

GEMS of the Week

SPOTLIGHT

**Which is Best for Dense Breasts?
Abbreviated MRI, Automated Whole
Breast Ultrasound, or Contrast-Enhanced
Mammography?**

Flora Gone Awry:

Effects of Bacterial Vaginosis in Pregnancy

Can Probiotics Help Prevent Recurrent UTIs?

Antivirals and Mpox:

Helpful or Hype?

Not all Hypertension is Equal:

Long-Term Cardiovascular Risk by Subtype

**Is Oral Tecovirimat Effective in the Treatment of
Mpox?**

Which is Best for Dense Breasts? Abbreviated MRI, Automated Whole Breast Ultrasound, or Contrast-Enhanced Mammography?

Comparison of Supplemental Breast Cancer Imaging Techniques-Interim Results from the BRAID Randomized Controlled Trial

Gilbert FJ, Payne NR, Allajbeu I, et al. Comparison of Supplemental Breast Cancer Imaging Techniques-interim Results from the BRAID Randomized Controlled Trial. *Lancet*. 2025;405(10493):1935-1944. doi:10.1016/S0140-6736(25)00582-3

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KEY TAKEAWAY: Abbreviated magnetic resonance imaging (MRI), automated whole breast ultrasound (ABUS), and contrast-enhanced mammography (CEM) are superior supplemental imaging modalities in breast cancer detection compared to full-field digital mammography (FFDM) among women with dense breasts.

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Dense breasts are a risk factor for breast cancer, and women with higher breast density are at an increased risk of their cancer being diagnosed at a later stage. This study aimed to compare different supplemental imaging modalities for breast cancer screening for women with increased breast density.

PATIENTS: Women with dense breasts and negative mammograms

INTERVENTION: Abbreviated MRI, ABUS, and CEM

CONTROL: FFDM

PRIMARY OUTCOME: Detection rate of breast cancer

Secondary Outcome: Recall rates, tumor characteristics

METHODS (BRIEF DESCRIPTION):

- Patients who attended the three-yearly UK National Health Service Breast Cancer Screening Program with normal mammograms and Breast Imaging Reporting and Data System (Bi-RADS)-graded breast density C or D were invited to participate.
- Patients were randomized 1:1:1:1 among ten different sites to the abbreviated MRI, ABUS, CEM, or FFDM arm.
- The primary outcome was cancer detection rates defined by histologically confirmed breast cancers.
- Secondary outcomes were:

- Recall rates defined by women with positive supplemental imaging who underwent repeat examination or had further assessment.
- Tumor characteristics including size, type and grade of cancer.
- Statistical analysis: Network meta-analysis by imaging received. Each site was treated as a study in the meta-analysis.
- Primary analysis: Three active intervention arms that compared the three supplemental imaging techniques to full-field digital mammography alone with respect to cancer detection, recall, and biopsy rates
- Secondary Analysis: Observational data from Cambridge on full-field digital mammography alone.

INTERVENTION (# IN THE GROUP):

- Abbreviated MRI: 2,318
- ABUS: 2,240
- Contrast-enhanced MRI: 2,235

COMPARISON (# IN THE GROUP): 2,568

FOLLOW-UP PERIOD: Supplemental imaging performed within six months from normal mammogram

RESULTS:

Primary Outcome –

- When analyzed by the intervention, the cancer detection rates were:
 - Abbreviated MRI (17 per 1,000 exams; 95% CI, 12–24)
 - ABUS (4.2 per 1,000 exams; 95% CI, 1.9–8.0)
 - CEM (19 per 1,000 exams; 95% CI, 14–26)
- Abbreviated-MRI had a higher cancer detection rate compared to FFDM (odds ratio [OR] 4.4; 95% CI, 2.7–6.2).
- ABUS had a higher cancer detection rate compared to FFDM (OR 2.1; 95% CI, 1.4–3.2).
- CEM had a higher cancer detection rate compared to full-field digital mammography FFDM (OR 4.9; 95% CI, 3.2–7.4).

Secondary Outcome –

- Abbreviated MRI increased the recall rate compared to FFDM (OR 2.6; 95% CI, 1.7–4.1).
- ABUS increased the recall rate compared to FFDM (OR 1.7; 95% CI, 1.1–2.8).

- CEM increased recall rate compared to FFDM (OR 2.4; 95% CI, 1.4–3.9).
 - Abbreviated MRI (10 mm, IQR 8–15) and contrast-enhanced MRI (11 mm, IQR 7–15) detected invasive cancers that were about half as small as those detected by ABUS (22 mm, IQR 14–35).
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LIMITATIONS:

- Unable to compare cancer detection rates and recall rates among all four arms due to logistical reasons at participating centers; additional analysis will be possible in the future.
 - Does not measure the benefit of supplemental screening (breast cancer mortality reduction or overdiagnosis/long-term harm).
 - Unable to differentiate by modality detection of high/intermediate grade with low grade cancers due to insufficient power.
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Flora Gone Awry: Effects of Bacterial Vaginosis in Pregnancy

Maternal and Fetal Outcomes of Pregnant Women with Bacterial Vaginosis

Ng BK, Chuah JN, Cheah FC, et al. Maternal and fetal outcomes of pregnant women with bacterial vaginosis.

Front Surg. 2023;10:1084867.

doi:10.3389/fsurg.2023.1084867

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KEY TAKEAWAY: Bacterial vaginosis (BV) is associated with adverse fetal outcomes, including lower median birth weight and increased incidence of preterm birth, neonatal intensive care unit (NICU) admissions, respiratory distress syndrome (RDS), and intubation. BV is associated with increased incidence of histological chorioamnionitis but is not associated with clinically significant maternal outcomes, such as clinical chorioamnionitis or endometritis.

STUDY DESIGN: Prospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: BV is a common disorder of women of childbearing age which has been linked to obstetrical complications including preterm prelabor rupture of membranes (PPROM), preterm labor, and intra-amniotic infections as well as neonatal complications including RDS, NICU admissions, and lower median birth weight. The study aimed to assess the fetal and maternal outcomes in women diagnosed with BV during pregnancy

PATIENTS: Pregnant persons between 22–34 weeks gestation with abnormal vaginal discharge and preterm labor or PPRM

INTERVENTION: Presence of BV

CONTROL: Absence of BV

PRIMARY OUTCOME: Maternal and neonatal outcomes

METHODS (BRIEF DESCRIPTION):

- Single tertiary care academic medical center in Malaysia
- Pregnant women between 22- and 34-weeks' gestation with singleton pregnancies who presented with abnormal vaginal discharge, preterm labor or PPRM were included in the study (n=251; but 14 were excluded from analysis due to being lost to follow up)
- Eligibility for enrollment included the presence of abnormal vaginal discharge (defined as a change in

color to grey, green, yellow, or blood-stained, copious, malodorous fluid associated with itchiness or soreness). Preterm labor was defined as regular contractions (at least 2 in 10 minutes with cervical effacement and os dilatation).

- The median maternal age was 30 years old, with predominantly married women and an ethnic distribution reflective of the local population (primarily Malay, followed by Chinese and Indian populations).
- Median gestational age at recruitment was 32 weeks.
- Patients with major medical comorbidities or obstetric complications were excluded.
- The exposure group consisted of people with a diagnosis of BV (detected using the BV Blue Test).
- The comparison group was those without a diagnosis of BV. People diagnosed with BV were treated with dequalinium chloride (Fluomizin).
- The following were measured as the maternal outcomes:
 - Mode of delivery, wound breakdown, postpartum hemorrhage
 - Clinical chorioamnionitis and postpartum endometritis were defined by the presence of signs and symptoms, including fever, uterine tenderness, foul-smelling discharge, abnormal lochia, and wound discharge.
 - Histological chorioamnionitis was based on placental histopathology examination.
 - Duration from time of enrollment to delivery was measured in weeks.
- The following were measured as the neonatal outcomes:
 - Preterm birth was defined as delivery before 34 weeks gestation.
 - Neonatal birth weight was measured in grams.
 - Respiratory outcomes were defined by the need for endotracheal intubation and the presence/absence of RDS diagnosed clinically by the neonatal team.
 - Umbilical cord pH was measured using cord blood.

- Apgar scores were calculated by the neonatal team.

INTERVENTION (# IN THE GROUP): 24

COMPARISON (# IN THE GROUP): 213

FOLLOW-UP PERIOD: Up to six weeks postpartum

RESULTS:

Primary Outcome –

- There were no statistically significant differences in any maternal outcomes, including mode of delivery, postpartum hemorrhage, endometritis, wound breakdown, or clinically diagnosed chorioamnionitis.
 - BV exposure was associated with a high rate of histologic chorioamnionitis on placental pathology (present in 56% of BV positive placentas); however, no statistical comparison was made with non-BV placentas.
 - BV exposure was associated with an increase in the following neonatal outcomes:
 - Percentage of preterm deliveries (<34 weeks) (23% vs 6.2%; $p=.019$)
 - NICU admissions (42% vs 19%; $p=.010$)
 - Need for neonatal intubation (29% vs 7.6%; $p=.004$)
 - Neonatal RDS (33% vs 9.0%; $p=.002$)
 - BV exposure was associated with a decrease in the following neonatal outcomes:
 - Median gestational age at delivery (37 weeks vs 38 weeks; $p=.010$).
 - Median time from enrollment to delivery (4.8 weeks vs 7.2 weeks; $p=.026$)
 - Median birth weight (2,450 g vs 2,950 g; $p=.007$)
 - Median umbilical cord pH (7.25 vs 7.33; $p=.004$; still within the normal range)
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LIMITATIONS:

- Only patients with abnormal vaginal discharge and preterm labor or PPRM were included.
- GV was considered as sole etiology of BV.
- The need for tocolytics was individualized, which may have altered neonatal and maternal outcomes.
- BV was treated with Fluomizin rather than the Center of Disease Control (CDC) recommended treatments of metronidazole or clindamycin, and outcomes may have been altered by treatment.

- The researchers did not include data on potential confounding factors such as cervical length, fetal fibronectin levels, prenatal care, or substance exposures.
 - The researchers were not blinded to the diagnoses of BV.
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Can Probiotics Help Prevent Recurrent UTIs?

Effectiveness of Prophylactic Oral and/or Vaginal Probiotic Supplementation in the Prevention of Recurrent Urinary Tract Infections: A Randomized, Double-Blind, Placebo-Controlled Trial

Gupta V, Mastromarino P, Garg R. Effectiveness of Prophylactic Oral and/or Vaginal Probiotic Supplementation in the Prevention of Recurrent Urinary Tract Infections: A Randomized, Double-Blind, Placebo-Controlled Trial. *Clin Infect Dis*. 2024;78(5):1154-1161. doi:10.1093/cid/ciad766

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KEY TAKEAWAY: Vaginal probiotics, alone or with oral probiotics, reduce the number of symptomatic urinary tract infection (UTI) recurrences and increase the mean time to first symptomatic recurrence in premenopausal women 18–45 years old with a history of ≥ 3 uncomplicated UTIs in the past year.

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small sample size)

BRIEF BACKGROUND INFORMATION: UTIs are a very common condition affecting all women, with 20–30% of women experiencing recurrent UTIs. Lactobacilli are part of normal, healthy vaginal flora, and a reduced number of lactobacilli can allow colonization of common bacterial uropathogens. This study investigated whether probiotic supplementation affected recurrent UTI rates.

PATIENTS: Premenopausal women 18–45 years old with a history of ≥ 3 uncomplicated UTIs in the past year

INTERVENTION: Vaginal probiotics + oral placebo, oral probiotics + vaginal placebo, and oral + vaginal probiotics

CONTROL: Oral placebo + vaginal placebo

PRIMARY OUTCOME: Number of symptomatic UTI recurrences, UTI incidence, and time to first symptomatic UTI

Secondary Outcome: Vaginal microbiota, patient-rated global assessment of overall improvement in UTI condition, adverse events

METHODS (BRIEF DESCRIPTION):

- A total of 174 premenopausal, non-pregnant women 18–45 years old with a history of ≥ 3 uncomplicated UTIs in the past year were selected. The study was conducted at a tertiary care teaching hospital in Chandigarh, India.

- The study excluded patients who were pregnant, consumed antibiotics within two weeks of baseline urine screen, had abnormal liver or kidney labs, were on systemic steroids, were immunocompromised, had comorbid conditions, or were unwilling to sign informed consent.
- Women were randomly selected, in a blinded fashion, for different treatment groups.
 - Group 2 (G2) received vaginal probiotics + oral placebo.
 - Group 3 (G3) received oral probiotics + vaginal placebo.
 - Group 4 (G4) received both oral and vaginal probiotics for prevention of recurrent UTIs.
- Women were randomized to Group 1 (G1), where they received placebo for both oral and vaginal routes of administration.
- The probiotic oral capsules (Visbiome or Florimax brands) contained 113 billion live, lyophilized lactic acid bacteria and bifidobacteria.
- The vaginal probiotic tablet (FloraBalance or Evanev brands) contained one billion colony-forming units of three lactobacilli strains.
- The placebo had identical packaging and contained the same ingredients without the bacterial strains.
- Initially, patients provided a baseline urine sample and vaginal swab for wet mount and culture evaluation.
 - Patients logged daily UTI symptoms (dysuria, frequency, urgency, suprapubic pain, or hematuria).
 - Symptoms, midstream urine sample, periurethral swab, and vaginal swabs were evaluated at the end of months one, two, three, four, and six. Patients also reported symptoms by phone each subsequent month.
 - Vaginal swabs were evaluated by real-time quantification polymerase chain reaction (qRT-PCR) to quantitatively assess the vaginal microbiome.
 - If UTI symptoms or other adverse symptoms (fever, diarrhea, nausea, vomiting, constipation, abdominal pain, or vaginal symptoms) were

experienced, it was asked that patients be evaluated immediately by the clinic.

- If a participant was diagnosed with a symptomatic UTI during the trial period, they were treated with an antibiotic selected based on culture sensitivity report and retested after two weeks to confirm resolution of UTI.
- Overall improvement in UTI condition was assessed by using a seven-point Likert scale patient-rated global assessment that ranged from “very much improvement” to “very much worse” at the end of four months.

INTERVENTION (# IN THE GROUP):

- G2: 43
- G3: 43
- G4: 44

COMPARISON (# IN THE GROUP): 44

FOLLOW-UP PERIOD: Four and 12 months

RESULTS:**Primary Outcome –**

- Probiotic supplementation decreased the number of symptomatic UTI recurrences after four months in G2, G3, and G4 compared to G1 (mean 1.6, 1.1, and 1.1 vs 2.1, respectively; $p < .001$).
- Probiotic supplementation decreased the number of symptomatic UTI recurrences after 12 months in G2, G3, and G4 compared to G1 (mean 3.4, 2.2, and 2.0 vs 3.8, respectively, $p < .001$).
- G3 and G4 decreased the incidence of UTIs at four months compared to G1:
 - G3 (relative risk [RR] 0.59; 95% CI, 0.39–0.88)
 - G4 (RR 0.45; 95% CI, 0.28–0.72)
- There was no significant difference in the incidence of UTIs in G2 at four months compared to G1 (RR 0.89; 95% CI, 0.66–1.2).
- G2, G3, and G4 decreased the incidence of symptomatic UTIs at 12 months compared to G1:
 - G2 (RR 0.83; 95% CI, 0.70–0.97)
 - G3 (RR 0.66; 95% CI, 0.51–0.83)
 - G4 (RR 0.57; 95% CI, 0.43–0.75)
- G3 and G4 increased mean time to first symptomatic UTI recurrence compared to G1 and

G2 (124 days vs 142 days vs 69 days vs 72 days, respectively; $P < .05$).

Secondary Outcome –

- Patients receiving G3 or G4 reported greater global improvement in symptoms than G1 or G2 ($\chi^2 = 113$; $P < .001$).
- G4, G3, and G2 decreased vaginal *Escherichia coli* counts compared to G1 (1.0, 0.96, 1.7 vs 4.6, respectively; $p < .001$).
- G4 and G3 decreased *Proteus mirabilis* counts compared to G1 and G2 (1.6 and 2.5 vs 3.1 and 4.2, respectively; $p < .05$).
- G4 increased vaginal *Lactobacillus* count compared to G3, G2, and G1 (6.0 vs 4.1, 5.7, and 2.2, respectively; $P = .008$).
- There was no significant difference in *Klebsiella pneumoniae* and *Bifidobacterium* counts between the groups.
- No participant experienced significant treatment-related adverse events.

LIMITATIONS:

- The small sample size of 174 patients, limited to only premenopausal women, reduces the generalizability to postmenopausal women, who are recognized to be at a higher risk for recurrent UTIs.
- Other modalities of UTI prevention, such as prophylactic antibiotics, were not compared for reduction in recurrent UTI.
- Immunological biomarkers were not measured or monitored, which may have reflected immune activity.
- No comment was made on the use of medications, such as contraceptives, that could potentially alter existing vaginal flora.

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Clinical Features, Antiviral Treatment, and Patient Outcomes: A Systematic Review and Comparative Analysis of the Previous and the 2022 Mpox Outbreaks

Li P, Li J, Ayada I, et al. Clinical Features, Antiviral Treatment, and Patient Outcomes: A Systematic Review and Comparative Analysis of the Previous and the 2022 Mpox Outbreaks. *J Infect Dis*. 2023;228(4):391-401. doi:10.1093/infdis/jiad034

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KEY TAKEAWAY: The 2022 mpox outbreak is associated with increased incidence of men who have sex with men (MSM), high-risk behaviors, and a different distribution of skin lesions compared with prior outbreaks in patients with mpox.

STUDY DESIGN: Systematic review of 73 studies, with 33 studies included in the meta-analysis. Only 17 studies contained any information on therapeutics (N=592)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to paucity of cases to perform meta-analysis on treatment outcomes)

BRIEF BACKGROUND INFORMATION: Mpox is an orthopoxvirus causing smallpox-like illness, most often manifesting with distinct skin lesions. While historically endemic to Africa, a 2022 global outbreak occurred predominantly in adult males without travel history to endemic areas. Understanding the clinical features, management, and outcomes across different mpox outbreaks is critical for guiding effective treatment options and adequate response to future outbreaks.

PATIENTS: Patients infected with mpox

INTERVENTION: Treatment varies between mono- or poly-therapy of antibiotics and/or antivirals

CONTROL: No intervention

PRIMARY OUTCOME: Incidence of MSM and high-risk behaviors, clinical symptoms, and distribution of skin lesions

Secondary Outcome: Hospitalization rate, fatality rate, HIV prevalence

METHODS (BRIEF DESCRIPTION):

- Medline, Embase, Web of Science, Cochrane Central, Google Scholar was searched to identify articles.
- Studies lacking clinical or outcome data were excluded.

- Only moderate- to high-quality studies were included in the meta-analysis, based on Joanna Briggs Institute checklist scores of 4–9 points.
- Included mpox studies reporting clinical symptoms, management, or patient outcomes confirmed by lab or clinical diagnosis. Cases were further divided into two sections: Mpox outbreaks/cases before 2022 and after May 2022.
- Intervention: Exact interventions varied amongst the 17 included trials, with tecovirimat being the most common antiviral reported. In total, 19 patients received antibiotics, and 63 patients received antiviral therapy. Tecovirimat was only used during the 2022 outbreak. The most common intervention prior to the 2022 outbreak was antibiotics ± supportive measures.
- Comparator: No intervention.
- Extracted patient demographics, symptoms, treatment, outcomes, HIV status, and high-risk sexual behavior data.
- The primary outcome assessed the incidence of MSM and high-risk behaviors, clinical symptoms, and distribution of skin lesions.
- The secondary outcomes assessed the hospitalization rate, fatality rate, and HIV prevalence.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Varied by study

RESULTS:

Primary Outcome –

- The 2022 mpox outbreak primarily affected MSM (18 studies, n=3,271; pooled prevalence 95%; 95% CI, 88–99; I²=98%).
- High-risk sexual activity was reported in most patients in the 2022 outbreak (5 studies, n=881; pooled prevalence 72%; 95% CI, 51–90; I²=98%).
- The most common clinical symptom reported was fever, both prior to the 2022 outbreak (9 studies, n=1,193; incidence rate 81%; 95% CI, 60–96; I²=94%) and for the 2022 outbreak (16 studies, n=3,904; incidence rate 59%; 95% CI, 54–65; I²=89%).
- The most common lesion location reported prior to the 2022 outbreak was facial (5 studies, n=1,182;

incidence rate 98%; 95% CI, 96–100; $I^2=15\%$) and genital for the 2022 outbreak (14 studies, $n=2,836$; incidence rate 51%; 95% CI, 40–62; $I^2=96\%$).

Secondary Outcome –

- The 2022 mpox outbreak had a low rate of hospitalization (9 studies, $n=2,275$; pooled prevalence 6.3%; 95% CI, 3.4–10; $I^2=91\%$).
- The overall reported fatality rate in these studies was nearly 5% (10 studies, $n=831$; pooled prevalence 4.6%; 95% CI, 2.4–7.4; $I^2=53\%$).
- HIV positivity rate was reported in most studies for the 2022 outbreak (15 studies, $n=3,226$; pooled prevalence 38%; 95% CI, 30–46; $I^2=93\%$).

LIMITATIONS:

- There was very high heterogeneity among included studies reporting different symptoms.
- Observational nature and variability of reporting.
- Extremely limited data on antiviral treatment and efficacy.
- Only included studies in English.

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Not all Hypertension is Equal: Long-Term Cardiovascular Risk by Subtype

Hypertensive Disorders of Pregnancy Subtypes and Long-Term Cardiovascular Risk

Kwak S, Park CS, Park Y, et al. Hypertensive Disorders of Pregnancy Subtypes and Long-Term Cardiovascular Risk. *JAMA Intern Med.* 2026;186(4):469-478.

doi:10.1001/jamainternmed.2025.7802

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KEY TAKEAWAY: Hypertensive disorders of pregnancy (HDP) significantly and independently increase the risk of long-term cardiovascular (CV) events, including CV death, heart failure (HF), myocardial infarction (MI), stroke, and atrial fibrillation (AF), compared to pregnant patients with normal blood pressure in South Korea.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 4 (downgraded due to lack of generalizability)

BRIEF BACKGROUND INFORMATION: HDP are a common complication in pregnancy, complicating approximately 5–10%. While previous studies have mainly focused on preeclampsia, they have not addressed whether specific HDP subtypes have different long-term CV risks. This study aimed to assess a nationwide study analyzing the South Korean population and the risk HDPs pose beyond their immediate obstetric impact.

PATIENTS: Women with deliveries in South Korea from January 2010 to December 2018

INTERVENTION: Women with HDPs

CONTROL: Women without HDPs

PRIMARY OUTCOME: Composite CV outcomes
Secondary Outcome: Individual components of the primary outcome

METHODS (BRIEF DESCRIPTION):

- Used the National Health Insurance Service database of South Korea and obtained delivery records between January 2010 and December 2018.
- Exclusion criteria include women <19 years old and >50 years old, end-stage kidney disease (ESKD), or cancer, prior CV events, or events that occurred within the first year after delivery.
- Required general health exam within two years prior to pregnancy.
- HDPs were identified using ICD-10-CM codes with definition of HTN as systolic blood pressure (SBP) of ≥ 140 mmHg or diastolic blood pressure (DBP) of ≥ 90

mmHg and were classified into subtypes of HDP that included preeclampsia or eclampsia, superimposed preeclampsia, gestational HTN, chronic HTN, or unspecified HDPs.

- Primary outcome was measured by a composite of CV events including CV death, HF, MI, stroke, and AF.
- Secondary outcomes were individual outcomes of the above-mentioned conditions.
- Statistical analysis was completed using chi-square tests for categorical variables and ANOVA/t-test for continuous variables.
- Cox proportional hazard models were applied to estimate adjusted hazard ratios.
- The primary and secondary outcome results were controlled for age, body mass index (BMI) (>25 vs <25), diabetes, dyslipidemia, chronic kidney disease (CKD), low income, metropolitan area residence, nulliparity, spontaneous vaginal delivery, history of abortion, gestational diabetes, current smoker, heavy alcohol use, and regular physical activity.

INTERVENTION (# IN THE GROUP):

- 22,876 women with HDP
 - Chronic HTN: 2,810
 - Gestational HTN (gHTN): 7,954
 - Superimposed preeclampsia: 644
 - Preeclampsia or eclampsia: 7,411
 - Unspecified HTN: 4,057

COMPARISON (# IN THE GROUP): 547,967

FOLLOW-UP PERIOD: Patients were followed until December 2022 (median 6.5 years)

RESULTS:

Primary Outcome –

- HDPs increased the risk of composite CV events compared to patients without HDPs (adjusted hazard ratio [aHR] 1.6; 95% CI, 1.5–1.8).
- All subtypes of HDP significantly increased the risk of composite cardiac events compared to patients without HDP.
 - Chronic HTN (aHR 1.8; 95% CI, 1.5–2.2)
 - gHTN (aHR 1.5; 95% CI, 1.3–1.8)
 - Superimposed preeclampsia (aHR 2.9; 95% CI, 2.2–4.0)

- Preeclampsia or eclampsia (aHR 1.5; 95% CI, 1.3–1.7)
- Unspecified HTN (aHR 1.6; 95% CI, 1.3–2.0)

Secondary Outcome –

- HDPs increased the risk of CV death compared to patients without HDP (aHR 2.6; 95% CI, 1.4–4.9).
- HDPs increased the risk of HF compared to patients without HDP (aHR 1.6; 95% CI, 1.5–1.8).
- HDPs increased the risk of MI compared to patients without HDP (aHR 1.3; 95% CI, 1.1–1.7).
- HDPs increased the risk of stroke compared to patients without HDP (aHR 2.4; 95% CI, 1.9–2.9).
- HDPs increased the risk of AF compared to patients without HDP (aHR 1.5; 95% CI, 1.2–1.9).
- Chronic HTN, gHTN, and preeclampsia or eclampsia increased the risk of CV death compared to patients without HDP.
 - Chronic HTN (aHR 3.4; 95% CI, 1.01–11)
 - gHTN (aHR 2.9; 95% CI, 1.1–8.1)
 - Preeclampsia or eclampsia (aHR 3.5; 95% CI, 1.4–8.8)
- There was no significant relationship between superimposed preeclampsia or unspecified HTN and CV death due to a lack of data.
- All subtypes of HDP increased the risk of developing HF compared to patients without HDP.
 - Chronic HTN (aHR 1.9; 95% CI, 1.5–2.4)
 - gHTN (aHR 1.5; 95% CI, 1.3–1.8)
 - Superimposed preeclampsia (aHR 2.8; 95% CI, 1.9–4.1)
 - Preeclampsia or eclampsia (aHR 1.5; 95% CI, 1.3–1.8)
 - Unspecified HTN (aHR 1.5; 95% CI, 1.2–1.9)
- Unspecified HTN increased the risk of MI compared to patients without HDP (aHR 1.6; 95% CI, 1.02–2.5).
- Chronic HTN, gHTN, superimposed preeclampsia, and preeclampsia or eclampsia did not individually increase the risk of MI compared to patients without HDP.
- All subtypes of HDP increased the risk of stroke compared to patients without HDP.
 - Chronic HTN (aHR 2.0; 95% CI, 1.2–3.3)
 - gHTN (aHR 2.1; 95% CI, 1.4–3.0)

- Superimposed preeclampsia (aHR 4.8; 95% CI, 2.4–9.3)
- Preeclampsia or eclampsia (aHR 2.3; 95% CI, 1.6–3.2)
- Unspecified HTN (aHR 3.0; 95% CI, 2.0–4.6)
- Chronic HTN and unspecified HTN increased the risk of developing AF compared to patients without HDP.
 - Chronic HTN (aHR 2.3; 95% CI, 1.4–3.9)
 - Unspecified HTN (aHR 1.8; 95% CI, 1.01–3.1)
- gHTN, superimposed preeclampsia, and preeclampsia or eclampsia did not individually significantly increase the risk of developing AF.

LIMITATIONS:

- Population limited to South Korea, and patients were required to have had a general health exam within the last two years, which both limit generalizability.
- Risk of misclassified data sets using claims data to establish diagnosis of HDP.
- Overall incidence of CV events was low, which may limit the power of the study.
- No information available to study on patient's history of prior HDP.
- Subgroups were not assessed for baseline CV risk (family history, diet, CV markers).
- Did not mention severity of HDP, including onset, need for medication, postpartum treatment impacting CV risk.

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Navy Medical Department, the Navy at large, or the Department of Defense.

Is Oral Tecovirimat Effective in the Treatment of Mpox?

Tecovirimat for Clade I MPXV Infection in the Democratic Republic of Congo

PALM007 Writing Group, Ali R, Alonga J, et al.

Tecovirimat for Clade I MPXV Infection in the Democratic Republic of Congo. *N Engl J Med*. 2025;392(15):1484-1496. doi:10.1056/NEJMoa2412439

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KEY TAKEAWAY: Oral tecovirimat therapy does not reduce the time to lesion resolution compared to standard supportive care in patients in the Democratic Republic of Congo (DRC) with PCR-confirmed clade I monkeypox virus (MPXV) and at least one skin lesion.

STUDY DESIGN: Double-blind randomized controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to limited external validity with primarily pediatric population conducted exclusively in the geographic area of DRC)

BRIEF BACKGROUND INFORMATION: MPXV is an orthopoxvirus infection that can cause significant morbidity and mortality, particularly with clade I strains circulating in Central Africa. Tecovirimat, an antiviral approved based largely on animal studies and limited human observational data, has been widely stockpiled and used despite a lack of high-quality randomized clinical trial evidence demonstrating clinical benefit in humans. There is uncertainty whether tecovirimat improves outcomes, making rigorous evaluation in an endemic population essential to guide treatment recommendations and public health policy. This study aimed to determine whether tecovirimat improves time to lesion resolution in patients with clade I MPXV infection compared with placebo.

PATIENTS: Adults and children in the DRC with PCR-confirmed clade I MPXV and at least one skin lesion

INTERVENTION: Tecovirimat

CONTROL: Placebo

PRIMARY OUTCOME: Resolution of skin lesions

Secondary Outcome: Viral clearance by PCR, mortality, safety/adverse events, recrudescence

METHODS (BRIEF DESCRIPTION):

- Randomized, double-blind, placebo-controlled clinical trial conducted at two treatment centers in the DRC.

- The study enrolled patients with lab-confirmed clade I MPXV infection who had at least one active skin lesion at presentation.
- Included both pediatric and adult patients, with a median age in early adolescence.
- Many patients had moderate to severe disease, with a sizable proportion presenting with >100 lesions and systemic symptoms at enrollment.
- Exclusion criteria included weight <3 kg, Hgb <7, or current use/plan to use meglitinide or midazolam.
- All patients were hospitalized and received supportive care, including monitoring, nutrition, and management of complications.
- Patients were followed daily for clinical progression, lesion healing, adverse events, and virologic testing until recovery or study completion.
- Patients were randomized 1:1 to tecovirimat or placebo and were stratified according to the number of days since the onset of symptoms (≤7 days vs >7 days).
 - Patients receiving tecovirimat received a dose based on body weight x 14 days.
 - Both groups received supportive care consisting of symptom management, skin care, dietary support, and oropharyngeal care.
- The primary outcome measured resolution of skin lesions by having a trained clinician assess lesions daily until resolution. At baseline, an entire-body count of active lesions was obtained and then monitored daily. Illness severity was also classified using the modified WHO criteria.
- Secondary outcomes were measured using the following:
 - Viral clearance was assessed by real-time PCR testing for MPXV in blood and oropharyngeal samples.
 - Mortality was assessed by the documentation of death of an enrolled patient.
 - Safety/adverse events were assessed by documentation of serious adverse events, to include malaria diagnosis and GI adverse events (such as abdominal pain).
 - Recrudescence was assessed at an optional visit, with recrudescence being defined as the

presence of a new skin lesion and an MPXV-positive result from a PCR of either a skin swab or blood sample after initial lesion resolution.

- After being hospitalized for a 14-day dosing period and being discharged when lesions resolved and two consecutive blood samples were negative for MPXV by PCR, patients attended a follow-up visit 28 days after randomization, with an optional visit at 58 days.

INTERVENTION (# IN THE GROUP): 295

COMPARISON (# IN THE GROUP): 302

FOLLOW-UP PERIOD: 28 days after randomization, with an optional visit at 58 days

RESULTS:

Primary Outcome –

- Tecovirimat did not reduce time to lesion resolution compared to placebo (hazard ratio [HR] 1.1; 95% CI, 0.97–1.3).
- Stratification by timing of symptom onset showed no significant benefit of tecovirimat in either subgroup.
 - Symptom onset ≤ 7 days before randomization (HR 1.2; 95% CI, 0.98–1.4)
 - Symptom onset > 7 days before randomization (HR 1.0; 95% CI, 0.71–1.4)

Secondary Outcome –

- There was no significant reduction in viral clearance or mortality with the use of tecovirimat compared to placebo.
- Adverse events occurred at similar rates in both groups, and tecovirimat was not associated with any major safety concerns.
- Of 20 patients experiencing recrudescence, 55% had received tecovirimat and 45% had received placebo.

LIMITATIONS:

- This study was conducted in the DRC, which limits geographic generalizability.
 - A pediatric-heavy and 49% female study population may not reflect global outbreaks.
 - Mucosal lesions were excluded, which may underestimate the disease burden.
 - Low interobserver reliability when assessing skin lesions.
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