Bacterial vaginosis (BV) is characterized by a vaginal microbiota low in lactobacilli; it affects one-quarter to one-third of reproductive-age cisgender women. Approximately one-half of cases are symptomatic, with abnormal vaginal discharge and/or amine or fishy vaginal odor. BV contributes to adverse sexual and reproductive outcomes, including HIV and/or sexually transmitted infection (STI) acquisition and preterm birth, and symptoms can negatively impact psychosocial well-being and sexual satisfaction. The BV treatment landscape has not appreciably changed in decades: in the US, metronidazole and clindamycin are recommended as first-line treatments for symptomatic BV, and secnidazole and tinidazole are used as alternatives. Although these treatments are effective in the short term, up to 60% of women experience BV recurrence within 1 year of treatment. Some have frequent recurrences, and options are limited for these individuals and may involve onerous suppressive regimens with twice-weekly application of intravaginal antibiotics for extended time periods. Suppressive vaginal metronidazole fails for 25% of patients and leads to secondary vulvovaginal candidiasis (VVC) in up to 40%, and many patients have BV recurrence after stopping suppressive therapy.

It is imperative that we expand the toolkit of available BV treatments. Alternatives that are at least as effective as nitroimidazoles and clindamycin would be welcome additions. Treatments that effect a lasting cure would be paradigm-shifting.

One option may be dequalinium chloride (DQC), a locally delivered antiseptic with broad antibacterial and antifungal activity. Its antibacterial activity is attributed to interaction with the bacterial cytoplasmic membrane and perturbation of cellular permeability, protein denaturation and subsequent alteration of ribosomal protein synthesis, and nucleic acid precipitation. A prior trial reported that intravaginal DQC was noninferior to intravaginal clindamycin for BV treatment (discussed later), motivating Raba and colleagues to evaluate its efficacy vs metronidazole. In a European, phase 4, multicenter, triple-blinded, randomized trial including 147 women, Raba et al found that intravaginal DQC (10 mg tablet daily for 6 days) was noninferior to oral metronidazole (500 mg twice daily for 7 days) for treating BV defined by all four Amsel criteria. Clinical cure rates in both groups were 92.8% to 93.2% upon completing treatment, and DQC tolerability was significantly higher than for metronidazole. Notably, 27.9% of participants had a Nugent score of 3 or lower at enrollment (indicating non-BV microbiota) despite all 4 Amsel criteria being present; although there is some variation in the literature, this discrepancy is greater than the approximately 10% reported in a sentinel study. However, these participants were evenly distributed across groups.

The trial by Raba et al is the second to compare DQC with standard-of-care BV treatment. In 2012, Weissenbacher and colleagues reported that intravaginal DQC was noninferior to intravaginal clindamycin (2% cream for 7 days) in a trial of 315 participants. Like Raba et al, they enrolled women presenting with 4 Amsel criteria from multiple European clinical sites. Clinical cure rates for DQC and antibiotic groups at early and late time points were somewhat lower than in the trial by Raba et al, which may reflect slightly different clinical cure definitions and outcome assessment timing (7 and 20-40 days after starting treatment for Raba et al and 7 and 25 days after completing treatment for Weissenbacher et al). It is encouraging that both trials demonstrated noninferiority using the same 15% noninferiority margin and showed 75% to 80% clinical cure up to 5 weeks after DQC.
Likewise, in a case series of Spanish women receiving DQC for BV, 84.8% self-reported symptom resolution 4 to 6 weeks after treatment; clinical and microbiologic outcomes were not available.³⁸

Collectively, these data suggest DQC could be a viable BV treatment. Intravaginal DQC is not approved by the US Food and Drug Administration, but it is available in much of Europe, where it has been used in BV care for several decades.⁴ It is recommended as alternative or second-line BV treatment in guidelines from the International Union Against STIs; World Health Organization; International Society for the Study of Vulvovaginal Disease; and the Austrian, German, Portuguese, Spanish, and Swiss Societies of Gynecology and Obstetrics. To our knowledge, the Polish Society of Gynecologists and Obstetricians issued the only guidelines recommending DQC as first-line treatment. However, the evidence supporting its use is limited, and we will highlight 3 important gaps.

First, both completed trials comparing DQC with standard-of-care BV treatment (those by Weissenbacher et al⁵ and Raba et al⁶) were conducted in Europe. Vaginal microbiota composition and response to antibiotic BV treatment may vary over geographic regions.⁹ Response to DQC may be similarly heterogeneous, so its efficacy must be evaluated in various global populations.

Second, long-term data on post-DQC BV recurrence are sparse. Weissenbacher et al⁵ observed declining clinical cure rates from 1 to 4 weeks after treatment, but DQC remained noninferior to clindamycin at both time points (DQC clinical cure rates of 79.7% and 74.8%, respectively). Raba et al⁶ similarly reported lower clinical cure rates for both groups at 2 to 5 weeks after treatment vs at treatment completion. Although the DQC group showed 79.7% clinical cure at the later time point, results indicated DQC was inferior to metronidazole at 2 to 5 weeks.⁶ In subgroup analysis considering participants with BV by Nugent score (7-10) at enrollment, DQC was noninferior to metronidazole upon completing treatment, with a cure rate of 94.6%, but inferior 2 to 5 weeks later, with a clinical cure rate of 75.7%.⁶ These 1-month data are informative; however, postmetronidazole recurrence nearly doubles from 1 to 3 months.⁷ It is unknown whether recurrence patterns are similar following DQC, and longer-term data are critical to inform its use vs nitroimidazoles and clindamycin.

Third, there are limited data on the safety of intravaginal DQC during pregnancy. In 2 trials, placental dysfunction at 16 weeks' gestation and early pregnancy loss were lower among those receiving DQC vs intravaginal povidone-iodine during their first trimester.⁴ These data only represent 66 DQC-exposed and 70 povidone-iodine–exposed pregnancies, and they lack standard-of-care comparators.⁴

Robust clinical trials are needed to fill these gaps. Accordingly, Haydock and colleagues are currently enrolling participants into the UK-based Dequalinium Versus Usual Care Antibiotics for the Treatment of Bacterial Vaginosis (DEVA) trial, a multicenter, randomized, open-label, noninferiority trial of DQC vs standard-of-care antibiotics for BV. Follow-up will last 3 months and generate longer-term recurrence data than prior trials. Pregnant individuals are eligible for DEVA, expanding available data on DQC safety during pregnancy. Additional trials are still needed to evaluate DQC's efficacy vs antibiotics in various global populations.

If DQC is shown to effect a more lasting cure than current first-line antibiotics, it could mark a major advancement. However, if research continues to demonstrate that DQC is at least comparable to current treatments, it could still be a useful addition to the BV management toolkit for several reasons. As an intravaginal tablet, systemic DQC exposure is negligible, and systemic adverse effects are rare,⁴ which are advantages over current oral regimens. Some individuals may also prefer tablet formulation to intravaginal creams or gels. Because DQC is a broad-spectrum antiseptic, resistance may be less of a concern than with antibiotics.⁴ Furthermore, DQC's antifungal activity could help prevent secondary VVC, which many women develop following antibiotic BV treatment. The trial by Weissenbacher et al⁵ showed more secondary VVC cases among the clindamycin group than the DQC group, and a trial conducted in Thailand found that DQC was noninferior to clotrimazole for resolving VVC signs and symptoms.¹⁰ Finally, nitroimidazoles and/or clindamycin are contraindicated for some individuals, and DQC could provide an additional option in these cases.
Recent years have seen growing investment in developing innovative BV treatments, including live biotherapeutic products and vaginal microbiome transplantation. These are in the early stages of development, and bringing them to market will be costly and slow. In contrast, the trial by Raba et al.\(^5\) and others indicate that DQC could be a viable, well-tolerated alternative BV treatment that warrants further investigation.