THE ARISING

OCTOBER 28, 2026 · JOHN GRIFFIN, MD

The care around the technology



Original conceptual illustration · The people around the technology

Good technology needs good care around it. These ten investigations move from a coordinated heart-failure program to diagnostic labels, metabolic health, wearables and new research tools. The recurring question is whether an intervention changes a meaningful outcome, and what remains uncertain when it does not.

Ten full written articles · Alive. Awake. Aware.

In this edition

01 The care team, not the algorithm, made the difference in heart failure

02 Opening a narrowed carotid artery did not restore cognition

03 Lowering pediatric blood-pressure targets reduced drugs—not the main clinical outcome

04 GLP-1 cardiovascular protection appears similar across age groups

05 Removing inaccurate penicillin-allergy labels may improve antibiotic care

06 The new Cochrane review finds little proof that ergonomic fixes treat established arm and neck pain

07 Normal body weight does not guarantee protection from fatty liver disease

08 The economics of Parkinson monitoring are a warning for wearable-health startups

09 Liquid AI brings small, multimodal, open-weight models to the edge

10 A wireless patch reads cardiac motion, but the evidence is still in rodents

About this copy

Recovered and prepared October 31, 2026, from the dated source issue or existing reader selection. The issue date is preserved; this PDF does not establish a publication date. Source qualifications are retained. This packaging pass is not a fresh independent audit of every study.

Use NEWSLETTER.html for copying into Substack and upload the image files separately. The longer original written-article reference, where supplied, is separate from this reader selection.

01 / The care team, not the algorithm, made the difference in heart failure

Published October 27, 2026 · Clinical effectiveness · Cluster-randomized trial · Potentially actionable in supervised care models
Primary source: TIME-HF trial, Circulation, PMID 42668439

The TIME-HF trial enrolled **1,507 adults with heart failure with reduced ejection fraction** at 22 centers in India. Centers were randomized to usual care or a nurse-coordinated, mobile-health-supported program incorporating risk stratification, medication and lifestyle optimization, education, outpatient monitoring, and active follow-up. The primary endpoint was days alive and out of hospital over two years.

The modeled probability of surviving the entire 730 days without hospitalization was **46.5% versus 34.7%** with usual care—an absolute **11.8-percentage-point difference**. There were **163 deaths among 755 intervention participants (21.6%) versus 201 among 752 controls (26.7%)**, an absolute 5.1-point difference and adjusted mortality hazard ratio **0.78 (95% CI 0.63–0.95)**. Nearly all participants completed follow-up.

Strength and limitations. Randomization at the center level and two-year clinical endpoints are major strengths. The intervention was multifaceted and cannot identify which component caused the improvement. It was conducted in a predominantly male, often rural population in India; generalizability to U.S. systems, staffing costs, and standard background therapy require evaluation.

Clinical practice: A strong basis for local implementation research around nurse-led follow-up, guideline-directed therapy, access, and adherence—not a mandate to copy the protocol unchanged.

Source edition: October 28, 2026 · AR-20261028-READER-01 · existing reader feature

02 / Opening a narrowed carotid artery did not restore cognition

Published October 27, 2026 · Negative clinical result · Prespecified secondary outcomes of two randomized trials
Primary source: CREST-2 cognition analysis, JAMA, PMID 42747844

A common rationale for treating severe asymptomatic carotid stenosis is that restoring blood flow might protect thinking. CREST-2 tested the cognitive part of that premise within two randomized comparisons: carotid stenting plus intensive medical management versus medical management alone, and carotid endarterectomy plus the same medical management versus medical management alone.

Among **2,366 U.S. patients**, **2,165** completed baseline cognitive assessments. Composite cognitive z-score differences at four years were small and uncertain: **0.03 SD (95% CI −0.09 to 0.15)** for stenting and **0.02 SD (−0.09 to 0.14)** for endarterectomy. Neither comparison showed a significant benefit on the five individual cognitive tests. Follow-up testing averaged 2.24 years, despite the four-year modeled endpoint.

Strength and limitations. Large multicenter randomized parent trials, blinded central cognitive assessment, and prespecified analysis support the conclusion that clinically important cognitive benefit was not demonstrated. This was a secondary outcome, not a comprehensive test of every revascularization indication or stroke outcome. A smaller hemodynamic substudy also did not show cognitive advantage and shares the underlying CREST-2 population; it is not an independent trial. CREST-H substudy, PMID 42747834.

Clinical practice: Do not offer carotid revascularization solely in expectation of cognitive improvement on these data; assess stroke-prevention indications separately.

Source edition: October 28, 2026 · AR-20261028-READER-02 · existing reader feature

03 / Lowering pediatric blood-pressure targets reduced drugs—not the main clinical outcome

Published October 27, 2026 · Important negative randomized trial · Pediatric critical care
Primary source: PRESSURE trial, JAMA, PMID 42806496

The pragmatic PRESSURE trial randomized **1,900 critically ill children** at 23 pediatric intensive care units in three countries. All required mechanical ventilation and vasoactive therapy for hypotension. The experimental strategy targeted a mean arterial pressure above the fifth percentile for age, while controls received attending-physician-selected targets.

Children receiving the permissive strategy were exposed to a **37.5% lower median norepinephrine-equivalent total dose**. Median mean arterial pressure while on vasoactives was **58 versus 61 mm Hg**. Yet the prespecified combined outcome of 30-day mortality and duration of invasive ventilation **did not significantly improve** (probabilistic index **0.52; 95% CI 0.49–0.54; P=.23**). Most secondary outcomes were also similar; survivor PICU stay was modestly shorter, and kidney replacement therapy and adverse events did not differ detectably.

Strength and limitations. Large pragmatic randomized comparison with patient-important outcomes. It was unblinded; the composite endpoint needs clinical interpretation, and children receiving different forms of circulatory support may not behave alike. Reduced drug exposure is a process outcome, not proof of improved survival.

Clinical practice: Supports careful reassessment of automatically escalating vasopressors to higher targets, under local critical-care protocols—not generalized hypotension tolerance.

Source edition: October 28, 2026 · AR-20261028-READER-03 · existing reader feature

04 / GLP-1 cardiovascular protection appears similar across age groups

Published October 27, 2026 · Systematic synthesis of eight randomized outcome trials · Clinically relevant
Primary source: Age-stratified GLP-1RA meta-analysis, PMID 42946897

Older adults are often underrepresented in trials, and relative treatment effects might differ with age. This analysis pooled age-stratified major adverse cardiovascular event data from **eight placebo-controlled GLP-1 receptor agonist trials involving 71,926 participants** with diabetes or overweight/obesity.

Pooled hazard ratios for major adverse cardiovascular events were **0.81 (95% CI 0.69–0.94)** for participants younger than 65 and **0.84 (0.79–0.90)** for those 65 and older. The between-age-group ratio of hazard ratios was **1.03 (0.85–1.25)**: **no clear evidence of age modification**. But that interval does not prove identical effects. Only four trials supplied the finer ≥75-year subgroup, which remained relatively small. Absolute event reductions were not consistently reported in the abstract and are not inferred here.

Strength and limitations. These are randomized cardiovascular endpoint trials synthesized at the subgroup level, but heterogeneity and differences in drugs, risk, and age distributions remain. It is not an age-specific randomized assignment to different drugs, and a null interaction test does not demonstrate equivalence.

Clinical practice: Age alone need not exclude indicated GLP-1 treatment, but individual frailty, nutrition, muscle and bone health, contraindications, and costs still matter.

Source edition: October 28, 2026 · AR-20261028-READER-04 · existing reader feature

05 / Removing inaccurate penicillin-allergy labels may improve antibiotic care

Published October 28, 2026 · Systematic review of nine comparative studies · Actionable within structured hospital pathways
Primary source: Hospital penicillin delabeling systematic review, PMID 42946949

Many hospitalized patients carry a penicillin-allergy label that does not reflect a true clinically relevant allergy. A new systematic review examined **nine controlled studies—three randomized trials and six nonrandomized studies**—of structured delabeling interventions.

Reported delabeling success ranged from **approximately 4% to more than 95%**, largely because methods and case selection differed. Carefully selected low-risk patients undergoing direct oral challenge were among the most successfully delabeled. Pharmacist- and antimicrobial-stewardship-led programs also identified inaccurate labels and supported more appropriate narrow-spectrum antibiotic use. Adverse events were uncommon and predominantly mild in the included studies.

Strength and limitations. The intervention is practical, but the extreme range is a warning against quoting a universal success rate. Heterogeneous protocols, risk definitions, designs, and outcomes prevented meaningful pooling. Structured allergy history and supervised challenges are not equivalent to telling patients to ignore reported reactions.

Clinical practice: A credible near-term clinical implementation candidate where trained personnel, clear exclusions, documentation, and rescue procedures exist.

Source edition: October 28, 2026 · AR-20261028-READER-05 · existing reader feature

06 / The new Cochrane review finds little proof that ergonomic fixes treat established arm and neck pain

Published October 28, 2026 · Cochrane systematic review of randomized trials · Important negative finding
Primary source: Ergonomics review, PMID 42946017

Workstation redesign and ergonomic instruction seem intuitively helpful. But preventing symptoms and treating an established disorder are different questions. This update synthesized **20 studies involving 2,478 adults** with work-related complaints of the arm, neck, or shoulder.

Compared with no treatment/usual care/placebo, ergonomic interventions produced **little or no clear improvement in pain** (standardized mean difference **−0.23; 95% CI −0.54 to 0.08**, four RCTs, 692 participants; low certainty). For function, a comparison against waiting-list control yielded **RR 1.06 (0.84–1.34)** with moderate certainty. Evidence for sickness absence, recovery, and quality of life also did not show consistent, meaningful gains. Comparisons against exercise were especially uncertain.

Strength and limitations. Prespecified Cochrane synthesis with GRADE evaluation, but protocols, patient populations, outcome metrics, and certainty differ substantially. The review does not establish that all ergonomics is useless, nor does it assess every prevention or workplace-safety program.

Clinical practice: Do not promise pain resolution from ergonomic equipment alone; evaluate occupational demands, exercise, rehabilitation, and specific diagnoses.

Source edition: October 28, 2026 · AR-20261028-READER-06 · existing reader feature

07 / Normal body weight does not guarantee protection from fatty liver disease

Published October 28, 2026 · Large retrospective observational analysis · Risk stratification, not causal treatment evidence
Primary source: Normal-BMI MASLD study, PMID 42947552

Clinicians often equate metabolic dysfunction-associated steatotic liver disease with obesity. An analysis of a U.S. electronic health-record network included **619,171 patients**, creating **51,940 matched pairs** with normal-BMI and overweight/obesity-associated MASLD under ethnicity-informed BMI definitions.

Reported survival was **77.49% in the normal-BMI MASLD group versus 83.93%** in the comparator group, corresponding to a mortality hazard ratio **1.735 (95% CI 1.653–1.822)**. The authors also reported differences in certain cardiovascular, renal, and cancer outcomes across ethnic groups. Incretin-based treatment was used less frequently in the normal-BMI group, and its use correlated with better survival.

Strength and limitations. Large datasets and matching help identify a potentially overlooked population, but coding, residual confounding, selection, disease-severity imbalance, and care-access differences can distort the comparisons. An association between incretin use and survival is **not evidence** that these medicines should be prescribed to normal-BMI MASLD patients for longevity.

Clinical practice: Evaluate steatotic liver disease and metabolic risk on their own merits, not BMI alone.

Source edition: October 28, 2026 · AR-20261028-READER-07 · existing reader feature

08 / The economics of Parkinson monitoring are a warning for wearable-health startups

Published October 28, 2026 · Early health technology assessment and simulation · Negative economic base case
Primary source: Parkinson ML remote-monitoring assessment, PMID 42947537

Wearables and machine learning could identify progression to advanced Parkinson disease sooner. But detecting progression is not itself a patient outcome. Investigators modeled a 16-year Finnish care pathway comparing standard management with machine-learning-enabled remote monitoring, assuming **88% sensitivity** and **62% specificity** in the base case.

The modeled system generated **0.0044 additional quality-adjusted life-years** at **€761 additional cost per patient**, an incremental cost-effectiveness ratio of **€172,023 per QALY**. At a €35,000/QALY willingness-to-pay threshold, net monetary benefit was negative. Some scenarios became favorable if monitoring produced direct quality-of-life gains or delayed entry into institutional care.

Strength and limitations. This is a transparent model-based assessment, not an outcome trial. Many inputs are assumed; results depend on the health system, intervention costs, prevalence, and how clinicians respond to alerts. It should be treated as a design challenge rather than a verdict against all Parkinson wearables.

Clinical practice: Monitoring needs a defined action pathway and evidence that action changes outcomes.

Source edition: October 28, 2026 · AR-20261028-READER-08 · existing reader feature

09 / Liquid AI brings small, multimodal, open-weight models to the edge

Announced October 27, 2026 · First-party technology release · Technology announcement, not clinical evidence
Primary source: Liquid AI, Introducing LFM3

Liquid AI announced **LFM3**, a new family built around a common hybrid architecture supporting text, vision, audio, multimodal, and decision-model use cases. The first release is in the **roughly 2-billion-parameter class**; the company describes **22 trillion pretraining tokens** and emphasizes local fine-tuning and device deployment. Open-weight checkpoints are announced as available through its distribution channels.

Evidence strength and limitations. These are first-party model specifications and performance claims—not independently established superiority and certainly not medical-device authorization. Hardware feasibility, benchmark transfer, model cards, licenses, hallucination rate, and safety need a hands-on evaluation. A general release does not mean every modality or model is equally production-ready.

Clinical practice: None directly.

Source edition: October 28, 2026 · AR-20261028-READER-09 · existing reader feature

10 / A wireless patch reads cardiac motion, but the evidence is still in rodents

Published October 28, 2026 · Materials engineering and animal experimentation · Preclinical discovery
Primary source: Wireless myocardial-motion patch study, PMID 42947659

Researchers report a biocompatible magnetic-particle patch placed on the epicardium during surgery. An external magnetometer and a machine-learning regression model reconstruct three-dimensional cardiac motion from magnetic-field changes. Unlike an ECG, which measures electrical activity, this approach targets mechanical movement and may detect abnormalities of contraction and relaxation.

The researchers demonstrated motion tracking and recognition of acute diastolic abnormalities **in rodent experiments**. They report no important local tissue reactions or detectable systemic toxicity over **12 weeks** of implantation in their experimental setting.

Strength and limitations. This is a promising engineering proof of concept, not evidence of safety, accuracy, clinical utility, or improved outcomes in people. It requires invasive implantation, and 'clinical-grade velocity profiles' in a laboratory report should not be confused with clinical validation.

Clinical practice: None yet.

Source edition: October 28, 2026 · AR-20261028-READER-10 · existing reader feature

---

Alive. Awake. Aware.

GO DEEPER

Keep following the question.

The daily issue is a beginning. Choose a reading companion, explore a connection, or return to the wider Arising universe.

Reading the evidence →

GLP-1, in context →

Browse all public booklets →

Explore the collections →

Follow connections in the Atlas →

Visit Arising Health →

Meet the book →

Meet The Long Game →

The public Atlas connects questions across topics. The book and game pages introduce projects in development.

Alive. Awake. Aware.