

Prostate cancer screening in low- and middle- income countries: the Mexican case

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Abstract

Prostate-specific antigen (PSA)-based early detection for prostate cancer is the subject of intense debate. Implementation of organized prostate cancer screening has been challenging, in part because the PSA test is so amenable to opportunistic screening. To the extent that access to cancer screening tests increases in low- and middle-income countries (LMICs), there is an urgent need to thoughtfully evaluate existing and future cancer screening strategies to ensure benefit and control costs. We used Mexico's prostate cancer screening efforts to illustrate the challenges LMICs face. We provide five considerations for policymakers for a smarter approach and implementation of PSA-based screening.

Keywords: early detection of cancer; prostate; early diagnosis

Resumen

El uso del Antígeno Prostático Específico (APE) para tamizaje para cáncer de próstata sigue siendo tema de amplio debate. La implementación de estrategias de tamiz organizado de cáncer de próstata ha sido un reto en parte porque la prueba de APE se presta para detección oportunista. A medida que aumenta el acceso a las pruebas de detección de cáncer en los países de ingresos bajos y medianos (PIBM), existe la necesidad urgente de evaluar cuidadosamente las estrategias actuales y futuras de detección oportuna de cáncer para garantizar su beneficio y controlar sus costos. Utilizamos los esfuerzos de tamizaje de cáncer de próstata de México para ilustrar los retos para PIBM. Ofrecemos cinco consideraciones dirigidas a tomadores de decisión que permitan contar con estrategias racionales de implementación de tamizaje para cáncer de próstata basado en el uso de APE.

Palabras clave: detección precoz del cáncer; próstata; diagnóstico precoz

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International organizations consider prostate cancer screening low-priority and provide minimal guidance on implementation for low- and middle-income countries (LMICs).¹ While seeking strategies to increase prostate cancer screening access, LMICs may rely on recommendations that may not be transferable to their settings and seek cost-cutting strategies with suboptimal health benefits. We used Mexico's prostate cancer screening efforts to illustrate the challenges LMICs face and, although not completely transferable, provide considerations to be made by policymakers.

PSA-based early detection for prostate cancer is the subject of an intense debate. Implementation of organized prostate cancer screening has been challenging, in part because the PSA test is so amenable to opportunistic screening. In the US, younger men (i.e. 50-54 years) have been under-screened while older men have been screened without considering life-expectancy. The widespread adoption of the threshold of a 4 ng/mL PSA independent of age or other risk factors led to clinically significant tumors being missed, while also prompting substantial follow-up testing for clinically irrelevant disease or benign conditions.² The "normal" PSA level is much <4 ng/mL. Robust prospective data show that median PSA levels in men in their 40s and 50s are below 0.9 ng/mL and that a threshold ≥ 1.0 ng/mL in men aged 40-54 years would identify a large majority of aggressive cancers.^{3,4} Thus, men aged 40-49 years with PSA levels below 0.68 ng/mL could safely forgo repeated screening for a decade. There is growing agreement that PSA-based early detection of high-risk disease reduces prostate cancer mortality and with a smarter PSA-based screening approach the potential harms of screening could be avoided.

The Global Burden of Disease study ranks prostate cancer as the leading cause of cancer mortality in Mexican men (age standardized mortality=19 per 100 000), while increased public awareness and the ease of PSA testing have placed prostate cancer as a public health priority. Currently, the major publicly funded insurance schemes (covering 85% of the population) offers full treatment coverage for prostate cancer. Late in 2017, health authorities in Mexico published a legally binding national prostate cancer screening guideline stating that all Mexican men ≥ 45 years should be screened using digital rectal examination and PSA (men with a family history of prostate cancer should begin at age 40).⁵ Implementation of this recommendation would require regular screening of more than 15 million Mexican men in an already under-resourced healthcare system. The controversial feature of this guideline is underscoring ≥ 4 ng/mL PSA as the threshold for early detection of prostate cancer, with the additional endorsement of capillary

blood *qualitative* PSA test based on this threshold.⁶ Only when PSA is ≥ 4 ng/mL will the *qualitative* test read "positive," a result that, according to the guideline, should indicate a subsequent confirmatory quantitative PSA test. The use of this *qualitative* test may appear to be of lower cost and increase access to screening. However, as noted above the *qualitative* test ignores our current knowledge of prostate biology. Clearly a one-size-fits-all construction of PSA as a binary variable is suboptimal for a population with mixed age and genetic risk, and use of a *qualitative* test may result in high proportion of false negatives in men with high-risk disease and increase health costs rather than lower them.

Consideration 1. Screen for prostate cancer only after careful evaluation of availability of infrastructure for counseling, and referral for diagnosis and treatment

Effective cancer screening requires access to diagnostic tests, optimal treatment, and adequate clinical follow-up. In LMICs, these downstream factors need to be considered with care due to often fragmented and under-resourced health systems. In this setting, national screening program for prostate cancer may not be feasible. Targeting specific geographic areas where infrastructure is adequate may be a first step to develop and validate national organized cancer screening programs.

Consideration 2. Interpret PSA levels according to age

The interpretation of a PSA differs according to age. A 45-year-old man with a PSA of 3.8 ng/mL is at high risk for developing aggressive prostate cancer. In contrast, this same PSA level in a 75-year-old man is likely to be the result of a benign condition or low-risk for prostate cancer. Applying this threshold without considering age and/or using a *qualitative* test based on this threshold, may result in false negatives in men with high-risk disease, particularly in younger men.

Consideration 3. Screen younger men and screen less often to ensure the largest benefit

PSA performs better in younger men because of the lower prevalence of benign conditions that increase PSA. Also, younger men have the most life-years to gain from early detection of aggressive prostate cancer. Considerations should be made to focus screening efforts in relatively young men (e.g. <60 years). As mentioned

above, men with low PSA levels could potentially forgo frequent testing lowering the cost of the screening program, the burden on the healthcare system, and averting potential overtreatment.

Consideration 4. Collect data for health outcomes research on prostate cancer for effective policy-making

Recommendations on prostate cancer screening are constantly evolving and monitoring and evaluating downstream outcomes is essential to guide policy changes. Joining international efforts to standardize the measurement and reporting of prostate cancer patient outcomes (i.e. International Consortium of Health Outcomes Measurement) and to model prostate cancer screening strategies (i.e. Cancer Intervention and Surveillance Modeling Network) could provide policymakers with high quality locally-based decision making tools.

Consideration 5. Increase prostate cancer awareness through education

Health-related decision-making may be challenging for men living in LMICs because of limited access to prostate cancer information. National and international organizations should engage in population-based strategies and educational programs to improve cancer knowledge and awareness at early ages.

Effective cancer screening policy not only requires robust evidence but an understanding of healthcare structure and capacity as well as health awareness. As access to cancer screening tests increase in LMICs there is an urgent need to thoughtfully evaluate existing and future cancer screening strategies to ensure benefit and control costs in limited resource settings.

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Declaration of conflict of interests. The authors declare that they have no conflict of interests.

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