

Author's response to reviews

Title: Urogenital Abnormalities in Men Exposed to Diethylstilbestrol in Utero: A Cohort Study

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Dear Editors:

Thank you for the opportunity to submit a revised version of our manuscript. The manuscript now conforms to the journal style. We have also made revisions in response to comments from the reviewers. Our specific responses to the reviewers are outlined below:

Reviewer 1 (Robboy)

1. We have deleted the sentence as requested by the reviewer.
2. The reviewer asks that we elaborate on the data of “the 20 patients from the Mayo Clinic study who have cumulative dose information.” Our text states that cumulative dose data were available for 20 percent of participants from the Mayo Clinic, not 20 patients. Thus, of the 21 Mayo Clinic participants who reported an epididymal cyst (Table 3), cumulative dose data was available for only five, one of whom had a cumulative dose of 9,745 mg and was classified as >5 grams and four of whom had cumulative doses under 5 grams (100, 240, 2,100, 2,395). Our point in that section (last paragraph of Results) is that there was not enough data to examine a dose effect in the Mayo Clinic subgroup. We have not made changes to that section. Adding more information on the specific doses will likely take away from the main point – that cumulative dose was only available for 20% of participants.
3. We appreciate Dr. Robboy’s comment and agree with his speculation as to a possible reason for observing a significant association of DES exposure with

inflammation/infection of the testes. We have added a sentence to that effect.

Reviewer 2 (Newbold)

1. The ages of the exposed and unexposed cohorts were quite similar (median 43, interquartile range 38-46; median 42, interquartile range 38-45). We have added a sentence to this effect at the end of the first paragraph of the Results section.

2. We agree with Dr. Newbold's comment and have added the following sentence to the end of the manuscript: "As cohort participants age, it will become possible to investigate whether DES-exposed men have an increased risk of conditions such as benign urethral hypertrophy and prostate cancer, which occur more often in older men."

Sincerely yours,

Julie R. Palmer, ScD