

teaching low-level diagnostic skills, rather than demonstrating isolated Hi-Tech procedures, has been Urolink's maxim. The world is, and the needs of LMIC urologists are, changing; Urolink anticipates being there to help.


Disclosure of Interests

I did not receive, at any time payment or services from a third party for any aspect of the submitted work.

I do not have financial relationships with entities as described in the instructions during the 36 months prior to publication.

I do not have any patents planned, pending, or issued, broadly relevant to the work.

I have no other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what have written in the submitted work.

Stephen R. Payne 

Urolink, British Association of Urological Surgeons, London, UK

Is Gleason 6 cancer? The answer is more than just a 'name'

The Cambridge dictionary defines cancer as 'a serious disease that is caused when cells in the body grow in a way that is uncontrolled and not normal, killing normal cells and often causing death' [1]. In this issue of *BJUI*, Iczkowski and a group mainly of urologists make an argument in favour of maintaining the existing nomenclature for Gleason score 6 (GS6) disease, stating it should still be labelled 'cancer' based largely on histopathological features consistent with the above definition [2]. Their article rebuts a commentary by Eggener et al. [3] that argues that the histological entity termed GS6 disease (now Grade Group 1) should not be labelled 'cancer'. Eggener et al. argue that GS6 is exceedingly prevalent, especially in aging men, and rarely leads to metastasis and death. Thus, GS6 does not meet a definition of cancer. Rather its biological behaviour is more like a precancer, rarely transforming into a more life-threatening disease. The emotional and psychosocial weight of the term 'cancer', they argue, represents a major barrier to deferring treatment with curative intent. Addressing this issue is complex and should include broad clinical and public stakeholder input from those experienced in disease definitions and labelling. Such efforts would substantially reduce overdiagnosis and overtreatment.

Emphasizing the broad support among urologists, the central arguments put forward by Iczkowski et al. [2] are: that GS6 demonstrates histological features that define cancer; that this scenario is different from carcinoma *in situ* in settings such as thyroid and breast cancer and atypical small acinar proliferation; and that information from randomized trials and observational studies conducted prior to widespread PSA screening demonstrated that GS6 disease can, over decades, lead to prostate cancer metastases and death in some men treated with watchful waiting [4,5]. Also, they argue,

progress has been made in reducing unwarranted prostatectomies in favour of increased use of active surveillance (AS). Lastly, if GS6 disease remains undetected, an unacceptable degree of synchronous or subsequent high-grade cancer would occur.

We acknowledge the urology expertise included by Iczkowski et al. [2] but support much of the clinical perspective of Eggener et al., focusing on the beneficial downstream effects of renaming GS6, particularly in the current era of widespread PSA testing, use of multiparametric MRI for evaluation and targeted biopsies, and classification of nearly all GS6 as low to very low risk. Screening should only be conducted if benefits justify harms and costs, rather than to identify an entity based on histopathological criteria. Prostate cancer screening trials have shown, at best, a small long-term benefit at the expense of harms including overdiagnosis and overtreatment [6]. Removing GS6 from the classification equation could substantially shift the balance of benefits to harms. Renaming would reduce the number receiving a cancer diagnosis, the psychological, physical, and financial harms of disease labelling, and unnecessary treatment. As Eggener et al. [3] argue, in most cases, $GS \geq 7$ disease should be a prerequisite for contemplating radical treatment. Notably, even men with GS6 tumours diagnosed prior to widespread PSA testing had excellent long-term outcomes even though up to one-third had undetected higher-grade cancers. Additionally, the presence of higher-grade cancers unsampled on initial biopsy is not associated with worse long-term outcomes [3,4]. However, in an era of multiparametric MRI-based diagnosis and biopsy-based AS, these individuals are reclassified as Grade Group 2 and risk overtreatment. AS also contributes to overtreatment because

delayed intervention is triggered by poorly validated radiographic and histological markers of asymptomatic progression, and repeated prostate biopsies have harms and costs. Yet most patients would never experience symptomatic progression and would have better outcomes if managed with a less burdensome, observant approach.

Despite strong disagreements between them, both author teams share the belief that radical treatment for GS6 disease should be rare. We agree. But fully answering the question of whether to rename low-risk prostate cancer (including any GS6) is more than semantics. Words matter. What we say and how we say (name) it have important health and healthcare implications. In addition to the question of whether GS6 should be labelled a cancer, other steps should be taken to mitigate overdiagnosis and overtreatment harms while focusing treatments on those for whom it is effective and needed. We believe that, given the favourable natural history of GS6 disease in the PSA era, reducing intensity of AS protocols, including decreasing use of expensive and poorly validated biomarkers not demonstrated to have more than minimal incremental prognostic value, would decrease harms, complexity, and costs [7]. Recent data also suggest the same is true for favourable intermediate-risk (Grade Group 3) cancer. While MRI and biopsy-based AS represents advancement in the diagnosis and management paradigm, its effectiveness has never been established in randomized trials. Such trials should be conducted. Furthermore, watchful waiting deserves a larger role than current guidelines recommend, i.e. limiting use of watchful waiting only to men with very low-risk disease and life expectancy <5 years [8]. This is especially important given the effectiveness of newer medications in the small minority who develop advanced disease.

In conclusion, answering the question of whether to call GS6 'cancer' has important health and healthcare implications that go beyond a simple name or word. The answers to other important screening, diagnosis, monitoring and treatment questions are needed and to do this ideally requires large long-term trials. Until then, clinical guidelines can lead by

aligning their recommendations and corresponding wording with current best evidence demonstrating that, for many men, less intensive screening, evaluation, surveillance and treatment leads to better health outcomes at lower cost. Their words matter.

Disclosure of Interests

The authors declare no conflicts of interest.

Timothy J. Wilt^{1,2}  and Philipp Dahm³ 

¹Minneapolis VA Center for Care Delivery and Outcomes Research, Minneapolis, MN, ²Lisa Schwarz Foundation for Truth in Medicine, Norwich, VT, and ³Minneapolis VA Healthcare System and the University of Minnesota Department of Urology, Minneapolis, MN, USA

References

- 1 Cambridge Dictionary. Available at: <https://dictionary.cambridge.org/us/dictionary/english/cancer>. Accessed 22 August 2022
- 2 Iczkowski K, Molina M, Egevad L, Bostwick D, van Leenders G. Low-grade prostate cancer should still be labeled cancer. *BJU Int* 2022
- 3 Eggener SE, Berlin A, Vickers AJ, Paner GP, Wolinsky H, Cooperberg MR. Low-grade prostate cancer: time to stop calling it cancer. *J Clin Oncol* 2022 Apr 18;JCO2200123; 40: 3110–4
- 4 Wilt TJ, Vo TN, Langsetmo L et al. Radical prostatectomy or observation for clinically localized prostate cancer: extended follow-up of the prostate cancer intervention versus observation trial (PIVOT). *Eur Urol* 2020; 77: 713–24
- 5 Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. *JAMA* 2005; 4: 2095–101
- 6 Ilic D, Djulbegovic M, Jung JH et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. *BMJ* 2018; 5: k3519
- 7 Wilt TJ, Dahm P. Value of prostate cancer care: new information on new therapies suggest less is more. *Eur Urol* 2017; 72: 736–7
- 8 Eastham JA, Aufferberg GB, Barocas DA et al. Clinically localized prostate cancer: AUA/ASTRO guideline, part I: introduction, risk assessment, staging, and risk-based management. *J Urol* 2022; 208: 10–8

Abbreviations: AS active surveillance, GS6 Gleason score 6.

Post-prostatectomy radiotherapy: does late toxicity lead the game?

In the current issue of *BJUI*, Swedish researchers report on late toxicity induced by post-prostatectomy radiation (PPR). This late toxicity includes urinary and rectal toxicity and data on induced secondary malignancies [1]. Based on patient and outcome data available in the Prostate Cancer Database

Sweden (PCBaSe) the authors compared the toxicity data of patients treated with PPR and patients treated with prostatectomy alone (PRAL). Using 1:2 matching, the data of 2789 patients who received PPR and 5578 patients who underwent PRAL were analysed [1].