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# Technical comment on: Würnschimmel C, et al. Prostate cancer screening in Switzerland: a literature review and consensus statement from the Swiss Society of Urology

**Takeshi Takahashi**[a]

[a] Health and Welfare Bureau, Kitakyushu, Japan

The article "Prostate cancer screening in Switzerland: a literature review and consensus statement from the Swiss Society of Urology" by Würnschimmel and colleagues [1] reviews guidelines and clinical trials of prostate-specific antigen (PSA) screening conducted subsequent to the issuance of the US Preventive Services Task Force (USPSTF) statement. Urologists, while cautiously accepting the USPSTF statement, identify challenges with the three primary randomised controlled trials (RCTs) and offer their interpretations. They advocate for further investigation into risk factors such as pathological findings, MRI and biomarkers to mitigate the harms associated with overdiagnosis.

The article represents a consensus expert opinion from the Swiss Society of Urology regarding PSA screening. RCTs constitute the highest level of evidence, followed by prospective cohort studies and case-control studies, while case reports and expert opinions are not considered evidentiary. In contrast, public health physicians specialise in evaluating evidence, albeit not specifically in the context of prostate cancer. Therefore, the USPSTF statement is regarded as an evidence-based guideline rather than an expert opinion, meriting greater respect than guidelines from urology societies, which are grounded in expert consensus rather than robust evidence.

Unlike clinically apparent prostate cancer, characterised by detectable tumours with symptoms such as local invasion and metastasis, screen-detected prostate cancer is diagnosed exclusively through histopathology. This concept traces its origins to the Bowery series in the 1950s, where diagnostic criteria were established based on latent cancers identified posthumously through autopsy [2, 3], originally proposed by a pathologist at that time [4]. The malignant potential of screen-detected cancers remains scientifically unvalidated. Dr Chadok's review of prostate cancer screening in the 1980s, prior to the introduction of PSA testing, cautioned, "Prostate cancer screening should be considered investigational until definitive evidence is available" [5]. Consequently, the foundation of PSA screening, encompassing criteria such as Gleason grade, PSA screening thresholds and the introduction of the T1c stage in the TNM classification, remains experimental. Subsequent imaging modalities and treatments are empirically applied, despite widespread adoption. Clinical research papers on these modalities are typically case series, as the natural history of screen-detected cancers, which should ideally serve as the control group, remains unknown.

Public health physicians raised questions about this situation [6, 7]. Efforts to elucidate its natural history through active surveillance underscore the necessity for a no-treatment control group, pending conclusive outcomes from RCTs [8, 9].

In 2018, the USPSTF reviewed three RCTs (PLCO, ERSPC, CAP), finding no reduction in all-cause mortality and inconsistent impacts on cancer-specific mortality [1]. PSA screening received a Grade C rating with no recommendation, with authors citing inadequate evidence to support benefits outweighing harms. Urologists have contested this, highlighting issues such as contamination in the non-screening group of the PLCO and a subgroup of the ERSPC resulting in a 20% reduction in cancer mortality [1]. However, the USPSTF review determined the RCTs' quality as fair after addressing these concerns, and noted consistent statistical errors accounting for discrepancies among RCTs and their subgroups. Public health professionals provide an impartial and objective evaluation of RCT findings, contrasting with urologists' expert opinions. At the very least, the results of these RCTs do not provide definite evidence of what Dr Chadok says. It is urologists who advocate for prostate cancer screening, assuming the responsibility to provide the conclusive evidence, rather than public health professionals [10]. Additionally, the SPCG4 RCT evaluating clinical cancer treatments demonstrated superior outcomes with surgery than with surveillance. Conversely, the ProtecT trial focused on screen-detected cancers revealed no advantage of surgery over radiation therapy or surveillance. Therefore, surveillance may be considered equivalent to no treatment, and radiation therapy comparable to placebo surgery. Thus, achieving a 10-year cancer-specific survival rate as high as 99%, with no significant disparities among treatment

Takeshi Takahashi MD, PhD
Health and Welfare Bureau
Kitakyushu city office
Jyonai 1-1
JP-803-8501 Kitakyushu
jazzy[at]kuhp.kyoto-u.ac.jp

arms, characterises the natural progression of screen-detected cancer, analogous to that of normal tissue [11].

Therefore, from PSA thresholds and T1c categories to pathological findings like Gleason score, biomarkers such as PHI, 4Kscore, Stockholm3, etc, as well as imaging modalities including ultrasound and MRI, and treatment modalities such as surgery, radiation therapy and surveillance therapy – all aspects of clinical practice concerning prostate cancer screening remain empirical and experimental. Furthermore, these clinical studies predominantly constitute case series lacking a control group, precluding comparative statistical analysis and detracting from their evidentiary value. Claims regarding the use of prognostic factors to stratify risk and mitigate the harms of overdiagnosis lack substantiation [1].

Prostate cancer diagnoses continue to rise, with 90% detected through screening [12]. Can we simply observe passively? Diagnosis and treatment approaches for prostate cancer have not been uniformly guided by scientific evidence, often relying on case series outcomes and expert opinions. While Switzerland lacks a national prostate cancer screening programme, the matter of insurance coverage warrants consideration. In countries with private insurance coverage, such as the United States and the United Kingdom, subjects are fully informed before undergoing PSA testing and subsequent treatment, with costs borne by either the subject or the study sponsor, posing no significant issues. In contrast, in nations with public health insurance systems, including many European countries, Japan and Australia, subjects may be less resistant to testing and treatment due to lower costs, potentially influenced by authorities promoting the scientific validity of PSA screening, though achieving inadequate shared decision-making [2]. Therefore, if research presented in this review by Würnschimmel and colleagues aims to mitigate the harms of PSA screening within a medically insured practice, ethical concerns under the Declaration of Helsinki may arise, alongside substantial national health economic implications. Urologists in Switzerland must reaffirm that prostate cancer screening remains an empirical clinical practice grounded in hypothesis, not evidence-based medicine (EBM), effectively communicating these points to the public, government health officials and ethics committees within their institutions.

**Potential competing interests**

The author has completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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