GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of April 28- May 2, 2025

SPOTLIGHT:

Does Cerebral Tissue Oxygenation Monitoring Improve Cerebral Injury Outcomes in Preterm Neonates?

- Benefits of Intermittent Fasting in Adults with Metabolic Syndrome
- Do Adaptive Behavioral Interventions Affect Weight Loss Management?

Does Cerebral Tissue Oxygenation Monitoring Improve Cerebral Injury Outcomes in Preterm Neonates?

Cerebral Regional Tissue Oxygen Saturation to Guide Oxygen Delivery in Preterm Neonates During Immediate Transition After Birth (COSGOD III): Multicenter Randomized Phase 3 Clinical Trial

Pichler G, Goeral K, Hammerl M, et al. Cerebral regional tissue Oxygen Saturation to Guide Oxygen Delivery in preterm neonates during immediate transition after birth (COSGOD III): multicentre randomised phase 3 clinical trial [published correction appears in BMJ. 2023 May 15;381:p1102. doi: 10.1136/bmj.p1102.]. *BMJ*. 2023;380:e072313. Published 2023 Jan 24. doi:10.1136/bmj-2022-072313

KEY TAKEAWAY: The use of near-infrared spectroscopy as a guide for oxygen therapy over traditional peripheral pulse oximetry does not decrease neonatal cerebral injury or mortality.

STUDY DESIGN: Multicenter, multinational, randomized trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: The immediate transition period for neonates involves complex physiological changes in breathing, lung aeration and the transition from intrauterine to extra-uterine circulation. In neonatal resuscitation, it is recommended to target arterial oxygen saturation (SpO_2) to guide delivery of oxygen and respiratory support. After initiation of spontaneous breathing, the partial pressure of oxygen rapidly increases. Delivery of oxygen of cerebral tissue normalizes faster than peripheral SpO_2, suggesting that there is a preferential shunting of oxygenated blood to the brain. Measuring cerebral oxygenation ($crSO_2$) may provide a more accurate target in preventing cerebral hypoxia.

PATIENTS: Neonates born before 32 weeks without severe congenital malformation

INTERVENTION: Near infrared spectroscopy + standard care

CONTROL: Standard care

PRIMARY OUTCOME: Composite of survival without cerebral Injury

Secondary Outcome: Respiratory distress syndrome, culture proven infection, necrotizing enterocolitis, bronchopulmonary dysplasia, retinopathy of prematurity, persistent ductus arteriosus

METHODS (BRIEF DESCRIPTION):

- Participants were recruited from 11 neonatal intensive care units (ICU) in Europe and Canada.
- Participants included neonates born before 32 weeks without severe congenital malformation including brain, heart, lung or the presence of prenatal cerebral injury.
- Participants were randomized 1:1 to either monitored cerebral oxygen saturation or standard care via a web-based randomization service.
    - Intervention: Oxygen therapy guided by cerebral oxygen levels obtained via infrared spectroscopy. A member of the research team documented the $crSO_2$ values for every minute during resuscitation.
    - Control: Oxygen therapy guided by traditional peripheral pulse oximetry, applied to the right hand. A member of the research team documented the $crSO_2$ values for every minute from the device's storge after resuscitation.
- The resuscitation team was masked to the $crSO_2$ in the control group by either concealing the near infrared spectroscopy monitor or turning the monitor away.
    - Group allocation was concealed during statistical analysis.
- Pulse oximetry was used to monitor SpO_2 and heart rate (HR). Electrocardiography was performed according to local guidelines.
- In the immediate transition after birth, patients were either monitored with standard peripheral pulse oximetry or infrared cerebral spectroscopy to guide oxygen delivery.
- The primary composite outcome was survival without cerebral injury, defined as intraventricular hemorrhage or periventricular leukomalacia, assessed using all-cause mortality and cerebral ultrasonography.
    - Cerebral injury was defined as any grade of intraventricular hemorrhage or cystic periventricular leukomalacia.

- Secondary outcome measures were individual components of the primary outcome, which included presence of respiratory distress syndrome, culture proven infection, necrotizing enterocolitis, bronchopulmonary dysplasia, retinopathy of prematurity, and persistent ductus arteriosus requiring intervention.

INTERVENTION (# IN THE GROUP): 304
COMPARISON (# IN THE GROUP): 303

FOLLOW-UP PERIOD: 24 hours, 2–5 days, 6–8 days, 12–16 days and before discharge or term equivalent, whichever came first

RESULTS:

Primary Outcome –

- There was no statistical difference in survival without cerebral injury in patients assigned to near-infrared spectroscopy compared to standard care (relative risk [RR] 1.1; 95% CI, 0.98–1.1).

Secondary Outcome –

- There was no significant difference in respiratory distress syndrome, culture proven infection, necrotizing enterocolitis, bronchopulmonary dysplasia, retinopathy of prematurity, or persistent ductus arteriosus in patients assigned to near-infrared spectroscopy compared to standard care.

LIMITATIONS:

- The majority of included neonates were born by caesarean section.
- Full masking could not be guaranteed as cerebral ultrasonography was performed locally.
- No follow up period was included in the study design and may be beneficial in the future when assessing sequelae and additional secondary outcomes.

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The views expressed herein are those of the author and do not necessarily reflect the official policy of the Department of the Army, Defense Health Agency, Department of Defense, or the US Government.

Benefits of Intermittent Fasting in Adults with Metabolic Syndrome

Time-Restricted Eating in Adults with Metabolic Syndrome: A Randomized Controlled Trial

Manoogian ENC, Wilkinson MJ, O'Neal M, et al. Time-Restricted Eating in Adults With Metabolic Syndrome: A Randomized Controlled Trial. *Ann Intern Med*. 2024;177(11):1462-1470. doi:10.7326/M24-0859

KEY TAKEAWAY: Time-restricted eating (TRE) significantly improves insulin sensitivity and fasting glucose levels in adults with metabolic syndrome, offering a promising non-pharmacological intervention to reduce metabolic risk factors.

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Metabolic syndrome has been a major contributor to the development of type 2 diabetes and cardiovascular disease. This study aimed to evaluate the effects of intermittent fasting on key metabolic parameters in adults with metabolic syndrome.

PATIENTS: Adults 18–75 years old with metabolic syndrome, an elevated body mass index (BMI), and elevated fasting glucose or hemoglobin A1C (HbA1c)

INTERVENTION: TRE

CONTROL: Standard of care (SOC)

PRIMARY OUTCOME: Insulin sensitivity

Secondary Outcome: Cardiometabolic factors, trunk fat

METHODS (BRIEF DESCRIPTION):

- Eligible participants were 18–75 years old with metabolic syndrome (fasting glucose 5.6–6.9 mmol/L), elevated BMI (BMI ≥25 and ≤41 kg/m²), and a prediabetic HbA1c, or (HbA1c 5.7–7.0%).
- Participants were allowed to be on medications for lipid management (statins), antihypertensive drugs, and antidiabetic drugs.
- Patients who were pregnant, breastfeeding, had sleep disruption from shift work, were on unstable medication regimens, and had completed recent weight loss interventions were excluded from the study.
- Participants in the TRE group were assigned to an 8–10 hour eating window with at least 14 hours of fasting daily. Patients were also given lifestyle and nutritional recommendations.
- The SOC group continued their usual eating patterns with no restriction on meal timing and were given lifestyle and nutritional recommendations.
- At visit one, participants completed baseline assessments and were also instructed to track their food intake via the myCircadianClock (mCC) app, wear a continuous glucose monitor (CGM), and an actigraphy device for two weeks.
- At visit two, further baseline assessments were conducted, including body composition analysis (via dual-energy x-ray absorptiometry) and a 24-hour dietary recall.
- The following were measured as the primary outcomes:
  - HbA1c was measured via a blood sample analysis.
  - Fasting glucose levels were measured after an overnight fast via venous or capillary blood analysis.
  - Fasting insulin levels were measured after an overnight fast to assess pancreatic insulin secretion via a blood sample analysis.
  - Mean glucose levels were assessed over 24 hours using CGM.
  - Insulin resistance was assessed using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), a formula that evaluates insulin sensitivity based on fasting glucose and insulin levels. Scores range from 0.5–5.0, with higher values indicating worse insulin sensitivity and greater insulin resistance.
  - Continuous overall net glycemic action (CONGA) was measured to reflect glycemic variability, calculated using CGM data to assess the overall glycemic excursion. A lower percentage of CONGA indicates less glycemic variability, suggesting better metabolic stability.
  - The glycemic mean of daily differences (MODD) measures glycemic variability, calculated from CGM data. Lower values indicate reduced daily glucose fluctuations, which is associated with better metabolic control.
- The following were measured as the secondary outcomes of the study:

- Low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were measured via a lipid panel blood test.
- High-sensitivity C-reactive protein (hs-CRP) was measured via a blood test to assess inflammation levels.
- Trunk fat percentage was measured using a Dual-energy X-ray absorptiometry (DXA) scan.

INTERVENTION (# IN THE GROUP): 60

COMPARISON (# IN THE GROUP): 60

FOLLOW-UP PERIOD: 12 weeks

RESULTS:

Primary Outcome –

- TRE decreased HbA1c compared to SOC (between-group difference −0.77; 95% CI, −1.4 to −0.17).
- TRE decreased fasting glucose levels compared to SOC (between-group difference −1.4; 95% CI, −2.4 to −0.43).
- TRE decreased glycemic MODD compared to SOC (between-group difference −1.5%; 95% CI, −3.0 to −0.06).
- TRE did not significantly improve fasting insulin levels compared to SOC (between-group difference −0.19; 95% CI, −0.66 to 0.28).
- TRE did not significantly improve mean glucose levels compared to SOC (between-group difference −0.04; 95% CI, −0.07 to 0.0).
- TRE did not significantly improve CONGA compared to SOC (between-group difference −0.51; 95% CI, −1.7 to 0.65).

Secondary Outcome –

- There was no significant difference in LDL cholesterol, HDL cholesterol, triglycerides, and hs-CRP between TRE and SOC.
- TRE decreased trunk fat mass compared to SOC (between-group difference −0.27%; 95% CI, −0.41 to −0.13).

LIMITATIONS:

- Participants were aware of their group allocation, which could lead to bias in self-reported adherence to the eating regimen.
- The 12-week duration limited the ability to assess the long-term sustainability of the benefits associated with TRE.
- While the study utilized the mCC app and CGM to monitor adherence, there may have been differences in adherence levels between participants, which were not fully explored. Also, CGM might not detect when participants eat food that has a low glycemic index.
- The study population was relatively homogenous, with participants recruited from UCSD Health. The findings may not apply to individuals from other geographical areas or with different cultural eating habits.
- The study did not control for caloric intake or dietary composition, which could have influenced the outcomes.

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Do Adaptive Behavioral Interventions Affect Weight Loss Management?

An Adaptive Behavioral Intervention for Weight Loss Management: A Randomized Clinical Trial

Spring B, Pfammatter AF, Scanlan L, et al. An Adaptive Behavioral Intervention for Weight Loss Management: A Randomized Clinical Trial. *JAMA*. 2024;332(1):21-30. doi:10.1001/jama.2024.0821

KEY TAKEAWAY: For individuals attempting weight loss, a wireless feedback system (WFS) + coaching leads to greater weight loss at six months compared to WFS alone.

STUDY DESIGN: Noninferiority, single-blinded, randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Obesity is a growing health concern leading to increased incidence of comorbid health conditions and substantial medical costs. Current obesity treatments fail to balance effectiveness, costs, and available resources. This study aimed to evaluate if a less resource-intensive behavioral weight loss strategy (WFS without coaching) in the context of social and healthcare constraints is noninferior to a more resource-intensive program (WFS + coaching).

PATIENTS: Adults with body mass index (BMI) of 27–45

INTERVENTION: WFS + coaching

CONTROL: WFS alone

PRIMARY OUTCOME: Weight change at six months

Secondary Outcome: Weight change at three and 12 months with and without step-up therapy

METHODS (BRIEF DESCRIPTION):

- This noninferiority randomized trial was conducted at Northwestern University from June 2017 to March 2021, recruiting participants based on age, BMI, and suboptimal weight loss.
- Adults 18–60 years old with a BMI of 27–45 and no weight changes >11 kg in the past six months were included in the study.
- Participants received a WFS which included a Wi-Fi activity tracker and scale that transmits data to a smartphone app, to provide daily feedback on a participant's progress in their lifestyle changes and weight loss. The WFS was returned after 12 weeks.
- Patients were randomized to either WFS alone or WFS + health coaching.
- Health coaches monitored progress, provided feedback, and adjusted strategies to enhance adherence, tailoring coaching to participants' evolving needs and challenges.
- Patients who did not achieve clinically significant weight loss of at least 5% of their baseline weight by 12 months were considered non-responsive to the initial study.
    - Stage two randomization occurred at the 12-month mark for those who were deemed nonresponsive, allowing for adjustments in their intervention strategy.
- Step-up strategies included supportive push notifications, increased counseling sessions, and personalized dietary and exercise plans.
- Weight changes were recorded at three, six, and 12 months for all participants.
- Weight changes among non-responders who received step up therapy were evaluated at three, six, and 12 months.
- The primary outcome was measured by evaluating weight change in kilograms (kg) in six months.
- The secondary outcome was measured by evaluating the weight change at three months and 12 months, with and without step-up therapy.
- Weight change among non-responders were assessed by examining the differences in weight change at three, six, and 12 months between step-up interventions.

INTERVENTION (# IN THE GROUP): 201

COMPARISON (# IN THE GROUP): 199

FOLLOW-UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- WFS + coaching resulted in greater weight loss at six months compared to WFS alone (between-group difference –2.0 kg; 95% CI, –2.9 to –1.1).

Secondary Outcome –

- WFS + coaching led to greater weight loss than WFS alone for responders at three months (between-group difference –1.6 kg; 95% CI, –2.2 to –1.0).
- WFS + coaching led to greater weight loss than WFS alone for responders at 12 months (between-group difference –1.7 kg; 95% CI, –2.9 to –0.5).

- There were no statistically significant differences in weight change between step-up interventions for non-responders at three and 12 months.
- Various treatment sequences yielded similar weight loss patterns over time, with no optimal sequence determined.

LIMITATIONS:

- The participants in this study consisted of mostly well-educated, technology literate, and majority female participants with smartphone access, which limits the generalizability of its findings to broader and more diverse populations.
- Removing the WFS and having a shorter intervention period (3 months) most likely impacted on the overall potential for continued weight loss and long-term efficacy of the weight loss strategies.

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