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FPIN
Family Physicians Inquiries Network

Volume 6 Issue 7

Intense Exercise with Asthma?!

Effects of Moderate vs Vigorous-Intensity Exercise Training on Asthma Outcomes in Adults

Valkenborghs SR, Wood LG, Callister R, et al. Effects of Moderate- Versus Vigorous-Intensity Exercise Training on Asthma Outcomes in Adults. *J Allergy Clin Immunol Pract*. 2024;12(10):2744-2753.e8. doi:10.1016/j.jaip.2024.06.015

KEY TAKEAWAY: Moderate and vigorous exercise training is associated with improved asthma-related quality of life (ASQL) and could be considered as an adjunct treatment in adults.

STUDY DESIGN: Multi-center, randomized controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small sample size and unclear/lack of blinding)

BRIEF BACKGROUND INFORMATION: Asthma is a common respiratory disease in the adult population worldwide. Multiple treatment modalities are available including the use of both moderate and intense aerobic exercise. Specific exercise parameters and optimal durations had not been previously defined. This study investigated various exercise intensities/durations and its impact on ASQL.

PATIENTS: Adults with asthma

INTERVENTION: Moderate and vigorous exercise

CONTROL: Current/unchanged physical activity levels

PRIMARY OUTCOME: ASQL

Secondary Outcome: Clinical asthma outcomes, cardiorespiratory fitness, body composition, airway/systemic inflammation

METHODS (BRIEF DESCRIPTION):

- Patients were recruited through the Hunter Medical Research Institute (HMRI) in Australia and were self-referred.
- Adults 18–55 years old, body mass index (BMI) ≤40, with physician-diagnosed asthma and current episodic symptoms.
  - Post-bronchodilator forced expiratory volume in 1 second (FEV1) ≥50% predicted.
  - Able to participate in structured moderate and/or vigorous intensity physical activity per week of ≤90 minutes.
- Patients with other primary respiratory diseases, required steroids/antibiotics (4 weeks prior), required hospitalization (3 months prior), resting oxygen saturation of ≤95% on room air, had contraindications to exercise, cancer, pregnancy, breastfeeding, diabetes, uncontrolled hypertension or thyroid disease were excluded from the study.
- Patients were randomized to:
  - Moderate intensity exercise group: 45 minutes of moderate exercise three times per week for 12 weeks. Parameters included 55–70% age-predicted heart rate maximum (measured via ergometers).
  - Vigorous intensity exercise group: 30 minutes of vigorous exercise three times per week for 12 weeks. Parameters included 70–90% age-predicted heart rate maximum (measured via ergometers).
  - Control group: Participants maintained their current physical activity levels for 12 weeks. Measurements via Fitbit device.
- The primary outcome was measured using the Juniper Asthma Related Quality of Life Questionnaire (AQLQ) where a 0.5 unit increase in scoring was considered a significant improvement.
- Secondary outcomes were measured using the following:
  - Asthma control was measured using the Juniper Asthma Control Questionnaire (ACQ7). This uses an average range of 0–7, with a score of seven being the most severe score. A 0.5-point decrease was considered a significant improvement in this study.
  - Prebronchodilator lung function was measured by spirometry.
  - Sputum collection/analysis included using nebulized hypertonic saline (4.5%) followed by use of dithiothreitol to disperse the sample and a hemocytometer to determine total cell counts. From here cell count was obtained from spinning/staining.
  - Cardiorespiratory fitness was assessed with an ergometer from an upright cycle combined with

a portable metabolic system to determine volitional exhaustion measurements.
    - Height/weight measurements were used to calculate BMIs; Dual Energy X-ray Absorptiometry (DEXA) scans were used to determine body composition.

INTERVENTION (# IN THE GROUP): 32
COMPARISON (# IN THE GROUP): 14

FOLLOW-UP PERIOD: 12 weeks

RESULTS:

Primary Outcome –

- Moderate-intensity exercise both significantly and clinically improved ASQL compared to control (mean difference [MD] 0.63; 95% CI, 0.33–0.93).
- Vigorous-intensity exercise significantly, but not clinically, improved ASQL compared to control (MD 0.46; 95% CI, 0.02–0.73).

Secondary Outcome –

- Moderate-intensity exercise significantly and clinically improved asthma control compared to the control (MD –0.36; 95% CI, –0.69 to –0.02).
- There was no significant difference in asthma control between exercise groups.
- There was no significant difference in lung function for vigorous or moderate intensity exercise compared to control.
- Moderate-intensity exercise significantly and clinically improved asthma control compared to the control (MD –0.36; 95% CI, –0.69 to –0.02).
- There was no significant difference in asthma control between exercise groups.
- There was no significant difference in lung function for vigorous or moderate intensity exercise compared to control.
- Moderate-intensive exercise did not significantly decrease relative volitional exhaustion compared to control.
- Vigorous-intensive exercise improved relative volitional exhaustion compared to control (MD 4.0; 95% CI, 1.5–6.5).
- Moderate-intensity exercise did not significantly reduce gynoid fat mass compared to control.
- Moderate-intensive exercise decreased sputum macrophage count compared to control (MD –1,341; 95% CI, –2,491 to –191).
- Moderate-intensity exercise decreased sputum lymphocyte count compared to control (MD –114; 95% CI, –220 to –8).
- There was no significant difference in sputum macrophage count and sputum lymphocyte count for vigorous intensity exercise.

LIMITATIONS:

- There may have been inconsistencies between intervention groups.
- Fitness data that was pulled from the treadmills and cycle ergometers were subject to variation
- Smaller sample size of the stay may have been underpowered when detecting secondary outcomes.
- Per-protocol analysis of the study instead of intention-to-treat ITT analysis.

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From Prompt to Plan - Helping Doctors See the Whole Story

Effect of Electronic Health Record Clinical Decision Support on Contextualization of Care: A Randomized Clinical Trial

Weiner SJ, Schwartz A, Weaver F, et al. Effect of Electronic Health Record Clinical Decision Support on Contextualization of Care: A Randomized Clinical Trial. *JAMA Netw Open*. 2022;5(10):e2238231. Published 2022 Oct 3. doi:10.1001/jamanetworkopen.2022.38231

KEY TAKEAWAY: Integrating prompts about patients' real-life challenges into the electronic health record (EHR) using clinical decision support (CDS) tools does not improve resolution of patients' problems compared with usual care in adult primary-care patients.

STUDY DESIGN: Multicenter randomized clinical trial

LEVEL OF EVIDENCE: STEP 3 (downgraded because of lack of blinding and possible underpowering)

BRIEF BACKGROUND INFORMATION: Clinicians frequently miss or overlook contextual factors in patient care, such as financial hardship, transportation issues, or low health literacy, which may impact treatment adherence and outcomes. This study evaluated whether integrating these factors into the EHR via CDS tools could improve clinician behavior and ultimately patient outcomes.

PATIENTS: Adult primary care patients

INTERVENTION: Contextualized CDS

CONTROL: Usual care

PRIMARY OUTCOME: Resolution or improvement of contextual red flags

Secondary Outcome: Proportion of red flags probed by clinicians and proportion of contextual factors incorporated into care plans

METHODS (BRIEF DESCRIPTION):

- English-speaking patients (≥18 years old) were selected from two academic primary care systems (Chicago), using Cerner (site 1) and Epic (site 2).
- 452 recorded encounters (291 women, mean age 56 years old) with 39 clinicians; from 2018–2021.
- Patients were randomized to intervention vs control; analyses were intention-to-treat and adjusted for site and multiple red flags/factors per visit.
- Patient portal pre-visit questionnaire elicited patient challenges with taking their medications, keeping their appointments, completing recommended tests, using medical equipment, and engaging in healthy behaviors.
- EHR algorithms identified red flags (e.g., missed appointments, multiple ED visits, loss of control of diabetes/hypertension, self-pay).
- Patient-reported challenges and EHR-identified red flags populated a contextual care box (CCB) incorporated into the visit note template of the EHR
- Algorithm-based interruptive alerts encouraged providers to probe patient circumstances during the visit and to consider context-sensitive orders such as consults to a social worker, pharmacist, or visiting nurse.
- Visits were audio-recorded and coded using Content Coding for Contextualization of Care (4C) to determine whether contextual factors were probed or addressed.
- Patients were blinded to which group they were randomized, as well as the research assistants coding the visits. Clinicians inherently could not be blinded to the randomization.
- EHR was reviewed at six months to classify each predefined red flag as "improved", "worsened" or "unchanged". Examples of "improved" included better control of diabetes or blood pressure, better adherence to medications and appointments, and fewer emergency department visits.
- Mixed-effects models estimated adjusted odds ratios for probing, contextualization, and red-flag improvement; prespecified exploratory analyses examined alert/CCB effects.

INTERVENTION (# IN THE GROUP): 177

COMPARISON (# IN THE GROUP): 275

FOLLOW-UP PERIOD: Six months

RESULTS:

Primary Outcome –

- Contextualized CDS did not improve resolution of contextual red flags compared to usual care (adjusted odds ratio [aOR] 0.96; 95% CI, 0.57–1.6).

Secondary Outcome –

- Contextualized CDS improved clinicians' probing of contextual red flags compared to usual care (aOR 2.1; 95% CI, 1.1–3.9).
- Contextualized CDS improved clinicians' incorporating of contextual factors into care plans compared to usual care (aOR 2.7; 95% CI, 1.3–5.4).

LIMITATIONS:

- Primary outcome may have been underpowered to detect modest differences due to an imbalance in randomization counts.
- Clinicians were not blinded, which may have introduced performance bias.
- Differences in EHRs across both sites can cause variability in exposure of alerts to clinicians.
- Contextualization captured via audio-coding may introduce variability in classification.
- Generalizability may be limited as the study was conducted at two academic centers with high EHR integration.
- Patients in both arms completed a questionnaire, potentially priming all participants to disclose contextual factors.
- Some outcome measures were subjective, such as self-reported behavior changes.

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Cashing In for Losing Weight: A Teenage Dream?

Financial Incentives and Treatment Outcomes in Adolescents with Severe Obesity: A Randomized Clinical Trial

Gross AC, Freese RL, Bensignor MO, et al. Financial Incentives and Treatment Outcomes in Adolescents With Severe Obesity: A Randomized Clinical Trial. *JAMA* Pediatr. 2024;178(8):753-762. doi:10.1001/jamapediatrics.2024.1701

KEY TAKEAWAY: Adding financial incentives (FI) to meal replacement therapy (MRT) reduces body mass index (BMI) and body fat at 52 weeks in adolescents with severe obesity compared with MRT alone.

STUDY DESIGN: Single-blind, randomized controlled trial (RCT)

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

BRIEF BACKGROUND INFORMATION: Severe pediatric obesity affects approximately 8% of United States youth and is important to treat before adulthood because it is linked to adult obesity, cardiovascular disease, and type 2 diabetes. MRT has been shown to effectively reduce BMI in adolescents; however, long term adherence is poor. FI are a potential way to promote adherence. They have been studied to be effective in adherence to lifestyle modifications in adults with obesity, but not in adolescents yet. FI have been shown to improve some health-related behaviors in adolescents such as smoking cessation, exercise duration, and type 1 diabetes medication adherence. This study aimed to determine whether adding FI to MRT leads to a reduction in BMI in adolescents.

PATIENTS: Adolescents with severe obesity

INTERVENTION: MRT + FI

CONTROL: MRT alone

PRIMARY OUTCOME: Change in BMI

Secondary Outcome: Total body fat, blood pressure (BP), triglyceride to high-density lipoprotein (HDL) ratio, heart rate variability, arterial stiffness, cost-effectiveness, quality of life

METHODS (BRIEF DESCRIPTION):

- On recruitment, participants were blinded to financial incentives and were informed only that the study was testing the effectiveness of MRT on BMI reduction.
- Only participants randomly allocated to the FI group were later informed that they were receiving FIs. Those in the MRT alone group were not made aware that others were receiving FI. Staff and study investigators were blinded to treatment conditions.
- Inclusion criteria were adolescents 13–17 years old with obesity. Obesity was defined as a BMI at ≥120% of the 95th percentile based on age and sex or a BMI of ≥35, whichever was lower.
- Exclusion criteria included a history of diabetes, bariatric surgery, eating disorders or unhealthy compensatory behaviors, and recent or current use of MRT or weight loss medication.
- MRT consisted of 1,200 calorie Healthy for Life meals provided free of charge with home delivery throughout the trial.
- $20 gift cards were provided for every 0.5% reduction in body weight from baseline.
- Height and weight were measured using standard calibrated equipment to calculate BMI which was the primary endpoint.
- The secondary outcomes assessed various aspects of body composition measured via:
  - Advanced Dual-Energy X-ray Absorptiometry (DXA) system
  - BP
  - Triglyceride- to-HDL ratio
  - Heart rate variability, measured via the SphygmoCor MM3 system, a noninvasive device that measures central BP and arterial stiffness by analyzing peripheral pulse waveforms.
  - Arterial stiffness, measured via carotid-radial pulse wave velocity
  - Quality of life measures included body esteem, social life, physical comfort, family relations, and total Impact of Weight on Quality of Life-Kids (IWQOL-Kids). Scores on the IWQOL-Kids range from 0–100, with higher score meaning better quality of life, which includes physical, social and emotional subscales.

INTERVENTION (# IN THE GROUP): 63

COMPARISON (# IN THE GROUP): 63

FOLLOW-UP PERIOD: 52 weeks

RESULTS:

Primary Outcome –

- The MRT + FI group had a significantly greater BMI percentage reduction than MRT alone (estimated treatment difference −5.9%; 95% CI, −9.9 to −1.9).
- The MRT + FI group had a greater reduction in total body fat mass compared to MRT alone (estimated treatment difference −4.8 kg; 95% CI, −9.1 to −0.6).

Secondary Outcomes –

- There were no significant differences between groups in cardiometabolic outcomes, including blood pressure, triglyceride-to-HDL ratio, heart rate variability, or pulse wave velocity.
- Quality of life outcomes showed no significant differences at 52 weeks.

LIMITATIONS:

- Adherence data were incomplete, preventing confirmation that FIs improved adherence to MRT.
- The study was conducted during the COVID-19 pandemic, contributing to nearly 30% attrition and missing data due to suspended in-person visits
- Blinding of participants to the FI component was not guaranteed; although participants in the MRT group were intended to be unaware, they may have learned about incentives through outside sources.
- All participants received meal provisions and reimbursement, potentially minimizing observed differences between groups and underestimating the true effect of FIs.
- The intervention was only tested for one year, limiting understanding of long-term sustainability and effects after FI withdrawal.
- Scalability and feasibility in real-world clinical or community settings remain uncertain, especially when considering broader implementation beyond the research setting.

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BCAAs to the Brain: Can Branched Chain Amino Acids Help Teens and Young Adults Bounce Back from Concussions?

Head Injury Treatment with Healthy and Advanced Dietary Supplements: A Pilot Randomized Controlled Trial of the Tolerability, Safety, and Efficacy of Branched Chain Amino Acids in the Treatment of Concussion in Adolescents and Young Adults

Corwin DJ, Myers SR, Arbogast KB, et al. Head Injury Treatment with Healthy and Advanced Dietary Supplements: A Pilot Randomized Controlled Trial of the Tolerability, Safety, and Efficacy of Branched Chain Amino Acids in the Treatment of Concussion in Adolescents and Young Adults. *J Neurotrauma*. 2024;41(11-12):1299-1309. doi:10.1089/neu.2023.0433

KEY TAKEAWAY: Branched chain amino acid (BCAA) supplementation does not reduce neurocognitive recovery time compared to usual care in concussed adolescents and young adults.

STUDY DESIGN: Pilot, double-blinded, randomized controlled trial

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

BRIEF BACKGROUND INFORMATION: Concussions are a common injury in the adolescent and young adult age group, and there has been a lot of recent research regarding concussion recovery with little consensus on pharmacological intervention/supplementation. However, it has been noted that in both mice and human studies, there has been shown a reduction in BCAA's in individuals with concussions compared to individuals without concussions. This pilot study studied the effect of BCAA supplementation on concussion recovery in adolescents and young adults.

PATIENTS: Adolescents and young adults with diagnosed mild concussion

INTERVENTION: Oral BCAA supplementation

CONTROL: Usual care

PRIMARY OUTCOME: Neurocognitive recovery time

Secondary Outcome: Concussion symptoms, physical and cognitive activity, sleep efficacy, treatment compliance, adverse events

METHODS (BRIEF DESCRIPTION):

- Participants enrolled from outpatient sports medicine and primary clinics, urgent care centers, and emergency rooms of a tertiary care pediatric children's hospital.
- Participants 11–34 years old, diagnosed with a mild concussion with the injury occurring within the prior 72 hours, negative pregnancy test with acceptable birth control, weight of at least 40 kg were included in the study.
- Participants with signs of moderate-severe traumatic brain injury (TBI), prior concussion within preceding 90 days, history or family history of Maple Syrup Urine Disease (MSUD), actively taking neurological or psychoactive medications, and allergy to Red Dye #40 or sucralose were excluded from the study.
- Participants blindly randomized into one of five groups (placebo, BCAA 15 g daily dose, BCAA 30 g daily dose, BCAA 45 g daily dose, BCAA 54 g daily dose).
- Patients were monitored for 21 days following enrollment.
    - Daily electronic surveys were used including questions regarding concussion symptoms, physical activity, cognitive activity, drug compliance, adverse effects, and cognitive testing.
    - Continuous actigraphy
    - In-person visits conducted at days five, nine, 12, 16, 22, and 24.
- Neurocognitive testing performed using the CogSport/Axon Sports Computerized Cognitive Assessment Tool (CCAT) tool which measures processing speed, attention, visual learning, working memory.
- Concussion symptoms were assessed via self-reporting nine-item symptom instrument. Scores range from 0–54, with lower scores indicating fewer symptoms.
- Physical activity was rated on a six-point Likert scale of return to baseline physical activity.
- Cognitive activity was rated in a five-point Likert scale or return to baseline cognitive activity at school or work.
- Sleep was assessed using actigraphy worn 24/7 during study participation on non-dominant wrist

and analyzed bedtime, wake time, total sleep time, sleep efficiency, wake after sleep onset, number and length of awakenings, activity, and movement/sleep fragmentation.
- Compliance was assessed by self-report.
- Adverse effects were collected via daily self-reports.
- For analysis of results, linear regression was used to conduct a dose-response analysis with total study dose received as independent variable and change in outcome as the dependent variable.

INTERVENTION (# IN THE GROUP):
- BCAA 15 mg: 8
- BCAA 50 mg: 9
- BCAA 46 mg: 9
- BCAA 54 mg: 8

COMPARISON (# IN THE GROUP): 8

FOLLOW-UP PERIOD: 21 days

RESULTS:

Primary Outcome –
- BCAA supplementation did not significantly change neurocognitive testing: Processing speed (p=.62), attention (p=.26), working memory (p=.80), or visual learning (p=.77). All results were presented via figure.

Secondary Outcome –
- BCAA supplementation showed dose-dependent reduction in total symptom score compared to usual care (p=.0036; results presented via figure).
- BCAA supplementation showed dose-dependent improvement in return to baseline physical activity compared to usual care (p=.0053; results presented via figure).
- BCAA supplementation did not significantly change cognitive activity for any of the intervention dosages compared to usual care.
- BCAA supplementations effect on sleep efficacy was unable to be concluded accurately given limited number of participants with complete actigraphy data.
- BCAA supplementation did not significantly change patient compliance for any of the intervention dosages compared to usual care.
- BCAA supplementation had no statistically significant change in adverse effects for any of the intervention dosages compared to usual care.

LIMITATIONS:
- Small sample size
- Poor follow-up and missing data
- Long testing period with multiple temporal trends in the management of concussion during the study time frame
- Several new symptom testing methods have come out since study onset as a standard of care for assessing concussion symptoms, possibly making study sample non-representative of overall population of acutely concussed adolescents and young adults.
- There is a need for a larger, more definitive trial before routine clinical implementation of BCAA therapy for concussion.

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