Reviewer’s report

Title: Tall height and obesity are associated with an increased risk of aggressive prostate cancer: results from the EPIC cohort study

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Reviewer: Emma Allott

Reviewer's report:

Body size and adiposity are associated with an increased risk of aggressive prostate cancer: results from the EPIC cohort study

The authors examined associations between body size (height and obesity) and prostate cancer risk in EPIC, a prospective cohort of ~140,000 men, ~7,000 of whom were diagnosed with prostate cancer during a follow up period of 13.9 years. Study strengths include the relatively large number of cases and the range of obesity measures (waist circumference, waist-to-hip ratio and BMI; either measured or self-reported and validated). However, it does not appear that prostate cancer screening was taken into account in the analysis, and this is an important variable to consider. I have several comments:

1. The authors state throughout the manuscript that the relationship between obesity and aggressive prostate cancer is unclear. However, there have been quite a number of studies published in this area, including the most recent last year (Kelly et al JNCI - a study using PLCO data), and there have also been meta-analyses completed based on these studies, although the most recent was published in 2012 (Discacciati et al). Studies fairly consistently show that obesity is associated with increased risk of aggressive prostate cancer. Therefore, I do not think that it is accurate to state that the relationship between obesity and prostate cancer is unclear. Rather, the authors could focus on a less clear aspect of this question - perhaps it is the different measures of obesity used in this study that distinguishes it from past studies.

2. The authors could cite the Health Professionals study in their Discussion, which showed a positive association between obesity and lethal prostate cancer only in ERG+ tumors (Pettersson et al JNCI 2013). Given that ERG is an androgen-responsive gene fusion, this may shed light on mechanisms linking obesity and prostate cancer.

3. What was the impact of excluding men with missing data for tumor characteristics and how many men were missing data for tumor characteristics? If this was a large number, the authors should compare characteristics of men with tumor data vs. missing tumor data to assess if these data are missing at random. Also, what was the impact of excluding men with
missing data for important covariates? These sensitivity analyses are mentioned in the Methods, but the results of these sensitivity analyses are not included.

4. There is a large amount of missing data for the variable "married". The last sentence of the first paragraph of the Results section states that obese men were more likely to be married than men of normal BMI, but this is not what the results presented in Table 1 show. In fact, given the large amount of missing data, I am not sure how confident we can be in the distribution of this variable across BMI category. Perhaps the results section should mention that obese men were more likely to be missing this variable.

5. The lack of screening data is an important limitation of this analysis, and should be mentioned particularly in the limitations section of the Discussion, and also in the relevant section of the Methods.

6. The term "fifth" is mentioned in the Abstract results, but not defined. It should be clarified in the abstract that these are fifths of height. Consider replace the term "fifths" with "quintiles"?

7. The term "prostate cancer subtype" could perhaps be replaced with "tumor characteristics" or "high grade prostate cancer", given that this study is not examining molecular subtypes (as other studies are now beginning to do).

8. The conclusion states that associations between body size and aggressive prostate cancer risk were strongest for height and waist circumference. However, the title does not reflect that height was examined. Consider modifying the title to reflect the main analyses and findings of the study.

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

Yes

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

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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