life-threatening PCa [1]. Risk assessment can be further refined by considering other factors such as age, race, family history, and prostate volume along with the PSA measurement [6]. It is becoming increasingly clear that a risk-adapted strategy for PCa screening is superior to a "one size fits all" approach [7]. Future studies will help to better define the optimal combination of variables for a customized PCa screening program.

Conflicts of interest: The author has nothing to disclose.

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Platinum Priority

Reply from Authors re: Stacy Loeb. Use of Baseline Prostate-Specific Antigen Measurements to Personalize Prostate Cancer Screening. Eur Urol 2012;61:875–6

David D. Ørsted[a,b], *Børge G. Nordestgaard*[a,b,c], *Gorm B. Jensen*[c], *Peter Schnohr*[c], *Stig E. Bojesen*[a,b,c,*]

[a] *Department of Clinical Biochemistry, Herlev Hospital, Copenhagen University Hospital, Denmark;* [b] *Faculty of Health Sciences, University of Copenhagen, Denmark;* [c] *The Copenhagen City Heart Study, Bispebjerg Hospital, Copenhagen University Hospital, Denmark*

We thank Loeb for the positive and insightful editorial [1] regarding our study on prostate-specific antigen (PSA) for long-term prediction of prostate cancer (PCa) incidence and mortality [2]. We fully agree that our data strongly support the use of personalized PSA screening rather than a "one size fits all" approach.

As also pointed out by Loeb, major strengths of our study include that screening for PCa is not recommended in Denmark and that, in subanalyses, we studied the period 1981–1995, before PSA testing was available in Denmark. Thus in our study, a diagnosis of PCa was not a result of PSA-based screening but rather was based on clinical symptoms leading to further examination and subsequent diagnosis. In addition, we were able to examine the association between PSA at first date of testing and PCa mortality. These factors add strength to the interpretation of our results by eliminating the influence of ascertainment bias, at least in 1981–1995. In this way, we could study the natural history between elevated PSA and PCa incidence and mortality.

The use of a baseline PSA measurement for personalized risk stratification is gaining support [3] and is already included in some PCa-screening recommendations [4]. Furthermore, previous results from randomized screening trials have shown that the use of screening intervals based on PSA levels allows detection of clinically significant cancers while reducing harmful effects of screening [5,6]. Our results support such a personalized approach, and we suggest that PSA levels at first date of testing can be used to stratify men into groups with different screening intervals (Fig. 1). Such a personalized screening strategy might reduce the number of unnecessary PSA measurements and, thus, the risk of overdiagnosis and treatment of latent PCa. It might also allow physicians to focus on high-risk individuals and hopefully ease the increasing unnecessary pressure on urology departments responsible for PCa patients.

Despite the common use of PSA in clinical practice worldwide, there is continued, and sometimes heated, debate regarding PSA-based screening. Recently, the US Preventive Services Task Force issued a recommendation against use of PSA for screening purposes in asymptomatic low-risk men [7]; this guidance is in line with recommendations in most European countries. However, in the past, PSA has been used differently in the United States compared to many countries in Europe. This may be due to cultural and economic factors influencing patients' and physicians' incentives to diagnose and treat PCa. A health system providing direct remuneration per service to physicians,

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* Corresponding author. Department of Clinical Biochemistry, Herlev Hospital, Copenhagen University Hospital, Herlev Ringvej 75, DK-2730 Herlev, Denmark. Tel. +45 3868 3843; Fax: +45 3868 3311.
E-mail address: stebo@heh.regionh.dk (S.E. Bojesen).

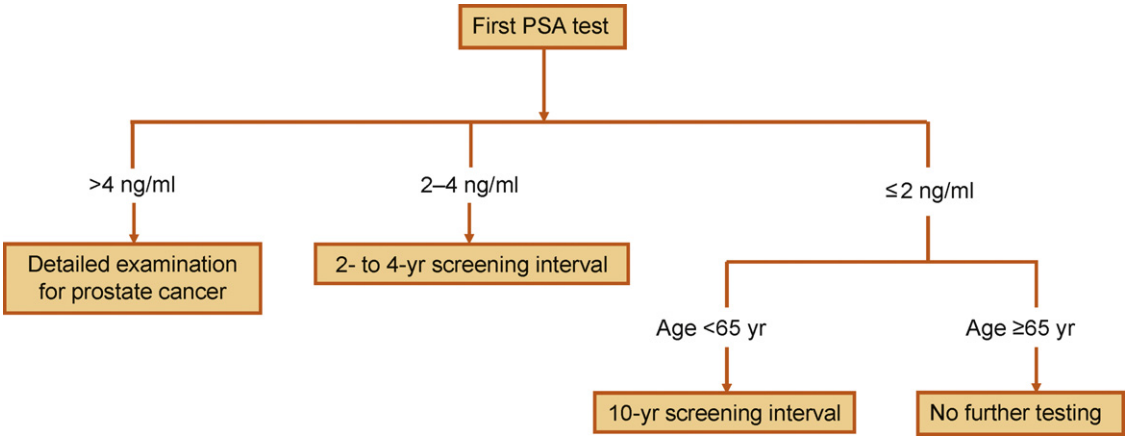

Fig. 1 – Algorithm for personalized prostate cancer (PCa) screening intervals for asymptomatic men based on plasma prostate-specific antigen levels and age at first date of testing. Based on absolute 10-yr risk of PCa incidence and mortality (Fig. 4 and 5 in [2]).
PSA = prostate-specific antigen.

as seen in the United States, may result in a more aggressive approach to finding and treating PCa. In addition, private insurance systems may allow some patients a more direct influence on screening practices. Conversely, systems using restrictive budget frames, as seen in many European countries, may lead to an insufficient use of PSA and subsequently to underdiagnosis and undertreatment of many PCa patients with aggressive cancers. A more personalized screening strategy, as supported by our data [2], might help combine the best parts of the two systems and hopefully result in a more balanced use of PSA testing in asymptomatic men.

Treatment of PCa has improved greatly over the past decade, and new treatment modalities continue to appear. However, to further balance the positive and negative effects of PSA screening, it appears that increased implementation of personalized active surveillance and watchful waiting has the potential to reduce overtreatment of men with more latent cancer, especially in men >70 yr of age, who are more likely to die from competing events than from PCa [8]. A combination of better personalized risk stratification and improved treatment strategies is likely to decrease the harms of PSA screening to the benefit of patients and health care systems.

Personalized risk stratification can possibly be further enhanced by the inclusion of yet other risk factors (eg, age and family history) as well as previous history of clinical benign prostatic hyperplasia [9]. These factors can be included in risk calculators used clinically [3]. In addition, PSA velocity, that is, the change of PSA concentration over time in an individual man, could have a role in long-term prediction of PCa incidence and mortality, but results have been conflicting [10]. Finally, it remains unclear whether and to what extent PSA measurements and risk estimates need to be corrected for genetic factors to enhance both predictive and diagnostic performance. Future well-designed studies are needed to improve the clinical use of what remains the most important tumor risk marker in clinical practice today.

Conflicts of interest: The authors have nothing to disclose.

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