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EDITORIAL

A Norwegian perspective on the Swedish national guidelines on prostate cancer for non-metastatic disease

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Almost two decades ago, Wiking Månsson reviewed the state of urological guidelines in an editorial in *European Urology* titled 'Evidence-Based Urology – A Utopia?' [1]. In his article, he posed the question: How are we doing in urology? and provided the rather unflattering answer: Not that good. He lamented that '… most of what is published in the urological journals has low level of evidence and as a consequence, low grade of recommendation'.

A lot has changed since Månsson voiced his dismay and the change has mostly been for the better. Today, urological guidelines are based on a large number of randomized clinical trials and high-quality register studies. We can, with considerable pride, state that prostate cancer researchers from Scandinavia, with Sweden often in the lead, have made decisive contributions to these improvements. The Scandinavian Prostate Cancer Group (SPCG) has been the incubator of the major Nordic randomized trials, with SPCG-4 and SPCG-7 as the most widely known trials [2,3]. Furthermore, the National Prostate Cancer Register, a Swedish population-based, clinical register, has generated multiple high impact publications [4,5]. Clinical cancer registers are cost-efficient tools to study the often decade-long prostate cancer disease trajectory. In Scandinavia in general and in Sweden in particular, there is a strong scientific environment that has enabled the creation of evidence-based urological cancer guidelines.

Clinical guidelines are formulated according to standard procedure, based on a transparent methodology, discussed in professional panels including representatives from other relevant professions and patient organizations. Modern guidelines are largely based on clinical evidence, with prospective randomized control trials having the highest, and retrospective studies from single institutions having the lowest impact. Changes in guidelines can have major implications for patient management, organization of the health care system and on health care economy. However, due to the high level of evidence required for strong recommendations, changes are often slow in the coming.

In Europe, most countries adhere to the European Urological Association (EAU) guidelines [6]. While the recommendations in the EAU Guidelines are based on strict rules, the implementation has to be flexible since the health care systems and 'health care culture' varies to a certain degree across Europe. In some European countries, urologists and oncologists have adopted EAU guidelines as their own guidelines, while in other countries national guidelines have been issued. In contrast to the EAU guidelines, National guidelines can be written to suit the specific requirements, opportunities and limitations of a national health care system.

For the first time a summary of the Swedish prostate cancer guidelines is published in English by Bratt et al. in this issue of the Scandinavian Journal of Urology [7]. Why is it important guidelines written by Swedish urologists and oncologists are published in an international scientific journal? It is important for several reasons: First, despite universally available publications of randomized and other important clinical trials, the interpretation of the evidence presented in these trials can vary substantially. Publication ensures that the selection of studies and their interpretation in the formulation of the guidelines are transparent. Furthermore, publication of national guidelines in peer-reviewed journals opens for scrutiny, scientific discussion and criticism which in turn may lead to improvements of both the national and possibly, by way of inspiration and reflection, international guidelines, thus, leading to the development of 'collective intelligence'.

The current Swedish guidelines contain inspiring innovations and some notable deviations from international guidelines.

On the innovative side, we take notice that ongoing and relevant clinical trials are listed in the summary of

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recommendations at the end of each chapter. This emphasizes the central importance of clinical trials for the continuous improvement and modification of clinical guidelines and serves as a constant reminder that these studies require recruitment of patients. Furthermore, it ensures that eligible patients are informed about and recruited to ongoing trials irrespective of their place of residence. This is an example that could and should be followed by other national and international urological societies in their guidelines.

Further, the guidelines state that the Swedish urologic community has taken the first step toward an organized prostate cancer testing program (OPT). As the Swedish National Board of Health and Welfare recommended against a formal population-based prostate cancer screening program, the Board 'acknowledges(d) that individual men may consider the potential benefits and harms from PSA testing differently' [7]. The Board also acknowledged 'widespread, ineffective, unorganized PSA testing'. So far OPT has been launched in 3/21 regions in Sweden with the aim to extend further to the whole country. The program is launched to improve 'pre-testing information to men, reducing socioeconomic inequality, making the testing and subsequent diagnostics more effective, and gaining knowledge and experience to prepare for a future national screening program' [7]. It is further stated,

> Men who opt for testing are managed according to a strict algorithm in a separate pathway outside routine health-care, very much like in a formal screening program. Birth cohorts of men are gradually invited with the aim of including the entire target population of men between 50 and 74 years of age within 7–9 years. All data are registered in regional databases for quality control and research.

Of note, the OPT algorithm in the Swedish guidelines states that with a PSA density $<0.15\,\mu g/l/cm^3$, an MRI PI-RADS score 1–3 and benign digital rectal examination, prostate biopsies are not recommended. These recommendations are interesting to read and further outcomes from Swedish studies will be very interesting to follow e.g. the Gothenburg II trial [8], and how these might change future recommendations of PSA cut-off for initiating a prostate MRI and biopsy.

A deviation from international consensus that deserves discussion is found in the chapter on treatment of patients with non-metastatic disease. While international guidelines generally recommend a life expectancy of at least 10 years to warrant treatment with curative intent [6], the Swedish guidelines recommend treatment for patients with high-risk and very high-risk prostate cancer with a life expectancy of more than 5 years. The argument for lowering the age threshold is that prostate cancer mortality in these risk groups is as high as 20–30% during the first five years following diagnosis. This is certainly true and focusing on the patients at highest risk of dying of prostate cancer is recommendable. However, this policy change should also warrant some words of caution: The available evidence suggests that the considerable effects of early curative treatment are time-dependent with no significant differences between intervention and control groups in metastasis-free survival, prostate cancer, and overall mortality during the first five to seven years, also in high-risk patients [2,9]. So the question is what effects of curative treatment patients can expect during the first five years following treatment? Moreover, could this policy change lead to more overtreatment particularly of elderly patients? To illustrate the problem, an 85-year-old man with an average life expectancy of six years (according to Statistics Norway/Sweden/Denmark) and a localized Gleason 8 prostate cancer should receive curative treatment according to the Swedish guidelines. Are we sure that this is a sound recommendation? Moreover, will curative treatment be a boon or a burden for this man in terms of quality of life? We think there is currently no clear answer to these questions. More research is needed on the large group of older patients with high-risk prostate cancer to better define their specific needs. Willet Whitemore's warning, put in writing almost 50 years ago, is still relevant today: 'Appropriate treatment implies that therapy be applied neither to those patients for whom it is unnecessary nor to those for whom it will prove ineffective'. [10].

Urological guidelines have developed significantly in terms of quality and relevance during the past twenty years and now represent the most important pillar of evidence-based medicine. Their influence is indeed so strong that clinicians are increasingly reluctant to deviate from them even if guideline recommendations run contrary to their clinical experience and intuition in their meeting with individual patients. It is thus important to remember that the other two pillars of evidence-based medicine, clinical experience and patient preference [11] retain their importance in our evaluation of individual patients even in the age of ever-improving and more detailed clinical guidelines. In many respects, clinical guidelines have made our job of giving patients balanced and informative advice both easier and sometimes more cumbersome. In conclusion, Guidelines remain tools 'for the obedience of fools and the guidance of wise men' [12].

Disclosure statement

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