Author's response to reviews

Title: Impact of urinary incontinence on health-related quality of life, daily activities, and healthcare resource utilization in patients with neurogenic detrusor overactivity.

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Author's response to reviews: see over
A Note to Our Reviewers…

The authors would like to thank the reviewers for taking the time to evaluate our manuscript. The comments received were insightful and the resulting revisions will help to make this research report stronger. **Author responses are highlighted in blue.**

**MAJOR COMPULSORY REVISIONS**

Page 10: The authors state that the quality of life data and the productivity data were distributed similarly and therefore OLS is appropriate. However, there is no evidence that those variables are distributed similarly. The authors referred to Table 2 as evidence for this but Table 2 only has minimum and maximum. I would think to assess whether two variables are distributed similarly one would want to consider statistics such as mean, standard deviation/variance, skewness, kurtosis. Is there evidence that the distributions are the same when looking at this basic statistics? The authors also state that, even if productivity is non-normal this is not inherently problematic given the central limit theorem and recent literature (they provide a helpful reference, Lumley et al 2002). Although I appreciate the reference, I have methodological criticisms of the simulation by Lumley et al 2002 and remain unconvinced. Also, Lumley et al mentions that skewed cost data could be analyzed with OLS with samples of 500 or more; the current paper has less than this (n=324) so I’m unclear why this reference would be justification for the current approach. If the authors genuinely believe in the OLS approach, I’m okay with this but would ask they do sensitivity analyses using a generalized linear model as well (most likely a negative binomial distribution and a log-link function, though I will leave it to them). These results can be presented in an Appendix or as additional rows in Table 7. I think this would help readers have additional confidence in the results. Also, the authors imply (though I may have misinterpreted) that the Poisson-like models do not generate differences in magnitude of outcomes; this is not correct, as any statistical package could provide adjusted means for these models making them completely analogous to what is presented currently in Table 7 (except for an R2 value, of course).

Additional sensitivity analyses were conducted on all quality of life and productivity outcome variables using negative binomial regression models (with “country” added as covariates). This has been additionally indicated in the methods section; additional results are added as Table 8.

Page 10: I appreciate that the overall study goal of assessing the burden of variations between incontinent and continent NDO patients, but I think the current approach which does not control for country has a serious flaw in assessing this burden. By not controlling for country, the authors are implicitly given more weight to countries/regions with higher sample size (Europe more than the US; Spain more than all other countries, apparently). Even if the authors are not interested in how the burden varies by country, it would make the interpretation of the overall outcomes more accurate. I’m also surprised by the author’s comment saying there has been “no substantial evidence demonstrating a difference of health or resource burden in NDO across Western European countries and the US”. I suppose if
there was very convincing evidence for this then I would be okay with their approach. However, are the authors saying studies have been done showing no differences or that no studies have been done? Absence of evidence does not equate to evidence of absence. Regardless, on page 13 the authors note the differences in hospitalizations between US and Europe; also, Table 6 seems to show fairly large differences between the US and Europe. To me, this provides more than enough evidence to warrant controlling for country. Naturally, adding a covariate does affect power but, given the rule of thumb for 20 cases per predictor, this should not be an issue.

“Country” has been added as covariates (coded as 4 dummy variables for the 5 countries) in all regression models employed in this study. Altered study results have been comprehensively updated in the results section and Table 7 and 8.