PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study
AUTHORS	Nwogu-Onyemkpa, Eberechi; Dongarwar, Deepa; Salihu, HM; Akpati, Lois; Marroquin, Maricarmen; Abadom, Megan; Naik, Aanand

VERSION 1 – REVIEW

REVIEWER	Joanne Stubbs Western Sydney Local Health District, Epidemiology and Health Analytics
REVIEW RETURNED	10-Dec-2021

GENERAL COMMENTS	Bmjopen-2021-057361
	Reviewer feedback
	This is an interesting study examining the prevalence of inpatient palliative care for patients with SDC and factors associated with the provision of palliative care.
	General comment The word 'utilize' is used throughout the manuscript, but 'use' is generally better and more appropriate (this can be confirmed by a quick Google search). Having said that, use of palliative care depends on a variety of factors including availability, access and patient choice. As such I think that in many cases 'received' (or a similar word) would be preferable. In some instances it would be sufficient to simply state 'palliative care' or 'palliative care services'.
	Abstract P2 line 48 'were associated with' – it is more correct to say 'received'
	Introduction P4, line 24 – I assume that '(42-48 years)' refers to the life expectancy of people with SCD, not the general population, as such it should be moved to after 'adulthood'
	It would be helpful to include a brief statement about the coding criteria for allocation of an ICD palliative care code.
	Method Are the coding instructions for V66.7 and Z51.5 the same? – i.e. are there any instances where a hospitalization would be coded as palliative care by one version of ICD but not the other? A statement about this should be included, otherwise it could be suggested that

the change from ICD9 to ICD10 could contribute to changes in the prevalence of palliative care diagnosis codes.

P8 line 30 – 'allows to examine' is awkward wording, perhaps 'enables examination of ...'

P8 line 48 – please provide details about what variables were adjusted for in the analysis. Also I don't think 'survey' is needed, 'adjusted logistic regression' is sufficient.

Results

When describing rates, wording should be per 1000 hospitalizations (plural not singular)

I am not a statistician, but I have been told that it is not correct to report an OR of 1.81 as '81% more likely'. I think it is more correct to say something like 'the odds were 1.81 times greater', or '... were more likely (OR=1.81)'. This applies to a number of sentences in the Results section.

P10 line 14 - 'associated with' – more appropriate to say 'that received'

p10 line 17 - trends, not trend

P10 line 17 – please report the rate of palliative care at the beginning and end of the study period for all SCD hospitalizations and terminal hospitalizations

p10 line 19 – I think the increase is an average of 9.2% ...?

P10 line 27 - 'for' rather than 'among'

P10 line 39 - it is more correct to say 'highest' rather than 'most pronounced'

P10 line 43 - 'frequency' is not correct, the prevalence is being reported

P11 line 9 - should read '... had the highest levels ...'. It would be good to also report that these types of hospitals also had the highest prevalence of SCD hospitalizations

P11 line 21 – 'end of life' is not correctly used here, 'terminal hospitalizations' is what is being reported

P12 line 8 – 'were' not 'was', and differences

P12 line 16 - 'or' not 'and'

Discussion

The finding that very few of the examined factors increased the odds of palliative care at the terminal hospitalization is interesting but has not been mentioned. It would be good to include a statement about this, and a possible explanation for this.

P13 line 9-13 – is this summary of results based on table 1 or 2? It seems to be a combination of prevalence and adjusted odds results without any clear differentiation between the two.

P13 line 30-35 – the wording of this sentence is a bit awkward, rearranging the sentence would improve it, e.g. something like '... several opportunities arise earlier in the course of SCD for palliative care involvement facilitating more holistic care of patients'

P13 line 38-47 – this sentence would benefit from being re-worded. It also needs a reference

P13 line 54 – race/ethnicity was the only factor clearly associated with palliative care during both SDC hospitalizations and terminal hospitalizations. This should be noted in the discussion.

P14 line 17 - 'in', not 'for'

P14 line 24 - 'the difference' is not needed

P14 line 26 – differences not difference and patients not patient

P14 line 31 – differences not difference

P14 line 45 – perhaps it should say that 'hospitalizations primarily involve ...'

P15 line 10 - 'differences in the ...'

P15 line 13 – judging by their titles, these other studies seem to have examined diseases other than SCD, as such 'diseases' is more appropriate than 'studies'

P15 line 15 – please specify the comparison groups (i.e. zip code lowest quartile and Medicare)

P15 line 22 - this statement should be referenced

P15 line 29 – my reading of the results indicates that this difference was not significant

P15 line 36 – I think you are describing the results of large hospitals and urban teaching hospitals, so such it should be 'large and urban teaching hospitals' (i.e. move the 'and'). Palliative care was also more likely at Medium hospitals, so this should be included

P15 line 46 – 'small and rural...

P16 line 20-27 – the authors should state more explicitly that because of this the reported prevalence rates over-estimate the number of patients benefitting from palliative care

P16 line 34 - 'have' not 'has'

P16 line 36 – could the authors please modify this sentence so as to make a stronger comment regarding the role of the 'provider' (I assume you mean the hematologist or other medical practitioners treating/caring for people with SCD) in referring their patients for a palliative care consultation or liaising with a palliative care specialist. Awareness alone is not sufficient, providers need to take the initiative to discuss palliative care options with the patient or arrange a consultation at an earlier stage of the disease is also needed. It would strengthen the paper if the authors could also make some

suggestion/s as to how this could be achieved, e.g. do they fail to initiate such discussions because they are not aware of the benefits of early palliative care, they do not feel comfortable raising palliative care with their patients, they do not know how to raise it, etc

P16 line 41-46 – the benefits of early palliative care in symptom control and subsequently improved quality of life should also be mentioned here

P16 line 53 – 'life limiting illnesses' is a better term to use than 'chronic serious illnesses'

Table 1 col 5 heading – 'Hospitalizations among ...' this heading does not correctly describe the data in this column. Please reword, e.g. 'Hospitalized patients with SCD receiving palliative care'

Table 2 – please change order of age group and race/ethnicity to be consistent with Table 1

Figure 1 – both axes need to be labelled. The * is not explained.

Figures 2 & 3 – I am not sure that these figures are needed as the data are presented in Table 1. If they are kept, I suggest they are combined into one figure showing both the prevalence of both hospitalizations and palliative care. The x-axis should be labelled.

REVIEWER	Clement Narh
	School of Public Health, University of Health and Allied Sciences,
	Epidemiology and Biostatistics
REVIEW RETURNED	07-Jan-2022

GENERAL COMMENTS

Very interesting manuscript. However, I have a few comments on the analysis that would require some amount of reworking by the authors

How was each hospitalization for SCD counted? A statement should be included in the manuscript to guide on how readmissions were handled as one patient could have contributed several admissions between the study of 2008 to 2018.

Palliative care service utilization was not clearly defined for use in a logistic regression model

It good if the authors could report the simple proportions of Palliative care service utilization in their study population.

Table 2 does not seem to have an outcome variable and does not also indicate whether the model was an unadjusted or adjusted model. For instance, it would be great to have the OR for 4442 receiving palliative care out of the 987555 SCD related hospitalizations. A similar, outcome for in-hospital deaths vs discharged alive should be reported.

I would like to believe that the authors' main objective is palliative care utilization among SCD inpatients, hence, they should try to stick to this objective without focusing so much on the other/confounding variables in the model such as age, race, sex, etc.

Figure 2: the "other category" with a prevalence rate of 1.3 in figure 2 should be split into the different race/ethnicity or the BH-White category added to this group with a footnote indicating the different races forming this group.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1

This is an interesting study examining the prevalence of inpatient palliative care for

patients with SDC and factors associated with the provision of palliative care.

Response to Reviewer: Thank you for your interest in this topic.

General comment

The word 'utilize' is used throughout the manuscript, but 'use' is generally better and

more appropriate (this can be confirmed by a quick Google search). Having said

that, use of palliative care depends on a variety of factors including availability,

access and patient choice. As such I think that in many cases 'received' (or a similar

word) would be preferable. In some instances it would be sufficient to simply state

'palliative care' or 'palliative care services'.

Response to Reviewer: We agree with 'use' and 'received' being the more appropriate words of

choice. These changes have been made throughout the manuscript.

Location of Modification: Throughout the manuscript.

P2 line 48 'were associated with' – it is more correct to say 'received'

Response to Reviewer: We accept this change.

Location of Modification: Abstract

Modified Text: "987,555 SCD-related hospitalizations were identified, of which 4442 (0.45%) received

palliative care service."

P4, line 24 – I assume that '(42-48 years)' refers to the life expectancy of people with

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SCD, not the general population, as such it should be moved to after 'adulthood'

Response to Reviewer: We accept this change.

Location of Modification: Introduction

Modified Text: "Currently, life expectancy with SCD extends into adulthood (42-48 years) but remains significantly lower than the general population, especially for sickle cell anemia—the most severe

form of SCD."

It would be helpful to include a brief statement about the coding criteria for allocation

of an ICD palliative care code.

Response to Reviewer: There is one ICD9 and one ICD10 code for palliative care. This was described in the methods section, "The study's primary outcome was palliative care utilization which

was identified using ICD-9-CM diagnosis code V66.7 and ICD-10-CM diagnosis code Z51.5."

Are the coding instructions for V66.7 and Z51.5 the same? – i.e. are there any

instances where a hospitalization would be coded as palliative care by one version of

ICD but not the other? A statement about this should be included, otherwise it could

be suggested that the change from ICD9 to ICD10 could contribute to changes in the

prevalence of palliative care diagnosis codes.

Response to Reviewer: There were no changes in the criteria for palliative care code with the change

from ICD9 to ICD10.

Location of Modification: Methods

Modified Text: "There were no changes in the criteria for palliative care code with the transition from

ICD-9-CM to ICD-10-CM."

P8 line 30 - 'allows to examine' is awkward wording, perhaps 'enables examination

of ...'

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Response to Reviewer: We accept this change.

Location of Modification: Methods

Modified Text: "Temporal trends analyses were performed using Joinpoint regression technique, which enables examination of the trend of an outcome (in this case, palliative care use) over the study period."

P8 line 48 – please provide details about what variables were adjusted for in the analysis. Also I don't think 'survey' is needed, 'adjusted logistic regression' is sufficient.

Response to Reviewer: We used 'survey logistic regression model' and not plain 'logistic regression'. Survey logistic regression accounts for complex survey design components such as cluster, stratum and weights in the model. We looked at independent association between each of the patient's demographic and hospitalization characteristics (exposure) and palliative care (outcome). We have now added this to the manuscript.

Location of Modification: Methods

Modified Text: "Furthermore, we conducted adjusted survey logistic regression models to examine the patient socio-demographic and hospitalization characteristics (exposures) associated with palliative care utilization (outcome variable) among all SCD hospitalizations and among those which resulted in patients' death in-hospital."

When describing rates, wording should be per 1000 hospitalizations (plural not singular)

Response to Reviewer: We accept this change. This change has been made throughout the result section.

Location of Modification: Results

I am not a statistician, but I have been told that it is not correct to report an OR of 1.81 as '81% more likely'. I think it is more correct to say something like 'the odds were 1.81 times greater', or '... were more likely (OR=1.81)'. This applies to a

number of sentences in the Results section.

Response to Reviewer: '81% more likely' is another way of presenting OR of 1.81. See below papers which have used this terminology - https://pubmed.ncbi.nlm.nih.gov/18316266/

https://pubmed.ncbi.nlm.nih.gov/18562153/

P10 line 14 - 'associated with' - more appropriate to say 'that received'

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "There were 4442 (0.45%) SCD-related hospitalizations that received palliative care service."

p10 line 17 - trends, not trend

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "Figure 1 shows temporal trends in palliative care usage."

P10 line 17 – please report the rate of palliative care at the beginning and end of the study period for all SCD hospitalizations and terminal hospitalizations

Response to Reviewer: We have now added the requested details in the manuscript results.

Location of Modification: Methods

Modified Text: "The rate of inpatient palliative care service utilization increased at an average of 9.2% per year (95% CI, 5.6-12.9) for all SCD-related hospitalizations – from 2.86 per 1000 hospitalizations in 2008 to 6.32 per 1000 hospitalizations in 2017; and an average of 10.7% (95% CI, 3.4-18.5) for terminal hospitalizations – 6.34 per 1000 hospitalizations in 2008 to 15.82 per 1000 hospitalizations in 2017."

p10 line 19 - I think the increase is an average of 9.2% ...?

Response to Reviewer: Yes, the numbers presented are average annual percentage change. We have now added the requested details in the manuscript results.

Location of Modification: Methods

Modified Text: "The rate of inpatient palliative care service utilization increased at an average of 9.2% per year (95% CI, 5.6-12.9) for all SCD-related hospitalizations – from 2.86 per 1000 hospitalizations in 2008 to 6.32 per 1000 hospitalizations in 2017; and an average of 10.7% (95% CI, 3.4-18.5) for terminal hospitalizations – 6.34 per 1000 hospitalizations in 2008 to 15.82 per 1000 hospitalizations in 2017."

P10 line 27 - 'for' rather than 'among'

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "Table 1 shows patient characteristics for SCD related hospitalizations and patients utilizing palliative care services."

P10 line 39 - it is more correct to say 'highest' rather than 'most pronounced'

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "The prevalence of SD-related hospitalization was highest among NH-Blacks (20.7 per 1000 SCD hospitalizations) and lowest in NH-Whites (0.1 per 1000 SCD hospitalizations)..."

P10 line 43 - 'frequency' is not correct, the prevalence is being reported

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "...while the prevalence of inpatient palliative care services was highest in NH-Whites (12.6 per 1000 SCD hospitalizations) and lowest in Hispanics (3.6 per 1000 SCD hospitalizations)."

P11 line 9 - should read '... had the highest levels ...'. It would be good to also report that these types of hospitals also had the highest prevalence of SCD hospitalizations

Response to Reviewer: We agree with these changes.

Location of Modification: Results

Modified Text: "Large and urban teaching hospitals had the highest prevalence of SCD hospitalization (3.4 and 4.3 per 1000 hospitalizations, respectively) and highest level of inpatient palliative care service use (5.1 and 5.1 per 1000 SCD hospitalizations, respectively)."

P11 line 21 – 'end of life' is not correctly used here, 'terminal hospitalizations' is what is being reported

Response to Reviewer: We agree with this change.

Location of Modification: Results

Modified Text: "During terminal hospitalizations patients between 40-59 years were 81% more likely to receive palliative care services than patients 18-39 years old (odds ratio [OR], 1.81, 95% confidence interval [CI], 1.19-2.75)."

P12 line 8 - 'were' not 'was', and differences

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "During terminal admissions, there were no significant differences in palliative care usage across different payors."

P12 line 16 - 'or' not 'and'

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "Patients admitted in a medium or large hospital were 47% and 91%, respectively more

likely..."

The finding that very few of the examined factors increased the odds of palliative care at the terminal hospitalization is interesting but has not been mentioned. It would be good to include a statement about this, and a possible explanation for this.

Response to Reviewer: We appreciate this observation. We have added the statement below noting that race and ethnicity was the only factor that was associated with palliative care use in both SCD-related and terminal hospitalizations. There is no obvious explanation for this observation however, one might speculate that palliative care use during terminal admissions were likely related to patient reception of comfort care during these events.

Location of Modification: Discussions

Modified Text: "Our study found higher prevalence of palliative care service usage in terminal admissions when compared to admissions with routine discharge or transfer to another level of care. Furthermore, race/ethnicity was the only factor associated with PC use during both SCD-related and terminal hospitalizations."

P13 line 9-13 – is this summary of results based on table 1 or 2? It seems to be a combination of prevalence and adjusted odds results without any clear differentiation between the two.

Response to Reviewer: This is a summary of results presented in table 2. We have removed 'in the northeast" for accuracy.

Location of Modification: Discussion

Modified Text: "Palliative care use was more likely among patients who are NH-White male, in higher income quartiles, with private insurance, who receive care in large academic hospitals in the northeast."

P13 line 30-35 – the wording of this sentence is a bit awkward, re-arranging the sentence would improve it, e.g. something like '... several opportunities arise earlier in the course of SCD for palliative care involvement facilitating more holistic care of Patients'

Response to Reviewer: We accept this change. Sentence has been revised as noted below.

Location of Modification: Discussion

Modified Text: "This highlights an opportunity earlier in the progression of SCD for palliative care involvement, facilitating more holistic care of patients."

P13 line 38-47 – this sentence would benefit from being re-worded. It also needs a Reference

Response to Reviewer: The sentence has been reworded and a reference included.

Location of Modification: Discussion

Modified Text: "This highlights an opportunity earlier in the progression of SCD for palliative care involvement, facilitating more holistic care of patients. Earlier initiation of palliative care grants patients psychosocial support and symptom management from an interdisciplinary team, as well as honest discussions regarding goals of care and patient's preference for end of life."

P13 line 54 – race/ethnicity was the only factor clearly associated with palliative care during both SDC hospitalizations and terminal hospitalizations. This should be noted in the discussion.

Response to Reviewer: Thank you for the recommendation. We have added this observation.

Location of Modification: Discussion

Modified Text: "Notably, race/ethnicity was the only factor associated with palliative care use in both SCD and terminal hospitalizations."

P14 line 17 - 'in', not 'for'

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Similar studies are lacking to elucidate factors implicated in the racial difference in non-hospice palliative care usage across all life limiting diseases."

P14 line 24 – 'the difference' is not needed

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Palliative care has a strong perceived association with hospice with many patients and families unable to differentiate between the two."

P14 line 26 – differences not difference and patients not patient

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Therefore, the above factors identified are likely to also play a role in racial differences observed in palliative care use in patients with chronic conditions such as SCD."

P14 line 31 - differences not difference

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Further studies are needed to investigate patient and system factors associated with racial differences in palliative care usage in SCD."

P14 line 45 – perhaps it should say that 'hospitalizations primarily involve ...'

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Pain is the most prominent feature of SCD and hence it is plausible that inpatient palliative care services in SCD hospitalizations primarily involve pain management."

P15 line 10 - 'differences in the ...'

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "We also found socioeconomic differences in the usage of palliative care in SCD similar to other diseases."

P15 line 13 – judging by their titles, these other studies seem to have examined

diseases other than SCD, as such 'diseases' is more appropriate than 'studies'

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "We also found socioeconomic differences in the usage of palliative care in SCD similar to other diseases."

P15 line 15 – please specify the comparison groups (i.e. zip code lowest quartile and Medicare)

Response to Reviewer: We had already included the comparison group for payor, but now we have also included the referent group for income quartile

Location of Modification: Results

Modified Text: "Patients with zip code in the highest income quartile were 58% more likely to utilize inpatient palliative care services (OR, 1.58; 95% CI 1.02-2.45) than those in the lowest quartile."

P15 line 22 – this statement should be referenced

Response to Reviewer: References have been added.

Location of Modification: Discussion

P15 line 29 – my reading of the results indicates that this difference was not Significant

Response to Reviewer: We agree that this finding was not significant. This sentence has been removed.

Location of Modification: Discussion

P15 line 36 – I think you are describing the results of large hospitals and urban teaching hospitals, so such it should be 'large and urban teaching hospitals' (i.e. move the 'and'). Palliative care was also more likely at Medium hospitals, so this should be included

Response to Reviewer: We accept these changes.

Location of Modification: Discussion

Modified Text: "Hospital characteristics were also predictive of palliative care usage with medium, large and urban teaching hospitals associated with greater usage of palliative care in SCD similar to findings from other studies."

P15 line 46 – 'small and rural...

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "...this study highlights the need for improvement in access to palliative care services across all settings in the US, particularly in small and rural hospitals."

P16 line 20-27 – the authors should state more explicitly that because of this the reported prevalence rates over-estimate the number of patients benefitting from palliative care

Response to Review: We accept this suggestion and have added a sentence to clarify this.

Location of Modification: Discussion

Modified Text: "As such, we suspect that our study overestimates the prevalence of palliative care usage in SCD."

P16 line 34 - 'have' not 'has'

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "SCD related morbidity and mortality have a significant impact on patient self-reported quality of life outcomes and healthcare utilization and cost."

P16 line 36 – could the authors please modify this sentence so as to make a stronger comment regarding the role of the 'provider' (I assume you mean the hematologist or other medical practitioners treating/caring for people with SCD) in referring their patients for a palliative care consultation or liaising with a palliative care specialist. Awareness alone is not sufficient, providers need to take the initiative to discuss palliative care options with the patient or arrange a consultation at an earlier stage of the disease is also needed. It would strengthen the paper if the authors could also make some suggestion/s as to how this could be achieved, e.g. do they fail to initiate such discussions because they are not aware of the benefits of early palliative care, they do not feel comfortable raising palliative care with their patients, they do not know how to raise it, etc

Response to Reviewer: 'Provider' was inclusive of members of SCD care team (hematologists and other medical providers providing care to this population) as well as palliative care specialists. This sentence has been removed to eliminate ambiguity and replaced with the new statement listed below. It is difficult for the authors to comment on ways to achieve early palliative care in SCD as there are no studies to date exploring barriers to early palliative care in this population. As such any statement made would lack a reference to support it.

Location of Modification: Discussion

Modified Text: "Studies exploring barriers and facilitators to early palliative care at the provider (SCD providers, palliative care specialists), patient, and system levels do not exist and are needed for future recommendation for PC interventions in this population."

P16 line 41-46 – the benefits of early palliative care in symptom control and subsequently improved quality of life should also be mentioned here

Response to Reviewer: We accept this suggestion and have included a sentence to this effect.

Location of Modification: Discussion

Modified Text: "Early palliative care also has the potential to improve symptom management and consequently improve quality of life for individuals with SCD."

P16 line 53 – 'life limiting illnesses' is a better term to use than 'chronic serious Illnesses'

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Furthermore, studies addressing system barriers to palliative care use among minority patients are needed as the implication spans across other life limiting illnesses."

Table 1 col 5 heading – 'Hospitalizations among ...' this heading does not correctly describe the data in this column. Please reword, e.g. 'Hospitalized patients with SCD receiving palliative care'

Response to Reviewer: We agree with this revision.

Location of Modification: Table 1

Modified Text: "SCD-related hospitalizations receiving palliative care"

Table 2 – please change order of age group and race/ethnicity to be consistent with

Table 1

Response to Reviewer: We have now modified table 2 as per reviewer's recommendation

Location of Modification: Table 2

Figure 1 – both axes need to be labelled. The * is not explained.

Response to Reviewer: We have added the axes labels now.

Figures 2 & 3 – I am not sure that these figures are needed as the data are presented in Table 1. If they are kept, I suggest they are combined into one figure showing both the prevalence of both hospitalizations and palliative care. The x-axis should be labelled.

Response to Reviewer: We agree that the information is repeated in table 2 and therefore, we have now removed figures 2 and 3 based on the reviewer's suggestion.

Reviewer #2

Very interesting manuscript. However, I have a few comments on the analysis that would require some amount of reworking by the authors. How was each hospitalization for SCD counted? A statement should be included in the manuscript to guide on how readmissions were handled as one patient could have contributed several admissions between the study of 2008 to 2018.

Response to Reviewer: Thank you for your interest in this topic. The HCUP NIS presents data at the hospitalization level rather than patient level. In each patient's discharge records, there are up to 30 diagnoses codes in ICD-09 or ICD-10 format, which are used to identify SCD. There is no way to identify readmissions in the NIS dataset. We mention this in the discussion section of the manuscript – "Given utilization of aggregate data in which a hospitalization is considered a single event, we are unable to identify the number of patients who benefited from palliative care services as multiple admissions could be associated with one patient."

Palliative care service utilization was not clearly defined for use in a logistic regression model.

Response to Reviewer: This was addressed in the methods section. "Furthermore, we conducted adjusted survey logistic regression models to examine the patient socio-demographic and hospitalization characteristics (exposures) associated with palliative care utilization (outcome variable) among all SCD hospitalizations and among those which resulted in patients' death in-hospital."

It good if the authors could report the simple proportions of Palliative care service utilization in their study population.

Response to Reviewer: This is reported in results section, "There were 4442 (0.45%) SCD-related hospitalizations associated with palliative care service."

Table 2 does not seem to have an outcome variable and does not also indicate whether the model was an unadjusted or adjusted model. For instance, it would be great to have the OR for 4442 receiving palliative care out of the 987555 SCD related hospitalizations. A similar, outcome for inhospital deaths vs discharged alive should be reported.

Response to Reviewer: We understand that the way the results were presented earlier, it could have created confusion for the readers. Therefore, we have now modified the text to make it clearer.

Location of Modification: Methods

Modified Text: "Furthermore, we conducted adjusted survey logistic regression models to examine the patient socio-demographic and hospitalization characteristics (exposures) associated with palliative care utilization (outcome variable) among all SCD hospitalizations and among those which resulted in patients' death in-hospital."

I would like to believe that the authors' main objective is palliative care utilization among SCD inpatients, hence, they should try to stick to this objective without focusing so much on the other/confounding variables in the model such as age, race, sex, etc.

Response to Reviewer: We agree that the primary objective of our study was to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations. Our secondary objective was to identify patient and hospital characteristics associated with use of hospital-based palliative care services in SCD hence the inclusion of variables such as age, race, sex, hospital type, etc.

Figure 2: the "other category" with a prevalence rate of 1.3 in figure 2 should be split into the different race/ethnicity or the BH-White category added to this group with a footnote indicating the different races forming this group.

Response to Reviewer: We have now removed figure 2 based on the first reviewer's feedback.

VERSION 2 - REVIEW

REVIEWER	Joanne Stubbs Western Sydney Local Health District, Epidemiology and Health Analytics
REVIEW RETURNED	23-Mar-2022

GENERAL COMMENTS

Thank you for the thorough revision of your manuscript, it is noticeably improved. Most of my comments on the previous version have been adequately addressed. I have noted below the couple that were not. My comments on this version primarily relate to grammatical issues or are suggestions for sentences that I thought could be improved by rewording. Apologies, some of these I missed picking up in my previous review.

General comments

As requested, you have replaced "utilization" throughout much of the manuscript. I noticed however that in some places (main text and figure) the word "usage" has been inserted. "Use" is preferable, as indicated in the English Language Blog: 'In general, if either "use" or "usage" seems like it could work in a sentence the best choice is probably "use" as this is a more commonly used word with more meanings.' https://blogs.transparent.com/english/use-versus-usage/

I have consulted further about the correct reporting of ORs and stand by my original statement that it is not correct to report an OR of 1.81 as '81% more likely'. An OR is as it says, a ratio of two odds, differences between ORs are therefore differences between the odds. As such, results should be reported as 'there was an 81% increase in the odds of X' or 'the odds were 1.81 times greater' or '... were more likely (OR=1.81)'. Unfortunately, the terminology used to describe OR results is sometimes incorrect even in reviewed journal articles, as noted in these articles:

https://pubmed.ncbi.nlm.nih.gov/22569219/https://pubmed.ncbi.nlm.nih.gov/11576589/

Specific comments

Abstract Participants – replace "and" with "or" in "ICD-9-CM and ICD-10-CM" (admissions were coded with one or the other version of ICD, not both)

Abstract p2, line 53 – "... compared to NH-White patients" (add "patients")

Abstract p3, line 3 – reword to "... each had a lower likelihood of ..."

P6, line 3 – health care costs (plural)

P7, 1st para – after United States provide abbreviation in brackets. The abbreviation U.S. is used in the same paragraph and in the Abstract but US is used in the Discussion (p15). Please chose one and use throughout the paper.

P7, 2nd para – "To assess the study's primary exposure". I don't think this is the correct use of the term "exposure" – you are talking about the study sample. Please reword to something like "To identify

the hospitalizations of interest" or "To identify the study sample".

P7, 2nd para – the authors misunderstood my previous comment about including a brief statement about the coding criteria for allocation of an ICD palliative care code. I did not mean could you provide the relevant ICD codes, but rather could you please briefly outline the coding instructions (i.e. what constitutes palliative care). This sentence might be best placed before the inserted sentence about there being no changes between ICD-9-CM and ICD-10-CM.

P8, 3rd para, line 46 – "during their hospitalization." (singular)

P9, line 3 – "exposure variables", not "exposures".

P10, line 10 – "During" rather than "between". Also, the year 2018 is not included on the figure, so is the study period actually 1 January 2008 to 31 December 2017? Could the authors please provide exact dates.

P10, line 32 - "use" rather than "utilizing"

P11, line 10 – "lowest use" rather than "lowest level of usage"

P12, line 3 – reword to "Patients living in zip codes"

P12, line 21 – reword to "Patients admitted to" and "... hospitals" (plural)

P12, line 30 - "hospitals" (plural)

P13, line 9 – "patients who were ..." (change to past tense for consistency)

P13, line 11 – reword to "the highest income quartile" (it was only the highest quartile, not the higher quartiles that were significant)

P13, line 11 to 14 – reword to "...private insurance, and who received care in large or urban academic hospitals." Also remove "in the northeast" as previously requested.

P13, line 28 – reword to "some patients with SCD" (not "some SCD patients")

P13, line 31 - "... found a higher ..."

P13, line 35 – sentence starting "This highlights ..." is a bit awkward. Suggest re-arranging words to say "This highlights an opportunity for palliative care involvement earlier in ..."

P13, line 50-"...analysis accounting for covariates" has not been described in the analysis section and Table 2 does not indicate that the ORs were adjusted. Could the authors please address this by either rewording the sentence to more accurately describe the further analysis or by adding information to the analysis section and Table 2- whichever is appropriate.

P14, line 6 – "disparities in the use"

P14, line 17 – the authors applied my suggested change to the wrong sentence. Pease revert wording to "preference for more

aggressive"
P14, line 24 – the sentence "Therefore, the above factors …" is awkward, suggest rewording it to "Therefore, the factors identified above relating to hospice use are likely…" or something similar
P14, line 34 – add "the" to "Gender differences in the …"
P14, line 36 – add "a" to "female patients had a similar prevalence"
P14, line 50 – "than" not "then"
P15, line 53 – add a reference to the sentence starting "Furthermore,", suggest Stubbs, J. M., Assareh, H., Achat, H. M., Greenaway, S., & Muruganantham, P. (2021). Specialist palliative care activity at an acute care tertiary hospital and its representation in administrative data. Am J Hosp Palliat Care, 38(3), 216-222. doi:10.1177/1049909120939861
P16, line 27 – the sentence starting "As such …" fits better before (not after) the sentence starting "Lastly …"
Figure 1 Title – Are the 2 lines on the figure the AAPC or the yearly rate? I assume they are yearly rates, in which case the newly added phrase "represented as average annual percentage change (AAPC)" is incorrect.
Legend on the actual figure – "Rate of 1000 hospitalizations)" not hospitalization

REVIEWER	Clement Narh School of Public Health, University of Health and Allied Sciences, Epidemiology and Biostatistics
REVIEW RETURNED	26-Mar-2022

GENERAL COMMENTS	The authors have responded to comments to my satisfaction and
	updated the manuscript accordingly.
	I recommend the manuscript for acceptance.
	Many thanks

VERSION 2 – AUTHOR RESPONSE

Reviewer #2

Comments to the Author:

Thank you for the thorough revision of your manuscript, it is noticeably improved. Most of my comments on the previous version have been adequately addressed. I have noted below the couple that were not. My comments on this version primarily relate to grammatical issues or are suggestions for sentences that I thought could be improved by rewording. Apologies, some of these I missed picking up in my previous review.

General comments

As requested, you have replaced "utilization" throughout much of the manuscript. I noticed however

that in some places (main text and figure) the word "usage" has been inserted. "Use" is preferable, as indicated in the English Language Blog: 'In general, if either "use" or "usage" seems like it could work in a sentence the best choice is probably "use" as this is a more commonly used word with more meanings.' https://urldefense.proofpoint.com/v2/url?u=https-3A blogs.transparent.com_english_use-2Dversus-2Dusage_&d=DwIFaQ&c=ZQs-

 $\frac{KZ80xEw0p81sqgiaRA\&r=X71_luslpz6OKfFNaYwYkvflEmKTfpwPPQ5Lv9kOix4\&m=VxSgXPOutlq2lFxo4TVOMk2rffa0436Kt9ykgRhUnBSFryC0msMnxqvA5cv150f5\&s=JHc7-SYhulR6L9wpRq0a1c-VCW4RE 21kah2kYoQhls&e=$

Response to Reviewer: We accept this change.

Location of Modification: Throughout manuscript.

I have consulted further about the correct reporting of ORs and stand by my original statement that it is not correct to report an OR of 1.81 as '81% more likely'. An OR is as it says, a ratio of two odds, differences between ORs are therefore differences between the odds. As such, results should be reported as 'there was an 81% increase in the odds of X' or 'the odds were 1.81 times greater' or '... were more likely (OR=1.81)'. Unfortunately, the terminology used to describe OR results is sometimes incorrect even in reviewed journal articles, as noted in these articles:

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<u>I54pQvkKDdyZPnqqI7IPUATVtYMNeIgKR5Egc&e=</u>

Response to Reviewer: Thank you for this clarification. We accept the revision requested.

Location of Modification: Throughout results section.

Specific comments

Abstract Participants – replace "and" with "or" in "ICD-9-CM and ICD-10-CM" (admissions were coded with one or the other version of ICD, not both)

Response to Reviewer: We accept this change.

Location of Modification: Abstract

Modified Text: "Patients >18 years old hospitalized with a primary or secondary ICD-9-CM or ICD-10-CM diagnosis of SCD were included."

Abstract p2, line 53 – "... compared to NH-White patients" (add "patients")

Response to Reviewer: We accept this change.

Location of Modification: Abstract

Modified Text: "NH-Black and Hispanic patients were 33% and 53% less likely to have palliative care services compared to NH-White patients (OR 0.67; CI 0.45-0.99 and OR 0.47; CI, 0.26-0.84)."

Abstract p3, line 3 - reword to "... each had a lower likelihood of ..."

Response to Reviewer: We accept this change.

Location of Modification: Abstract

Modified Text: "Female patients (OR 0.40; CI, 0.21-0.76), Medicaid use (OR 0.40; CI, 0.21-0.78), rural (OR 0.47; CI 0.28-0.79) and urban non-teaching hospitals (OR 0.61; CI 0.47-0.80) each had a lower likelihood of palliative care services use."

P6, line 3 – health care costs (plural)

Response to Reviewer: We accept this change.

Location of Modification: Introduction

Modified Text: "Palliative care has been shown to increase patient's quality of life and decrease health care costs but the impact of palliative care on SCD is not well characterized."

P7, 1st para – after United States provide abbreviation in brackets. The abbreviation U.S. is used in the same paragraph and in the Abstract but US is used in the Discussion (p15). Please chose one and use throughout the paper.

Response to Reviewer: We accept this change and have used the abbreviation "US" throughout the paper.

Location of Modification: Throughout the manuscript

P7, 2nd para — "To assess the study's primary exposure". I don't think this is the correct use of the term "exposure" — you are talking about the study sample. Please reword to something like "To identify the hospitalizations of interest" or "To identify the study sample".

Response to reviewer: We accept this change.

Location of Modification: Methods

Modified Text: "To identify the hospitalizations of interest, we first scanned the diagnosis codes (the principal diagnosis and up to 29 secondary diagnoses) in each patient's discharge record for an indication of SCD..."

P7, 2nd para – the authors misunderstood my previous comment about including a brief statement about the coding criteria for allocation of an ICD palliative care code. I did not mean could you provide the relevant ICD codes, but rather could you please briefly outline the coding instructions (i.e. what constitutes palliative care). This sentence might be best placed before the inserted sentence about there being no changes between ICD-9-CM and ICD-10-CM.

Response to reviewer: A sentence on the coding criteria for palliative care ICD code has been added

Location of Modification: Methods

Modified Text: "ICD-9-CM and ICD-10-CM palliative care codes capture hospital encounters by a palliative care specialist or service, patients admitted for palliative care, and patients on comfort measures only status."

P8, 3rd para, line 46 – "during their hospitalization." (singular)

Response to reviewer: We accept this change

Location of Modification: Methods

Modified Text: "Next, we examined the socio-demographic and hospitalization characteristics of patients with SCD and those with SCD who received palliative care during their hospitalization."

P9, line 3 – "exposure variables", not "exposures".

Response to reviewer: We accept this change.

Location of Modification: Methods

Modified Text: "Furthermore, after excluding records with missing values in model variables, we conducted adjusted survey logistic regression models to examine the patient socio-demographic and hospitalization characteristics (exposure variables) associated with palliative care use (outcome variable) among all SCD hospitalizations and among those which resulted in patients' death inhospital."

P10, line 10 – "During" rather than "between".

Also, the year 2018 is not included on the figure, so is the study period actually 1 January 2008 to 31 December 2017? Could the authors please provide exact dates.

Response to reviewer: We accept this change. We have now modified the study period in the results.

Location of Modification: Results

Modified Text: "During the study period of 1 January 2008 to 31 December 2017, the NIS contained 987,555 SCD-related hospitalizations of which 6,327 (0.64%) were terminal admissions."

P10, line 32 - "use" rather than "utilizing

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "Table 1 shows patient characteristics for SCD related hospitalizations and patients who received palliative care services."

P11, line 10 – "lowest use" rather than "lowest level of usage"

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "Conversely the South region had the highest prevalence of SCD hospitalization (4.3 per 1000 SCD hospitalizations) but the lowest use of inpatient palliative care services (3.6 per 1000 SCD hospitalizations)."

P12, line 3 – reword to "Patients living in zip codes"

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "Patients living in zip codes in the highest income quartile were 58% more likely to receive inpatient palliative care services..."

P12, line 21 – reword to "Patients admitted to" and "... hospitals" (plural)

Response to Reviewer: We accept this change.

Location of Modification: Results

Modified Text: "Patients admitted to medium or large hospitals were more likely..."

P12, line 30 – "hospitals" (plural)

Response to Reviewer: We accept this change.

Location of Modification: Results

P13, line 9 – "patients who were ..." (change to past tense for consistency)

Response to Reviewer: We accept this change.

Location of Modification: Discussion

P13, line 11 – reword to "the highest income quartile" (it was only the highest quartile, not the higher quartiles that were significant)	
Response to Reviewer: We accept this change.	
Location of Modification: Discussion	
Modified Text: "Palliative care use was more likely among patients who were NH-White male, in the highest income quartile"	
P13, line 11 to 14 – reword to "private insurance, and who received care in large or urban academic hospitals."	
Response to Reviewer: We accept this change.	
Location of Modification: Discussion	
P13, line 28 – reword to "some patients with SCD" (not "some SCD patients")	
Response to Reviewer: We accept this change.	
ocation of Modification: Discussion	
Modified Text: "Furthermore, some patients with SCD experience complications"	

Modified Text: "Palliative care use was more likely among patients who were NH-White male, in

higher income quartiles, with private insurance..."

P13, line 31 – "... found a higher ..."

Location of Modification: Discussion

Response to Reviewer: We accept this change.

Modified Text: "Our study found a higher prevalence of palliative care service use in terminal admissions..."

P13, line 35 – sentence starting "This highlights ..." is a bit awkward. Suggest re-arranging words to say "This highlights an opportunity for palliative care involvement earlier in ..."

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "This highlights an opportunity for palliative care involvement earlier in the disease course in SCD, facilitating more holistic care of patients."

P13, line 50 – "...analysis accounting for covariates" has not been described in the analysis section and Table 2 does not indicate that the ORs were adjusted. Could the authors please address this by either rewording the sentence to more accurately describe the further analysis or by adding information to the analysis section and Table 2 – whichever is appropriate.

Response to Reviewer - We thank the reviewer for the feedback. We have now added the details in the methods - statistical analysis section.

Location of Modification - Methods

Modified text - "All the patient demographic and hospital characteristics were loaded into the association models to obtain adjusted odds ratio and 95% confidence intervals

P14, line 6 - "disparities in the use"

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: Other studies have shown racial disparities in the use of palliative care services in other chronic diseases.

P14, line 17 – the authors applied my suggested change to the wrong sentence. Pease revert wording to "preference for more aggressive..."

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Factors identified to drive this racial disparity in hospice use include knowledge deficits, mistrust of the health care system, miscommunication and misunderstanding of treatment options, and preference for more aggressive."

P14, line 24 – the sentence "Therefore, the above factors ..." is awkward, suggest rewording it to "Therefore, the factors identified above relating to hospice use are likely..." or something similar

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Therefore, the above factors identified above relating to hospice use are likely are likely to also play a role in racial differences observed in palliative care use in patients with chronic conditions such as SCD."

P14, line 34 – add "the" to "Gender differences in the ..."

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Gender differences in the use of inpatient palliative care services were found."

P14, line 36 – add "a" to "...female patients had a similar prevalence..."

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Although male and female patients had a similar prevalence of SCD-related hospitalization..."

P14, line 50 - "than" not "then"

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "Studies have shown that although most chronic pain conditions are more prevalent in women than men, and women report greater pain than men after invasive procedures..."

P15, line 53 – add a reference to the sentence starting "Furthermore,...", suggest Stubbs, J. M., Assareh, H., Achat, H. M., Greenaway, S., & Muruganantham, P. (2021). Specialist palliative care activity at an acute care tertiary hospital and its representation in administrative data. Am J Hosp Palliat Care, 38(3), 216-222. doi:10.1177/1049909120939861

Response to Reviewer: Thank you for this recommendation. We have added this reference.

Location of Modification: Discussion

P16, line 27 – the sentence starting "As such ..." fits better before (not after) the sentence starting "Lastly ..."

Response to Reviewer: We accept this change.

Location of Modification: Discussion

Modified Text: "As such, we suspect that our study overestimates the prevalence of palliative care use in SCD. Lastly, our study investigated inpatient palliative care use and hence, our findings cannot be extrapolated to outpatient settings where patients with SCD patient receive most of their care."

Figure 1

Title – Are the 2 lines on the figure the AAPC or the yearly rate? I assume they are yearly rates, in which case the newly added phrase "represented as average annual percentage change (AAPC)" is incorrect.

Response to reviewer: We thank the reviewer for the feedback. We have now corrected the phrase for the figure legend.

Location of modification: Figure 1 legend

Modified text: "Figure 1: Temporal trends in the rates of palliative care use. Average annual percentage change (AAPC) represents the overall change in rates of palliative care use during the study period 2008-2017."

Legend on the actual figure – "Rate of ... 1000 hospitalizations)" not hospitalization

Response to Reviewer: We accept this change.

Location of Modification: Figure 1

VERSION 3 - REVIEW

REVIEWER	Joanne Stubbs Western Sydney Local Health District, Epidemiology and Health
	Analytics
REVIEW RETURNED	18-May-2022

GENERAL COMMENTS	Thank you for revising your manuscript in line with my previous comments. There are just a couple of minor issues relating to the revisions which should be corrected prior to publication.
	P14, line 17 the word 'care' has been omitted from the end of the sentence and needs to be re-inserted after 'aggressive'
	P14, line 24 it looks like the authors missed deleting some of the words when revising this sentence. I think it is meant to read: 'Therefore, the factors identified above relating to hospice use are likely to also play a role in racial differences observed in palliative care use in patients with chronic conditions such as SCD.'
	Figure 1 title I still find the revised title a bit confusing and potentially misleading. I think the sentence 'Average annual percentage change (AAPC) represents the overall change in rates of palliative care use during the study period 2008-2017.'
	should probably be omitted as the figure only graphs the annual rates, not the AAPC.

VERSION 3 – AUTHOR RESPONSE

Reviewer #2

P14, line 17

the word 'care' has been omitted from the end of the sentence and needs to be re-inserted after 'aggressive'

Response to Reviewer: The suggested change has been made

Location of Modification: Discussion

Modified Text now reads: "Factors identified to drive this racial disparity in hospice use include knowledge deficits, mistrust of the health care system, miscommunication and misunderstanding of treatment options, and preference in more aggressive care."

P14, line 24

it looks like the authors missed deleting some of the words when revising this sentence. I think it is meant to read:

'Therefore, the factors identified above relating to hospice use are likely to also play a role in racial differences observed in palliative care use in patients with chronic conditions such as SCD.'

Response to Reviewer: We thank the review for pointing out this omission.

Location of Modification: Discussion

Modified Text now reads: "Therefore, the factors identified above relating to hospice use are likely to also play a role in racial differences observed in palliative care use in patients with chronic conditions such as SCD."

Figure 1 title

I still find the revised title a bit confusing and potentially misleading. I think the sentence 'Average annual percentage change (AAPC) represents the overall change in rates of palliative care use during the study period 2008-2017.' should probably be omitted as the figure only graphs the annual rates, not the AAPC.

Response to Reviewer: The title to Figure 1 is now modified as suggested.

Location of Modification: Figure title

Modified Text now reads: "Temporal trends in the rates of palliative care use 2008-2017."