BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-057361
Article Type:	Original research
Date Submitted by the Author:	07-Oct-2021
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Keywords:	Adult palliative care < PALLIATIVE CARE, HAEMATOLOGY, Anaemia < HAEMATOLOGY

Title: Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

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Word count: 2,952

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Abstract:

Objective: Sickle cell disease (SCD) is a highly morbid condition notable for recurrent hospitalizations due to vaso-occlusive crises and complications of end organ damage. Little is known about the use of inpatient palliative care services in adult patients with SCD. This study aims to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations. We hypothesize that use of palliative care is low in SCD hospitalizations.

Design: A retrospective cross-sectional study utilizing data from the National Inpatient Sample (NIS) from 2008-2017 was conducted.

Setting: U.S. hospitals from 47 states and the District of Columbia.

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

Primary and secondary outcome measures: Palliative care service utilization using ICD-9-CM and ICD-10-CM diagnosis codes V66.7 and Z51.5.

Results: 987,555 SCD-related hospitalizations were identified, of which 4442 (0.45%) were associated with palliative care service. Palliative care service utilization increased at a rate of 9.2% per year (CI, 5.6-12.9). NH-Black and Hispanic patients were 33% and 53% less likely to have palliative care services compared to NH-White (OR 0.67; CI 0.45-0.99 and OR 0.47; CI, 0.26-0.84). 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) had decreased likelihood of palliative care services use.

Conclusion: Utilization of palliative care during SCD-related hospitalizations is increasing but remains low. Disparities associated with race and gender exist for use of palliative care services during SCD related hospitalization. Further studies are needed to guide evidence-based palliative care interventions for more comprehensive and equitable care of adult patients with SCD.

Strengths and limitations of this study

- Our study is the first of its kind to investigate palliative care utilization among SCD patients using a national database.
- ICD-9-CM and ICD-10-CM codes for palliative care are not specific to palliative care provided by a palliative care specialist as these codes also encompass patients who are in comfort care status.
- Our study investigated inpatient palliative care utilization and hence, our findings cannot be extrapolated to outpatient setting where patients with SCD patient receive most of their care.

Introduction:

Sickle cell disease (SCD) is a group of inherited red blood cell disorders in which abnormality in Hemoglobin (Hb) beta gene results in abnormal shape and sickling of red blood cells under stress. Physiologic manifestations of the illness arise from end organ ischemia, including acute pain from vaso-occlusive crises, cerebrovascular accident, acute chest syndrome, pulmonary hypertension, heart failure, renal failure, severe anemia, and recurrent infections.[1] Approximately 100,000 Americans predominantly of African (90%), Middle Eastern, and Mediterranean descent are affected by SCD.[2] Historically, SCD was a childhood disease – life expectancy for those with the disease was 20 years in 1970. Currently, life expectancy with SCD extends into adulthood but remains significantly lower than the general population (42-48 years), especially for sickle cell anemia—the most severe form of SCD.[3] As an increasing number of people with SCD survive into adulthood, there is a rising need for effective transitions to adult medicine involving multidisciplinary care teams.[4]

SCD is a highly morbid condition. Recurrent hospitalization is common in SCD due to vaso-occlusive crises and complications of end organ damage.[5] [6] During their last year of life, people with SCD were hospitalized for an average of forty-two days over five admissions.[7] Hospital admissions and ED visits increase sharply a month before death and most patients with SCD die in the hospital (63%) or emergency department (15%).[7] Patients with SCD experience increased rates of depression and anxiety,[8] [9] [10] chronic pain,[11] and decreased health-related quality of life. [12]. Increased healthcare use [13] and symptom burden are salient opportunities for palliative care intervention in this patient population. Palliative care provides holistic care for patients with serious chronic illnesses using a multidisciplinary team approach.[14] Palliative care has been

shown to increase patient's quality of life and decrease health care cost [15] [16] but the impact of palliative care on SCD is not well characterized.[17]

Furthermore, little is known about the use of *inpatient* palliative care services in adult patients with SCD. To address this gap, we used national data to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations (hospitalizations that resulted in patients' death in-hospital regardless of cause of death). We identified patient and hospital characteristics associated with use of hospital-based palliative care services in SCD. We hypothesize that use of palliative care is low in SCD hospitalizations.

Methods:

Data Source

Data from the 2008 to 2017 National Inpatient Sample (NIS), the largest all-payer, nationally representative inpatient database in the United States was used. The NIS is part of a group of databases developed by the Healthcare Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ).[18] This public database contains longitudinal data from a stratified sample of all discharges from U.S. hospitals from 47 states and the District of Columbia, excluding rehabilitation and long-term acute care hospitals, thereby estimating about a 20% sample of all hospital discharges. When weighted, each year, NIS contains data from about 35 million hospitalizations.

Study Population and Variables

The analysis was restricted to hospitalizations in adults aged 18 years and above. Diagnoses and procedures are coded using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes till the 3rd quarter of 2015, after which HCUP transitioned to ICD-10-CM format. To assess the study's primary exposure, 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 (ICD-9-CM - 282.41, 282.42, 282.61, 282.62, 282.63, 282.64, 282.60, 282.68, 282.69; ICD-10-CM - D57.4x, D57.0x, D57.2x, D57.1x, D57.8x). 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. Covariates included in the study were socio-demographics for the patient which consisted of patients' age, race/ethnicity –

categorized as Non-Hispanic (NH)-White, NH-Black, Hispanic and NH-Others, sex, insurance type – Medicare, Medicaid, private insurance, self-pay and others, median household income based on zipcodes; and hospital characteristics such as hospital location, hospital type (urban vs. rural and teaching vs. non-teaching), and hospital bed size.

Statistical Analysis

Since the NIS data was de-identified and publicly available, the study was approved as exempt by the Institutional Review Board (IRB) of Baylor College of Medicine. All statistical tests were two-tailed with the type-I error of 5% and were conducted using R version 3.5.1 (University of Auckland, Auckland, New Zealand) and R Studio Version 1.1.423 (Boston, MA) and Joinpoint Regression Program, version 4.7.0.0 (National Cancer Institute).

Temporal trends analyses were performed using Joinpoint regression technique, which allows to examine the trend of an outcome (in this case, palliative care utilization) over the study period.[19] The results are represented in the form of average annual percentage change (AAPC) and its 95% confidence interval (CI). We scrutinized the temporal trends in the rates of palliative care utilization among SCD patients overall, and among those who died in-hospital. Next, we examined the socio-demographic and hospitalization characteristics of patients with SCD and those with SCD who utilized palliative care during their hospitalization. Prevalence rates of SCD and palliative care utilization among SCD hospitalizations were calculated, stratified by patients' race/ethnicity. Furthermore, we conducted adjusted survey logistic regression models to examine the factors associated with palliative care utilization among all SCD hospitalizations and among those which resulted in patients' death in-hospital.

Patient and public involvement

Patients were not involved in this retrospective analysis of an anonymized national inpatient database.

Results:

Trends in the rate of palliative care utilization in SCD-related hospitalizations

Between the study period of 2008 to 2018 the NIS contained 987,555 SCD-related hospitalizations of which 6,327 (0.64%) were terminal admissions. There were 4442 (0.45%) SCD-related hospitalizations associated with palliative care service. Figure 1 shows temporal trend in palliative care utilization. The rate of inpatient palliative care service utilization increased at 9.2% per year (95% CI, 5.6-12.9) for all SCD-related hospitalizations and 10.7% (95% CI, 3.4-18.5) for terminal hospitalizations.

Patient characteristics – SCD hospitalizations with palliative care utilization

Table 1 shows patient characteristics among SCD related hospitalizations and patients utilizing palliative care services. The prevalence of SCD-related hospitalization was highest among the 18-39 age group (9.7 per 1000 SCD hospitalizations) and decreased with increasing age. Conversely, the prevalence of inpatient palliative care use was highest in the oldest age group (34.8 per 1000 SCD hospitalization) and lowest in the 18-39 age group (3.8 per 1000 SCD hospitalization). In Figures 2 and 3 the prevalence of SCD-related hospitalization was most pronounced among NH-Blacks (20.7 per 1000 SCD hospitalization) and lowest in NH-Whites (0.1 per 1000 SCD hospitalization) while the frequency 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 hospitalization).

Regional and hospital characteristics – SCD hospitalizations with palliative care utilization

SCD hospitalization was lowest in the Northeast (1.4 per 1000 SCD hospitalization) but the prevalence of inpatient palliative care service was highest in this region (6.1 per 1000 SCD hospitalization). Conversely the South region had the highest prevalence of SCD hospitalization (4.3 per 1000 SCD hospitalization) but the lowest level of utilization of inpatient palliative care services (3.6 per 1000 SCD hospitalization). Large and urban teaching hospitals had highest level of inpatient palliative care service utilization (5.1 and 5.1 per 1000 SCD hospitalization, respectively).

Factors associated with inpatient palliative care utilization in SCD

Table 2 shows factors associated with inpatient palliative care utilization in SCD hospitalizations. At end-of-life patients between 40-59 years were 81% more likely to utilize palliative care services than patients 18-39 years old (odds ratio [OR], 1.81, 95% confidence interval [CI], 1.19-2.75). NH-Black and Hispanic patients were 33% and 53% respectively less likely to utilize inpatient palliative care services compared to NH-White (OR, 0.67; 95% CI, 0.45-0.99 and OR, 0.47; 95% CI, 0.26-0.84, respectively). Likewise, during terminal admissions utilization of palliative care services was 67% and 72% less likely among NH-Black and Hispanic patients, respectively when compared to NH-White (OR, 0.33; 95% CI, 0.16-0.68 and OR, 0.28; 95% CI, 0.09-0.91, respectively). Female patients were 60% less likely to utilize palliative care services than male patients (OR, 0.40; 95% CI, 0.21-0.76). Compared to routine discharges, hospitalizations resulting in death and transfer to another health care facility were associated with increased usage of inpatient palliative care services (OR, 39.36; 95% CI, 30.83-49.98, and OR, 3.71; 95% CI, 2.73-5.03, respectively) while discharge against medical advice (DAMA) was associated with decreased utilization of inpatient palliative care services (OR, 0.48; 95% CI 0.28-0.84).

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). Compared to Medicare patients, those with Medicaid were 60% less likely (OR, 0.40; 95% CI, 0.21-0.78), while patients with private insurance were 30% more likely (OR, 1.30; 95% CI, 0.93-1.59) to utilize palliative care services. During terminal admissions, there was no significant difference in palliative care utilization across different payors.

Patients admitted in a medium and large hospital were 47% and 91%, respectively more likely (OR, 1.47; 95% CI, 1.02-2.12 and OR, 1.91; 95% CI, 1.30-2.82, respectively) to utilize palliative care services than patients in small hospitals while patients admitted to rural or urban non-teaching hospitals were less likely to utilize palliative care services than those in urban teaching hospital (OR, 0.47; 95% CI 0.28-0.79) and OR, 0.61; 95% CI 0.47-0.80, respectively).

Discussion:

In this study of national trends, we found overall low utilization of palliative care services during SCD-related hospitalizations. Palliative care utilization 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. NH-Black and Hispanic patients were less likely to utilize palliative care services especially during terminal hospitalizations.

While early palliative care has gained acceptance in cancer care,[20] its adoption in other serious life limiting conditions such as congestive heart failure, chronic kidney disease, and SCD lags. SCD has traditionally been viewed as a childhood disease as most patients did not survive to adulthood in the past. Currently, most patients with SCD survive to adulthood.[3] Furthermore, some patients with SCD experience more complications and end organ damage from their disease than others resulting in shortened life expectancy. As such, several opportunities are present for palliative care intervention in provision of holistic care to patients earlier in the SCD course. 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. This highlights the need for early provision of palliative care during non-terminal admissions, as patients benefit from the psychosocial support and symptom management from an interdisciplinary team, as well as early initiation of discussions regarding goals of care and patient's preference for end of life.

Our study showed most SCD-related hospitalizations and palliative care service usage were in the NH-Black group. However, further analysis accounting for covariates revealed that NH-Black patients were significantly less likely to utilize palliative care during hospitalization compared to NH-white patients. Other studies have shown racial disparities in utilization of palliative care services in other chronic diseases.[21, 22] Furthermore, studies have shown that black patients are less likely to utilize hospice services and more likely to received intensive life-sustaining procedures at end of life compared to white patients.[23] Factors identified to drive this racial disparity in hospice use include knowledge deficit,[24] mistrust of the health care system,[25] miscommunication and misunderstanding of treatment options,[26] and preference for more aggressive care.[27] Similar studies are lacking to elucidate factors implicated for the racial difference in non-hospice palliative care utilization across all life limiting diseases.[28] Palliative care has a strong association with hospice with many patients and families unable to differentiate the difference between the two. Therefore, the above factors identified are likely to also play a role in racial difference observed in palliative care utilization in patient with chronic conditions such as SCD. Further studies are needed to investigate patient and system factors associated with racial difference in palliative care utilization in SCD.

Gender differences in utilization of inpatient palliative care services were found. Although male and female patients had similar prevalence of SCD-related hospitalization, female patients were 60% less likely to utilize palliative care services. This finding is contrary to that of other studies which show that women are more receptive to palliative care than men.[29] Pain is the most prominent feature of SCD and hence it is plausible that inpatient palliative care services in SCD hospitalizations involve pain management. Studies have shown that although most chronic pain conditions are more prevalent in women than men, and women report greater pain then men after invasive procedures, women receive less analgesia and are more likely to have their pain attributed to psychological causes.[30] It is possible that palliative care consultants are more frequently involved for specialist level pain management for male than female patients

accounting for the gender difference observed in our study. This finding requires further investigation as the study by McClish et al. demonstrates that men and women with SCD report similar pain experiences.[31]

We also found socioeconomic differences in utilization of palliative care in SCD similar to other studies.[22, 32, 33] Patients with zip codes in the highest income quartile and those with private insurance were more likely to utilize palliative care, while patients with Medicaid were less likely to utilize palliative care services. Insurance dictates patient's access to specialty care with patients on Medicaid reporting more challenge than those with private insurance accessing certain specialty care particularly in the outpatient setting.

Regional differences were detected in our study. The South region had the highest number of SCD hospitalizations but the lowest prevalence of palliative care utilization. A patient in the South was significant less likely to utilize palliative care services when compared to a patient in the Northeast. This finding is notable as two of the three states (Florida, Texas, and New York) with the highest population of SCD patients are in the South. Hospital characteristics were also predictive of palliative care utilization with large, urban and teaching hospitals associated with greater utilization of palliative care in SCD similar to findings from other studies.[32] [21] [33] While many sickle cell patients utilize larger, urban hospitals for their care,[34] this study highlights the need for improvement in access to palliative care services across all settings in the US, particularly in smaller, rural hospitals.

To our knowledge, our study is the first of its kind to investigate palliative care utilization among SCD patients using a national data base. Limitations exist in our study one of which is the validity of the ICD-9 and ICD-10 codes for identification of palliative care consultations. Investigators have sought to validate these codes however these studies utilize data from a single institution [35] or from the VA system.[36] Furthermore, the ICD-9 and ICD-10 codes for palliative care are not specific to palliative care provided by a palliative care specialist as these codes also encompass patients who are in comfort care status. Not all patients in comfort care are managed by a palliative care specialist and as such it is difficult to delineate which hospitalizations were indeed associated with the involvement of a palliative care specialist. In addition, our dataset does not allow us to elucidate the nature of palliative care intervention provided during admissions hence it is unclear if these interventions were for symptom management, goals of care discussion, counseling and support, or transition to comfort care. 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. Lastly, our study investigated inpatient palliative care utilization and hence, our findings cannot be extrapolated to outpatient setting where patients with SCD patient receive most of their care.

SCD related morbidity and mortality has a significant impact on patient self-reported quality of life outcomes and healthcare utilization and cost. Awareness of the complexity of SCD and its end organ complications is needed at the provider level to highlight the need for early palliative care involvement in this patient population. Early palliative care might guide patients' treatment decisions and mitigate initiation of interventions that are not in line with a patients' wishes at the end of life. Racial disparity in the utilization of palliative care by SCD patients should be investigated with studies assessing knowledge of palliative care and barriers to palliative care utilization by SCD patients. Furthermore, studies addressing system barriers to palliative care utilization among minority patients are needed as the implication spans across other chronic serious illnesses.

Acknowledgements

Conflict of Interest Disclosures: Authors without conflicts of interest, including relevant financial interests, activities, relationships, and affiliations.

Funding/Support: Research funding support was provided by the U.S. Department of Health and Human Services and Health Resources and Services Administration for Baylor College of Medicine Center of Excellence in Health Equity, Training, and Research (Grant No: D34HP31024). Additional support is provided to Dr. Naik from the Houston VA HSR&D Center for Innovations in Quality, Effectiveness, and Safety (CIN 13-413).

Authorship Contribution:

Eberechi Nwogu-Onyemkpa was involved in the conception of the study, interpretation of data, drafting, and revision of the manuscript.

Deepa Dongarwar was involved in the conception of the study, analysis of the data, drafting, and revision of the manuscript.

Hamisu Salihu was involved in the conception of the study and revision of the manuscript.

Chioma Akpati was involved in the interpretation of data and drafting of the manuscript.

Maricarmen Marroquin was involved in the interpretation of data and drafting of the manuscript.

Megan Abadom was involved in the interpretation of data and drafting of the manuscript.

Aanand D. Naik was involved in the conception of the study and revision of the manuscript.

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Table 1: Patient characteristics among SCD-related hospitalizations and among those with SCD who utilized palliative care during their hospitalization

	Total N=307709982	SCD related hospitalizations N=987555	Prevalence of SCD-related hospitalizations (per 1000 hospitalizations)	Hospitalizations among patients with SCD receiving palliative care N=4442	Prevalence of palliative care usage (per 1000 SCD hospitalizations)
Age Group					
18-39 years	75567499	733837	9.7	2824	3.8
40-59 years	78526326	214939	2.7	1160	5.4
60-79 years	101611492	35362	0.3	339	9.6
80+ years	52004665	3417	0.1	119	34.8
Race/Ethnicity					
NH-White	192567014	16962	0.1	214	12.6
NH-Black	41490748	857006	20.7	3773	4.4
Hispanic	29897432	32676	1.1	116	3.6
Others	17422072	23026	1.3	157	6.8
Missing	26332714	57883	2.2	181	3.1
Sex					
Male	125745784	427285	3.4	1921	4.5
Female	181778482	559845	3.1	2521	4.5
Missing	185716	424	2.3	0	0.0
Discharge Status					
Routine	202797074	853218	4.2	2619	3.1
Transfer	55186460	37409	0.7	447	11.9
Died	6740712	6327	0.9	685	108.3
DAMA	3847845	44520	11.6	69	1.5
Other	38933666	45507	1.2	622	13.7
Missing	204225	573	2.8	0	0.0
Zip code income quartile					
Lowest quartile	89460128	478674	5.4	2053	4.3
2nd quartile	78497949	219619	2.8	801	3.6
3rd quartile	71474969	163233	2.3	836	5.1
Highest quartile	61340502	100769	1.6	703	7.0
Missing	6936433	25259	3.6	48	1.9
Primary Payer					
Medicare	141357438	315777	2.2	1736	5.5
Medicaid	50563783	428967	8.5	1725	4.0
Private Insurance	88933878	170459	1.9	671	3.9
Self-Pay	26247689	70526	2.7	304	4.3
Missing	607194	1825	3.0	5	2.7
Hospital Characteristics					
Hospital Region					
Northeast	33888883	46282	1.4	1226	6.1
Midwest	107572349	234180	2.2	1014	5.4
South	164884575	701680	4.3	1820	3.6

West	1364173	5411	4.0	382	4.4
Hospital Bed Size					
Small	46455596	114366	2.5	331	2.9
Medium	81563430	258481	3.2	998	3.9
Large	178326782	609296	3.4	3108	5.1
Missing	1364173	5411	4.0	4	0.7
Hospital Location and Teaching Status					
Rural	33888883	46282	1.4	96	2.1
Urban non-teaching	107572349	234180	2.2	749	3.2
Urban teaching	164884575	701680	4.3	3591	5.1
Missing	1364173	5411	4.0	4	0.7

SCD-Sickle Cell Disease
NH-Non-Hispanic
DAMA-Discharged Against Medical Advice
Prevalence is the rate of the outcome (SCD or palliative care usage) among each patient characteristics

Table 2: Factors associated with palliative care utilization in SCD patients – overall and among those who died in-hospital

	Palliative care utilization in SCD hospitalizations	Palliative care utilization among SCD patients who died in-hospital
	OR(95% CI)	OR(95% CI)
Race/Ethnicity		
NH-White	reference	reference
NH-Black	0.67(0.45-0.99)*	0.33(0.16-0.68)*
Hispanic	0.47(0.26-0.84)*	0.28(0.09-0.91)*
Others	0.83(0.49-1.39)	0.41(0.12-1.42)
Age Group		
18-39 years	reference	reference
40-59 years	0.98(0.81-1.18)	1.81(1.19-2.75)*
60-79 years	0.95(0.70-1.30)	1.13(0.60-2.12)
80+ years	2.34(1.41-3.88)*	2.29(0.79-6.64)
Sex		
Male	reference	reference
Female	0.40(0.21-0.76)*	1.45(1.00-2.11)
Discharge Status		
Routine	reference	reference
Transfer	3.71(2.73-5.03)*	
Died	39.26(30.83-49.98)*	—
DAMA	0.48(0.28-0.84)*	—
Other	4.14(3.20-5.35)*	—
Zip code income quartile		
Lowest quartile	reference	reference
2nd quartile	0.89(0.71-1.11)	0.69(0.42-1.14)
3rd quartile	1.24(0.85-1.80)	0.48(0.25-0.91)*
Highest quartile	1.58(1.02-2.45)*	1.46(0.79-2.71)
Primary Payer		
Medicare	reference	reference
Medicaid	0.40(0.21-0.78)*	0.72(0.21-2.48)
Private Insurance	1.30(1.02-1.65)*	1.03(0.59-1.79)
Self-Pay	1.22(0.93-1.59)	1.12(0.64-1.99)
Hospital Characteristics		
Hospital Region		
Northeast	reference	reference
Midwest	1.00(0.57-1.75)	1.18(0.57-2.46)
South	0.69(0.42-1.11)	1.47(0.78-2.78)
West	0.72(0.40-1.31)	1.63(0.77-3.41)
Hospital Bed Size		
Small	reference	reference
Medium	1.47(1.02-2.12)*	1.18(0.57-2.44)
Large	1.91(1.30-2.82)*	1.52(0.78-2.96)

Hospital Location and Teaching Status		
Urban teaching	reference	reference
Rural	0.47(0.28-0.79)*	0.75(0.33-1.73)
Urban non-teaching	0.61(0.47-0.80)*	0.63(0.40-0.99)

SCD-Sickle Cell Disease
NH-Non-Hispanic
DAMA-Discharged Against Medical Advice
OR- odds ratio, CI- confidence interval

Figure legend/caption

Figure 1: Temporal trends in the rates of palliative care utilization represented as average annual percentage change (AAPC). Rate of inpatient palliative care service utilization increased at 9.2% per year (95% CI, 5.6-12.9) for all SCD-related hospitalizations and 10.7% (95% CI, 3.4-18.5) for terminal hospitalizations.

Figure 2: Prevalence of SCD-related hospitalization was highest among NH-Blacks (20.7 per 1000 SCD hospitalization) and lowest in NH-Whites (0.1 per 1000 SCD hospitalization).

Figure 3: Prevalence of inpatient palliative services was highest in NH-Whites (12.6 per 1000 SCD hospitalizations) and lowest in Hispanics (3.6 per 1000 SCD hospitalization).

Figure 1: Trends in the rates of palliative care utilization in SCD-related hospitalizations, overall and among those who died in-hospital

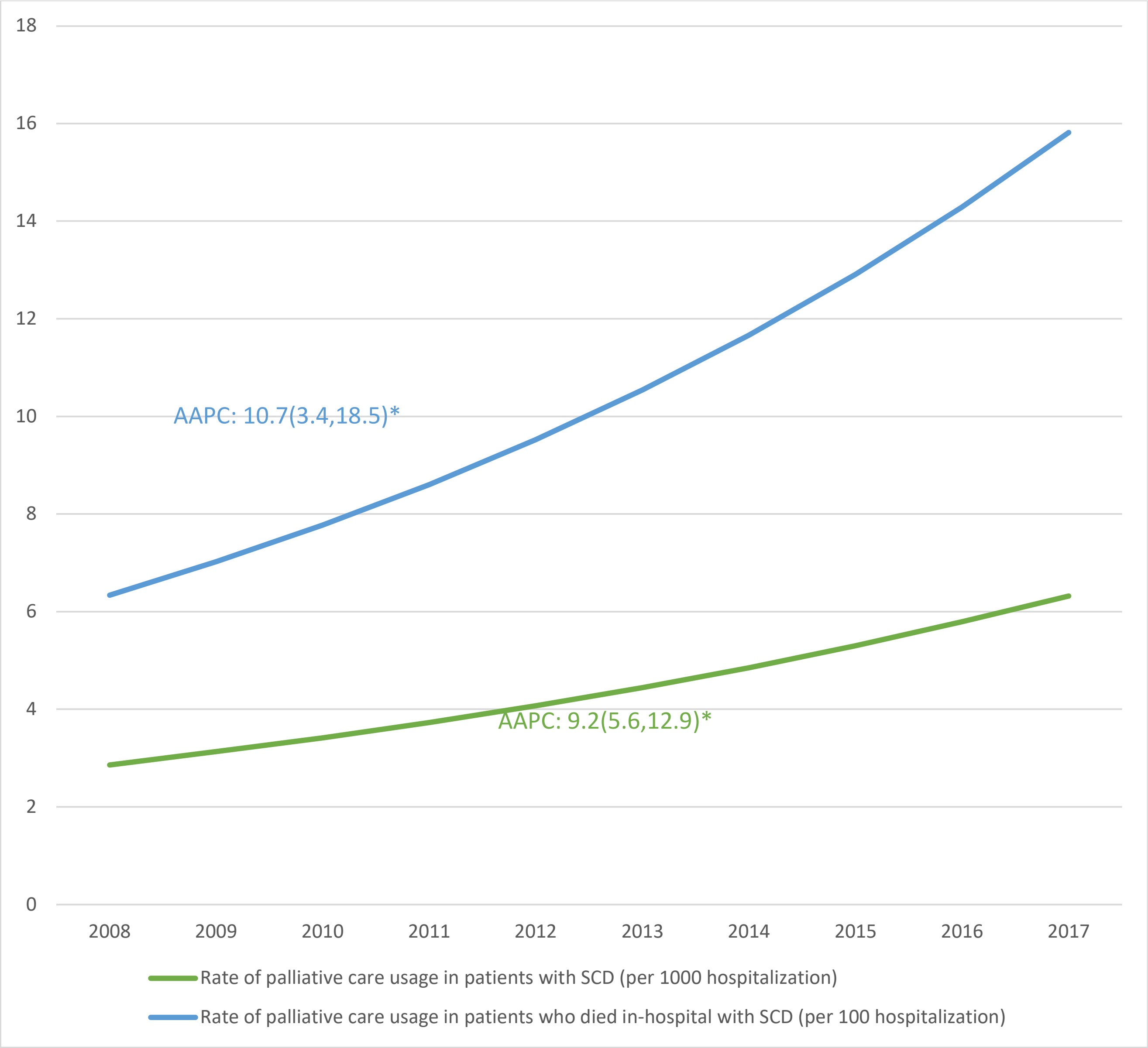


Figure 2- Prevalence rates of SCD-related hospitalizations (per 1000 hospitalizations) by race/ethnicity

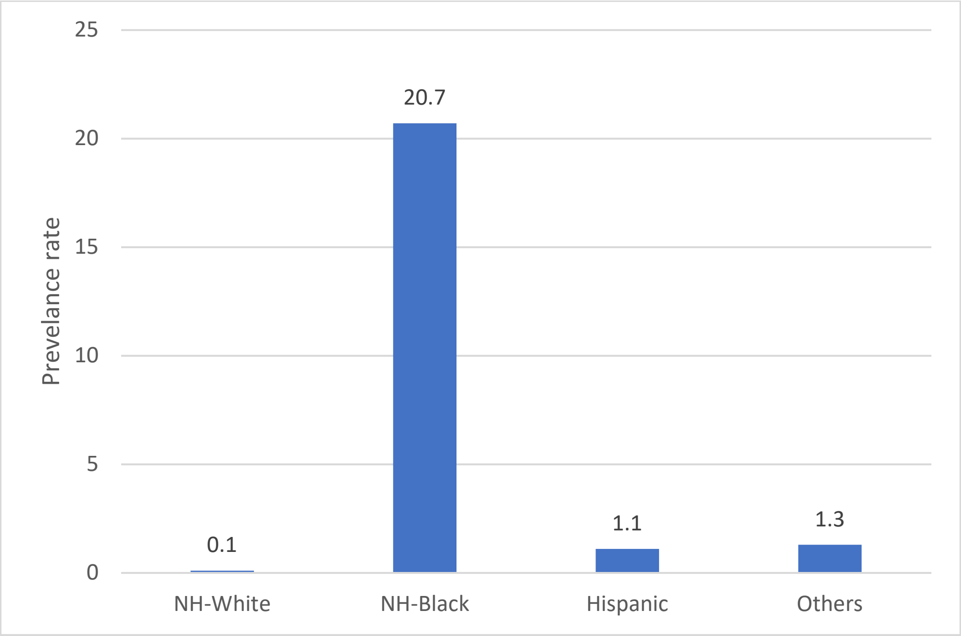
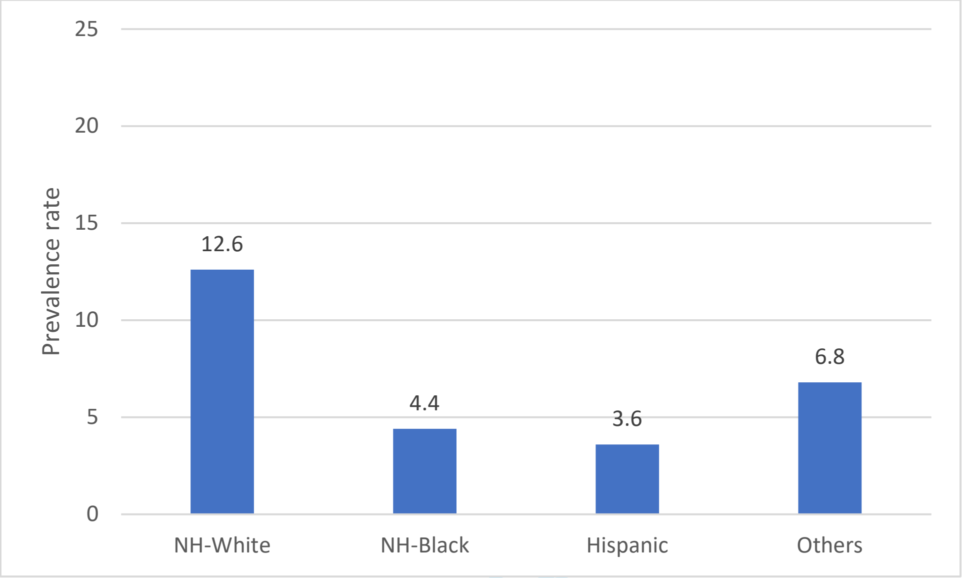


Figure 3 – Prevalence rates of palliative care usage in SCD-related hospitalizations (per 1000 SCD hospitalizations) by race/ethnicity



Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7,8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11,12
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15,16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13,14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-057361.R1
Article Type:	Original research
Date Submitted by the Author:	09-Mar-2022
Complete List of Authors:	Nwogu-Onyemkpa, Eberechi; Baylor College of Medicine, Department of Medicine, Center of Excellence in Health Equity, Training and Research; Baylor College of Medicine, Section of Geriatrics and Palliative Medicine Dongarwar, Deepa; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Salihu, HM; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Akpati, Lois; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Marroquin, Maricarmen; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Abadom, Megan; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Naik, Aanand; UTHealth School of Public Health, Management, Policy and Community Health; Michael E DeBakey VA Medical Center, Houston Center for Innovations in Quality, Effectiveness, and Safety
Primary Subject Heading:	Palliative care
Secondary Subject Heading:	Haematology (incl blood transfusion)
Keywords:	Adult palliative care < PALLIATIVE CARE, HAEMATOLOGY, Anaemia < HAEMATOLOGY

Title: Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

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Word count: 3,059

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Abstract:

Objective: Sickle cell disease (SCD) is a highly morbid condition notable for recurrent hospitalizations due to vaso-occlusive crises and complications of end organ damage. Little is known about the use of inpatient palliative care services in adult patients with SCD. This study aims to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations. We hypothesize that use of palliative care is low in SCD hospitalizations.

Design: A retrospective cross-sectional study utilizing data from the National Inpatient Sample (NIS) from 2008-2017 was conducted.

Setting: U.S. hospitals from 47 states and the District of Columbia.

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

Primary and secondary outcome measures: Palliative care service usage (documented by ICD-9-CM and ICD-10-CM diagnosis codes V66.7 and Z51.5).

Results: 987,555 SCD-related hospitalizations were identified, of which 4442 (0.45%) received palliative care service. Palliative care service usage increased at a rate of 9.2% per year (CI, 5.6-12.9). NH-Black and Hispanic patients were 33% and 53% less likely to have palliative care services compared to NH-White (OR 0.67; CI 0.45-0.99 and OR 0.47; CI, 0.26-0.84). 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) had decreased likelihood of palliative care services use.

Conclusion: Usage of palliative care during SCD-related hospitalizations is increasing but remains low. Disparities associated with race and gender exist for use of palliative care services during SCD related hospitalization. Further studies are needed to guide evidence-based palliative care interventions for more comprehensive and equitable care of adult patients with SCD.

Strengths and limitations of this study

- Our study is the first of its kind to investigate palliative care use among SCD patients using a national database.
- ICD-9-CM and ICD-10-CM codes for palliative care are not specific to palliative care provided by a palliative care specialist as these codes also encompass patients who are in comfort care status.
- Our study investigated inpatient palliative care usage and hence, our findings cannot be extrapolated to outpatient setting where patients with SCD patient receive most of their care.

Introduction:

Sickle cell disease (SCD) is a group of inherited red blood cell disorders in which abnormality in Hemoglobin (Hb) beta gene results in abnormal shape and sickling of red blood cells under stress. Physiologic manifestations of the illness arise from end organ ischemia, including acute pain from vaso-occlusive crises, cerebrovascular accident, acute chest syndrome, pulmonary hypertension, heart failure, renal failure, severe anemia, and recurrent infections.[1] Approximately 100,000 Americans predominantly of African (90%), Middle Eastern, and Mediterranean descent are affected by SCD.[2] Historically, SCD was a childhood disease – life expectancy for those with the disease was 20 years in 1970. 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.[3] As an increasing number of people with SCD survive into adulthood, there is a rising need for effective transitions to adult medicine involving multidisciplinary care teams.[4]

SCD is a highly morbid condition. Recurrent hospitalization is common in SCD due to vaso-occlusive crises and complications of end organ damage.[5] [6] During their last year of life, people with SCD were hospitalized for an average of forty-two days over five admissions.[7] Hospital admissions and ED visits increase sharply a month before death and most patients with SCD die in the hospital (63%) or emergency department (15%).[7] Patients with SCD experience increased rates of depression and anxiety,[8] [9] [10] chronic pain,[11] and decreased health-related quality of life. [12]. Increased healthcare use [13] and symptom burden are salient opportunities for palliative care intervention in this patient population. Palliative care provides holistic care for patients with serious chronic illnesses using a multidisciplinary team approach.[14] Palliative care has been

shown to increase patient's quality of life and decrease health care cost [15] [16] but the impact of palliative care on SCD is not well characterized.[17]

Furthermore, little is known about the use of *inpatient* palliative care services in adult patients with SCD. To address this gap, we used national data to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations (hospitalizations that resulted in patients' death in-hospital regardless of cause of death). We identified patient and hospital characteristics associated with use of hospital-based palliative care services in SCD. We hypothesize that use of palliative care is low in SCD hospitalizations.

Methods:

Data Source

Data from the 2008 to 2017 National Inpatient Sample (NIS), the largest all-payer, nationally representative inpatient database in the United States was used. The NIS is part of a group of databases developed by the Healthcare Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ).[18] This public database contains longitudinal data from a stratified sample of all discharges from U.S. hospitals from 47 states and the District of Columbia, excluding rehabilitation and long-term acute care hospitals, thereby estimating about a 20% sample of all hospital discharges. When weighted, each year, NIS contains data from about 35 million hospitalizations.

Study Population and Variables

The analysis was restricted to hospitalizations in adults aged 18 years and above. Diagnoses and procedures are coded using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes till the 3rd quarter of 2015, after which HCUP transitioned to ICD-10-CM format. To assess the study's primary exposure, 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 (ICD-9-CM - 282.41, 282.42, 282.61, 282.62, 282.63, 282.64, 282.60, 282.68, 282.69; ICD-10-CM - D57.4x, D57.0x, D57.2x, D57.1x, D57.8x). The study's primary outcome was palliative care use which was identified using ICD-9-CM diagnosis code V66.7 and ICD-10-CM diagnosis code Z51.5. There were no changes in the criteria for palliative care code with the transition from ICD-9-CM to ICD-10-CM. Covariates included in the study were socio-demographics for the patient which consisted of patients' age, race/ethnicity – categorized as Non-Hispanic (NH)-White, NH-Black, Hispanic and NH-Others, sex, insurance type – Medicare, Medicaid, private insurance, self-pay and others, median household income based on zipcodes; and hospital characteristics such as hospital location, hospital type (urban vs. rural and teaching vs. non-teaching), and hospital bed size.

Statistical Analysis

Since the NIS data was de-identified and publicly available, the study was approved as exempt by the Institutional Review Board (IRB) of Baylor College of Medicine. All statistical tests were two-tailed with the type-I error of 5% and were conducted using R version 3.5.1 (University of Auckland, Auckland, New Zealand) and R Studio Version 1.1.423 (Boston, MA) and Joinpoint Regression Program, version 4.7.0.0 (National Cancer Institute).

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.[19] The results are represented in the form of average annual percentage change (AAPC) and its 95% confidence interval (CI). We scrutinized the temporal trends in the rates of palliative care use among SCD patients overall, and among those who died in-hospital. Next, we examined the socio-demographic and hospitalization characteristics of patients with SCD and those with SCD who received palliative care during their hospitalizations. Prevalence rates of SCD and palliative care use among SCD hospitalizations were calculated, stratified by patients' race/ethnicity. 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 (exposures) associated with palliative care use (outcome variable) among all SCD hospitalizations and among those which resulted in patients' death in-hospital.

Patient and public involvement

Patients were not involved in this retrospective analysis of an anonymized national inpatient database.

Results:

Trends in the rate of palliative care usage in SCD-related hospitalizations

Between the study period of 2008 to 2018 the NIS contained 987,555 SCD-related hospitalizations of which 6,327 (0.64%) were terminal admissions. There were 4442 (0.45%) SCD-related hospitalizations that received palliative care service. Figure 1 shows temporal trends in palliative care usage. The rate of inpatient palliative care service use 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.

Patient characteristics – SCD hospitalizations with palliative care usage

Table 1 shows patient characteristics for SCD related hospitalizations and patients utilizing palliative care services. The prevalence of SCD-related hospitalization was highest among the 18-39 age group (9.7 per 1000 SCD hospitalizations) and decreased with increasing age. Conversely, the prevalence of inpatient palliative care use was highest in the oldest age group (34.8 per 1000 SCD hospitalization) and lowest in the 18-39 age group (3.8 per 1000 SCD hospitalizations). The prevalence of SCD-related hospitalization was highest among NH-Blacks (20.7 per 1000 SCD hospitalizations) and lowest in NH-Whites (0.1 per 1000 SCD hospitalizations) 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).

Regional and hospital characteristics – SCD hospitalizations with palliative care usage

SCD hospitalization was lowest in the Northeast (1.4 per 1000 SCD hospitalizations) but the prevalence of inpatient palliative care service was highest in this region (6.1 per 1000 SCD hospitalizations). Conversely the South region had the highest prevalence of SCD hospitalization (4.3 per 1000 SCD hospitalizations) but the lowest level of usage of inpatient palliative care services (3.6 per 1000 SCD hospitalizations). 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).

Factors associated with inpatient palliative care usage in SCD

Table 2 shows factors associated with inpatient palliative care usage in SCD hospitalizations. 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). NH-Black and Hispanic patients were 33% and 53% respectively less likely to receive inpatient palliative care services compared to NH-White (OR, 0.67; 95% CI, 0.45-0.99 and OR, 0.47; 95% CI, 0.26-0.84, respectively). Likewise, during terminal admissions usage of palliative care services was 67% and 72% less likely among NH-Black and Hispanic patients, respectively when compared to NH-White (OR, 0.33; 95% CI, 0.16-0.68 and OR, 0.28; 95% CI, 0.09-0.91, respectively). Female patients were 60% less likely to receive palliative care services than male patients (OR, 0.40; 95% CI, 0.21-0.76). Compared to routine discharges, hospitalizations resulting in death and transfer to another health care facility were associated with increased usage of inpatient palliative care services (OR, 39.36; 95% CI, 30.83-49.98, and OR, 3.71; 95% CI, 2.73-5.03, respectively) while discharge against medical advice (DAMA) was associated with decreased use of inpatient palliative care services (OR, 0.48; 95% CI 0.28-0.84).

Patients with zip code in the highest income quartile were 58% more likely to receive inpatient palliative care services (OR, 1.58; 95% CI 1.02-2.45) than those in the lowest quartile. Compared to Medicare patients, those with Medicaid were 60% less likely (OR, 0.40; 95% CI, 0.21-0.78), while patients with private insurance were 30% more likely (OR, 1.30; 95% CI, 0.93-1.59) to receive palliative care services. During terminal admissions, there were no significant differences in palliative care usage across different payors.

Patients admitted in a medium or large hospital were 47% and 91%, respectively more likely (OR, 1.47; 95% CI, 1.02-2.12 and OR, 1.91; 95% CI, 1.30-2.82, respectively) to receive palliative care services than patients in small hospitals while patients admitted to rural or urban non-teaching hospitals were less likely to receive palliative care services than those in urban teaching hospital (OR, 0.47; 95% CI 0.28-0.79 and OR, 0.61; 95% CI 0.47-0.80, respectively).

Discussion:

In this study of national trends, we found overall low usage of palliative care services during SCD-related hospitalizations. 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. NH-Black and Hispanic patients were less likely to receive palliative care services especially during terminal hospitalizations.

While early palliative care has gained acceptance in cancer care,[20] its adoption in other serious life limiting conditions such as congestive heart failure, chronic kidney disease, and SCD lags. SCD has traditionally been viewed as a childhood disease as most patients did not survive to adulthood in the past. Currently, most patients with SCD survive to adulthood.[3] Furthermore, some SCD patients experience complications and end organ damage from their disease resulting in a shortened life expectancy than the general population. 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. 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,[21] as well as honest discussions regarding goals of care and patient's preference for end of life.

Our study showed most SCD-related hospitalizations and palliative care service usage were in the NH-Black group. However, further analysis accounting for covariates revealed that NH-Black patients were significantly less likely to receive palliative care during hospitalization compared to NH-white patients. Notably, race/ethnicity was the only factor associated with palliative care use in both SCD and terminal hospitalizations. Other studies have shown racial disparities in use of palliative care services in other chronic diseases.[22,23] Furthermore, studies have shown that black patients are less likely to use hospice services and more likely to receive intensive life-sustaining procedures at end of life compared to white patients.[24] Factors identified to drive this racial disparity in hospice use include knowledge deficits,[25] mistrust of the health care system,[26] miscommunication and misunderstanding of treatment options,[27] and preference in more aggressive care.[28] Similar studies are lacking to elucidate factors implicated in the racial difference in non-hospice palliative care usage across all life limiting diseases.[29] Palliative care has a strong perceived association with hospice with many patients and families unable to differentiate between the two. 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. Further studies are needed to investigate patient and system factors associated with racial differences in palliative care usage in SCD.

Gender differences in use of inpatient palliative care services were found. Although male and female patients had similar prevalence of SCD-related hospitalization, female patients were 60% less likely to receive palliative care services. This finding is contrary to that of other studies which show that women are more receptive to palliative care than men.[30] 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. Studies have shown that although most chronic pain conditions are more prevalent in women than men, and women report greater pain then men after invasive procedures, women receive less analgesia and are more likely to have their pain attributed to psychological causes.[31] It is possible that palliative care consultants are more frequently involved for specialist level pain management for male than female patients

accounting for the gender difference observed in our study. This finding requires further investigation as the study by McClish et al. demonstrates that men and women with SCD report similar pain experiences.[32]

We also found socioeconomic differences in the usage of palliative care in SCD similar to other diseases.[23,33,34] Patients with zip codes in the highest income quartile and those with private insurance were more likely to receive palliative care, while patients with Medicaid were less likely to receive palliative care services. Insurance dictates patient's access to specialty care with patients on Medicaid reporting more challenge than those with private insurance accessing certain specialty care particularly in the outpatient setting.[35,36]

Regional differences were detected in our study. The South region had the highest number of SCD hospitalizations but the lowest prevalence of palliative care use. This finding is notable as two of the three states (Florida, Texas, and New York) with the highest population of SCD patients are in the South. 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.[33] [22] [34] While many sickle cell patients use larger, urban hospitals for their care,[37] 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.

To our knowledge, our study is the first of its kind to investigate palliative care use among SCD patients using a national data base. Limitations exist in our study one of which is the validity of the ICD-9 and ICD-10 codes for identification of palliative care consultations. Investigators have sought to validate these codes however these studies utilize data from a single institution [38] or from the VA system.[39] Furthermore, the ICD-9 and ICD-10 codes for palliative care are not specific to palliative care provided by a palliative care specialist as these codes also encompass

patients who are in comfort care status. Not all patients in comfort care are managed by a palliative care specialist and as such it is difficult to delineate which hospitalizations were indeed associated with the involvement of a palliative care specialist. In addition, our dataset does not allow us to elucidate the nature of palliative care interventions provided during admissions hence it is unclear if these interventions were for symptom management, goals of care discussion, counseling and support, or transition to comfort care. 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. 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. As such, we suspect that our study overestimates the prevalence of palliative care usage in SCD.

SCD related morbidity and mortality have a significant impact on patient self-reported quality of life outcomes and healthcare utilization and cost. Early palliative care might guide patients' treatment decisions and mitigate initiation of interventions that are not in line with a patients' wishes at the end of life. Early palliative care also has the potential to improve symptom management and consequently improve quality of life for individuals with SCD. 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. Racial disparity in the use of palliative care by SCD patients should be investigated with studies assessing knowledge of palliative care and barriers to palliative care use by SCD patients. Furthermore, studies addressing system

barriers to palliative care use among minority patients are needed as the implication spans across other life limiting illnesses.

Acknowledgements

Conflict of Interest Disclosures: Authors without conflicts of interest, including relevant financial interests, activities, relationships, and affiliations.

Funding/Support: Research funding support was provided by the U.S. Department of Health and Human Services and Health Resources and Services Administration for Baylor College of Medicine Center of Excellence in Health Equity, Training, and Research (Grant No: D34HP31024). Additional support is provided to Dr. Naik from the Houston VA HSR&D Center for Innovations in Quality, Effectiveness, and Safety (CIN 13-413).

Authorship Contribution:

Eberechi Nwogu-Onyemkpa was involved in the conception of the study, interpretation of data, drafting, and revision of the manuscript.

Deepa Dongarwar was involved in the conception of the study, analysis of the data, drafting, and revision of the manuscript.

Hamisu Salihu was involved in the conception of the study and revision of the manuscript.

Chioma Akpati was involved in the interpretation of data and drafting of the manuscript.

Maricarmen Marroquin was involved in the interpretation of data, drafting and revision of the manuscript.

Megan Abadom was involved in the interpretation of data and drafting of the manuscript.

Aanand D. Naik was involved in the conception of the study and revision of the manuscript.

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Table 1: Patient characteristics among SCD-related hospitalizations and among those with SCD who received palliative care during their hospitalization

	Total N=307709982	SCD-related hospitalizations N=987555	Prevalence of SCD-related hospitalizations (per 1000 hospitalizations)	SCD-related hospitalizations receiving palliative care N=4442	Prevalence of palliative care use (per 1000 SCD hospitalizations)
Age Group					
18-39 years	75567499	733837	9.7	2824	3.8
40-59 years	78526326	214939	2.7	1160	5.4
60-79 years	101611492	35362	0.3	339	9.6
80+ years	52004665	3417	0.1	119	34.8
Race/Ethnicity					
NH-White	192567014	16962	0.1	214	12.6
NH-Black	41490748	857006	20.7	3773	4.4
Hispanic	29897432	32676	1.1	116	3.6
Others	17422072	23026	1.3	157	6.8
Missing	26332714	57883	2.2	181	3.1
Sex					
Male	125745784	427285	3.4	1921	4.5
Female	181778482	559845	3.1	2521	4.5
Missing	185716	424	2.3	—	—
Discharge Status					
Routine	202797074	853218	4.2	2619	3.1
Transfer	55186460	37409	0.7	447	11.9
Died	6740712	6327	0.9	685	108.3
DAMA	3847845	44520	11.6	69	1.5
Other	38933666	45507	1.2	622	13.7
Missing	204225	573	2.8	—	—
Zip code income quartile					
Lowest quartile	89460128	478674	5.4	2053	4.3
2nd quartile	78497949	219619	2.8	801	3.6
3rd quartile	71474969	163233	2.3	836	5.1
Highest quartile	61340502	100769	1.6	703	7.0
Missing	6936433	25259	3.6	48	1.9
Primary Payer					
Medicare	141357438	315777	2.2	1736	5.5
Medicaid	50563783	428967	8.5	1725	4.0
Private Insurance	88933878	170459	1.9	671	3.9
Self-Pay	26247689	70526	2.7	304	4.3
Missing	607194	1825	3.0	—	—
Hospital Characteristics					
Hospital Region					
Northeast	33888883	46282	1.4	1226	6.1
Midwest	107572349	234180	2.2	1014	5.4
South	164884575	701680	4.3	1820	3.6

West	1364173	5411	4.0	382	4.4
Hospital Bed Size					
Small	46455596	114366	2.5	331	2.9
Medium	81563430	258481	3.2	998	3.9
Large	178326782	609296	3.4	3108	5.1
Missing	1364173	5411	4.0	—	—
Hospital Location and Teaching Status					
Rural	33888883	46282	1.4	96	2.1
Urban non-teaching	107572349	234180	2.2	749	3.2
Urban teaching	164884575	701680	4.3	3591	5.1
Missing	1364173	5411	4.0	—	—

SCD-Sickle Cell Disease
NH-Non-Hispanic
DAMA-Discharged Against Medical Advice
Prevalence is the rate of the outcome (SCD or palliative care usage) among each patient characteristics
'—' represents cell values <10, which have been suppressed to preserve patient confidentiality, as per HCUP guidelines.

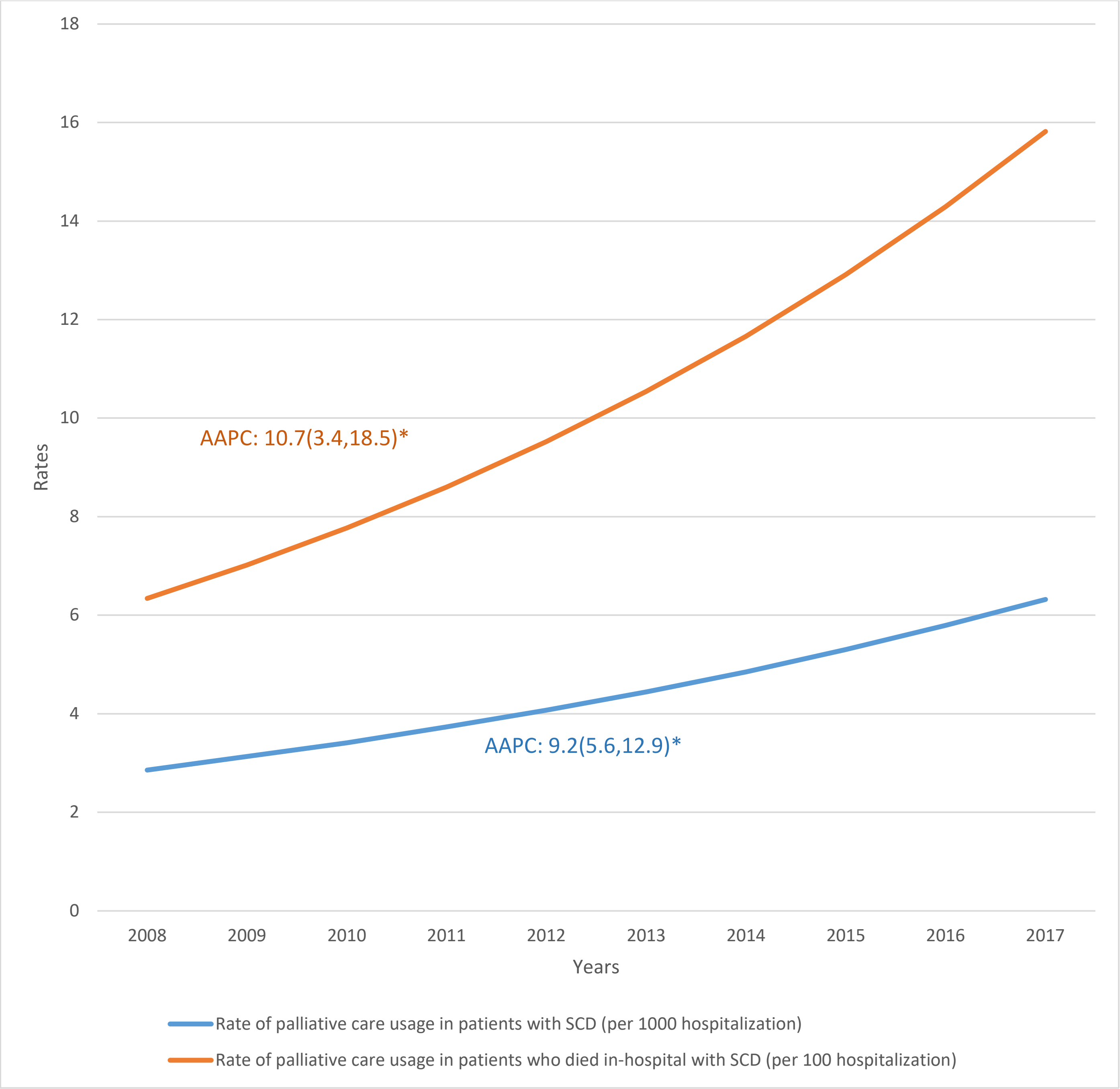
Table 2: Factors associated with palliative care use in SCD patients – overall and among those who died in-hospital

	Palliative care use in SCD hospitalizations	Palliative care use among SCD patients who died in-hospital
	OR(95% CI)	OR(95% CI)
Age Group		
18-39 years	reference	reference
40-59 years	0.98(0.81-1.18)	1.81(1.19-2.75)*
60-79 years	0.95(0.70-1.30)	1.13(0.60-2.12)
80+ years	2.34(1.41-3.88)*	2.29(0.79-6.64)
Race/Ethnicity		
NH-White	reference	reference
NH-Black	0.67(0.45-0.99)*	0.33(0.16-0.68)*
Hispanic	0.47(0.26-0.84)*	0.28(0.09-0.91)*
Others	0.83(0.49-1.39)	0.41(0.12-1.42)
Sex		
Male	reference	reference
Female	0.40(0.21-0.76)*	1.45(1.00-2.11)
Discharge Status		
Routine	reference	reference
Transfer	3.71(2.73-5.03)*	
Died	39.26(30.83-49.98)*	—
DAMA	0.48(0.28-0.84)*	—
Other	4.14(3.20-5.35)*	—
Zip code income quartile		
Lowest quartile	reference	reference
2nd quartile	0.89(0.71-1.11)	0.69(0.42-1.14)
3rd quartile	1.24(0.85-1.80)	0.48(0.25-0.91)*
Highest quartile	1.58(1.02-2.45)*	1.46(0.79-2.71)
Primary Payer		
Medicare	reference	reference
Medicaid	0.40(0.21-0.78)*	0.72(0.21-2.48)
Private Insurance	1.30(1.02-1.65)*	1.03(0.59-1.79)
Self-Pay	1.22(0.93-1.59)	1.12(0.64-1.99)
Hospital Characteristics		
Hospital Region		
Northeast	reference	reference
Midwest	1.00(0.57-1.75)	1.18(0.57-2.46)
South	0.69(0.42-1.11)	1.47(0.78-2.78)
West	0.72(0.40-1.31)	1.63(0.77-3.41)
Hospital Bed Size		
Small	reference	reference
Medium	1.47(1.02-2.12)*	1.18(0.57-2.44)
Large	1.91(1.30-2.82)*	1.52(0.78-2.96)
Hospital Location and Teaching Status		
Urban teaching	reference	reference
Rural	0.47(0.28-0.79)*	0.75(0.33-1.73)
Urban non-teaching	0.61(0.47-0.80)*	0.63(0.40-0.99)

SCD-Sickle Cell Disease
NH-Non-Hispanic
DAMA-Discharged Against Medical Advice
OR- odds ratio, CI- confidence interval
'–' represents the absence of variable in the model

Figure legend/caption

Figure 1: Temporal trends in the rates of palliative care use represented as average annual percentage change (AAPC). '*' represents statistically significant findings ($p<0.05$). Rate of inpatient palliative care service usage increased at average of 9.2% per year (95% CI, 5.6-12.9) for all SCD-related hospitalizations and 10.7% (95% CI, 3.4-18.5) for terminal hospitalizations.


18
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Rates
2008
2009
2010
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2016
2017
Years
AAPC: 10.7(3.4,18.5)*
AAPC: 9.2(5.6,12.9)*
Rate of palliative care usage in patients with SCD (per 1000 hospitalization)
Rate of palliative care usage in patients who died in-hospital with SCD (per 100 hospitalization)

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	**Recommendation**	**Page No**
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7,8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8,9
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	22, 23
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11,12
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15,16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13,14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-057361.R2
Article Type:	Original research
Date Submitted by the Author:	16-May-2022
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Primary Subject Heading:	Palliative care
Secondary Subject Heading:	Haematology (incl blood transfusion)
Keywords:	Adult palliative care < PALLIATIVE CARE, HAEMATOLOGY, Anaemia < HAEMATOLOGY

Title: Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

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Word count: 3,116

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Abstract:

Objective: Sickle cell disease (SCD) is a highly morbid condition notable for recurrent hospitalizations due to vaso-occlusive crises and complications of end organ damage. Little is known about the use of inpatient palliative care services in adult patients with SCD. This study aims to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations. We hypothesize that use of palliative care is low in SCD hospitalizations.

Design: A retrospective cross-sectional study utilizing data from the National Inpatient Sample (NIS) from 2008-2017 was conducted.

Setting: US hospitals from 47 states and the District of Columbia.

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

Primary and secondary outcome measures: Palliative care service use (documented by ICD-9-CM and ICD-10-CM diagnosis codes V66.7 and Z51.5).

Results: 987,555 SCD-related hospitalizations were identified, of which 4442 (0.45%) received palliative care service. Palliative care service use increased at a rate of 9.2% per year (CI, 5.6-12.9). 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). 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.

Conclusion: Use of palliative care during SCD-related hospitalizations is increasing but remains low. Disparities associated with race and gender exist for use of palliative care services during SCD related hospitalization. Further studies are needed to guide evidence-based palliative care interventions for more comprehensive and equitable care of adult patients with SCD.

Strengths and limitations of this study

- Our study is the first of its kind to investigate palliative care use among SCD patients using a national database.
- ICD-9-CM and ICD-10-CM codes for palliative care are not specific to palliative care provided by a palliative care specialist as these codes also encompass patients who are in comfort care status.
- Our study investigated inpatient palliative care use and hence, our findings cannot be extrapolated to outpatient setting where patients with SCD patient receive most of their care.

Introduction:

Sickle cell disease (SCD) is a group of inherited red blood cell disorders in which abnormality in Hemoglobin (Hb) beta gene results in abnormal shape and sickling of red blood cells under stress. Physiologic manifestations of the illness arise from end organ ischemia, including acute pain from vaso-occlusive crises, cerebrovascular accident, acute chest syndrome, pulmonary hypertension, heart failure, renal failure, severe anemia, and recurrent infections.[1] Approximately 100,000 Americans predominantly of African (90%), Middle Eastern, and Mediterranean descent are affected by SCD.[2] Historically, SCD was a childhood disease – life expectancy for those with the disease was 20 years in 1970. 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.[3] As an increasing number of people with SCD survive into adulthood, there is a rising need for effective transitions to adult medicine involving multidisciplinary care teams.[4]

SCD is a highly morbid condition. Recurrent hospitalization is common in SCD due to vaso-occlusive crises and complications of end organ damage.[5 6] During their last year of life, people with SCD were hospitalized for an average of forty-two days over five admissions.[7] Hospital admissions and ED visits increase sharply a month before death and most patients with SCD die in the hospital (63%) or emergency department (15%).[7] Patients with SCD experience increased rates of depression and anxiety,[8 9 10] chronic pain,[11] and decreased health-related quality of life. [12]. Increased healthcare use [13] and symptom burden are salient opportunities for palliative care intervention in this patient population. Palliative care provides holistic care for patients with serious chronic illnesses using a multidisciplinary team approach.[14] Palliative care has been shown to increase patient’s quality of life and decrease health care costs [15 16] but the impact of palliative care on SCD is not well characterized.[17]

Furthermore, little is known about the use of *inpatient* palliative care services in adult patients with SCD. To address this gap, we used national data to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations (hospitalizations that resulted in patients’ death in-hospital regardless of cause of death). We identified patient and hospital characteristics associated with use of hospital-based palliative care services in SCD. We hypothesize that use of palliative care is low in SCD hospitalizations.

Methods:

Data Source

Data from the 2008 to 2017 National Inpatient Sample (NIS), the largest all-payer, nationally representative inpatient database in the United States (US) was used. The NIS is part of a group of databases developed by the Healthcare Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ).[18] This public database contains longitudinal data from a stratified sample of all discharges from US hospitals from 47 states and the District of Columbia, excluding rehabilitation and long-term acute care hospitals, thereby estimating about a 20% sample of all hospital discharges. When weighted, each year, NIS contains data from about 35 million hospitalizations.

Study Population and Variables

The analysis was restricted to hospitalizations in adults aged 18 years and above. Diagnoses and procedures are coded using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes till the 3rd quarter of 2015, after which HCUP transitioned to ICD-10-CM format. 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 (ICD-9-CM - 282.41, 282.42, 282.61, 282.62, 282.63, 282.64, 282.60, 282.68, 282.69; ICD-10-CM - D57.4x, D57.0x, D57.2x, D57.1x, D57.8x). The study's primary outcome was palliative care use which was identified using ICD-9-CM diagnosis code V66.7 and ICD-10-CM diagnosis code Z51.5. The 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. There were no changes in the criteria for palliative care code with the transition from ICD-9-CM to ICD-10-CM. Covariates included in the study were socio-demographics for the patient which consisted of patients' age, race/ethnicity – categorized as Non-Hispanic (NH)-White, NH-Black, Hispanic and NH-Others, sex, insurance type – Medicare, Medicaid, private insurance, self-pay and others, median household income based on zipcodes; and hospital characteristics such as hospital location, hospital type (urban vs. rural and teaching vs. non-teaching), and hospital bed size.

Statistical Analysis

Since the NIS data was de-identified and publicly available, the study was approved as exempt by the Institutional Review Board (IRB) of Baylor College of Medicine. All statistical tests were two-tailed with the type-I error of 5% and were conducted using R version 3.5.1 (University of Auckland, Auckland, New Zealand) and R Studio Version 1.1.423 (Boston, MA) and Joinpoint Regression Program, version 4.7.0.0 (National Cancer Institute).

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.[19] The results are represented in the form of average annual percentage change (AAPC) and its 95% confidence interval (CI). We scrutinized the temporal trends in the rates of palliative care use among SCD patients overall, and among those who died in-hospital. Next, we examined the socio-demographic and hospitalization characteristics of patients with SCD and those with SCD who received palliative care during their hospitalization. Prevalence rates of SCD and palliative care use among SCD hospitalizations were calculated, stratified by patients' race/ethnicity. 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 in-hospital. All the patient demographic and hospital characteristics were loaded into the association models to obtain adjusted odds ratio and 95% confidence intervals.

Patient and public involvement

Patients were not involved in this retrospective analysis of an anonymized national inpatient database.

Results:

Trends in the rate of palliative care use in SCD-related hospitalizations

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. There were 4442 (0.45%) SCD-related hospitalizations that received palliative care service. Figure 1 shows temporal trends in palliative care use. The rate of inpatient palliative care service use 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.

Patient characteristics – SCD hospitalizations with palliative care use

Table 1 shows patient characteristics for SCD related hospitalizations and patients who received palliative care services. The prevalence of SCD-related hospitalization was highest among the 18-39 age group (9.7 per 1000 SCD hospitalizations) and decreased with increasing age. Conversely, the prevalence of inpatient palliative care use was highest in the oldest age group (34.8 per 1000 SCD hospitalization) and lowest in the 18-39 age group (3.8 per 1000 SCD hospitalizations). The prevalence of SCD-related hospitalization was highest among NH-Blacks (20.7 per 1000 SCD hospitalizations) and lowest in NH-Whites (0.1 per 1000 SCD hospitalizations) 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).

Regional and hospital characteristics – SCD hospitalizations with palliative care use

SCD hospitalization was lowest in the Northeast (1.4 per 1000 SCD hospitalizations) but the prevalence of inpatient palliative care service was highest in this region (6.1 per 1000 SCD hospitalizations). 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). 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).

Factors associated with inpatient palliative care use in SCD

Table 2 shows factors associated with inpatient palliative care use in SCD hospitalizations. During terminal hospitalizations patients between 40-59 years were 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). NH-Black and Hispanic patients were less likely to receive inpatient palliative care services compared to NH-White (OR, 0.67; 95% CI, 0.45-0.99 and OR, 0.47; 95% CI, 0.26-0.84, respectively). Likewise, during terminal admissions use of palliative care services was less likely among NH-Black and Hispanic patients, respectively when compared to NH-White (OR, 0.33; 95% CI, 0.16-0.68 and OR, 0.28; 95% CI, 0.09-0.91, respectively). Female patients were less likely to receive palliative care services than male patients (OR, 0.40; 95% CI, 0.21-0.76). Compared to routine discharges, hospitalizations resulting in death and transfer to another health care facility were associated with increased odds of use of inpatient palliative care services (OR, 39.36; 95% CI, 30.83-49.98, and OR, 3.71; 95% CI, 2.73-5.03, respectively) while discharge against medical advice (DAMA) was associated with decreased odds of use of inpatient palliative care services (OR, 0.48; 95% CI 0.28-0.84).

Patients living in zip codes in the highest income quartile were more likely to receive inpatient palliative care services (OR, 1.58; 95% CI 1.02-2.45) than those in the lowest quartile. Compared to Medicare patients, those with Medicaid had lesser odds (OR, 0.40; 95% CI, 0.21-0.78), while patients with private insurance had higher odds (OR, 1.30; 95% CI, 0.93-1.59) of receiving palliative care services. During terminal admissions, there were no significant differences in palliative care use across different payors.

Patients admitted to medium or large hospitals were more likely (OR, 1.47; 95% CI, 1.02-2.12 and OR, 1.91; 95% CI, 1.30-2.82, respectively) to receive palliative care services than patients in small hospitals while patients admitted to rural or urban non-teaching hospitals were less likely to receive palliative care services than those in urban teaching hospitals (OR, 0.47; 95% CI 0.28-0.79 and OR, 0.61; 95% CI 0.47-0.80, respectively).

Discussion:

In this study of national trends, we found overall low use of palliative care services during SCD-related hospitalizations. Palliative care use was more likely among patients who were NH-White male, in the highest income quartile, with private insurance, and who received care in large or urban academic hospitals. NH-Black and Hispanic patients were less likely to receive palliative care services especially during terminal hospitalizations.

While early palliative care has gained acceptance in cancer care,[20] its adoption in other serious life limiting conditions such as congestive heart failure, chronic kidney disease, and SCD lags. SCD has traditionally been viewed as a childhood disease as most patients did not survive to adulthood in the past. Currently, most patients with SCD survive to adulthood.[3] Furthermore, some patients with SCD experience complications and end organ damage from their disease resulting in a shortened life expectancy than the general population. Our study found a higher prevalence of palliative care service use in terminal admissions when compared to admissions with routine discharge or transfer to another level of care. This highlights an opportunity for palliative care involvement earlier in the disease course in SCD, facilitating more holistic care of patients. Earlier initiation of palliative care grants patients psychosocial support and symptom management from an interdisciplinary team,[21] as well as honest discussions regarding goals of care and patient's preference for end of life.

Our study showed most SCD-related hospitalizations and palliative care service use were in the NH-Black group. However, further analysis accounting for covariates revealed that NH-Black patients were significantly less likely to receive palliative care during hospitalization compared to NH-white patients. Notably, race/ethnicity was the only factor associated with palliative care use in both SCD and terminal hospitalizations. Other studies have shown racial disparities in the use of palliative care services in other chronic diseases.[22,23] Furthermore, studies have shown that black patients are less likely to use hospice services and more likely to receive intensive life-sustaining procedures at end of life compared to white patients.[24] Factors identified to drive this racial disparity in hospice use include knowledge deficits,[25] mistrust of the health care system,[26] miscommunication and misunderstanding of treatment options,[27] and preference for more aggressive.[28] Similar studies are lacking to elucidate factors implicated in the racial difference in non-hospice palliative care use across all life limiting diseases.[29] Palliative care has a strong perceived association with hospice with many patients and families unable to differentiate between the two. 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. Further studies are needed to investigate patient and system factors associated with racial differences in palliative care use in SCD.

Gender differences in the use of inpatient palliative care services were found. Although male and female patients had a similar prevalence of SCD-related hospitalization, female patients were 60% less likely to receive palliative care services. This finding is contrary to that of other studies which show that women are more receptive to palliative care than men.[30] 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. 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, women receive less analgesia and are more likely to have their pain attributed to psychological causes.[31] It is possible that palliative care consultants are more frequently involved for specialist level pain management for male than female patients

accounting for the gender difference observed in our study. This finding requires further investigation as the study by McClish et al. demonstrates that men and women with SCD report similar pain experiences.[32]

We also found socioeconomic differences in the use of palliative care in SCD similar to other diseases.[23,33,34] Patients with zip codes in the highest income quartile and those with private insurance were more likely to receive palliative care, while patients with Medicaid were less likely to receive palliative care services. Insurance dictates patient's access to specialty care with patients on Medicaid reporting more challenge than those with private insurance accessing certain specialty care particularly in the outpatient setting.[35,36]

Regional differences were detected in our study. The South region had the highest number of SCD hospitalizations but the lowest prevalence of palliative care use. This finding is notable as two of the three states (Florida, Texas, and New York) with the highest population of SCD patients are in the South. Hospital characteristics were also predictive of palliative care use with medium, large and urban teaching hospitals associated with greater use of palliative care in SCD similar to findings from other studies.[33] [22] [34] While many sickle cell patients use larger, urban hospitals for their care,[37] 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.

To our knowledge, our study is the first of its kind to investigate palliative care use among SCD patients using a national data base. Limitations exist in our study one of which is the validity of the ICD-9 and ICD-10 codes for identification of palliative care consultations. Investigators have sought to validate these codes however these studies utilize data from a single institution [38] or from the VA system.[39] Furthermore, the ICD-9 and ICD-10 codes for palliative care are not specific to palliative care provided by a palliative care specialist as these codes also encompass

patients who are in comfort care status.[40] Not all patients in comfort care are managed by a palliative care specialist and as such it is difficult to delineate which hospitalizations were indeed associated with the involvement of a palliative care specialist. In addition, our dataset does not allow us to elucidate the nature of palliative care interventions provided during admissions hence it is unclear if these interventions were for symptom management, goals of care discussion, counseling and support, or transition to comfort care. 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. 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.

SCD related morbidity and mortality have a significant impact on patient self-reported quality of life outcomes and healthcare utilization and cost. Early palliative care might guide patients' treatment decisions and mitigate initiation of interventions that are not in line with a patients' wishes at the end of life. Early palliative care also has the potential to improve symptom management and consequently improve quality of life for individuals with SCD. 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. Racial disparity in the use of palliative care by SCD patients should be investigated with studies assessing knowledge of palliative care and barriers to palliative care use by SCD patients. Furthermore, studies addressing system

barriers to palliative care use among minority patients are needed as the implication spans across other life limiting illnesses.

Acknowledgements

Conflict of Interest Disclosures: **A**uthors *without* conflicts of interest, including relevant financial interests, activities, relationships, and affiliations.

Funding/Support: Research funding support was provided by the US Department of Health and Human Services and Health Resources and Services Administration for Baylor College of Medicine Center of Excellence in Health Equity, Training, and Research (Grant No: D34HP31024). Additional support is provided to Dr. Naik from the Houston VA HSR&D Center for Innovations in Quality, Effectiveness, and Safety (CIN 13-413).

Authorship Contribution:

Eberechi Nwogu-Onyemkpa was involved in the conception of the study, interpretation of data, drafting, and revision of the manuscript.

Deepa Dongarwar was involved in the conception of the study, analysis of the data, drafting, and revision of the manuscript.

Hamisu Salihu was involved in the conception of the study and revision of the manuscript.

Chioma Akpati was involved in the interpretation of data and drafting of the manuscript.

Maricarmen Marroquin was involved in the interpretation of data, drafting and revision of the manuscript.

Megan Abadom was involved in the interpretation of data and drafting of the manuscript.

Aanand D. Naik was involved in the conception of the study and revision of the manuscript.

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Table 1: Patient characteristics among SCD-related hospitalizations and among those with SCD who received palliative care during their hospitalization

	Total N=307709982	SCD-related hospitalizations N=987555	Prevalence of SCD-related hospitalizations (per 1000 hospitalizations)	SCD-related hospitalizations receiving palliative care N=4442	Prevalence of palliative care use (per 1000 SCD hospitalizations)
Age Group					
18-39 years	75567499	733837	9.7	2824	3.8
40-59 years	78526326	214939	2.7	1160	5.4
60-79 years	101611492	35362	0.3	339	9.6
80+ years	52004665	3417	0.1	119	34.8
Race/Ethnicity					
NH-White	192567014	16962	0.1	214	12.6
NH-Black	41490748	857006	20.7	3773	4.4
Hispanic	29897432	32676	1.1	116	3.6
Others	17422072	23026	1.3	157	6.8
Missing	26332714	57883	2.2	181	3.1
Sex					
Male	125745784	427285	3.4	1921	4.5
Female	181778482	559845	3.1	2521	4.5
Missing	185716	424	2.3	—	—
Discharge Status					
Routine	202797074	853218	4.2	2619	3.1
Transfer	55186460	37409	0.7	447	11.9
Died	6740712	6327	0.9	685	108.3
DAMA	3847845	44520	11.6	69	1.5
Other	38933666	45507	1.2	622	13.7
Missing	204225	573	2.8	—	—
Zip code income quartile					
Lowest quartile	89460128	478674	5.4	2053	4.3
2nd quartile	78497949	219619	2.8	801	3.6
3rd quartile	71474969	163233	2.3	836	5.1
Highest quartile	61340502	100769	1.6	703	7.0
Missing	6936433	25259	3.6	48	1.9
Primary Payer					
Medicare	141357438	315777	2.2	1736	5.5
Medicaid	50563783	428967	8.5	1725	4.0
Private Insurance	88933878	170459	1.9	671	3.9
Self-Pay	26247689	70526	2.7	304	4.3
Missing	607194	1825	3.0	—	—
Hospital Characteristics					
Hospital Region					
Northeast	33888883	46282	1.4	1226	6.1
Midwest	107572349	234180	2.2	1014	5.4
South	164884575	701680	4.3	1820	3.6

West	1364173	5411	4.0	382	4.4
Hospital Bed Size					
Small	46455596	114366	2.5	331	2.9
Medium	81563430	258481	3.2	998	3.9
Large	178326782	609296	3.4	3108	5.1
Missing	1364173	5411	4.0	—	—
Hospital Location and Teaching Status					
Rural	33888883	46282	1.4	96	2.1
Urban non-teaching	107572349	234180	2.2	749	3.2
Urban teaching	164884575	701680	4.3	3591	5.1
Missing	1364173	5411	4.0	—	—

SCD-Sickle Cell Disease
NH-Non-Hispanic
DAMA-Discharged Against Medical Advice
Prevalence is the rate of the outcome (SCD or palliative care use) among each patient characteristics
'—' represents cell values <10, which have been suppressed to preserve patient confidentiality, as per HCUP guidelines.

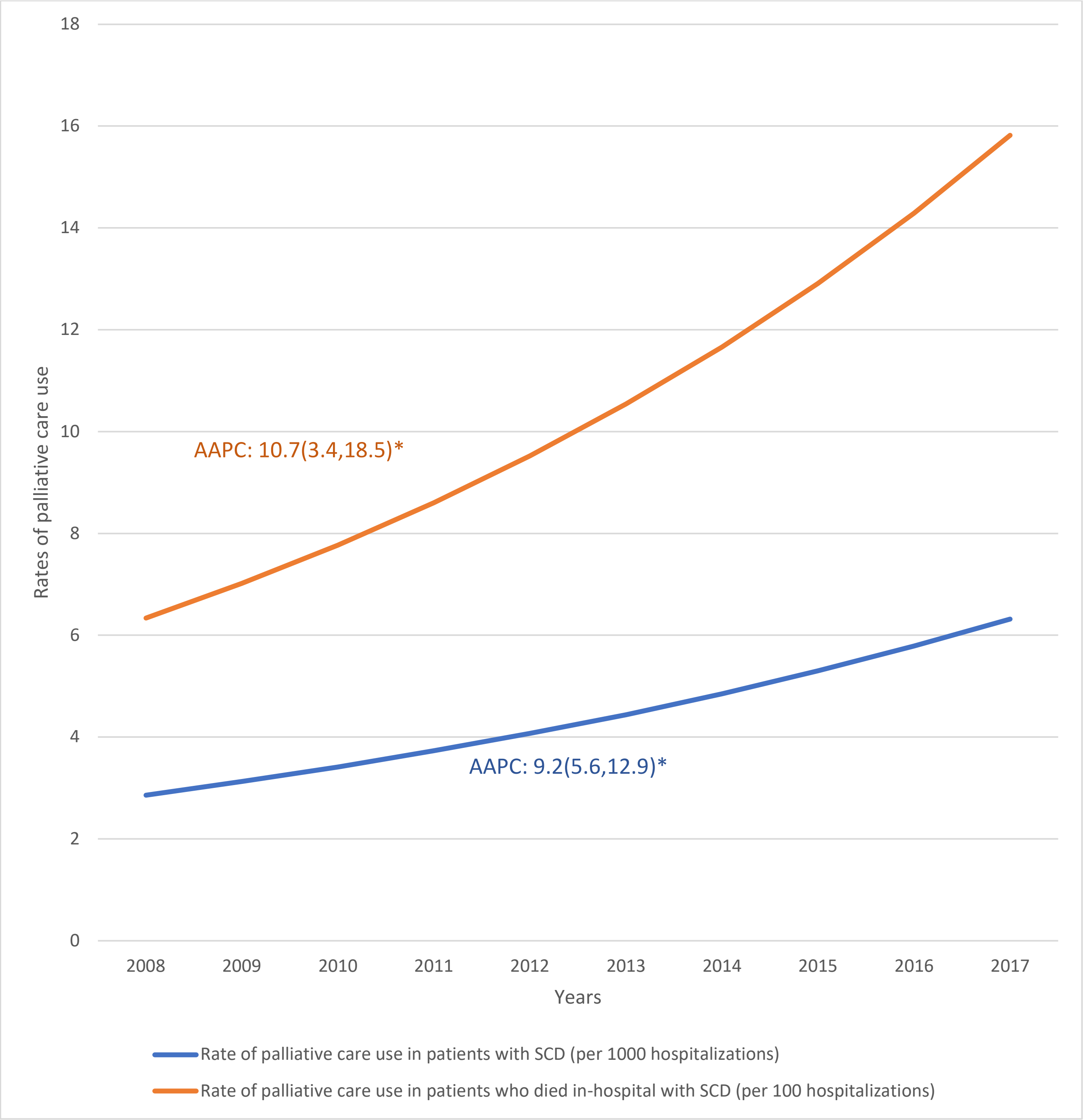
Table 2: Factors associated with palliative care use in SCD patients – overall and among those who died in-hospital

	Palliative care use in SCD hospitalizations	Palliative care use among SCD patients who died in-hospital
	OR(95% CI)	OR(95% CI)
Age Group		
18-39 years	reference	reference
40-59 years	0.98(0.81-1.18)	1.81(1.19-2.75)*
60-79 years	0.95(0.70-1.30)	1.13(0.60-2.12)
80+ years	2.34(1.41-3.88)*	2.29(0.79-6.64)
Race/Ethnicity		
NH-White	reference	reference
NH-Black	0.67(0.45-0.99)*	0.33(0.16-0.68)*
Hispanic	0.47(0.26-0.84)*	0.28(0.09-0.91)*
Others	0.83(0.49-1.39)	0.41(0.12-1.42)
Sex		
Male	reference	reference
Female	0.40(0.21-0.76)*	1.45(1.00-2.11)
Discharge Status		
Routine	reference	reference
Transfer	3.71(2.73-5.03)*	
Died	39.26(30.83-49.98)*	—
DAMA	0.48(0.28-0.84)*	—
Other	4.14(3.20-5.35)*	—
Zip code income quartile		
Lowest quartile	reference	reference
2nd quartile	0.89(0.71-1.11)	0.69(0.42-1.14)
3rd quartile	1.24(0.85-1.80)	0.48(0.25-0.91)*
Highest quartile	1.58(1.02-2.45)*	1.46(0.79-2.71)
Primary Payer		
Medicare	reference	reference
Medicaid	0.40(0.21-0.78)*	0.72(0.21-2.48)
Private Insurance	1.30(1.02-1.65)*	1.03(0.59-1.79)
Self-Pay	1.22(0.93-1.59)	1.12(0.64-1.99)
Hospital Characteristics		
Hospital Region		
Northeast	reference	reference
Midwest	1.00(0.57-1.75)	1.18(0.57-2.46)
South	0.69(0.42-1.11)	1.47(0.78-2.78)
West	0.72(0.40-1.31)	1.63(0.77-3.41)
Hospital Bed Size		
Small	reference	reference
Medium	1.47(1.02-2.12)*	1.18(0.57-2.44)
Large	1.91(1.30-2.82)*	1.52(0.78-2.96)
Hospital Location and Teaching Status		
Urban teaching	reference	reference
Rural	0.47(0.28-0.79)*	0.75(0.33-1.73)
Urban non-teaching	0.61(0.47-0.80)*	0.63(0.40-0.99)

SCD-Sickle Cell Disease
NH-Non-Hispanic
DAMA-Discharged Against Medical Advice
OR- odds ratio, CI- confidence interval
'—' represents the absence of variable in the model

Figure legend/caption

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. '*' represents statistically significant findings ($p<0.05$). Rate of inpatient palliative care service use increased at average of 9.2% per year (95% CI, 5.6-12.9) for all SCD-related hospitalizations and 10.7% (95% CI, 3.4-18.5) for terminal hospitalizations.


18
16
14
12
10
8
6
4
2
0
Rates of palliative care use
AAPC: 10.7(3.4,18.5)*
AAPC: 9.2(5.6,12.9)*
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Years
Rate of palliative care use in patients with SCD (per 1000 hospitalizations)
Rate of palliative care use in patients who died in-hospital with SCD (per 100 hospitalizations)

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7,8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8,9
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	22, 23
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11,12
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15,16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13,14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-057361.R3
Article Type:	Original research
Date Submitted by the Author:	12-Jul-2022
Complete List of Authors:	Nwogu-Onyemkpa, Eberechi; Baylor College of Medicine, Department of Medicine, Center of Excellence in Health Equity, Training and Research; Baylor College of Medicine, Section of Geriatrics and Palliative Medicine Dongarwar, Deepa; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Salihu, HM; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Akpati, Lois; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Marroquin, Maricarmen; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Abadom, Megan; Baylor College of Medicine, Center of Excellence in Health Equity, Training and Research Naik, Aanand; UTHealth School of Public Health, Management, Policy and Community Health; Michael E DeBakey VA Medical Center, Houston Center for Innovations in Quality, Effectiveness, and Safety
Primary Subject Heading:	Palliative care
Secondary Subject Heading:	Haematology (incl blood transfusion)
Keywords:	Adult palliative care < PALLIATIVE CARE, HAEMATOLOGY, Anaemia < HAEMATOLOGY

Title: Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

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Word count: 3,551

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Abstract:

Objective: Sickle cell disease (SCD) is a highly morbid condition notable for recurrent hospitalizations due to vaso-occlusive crises and complications of end organ damage. Little is known about the use of inpatient palliative care services in adult patients with SCD. This study aims to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations. We hypothesize that use of palliative care is low in SCD hospitalizations.

Design: A retrospective cross-sectional study utilizing data from the National Inpatient Sample (NIS) from 2008-2017 was conducted.

Setting: US hospitals from 47 states and the District of Columbia.

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

Primary and secondary outcome measures: Palliative care service use (documented by ICD-9-CM and ICD-10-CM diagnosis codes V66.7 and Z51.5).

Results: 987,555 SCD-related hospitalizations were identified, of which 4442 (0.45%) received palliative care service. Palliative care service use increased at a rate of 9.2% per year (CI, 5.6-12.9). 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). 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.

Conclusion: Use of palliative care during SCD-related hospitalizations is increasing but remains low. Disparities associated with race and gender exist for use of palliative care services during SCD related hospitalization. Further studies are needed to guide evidence-based palliative care interventions for more comprehensive and equitable care of adult patients with SCD.

Strengths and limitations of this study

- Our study is the first of its kind to investigate palliative care use among SCD patients using a national database.
- ICD-9-CM and ICD-10-CM codes for palliative care are not specific to palliative care provided by a palliative care specialist as these codes also encompass patients who are in comfort care status.
- Our study investigated inpatient palliative care use and hence, our findings cannot be extrapolated to outpatient setting where patients with SCD patient receive most of their care.

Introduction:

Sickle cell disease (SCD) is a group of inherited red blood cell disorders in which abnormality in Hemoglobin (Hb) beta gene results in abnormal shape and sickling of red blood cells under stress. Physiologic manifestations of the illness arise from end organ ischemia, including acute pain from vaso-occlusive crises, cerebrovascular accident, acute chest syndrome, pulmonary hypertension, heart failure, renal failure, severe anemia, and recurrent infections.[1] Approximately 100,000 Americans predominantly of African (90%), Middle Eastern, and Mediterranean descent are affected by SCD.[2] Historically, SCD was a childhood disease – life expectancy for those with the disease was 20 years in 1970. 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.[3] As an increasing number of people with SCD survive into adulthood, there is a rising need for effective transitions to adult medicine involving multidisciplinary care teams.[4]

SCD is a highly morbid condition. Recurrent hospitalization is common in SCD due to vaso-occlusive crises and complications of end organ damage.[5] [6] During their last year of life, people with SCD were hospitalized for an average of forty-two days over five admissions.[7] Hospital admissions and ED visits increase sharply a month before death and most patients with SCD die in the hospital (63%) or emergency department (15%).[7] Patients with SCD experience increased rates of depression and anxiety,[8] [9] [10] chronic pain,[11] and decreased health-related quality of life. [12]. Increased healthcare use [13] and symptom burden are salient opportunities for palliative care intervention in this patient population. Palliative care provides holistic care for patients with serious chronic illnesses using a multidisciplinary team approach.[14] Palliative care has been

shown to increase patient's quality of life and decrease health care costs [15] [16] but the impact of palliative care on SCD is not well characterized.[17]

Furthermore, little is known about the use of *inpatient* palliative care services in adult patients with SCD. To address this gap, we used national data to evaluate inpatient palliative care use during SCD related hospitalizations overall and during terminal hospitalizations (hospitalizations that resulted in patients' death in-hospital regardless of cause of death). We identified patient and hospital characteristics associated with use of hospital-based palliative care services in SCD. We hypothesize that use of palliative care is low in SCD hospitalizations.

Methods:

Data Source

Data from the 2008 to 2017 National Inpatient Sample (NIS), the largest all-payer, nationally representative inpatient database in the United States (US) was used. The NIS is part of a group of databases developed by the Healthcare Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ).[18] This public database contains longitudinal data from a stratified sample of all discharges from US hospitals from 47 states and the District of Columbia, excluding rehabilitation and long-term acute care hospitals, thereby estimating about a 20% sample of all hospital discharges. When weighted, each year, NIS contains data from about 35 million hospitalizations.

Study Population and Variables

The analysis was restricted to hospitalizations in adults aged 18 years and above. Diagnoses and procedures are coded using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes till the 3rd quarter of 2015, after which HCUP transitioned to ICD-10-CM format. 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 (ICD-9-CM - 282.41, 282.42, 282.61, 282.62, 282.63, 282.64, 282.60, 282.68, 282.69; ICD-10-CM - D57.4x, D57.0x, D57.2x, D57.1x, D57.8x). The study's primary outcome was palliative care use which was identified using ICD-9-CM diagnosis code V66.7 and ICD-10-CM diagnosis code Z51.5. The 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. There were no changes in the criteria for palliative care code with the transition from ICD-9-CM to ICD-10-CM. Covariates included in the study were socio-demographics for the patient which consisted of patients' age, race/ethnicity – categorized as Non-Hispanic (NH)-White, NH-Black, Hispanic and NH-Others, sex, insurance type – Medicare, Medicaid, private insurance, self-pay and others, median household income based on zipcodes; and hospital characteristics such as hospital location, hospital type (urban vs. rural and teaching vs. non-teaching), and hospital bed size.

Statistical Analysis

Since the NIS data was de-identified and publicly available, the study was approved as exempt by the Institutional Review Board (IRB) of Baylor College of Medicine. All statistical tests were two-tailed with the type-I error of 5% and were conducted using R version 3.5.1 (University of Auckland, Auckland, New Zealand) and R Studio Version 1.1.423 (Boston, MA) and Joinpoint Regression Program, version 4.7.0.0 (National Cancer Institute).

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.[19] The results are represented in the form of average annual percentage change (AAPC) and its 95% confidence interval (CI). We scrutinized the temporal trends in the rates of palliative care use among SCD patients overall, and among those who died in-hospital. Next, we examined the socio-demographic and hospitalization characteristics of patients with SCD and those with SCD who received palliative care during their hospitalization. Prevalence rates of SCD and palliative care use among SCD hospitalizations were calculated, stratified by patients' race/ethnicity. 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 in-hospital. All the patient demographic and hospital characteristics were loaded into the association models to obtain adjusted odds ratio and 95% confidence intervals.

Patient and public involvement

Patients were not involved in this retrospective analysis of an anonymized national inpatient database.

Results:

Trends in the rate of palliative care use in SCD-related hospitalizations

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. There were 4442 (0.45%) SCD-related hospitalizations that received palliative care service. Figure 1 shows temporal trends in palliative care use. The rate of inpatient palliative care service use 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.

Patient characteristics – SCD hospitalizations with palliative care use

Table 1 shows patient characteristics for SCD related hospitalizations and patients who received palliative care services. The prevalence of SCD-related hospitalization was highest among the 18-39 age group (9.7 per 1000 SCD hospitalizations) and decreased with increasing age. Conversely, the prevalence of inpatient palliative care use was highest in the oldest age group (34.8 per 1000 SCD hospitalization) and lowest in the 18-39 age group (3.8 per 1000 SCD hospitalizations). The prevalence of SCD-related hospitalization was highest among NH-Blacks (20.7 per 1000 SCD hospitalizations) and lowest in NH-Whites (0.1 per 1000 SCD hospitalizations) 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).

Regional and hospital characteristics – SCD hospitalizations with palliative care use

SCD hospitalization was lowest in the Northeast (1.4 per 1000 SCD hospitalizations) but the prevalence of inpatient palliative care service was highest in this region (6.1 per 1000 SCD hospitalizations). 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). 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).

Factors associated with inpatient palliative care use in SCD

Table 2 shows factors associated with inpatient palliative care use in SCD hospitalizations. During terminal hospitalizations patients between 40-59 years were 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). NH-Black and Hispanic patients were less likely to receive inpatient palliative care services compared to NH-White (OR, 0.67; 95% CI, 0.45-0.99 and OR, 0.47; 95% CI, 0.26-0.84, respectively). Likewise, during terminal admissions use of palliative care services was less likely among NH-Black and Hispanic patients, respectively when compared to NH-White (OR, 0.33; 95% CI, 0.16-0.68 and OR, 0.28; 95% CI, 0.09-0.91, respectively). Female patients were less likely to receive palliative care services than male patients (OR, 0.40; 95% CI, 0.21-0.76). Compared to routine discharges, hospitalizations resulting in death and transfer to another health care facility were associated with increased odds of use of inpatient palliative care services (OR, 39.36; 95% CI, 30.83-49.98, and OR, 3.71; 95% CI, 2.73-5.03, respectively) while discharge against medical advice (DAMA) was associated with decreased odds of use of inpatient palliative care services (OR, 0.48; 95% CI 0.28-0.84).

Patients living in zip codes in the highest income quartile were more likely to receive inpatient palliative care services (OR, 1.58; 95% CI 1.02-2.45) than those in the lowest quartile. Compared to Medicare patients, those with Medicaid had lesser odds (OR, 0.40; 95% CI, 0.21-0.78), while patients with private insurance had higher odds (OR, 1.30; 95% CI, 0.93-1.59) of receiving palliative care services. During terminal admissions, there were no significant differences in palliative care use across different payors.

Patients admitted to medium or large hospitals were more likely (OR, 1.47; 95% CI, 1.02-2.12 and OR, 1.91; 95% CI, 1.30-2.82, respectively) to receive palliative care services than patients in small hospitals while patients admitted to rural or urban non-teaching hospitals were less likely to receive palliative care services than those in urban teaching hospitals (OR, 0.47; 95% CI 0.28-0.79 and OR, 0.61; 95% CI 0.47-0.80, respectively).

Discussion:

In this study of national trends, we found overall low use of palliative care services during SCD-related hospitalizations. Palliative care use was more likely among patients who were NH-White male, in the highest income quartile, with private insurance, and who received care in large or urban academic hospitals. NH-Black and Hispanic patients were less likely to receive palliative care services especially during terminal hospitalizations.

While early palliative care has gained acceptance in cancer care,[20] its adoption in other serious life limiting conditions such as congestive heart failure, chronic kidney disease, and SCD lags. SCD has traditionally been viewed as a childhood disease as most patients did not survive to adulthood in the past. Currently, most patients with SCD survive to adulthood.[3] Furthermore, some patients with SCD experience complications and end organ damage from their disease resulting in a shortened life expectancy than the general population. Our study found a higher prevalence of palliative care service use in terminal admissions when compared to admissions with routine discharge or transfer to another level of care. This highlights an opportunity for palliative care involvement earlier in the disease course in SCD, facilitating more holistic care of patients. Earlier initiation of palliative care grants patients psychosocial support and symptom management from an interdisciplinary team,[21] as well as honest discussions regarding goals of care and patient's preference for end of life.

Our study showed most SCD-related hospitalizations and palliative care service use were in the NH-Black group. However, further analysis accounting for covariates revealed that NH-Black patients were significantly less likely to receive palliative care during hospitalization compared to NH-white patients. Notably, race/ethnicity was the only factor associated with palliative care use in both SCD and terminal hospitalizations. Other studies have shown racial disparities in the use of palliative care services in other chronic diseases.[22,23] Furthermore, studies have shown that black patients are less likely to use hospice services and more likely to receive intensive life-sustaining procedures at end of life compared to white patients.[24] Factors identified to drive this racial disparity in hospice use include knowledge deficits,[25] mistrust of the health care system,[26] miscommunication and misunderstanding of treatment options,[27] and preference for more aggressive care.[28] Similar studies are lacking to elucidate factors implicated in the racial difference in non-hospice palliative care use across all life limiting diseases.[29] Palliative care has a strong perceived association with hospice with many patients and families unable to differentiate between the two. 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. Further studies are needed to investigate patient and system factors associated with racial differences in palliative care use in SCD.

Gender differences in the use of inpatient palliative care services were found. Although male and female patients had a similar prevalence of SCD-related hospitalization, female patients were 60% less likely to receive palliative care services. This finding is contrary to that of other studies which show that women are more receptive to palliative care than men.[30] 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. 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, women receive less analgesia and are more likely to have their pain attributed to psychological causes.[31] It is possible that palliative care consultants are more frequently involved for specialist level pain management for male than female patients

accounting for the gender difference observed in our study. This finding requires further investigation as the study by McClish et al. demonstrates that men and women with SCD report similar pain experiences.[32]

We also found socioeconomic differences in the use of palliative care in SCD similar to other diseases.[23,33,34] Patients with zip codes in the highest income quartile and those with private insurance were more likely to receive palliative care, while patients with Medicaid were less likely to receive palliative care services. Insurance dictates patient's access to specialty care with patients on Medicaid reporting more challenge than those with private insurance accessing certain specialty care particularly in the outpatient setting.[35,36]

Regional differences were detected in our study. The South region had the highest number of SCD hospitalizations but the lowest prevalence of palliative care use. This finding is notable as two of the three states (Florida, Texas, and New York) with the highest population of SCD patients are in the South. Hospital characteristics were also predictive of palliative care use with medium, large and urban teaching hospitals associated with greater use of palliative care in SCD similar to findings from other studies.[33] [22] [34] While many sickle cell patients use larger, urban hospitals for their care,[37] 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.

To our knowledge, our study is the first of its kind to investigate palliative care use among SCD patients using a national data base. Limitations exist in our study one of which is the validity of the ICD-9 and ICD-10 codes for identification of palliative care consultations. Investigators have sought to validate these codes however these studies utilize data from a single institution [38] or from the VA system.[39] Furthermore, the ICD-9 and ICD-10 codes for palliative care are not specific to palliative care provided by a palliative care specialist as these codes also encompass

patients who are in comfort care status.[40] Not all patients in comfort care are managed by a palliative care specialist and as such it is difficult to delineate which hospitalizations were indeed associated with the involvement of a palliative care specialist. In addition, our dataset does not allow us to elucidate the nature of palliative care interventions provided during admissions hence it is unclear if these interventions were for symptom management, goals of care discussion, counseling and support, or transition to comfort care. 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. 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.

SCD related morbidity and mortality have a significant impact on patient self-reported quality of life outcomes and healthcare utilization and cost. Early palliative care might guide patients' treatment decisions and mitigate initiation of interventions that are not in line with a patients' wishes at the end of life. Early palliative care also has the potential to improve symptom management and consequently improve quality of life for individuals with SCD. 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. Racial disparity in the use of palliative care by SCD patients should be investigated with studies assessing knowledge of palliative care and barriers to palliative care use by SCD patients. Furthermore, studies addressing system

barriers to palliative care use among minority patients are needed as the implication spans across other life limiting illnesses.

Contributorship:

Eberechi Nwogu-Onyemkpa was involved in the conception of the study, interpretation of data, drafting, and revision of the manuscript.

Deepa Dongarwar was involved in the conception of the study, analysis of the data, drafting, and revision of the manuscript.

Hamisu Salihu was involved in the conception of the study and revision of the manuscript.

Chioma Akpati was involved in the interpretation of data and drafting of the manuscript.

Maricarmen Marroquin was involved in the interpretation of data, drafting and revision of the manuscript.

Megan Abadom was involved in the interpretation of data and drafting of the manuscript.

Aanand D. Naik was involved in the conception of the study and revision of the manuscript.

Funding/Support: Research funding support was provided by the US Department of Health and Human Services and Health Resources and Services Administration for Baylor College of Medicine Center of Excellence in Health Equity, Training, and Research (Grant No: D34HP31024). Additional support is provided to Dr. Naik from the Houston VA HSR&D Center for Innovations in Quality, Effectiveness, and Safety (CIN 13-413).

Competing of Interests: Authors *without* conflicts of interest, including relevant financial interests, activities, relationships, and affiliations.

Ethics Approval: This study was approved as exempt by the Institutional Review Board (IRB) of Baylor College of Medicine.

Data Sharing: All data relevant to the study are included in the article or uploaded as supplementary information. We used data from the 2008 to 2017 National Inpatient Sample (NIS) which is provided by the Healthcare Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ). Data can be accessed through the HCUP website.

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Table 1: Patient characteristics among SCD-related hospitalizations and among those with SCD who received palliative care during their hospitalization

	Total N=307709982	SCD-related hospitalizations N=987555	Prevalence of SCD-related hospitalizations (per 1000 hospitalizations)	SCD-related hospitalizations receiving palliative care N=4442	Prevalence of palliative care use (per 1000 SCD hospitalizations)
Age Group					
18-39 years	75567499	733837	9.7	2824	3.8
40-59 years	78526326	214939	2.7	1160	5.4
60-79 years	101611492	35362	0.3	339	9.6
80+ years	52004665	3417	0.1	119	34.8
Race/Ethnicity					
NH-White	192567014	16962	0.1	214	12.6
NH-Black	41490748	857006	20.7	3773	4.4
Hispanic	29897432	32676	1.1	116	3.6
Others	17422072	23026	1.3	157	6.8
Missing	26332714	57883	2.2	181	3.1
Sex					
Male	125745784	427285	3.4	1921	4.5
Female	181778482	559845	3.1	2521	4.5
Missing	185716	424	2.3	—	—
Discharge Status					
Routine	202797074	853218	4.2	2619	3.1
Transfer	55186460	37409	0.7	447	11.9
Died	6740712	6327	0.9	685	108.3
DAMA	3847845	44520	11.6	69	1.5
Other	38933666	45507	1.2	622	13.7
Missing	204225	573	2.8	—	—
Zip code income quartile					
Lowest quartile	89460128	478674	5.4	2053	4.3
2nd quartile	78497949	219619	2.8	801	3.6
3rd quartile	71474969	163233	2.3	836	5.1
Highest quartile	61340502	100769	1.6	703	7.0
Missing	6936433	25259	3.6	48	1.9
Primary Payer					
Medicare	141357438	315777	2.2	1736	5.5
Medicaid	50563783	428967	8.5	1725	4.0
Private Insurance	88933878	170459	1.9	671	3.9
Self-Pay	26247689	70526	2.7	304	4.3
Missing	607194	1825	3.0	—	—
Hospital Characteristics					
Hospital Region					
Northeast	33888883	46282	1.4	1226	6.1
Midwest	107572349	234180	2.2	1014	5.4
South	164884575	701680	4.3	1820	3.6

West	1364173	5411	4.0	382	4.4
Hospital Bed Size					
Small	46455596	114366	2.5	331	2.9
Medium	81563430	258481	3.2	998	3.9
Large	178326782	609296	3.4	3108	5.1
Missing	1364173	5411	4.0	—	—
Hospital Location and Teaching Status					
Rural	33888883	46282	1.4	96	2.1
Urban non-teaching	107572349	234180	2.2	749	3.2
Urban teaching	164884575	701680	4.3	3591	5.1
Missing	1364173	5411	4.0	—	—

SCD-Sickle Cell Disease
NH-Non-Hispanic
DAMA-Discharged Against Medical Advice
Prevalence is the rate of the outcome (SCD or palliative care use) among each patient characteristics
'—' represents cell values <10, which have been suppressed to preserve patient confidentiality, as per HCUP guidelines.

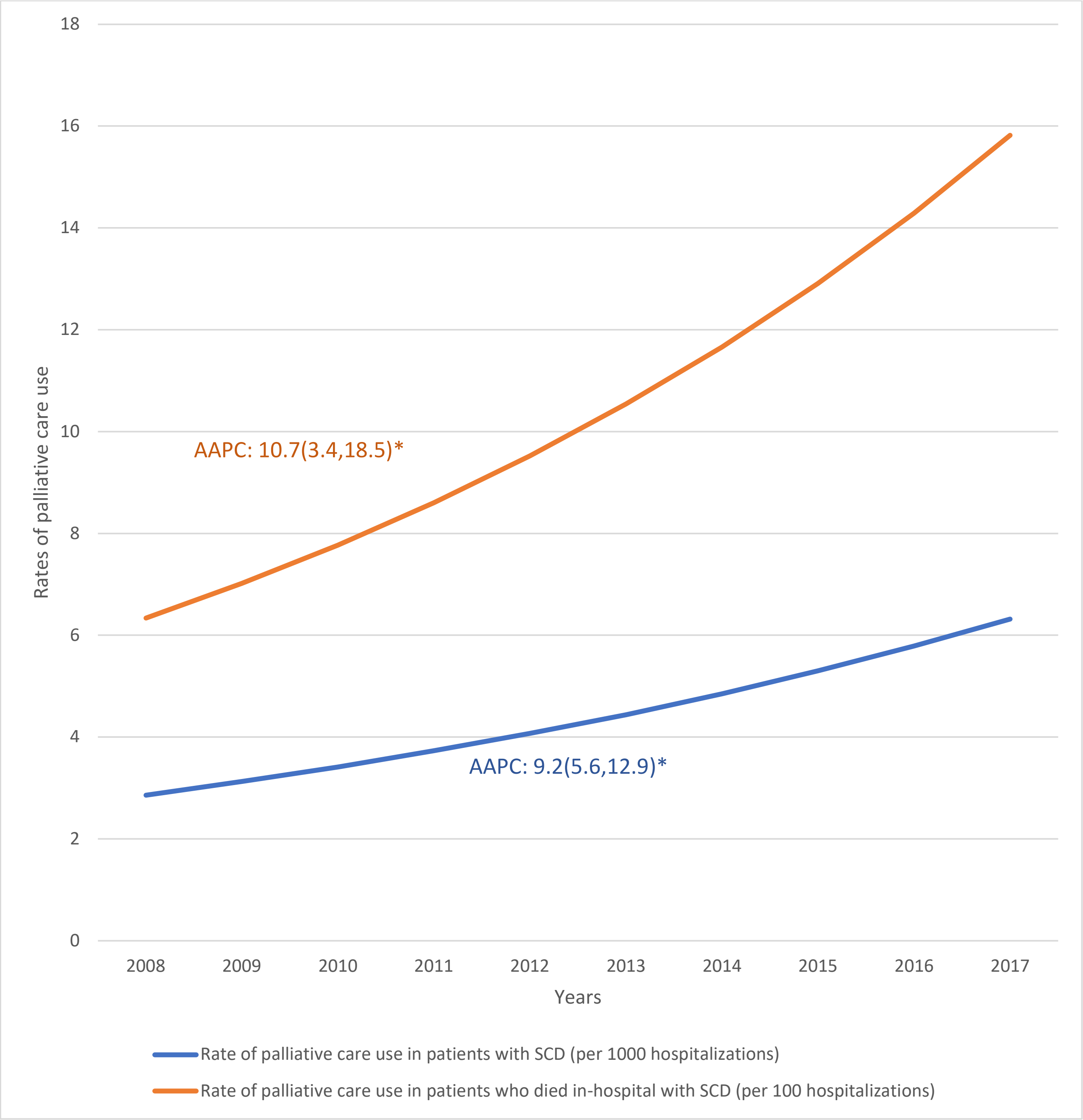
Table 2: Factors associated with palliative care use in SCD patients – overall and among those who died in-hospital

	Palliative care use in SCD hospitalizations	Palliative care use among SCD patients who died in-hospital
	OR(95% CI)	**OR(95% CI)**
Age Group		
18-39 years	reference	reference
40-59 years	0.98(0.81-1.18)	1.81(1.19-2.75)*
60-79 years	0.95(0.70-1.30)	1.13(0.60-2.12)
80+ years	2.34(1.41-3.88)*	2.29(0.79-6.64)
Race/Ethnicity		
NH-White	reference	reference
NH-Black	0.67(0.45-0.99)*	0.33(0.16-0.68)*
Hispanic	0.47(0.26-0.84)*	0.28(0.09-0.91)*
Others	0.83(0.49-1.39)	0.41(0.12-1.42)
Sex		
Male	reference	reference
Female	0.40(0.21-0.76)*	1.45(1.00-2.11)
Discharge Status		
Routine	reference	reference
Transfer	3.71(2.73-5.03)*	
Died	39.26(30.83-49.98)*	—
DAMA	0.48(0.28-0.84)*	—
Other	4.14(3.20-5.35)*	—
Zip code income quartile		
Lowest quartile	reference	reference
2nd quartile	0.89(0.71-1.11)	0.69(0.42-1.14)
3rd quartile	1.24(0.85-1.80)	0.48(0.25-0.91)*
Highest quartile	1.58(1.02-2.45)*	1.46(0.79-2.71)
Primary Payer		
Medicare	reference	reference
Medicaid	0.40(0.21-0.78)*	0.72(0.21-2.48)
Private Insurance	1.30(1.02-1.65)*	1.03(0.59-1.79)
Self-Pay	1.22(0.93-1.59)	1.12(0.64-1.99)
Hospital Characteristics		
Hospital Region		
Northeast	reference	reference
Midwest	1.00(0.57-1.75)	1.18(0.57-2.46)
South	0.69(0.42-1.11)	1.47(0.78-2.78)
West	0.72(0.40-1.31)	1.63(0.77-3.41)
Hospital Bed Size		
Small	reference	reference
Medium	1.47(1.02-2.12)*	1.18(0.57-2.44)
Large	1.91(1.30-2.82)*	1.52(0.78-2.96)
Hospital Location and Teaching Status		
Urban teaching	reference	reference
Rural	0.47(0.28-0.79)*	0.75(0.33-1.73)
Urban non-teaching	0.61(0.47-0.80)*	0.63(0.40-0.99)

SCD-Sickle Cell Disease
NH-Non-Hispanic
DAMA-Discharged Against Medical Advice
OR- odds ratio, CI- confidence interval
'—' represents the absence of variable in the model

Figure legend/caption

Figure 1: Temporal trends in the rates of palliative care use 2008-2017.


Rates of palliative care use
18
16
14
12
10
8
6
4
2
0
AAPC: 10.7(3.4,18.5)*
AAPC: 9.2(5.6,12.9)*
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Years
Rate of palliative care use in patients with SCD (per 1000 hospitalizations)
Rate of palliative care use in patients who died in-hospital with SCD (per 100 hospitalizations)

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7,8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8,9
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable

Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	22, 23
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11,12
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15,16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13,14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.