Flares of chronic pelvic pain syndrome: lessons learned from the MAPP Research Network.

Kessler, Thomas M

DOI: https://doi.org/10.1111/bju.14843

analyses of DALYs could enrich our understanding of the interaction between approaches to testicular cancer care and patient experience. For example, Pishgar et al. [4] report that Kiribati, Chile, and Argentina had the highest testicular cancer-specific age-standardised DALY rates. Focussed qualitative research in these countries, possibly incorporating comparisons with higher performing settings, could facilitate targeted improvements to patient care and experience. As more countries achieve the highest cure rates for testicular cancer, patient experience will assume increasing importance as a measure of care quality in this disease.

Analyses like this have the potential to provoke important conversations and to generate hypotheses in specialist clinical and health policy research. As clinicians, researchers and policy-makers, this study should encourage us to think critically about the policy context in which we see testicular cancer, the reasons patients might present late, and how equity of outcome might be achieved both within and beyond our own immediate surroundings. Pishgar et al. [4] invaluably remind us that we remain some way off being able to call testicular cancer a curable disease for all patients, in all settings.

Conflict of Interest

None.

John Withington

Urology, London Deanery and National Medical Director's Clinical Fellow, NHS England and NHS Improvement, London, UK

References

1 Global Cancer Observatory (GLOBOCAN). Available at: http://gco.iarc.fr. Accessed June 2019.

2 **Markt SC, Lago-Hernandez CA, Miller RE et al.** Insurance status and disparities in disease presentation, treatment, and outcomes for men with germ cell tumors. *Cancer* 2016; 122: 3127–35

3 **Withington J, Cole AP, Meyer CP et al.** Comparison of testis cancer-specific survival: an analysis of national cancer registry data from the USA, UK and Germany. *BJU Int* 2019; 123: 385–7

4 **Pishgar F, Haj-Mirzaian A, Ebrahimi H et al.** Global, regional, and national burden of testicular cancer, 1990–2016: results from the global burden of disease study 2016. *BJU Int* 2019; 124: 386–94

5 **Shanmugalingam T, Soultati A, Chowdhury S, Rudman S, Van Hemelrijck M.** Global incidence and outcome of testicular cancer. *Clin Epidemiol* 2013; 5: 417–27

6 **Rajpal S, Kumar A, Joe W.** Economic burden of cancer in India: evidence from cross-sectional nationally representative household survey, 2014. *PLoS One* 2018; 13: e0193320. https://doi.org/10.1371/journal.pone.0193320.

7 Lancet Global Health. Lifting the veil on cancer treatment. Lancet 2019; 7: PE281. DOI: 10.1016/ S2214-109X(19)30014-2

Flares of chronic pelvic pain syndrome: lessons learned from the MAPP Research Network

Chronic pelvic pain syndrome (CPPS) is one of the unresolved problems in urology. There are multiple recommendations for the management of CPPS, and the *BJUI* guideline of guidelines on bladder pain syndrome by Malde et al. [1] summarizes differences in nomenclature, definitions and recommended diagnostic tests and treatments between major national and international guidelines. CPPS is defined according to the European Association of Urology as chronic or persistent pain perceived in structures related to the pelvis without proven infection or other obvious local pathology that may account for the pain, and it is often associated with negative cognitive, behavioural, sexual and emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor or gynaecological dysfunction [2]. Despite exacerbations of CPPS symptoms, so-called 'flares' (i.e. sudden appearance or worsening of symptoms) that highly affect the patients' quality of life and strongly challenge their treating physicians, relevant characteristics of CPPS such as frequency, intensity, duration and risk factors are largely unknown.

In this month's issue of the *BJUI*, Sutcliffe et al. [3] bring light into this darkness and present their findings from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network. A total of 385 participants were eligible for participation in their 1-year, multi-site longitudinal study. Symptom flares were very common, with approximately three-quarters of the sample reporting at least one flare (23% reported one flare, 28% two to three flares and 25% four or more flares), flare duration ranged widely from 1 to 150 days, and variability in symptoms, frequency, and duration was very relevant both between and within participants. Risk factors for greater flare burden (greater flare frequency, symptom intensity and/or duration) were female gender, worse non-flare symptoms and bladder hypersensitivity or chronic overlapping pain conditions. These

new insights into the characteristics of CPPS close several gaps in our knowledge, but also raise many questions. What are the reasons that one-quarter of patients with CPPS did not experience flares and what can we learn from this specific subgroup to optimize our treatment strategies? What are the pathomechanisms involved? Can we use biomarkers to identify patients at risk of CPPS flares? Would there be protective factors to obviate CPPS flares? How can we optimize the management of CPPS flares to improve the quality of life of affected patients? Despite these many questions, there is light at the end of the tunnel: the aforementioned MAPP Research Network (www.mappnetwork.org). This network, established by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health in 2008, is a whole-body initiative which has enormously expanded our knowledge in the field of CPPS in recent years. Such research networks, unifying highly multidisciplinary approaches through the collaboration of scientists, epidemiologists and clinicians, are essential to push the borders of knowledge, paving the way for novel management strategies. Together we are strong, with basic and clinical research linked by translation and reverse translation enabling innovations and finally resulting in better patient care. However, although a customized, patient-tailored bio-psycho-social approach engaging the patient in a collaborative journey towards self-management is strongly recommended and generally accepted for CPPS [4], flares remain a major issue. We still have to solve this Gordian knot; however, *per aspera ad astra*! The next steps are to prevent flares and to find an optimal flare treatment.

Conflicts of Interest

None declared.

Thomas M. Kessler,
BJUI Associate Editor -Functional Urology
Department of Neuro-Urology, Balgrist University Hospital, University of Zürich, Zürich, Switzerland

References

1 **Malde S, Palmisani S, Al-Kaisy A, Sahai A.** Guideline of guidelines: bladder pain syndrome. *BJU Int* 2018; 122: 729–43
2 **Engeler D, Baranowski AP, Berghmans B et al.** EAU Guideline on Chronic Pelvic Pain 2019. Available at: https://uroweb.org/guideline/chronic-pelvic-pain. Accessed May 2019
3 **Sutcliffe S, Gallop R, Lai HH et al.** A longitudinal analysis of urologic chronic pelvic pain syndrome flares in the MAPP Research Network. *BJU Int* 2019; 124: 522–31
4 **Magistro G, Wagenlehner FM, Grabe M, Weidner W, Stief CG, Nickel JC.** Contemporary management of chronic prostatitis/chronic pelvic pain syndrome. *Eur Urol* 2016; 69: 286–97

Non-invasive diagnosis and monitoring of urothelial bladder cancer: are we there yet?

In this issue of *BJUI*, Ward et al. [1] describe the development of DNA-based urinary biomarkers for urothelial carcinoma (UC). The genomics of UC have been well characterized through interrogation of tumour issues in institutional series (e.g. the Memorial Sloan Kettering Cancer Center [MSKCC] experience), multi-institutional collaborations (e.g. The Cancer Genome Atlas [TCGA]) and commercial platforms (e.g. the Foundation Medicine experience) [2]. Until recently, these have been largely academic pursuits, with possible impact on prognostication but limited clinical applicability and utility for therapy selection and monitoring of response; however, with the US Food and Drug Administration approval of erdafitinib several weeks ago, patients with advanced UC will routinely receive genomic assessment for *FGFR2/3* mutation or fusion, the targets for this therapy [3]. In due time, it is anticipated that multiple other putative targets with associated therapies (e.g. *ERBB2*, *CDKN2A*), as well as potential predictive biomarkers, may also warrant testing.

The evolving landscape in advanced UC makes a non-invasive biomarker particularly attractive. The authors of the present commentary have previously reported results from a series of 369 patients with advanced UC, demonstrating that genomic alterations in ctDNA could be identified in 91% of patients using a commercially available 73 gene panel [4]. More recently, Christensen et al. [5] assessed a cohort of 68 patients receiving neoadjuvant chemotherapy for muscle-invasive disease, demonstrating 100% sensitivity and 98% specificity for the detection of relapsed disease with a patient-specific ctDNA assessment (sequenced to a median target coverage of 105 000×) after cystectomy. Impressively, the data also showed that the dynamics of ctDNA appeared to be more useful than pathological downstaging in predicting relapse.

In contrast to these studies, Ward et al. have developed a 23-gene panel based on frequently expressed genes in a cohort of 916 UC tissue specimens, largely derived from patients with