GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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Family Physicians Inquiries Network

What's in this week's issue?

Week of September 27 - October 1, 2021

SPOTLIGHT: Should RSV vaccination be recommended during pregnancy to help prevent medically significant RSV infection in infants?

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GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Respiratory Syncytial Virus Vaccination during Pregnancy and Effects in Infants

Madhi SA, Polack FP, Piedra PA, et al. Respiratory Syncytial Virus Vaccination during Pregnancy and Effects in Infants. *N Engl J Med*. 2020; 383(5):426-439.

KEY TAKEAWAY: Vaccinating pregnant women with a single intramuscular dose of nanoparticle RSV F-protein does not significantly reduce RSV-associated, medically significant lower respiratory tract infections in the infant.
STUDY DESIGN: Multi-country randomized, observer-blind, placebo-controlled trial
LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Respiratory Syncytial Virus, RSV, is a leading cause of lower respiratory tract infections in infants and young children. It can have major consequences on the healthcare system with hospitalization and even death. A licensed vaccine is not yet available, but a monoclonal antibody, palivizumab, has shown promising passive immunity.

PATIENTS: Pregnant women 28–36 weeks' gestation near RSV season and their infants
INTERVENTION: Single-dose RSV vaccine
CONTROL: Placebo
OUTCOME: Primary – RSV infection
Secondary – Severe RSV
Safety – Injection site reaction, pneumonia

METHODS (BRIEF DESCRIPTION):

- The patients were healthy, pregnant women 18–40 years old between 28–36 weeks' gestation who received the vaccination or placebo at least two weeks prior to delivery and their infants who were born, at the earliest, at 37 weeks' gestation.
- The intervention group received a single dose of the RSV vaccine. The comparison group was given placebo.
- The infants of the women were then evaluated weekly for symptoms of RSV until 180 days after delivery. Parents/caregivers were also able to report symptoms at any time during the 180 days.
- The primary outcome to show vaccine efficacy (RSV-associated, medically significant lower respiratory tract infection) was measured using a lower bound of the 97.52% confidence interval of 30% or greater set for the definition of success by the FDA. The secondary outcomes used a 95% CI of greater than 0%.
- The study also analyzed the safety of the vaccine compared to placebo.

INTERVENTION (# IN THE GROUP): 3,051 women; 3,014 infants
COMPARISON (# IN THE GROUP): 1,585 women; 1,565 infants

FOLLOW UP PERIOD: The infants were followed for 180 days to monitor for lower respiratory tract infection and then 364 days to assess safety.

RESULTS:
Primary Outcome –

- Vaccine efficacy did not meet the pre-specified success criterion for efficacy (39%; 97.52% CI, −1.0 to 63.7).
- Infants with RSV-associated, medically significant, lower respiratory tract infection through 90 days in the vaccine group vs placebo was 1.5% vs 2.4%.

Secondary Outcome –

- Vaccine efficacy did not meet the success criterion for efficacy against RSV-associated lower respiratory tract infection with severe hypoxemia (48%; 95% CI,−8.2 to 75) or against hospitalization for RSV-associated infection (44%; 95% CI, 20 to 62).

Safety Outcome –

- Local injection site reaction was increased in those who received the vaccine vs. placebo (41% vs. 9.9%; *P*<.001).
- Common and serious adverse events were similar between the two infant groups; however, pneumonia was more common in the placebo group (4.5%) compared to the vaccine group (2.2%).

LIMITATIONS:

- Underpowered as there was an overestimate in the number of infants with a primary endpoint event.
- Cord blood testing for certain antibodies was not completed.

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Financial Incentives for Homeless Patients to Quit Smoking: Do They Work?

Financial Incentives for Smoking Abstinence in Homeless Smokers: A Pilot Randomized Controlled Trial

Baggett TP, Chang Y, Yaqubi A, McGlave C, Higgins ST, Rigotti NA. Financial Incentives for Smoking Abstinence in Homeless Smokers: A Pilot Randomized Controlled Trial. *Nicotine Tob Res*. 2018; 20(12):1442–1450. doi:10.1093/ntr/ntx178

KEY TAKEAWAY: Financial incentives ranging from $15 to $35 per visit show promise in encouraging homeless smokers to engage in short-term smoking abstinence.
STUDY DESIGN: Non-blinded randomized controlled trial
LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Three-quarters of homeless adults are cigarette smokers. Homeless adults have higher tobacco-related mortality rates and are less likely to quit smoking compared to the general population. Pharmacologic treatments alone have not proven effective to sustain smoking abstinence among homeless smokers.

PATIENTS: Adult smokers wanting to quit with at least 100 lifetime cigarettes and current smoking of at least 5 cigarettes a day
INTERVENTION: Abstinence-contingent financial incentives
CONTROL: No financial incentives specifically for smoking abstinence
OUTCOME: Brief smoking abstinence
Secondary Outcome: Brief smoking abstinence at eight weeks

METHODS (BRIEF DESCRIPTION):

- Homeless adult smokers >18 years old were recruited from the Boston Health Care for the Homeless Program and were randomly assigned either to receive financial incentives for smoking abstinence or no abstinence-contingent incentives.
- All participants received nicotine patches, the opportunity for in-person counseling from a certified Master Tobacco Treatment Specialist, and $10 for attending each of 14 checkup visits over 8 weeks.
- At each checkup visit, exhaled carbon monoxide levels were measured, with brief smoking abstinence defined as less than 8 parts per million.
- Participants in the intervention arm received escalating amounts of financial incentives ranging from $15 to $35 for each consecutive visit of abstinence, with a maximum of $440 over 8 weeks.

INTERVENTION (# IN THE GROUP): 25
COMPARISON (# IN THE GROUP): 25

FOLLOW UP PERIOD: 8 weeks

RESULTS:
Primary Outcome:

- Brief smoking abstinence rates were higher for participants receiving financial incentives compared to participants without abstinence-contingent incentives (odds ratio [OR] 7.3; 95% CI, 2.9–18).

Secondary Outcome:

- More participants receiving financial incentives for abstinence were found to be in brief smoking abstinence at the last checkup visit at 8 weeks compared to the control group (48% vs 8%; *P*=.004).

Self-Reported Outcomes:

- Participants that were given financial incentives for abstinence were more likely to report one-day cigarette abstinence (OR 4.9; 95% CI, 1.7–14).
- The seven-day cigarette abstinence rate difference between groups was not statistically significant.
- No statistically different usage in nicotine patches or in-person counseling.

LIMITATIONS:

- Pilot study with only 50 participants.
- No follow-up to determine if abstinence continued after financial incentives stopped.
- Exhaled carbon monoxide does not reliably confirm smoking abstinence beyond 1 day, and checkup visits were more than 1 day apart.
- Potential participants who had used smoking cessation medication already within the past month were excluded.

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Jump In! Cultural Immersion in the Education of Healthcare Professionals

Cultural Immersion in the Education of Healthcare Professionals: A Systematic Review

Brock MJ, Fowler LB, Freeman JG, Richardson DC, Barnes LJ. Cultural Immersion in the Education of Healthcare Professionals: A Systematic Review. *J Educ Eval Health Prof*. 2019; 16:4. doi:10.3352/jeehp.2019.16.4

KEY TAKEAWAY: Implementing cultural immersion experiences into healthcare education produces multi-domain positive effects.

STUDY DESIGN: Systematic review of non-randomized studies

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Educational methods that increase cultural awareness are needed in health care education today more than ever. This review examined 10 years of publications to see if cultural immersion experiences increase awareness and sensitivity.

PATIENTS: Healthcare professional students

INTERVENTION: Immersion experience

CONTROL: None

OUTCOME: Five overarching domains including cognitive, affective, perceptual, cultural dissonance, and skills/engagement

METHODS (BRIEF DESCRIPTION):

- Nine observational studies out of 126 articles were identified and fit criteria to be evaluated.
- Participants with experiences in 14 difference environments across nine countries participated.
- The participants were graduate level students in nursing, counseling, occupational therapy, physical therapy, or allied health professions.
- Outcomes of the studies revealed 47 themes that were organized into five overarching domains through qualitative methodology.

INTERVENTION (# IN THE GROUP): 94

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW UP PERIOD: 10 years

RESULTS: Nine studies of cultural immersion experiences revealed 47 themes that were divided and arranged by the authors to be part of five overarching themes:

- Cognitive: Commitment to change, connection with community, others, future, increased knowledge, cognitive reactions, cultural immersion and development, encouragers/barriers, cultural pride and appreciation
- Affective: Appreciation of life, connection with self and internal peace, nursing, affective reactions, empathy, global connection, personal characteristics, emotional reaction, relational connections
- Perceptual: Meaning of being an American, cultural and socio-political awareness, mind, body, spirit connection, increased openness, connection with environment, increased awareness, perceptual reactions, recognizing and appreciating differences, witnessing peer growth, past experiences, discrimination and prejudice, cultural sensitivity
- Cultural Dissonance: Challenges of integrating Western and traditional medicine, one's own comfort level, increased vigilance and adaptation, coping, communications
- Skills/Engagement: Engagement with communities in which immersion took place, learning natural remedies, connection with underserved communities with local partners, personal/professional changes

LIMITATIONS:

- Risk of Bias: Using MMAT, four articles received a score of 100% indicating low risk of bias. Five articles scored 75% indicating one criteria of the assessment tool was not met.
- English only studies
- Needing wider variety of health care professionals and students such as physicians, resident physicians, medical students, and pharmacy students.

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Oh, baby! I'm not ready!

Levonorgestrel vs Copper Intrauterine Devices for Emergency Contraception

Turok DK, Gero A, Simmons RG, et al. Levonorgestrel vs. Copper Intrauterine Devices for Emergency Contraception. *N Engl J Med.* 2021; 384(4):335-344. doi:10.1056/NEJMoa2022141

KEY TAKEAWAY: Levonorgestrel 52 mg IUD is noninferior to Copper IUD as a form of emergency contraception within 5 days of unprotected intercourse.
STUDY DESIGN: Randomized control trial
LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Levonorgestrel IUDs are the preferred IUD for long term contraception among women in the United States given a favorable side effect profile. Currently, Copper IUDs are the only long-acting contraceptive offered as emergency contraception and tend to have unwanted side effects such as increased abdominal cramps and heavy bleeding.

PATIENTS: Women 18-35 years old seeking emergency contraception within 5 days of unprotected intercourse
INTERVENTION: Insertion of Levonorgestrel 52 mg IUD
CONTROL: Insertion of Copper IUD
OUTCOME: Positive urine pregnancy test at 1 month post-insertion

METHODS (BRIEF DESCRIPTION):

- Patients who sought out emergency contraception within 5 days of unprotected intercourse and desired an IUD were randomized to receive either Copper IUD or Levonorgestrel 52 mg IUD.
- Participants were followed for one-month post-insertion and repeat pregnancy test was obtained at a follow up visit at 28 days post-insertion.

INTERVENTION (# IN THE GROUP): 327
COMPARISON (# IN THE GROUP): 328

FOLLOW UP PERIOD: Patients were to return to the clinic after 28 days.

RESULTS:

- Hormonal IUD was noninferior to Copper IUD use in positive pregnancy test at 1 month.
  - 1 versus 0 patients
  - Absolute difference 0.3% (95% CI, –0.9 to 1.8)
- Seeking care for adverse events such as bleeding and cramping were similar in the levonorgestrel and Copper IUD group (no p-value provided).

LIMITATIONS:

- This study did not compare the efficacy of Levonorgestrel IUD to oral levonorgestrel (standard of care) as an emergency contraceptive.
- Follow up: 7.5% of participants did not provide a pregnancy test at one-month post-insertion. The authors did attempt to search EMR database to confirm positive or negative pregnancy status but were not always successful.
- Generalizability: Women with irregular menstrual cycles were not included in the study.

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Effective Ways to Heal the Heel

What Treatment is Most Effective for Patients with Achilles Tendinopathy? A Living Systematic Review with Network Meta-Analysis of 29 Randomised Controlled Trials

van der Vlist AC, Winters M, Weir A, et al. Which treatment is most effective for patients with Achilles tendinopathy? A living systematic review with network meta-analysis of 29 randomised controlled trials. *Br J Sports Med.* 2021; 55(5):249–256. doi:10.1136/bjsports-2019-101872

KEY TAKEAWAY: In adults with mid-portion Achilles tendinopathy, any therapy is more effective in the first three months than the wait and see approach.
STUDY DESIGN: Living systematic review with network meta-analysis
LEVEL OF EVIDENCE: STEP 2 (downgraded due to high risk of bias and low certainty of evidence)

BRIEF BACKGROUND INFORMATION: Achilles tendinopathy is a common overuse injury with many treatment options. Current literature does not provide sufficient data that compares the effectiveness among treatment options.

PATIENTS: Adults with insertional or mid-portion Achilles tendinopathy
INTERVENTION: Treatment
CONTROL: No treatment (wait and see)
OUTCOME: Pain and activity

METHODS (BRIEF DESCRIPTION):

- Living systematic review with network meta-analysis was prospectively registered on PROSPERO (international register of systematic reviews) with 29 RCTs (N=1,640).
- Inclusion Criteria:
  - Randomized controlled trials that investigated any treatment in adults with Achilles tendinopathy (insertional, mid-portion, or both).
  - Diagnosis based on clinical findings.
  - Imaging to confirm the diagnosis was not necessary.
- Exclusion Criteria: Patients with full thickness rupture
- VISA-A score quantified pain and activity level (0–100; 100 being no pain and full activity, 0 being severe pain and no activity).
  - Minimal Clinically Important Difference = 15
- 42 different treatments were investigated including exercise, injections, shockwave therapy, night splints, acupuncture, and mucopolysaccharides.
- Majority of trials (86%) investigated mid-portion Achilles tendinopathy, one investigated insertional Achilles tendinopathy and three trials did not specify the location.
- Each treatment modality was compared to no treatment and to each other using the VISA-A score.

INTERVENTION (# IN THE GROUP): Not available
COMPARISON (# IN THE GROUP): Not available

FOLLOW UP PERIOD: 1 to 52 weeks (median 27 weeks)

RESULTS:

- Any modality of treatment, except exercise + placebo injection, was more effective than wait and see approach at 3-month follow-up.
  - Injection therapy (mean difference [MD] 23 points; 95% CI, 8 to 38)
  - Exercise therapy (MD 20 points; 95% CI, 11 to 30)
  - Shockwave therapy (MD 15 points; 95% CI, 6 to 24)
  - Exercise + injection therapy (MD 22 points; 95% CI, 7 to 36)
  - Exercise + shockwave therapy (MD 34 points; 95% CI, 21 to 47)
  - Exercise + night splint therapy (MD 21 points; 95% CI, 4 to 39)
  - Acupuncture therapy (MD 35 points; 95% CI, 25 to 45)
  - Mucopolysaccharides supplement + exercise therapy (MD 28 points; 95% CI, 14 to 41)
- At 12 months, four RCTs showed that exercise therapy, exercise + injection therapy, and exercise + night splint therapy were all comparable with injection therapy alone.

LIMITATIONS:

- 22 of the 29 trials were at high risk of bias.
- Certainty of evidence for all treatment comparisons were low to very low.
- Small sample size of each treatment arm.

- Some treatments being investigated were not connected to the network hindering assessment of comparative effectiveness of all treatments.
- Data primarily based on mid-portion Achilles tendinopathy, so results cannot be generalized to other types of Achilles tendinopathy (e.g., insertional tendinopathy).

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