Reviewer's report

**Title:** Epidemiology aspects in 11,507 Mexican children with cancer under a national public health insurance program Running title: Childhood cancer among Mexican children

**Version:** 2  **Date:** 17 February 2014

**Reviewer:** Scott Howard

**Reviewer's report:**

In this review of children with cancer covered by the Mexican children covered by the national public health insurance program, the authors review the epidemiology and outcomes of 11,507 patients treated from 2007-2011. The paper includes a wealth of very important data about the types of patients treated on Seguro Popular, and also includes important outcome information, which will move the field forward significantly and provide a model to other middle-income countries implementing improved coverage for children with non-communicable diseases.

However, the analysis could be much more robust and include a lot of important additional information. Use of overall survival at 2 years is not a good outcome measure, since it does not account for abandonment/relapse in the first year since some patients may survive another year after these events. EFS should be used throughout.

**Title**
Please include more description of the components of the study, such as “epidemiology and outcomes of …”, remove the number of patients, and add the time interval reviewed.

**Abstract**
Please redo after revising the manuscript according to the recommendations below.

**Background**
Please provide a reference for the 148,000 number in LMIC and the “5 times higher than expected in developing countries”. This number is fairly close to what would be expected in LMIC, especially if about 35% of children do not get diagnosed.

**Methods**
1. Ethics – identifiable data on living human subjects in most countries would require review by ethics committee or IRB. What was the basis for a waiver of approval in this case?
2. Define abandonment
3. Scope – epidemiology, but outcomes were included
4. 51 institutions mentioned in Abstract and Methods, but 59 in Background
5. 6 areas mentioned, but no analysis by region
6. Incidence – measured as a whole? What about by region?
7. Minimum follow-up of 48 months is mentioned, but patients diagnosed in 2011 could have a maximum of 3 years of follow-up
8. When was the data frozen for analysis?
9. Please include 2005 and 2006 data for leukemia patients
10. The number of cases of cancer among children covered by PMI grew much more rapidly than the number of covered children in the plan. However, this could be the result of children with cancer being preferentially registered into the program, more so than children living in rural areas who do not develop a severe disease and therefore do not come to treatment centers where registration would occur.
   a. Please describe the process of registering in the system and how healthy children from rural areas are registered
   b. Please analyze incidence by region by year, which could help identify where the increases have come from (for example, the pattern of change in Chiapas may differ from that in Mexico City, where most children may have already been registered.
   c. How many children were eligible for PMI in 2007-2011 of the 31,972,300 children in Mexico?
11. When was each national protocol developed, approved, and activated? Were all protocols activated for all cancers before 2007?
12. Please include the protocols as appendices
13. What monitoring was done to assure that all patients were treated according to the national protocol for each cancer?
14. Increased treatment compliance is mentioned on page 8 – how was this measured? What source documentation was provided? Who did the audits?
15. The abstract mentions 2-year overall survival, but this is not mentioned in Results. Please provide Kaplan-Meier curves for EFS for the following groups of patients (ok to include in a supplementary appendix):
   a. All patients
   b. By the 6 regions
   c. By state
   d. By centers (without mentioning names of centers, just by a number is fine)
   e. By diagnosis (ALL, AML, etc.)
   f. By sex
   g. By diagnosis year
Results
1. Numbers in the text of the results should be identical to those in the Tables – please double check all of them (e.g. 49.8% leukemia, 9.2% CNS tumors)
2. Please carefully edit the manuscript, including all details (e.g. Table I, for example, should be Table 1).
3. Please review the English throughout.
4. Classification of LCH should be in Methods
5. Prevalence is used several times when incidence should be used.
6. 75.6 cases of leukemia per 1,000,000 children per year is almost double that observed in any population of the world.
   a. How do the authors explain this?
   b. What is the incidence among children in Mexico without PMI?
   c. This is accompanied by a 49.9% proportion of children with leukemia – how is this explained?
7. The number of Hodgkin and non-Hodgkin lymphomas is compared but was “not statistically significant” – what statistics were done? What is being compared?

Conclusions
Needs to be a short summary of the major finding (which will be determined by the analyses in the Methods comment #15). No references or explanations in the Conclusion please (move to Discussion)

Figures
1. Please label Figures
2. Figure 2 – M:F should be 1.2:1, should include “All patients” on the far right in Figure 2
3. Please add survival curves and cumulative incidence (see Results suggestions)

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Needs some language corrections before being
published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I have no competing interests.