Reply to ‘Comment on “Validation of a contemporary prostate cancer grading system using prostate cancer death as outcome”’

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Sir,

I thank Dell’oglio et al for their comments and interest in our paper (Berney et al, 2016), and their generally supportive comments. The authors conclude that the new grading system is merely a ‘user-friendly instrument’, however, it includes a number of pattern refinements based on previous work outlined fully in our article (Berney et al, 2016), including the fact that all cribriform glands and glomeruloid glands should be assigned a Gleason pattern 4 regardless of morphology, and the grading of mucinous carcinoma of the prostate should be based on its underlying growth pattern rather than grading them all as pattern (Epstein et al, 2016).

They ask whether the new prostate cancer grading system improves the prediction of prostate cancer death relative to the standard grading system. The problem with this question is that there is divergence on interpretation of the standard model. The revisions to the Gleason system have been driven by a lack of clarity in pattern assignment, particularly, but not exclusively centred on grade assignment in cribriform lesions, which have been variably assigned and interpreted (Dong et al, 2013; Kir et al, 2014; Kweldam et al, 2014). It is virtually impossible to compare the new grading system with variable interpretations of ISUP 2005, and more recent suggested revisions of pattern present in the 2005 classification (Epstein, 2010). Recently, this variable interpretation was examined in detail by the European Network of Uro-Pathology (Berney et al, 2013). The paper cited by the authors, which found no improvement in grading by grade groups, included no reassignment of grades based on these clarifications, but was a retrospective exercise mining old reports (Loeb et al, 2016). Such retrospective mining of old reports should always be treated with caution.

The second to fourth criticisms of Dell’Oglio et al are related to the cohort itself. Unfortunately the ‘perfect’ prostate cohort does not exist. No cohort can have both long follow-up and be to contemporary standards of diagnosis and treatment. The radical prostatectomy data is self-evidently not available at diagnosis.

Two criticisms by Dell’Oglio et al of our cohort are virtually mutually exclusive suggestions: not using radical prostatectomy as a more accurate assessment of Gleason score, and not including patients over 76.

The most vital questions we have to answer for the treatment of prostate cancer remains in the clinic prior to any proposed treatment. Conservation management is a reasonable surrogate for the natural history of prostate cancer and an indication of how many men are being treated unnecessarily. At present few other comparable cohorts have been published with long-term outcome available.

Finally, we consider the importance of a patient-centered system is not a trivial one, especially one that does improve the groupings considered for future analysis. Grade Group 1 out of 5 better conveys indolent behavior compared with a GS of 6 out of 10, and will permit more rational and less emotional decision-making in regards to active surveillance. Grade Group 2 out of 5 (as opposed to Gleason score 7 out of 10) has a very good prognosis with rare metastases. Grade Group 3

has a significantly worse prognosis than Grade 2 as opposed to Gleason score 7, which combines Gleason scores 3 + 4 and 4 + 3 and is often incorrectly combined together for treatment and prognosis protocols.

Finally, Grade Group 5 obviates the need to distinguish between Gleason scores 4 + 5, 5 + 4 and 5 + 5 just as Grade Group 1 makes irrelevant, the distinction between Gleason scores 2 + 2, 2 + 3, 3 + 2 and 3 + 3. These practical points are likely to be of immense use in patient management and their comprehension of the severity of their disease.

The authors declare no conflict of interest.

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