GOOD EVIDENCE MATTERS

GEMs of the Week

SPOTLIGHT

Treat the Bleed, Not the Bugs

Less Antibiotics for GI Bleeds

Is More Data Always Better for Type 2 Diabetes?

The "Love Drug" Legacy

Unpacking Oxytocin's Impact on Families Down the Line

180 Days of Defense

Nirsevimab's RSVictory

FPIN
Family Physicians Inquiries Network

Volume 6 Issue 5

Treat the Bleed, Not the Bugs: Less Antibiotics for GI Bleeds

Antibiotic Prophylaxis for Upper Gastrointestinal Bleed in Liver Cirrhosis; Less May Be More

B Hadi Y, Khan RS, Lakhani DA, et al. Antibiotic Prophylaxis for Upper Gastrointestinal Bleed in Liver Cirrhosis; Less May Be More. *Dig Dis Sci*. 2023;68(1):284-290. doi:10.1007/s10620-022-07481-0

KEY TAKEAWAY: A three-day course of prophylactic antibiotics for cirrhosis patients with upper gastrointestinal (GI) bleeding and no active infection may be safe compared to longer durations.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: The use of prophylactic antibiotics in patients with cirrhosis and upper GI bleeding is known to improve outcomes. There are very limited studies exploring the recommended duration of prophylactic antibiotics. This retrospective cohort study aimed to explore the impact of shorter prophylactic antibiotics course on patient outcomes of infection incidence, incidence of rebleeding, timing of bleeding, and death during hospitalization.

PATIENTS: Adults with cirrhosis presenting with upper GI bleeding who received endoscopic procedures

INTERVENTION: Prophylactic antibiotics

CONTROL: No antibiotic prophylaxis

PRIMARY OUTCOME: Incidence of infection

Secondary Outcome: Incidence of rebleeding, timing of rebleeding, death during hospitalization, readmission within 30 days

METHODS (BRIEF DESCRIPTION):

- Adults >18 years old who received endoscopic procedures after presenting with confirmed diagnosis of cirrhosis and upper GI bleeding at the University of Virginia Hospital from 2010–2018 (n=303) were included in the study.
- The treatment groups were divided into the following categories by duration, with antibiotic regimen and duration selected by the treating physician:
  - Group A: Antibiotic duration of 1–3 days
  - Group B: Antibiotic duration of 4–6 days
  - Group C: Antibiotic duration of 7+ days
- The comparison group were those with no antibiotic prophylaxis.
- The primary outcome measured the incidence of infections, including pneumonia, urinary tract infection (UTI), and bacteremia and were diagnosed by treating physicians.
- The secondary outcomes measured the incidence of rebleeding, timing of rebleeding, death during hospitalization, and readmission.
  - Rebleeding was defined by need for transfusion, melena/hematochezia, drop in hemoglobin >2 g/dL, or bleeding lesion on repeat endoscopy.
  - Timing of rebleeding was defined as early (7 days after resolution) or late (>7 days after resolution).
  - Readmissions were considered within the 30 days of discharge.

INTERVENTION (# IN THE GROUP):

- Group A: 77
- Group B: 69
- Group C: 97

COMPARISON (# IN THE GROUP): 60

FOLLOW-UP PERIOD: 30 days after hospital discharge

RESULTS:

Primary Outcome –

- Infections were more often diagnosed in patients with no prophylactic antibiotics compared to the prophylaxis cohort (27% vs 11%, respectively; *p*=.002).
- There was no difference in the infection rates for antibiotic duration between group A, B, and C (9.1% vs 12% vs 12%, respectively; *p*=.78).

Secondary Outcome –

- Rebleeding was observed in 41 patients (17%).
  - Early rebleeding was observed in 26 patients (11%)
  - Late rebleeding was observed in 15 patients (6.2%).
  - There was no difference in rebleeding rates between group A, B, and C (18% vs 12%, vs 20%, respectively; no statistical analysis completed).
- Mortality in the hospital setting was observed in 11 patients (4.5%).

- There was no difference in mortality rates for antibiotic duration between group A, B, and C (5.2% vs 4.3% vs 4.1%, respectively; *p*=.94).

LIMITATIONS:

- This is a retrospective study with nonrandom choice of antibiotic duration and with some differences among the three cohorts.
- Notably, individuals with an antibiotic duration of 1–3 days had a shorter length of stay which may have underestimated the rate of infection in that cohort.
- Clostridioides infections are more likely to be diagnosed in patients with longer antibiotic duration and longer stays. Clostridioides infections are also independently correlated with mortality in cirrhosis patients, so this could have confounded the results. All the Clostridioides cases were in patients taking antibiotics for longer durations than three days.

Fatima Elwalid, MD
Northwest Washington FMRP
Bremerton, WA

Is More Data Always Better for Type 2 Diabetes?

Efficacy and Safety of Continuous Glucose Monitoring and Intermittently Scanned Continuous Glucose Monitoring in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Interventional Evidence

Seidu S, Kunutsor SK, Ajjan RA, Choudhary P. Efficacy and Safety of Continuous Glucose Monitoring and Intermittently Scanned Continuous Glucose Monitoring in Patients with Type 2 Diabetes: A Systematic Review and Meta-analysis of Interventional Evidence. *Diabetes Care*. 2024;47(1):169-179. doi:10.2337/dc23-1520

KEY TAKEAWAY: Self monitoring of blood glucose (SMBG), both continuous glucose monitoring (CGM) and intermittently scanned continuous glucose monitoring (isCGM) improves A1C but increases the risk of adverse events compared to usual care in patients with type 2 diabetes mellitus (T2DM). Neither method demonstrated consistent improvement in body composition, blood pressure, or lipid levels over SMBG.

STUDY DESIGN: Systematic review and meta-analysis of 29 studies from 26 distinct randomized controlled trials (RCTs) (N=2,783)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Blood glucose home-monitoring in T2DM has traditionally required frequent finger pricks. New technology has provided increased blood glucose data via CGM and isCGM. This study evaluated the benefits and potential risks of CGM and is CGM compared with usual care or SMBG in patients with T2DM.

PATIENTS: Patients with T2DM

INTERVENTION: CGM and isCGM

CONTROL: Usual care or SMBG

PRIMARY OUTCOME: Change in A1C

Secondary Outcome: Other glycemic measures, CGM metrics, body composition measures, metabolic outcomes, medication changes, safety events, psychological outcomes

METHODS (BRIEF DESCRIPTION):

- Studies were screened using Rayyan, an online bibliographic tool.
- Selected studies were RCTs that reported glycemic and relevant data, and compared at least two interventions for a minimum of eight weeks including CGM in real-time/retrospective mode, short/long-term use of CGM, isCGM, and SMBG in patients with T2DM.
- Selected studies ranged from publication dates 2008-2023.
- Studies which looked at CGM vs usual care/SMBG involved 17 RCTs with 1,146 patients with T2DM. 632 in the CGM group, and 514 in the usual care/SMBG group.
- Studies which looked at isCGM vs usual care/SMBG involved nine RCTs with 1,637 patients with T2DM. 871 in the isCGM group and 766 in the usual care/SMBG group.
- Patients ranged from 53–70 years old.
- T2DM duration ranged from 5.6–22 years.
- Baseline A1c ranged from 6.9–9.9%.
- CGM studies ranged in intervention duration from 8.0–35 weeks.
- isCGM studies ranged in intervention duration from 10–52 weeks.
- The primary outcome measured the change in A1C.
- The secondary outcomes measured the following:
  - Other glycemic measures: Fasting glucose concentration
  - CGM metrics: Blood glucose time in range (TIR), time below range (TBR), time above range (TAR)
  - Body composition: Weight, body mass index (BMI)
  - Metabolic outcomes: Blood pressure, lipid panel
  - Medication changes
  - Safety events
  - Psychological outcomes: Satisfaction, distress, and quality of life
- Outcomes were measured as effects that were presented as mean differences with 95% confidence intervals (CI), or as relative risks with 95% confidence intervals for binary outcomes.
- Heterogeneity across studies was measured using standardized X^2 and I^2 statistics.

INTERVENTION (# IN THE GROUP):

- CGM: 632 (17 RCTs)
- isCGM: 871 (9 RCTs)

COMPARISON (# IN THE GROUP):

- Usual care/SMBG (vs CGM): 514

- Usual care/SMBG (vs isCGM): 766

FOLLOW-UP PERIOD: Eight weeks (ranged from 8.0–52 weeks)

RESULTS:

Primary Outcome –

- CGM decreased A1C compared to SMBG (mean difference [MD] –0.19%; 95% CI, –0.34 to –0.04; I^2=19%).
- isCGM decreased A1c compared to SMBG (MD –0.31%; 95% CI, –0.46 to –0.17; I^2=43%).

Secondary Outcome –

- CGM resulted in no significant difference in fasting or mean glucose concentration compared to SMBG.
- isCGM reduced fasting and mean glucose concentration compared to SMBG:
  - Fasting glucose concentration (MD –7.5; 95% CI, –14 to –0.75)
  - Mean glucose concentration (MD –18; 95% CI, –32 to –4.0)
- CGM resulted in no significant difference in TIR compared to SMBG.
- isCGM significantly increased TIR compared to SMBG (MD 8.9%; 95% CI, 4.1–14).
- CGM and isCGM resulted in no significant difference in TBR compared to SMBG.
- Time Above Range (TAR)
- CGM increased TAR >140 mg/dL and >180 mg/dL compared to SMBG:
  - TAR >140 mg/dL (MD 10%; 95% CI, 3.7–17)
  - TAR >180 mg/dL (MD –7.70%; 95% CI, –15 to –0.7)
- CGM resulted in no significant difference in TAR >250 mg/dL compared to SMBG.
- isCGM decreased time per day with glucose >240 mg/dL compared to SMBG (MD –0.91 hours; 95% CI, –1.5 to –0.31).
- CGM resulted in no significant difference in body composition compared to SMBG.
- isCGM reduced waist circumference compared to SMBG (1 study; MD –4.7; 95% CI, –8.2 to –1.2).
- CGM resulted in no significant difference in vascular risk factors compared to SMBG.
- isCGM increased systolic blood pressure compared to SMBG (1 study; MD 10; 95% CI 3.7–16).
- CGM decreased glycemic medication use compared to SMBG (MD –0.67; 95% CI, –1.2 to –0.13).
- CGM increased the risk for any adverse event compared to SMBG (risk ratio [RR] 1.2; 95% CI, 1.01–1.5).
- isCGM increased the risk of any adverse event (RR 1.3; 95% CI, 1.05–1.6), and device-related adverse events (RR 4.2; 95% CI, 1.8–10).
- CGM reduced satisfaction scores compared to SMBG (standardized mean difference [SMD] –0.05; 95% CI, –0.29 to –0.19).
- isCGM increased satisfaction scores compared to SMBG (SMD 0.44; 95% CI, 0.29–0.59).

LIMITATIONS:

- The heterogeneity of data analyzed resulting from population variations, diverse interventions, and variation in definition of outcomes could limit the results.
- Some of the included studies had small sample sizes.
- The inclusion of single-study outcomes could limit the generalizability of the results.
- Applicability of the results to populations >53 years old remains uncertain because of most studies involved patients who were at least 53 years old.

Amanda White, MD
Community Health Care FMRP
Tacoma, WA

The "Love Drug" Legacy: Unpacking Oxytocin's Impact on Families Down the Line

Intrapartum Synthetic Oxytocin, Behavioral and Emotional Problems in Children, and the Role of Postnatal Depressive Symptoms, Postnatal Anxiety and Mother-to-Infant Bonding: A Dutch Prospective Cohort Study

Tichelman E, Warmink-Perdijk W, Henrichs J, et al. Intrapartum Synthetic Oxytocin, Behavioral and Emotional Problems in Children, and the Role of Postnatal Depressive Symptoms, Postnatal Anxiety and Mother-to-infant Bonding: A Dutch Prospective Cohort Study. *Midwifery*. 2021;100:103045. doi:10.1016/j.midw.2021.103045

KEY TAKEAWAY: Intrapartum oxytocin use was not associated with differences in child emotional or behavioral problems.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Synthetic oxytocin is commonly used for intrapartum labor management and for postpartum hemorrhage management. Since oxytocin is also an endogenous hormone, synthetic oxytocin may impact endogenous oxytocin signaling pathways in ways that could affect maternal-child bonding, maternal mood, and potentially child development as well. This study assessed the relationship between synthetic oxytocin use during labor with pediatric behavior for up to 60 months postpartum and maternal mood and infant-relationship for up to six months postpartum.

PATIENTS: Women with singleton gestations and term deliveries in the Netherlands

INTERVENTION: Synthetic oxytocin during labor

CONTROL: No synthetic oxytocin used during labor

PRIMARY OUTCOME: Pediatric emotional or behavioral problems for up to 60 months postpartum

Secondary Outcome: Maternal depressive or anxiety symptoms, mother-to-infant bonding

METHODS (BRIEF DESCRIPTION):

- 5,748 women identified via two prior studies, singleton gestations with term deliveries and had children <60 months old at time of study.
- 1,578 women met the criteria and responded to the survey.
- Intravenous (IV) oxytocin use in labor was determined by medical chart review identifying use of oxytocin vs not used, registered as yes/no.
- Pediatric behavioral and emotional problems were measured using a published questionnaire at 18 months and 45–60 months.
    - The Child Behavior Checklist (CBCL]), 99-item raw score transformed into two scales: a 0–72 scale for “internalizing problems” and a 0–48 scale for “externalizing problems;” in both scales, a higher score indicates greater severity.
- The secondary outcomes used published questionnaires to assess maternal depression, maternal anxiety, and maternal-infant bonding at six months:
    - Maternal depression was measured using the Edinburgh Postpartum Depression Scale (EPDS). Scores range from 0–30, with higher scores indicating more depressive symptoms),
    - Maternal anxiety was measured using State Trait Anxiety Inventory short form (STAI-6). Scores range from 20–80, with higher scores indicating more anxious symptoms.
    - Maternal-infant bonding was measured at 6–45 months postpartum using the Mother-to-Infant Bonding Scale (MIBS). Score range from 0–24, with higher scores indicating a worse maternal-child bond.

INTERVENTION (# IN THE GROUP): 607

COMPARISON (# IN THE GROUP): 921

FOLLOW-UP PERIOD: 60 months postpartum

RESULTS:

Primary Outcome –

- Intrapartum oxytocin was not associated with differences in child emotional or behavioral scores.
    - Children exposed in utero (mean internalizing scores 5.7 vs 5.1, respectively; β=.02; *p*=.81)
    - Children exposed in utero (mean externalizing scores 9.8 vs 8.9, respectively; β=.09; *p*=.18)

Secondary Outcome –

- Mothers who received oxytocin during labor reported slightly higher depressive symptoms at six months postpartum (mean 5.1 vs 4.4; β=.17; *p*=.02).

- Oxytocin exposure was not associated with postpartum maternal anxiety or mother-infant bonding.

LIMITATIONS:

- The dose of oxytocin was not recorded, so it's impossible to determine if a dose-response relationship exists.
- There was no data measuring observational maternal behavior or clinical diagnoses, only self-reported questionnaires.
- The study did not differentiate among indications for oxytocin and did not evaluate for postpartum oxytocin use for hemorrhage management.
- The study did not discuss how correction was made for confounders, as the populations in the intervention vs control groups had statistically significantly different rates of Cesarean section, primiparity, and labor lengths.
- Different timing was used for the mother-to-infant bonding measure compared to the child behavior, anxiety, and depression questionnaires.

Gera Stancheva, MD
Northwest Washington FMRP
Bremerton, WA

180 Days of Defense: Nirsevimab's RSVictory

180-day Efficacy of Nirsevimab Against Hospitalization for Respiratory Syncytial Virus Lower Respiratory Tract Infections in Infants (HARMONIE): A Randomized, Controlled, Phase 3b Trial

Munro APS, Drysdale SB, Cathie K, et al. 180-day Efficacy of Nirsevimab against Hospitalization for Respiratory Syncytial Virus Lower Respiratory Tract Infections in Infants (HARMONIE): A Randomized, Controlled, Phase 3b Trial. *Lancet Child Adolesc Health*. 2025;9(6):404-412. doi:10.1016/S2352-4642(25)00102-6

KEY TAKEAWAY: A single intramuscular (IM) dose of Nirsevimab shielded healthy infants (born at 29 weeks gestation or later) throughout their entire first respiratory syncytial virus (RSV) season, cutting RSV-related lower respiratory tract infection (LRTI) hospitalizations by roughly 83% over 180 days with a reassuring safety profile.

STUDY DESIGN: Multinational, open-label pragmatic randomized controlled trial (RCT)

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: RSV is the leading cause of infant bronchiolitis and hospitalization each winter. Palivizumab provides protection only for very high-risk infants and requires monthly dosing. Earlier phase-3 data suggested Nirsevimab, a long-acting monoclonal antibody, could protect healthy infants for an entire season, but definitive evidence for full 180-day efficacy in routine clinical settings was lacking.

PATIENTS: Healthy infants up to 12 months

INTERVENTION: IM Nirsevimab

CONTROL: Standard care

PRIMARY OUTCOME: RSV/LRTI hospitalization within 180 days

Secondary Outcome: Very-severe RSV/LRTI, all-cause LRTI hospitalizations, adverse events

METHODS (BRIEF DESCRIPTION):

- The authors conducted a phase 3b pragmatic RCT using a computer-generated 1:1 random allocation stratified by site with central concealment.
- The study was open label to participants and clinicians; RSV diagnosis was confirmed by blinded central polymerase chain reaction (PCR) testing and independent adjudication.
- Healthy term or later-preterm infants (≥29 weeks gestation) ≤12 months at enrollment and entering their first RSV season were included in the study.
- Individuals with chronic lung disease, hemodynamically significant congenital heart disease, immunodeficiency, or prior RSV prophylaxis were excluded from the study.
- Participants were four months old on average; 52% were male while 48% were female. 85% of the participants were term deliveries. 58% received their first dose before and 42% during their first RSV season.
- Nirsevimab was administered as a single IM dose (50 mg for <5 kg; 100 mg for ≥5 kg).
- The control group infants received routine vaccinations only without placebo vaccination.
- Follow-up contacts were at three, six, and 12 months, at which parents/guardians completed secure electronic diaries (web-/app-based) with monthly automated prompts to record any respiratory symptoms, healthcare visits, or hospitalizations.
- The primary endpoint was defined as a hospitalization for LRTI with PCR-confirmed RSV occurring within 180 days of the dose or of study entry for controls.

INTERVENTION (# IN THE GROUP): 4,038

COMPARISON (# IN THE GROUP): 4,019

FOLLOW-UP PERIOD: 180 days

RESULTS:

Primary Outcome –

- Nirsevimab decreased the incidence of RSV-related LRTI hospitalizations compared to standard care (relative risk [RR] 0.18; 95% CI, 0.09–0.32).
  - This corresponded to a reduction from 17 to 3 hospitalizations per 1,000, or 14 fewer admissions per 1,000 treated infants.

Secondary Outcome –

- Nirsevimab decreased very-severe RSV/LRTI hospitalizations compared to standard care (RR 0.25; 95% CI, not reported).
- Nirsevimab decreased any-cause LRTI admissions compared to standard care (RR 0.57; 95% CI, not reported).

- Patients were tracked for 12 months in total, and the overall adverse-event rates were virtually identical for Nirsevimab compared to standard care, with no treatment-related serious adverse events observed.

LIMITATIONS:

- The open-label design introduces potential for performance bias, though this was mitigated by blinding of outcome adjudicators.
- Beyond providing funding, Sanofi & AstraZeneca coordinated site operations, managed data collection, performed the statistical analyses, and jointly interpreted the findings, heightening the potential for sponsorship bias despite independent endpoint adjudication.
- This study was conducted solely in temperate European countries; so, the results may not generalize to regions with year-round RSV circulation.
- Follow-up was limited to a single RSV season; durability of protection in subsequent seasons remains unknown.

Joshua George, MD
Northern Light Eastern Maine Medical Center
Bangor, ME