Article details: 2022-0145
Title: Sickle cell disease in Ontario: an epidemiologic profile based on health systems administrative data
Authors: Jacob Pendergrast, Lanre Tunji Ajayi, Eliane Kim, Michael A. Campitelli, Erin Graves

Reviewer 1: Mark A. Crowther
Institution: Medicine, McMaster University
General comments (author response in bold)

I suspect that their algorithm has underestimated the number of patients for the reasons articulated below. They may wish to increase the sensitivity of their screen by using OLIS data to capture patients who are missed by NACRS and who have not sought care in an inpatient or ER setting over the time that the study reviewed. Maximizing the yield of the search for patients is critically important so that we have accurate numbers too help us to understand what programs are required, and how they should be funded.
Laboratory tests for sickle cell disease have not yet been examined, cleaned, and made research-ready at ICES. We were therefore unable to incorporate OLIS data into the analysis. However, we agree that once these steps have been completed this would be an exciting area for future research

Generally: How certain are the authors that they have captured lower-risk sickle cell patients (those with elevated HbF or with SC disease, for example) given their strategy. Our hospital, which has a reasonable number of sickle cell patients, does not participate in NACRS and thus, for example, if they had not been hospitalized, any patients followed at our site would have been missed. The authors should comment on this. The fact that outpatient data is flawed is highlighted by the small number of outpatient visits they identified (4957)> I bet the Toronto clinic, alone, had more visits than this over the period of the study.
Clarification that non-ER visits in NACRS was limited to cancer and dialysis clinics has been added to the results section. All hospitals in Ontario contribute data to NACRS regarding ER visits; further discussion on the data quality of the NACRS database can be found in reference 35.

Generally: Why wouldn't the authors increase the yield of the lower-risk patients by querying OLIS for patients with a positive confirmatory test - they have effectively done this at the low end of the age range with the screening data but not in those who have prevalent disease? That would increase the yield of the strategy the authors have used, I would think, and would capture some lower-risk people who may be missed.
See above response regarding the availability of OLIS data

Reviewer 2: Andrew Binding
Institution: Department of Hematology, Brampton Civic Hospital
General comments (author response in bold)

Page 3, line 31 - Suggest pick date for median age or disclose methodology in abstract data sources.
The text has been changed for greater clarity

page 5, line 31 - define acronym ICES
The text has been updated as suggested

page 9, line 37 - In discussion of RNI important to comment on immigration patterns even if not described in this manuscript
A comment on the absence of immigration data on the RNI has been added

Figure 4 is a great addition but not clear to me if this represents specific encounters or patients? data from all sources or NBS rates only or other?
Clarification added to Figure title

Reviewer 3: Kaberi Dasgupta
Institution: Division of Clinical Epidemiology, McGill University Health Centre
General comments (author response in bold)

A 10-year period (2007 to 2017) was considered. ICD-10 codes were employed. Please consider specifying the code(s). While some basic demographic information was available, it would have been interested to know more about the ethnocultural background of the persons studied. In future studies, please consider the CanCHEC cohort which merges NACRS and DAD with census data on 25% of the Canadian population other than Quebec; these individuals have ethnocultural variables reported
This is an excellent suggestion and can be investigated further in future studies

Only Ontario residents (OHIP) number were included. The authors specify, however, that only 2.6% of the sickle cell disease records were not associated with an OHIP number. They enumerated 3418 unique individuals with a median age of 24 years and a roughly equal sex distribution. There were 229 deaths over this period and nearly 500 newborn cases (35 per year). Interestingly, they were able to ascertain from the Newborn Screening Database that about 60% were Hemoglobin SS and over one fifth were Hemoglobin SC disease. There were 2% with Hemoglobin Sbeta, SE, and S/HPFH but the remainder were unspecified: this should be explicitly noted (i.e., percent unspecified).
The specific ICD codes used for the search of DAD and NACRS have now been included in the manuscript body; these demonstrate, unfortunately, that specific genotypes are not discernible within these codes