate thorough knowledge of their dataset and its inherent limitations – this should guide extensive sensitivity analyses, which are necessary when using administrative data for research. • One would expect regional disparities (largely SES) to influence risk of injury, severity of injury, population-based injury mortality and long-term outcomes, but not in-hospital outcomes. If this was the case, quality of care would be in the causal pathway between SES and outcome. This would require mediation analysis. The analysis used by authors postulates independence of these two effects even though authors state in the Introduction that SES and quality of care not independent. • Any analysis on quality of care requires adjustment for patient casemix. Even though authors only had access to hospital discharge data, adjustment for age, sex, comorbidities, race, a measure of injury severity based on ICD codes (e.g. ICISS), transfer status etc.. should be conducted. Also, information on the type of hospital (for profit, teaching, designated trauma center with level) should be incorporated. The authors should add a table to the results section describing their sample according to all of these parameters. • Aggregate measures of SES exist for Zip code data – why weren't these used? • For costs analysis, were cost-to-charge ratios used? Limitations of using this kind of cost data for inter-hospital and inter-regional comparisons should be discussed. How were patients with missing data on charges different from those with complete data? Would a missing completely at random assumption be plausible? Was multiple imputation considered? • I understand that ED deaths were excluded from LOS analyses. How were in-hospital deaths treated? • Table 1 – what does last column represents? IC should be added to ICC estimates • Discussion paragraph 1 – there is a large body of literature on inter-hospital variation in injury outcomes which should be added.

REVIEWER	Molly Jarman Brigham and Women's Hospital, USA
REVIEW RETURNED	14-May-2018

GENERAL COMMENTS	This is a well written paper addressing sources of variation in trauma outcomes as a means of identifying injury disparity pathways. The results could be strengthened by examining additional individual, neighborhood, and hospital characteristics to identify specific sources of variation, rather than simply quantifying variation at three levels. Page 6, Line 17-19: Which ICD-9 diagnostic codes were included in the study sample? Page 6, Lines 26-28 and 34-36: What were the mean and IQR for number of observations per hospital and per neighborhood? PAge 6, Line 34: ZIP code as a neighborhood definition is understandable given the availability of data in the SID, but ZIP may not adequately capture patterns of care or neighborhood characteristics, especially in high density/urban areas. Did you look at other neighborhood definitions, including clusters of ZIP codes with similar characteristics?

	Page 8, Lines 10-29: Consider including a flow chart to illustrate composition of the sample. Did you examine variation in patient characteristics by neighborhood and hospital? This is easily addressed by including patient, neighborhood, and hospital characteristics as covariates in hierarchical regression models. Other potential strategies include sub-group analysis by injury severity (ISS >15) and/or by trauma center designation (available in SID data sets by linking with the AHA annual survey). Much of what we think of as neighborhood variation in trauma outcomes will show up mathematically at the individual or hospital level. For example, high risk injuries may cluster in certain neighborhoods, but the variation in outcomes due to injury characteristics is accounted for at the individual level. Likewise, geographic access to a trauma center can be thought of as a neighborhood characteristic, but a regression model will reflect this as hospital-level variation due to differences in patterns of care at trauma and non-trauma centers.

VERSION 1 – AUTHOR RESPONSE

Responses to Reviewer 1

R1.1. *Please give mean ages of the populations studied. Were younger people poorer or poorer people younger, i. e. do they live in "dangerous" neighborhoods? The lack of co-existent morbidities in younger ages might cover poorer trauma outcome from lower socioeconomic status and vice versa. Please discuss.*

RESPONSE: This information has been added, along with other demographic comparison by neighborhood poverty, in a new table (see page 11, Table 2). This point is now addressed in the discussion (see page 15, final paragraph, following on page 16).

R1.2. *Pre-hospital trauma mortality is a significant issue that was not addressed in this study. Please discuss this topic and add "Kleber C, Giesecke MT, Tsokos M, Haas NP, Schaser KD, Poloczek S, Buschmann C (2012) Overall Distribution of Trauma-related Deaths in Berlin 2010: Advancement or Stagnation of German Trauma Management? World J Surg 36:2125-2130." to the reference list.*

RESPONSE: We have added several sentences to the limitations section addressing this issue, and highlighting the absence of pre-hospital mortality data in this study as a limitation to be addressed in future research (see page 16, final paragraph, following on page 17).

R1.3. *Please give some information about the emergency medical infrastructure in your area and possibly differences with regard to different neighborhoods.*

RESPONSE: We have added information regarding this subject in the introduction (see page 5, end of first full paragraph).

Responses to Reviewer 2

R2.1. *One would expect regional disparities (largely SES) to influence risk of injury, severity of injury, population-based injury mortality and long-term outcomes, but not in-hospital outcomes. If this was the case, quality of care would be in the causal pathway between SES and outcome. This would*

require mediation analysis. The analysis used by authors postulates independence of these two effects even though authors state in the Introduction that SES and quality of care not independent.

RESPONSE: A mediation analysis of this type is beyond the scope of this study. We have added an additional set of stratified analyses (by injury severity), which further help to clarify the extent to which differences in injury type and severity may account for broader inter-hospital differences in outcomes (see page 7, second full paragraph; page 10, full paragraph; page 11, Table 3). These points are now addressed in the discussion section (see page 15, final paragraph, following on page 16).

R2.2. *Any analysis on quality of care requires adjustment for patient casemix. Even though authors only had access to hospital discharge data, adjustment for age, sex, comorbidities, race, a measure of injury severity based on ICD codes (e.g. ICISS), transfer status etc.. should be conducted. Also, information on the type of hospital (for profit, teaching, designated trauma center with level) should be incorporated. The authors should add a table to the results section describing their sample according to all of these parameters.*

RESPONSE: We have added a substantial amount of additional descriptive information regarding patient demographics, injury severity, and neighborhood SES (see page 7 paragraph 2 – 3; pages 9 – 12, Tables 1 – 3).

R2.3. *Aggregate measures of SES exist for Zip code data – why weren't these used?*

RESPONSE: Neighborhood-level poverty rate data is included in the new comparative data (see page 10, full paragraph; pages 9 – 12, Tables 1 – 3). See also the description of these data in the methods section (page 7, paragraph 3).

R2.4. *For costs analysis, were cost-to-charge ratios used? Limitations of using this kind of cost data for inter-hospital and inter-regional comparisons should be discussed. How were patients with missing data on charges different from those with complete data? Would a missing completely at random assumption be plausible? Was multiple imputation considered?*

RESPONSE: Cost-to-charge ratios were not available for the data source used. We discuss this issue in the limitations section (see page 16, first paragraph). We have also changed the terminology used to refer to this variable from "costs" to "charges" throughout the paper to enhance clarity on this point. Supplemental analyses showed that patients with missing charge data differed substantially on a number of points including gender, race, and neighborhood poverty.

The assumption of MCAR does not seem reasonable; the assumption of MAR would be questionable, because it is plausible that charges were waived or left unrecorded differentially for uninsured patients with no ability to pay, or that hospitals treating a large number of patients in this category reported charge data less reliably. Given these issues, we decided that multiple imputation was not warranted in this case. We now address this point in the results section (see page 12, end of full paragraph).

R2.5. *I understand that ED deaths were excluded from LOS analyses. How were in-hospital deaths treated?*

RESPONSE: In-hospital deaths were retained in the analysis. We conducted supplemental analyses excluding all deaths from the LOS analyses and found no substantial changes in the results. This point is clarified in the methods section (see page 8, final paragraph).

R2.6. *Table 1 – what does last column represents? IC should be added to ICC estimates*

RESPONSE: This column has been moved to a new and expanded descriptive table (see pages 9 – 10, Table 1). The requested edit has been made to the ICC heading (see pages 12 – 14, Table 4).

R2.7. *Discussion paragraph 1 – there is a large body of literature on inter-hospital variation in injury outcomes which should be added.*

RESPONSE: We have added references to a number of relevant studies in the discussion section (see page 14, final paragraph).

Responses to Reviewer 3

R3.1. *Page 6, Line 17-19: Which ICD-9 diagnostic codes were included in the study sample?*

RESPONSE: This information has been added to the methods section (see page 6, end of first full paragraph).

R3.2. *Page 6, Lines 26-28 and 34-36: What were the mean and IQR for number of observations per hospital and per neighborhood?*

RESPONSE: We have added a new table including group-level descriptive statistics at both the hospital and neighborhood levels (see pages 9 – 10, Table 1).

R3.3. *PAge 6, Line 34: ZIP code as a neighborhood definition is understandable given the availability of data in the SID, but ZIP may not adequately capture patterns of care or neighborhood characteristics, especially in high density/urban areas. Did you look at other neighborhood definitions, including clusters of ZIP codes with similar characteristics?*

RESPONSE: It was not practical to develop alternate definitions of neighborhood within the scope of this study, but we have added an acknowledgement of this issue to the limitations section (see page 16, final paragraph, following on page 17).

R3.4. *Page 8, Lines 10-29: Consider including a flow chart to illustrate composition of the sample.*

RESPONSE: We have expanded the text clarifying the two primary points of ambiguity in data loss – the treatment of in-hospital mortality (see our response to reviewer 2, point R2.5; manuscript page 8, final paragraph) and sources of lost charge data (see our response to reviewer 2, point R2.4; manuscript page 10, end of first full paragraph) – which we think will help to clarify the sources of the differences in sample size between models. We are naturally happy to also add a flow chart if these changes are not sufficient to make the nature of the sample clear.

R3.5. *Did you examine variation in patient characteristics by neighborhood and hospital? This is easily addressed by including patient, neighborhood, and hospital characteristics as covariates in hierarchical regression models. Other potential strategies include sub-group analysis by injury severity (ISS >15) and/or by trauma center designation (available in SID data sets by linking with the AHA annual survey). Much of what we think of as neighborhood variation in trauma outcomes will show up mathematically at the individual or hospital level. For example, high risk injuries may cluster in certain neighborhoods, but the variation in outcomes due to injury characteristics is accounted for at the individual level. Likewise, geographic access to a trauma center can be thought of as a neighborhood characteristic, but a regression model will reflect this as hospital-level variation due to differences in patterns of care at trauma and non-trauma centers.*

RESPONSE: See also our response to review #2 point R2.2 above. We have added a substantial amount of information regarding neighborhood-level variation in various patient and case characteristics, as well as differences related to injury severity (see page 7 paragraph 2 – 3; pages 9 – 12, Tables 1 – 3).

Unfortunately, unlike most of the state SIDs, the Michigan SID includes only anonymized hospital identifiers, which allow for clustering of data but not for linkage with AHA data.

We have added material in the discussion section addressing the difficulties inherent in interpreting overlapping effects at multiple levels (see page 15, final paragraph, following on page 16).

VERSION 2 – REVIEW

REVIEWER	Lynne Moore Laval University, Quebec, Canada
REVIEW RETURNED	18-Jun-2018

GENERAL COMMENTS	The authors have done a great job responding to reviewers' comments. I have a two unresolved concerns: 1. Authors state that they used random and fixed effects in their GLMM models. What were the fixed effects? Did they adjust for patient case mix? Inter-hospital variations may well be due to indication bias – different patient case mix in different hospitals particularly across designation levels. This is recognized as a limit in the Discussion but could have been addressed by adjusting at the very least for age, comorbidities, ISS, injury type, and mechanism. Stratifying by dichotomizing the ISS and mechanism is not sufficient to account for patient case mix. 2. LOS and charges are right censored for in-hospital deaths. They should therefore not be included in the analysis of either outcome. However, excluding them may lead to survivor bias. The ideal approach is a Fine and Grey competing risks model but this is analytically complex and hard to interpret. The authors should at least report the results of sensitivity analysis including in-hospital deaths and mention this approach in the limitations section of the discussion.

REVIEWER	Molly Jarman Brigham and Women's Hospital, Boston, Massachusetts, USA
REVIEW RETURNED	28-Jun-2018

GENERAL COMMENTS	Thank you for your thoughtful response to reviewers' comments. The revisions have largely address all of my previously stated concerns. I do have two minor notes: 1) It is not clear if patients with sole/primary injury diagnoses of late effects of injury, superficial injury, or foreign bodies in orifice were excluded. These are typical exclusions when studying traumatic injury outcomes. 2) While the response notes that concerns about neighborhood definition were addressed in the limitations, this particular limitation is not clear. Please include language addressing the limitation of using ZIP code as a proxy for neighborhood.

VERSION 2 – AUTHOR RESPONSE

RESPONSES TO REVIEWER 1:

R1.1. *Authors state that they used random and fixed effects in their GLMM models. What were the fixed effects? Did they adjust for patient case mix? Inter-hospital variations may well be due to indication bias – different patient case mix in different hospitals particularly across designation levels. This is recognized as a limit in the Discussion but could have been addressed by adjusting at the very least for age, comorbidities, ISS, injury type, and mechanism. Stratifying by dichotomizing the ISS and mechanism is not sufficient to account for patient case mix.*

RESPONSE: In addition to the stratified analyses, we have added a series of adjusted analyses which use fixed effects to control for ae, comorbidities, ISS, and mechanism (unfortunately, injury type data is not included in the SID). To facilitate comparison of the random effects-only models (i.e., the analyses on which the previous draft was based) with the adjusted models, we also now report 95% confidence intervals for all ICC statistics. The adjusted ICC estimates are somewhat lower than the unadjusted estimates in most models, but comparison of confidence intervals indicates that none of these changes are statistically significant. See Tables 4, 5, and 6, as well as the Discussion in the first full paragraph of page 20.

R1.2. *LOS and charges are right censored for in-hospital deaths. They should therefore not be included in the analysis of either outcome. However, excluding them may lead to survivor bias. The ideal approach is a Fine and Grey competing risks model but this is analytically complex and hard to interpret. The authors should at least report the results of sensitivity analysis including in-hospital deaths and mention this approach in the limitations section of the discussion.*

RESPONSE: We conducted a sensitivity analysis, in which we re-ran the LOS and charge analyses both including and excluding in-hospital deaths. ICC estimates did not differ significantly between analyses using these alternate approaches. Sensitivity analyses are summarized at the end of the results section (see page 18, first full paragraph). This issue is also addressed in the limitations section (see the middle of page 21).

RESPONSES TO REVIEWER 3:

R3.1. *It is not clear if patients with sole/primary injury diagnoses of late effects of injury, superficial injury, or foreign bodies in orifice were excluded. These are typical exclusions when studying traumatic injury outcomes.*

RESPONSE: We have added a sentence in the methods section clarifying that these cases were not excluded from the present analyses (see page 6, first full paragraph). We conducted additional supplemental sensitivity analyses to determine whether excluding ICD-9 codes indicating late effects of trauma changed the results, and found no significant changes in the ICC estimates.

R3.2. *While the response notes that concerns about neighborhood definition were addressed in the limitations, this particular limitation is not clear. Please include language addressing the limitation of using ZIP code as a proxy for neighborhood.*

RESPONSE: We have expanded our discussion of this issue in the limitations section (see beginning of page 22).