Reviewer's report

Title: Effect of cinacalcet availability and formulary listing on parathyroidectomy rate trends

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Reviewer: Theresa I Shireman

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General overview:
In this paper, the investigators report on parathyroidectomy (PTX) rates for chronic dialysis patients over a 10-year period (2001-2010) using data from Quebec's provincial health care system. In particular, they describe PTX bi-monthly rates across essentially three periods anchored in the availability of cinacalcet. The methods and results are fairly straightforward with respect to PTX rates and suggest that the availability of cinacalcet has been associated with a decline in PTX rates, a logical conclusion. The importance and generalizability of this result, however, is limited given the unique structure and restrictions on cinacalcet use in place in Quebec during this period.

Specific comments:

Introduction:
1. there really is not a strong case made for undertaking this analysis. The authors cite prior research reporting changes in PTX rates over time in the US and suggest these change may be related to other treatment options and guidelines, but are vague on how these differences are important here.

2. Why is it important to analyze PTX trends in a “real world” setting? Is there an inherent “value” placed on PTX? Should we be trying to increase or decrease rates? The more relevant policy question is which alternative is most cost-effective way to manage SHPT, not whether PTX rates are increasing or decreasing.

3. The authors need to explain how the formulary process works in Canada for readers who are from other countries.

Subjects and Methods

4. Figure 1 shows a cohort catchment period of 1/1/99-12/31/10 whereas the methods report the cohort catchment period as spanning 1/1/01-12/31/10. Please clarify this discrepancy.

5. How was a prior history of PTX or kidney transplant ascertained?

6. What were the criteria that Amgen used to “carefully select” patients who received cinacalcet between Sept 2004-June 2006?

7. What do the investigators mean by “rigorously analyzed” with respect to requests for cinacalcet use? This sounds like a prior authorization program
(that's what it would be called in the US).

8. Please explain why age, sex and dialysis modality would change over time. What evidence is there that these are related to PTX? (p. 7) What is meant by mean age (p. 8), as in, when was age calculated? We have data presented in different sets of time periods: bimonthly PTX rates, patient characteristics every two years, medication exposure every year. These should be reconciled to a more consistent time presentation, particularly given the high mortality rates in chronic dialysis patients.

9. Why was medication use calculated on an annual basis when the PTX rates were bimonthly? In addition, there is no justification for the study of medications at all, especially the dosing. The decision to calculate average daily dose over a 12 month period in chronic dialysis patients who may switch off/on and back & forth between these medications is problematic and undermines any potential conclusions. This whole section is distracting to the purpose of the study.

Results/Conclusions

10. The underlying study cohorts appear to have an increasing proportion of prevalent patients over time: wouldn’t this in turn increase SHPT rates over time and potentially increase PTX rates also?

11. The current study looks at PTX rates in Quebec and they are quite different from PTX rates reported in the US during overlapping time periods. What are the implications of these differences? How generalizable are the present findings outside the Quebec system? The authors suggest that wider availability of cinacalcet in Quebec may have had a stronger effect on lowering PTX rates as compared to the US, but cinacalcet was on prior authorization (approval) per the authors after it was approved. This would mean that use was more restricted in Canada.

12. The broad calculation of doses of other medications does little to explain how individual patients were being managed clinically. In addition, as noted before, this aspect of the study is not well justified.

Tables/Figures

Table 1: not sure why this is reported on two-year increments
Table 2: data does not need to be in a table and should just be incorporated into the text
Table 3: analysis does not fit into the purpose of the study
Figure 1: cohort catchment period does not match text in Subjects & Methods
Figure 3: no justification for breaking out PTX rates by these variables: when was age calculated?
Figure 4: This analysis does not fit into the purpose of the study as noted above.

Level of interest: An article of limited interest
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.