Letters to the Editor

Testosterone Replacement Therapy for Male Hypogonadism

To the Editor: In their review of testosterone replacement therapy for male hypogonadism,[1] Drs. Heidelbaugh and Belakovskiy noted that testosterone replacement therapy has been shown to increase bone mineral density. However, a recently published secondary analysis of the TRAVERSE trial provides important additional context.[2] In this large, randomized trial, testosterone therapy was associated with a statistically significant increase in the primary fracture outcome, with similar results in several sensitivity analyses and secondary outcomes. Although the mechanism for this increase is unknown, the effect could be mediated by behavioral changes (eg, increased participation in activities associated with fracture risk) in men randomized to testosterone rather than through a biologic effect on bone tissue.[3] However, this analysis provides an important reminder that a positive effect on a disease-oriented outcome (eg, bone mineral density) does not guarantee a favorable effect on the corresponding patient-oriented outcome (eg, fractures). Discussion of possible increased fracture risk should be part of the shared decision-making process with men considering testosterone replacement therapy.

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Editor's Note: This letter was sent to the authors of "Testosterone Replacement Therapy for Male Hypogonadism," who declined to reply.

Doxy PEP and Anal Cancer Screening for Men Who Have Sex With Men

To the Editor: We appreciate the recent article on preventive care for men who have sex with men (MSM).[1] It sheds light on crucial aspects of health maintenance for this key demographic. However, the article could have delved deeper into two specific areas: doxycycline postexposure prophylaxis (doxy PEP) and the updated anal cancer screening guidelines of the International Anal Neoplasia Society.

Doxy PEP is an emerging intervention for the prevention of sexually transmitted infection (STI) and has the potential to significantly reduce the risk of gonorrhea, chlamydia, and syphilis, particularly among MSM and transgender women. The regimen consists of a single 200-mg dose of doxycycline taken up to 72 hours after unprotected sex. A trial of doxy PEP in the United States found a substantial decrease in the incidence of STIs among MSM and transgender women, with a remarkable 67% reduction in all STIs and an 88% reduction in chlamydia.[2] Additionally, the DOXYVAC trial and other studies further validate the effectiveness of doxy PEP, showing significant reductions in STI incidence among MSM receiving HIV preexposure prophylaxis.[3] The US Centers for Disease Control and Prevention has published guidelines on appropriate use of doxy PEP for at-risk populations.[4]

Recent updates to the anal cancer screening guidelines of the International Anal Neoplasia Society add crucial insights into early detection and prevention strategies for anal cancer, especially for MSM and transgender women. The guidelines recommend initiating screening at 35 years of age in MSM and transgender women with HIV; other HIV-positive patients and MSM and transgender women without HIV should be screened beginning at 45 years of age. Screening can be performed via anal cytology with or without cotesting for high-risk human papillomavirus.[5] The guidelines are supported by multiple large studies, most notably the 2022 Anal Cancer HSIL Outcomes Research trial, which conclusively showed that treatment of high-grade anal precursor lesions significantly decreases incident anal cancer events.[6]

Family physicians should discuss doxy PEP and anal cancer screening with eligible MSM to improve long-term health outcomes for these patients.

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In Reply: We thank the authors for their letter regarding doxy PEP and anal cancer screening guidelines as outlined by the International Anal Neoplasia Society. These topics are very important, and we agree with their conclusion that the family physician who cares for eligible MSM and transgender women in their practice should be aware of these resources.

We acknowledge that doxy PEP has shown a risk reduction for the common bacterial STIs of chlamydia, gonorrhea, and syphilis. We do acknowledge awareness at the time of drafting our article of this strategy, and the referenced studies demonstrate reduced incidence of the target STIs when using doxycycline appropriately as PEP.[1,2] As of June 6, 2024, there are published guidelines on the use of doxy PEP by Bachmann, et al.[3] These guidelines clearly outline patients who would most benefit from doxy PEP and the implementation strategies. We agree that doxy PEP appears to be a relatively safe and effective strategy that the family physician can discuss with their patient when appropriate.

We used the International Anal Neoplasia Society guideline reference from 2019 for our recommendations in the article.[4] We acknowledge the new guidelines published in May 2024,[5] although the new guidelines would not change the age recommended for screening MSM with HIV (35) and would lower the age for screening MSM without HIV from 50 to 45. The recommended screening strategy for MSM without HIV should include the digital anal rectal examination and anal cytology with consideration for high risk human papillomavirus testing.[5]

We appreciate this updated information and agree that the family physician caring for MSM and transgender women should be knowledgeable and able to discuss doxy PEP and current screening guidelines with their patients.

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Questionnaires Enrich Care Conversations

To the Editor: In their recent editorial, Thombs, et al., explained why they disagree with the US Preventive Services Task Force (USPSTF) recommendation to screen adults for anxiety with questionnaires.[1] The USPSTF recommendation statement is based on a systematic review that likewise describes physicians having limited time during primary care visits to discuss anxiety issues with patients.[2]

We draw the opposite conclusion. Given limited physician time with patients, screening questionnaires provide clinical benefit backed by good evidence and have been recommended for a variety of wellness encounters.[3,4] Patients may not recall all of their concerns in the examination room, but questionnaires can be completed in advance of their office visit. Furthermore, some patients are more comfortable reporting issues in a questionnaire than during a face-to-face encounter with their physician.

Thombs, et al., also advocate that time is better spent on a focused, in-depth discussion as opposed to administration and interpretation of a questionnaire. Indeed, a complete diagnostic mental health assessment is ideal but often not possible or necessary, and understanding the degree and temporality of anxiety may make reassurance and a tincture of time the best remedy. However, one cannot have it both ways: a focused discussion is not as feasible without the guidance of a questionnaire. Primary care clinicians are well-placed to initiate such conversations.

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In Reply: It is the task of screening guideline developers to carefully review evidence and recommend screening only when there is credible evidence of sufficient benefit to justify resources and harms incurred. These recommendations should rely on well-conducted randomized controlled trials (RCTs) when such trials are feasible, as is the case with questionnaire-based screening for anxiety.[1] The USPSTF guideline did not meet this standard, and suggesting that others also recommend using screening questionnaires does not constitute evidence.

Untreated anxiety is a critical problem in patient health care, but there is no evidence that the addition of screening to already time-constrained primary care visits saves time or improves care. The USPSTF recommendation cited two trials that enrolled patients who had already received positive screening results for anxiety with only triage and treatment to implement, yet neither showed improvement in health outcomes.[2]

Members of our author group previously reviewed USPSTF, Canadian Task Force on Preventive Health Care (CTFPHC), and United Kingdom National Screening Committee (UKNSC) questionnaire-based screening guidelines, which were all based on systematic reviews.[3] However, we did not find any trials among these that randomized patients to be screened, provided participants in screened and unscreened trial arms with similar care options when identified as needing care, and determined that screening improved health outcomes. The CTFPHC and UKNSC have consistently recommended against questionnaire-based screening; the USPSTF recommends questionnaire-based screening for unhealthy use of alcohol and drugs, intimate partner violence, depression, and anxiety, all without RCT evidence of benefit and despite several well-conducted, large RCTs that did not find benefit.[3]

The hypothesis that screening may be better than standard care due to time constraints, or because patients might forget to discuss some of their health concerns once with their doctor, is unsupported by evidence. Unlike subclinical conditions like early-stage cancer, patients are very aware of their anxiety and can be forthcoming about their symptoms.

A major reason the United States spends more on health care than other high-income countries and achieves worse outcomes is the provision of low-value and no-value health services.[4] The USPSTF's questionnaire-based screening recommendations contribute to this problem by reducing the time physicians have to provide effective care and adding to documentation and compliance burdens without demonstrated benefits.[5]

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