**Peer Review File**

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**Reviewer A**

Your evaluation of the recent Remmers update of the ERSPC sheds further insight on the limitations of the original design of the ERSPC trial. One of the major critiques of that trial is that it did not include men older than 69 years of age. Interestingly, Remmers finds that there is an age related decline in rates of PSA<1ng/mL suggesting that older men may benefit from further screening. I am excited to see where the discussions for prostate cancer screening are headed in the coming years.

**Reply: We thank the reviewer for this comment.**

**Reviewer B**

The editorial is well written and the authors raise a valid argument. I have no major comments. A few minor comments can be considered:

p.2, l.7:

The authors express agreement with Remmers et al.'s assertion that there is a need to improve screening algorithms. From my perspective, numerous screening algorithms are already available, varying in quality, but many are of high caliber. Consequently, I believe the focus should be on augmenting and implementing improved existing screening algorithms instead of solely relying on the PSA test.

**Reply: We thank the reviewer for this comment. We agree with the reviewer and have elaborated about additional factors that need to be included in prostate cancer screening. This is elaborated on page 2 lines 14-22.**

P.2, l.9:

I would rather talk about modern healthcare than Western World since many healthcare systems in the Eastern part of the world use modern techniques for prostate cancer diagnostics.

**Reply: We thank the reviewer for this comment. This sentence has since been modified to reflect that of modern healthcare as opposed to the Western world, as can be seen in page 2, line 16.**

**Reviewer C**

I read with extreme interest this nicely written Editorial on a topic under spootlight. The point of view of the authors is very well described and reasonable. I sincerly have only few minor remarks before acceptance. In line 11 page 2 you state "We know that there are a multitude of factors that can affect the results of PCa screening". I would insert some references to make your statement stronger

Similarly I would add the fact that also PSA value itself can be affected by several factors ( DIETARY > Association of Total Dietary Intake of Sugars with Prostate-Specific Antigen (PSA) Concentrations: Evidence from the National Health and

Nutrition Examination Survey (NHANES), 2003-2010. Biomed Res Int. 2021 Jan 9;2021:4140767. doi: 10.1155/2021/4140767. PMID: 33506014; PMCID: PMC7811566. CRONIC ASPIRINE USE > Correlation Between Long-Term Acetylsalicylic Acid Use and Prostate Cancer Screening with PSA. Should We Reduce the PSA Cut-off for Patients in Chronic Therapy? A Multicenter Study. Res Rep Urol. 2022 Oct 21;14:369-377. doi: 10.2147/RRU.S377510. PMID: 36304173; PMCID: PMC9595058. SMOKE > Smoking reduces PSA accuracy for detection of prostate cancer: results from an Italian cross-sectional study. Minerva Urol Nefrol. 2019 Dec;71(6):583-589. doi: 10.23736/S0393-2249.19.03360-5. Epub 2019 May 28. PMID: 31144489. ) and therefore its use must be tailored on patients'.

**Reply: We thank the reviewer for this comment and completely agree with it. We have included references to support our statement highlighting factors such as race, family history and prostate volume that affect screening. The effect of diet and smoking on PSA levels can be seen in page 2, lines 11-13.**