Reviewer’s report

Title: The Societal Economic Burden of Autosomal Dominant Polycystic Kidney Disease in the United States

Version: 1 Date: 20 Oct 2019

Reviewer: Kuocherh Huang

Reviewer's report:

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1. First of all, I have concerns about the study design of this manuscript, specifically how the comparison group was chosen. Abstract, Methods, "The incremental costs associated with ADPKD were calculated as the difference between costs incurred over a one-year period by individuals with ADPKD and the US population." How reasonable is it to use the entire U.S. population, which encompasses a large variety of diseases, as the comparison group? On page 5, 2nd main para., "The incremental costs associated with ADPKD were estimated based on average cost difference between an individual with ADPKD and an individual from the US population, and thus constitute the "excess" costs attributed to ADPKD." Normally, to make a comparison group "comparable" authors of a study would perform a matching procedure (such as propensity score matching, and match on age, gender, comorbidity, and the like) to ensure that the study and comparison cohorts are as homogenous as possible except the variable of interest, in this study ADPKD. The authors please cite supporting references with respect to the manner they selected the comparison group as to calculate the "excess" costs.

2. Generally speaking, health care costs are mostly skewed to the right. However, in this paper the authors used average costs only to present descriptive statistics.

3. As regards direct non-healthcare costs (including research, training, advocacy, costs of matching donors and recipients for kidney transplant, and costs of transportation to and from dialysis center), they "were drawn directly from the estimates of funding for research on polycystic kidney diseases (PKD) reported by the National Institute of Health (NIH) and from the annual report of the PKD Foundation" (p. 6, under Direct non-healthcare costs). How could the authors obtain comparable direct non-healthcare costs of research, training, and advocacy, and particularly equivalent costs of matching donors and recipients for kidney transplant, from the U.S. population as to estimate the excess costs attributed to ADPKD? Correspondingly, I could not comprehend the following remark on page 10 under the Direct non-healthcare costs sub-section: "Collectively, excess direct non-healthcare costs were estimated at $124.7 million." Actually, the amount of excess direct non-healthcare costs is inexplicable since no comparable costs from individuals of the U.S. population were presented as to demonstrate the "excess" costs. Similar lack of clarity is also observed in other parts of the Results section.

5. P. 15, last papa., "Another limitation is that there was scant information on direct healthcare costs for individuals with Medicare or Medicaid coverage". It is challenging for me to agree with the argument.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
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No

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