Economic Burden of Sickle Cell Disease: A Targeted Global Literature Review

Naik AS[1], Bagga S[1], Senecal M[1]

[1]Complete HEOR Solutions, North Wales, PA, USA

Background

- Sickle cell disease (SCD) is a commonly inherited hematological disorder caused by a mutation in the beta-globin gene[1]
- It is estimated that of the more than 300,000 infants born with SCD annually worldwide, approximately 75% are in sub-Saharan Africa[2]
- The only curative therapy available for SCD is allogeneic hematopoietic stem cell transplantation (HSCT) but it's use is constrained by the paucity of suitable human leukocyte antigen (HLA)-matched donors. It has limited application among older patients with significant morbidity[3]
- The global burden of SCD is set to rise as a consequence of improved survival in high-prevalence countries. Hence, it's necessary to assess the economic costs and related burden in SCD patients[4]
- A lack of knowledge of SCD in the medical community results in sub-optimal treatment of pain crises[5,6]

Objectives

The aim of this study was to review the published evidence on the economic burden of SCD worldwide

Primary objective: To summarize the health care resource utilization (HCRU) associated with SCD;

- Hospital admissions
- Emergency department visits
- Length of hospital stay
- Inpatient and outpatient visits

Secondary objective: To summarize the economic costs associated with SCD;

- Direct costs
- Indirect costs
- Total costs

Methods

Study design and search methods:

- A targeted literature review was performed
- Databases used for the search: PubMed, Cochrane, and Embase
- Time Period: January 2014 to June 2019
- Geography: Global
- Language: English
- Key search terms: "anemia, sickle cell"[MeSH], "health care utilization", "health care costs", "direct service costs", "cost of illness"[MeSH] and "indirect cost"

Eligibility criteria:

Studies reporting HCRUs and costs in SCD patients with comorbidities and any age were included. We excluded interventional, animal studies, narrative reviews, case report, case series, protocols, validation studies, magazine, expert opinions, books, letters, editorials, comments and erratum's

Publication review:

After duplicates were removed, the first selection of articles was made based on title and abstract screening. Articles selected for full-text review were screened according to the eligibility criteria

Data extraction:

One reviewer extracted the data and was verified by the same reviewer. From each article, study details, population, sample size, HCRUs, direct costs, indirect costs and the total costs were extracted

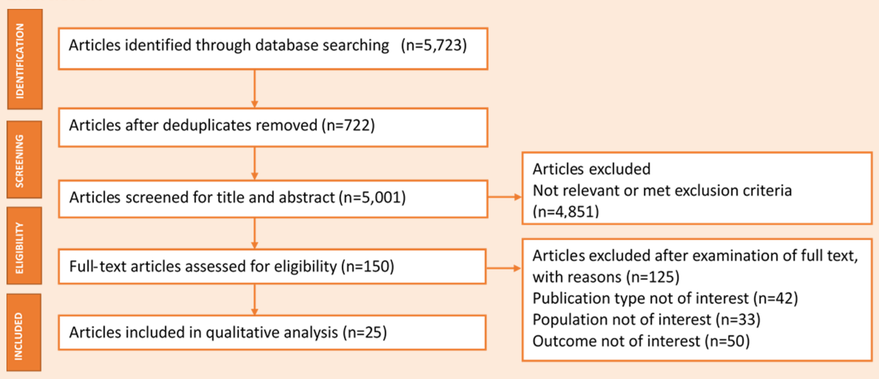
Data analysis:

To facilitate comparison across studies, all costs were inflated to 2019 values using the consumer price index (CPI) inflation rates provided by the World Bank. These values were then converted to US dollar based on exchange rate converter available online as of October 24, 2019

Results

- The electronic database search yielded 5,723 records. After removing duplicates (n=722), 5,001 citations were screened through title and abstract and excluded 4,851 citations as they did not meet the eligibility criteria
- Full text of the remaining 150 studies were evaluated and 125 articles were excluded, thus 25 records were finally included in the study
- Most of the included studies were conducted in the USA (n=18) followed by England (n=2), Nigeria (n=2), Canada (n=1), Columbia (n=1) and Tanzania (n=1)
- A flow diagram of the selection process is illustrated in Figure 1

Figure 1. Details on Number of Studies at Each Step along with Reason for Exclusion



Hospital Admissions

- Hospital admissions ranged from 146 to 1,101 over the 5-year period 2006-2014[7]
- The per patient per year (PPPY) median hospitalization ranged from 0.79 to 1.5 in 2006-2010 and 2007-2012, respectively while the per patient (PP) median hospitalization ranged from 1.8 to 7 in 2014 and 2011-2014, respectively[8]

Emergency Department (ED) Visits

- The total ED visits widely ranged from 185 to 1,456 across studies in 2016 and 2007-2011, respectively[9]
- The PPPY median ED visits ranged from 1.33 to 3.2 in 2006-2010 and 2014, respectively while the PP median ED visits ranged from 1.7 to 13 in 2015 and 2011-2014, respectively[7]

Hospital Length of Stay (LOS)

- The total hospital LOS for children and adults was 445 days and 699 days, respectively in 2010-2011[10]
- The average (SD) PPPY LOS ranged from 4.68 (3.92) to 12 (17) in 2016 and 2005, respectively

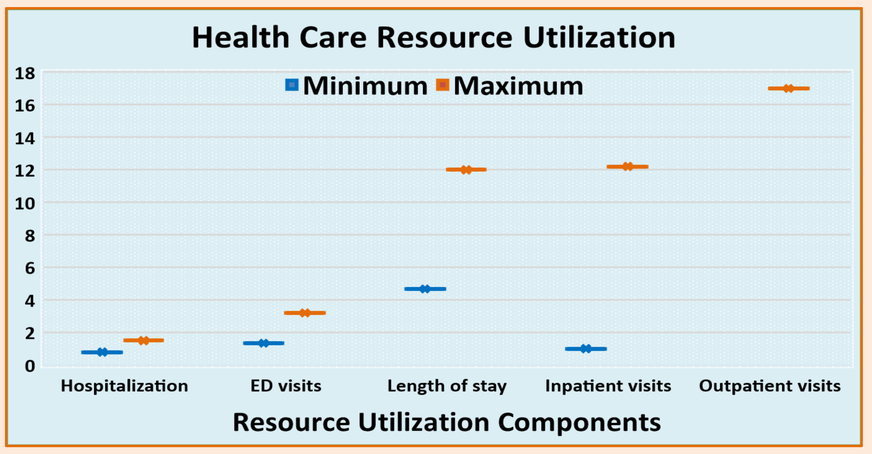
Inpatient Visits

- 76 inpatient visits were reported in the pre-allogeneic hematopoietic cell transplantation in 2002-2012 and 10 in the post-allogeneic hematopoietic cell transplantation while another publication reported 534 inpatient visits in 2015[11]
- The average PPPY inpatient visits ranged from 1 to 12.2 in 2005-2015 and 2013-2014, respectively while the pre-allogeneic hematopoietic cell transplantation and post-allogeneic hematopoietic cell transplantation range varied from 1 to 16 and 1 to 3, respectively in 2002-2012

Outpatient Visits

- 752 outpatient visits were reported in pre-allogeneic hematopoietic cell transplantation and 381 in post-allogeneic hematopoietic cell transplantation periods in 2002-2012[11]
- The mean PPPY, PP and per year outpatient visits were 17, 6.41 and 10.5, in 2005-2015, 2014 and 2009, respectively[12]
- The median PP outpatient visits in the pre-allogeneic hematopoietic cell transplantation period ranged from 5 to 139 while the range was 8 to 61 in the post-allogeneic hematopoietic cell transplantation period in 2002-2012

Figure 2: Per Patient Per Year Health Care Resource Utilization



*The minimum value for outpatient visits is not available

Table 1: Costs Associated with Sickle Cell Disease

Hospital admission	ED visits	LOS	Inpatient visits	Outpatient visits
Total cost: $29,755,548[10]	Total cost: $1,112	• Per stay cost: $370 in children's • Per stay cost: $323 in adults • Total cost: $27,044,111	Mean cost: $8,960[13]	• Total cost: $5,505 • Median per visit cost: $13[14]
• Average PPPH cost: $148 (106) • Mean annual PP cost: $372[15]	NA	NA	Average PP cost: $16,292	Average PP cost: $10,918[12]
Median per stay cost: $17,157[16]	NA	NA	NA	Average PP cost: $1,401[12]*

ED: emergency department; NA: not available: LOS: length of stay; PPPH: per patient per hospitalization; PP: per patient; SCD: Sickle Cell Disease; $: united states dollar; *out of pocket expenses

Conclusions

- The current literature review found wide discrepancies between health care resource utilization data reported for SCD and it suggests the economic burden of the disease is considerable for health care systems
- ED visits and LOS are observed to be the main cost drivers, with LOS being higher contributor in both children and adults
- There is a scarcity of data on indirect costs which leads to the underestimation of the true economic burden of SCD
- This review highlights the need for cost effective treatments in the management of SCD
- Future research is needed; it can potentially lead to a better understanding of the unmet needs of patients affected by SCD and how interventions can address these needs

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