Reviewer's report

Title: Addressing the contribution of previously described genetic and epidemiological risk factors associated with increased prostate cancer risk and aggressive disease within men from South Africa

Version: 1 Date: 12 July 2013

Reviewer: Rick Kittles

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Tindall et al. use sample data from the Southern African Prostate Cancer Study (SAPCS) consisting of 837 participants, 522 cases and 315 controls to investigate 46 Pca risk alleles and 24 epidemiological measures for power to predict Pca.

They found that none of the risk alleles significantly predicted Pca within the SAPCS. Also, their genetic risk profiles did not improve the predictive power of PSA testing. They did find that several lifestyle/environmental factors were associated with Pca risk.

The manuscript is relatively well written however there are several issues which need to be addressed.

1. The study is extremely under powered and this should be stated in the paper.
2. The authors tried to put too much information in a short paper without describing or presenting important details. For instance: who are the subjects, their ethnicity, demographic, and clinical characteristics. Without knowing their cultural and genetic differences, one cannot say, if any of the subjects should be analyzed separately or not.
3. Did they do analyses pooling stage 1 and 2? Maybe, they could get a better estimate of OR.
4. For case only study, why did they do the association test with PSA in cases, not in controls? How did they define tumor grade?
5. For the analyses of AUC, they used up to 38 SNPs. They said predictability improved as they added more SNPs but most of the SNPs are not significantly associated with prostate cancer. They also should examine how adding SNPs to PSA, family history, etc. all the significant variables in stage 3 improve the predictability.
6. They could expand more about the Stage 3 epidemiological analysis. Their findings in this section are potentially important for explaining why African descent men have higher incidence of prostate cancer compared to other ethnic/racial groups. There is definitely a need for a more thorough analysis and description of methods and results. They need more detailed discussion to explain observed patterns, especially many of readers do not know about the
socio-cultural conditions that these men live in, i.e., access to health care, etc.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests