Reviewer’s report

Title: Prophylaxis in older Canadian adults with hemophilia A: Lessons and more questions

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Reviewer: Annette von Drygalski

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The manuscript “Prophylaxis in older Canadian adults with hemophilia A: Lessons and more questions” by Jackson SC, et al. is a well written report addressing current prophylactic use of FVIII-concentrates in adults with hemophilia and warrants publication in BMC-Hematology after some revisions and clarifications.

As the authors point out there is currently no uniform practice as to prophylactic use of factor concentrates in the adult population. The manuscript nicely describes the differences between primary, secondary and tertiary prophylaxis, the latter being implemented after significant amounts of joint bleeding with subsequent joint destruction have occurred. Given the high cost of treatment and unclear benefits on joint health at that stage of arthropathy, the use of tertiary prophylaxis is not uniformly performed and often questioned by physicians and patients likewise. While the study could not produce any data specifically addressing the incidence or prevalence of tertiary prophylaxis in adults, it still provided good data indicating that an ever increasing proportion of adults in Canada (>50%) is on prophylaxis (irrespective of type), although the use of prophylaxis went down with increasing age. The statistical methods are sound and support conclusions. A very interesting aspect of this data set is that in older individuals perceived joint bleeding episodes were frequent, and frequency was similar if patients were on prophylaxis or not. This finding underlines that the pain etiology in painful joint of adults with preexisting arthropathy may not be related to bleeding in the majority of cases, and that objective imaging methods such as point-of-care ultrasound may be helpful and warranted for more accurate diagnoses.

The described data raise a number of good questions that cannot be answered with the current data set, but warrant new investigations as the authors point out. The study warrants publications. There are no major concerns, but I have a few comments and suggestions:

1. Major Comments:

1) Abstract: Background and Conclusion: “…..Study was conducted to describe TERTIARY prophylaxis….“ or “A significant number of older adults us TERTIARY continuous prophylaxis….“. The authors may consider eliminating the word TERTIARY since the result section provides no data as to when in life
prophylaxis was started.

2) Patients and Methods: Patients with < or equal 2% FVIII:C are classified as severe hemophiliacs. I believe the current guidelines would classify patients as severe when < or equal than 1%, and as moderately severe < or equal than 2%.

3) Patients and Methods: Please clarify if this was a prospective observational study, or a retrospective review of prospectively collected data into a data base.

4) Patients and Methods: Can the authors comment how the bleed logs are derived; i.e. patient documented paper logs, calls into the center, questioning during visits?

5) Patients and Methods: What were the reasons for missing data in the patients excluded from the study. Since a significant number of eligible patients (approx. 15%) were excluded this may be important regarding reporting bias. For example, a severe hemophilia patient with no bleeds and no problems may never come to clinic or call the center, while a severe hemophilia patient with lots of bleeds and problems may. Hence, certain populations may be under- or over-represented. Would just be good to get an idea about that.

2. Minor Comments:

6) Figures: came out very small and hard to read, especially the legends. They should be revised for better legibility and clarity.

7) Background: Line 49: there are a few comma/semicolon mistakes to correct

8) Patients and Methods: Although the authors provide a citation for the CHARMS data base, it would be good to explain briefly what this data entry system encompasses (for non-Canadians). For example, who enters the data, which data are entered etc...


10) Results: Factor Utilization: could the authors clarify if in the prophylactic cohort factor utilization just comprises prophylactic factor use or also additional doses for break-through bleeding.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests