GOOD EVIDENCE MATTERS

GEMs of the Week

SPOTLIGHT

Running Away from Back Pain: Does Running Help Alleviate Chronic Low Back Pain?

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Long-Term Use of Dupilumab for Eczema Treatment

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Running Away from Back Pain: Does Running Help Alleviate Chronic Low Back Pain?

Running is Acceptable and Efficacious in Adults with Non-Specific Chronic Low Back Pain: The ASTEROID Randomized Controlled Trial

Neason C, Samanna CL, Tagliaferri SD, et al. Running is Acceptable and Efficacious in Adults with Non-specific Chronic Low Back Pain: The ASTEROID Randomized Controlled Trial. *Br J Sports Med*. 2025;59(2):99-108. Published 2025 Jan 2. doi:10.1136/bjsports-2024-108245

KEY TAKEAWAY: For patients with chronic low back pain (CLBP), a run-walk program can help improve pain intensity and disability.

STUDY DESIGN: Two arm parallel individually randomized control trial

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

BRIEF BACKGROUND INFORMATION: CLBP affects 7.5% of people worldwide and contributes greatly to disability, decreased aerobic fitness and physical activity. Prior studies have evaluated running and CLBP but have not included details regarding running intervention and have also included non-running treatments making it difficult to ascertain the efficacy of a running program. This study evaluated changes in subjective pain by using a community-based running program for people with nonspecific CLBP.

PATIENTS: Adults with CLBP

INTERVENTION: Exercise training program

CONTROL: Standard care

PRIMARY OUTCOME: Self-reported pain and disability
Secondary Outcome: Recorded run distance, speed, surface for each run

METHODS (BRIEF DESCRIPTION):

- Adults 18–45 years old with non-specific CLBP (≥3 months) with symptoms most days of the week, with/without leg pain, recruited from non-marginalized communities in Melbourne, Australia.
- Patients with a history of spinal surgery, spine trauma, cauda equina symptoms, structural scoliosis, symptomatic radiculopathy, inflammatory spondyloarthropathies, non-musculoskeletal causes of LBP, unable to communicate in English, pregnant, lactating or <1 year postnatal, current or prior state or national athletes, any contraindications to MRI, those involved in running or sport with running three months prior to study, those with lower limb injury six weeks preceding enrolment and those who have any contraindication to exercise training, or inability to use a smartphone with internet connection were excluded from the study.
- Patients were randomized 1:1 to either the running group or standard care.
- The exercise training group had three, 30-minute training sessions per week over 12 weeks by an accredited exercise physiologist. Data was collected on the Runkeeper application.
    - Training programs included short running intervals and rest periods of walking. These started at stage 1/2/3 determined by tolerance to two-minute run test during initial physical assessment or self-selected. Progression to the next stage was achieved if participants could complete the upper repeat range in at least two of the training sessions during their week.
    - Weekly video consultations during weeks 1–4 and fortnightly during weeks 6–12; patients could also consult the physiologist PRN.
    - Education (on running speed, footwear, safety of running and dealing with setbacks) was delivered via email.
- Patients in the standard care group were asked to manage their backpain as they normally would with over-the-counter medications, seeing their general physician, and asked to avoid a running program.
- The primary outcomes measured the average pain intensity and disability and were recorded at baseline, six weeks and 12 weeks via Research Electronic Data Capture (REDCap).
    - Pain intensity was measured on visualized analogue scale (VAS). Scores range from 0–100, with higher scores indicating worse pain. A 20-point reduction was considered meaningful difference.
    - Disability was measured on Oswestry Disability Index. Scores range from 0–5, with a higher score indicating greater disability. A 10-point reduction was considered meaningful difference.

- The secondary outcomes were measured via RunKeeper application via smartphone of participants.

INTERVENTION (# IN THE GROUP): 20
COMPARISON (# IN THE GROUP): 20

FOLLOW-UP PERIOD: 12 weeks

RESULTS:

Primary Outcome –

- The exercise training program improved current pain intensity compared to standard care at 12 weeks, but not at six weeks.
  - Six weeks (difference –10; 95% CI, –23 to 2.4)
  - 12 weeks (difference –19; 95% CI, –32 to –6.7)
- The exercise training program improved average pain intensity compared to standard care at six and 12 weeks.
  - Six weeks (difference –10; 95% CI, –20 to –0.05)
  - 12 weeks (difference –15; 95% CI, –15 to –5.3)
- The exercise training program improved worst pain intensity compared to standard care at six weeks, but not at 12 weeks.
  - Six weeks (difference –5.2; 95% CI, –16 to –5.7)
  - 12 weeks (difference –8.3, 95% CI, –19 to 2.6)
- The exercise training program improved disability at 12 weeks, but not at six weeks.
  - Six weeks (difference –2.3; 95% CI, –7.3 to 2.6)
  - 12 weeks (difference –5.2; 95% CI, –10 to –0.24)

Secondary Outcome –

- There was no statistically significant difference in running distance, speed, or surface between the exercise group and the standard care group.

LIMITATIONS:

- Participants were unable to be blinded to treatment.
- Patients were self-referred based on advertisements, increasing the risk of selection bias.
- The studies population was limited to those with mild chronic nonspecific LBP; it is unclear how this would affect individuals with acute LBP.
- The control group did not have contact with researchers between testing sessions like the intervention group; the effects of intervention due to routine coaching and support cannot be quantified.
- It is unclear how generalizable the study findings are to individuals <18 years old or >45 years old.
- In the control group, it is unclear how the data is affected by a lack of change in scores from baseline and if this inflates the true intervention effects.

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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 Air Force, Defense Health Agency, Department of Defense, or the U.S. Government.

Get Clesrovimab: Forget Severe RSV Infection

Clesrovimab for Prevention of RSV Disease in Healthy Infants

Zar HJ, Simões EAF, Madhi SA, et al. Clesrovimab for Prevention of RSV Disease in Healthy Infants. *N Engl J Med*. 2025;393(13):1292-1303. doi:10.1056/NEJMoa2502984

KEY TAKEAWAY: A single dose of clesrovimab given to healthy preterm and full-term infants provides effective protection against respiratory syncytial virus (RSV) with no increase in adverse events compared to placebo.

STUDY DESIGN: Phase 2b-3 double-blind, randomized, placebo controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: RSV is the most common cause of lower respiratory tract infection (LRTI) in infants and toddlers <2 years old. RSV is highly prevalent and contagious, making it a leading cause of hospitalization in infancy. Currently Nirsevimab is the gold standard for RSV prevention in infancy, given as a one-time injection to all infants born in the winter season. Clesrovimab represents a new monoclonal antibody option undergoing this Phase 2b-3 trial to demonstrate efficacy and safety.

PATIENTS: Healthy infants of ≥29 weeks gestational age

INTERVENTION: Single dose of clesrovimab

CONTROL: Placebo injection

PRIMARY OUTCOME: RSV-associated medically attended lower respiratory infection (MALRI) through 150 days
Secondary Outcome: RSV-associated hospitalization through 150 days, and RSV associated MALRI with ≥1 indicator of LRI or disease severity through 180 days

METHODS (BRIEF DESCRIPTION):

- This was a phase 2b-3 double blind randomized, placebo-controlled trial conducted in 22 countries, designed and funded by Merck Sharp and Dohme.
- Those recovering from a recent febrile illness and those who had received any prior RSV preventive treatment were excluded.
- Healthy preterm and full-term infants, <1 year old, born at or later than 29 weeks gestation and entering their first RSV season were randomly assigned in a 2:1 ratio to receive one intramuscular dose of 105 mg clesrovimab or placebo injection (normal saline).
- At the start of the trial, male and female infants were almost equally distributed (51% vs 49%), 80% of the participants were <6 months old, 45% were White, 27% Asian, and 14% were Black.
- Most participants (83%) were born on or after 35 weeks gestational age, and 81% lived in a temperate climate.
- The primary endpoint was the rate of lower respiratory infection and severe disease requiring inpatient or outpatient medical attention through 150 days after the injection.
- Disease severity was defined by the presence of wheezing, crackles, hypoxemia, tachypnea, chest wall retractions and dehydration.
- Positive RT-PCR results were recorded within seven days prior to or 12 days after symptom onset or worsening.
- Secondary endpoints included RSV-associated hospitalization 150 days after injection, and RSV associated MALRI 180 days after injection.
- Rash, anaphylaxis or hypersensitivity reaction within 42 days of study intervention were the adverse events of special interest and safety events were collected in all infants for 240 days post-injection.

INTERVENTION (# IN THE GROUP): 2,412

COMPARISON (# IN THE GROUP): 1,202

FOLLOW-UP PERIOD: 515 days

RESULTS:

Primary Outcome –

- Clesrovimab significantly reduced the incidence of RSV-associated MALRI compared to placebo over 150 days (incidence rate 2.6% vs 6.5%, respectively; efficacy 60%; 95% CI, 44–72; number needed to immunize [NNI]=26).

Secondary Outcome –

- Clesrovimab reduced the incidence of RSV-associated hospitalization compared to placebo over 150 days (incidence rate 0.4% vs 2.4%, respectively; efficacy 84%; 95% CI, 67–94; NNI=50)
- Clesrovimab reduced the incidence of RSV-associated MALRI with one or more indicator of LRI or disease severity compared to placebo (incidence

rate 2.7% vs 6.8%, respectively; efficacy 60%; 95% CI, 43–71; NNI=25).

- Post hoc analysis revealed that clesrovimab reduced the incidence of RSV associated MALRI with ≥2 indicators of LRI or disease severity for days 1–150 (incidence rate 0.4% vs 2.5%, respectively; efficacy 88%; 95% CI, 76–94; NNI=33).
- Clesrovimab reduced the incidence of RSV-associated MALRI compared to placebo over 180 days (0.5% vs 2.5%, respectively; efficacy 87%; 95% CI, 75–93; NNI=32).
- Among the 1,650 infants followed into RSV season two, the rate and severity of RSV infection was similar in both groups in season two of the trial, indicating that protection against RSV in season one does not increase the severity of RSV thereafter.

Adverse Events –

- <0.1% of infants receiving clesrovimab developed anaphylaxis or hypersensitivity.
- There was no difference in rash, local reaction, irritability, or death between the two groups.

LIMITATIONS:

- There are no standard diagnostic criteria for MALRI, which is the primary end point of this study and expert opinion and CDC/WHO guidelines were used to define MALRI.
- This trial did not compare clesrovimab against nirsevimab which is currently the standard of care and differences in the population enrolled between the two trials made direct comparisons difficult.
- The trial was too small to detect rare serious adverse events.
- This was an industry designed and funded study which introduces the risk of sponsorship bias.

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Scratching the Surface: Long-Term Use of Dupilumab for Eczema Treatment

Long-Term Effectiveness and Reasons for Discontinuation of Dupilumab in Patients with Atopic Dermatitis

Boesjes CM, Kamphuis E, de Graaf M, et al. Long-Term Effectiveness and Reasons for Discontinuation of Dupilumab in Patients With Atopic Dermatitis. *JAMA Dermatol*. 2024;160(10):1044-1055. doi:10.1001/jamadermatol.2024.2517

KEY TAKEAWAY: Dupilumab demonstrates sustained clinical efficacy up to five years.

STUDY DESIGN: Prospective, multicenter observational cohort study

LEVEL OF EVIDENCE: STEP 4 (downgraded due to lack of statistical analysis for several outcomes)

BRIEF BACKGROUND INFORMATION: Atopic dermatitis is a common skin condition, with prevalence peaking in early childhood. Dupilumab, the first monoclonal antibody for atopic dermatitis treatment, was approved in 2017. This study aimed to determine long-term effectiveness of dupilumab, as well as examine reasons for discontinuation.

PATIENTS: Patients of all ages diagnosed with atopic dermatitis

INTERVENTION: Dupilumab

CONTROL: None

PRIMARY OUTCOME: Clinical effectiveness

Secondary Outcome: Cutoff scores, adverse events

METHODS (BRIEF DESCRIPTION):

- Patients were enrolled from 14 hospitals in the Netherlands.
- Patients ≥18 years old received a loading dose of 600 mg of subcutaneous dupilumab followed by 300 mg every other week. After one year, patients were eligible for off-label decreased dosing frequencies.
- Patients <18 years old (n=130) received weight-based dosages.
- Clinical effectiveness was measured using the following:
  - The Eczema Area and Severity Index (EASI). Scores range from 0–72, with higher scores indicating more severe disease.
  - The Investigator Global Assessment (IGA). Scores range from 0–4 with higher scores indicating more severe disease.
  - The Numeric rating scale (NRS) for pruritus. Scores range from 0–10, with a score of ≤4 indicating controlled itchiness.
  - Thymus- and activation-related chemokine (TARC), with higher levels indicating increased disease severity.
  - Eosinophil levels
- The majority (80%) of the patients were classified at initiation of dupilumab as moderate to severe AD by the IGA.
- Follow-up appointments were approximately every six months.
- The following were measured as the secondary outcomes:
  - Percentage of patients who reached predetermined cutoff scores (EASI ≤7, NRS for pruritus ≤4, IGA ≤1)
  - EASI responses (EASI improvement from baseline of 50%, 75%, or 90%)

INTERVENTION (# IN THE GROUP): 1,286

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW-UP PERIOD: Up to five years

RESULTS:

Primary Outcome –

- Dupilumab improved eczema severity after five years (mean EASI score 2.7; 95% CI, 1.2–4.2).
- Dupilumab resulted in >50% of patients reaching a ≥2-point reduction in IGA score at one, two, three, four, and five years (59%, 54%, 60%, 66%, and 62%; no statistical analysis completed).
- Dupilumab improved pruritus after five years (mean NRS scores 3.5; 95% CI, 2.7–4.3).
- Dupilumab reduced TARC after six months (390 pg/mL; 95% CI, 368–413).
- Dupilumab slightly increased eosinophil levels up to week 16, but consistently decreased below baseline levels during long-term follow-up and remained within normal range.

Secondary Outcome –

- Eczema severity and pruritus improved significantly on dupilumab at week four and maintained after five years (no statistical analysis completed).
- Dupilumab improved eczema severity according to the IGA ≤2 from week 28 through 4.5 years but decreased at five years.
- Treatment was discontinued by 306 patients (24%), primarily due to adverse events (7.6%) and ineffectiveness (6.6%).
    - Of these, 13% later restarted dupilumab
    - Ocular surface disease was the most commonly reported adverse event (3.9% of total patients), including conjunctivitis and other inflammatory ocular conditions.

LIMITATIONS:

- Some outcomes were missing due to the impact of COVID-19 patient loss to follow-up.
- The analysis by age group was limited as many pediatric patients did not have five years of follow-up data.
- The study did not report separate efficacy data for patients on prolonged dosing schedules; only total patient counts were provided.
- There was no exclusion criteria defined for the study population.
- Because this was not an inception cohort, not all patients reached five years of follow-up. The study remained ongoing at the time of publication.

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