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European Association of Urology

## Letter to the Editor

**Re: Jonas Hugosson, Monique J. Roobol, Marianne Månsson, et al. A 16-yr Follow-up of the European Randomized Study of Screening for Prostate Cancer. Eur Urol 2019;76:43–51**

### *Mortality in the Age Group ≥70 yr and the Case of Italy*

In their paper on prostate cancer (PCa) mortality and prostate-specific antigen (PSA) screening, Hugosson et al [1] conclude "Findings corroborate earlier results that PSA screening significantly reduces PCa mortality, showing larger absolute benefit with longer follow-up and a reduction in excess incidence. Repeated screening may be important to reduce PCa mortality on a population level." The patient summary states "... repeated screening reduces the risk of dying from prostate cancer".

Although both messages are formally correct, we disagree with their implications, resulting in a boost to measure PSA more often at the population level, regardless of age.

First, the rate ratio for PCa mortality was 0.80 at 16 yr, but a number of males, and maybe some doctors, might misunderstand, translating this to a 20% lower all-cancer mortality (or greatly overestimate the benefit in terms of cancer-specific mortality [2]) or even all-cause mortality. We know that PSA screening does not reduce all-cause mortality [3] and the ERSPC trial reconfirms this (rate ratio for all ages 0.99, 95% confidence interval [CI] 0.98–1.01) [1]. Why would a man aspire to not die from PCa if he understands that he could die from some other cause without any increase in his life expectancy? Indeed, in a randomized trial [4] primary care patients received an informed consent statement that included, among other information, "There is no evidence that having the test allows men to lead longer lives ..." (reconfirmed some 20 yr later) [1]. Informed men were much less likely to show high interest in screening (odds ratio 0.34, 95% CI 0.19–0.60) [4].

Second, all-cause and PCa mortality are not equally distributed: for men outside the core age group (summing ages 50–54 and ≥70 yr), published data allow calculation of a rate ratio of 1.0052171, which represents a nonsignificant increase in all-cause mortality. In the age group ≥70 yr, even PCa mortality tended to increase, with a rate ratio of 1.06 [1]. A strong message should be to stop screening men aged ≥70 yr rather than perform PSA testing more often.

Third, the data for Italy are particularly alarming. Among 14 515 participants over median follow-up of 15 yr, the PCa mortality rate ratio was 0.99 (95% CI 0.66–1.49), the number needed to invite to screening to prevent one PCa death was 44 232, and the number needed to detect PCa to prevent one PCa death was 673 [1], with a highly significant increase in PCa incidence, and thus in tests, visits, surgical, radiotherapeutic, and hormonal interventions, health consequences, and costs, without an overall benefit. These disappointing results (and the concept of all-cause mortality) should be clearly communicated to the population. Indeed, Italian males undergo PSA testing more frequently than women undergo mammography, although health authorities do not officially recommend PSA screening.

Fourth, the patient summary not only reiterates long-standing problems for complete informed consent but also undermines the opportunity costs. Decision-makers should consider the net results of any allocative intervention (treatment of men overdiagnosed via screening). The harms of displacing equivalent resources that could be used for other cost-effective interventions should also be deducted (and it is unlikely that PSA screening can be considered cost-effective, especially in the Italian health system).

There are many underused interventions for men's health with low costs per QALY that could be considered before promoting PSA screening. For example, a motivational interview or exercise prescription to increase physical activity [5] or a 5-min brief intervention plus self-help for smoking cessation [5] are at best orders of magnitude less expensive per QALY than very questionable screening.

***Conflicts of interest:*** The authors have nothing to disclose.

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Alberto Donzelli[a*]
Gianluca Castelluzzo[b]
Giulia Giudicatti[b]

[a]*Fondazione Allineare Sanità e Salute, Milan, Italy*
[b]*Department of Hygiene, Public Health and Preventive Medicine, University of Milano-Bicocca, Milan, Italy*

[*]Corresponding author. Fondazione Allineare Sanità e Salute, Via Carlo Giuseppe Merlo 3, Milan 20122, Italy.
E-mail address: adonzelli1@libero.it (A. Donzelli).

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