GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

Volume 5 - Issue 10

FPIN
Family Physicians Inquiries Network

What's in this week's issue?

Week of March 10-14, 2025

SPOTLIGHT:

Breathing Leads to Less Stress, Depression, and Anxiety

- Redesigning Behavioral Health for Those with Multiple Chronic Conditions
- Moderating Drinking Habits with Smartphones
- Get proBioticS for GBS
- Effectiveness of Multi-Component Non-Pharmacologic Interventions: Reducing Delirium Occurrence and Duration in Non-ICU Adult Patients

Breathing Leads to Less Stress, Depression, and Anxiety

Effect of Breathwork on Stress and Mental Health: A Meta-Analysis of Randomized Controlled Trials

Fincham GW, Strauss C, Montero-Marin J, Cavanagh K. Effect of breathwork on stress and mental health: A meta-analysis of randomized controlled trials. *Sci Rep*. 2023;13(1):432. Published 2023 Jan 9. doi:10.1038/s41598-022-27247-y

KEY TAKEAWAY: Breathwork improves self-reported stress with a small to medium effect compared to non-breathwork standard treatments.

STUDY DESIGN: Meta-analysis of 26 randomized controlled trials (RCTs) (N=785)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Stress, anxiety, and depression are becoming more common. Easy and accessible therapeutic approaches are needed to reduce and build resilience to stress worldwide. Given the possible mismatch between hype and evidence, it is paramount that breathwork is grounded in evidence.

PATIENTS: Adults with anxiety and depression

INTERVENTION: Therapeutic breathwork

CONTROL: Non-breathwork standard treatment

PRIMARY OUTCOME: Stress

Secondary Outcome: Anxiety, depression

METHODS (BRIEF DESCRIPTION):

- 26 RCTs that were published in English, included a breathwork intervention where breathwork formed ≥50% of the intervention, included an outcome measure of self-reported stress, anxiety, or depression, and included an adult participant sample >18 years old were included in the analysis.
- Adults with diagnoses of anxiety and depression were included.
- Individuals without stress, anxiety, or depression were excluded.
- Breathwork interventions included self-reported stress, anxiety, and depression following breathwork therapy which was compared to stress, anxiety, and depression prior to breathwork
- Non-breathwork interventions included self-reported stress, anxiety, and depression following therapy without breathwork interventions compared to stress, anxiety, and depression prior to therapy.
- The primary outcome measured the change in self-reported stress.
- The secondary outcomes measured the change in self-reported anxiety and depression.
- Outcomes were measured by the standardized between-group difference (g-value) where a lower value represents a smaller effect and a higher value represents a large effect.
  - Small effect=0.2
  - Medium effect=0.5
  - Large effect=0.8

INTERVENTION (# IN THE GROUP): 417

COMPARISON (# IN THE GROUP): 368

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- Patients who received breathwork treatments had significantly lower levels of self-reported stress compared to those who received standard treatments (12 studies; g −0.35; 95% CI, –0.55 to –0.14).

Secondary Outcome –

- Patients who received breathwork treatments had lower levels of self-reported anxiety compared to those who received standard treatments (20 studies; g −0.32; 95% CI, −0.48 to −0.16).
- Patients who received breathwork treatments had lower levels of self-reported depression compared to those who received standard treatments (18 studies; g −0.40; 95% CI, –0.58 to –0.22).

LIMITATIONS:

- Self-reported stress may lead to more bias depending on individuals' tolerance to stress and the variation of stress levels amongst different populations.
- Breathwork is a relatively new phenomenon in the West, and thus, the study populations are small.

Michael Swainston, MD
University of Wyoming Casper FMRP
Casper, WY

Redesigning Behavioral Health for Those with Multiple Chronic Conditions

A Cluster Randomized Trial of Primary Care Practice Redesign to Integrate Behavioral Health for Those Who Need It Most: Patients with Multiple Chronic Conditions

Littenberg B, Clifton J, Crocker AM, et al. A Cluster Randomized Trial of Primary Care Practice Redesign to Integrate Behavioral Health for Those Who Need It Most: Patients With Multiple Chronic Conditions. *Ann Fam Med*. 2023;21(6):483-495. doi:10.1370/afm.3027

KEY TAKEAWAY: Practices receiving integrated behavioral health (IBH) resources do not improve any of the quality of life measures among patients with multiple chronic conditions. Practices receiving IBH resources report better workflows than control practices.

STUDY DESIGN: Cluster randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Coordinating behavioral health and primary care services has shown improved outcomes for patients with depression and mixed depression and anxiety. Research has been lacking in testing the effects of IBH and primary care among patients with multiple chronic conditions. This study examined the effectiveness of a single approach to integrated primary care and IBH improvements on outcomes for primary care patients experiencing multiple chronic conditions (MCCs) and secondarily to study the effect on primary care efforts to enhance integration.

PATIENTS: Individuals with multiple chronic medical conditions or behavioral health conditions

INTERVENTION: Active primary care practices

CONTROL: Control primary care practices

PRIMARY OUTCOME: Quality of life

Secondary Outcome: Integration of behavioral health services

METHODS (BRIEF DESCRIPTION):

- Primary care practitioners from 42 randomized practices across internal medicine and family medicine specialties were recruited during 2016–2018.
- Recruited patients had ≥1 chronic medical condition, ≥1 chronic behavioral health condition, or three medical conditions.
- The study was divided into an active practice group and a control practice group.
    - Active practices had a facilitator for practice redesign support and quality improvement coaching, as well as access to workbooks detailing strategies for care management, registry and population reports, and team-based care.
    - Control practices had no specific intervention applied beyond regular ongoing activities.
- Participating patients completed an online survey via the Patient-Reported Outcomes Measurement Information System (PROMIS-29) at baseline, midpoint, and at two years.
- The primary outcome measured the patient's quality of life via the PROMIS-29 questionnaire.
    - Eight domains are assessed in the PROMIS-29 which include anxiety, depression, fatigue, sleep disturbance, pain interference, pain intensity, social participation, and physical function.
- The secondary outcome measured the integration of behavioral health services into practices assessed using the Practice Integration Profile (PIP).
    - A medical provider, behavioral health provider, administrator, and practice staff member completed a PIP at baseline, midpoint, and at two years.
    - Scores for the PIP ranged from 0–100, covering six domains, which include workflow, clinical services, workspace, integration of providers, patient identification, and patient engagement.

INTERVENTION (# IN THE GROUP): 1,190

COMPARISON (# IN THE GROUP): 1,755

FOLLOW-UP PERIOD: Two years

RESULTS:

Primary Outcome –

- Active practices did not improve any of the quality of life measures compared to control practices:
    - Anxiety (change 0.08; 95% CI, –0.53 to 0.69)
    - Depression (change 0.21; 95% CI, –0.37 to 0.79)
    - Fatigue (change 0.07; 95% CI, –0.54 to 0.68)
    - Sleep disturbance (change –0.05; 95% CI, –0.58 to 0.49)
    - Pain interference (change 0.19; 95% CI, –0.40 to 0.79)

- Pain intensity (change 0.1; 95% CI, –0.08 to 0.28)
- Social participation (change –0.06; 95% CI, –0.71 to 0.59)
- Physical function (change 0.1; 95% CI, –0.39 to 0.60)

Secondary Outcome –

- The 13 active practices that completed the intervention workbook had significantly better integration of behavioral health services compared to the seven active practices that did not complete workbooks (change 9.9; 95% CI, 2.0–18).
- Workflow improved in the active practices compared to control practices (change 9.3; 95% CI, 1.7–17).
- The mental health summary improvement in PROMIS-29 scores among active practices was not significantly better than the improvement among control practices.

LIMITATIONS:

- Patients who agreed to participate might be different from those who declined therefore possibly introducing selection bias.
- Researchers did not have access to individual patient electronic health records (EHRs) after enrollment to know which patients received behavioral health services.
- Both surveys relied on self-reporting, introducing the possibility of social desirability bias.

Reshma Vasu, MD
Central Michigan University FMRP
Saginaw, MI

Moderating Drinking Habits with Smartphones

Effect of a Smartphone Intervention as a Secondary Prevention for Use Among University Students with Unhealthy Alcohol Use: Randomized Controlled Trial

Bertholet N, Schmutz E, Studer J, et al. Effect of a smartphone intervention as a secondary prevention for use among university students with unhealthy alcohol use: randomized controlled trial. *BMJ*. 2023;382:e073713. Published 2023 Aug 16. doi:10.1136/bmj-2022-073713

KEY TAKEAWAY: A smartphone application with alcohol consumption resources is beneficial for reducing alcohol consumption among university students.

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Unhealthy alcohol use and drinking habits among university students are a prevalent and growing concern in numerous countries around the world. Spreading awareness and tracking alcohol consumption among university students is one method to address this problem. This study aimed to address this problem by using a smartphone application to make university students more aware of their drinking habits, to reduce alcohol consumption among this population.

PATIENTS: University students who screened positive for unhealthy alcohol use

INTERVENTION: Smartphone application with resources related to alcohol consumption

CONTROL: No intervention

PRIMARY OUTCOME: Weekly alcohol consumption

Secondary Outcome: Heavy drinking days

METHODS (BRIEF DESCRIPTION):

- Undergraduate and graduate university students ≥18 years old who screened positive for unhealthy alcohol use via AUDIT-C were included in the study.
- Major exclusion criteria were <18 years old, not owning a smartphone, individuals involved in the app's development, and not having a score on the AUDIT-C questionnaire that was indicative of alcohol use disorder
- The AUDIT-C is a three-question screening questionnaire that accurately assesses an individual's alcohol consumption habits. Scored from 0–12, with a score of ≥4 in men and ≥3 in women indicative of alcohol use disorder (AUD).
- Students were randomly selected to either have or not have access to a smartphone application.
- The smartphone application provided users access to personalized feedback on self-reported alcohol consumption, a blood alcohol content computation tool, a self-monitoring tool, a goal-setting tool, a designated driver tool, and fact sheets related to alcohol and alcohol consumption.
- Students filled out assessments at three, six, and 12 months regarding alcohol consumption.
- One standard drink in this study was defined as a drink containing 10–12 g of ethanol.

INTERVENTION (# IN THE GROUP): 884

COMPARISON (# IN THE GROUP): 886

FOLLOW-UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- Subjects using the smartphone application consumed fewer alcoholic drinks per week compared to the control group (incidence rate ratio [IRR] 0.90; 95% CI, 0.85–0.96).

Secondary Outcome –

- Subjects using the smartphone application reduced the average number of heavy drinking days over 30 days compared to the control group (IRR 0.89; 95% CI, 0.83–0.96).

LIMITATIONS:

- A standard drink is defined differently depending on the country which could cause individuals to inaccurately report their alcohol consumption.
- Students self-reported their alcohol consumption, which could have resulted in under-reporting.
- The control group could have accessed a smartphone application from a friend.

Eric Benca, DO
Community Health Care FMRP
Tacoma, WA

Supplementation of Probiotics in Pregnant Women Targeting Group B Streptococcus Colonization: A Systematic Review and Meta-Analysis

Menichini D, Chiossi G, Monari F, De Seta F, Facchinetti F. Supplementation of Probiotics in Pregnant Women Targeting Group B Streptococcus Colonization: A Systematic Review and Meta-Analysis. *Nutrients*. 2022;14(21):4520. Published 2022 Oct 27. doi:10.3390/nu14214520

KEY TAKEAWAY: Probiotic supplementation results in lower Group B streptococcus (GBS) positive rectovaginal cultures in pregnant women 35–37 weeks gestation compared to placebo.

STUDY DESIGN: Systematic review and meta-analysis of five randomized controlled trials (N=583)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to small sample size)

BRIEF BACKGROUND INFORMATION: GBS infection in pregnant women is the leading cause of neonatal sepsis. Around 98% of newborns who are exposed to GBS are not affected. Of the 1–3% of neonates who become acutely infected, the mortality is reported to be up to 50–60%. Pregnant patients are screened for GBS colonization between 35–37 weeks gestation with a rectovaginal swab. If positive for GBS, they are typically given antibiotics at the time of delivery. Probiotic administration is suspected to decrease GBS colonization rates in order to avoid antibiotic administration in labor.

PATIENTS: Pregnant patients at 35–37 weeks gestation

INTERVENTION: Probiotic supplmentation

CONTROL: Placebo

PRIMARY OUTCOME: GBS-positive rectovaginal cultures

Subgroup Analysis: Timing of treatment, positive vs unknown GBS status, duration of treatment

METHODS (BRIEF DESCRIPTION):

- The study included randomized controlled trials evaluating the effects of probiotic supplementation during pregnancy on GBS recto-vaginal colonization.
- An electronic database search was performed through Pubmed, Medline, Clinicaltrials.gov, Science Direct, and Cochrane for specific terms related to the study's focus, such as "GBS," "Group B streptococcus," "colonization," "probiotics," "recto-vaginal colonization," and "randomized trial."
- The inclusion criteria included evaluating pregnant patients undergoing GBS screening and the effects of probiotics during pregnancy. 132 publications were identified, with only five studies ultimately included.
- The intervention consisted of oral probiotic supplementation.
    - Four of the studies each used a different dose of probiotic, which ranged from 1×10^8 colony forming units (CFU) to 5.4×10^9 CFU daily of both *Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14 L.*
    - One study used 4×10^9 CFU daily of Lactobacillus *jensenii Lbv116*, Lactobacillus *crispatus Lbv88*, Lactobacillus *rhamnosus Lbv96,* and Lactobacillus *gasseri Lbv150*.
- The duration of the treatment ranged from 2–12 weeks depending on the study.
- Some studies began treatment at 23 weeks gestation (before GBS status was known) and others began after 30 weeks (after GBS status was known).
- GBS rectovaginal cultures were collected at 35–37 weeks of gestation following either placebo or probiotic supplementation.
- The presence of GBS in rectovaginal cultures was analyzed as the primary outcome.
- Timing of treatment, positive vs unknown GBS status, and duration of treatment were then analyzed as the subgroup analysis.

INTERVENTION (# IN THE GROUP): 301

COMPARISON (# IN THE GROUP): 282

FOLLOW-UP PERIOD: Varied (2–12 weeks)

RESULTS:

Primary Outcome –

- Oral probiotics reduced GBS-positive colonization in pregnant women taking oral probiotics compared to placebo at 35–37 weeks gestation (5 trials, N=583; 32% vs 39%, respectively; odds ratio [OR] 0.62; 95% CI, 0.40–0.94).

Subgroup Analysis –

- Oral probiotics started after 30 weeks gestation reduced GBS-positive colonization compared to placebo (3 trials, n=193; OR 0.41; 95% CI, 0.21–0.78).
- Oral probiotics started before 30 weeks gestation did not reduce GBS-positive colonization compared to placebo (2 trials, n=390; OR 0.81; 95% CI, 0.48–1.4).
- Oral probiotics reduced GBS-positive colonization in pregnant women with known positive GBS colonization at baseline compared to placebo (3 trials, n=193; OR 0.41; 95% CI, 0.21–0.78).
- Oral probiotics did not reduce GBS-positive colonization in pregnant women with unknown GBS colonization at baseline compared to placebo (2 trials, n=390; OR 0.81; 95% CI, 0.48–1.4).
- Oral probiotics for <12 weeks reduced GBS-positive colonization in pregnant women compared to placebo (3 trials, n=192; OR 0.41; 95% CI, 0.21–0.78).
- Oral probiotics for >12 weeks did not reduce GBS-positive colonization in pregnant women compared to placebo (2 trials, n=390; OR 0.81; 95% CI, 0.48–1.4).

LIMITATIONS:

- Only five randomized control trials were utilized in the study.
- The studies involved different populations with variations in ethnicity.
- One of the studies used a different combination of probiotic strains.
- Probiotic dosages were different in all five studies and ranged from 1×10^8 CFU to 5.4×10^9 CFU daily.
- One study used a different strain of probiotics compared to the other four studies.
- Compliance with probiotic supplementation was not addressed.
- In the known GBS baseline status group, the actual number of participants that converted from GBS positive to GBS negative was not mentioned.
- The forest plot graphs for the three subgroups are the same.
- The data for the duration subgroup analysis was not stated.

Samantha Sondermayer, DO
St Peter Hospital Program
Chehalis, WA

Effectiveness of Multi-Component Non-Pharmacologic Interventions: Reducing Delirium Occurrence and Duration in Non-ICU Adult Patients

Non-Pharmacological Interventions for Preventing Delirium in Hospitalized Non-ICU Patients

Burton JK, Craig L, Yong SQ, et al. Non-pharmacological interventions for preventing delirium in hospitalized non-ICU patients. *Cochrane Database Syst Rev*. 2021;11(11):CD013307. Published 2021 Nov 26. doi:10.1002/14651858.CD013307.pub3

KEY TAKEAWAY: Multi-component non-pharmacologic interventions may reduce the occurrence of delirium in hospitalized adult-aged, non-intensive care unit (ICU) patients compared to usual care. However, there is no difference in mortality.

STUDY DESIGN: Meta-analysis and systemic review of 22 randomized controlled trials (N=5,718)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to performance bias)

BRIEF BACKGROUND INFORMATION: Delirium is an acute neuropsychological disorder that is frequently seen in hospitalized patients. Patients with delirium have symptoms of sudden onset of confusion, decreased concentration, memory lapses, and cognitive impairment, all of which can be very distressing to patients, their families, and the care team. Due to limited treatment options for delirium, it is preferable to focus efforts on prevention. There are known multicomponent interventions that target several of the common risk factors for delirium (poor physical orientation, poor sleep, and lack of mental stimulation). The goal of this meta-analysis was to identify the effectiveness of these non-pharmacological interventions in preventing hospital delirium.

PATIENTS: Adults admitted to non-ICU inpatient service

INTERVENTION: Various non-pharmacological interventions

CONTROL: Usual care

PRIMARY OUTCOME: Occurrence of delirium and mortality

Secondary Outcome: Delirium event severity and duration, hospital length of stay, new care home admission

METHODS (BRIEF DESCRIPTION):

- Monthly searches were conducted in databases including Medline, Embase, CINAHL, PsychInfo, and Lili. Trial registers were searched monthly, Cochrane Library quarterly, and grey literature sources were searched bi-annually. Results were imported into Covidence software to eliminate duplicates, and two reviewers screened articles for relevance.
- Patients had a mean age of 70–79 years old from various countries, and gender representation varied from study to study
- Studies included adult participants (≥18 years old) in general hospital settings, focusing on non-pharmacological interventions to prevent delirium.
- Studies in community, long-term care, nursing homes, ICU, or high-dependency unit (HDU) settings were excluded, along with those related to substance misuse or withdrawal-induced delirium.
    - Pharmacological delirium prevention methods were also excluded
- 14 studies compared multicomponent delirium prevention interventions (specific protocols to lower the risk of sleep deprivation, immobility, dehydration, and impairment) with usual care (standard physiotherapy focused on walking exercises), while two studies compared liberal (intervention) and restrictive (control) blood transfusion thresholds and their impact on mentation.
- The rest of the trials examined various non-pharmacological interventions against usual care.
- Usual care of dementia was the control, which was not specifically specified in the research
- The following were measured as the primary outcomes of the study:
    - The incidence of delirium during hospital admission was measured using a validated diagnostic method, with studies that relied solely on positive screening tests without a formal diagnosis being excluded.
    - Mortality as an inpatient was assessed at various time intervals, including between 1–3 months, 6–12 months, and >12 months from randomization. Additionally, new diagnoses of dementia were recorded at the same time intervals.

- The following were measured as the secondary outcomes of the study:
  - The duration of delirium episodes was measured in days, while severity was assessed using the Memorial Delirium Assessment Scale (MDAS), Delirium Rating Scale (DRS), and the Delirium Rating Scale Revised 1998 (DRS-R-98).
  - Hospital admission length was recorded in days. New psychotropic medication use during admission was monitored.
  - Activities of daily living were evaluated using the Barthel and Katz Indexes, quality of life was measured through patient-reported metrics, and carer's quality of life was assessed using carer-reported measures.
  - These evaluations were conducted at 1–3 months, 6–12 months, and ≥12 months from randomization.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Varied with the longest being three years

RESULTS:

Primary Outcome –

- Multi-component non-pharmacological interventions reduce the occurrence of delirium compared to usual care (14 trials, n=3,693; risk ratio [RR] 0.57; 95% CI, 0.46–0.71; moderate-certainty evidence; I^2=39%).
- There was no significant difference in inpatient mortality between multicomponent interventions and usual care (10 trials, n=2,640; 5.2% vs 4.5%, respectively; RR 1.2; 95% CI, 0.79–1.7; low-certainty evidence; I^2=15%)

Secondary Outcome –

- There was no difference in the duration or severity of delirium episodes between multicomponent interventions and usual care.
- Multicomponent interventions may result in a reduction in hospital length of stay compared to usual care (10 trials, n=3,351; mean difference [MD] –1.3 days; 95% CI, –2.6 to –0.04; low-certainty evidence; I^2=91%).
- There was no difference in new care home admission at the time of hospital discharge between multicomponent interventions and usual care.

LIMITATIONS:

- No blinding of participants and personnel which could yield performance bias.
- The review encountered constraints in analyzing alternative combinations of non-pharmacological interventions attributable to a restricted pool of studies and a limited spectrum of components available for delirium management.
- The generalizability of the study to the broader US population is compromised as a majority of the studies analyzed were conducted outside of the United States.

Jae H You, DO
Tripler Army Medical Center FMRP
Honolulu, HI

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.