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TO THE EDITOR: We applaud the recent modeling study by Walensky et al. (Oct. 31 issue) as a compelling argument that, in principle, human immunodeficiency virus (HIV) treatment as prevention is cost-effective. However, the authors model only first- and second-order transmissions, thereby ignoring the dynamics of the full sexual network. Recent studies have shown that this modeling approach overestimates the effect of treatment as prevention, because many infections come from other parts of the network.\textsuperscript{2,3}

Using the same assumptions regarding the effectiveness of antiretroviral therapy (ART) as Walensky et al., we reran our simulation model of the South African HIV epidemic, STDSIM, which includes detailed sexual-network dynamics.\textsuperscript{3} We predict that, on a population level, treatment as prevention for serodiscordant couples would prevent 12\% of new infections in South Africa after 5 years, whereas treatment as prevention for all HIV-infected people (90\% coverage) would prevent 25\% of new infections (Fig. 1). Both values are much lower than the 69\% predicted by Walensky et al.

To maximize the effects of ART, policymakers require a comprehensive analysis of both treatment and prevention benefits. This is where traditional cohort models for cost-effectiveness analyses, such as the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) model,\textsuperscript{1} fall short.

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No potential conflict of interest relevant to this letter was reported.


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THE AUTHORS REPLY: There are several important differences between the CEPAC and STDSIM models, any one of which could account for our finding of more HIV cases prevented than in the analysis presented by Hontelez and de Vlas; two
are highlighted. First, we concentrate on serodiscordant couples in long-term partnerships (the target population of the HIV Prevention Trials Network 052 study); Hontelez and de Vlas simulate a generalized epidemic. Second, we focus on patients who are already identified and in care (treatment as prevention). In contrast, Hontelez and de Vlas describe an analysis of a test-and-treat strategy in which a patient’s choice not to undergo HIV testing, an inadequate linkage to care, and a lack of initiation of ART would all attenuate the intervention effect.

We respectfully disagree with the suggestion that by restricting attention to first- and second-order transmissions we failed to account for a substantial number of downstream infections. As noted in Table 2 of our article and in Figure S2 in the Supplementary Appendix (available with the full text of our article at NEJM.org), even second-order infections had no material effect on our findings over a period of 5 years. Projections beyond second-order infections in serodiscordant couples require assumptions about the future (e.g., ART efficacy, loss to follow-up, and sexual behavior) that are well beyond the trial data and unnecessary to reach our critical policy conclusions.

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Since publication of their article, the authors report no further potential conflict of interest.

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Circulatory Shock

TO THE EDITOR: In their review of circulatory shock, Vincent and De Backer (Oct. 31 issue) report that hypoperfusion can be apparent through the skin (cold extremities), the kidney (low urinary output), and the brain (altered mental state). We believe that the liver should also be included in this list of key organs that are markers of shock. In cardiogenic shock, in which hypoperfusion is usually associated with increased central venous pressure, hepatomegaly can be clinically apparent by palpation, and abdominal discomfort due to stretching of the liver capsule may be a symptom. There is often an increase in levels of conjugated bilirubin, alkaline phosphatase, and aminotransferases that mimics the increase observed in cholelithiasis. Alteration of coagulation can be present with an increase in the international normalized ratio. This cardio–hepatic interaction in shock generally results in the so-called hypoxic hepatitis or acute cardiogenic liver injury and has important prognostic implications. Can the authors comment on hepatic dysfunction as an indicator of shock?

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TO THE EDITOR: In their initial assessment of shock states, the authors do not reference the obtaining of an electrocardiogram (ECG) in the algorithm presented. The ECG is critical in evaluating a patient with circulatory shock and may