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Addressing uncertainty in PSA screening and testing intervals

Practice does not reflect evidence or guidelines

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Testing for prostate specific antigen (PSA) remains controversial, as reflected in clinical guidelines and different—and at times contradictory—recommendations. Testing, if recommended, is suggested for one of two indications: screening asymptomatic men to detect prostate cancer at an early stage amenable to curative treatment,[1] and diagnostic testing among men with symptoms potentially attributable to prostate cancer, such as haematuria, lower urinary tract symptoms, erectile dysfunction, low back pain, or weight loss. Notably, the National Institute for Health and Care Excellence (NICE) guideline does not recommend prostate cancer screening but rather sees its main role, alongside digital rectal examination, as a diagnostic test for men with symptoms or those considered at increased risk based on family history.[2]

Current guidelines disagree about whether screening has benefits that exceed harms. Guidelines recommending screening differ on age, PSA threshold for abnormality, and rescreening interval. Consensus is, however, growing that decision making about screening (and diagnostic testing) should be based on shared decision making that engages patients in conversations about benefits and harms, and their preferences and values for outcomes associated with the testing cascade. Indeed, almost no European country has population based screening programmes.[3]

While some guideline recommendations, such as those of the US Preventive Services Task Force, have changed over time, NICE guidelines have changed little since 2015 and focus on PSA testing for diagnostic purposes.[2 4] Importantly, and problematically, while the previously listed symptoms can occur in men with prostate cancer, other conditions such as benign prostatic hyperplasia, erectile dysfunction, and musculoskeletal back pain are more likely to be the cause of symptoms, with no strong association with a probable diagnosis of prostate cancer, and men with lower urinary tract symptoms are not at higher risk of prostate cancer than those without such symptoms.[5] Therefore, PSA testing in men with lower urinary tract symptoms or these other symptoms is screening by the "back door," but with poorer diagnostic yield. The concern is that false positive results lead to downstream consequences, including repeat PSA testing, magnetic resonance imaging, and biopsy, creating individual harms and burden as well as societal costs.

In a linked study, Collins and colleagues (doi:10.1136/bmj-2024-083800) evaluated the frequency and variability of primary care based PSA testing and retesting in England during 2000-19.[6] They found that testing increased fivefold during the study period, particularly in asymptomatic men and in those with values below age adjusted NICE referral thresholds.[2] Almost half of tested men underwent multiple tests, often without ever exceeding thresholds. Three quarters had no documented symptoms. Factors such as region, deprivation, ethnicity, age, family history, and symptoms substantially influenced testing and retesting intervals. Specifically, higher rates of PSA testing were observed in less deprived areas, although deprivation had a minimal effect on retesting intervals. Importantly, the highest testing rates occurred in men aged 70 and older, and a substantial portion occurred in men much younger (18-39 years) than recommended. Strengths of the study include its population based nature, likely capturing most testing over an extended period, as well as thorough analysis of retesting rates and association with previous PSA levels or symptoms. Limitations include the inability to link the reason for testing with symptoms in medical records.

A novelty of the paper lies in highlighting retesting rates—a more obscure area in guidelines. While no guidance on intervals exists in the UK, the American Urological Association recommends retesting every 2-4 years,[7] and the European Association of Urology states that 8-10 years may be offered to most men at low risk.[8] As 48% of men were retested with a median interval of 12.6 months and 73% of those with multiple testing never had raised PSA values, it seems that "annualised" screening was implemented, not following guideline protocols. Although repeated PSA testing might be helpful in men with a high baseline PSA level before biopsy,[9 10] repeating at shorter intervals leads to unnecessary biopsies and overdiagnosis.[11]

What are the take home messages? Firstly, the declining impact of national policies for PSA testing in England may have led to the substantial increase in testing frequency. Collins and colleagues attribute this to the influence of national celebrities publicly sharing their cancer diagnoses and advocating for screening. Interim changes in US Preventive Services Task Force recommendations from grade D in 2012 (against screening) to grade C (conditional for assuming shared decision making has taken place) in 2018 may have influenced practices as the world becomes increasingly interconnected.[12] Secondly, it speaks to the importance of "back door" PSA testing in men presenting with lower urinary tract symptoms or other symptoms poorly associated with prostate cancer, which is not supported by research evidence. This issue is relevant given the high prevalence of lower urinary tract symptoms, erectile dysfunction, and other symptoms in older men. Prostate cancer testing in men with these symptoms (especially those

in their 70s and 80s) results in considerable harms, overdiagnosis, overtreatment, and financial, resource, and opportunity costs, with little to no benefit. The authors noted that at most, randomised screening trials found small long term reductions in prostate cancer among generally healthy men aged 55-69. Men outside these ages and men with serious comorbidities were typically excluded from trials owing to the high likelihood that harms would exceed benefits. Thirdly, PSA testing in primary care does not closely follow randomised trial evidence or guidelines and likely results in net harm. Reasons for this are complex but include competing demands of primary care clinicians addressing patient, caregiver, and health system priorities in time focused visits, lack of knowledge of the predictors for prostate cancer or randomised trials' findings, advocacy sponsored initiatives supporting testing, and concern about underdiagnoses or missed diagnoses. Reducing low value care in older men and among men in their 20s and 30s should be a high priority initiative for practice improvement.[13] Doing so will require considerable efforts but would improve patients' health.

The major concern raised by Collins and colleagues' study and similar studies is that unregulated PSA testing will result in large costs and harms and increase the incidence of prostate cancer likely to remain undetected, while doing little to identify prostate cancer most likely to cause symptoms and death.[1] We welcome the European Commission's interest in population based cancer screening including prostate cancer. However, efforts need grounding in high quality evidence gleaned from randomised trials.[13] Collins and colleagues' study highlights the need for better NICE guidance, especially in men outside of recommended ages or men with lower urinary tract symptoms, erectile dysfunction, or other conditions unrelated to prostate cancer.

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