GOOD EVIDENCE MATTERS

GEMs of the Week

SPOTLIGHT

More Apnea, Less Problems: Tirzepatide for Moderate-to-Severe Sleep Apnea

It's Not Just Her Problem:
Bacterial Vaginosis Treatment for Him

A Shot At Prevention!

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More Apnea, Less Problems: Tirzepatide for Moderate-to-Severe Sleep Apnea

Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

Malhotra A, Grunstein RR, Fietze I, et al. Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity. *N Engl J Med.* 2024;391(13):1193-1205. doi:10.1056/NEJMoa2404881

KEY TAKEAWAY: Tirzepatide reduces sleep apnea events in patients with moderate-to-severe obstructive sleep apnea (OSA) and concurrent obesity.

STUDY DESIGN: Two randomized, multi-centered, placebo-controlled, phase 3 trials

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: There are no FDA-approved medications indicated for OSA treatment. Standard of care includes use of continuous positive airway pressure (CPAP) and interventions targeting weight loss. This study aimed to assess the efficacy and safety of tirzepatide as a pharmacologic option for moderate-to-severe OSA with concurrent obesity.

PATIENTS: Adults with moderate-to-severe OSA and obesity

INTERVENTION: Tirzepatide

CONTROL: Placebo

PRIMARY OUTCOME: Change in apnea-hypopnea index (AHI)

Secondary Outcome: Sleep-disordered breathing-related end points, cardiovascular risk factors

METHODS (BRIEF DESCRIPTION):

- SURMOUNT-OSA consisted of two similarly structured trials that differed only by the participant population: Trial one (T1) studied participants unable or unwilling to use CPAP and trial two (T2) studied participants who used CPAP for at least three months prior to screening.
- T2 participants were instructed to cease use of CPAP seven days prior to sleep study to lower risk for confounding.
- Inclusion criteria included patients with moderate to severe OSA (AHI >15 events/hour) and obesity with body mass index of >30
- Exclusion criteria included patients with a diagnosis of type 1 or type 2 diabetes, any self-reported change in body weight >5 kg in the three months pre-screening, those planning for surgery to treat sleep apnea or obesity, a diagnosis of central or mixed sleep apnea, and those with major craniofacial abnormalities.
- Participants were randomized 1:1 to receive tirzepatide (titrated up to 10 mg or 15 mg) or placebo group via once weekly autoinjector pen.
- Participants underwent non-pharmacologic intervention with diet and lifestyle, including maintaining an intake deficit (at least 500 kcal/day) and completing physical activity (at least 150 minutes per week).
- The primary outcome was measured by change in AHI score from baseline confirmed by polysomnography.
    - AHI measures the number of apneas and hypopneas during an hour of sleep that are categorized as:
        - Normal: <5 events per hour
        - Mild: 5–14.9 events per hour
        - Moderate-to-severe: >15 events per hour
- The secondary outcomes were measured using the following:
    - Sleep-disordered breathing-related end points: Percent change in AHI, percent reaching AHI reduction of >50%, percent reaching AHI score of <5 OR AHI score 5–14 and Epworth Sleepiness Scale (ESS) score of <10, sleep apnea-specific hypoxic burden.
    - Cardiovascular risk factors: Percent change in body weight, change in systolic blood pressure (SBP), change in high-sensitivity C-reactive protein (hsCRP) concentration, change in Patient-Reported Outcomes Measurement Information System (PROMIS) Short Form Sleep-related Impairment 8a (PROMIS-SRI) and PROMIS Short Form Sleep Disturbance 8b (PROMIS-SD).

INTERVENTION (# IN THE GROUP): 234

COMPARISON (# IN THE GROUP): 235

FOLLOW-UP PERIOD: 52 weeks

RESULTS:

Primary Outcome –

- Tirzepatide reduced AHI compared to placebo.
  - T1: (between-group difference –20; 95% CI, –26 to –14)
  - T2 (between-group difference –24; 95% CI, –30 to –18)

Secondary Outcome –

- Tirzepatide resulted in greater percent change of AHI compared to placebo.
  - T1 (between-group difference –48; 95% CI, –66 to –30)
  - T2 (between-group difference –56.2; 95% CI, –74 to –39)
- Tirzepatide resulted in more participants reaching AHI reduction of >50% compared to placebo.
  - T1 (relative risk [RR] 3.3; 95% CI, 2.1–5.1)
  - T2 (RR 3.1; 95% CI, 2.1–4.5)
- Tirzepatide resulted in more participants reaching AHI score of <5 OR AHI score 5–14 and ESS score of <10 compared to placebo.
  - T1 (RR 2.9; 95% CI, 1.8–4.8)
  - T2 (RR 3.3; 95% CI, 2.0–5.4)

LIMITATIONS:

- Since tirzepatide was an FDA-approved medication for weight loss, it becomes difficult to conclude that tirzepatide has an impact directly on OSA vs indirect benefit from weight loss.
- Tirzepatide arm would eventually start losing weight making blinding difficult to maintain.
- This study included participants with a body mass index (BMI) >30; however, following obesity treatment guidelines, expanding BMI to include participants with BMI >27 with one weight-related comorbidity would be appropriate as current study would represent a gap in that population.

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It's Not Just Her Problem: Bacterial Vaginosis Treatment for Him

Male-Partner Treatment to Prevent Recurrence of Bacterial Vaginosis

Vodstrcil LA, Plummer EL, Fairley CK, et al. Male-Partner Treatment to Prevent Recurrence of Bacterial Vaginosis. *N Engl J Med*. 2025;392(10):947-957. doi:10.1056/NEJMoa2405404

KEY TAKEAWAY: Treating male partners of women with bacterial vaginosis (BV) with oral metronidazole and topical clindamycin reduces the 12-week recurrence rate of BV compared to treating women alone.

STUDY DESIGN: Multicenter, open-label, randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: BV is common in pre-menopausal women and there is high recurrence rate after treatment. BV organisms have been shown to pass between sexual partners. Treatment of partners in past trials have not shown benefits, but this may have been related to poor treatment adherence and ineffective treatment regimens. This study compared recurrence rates of BV after treating male partners compared to standard therapy.

PATIENTS: Premenopausal women with BV receiving standard treatment

INTERVENTION: Male partner received oral metronidazole and topical clindamycin

CONTROL: No treatment for male partner

PRIMARY OUTCOME: Recurrence of BV within 12 weeks

Secondary Outcome: Recurrence of BV within four weeks, a Nugent score (NS) of 7–10 within four weeks and 12 weeks

METHODS (BRIEF DESCRIPTION):

- Women ≥18 years old with symptomatic BV with three of four Amsel Criteria (AC) and NS of 4–10 in monogamous heterosexual relationships for ≥8 weeks were enrolled at five health facilities across three Australian states: Two offered sexual health services and three offered family planning services.
  - AC: Characteristic discharge, vaginal pH >4.5, positive amine test, and clue cells.
  - NS: Microscopic evaluation of bacterial morphology or quantity, 0–3 is normal, 4–6 intermediate dysbiosis, 7–10 is consistent with BV.
- Couples were eligible to participate if male partner could enroll within a week after their partner.
- Sex workers and patients with HIV were excluded.
- All women received 400 mg metronidazole tablets twice daily for seven days, intravaginal 2% clindamycin cream for seven nights, or intravaginal 0.75% metronidazole gel for five nights.
- Intervention group male partners received metronidazole 500 mg tablets twice daily and clindamycin 2% cream topically twice daily for seven days.
- Couples were randomized 1:1 with stratification by site and contraceptive method.
- Primary outcome: BV recurrence at 12 weeks (≥3 AC + NS 4–10).
- Secondary outcomes: BV recurrence at four weeks, NS ≥7 at four and 12 weeks, and vaginal microbiota composition were assessed during clinic visits, and included symptom surveys, examinations, and vaginal swabs.
- Modified intention-to-treat analysis included women completing ≥1 follow-up.
- Male adherence was monitored via self-report, pill count, and returned cream.

INTERVENTION (# IN THE GROUP): 81 couples

COMPARISON (# IN THE GROUP): 83 couples

FOLLOW-UP PERIOD: 12 weeks

RESULTS:

Primary Outcome –

- Treating male partners with oral metronidazole and topical clindamycin decreased teh risk of recurrence of BV at 12 weeks compared to no partner treatment (35% vs 63%, respectively; hazard ratio [HR] 0.37; 95% CI, 0.22–0.61).

Secondary Outcome –

- Partner treatment reduced BV recurrence within four weeks (Amsel + Nugent criteria) compared to no partner treatment (17% vs 46%, respectively; HR 0.31; 95% CI, 0.16–0.59).
- Partner treatment reduced BV recurrence within four weeks (NS ≥7) compared to no partner

treatment (23% vs 37%, respectively; HR 0.49; 95% CI, 0.27–0.93).

- Partner treatment reduced BV recurrence within 12 weeks (NS ≥7) compared to no partner treatment (38% vs 57%, respectively; HR 0.46; 95% CI, 0.28–0.76).

LIMITATIONS:

- The study was terminated early after interim analysis showed significant efficacy, which may have overestimated treatment effect.
- Adherence was self-reported and high in the study, possibly limiting generalizability to real-world settings.
- The population was limited to monogamous heterosexual couples, limiting external validity.
- The population was recruited primarily from few facilities offering sexual health service, which may represent a higher-risk population and limit generalizability.
- Concurrent sexual partnerships may have been underreported, introducing potential misclassification and bias.
- Male partners in the control group received no placebo, raising the possibility of confounding behavior changes.

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A Shot At Prevention!

Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

Bekker LG, Das M, Abdool Karim Q, et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. *N Engl J Med*. 2024;391(13):1179-1192. doi:10.1056/NEJMoa2407001

KEY TAKEAWAY: Lenacapavir decreases human immunodeficiency virus (HIV) incidence compared to standard daily oral pre-exposure prophylaxis (PrEP) among cisgender women at elevated risk for HIV infection.

STUDY DESIGN: Double-blind, randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Cisgender women in sub-Saharan Africa face disproportionately high rates of new HIV infections. Daily oral PrEP options like emtricitabine/tenofovir alafenamide (F/TAF) and emtricitabine/tenofovir disoproxil fumarate (F/TDF) are effective, but adherence is a major challenge. Lenacapavir, a long-acting capsid inhibitor, offers a potential solution with only twice-yearly injections.

PATIENTS: Cisgender adolescent girls and young women (16–25 years old) in South Africa and Uganda at elevated risk for HIV infection

INTERVENTION: Subcutaneous Lenacapavir injections

CONTROL: Daily oral PrEP with either F/TAF or F/TDF

PRIMARY OUTCOME: Incidence of confirmed HIV infections

Secondary Outcome: Adverse events

METHODS (BRIEF DESCRIPTION):

- 5,338 sexually active cisgender women 16–25 years old initially HIV negative, were randomly included in the trial.
- Participants were randomly assigned in a 2:2:1 ratio to receive lenacapavir injections, oral F/TAF or oral F/TDF.
    - Subcutaneous Lenacapavir 927 mg administered q26 weekly (±7 days) with oral placebo
    - Daily oral F/TAF (200 mg/25 mg) with placebo injections
    - Daily oral F/TDF (200 mg/300 mg) with placebo injections
- Participants were followed at weeks four, eight, 13, and subsequently every 13 weeks.
- All participants received regular sexually transmitted infection (STI) testing, HIV prevention counseling, and follow-up.
- Drug levels for oral agents were checked periodically to monitor adherence.
- The primary outcome measured the incidence of confirmed HIV infections.
- The secondary outcome measured adverse events, particularly observance of injection site reactions.

INTERVENTION (# IN THE GROUP): 2,138

COMPARISON (# IN THE GROUP):

- FTAF: 2,137
- FTDF: 1,070

FOLLOW-UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- Lenacapavir reduced the incidence of HIV compared to oral F/TAF or F/TDF (incidence rate ratio [IRR] 0.0; 95% CI, 0.0–0.1).
- For the F/TDF group, incidence of HIV was similar to the background (IRR 1.2; 95% CI, 0.67–2.1).
- For the F/TAF group, incidence of HIV was similar to the background (IRR 0.84; 95% CI, 0.55–1.3).

Secondary Outcome –

- Adverse events of any grade occurred in 76% of the lenacapavir group, 78% in the FTAF group, and 78% in the FTDF group.
- Adverse events with injection sites occurred in 4% of the lenacapavir group, leading to discontinuation.

LIMITATIONS:

- The study was limited to a specific geographic location.

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