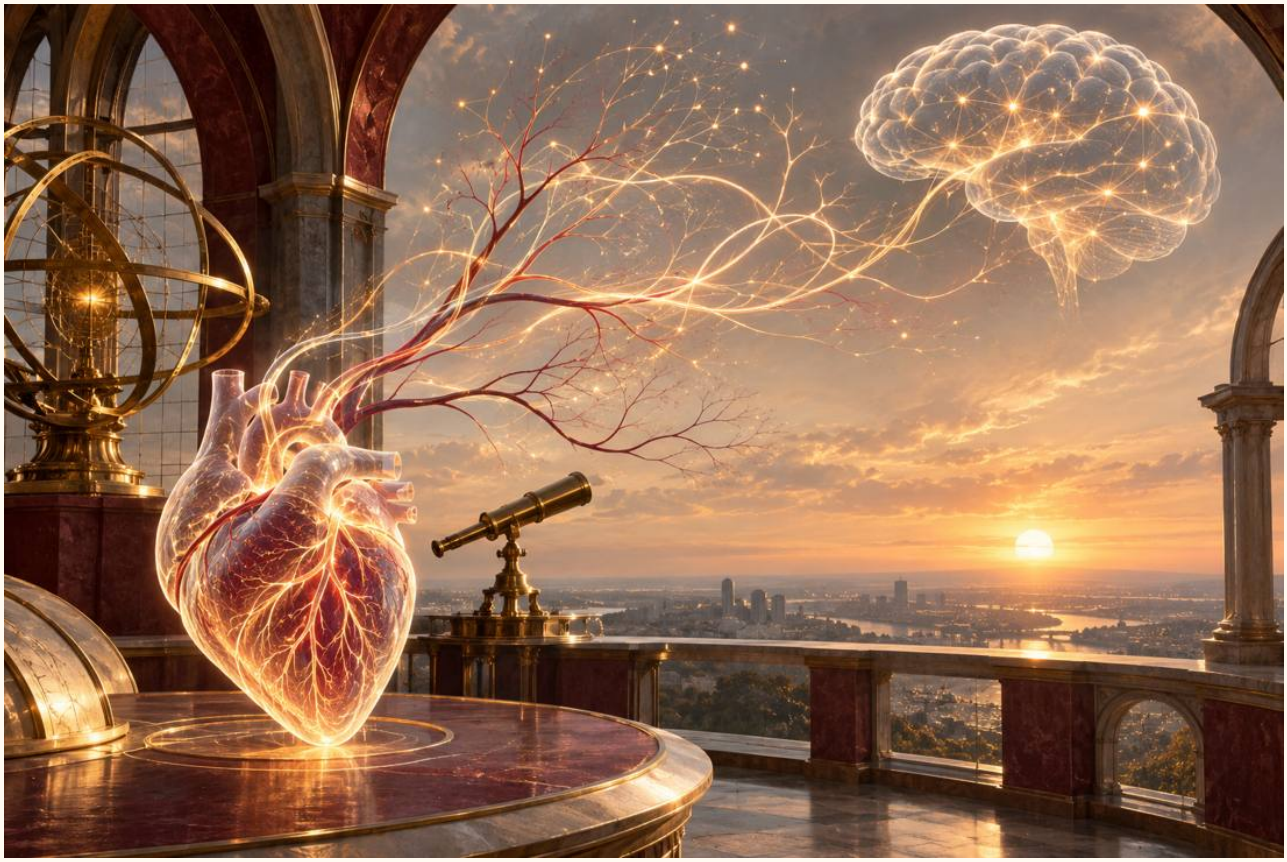
More Time, Better Function, Fewer Burdens

November 2, 2026 · John Griffin, MD



Conceptual editorial illustration for this edition of The Arising.

Alive. Awake. Aware.

The morning view

More effective cancer therapies, better metabolic medicines, meaningful functional training, and carefully deployed AI are changing medicine. They arrive with different kinds of evidence. Some results change treatment today; others identify an important possibility, a better research question or a treatment we should not adopt routinely.

Today's strongest clinical developments include an October 26 FDA expansion of gene-guided prostate cancer therapy; a randomized CAR T-cell trial in older, transplant-ineligible lymphoma patients; and a phase 3 hepatocellular-cancer combination that prolongs disease

control while overall survival remains uncertain. Equally important, a synthesis of nearly 12,000 randomized TAVR patients does not support routine cerebral embolic protection.

Closer to everyday healthspan, an exercise synthesis favors combined functional training and nutritional support; a small menopause-care trial examines practical estrogen application; and a perioperative cohort shows how cognitive impairment and frailty together identify patients at greater risk of delirium. Medical AI offers a useful operational gain in pharmacy outreach, but improved contact is not yet proof of better health.

Ten featured investigations

01. A prostate-cancer treatment moves earlier, guided by the tumor’s genes

Cancer and precision medicine · Source date: October 26, 2026 · Evidence: U.S. regulatory decision supported by randomized, double-blind phase 3 trial · Primary source

A genetic test can now change the treatment discussion earlier in metastatic prostate cancer. On October 26, the FDA expanded the approved use of talazoparib with enzalutamide to adults whose metastatic tumors carry specified homologous-recombination-repair (HRR) gene mutations and whose disease is still sensitive to, or has not received, androgen-pathway modulation. Eligibility depends on an FDA-authorized tissue or circulating-tumor-DNA test. That is a consequential clinical application of genomics: a result changes which treatment is indicated, not simply how risk is described.

The TALAPRO-3 study randomized 599 patients to talazoparib or placebo added to enzalutamide and androgen-deprivation therapy. Radiographic progression or death was less frequent with the combination (hazard ratio 0.48; 95% CI 0.36–0.65). Median radiographic progression-free survival had not been reached in the talazoparib arm, versus 45.8 months in the comparison arm. Overall-survival data were immature. The FDA label also warns about myelosuppression, myelodysplastic syndrome/acute leukemia, and embryo-fetal toxicity.

Timely molecular testing matters because an eligible result changes treatment options. Its benefit here was measured on imaging; a survival gain has not yet been established.

Clinical position: Clinically actionable for eligible patients under specialist management; verify exact label, assay, comedications and coverage before workflow adaptation.

02. An immune-cell treatment makes a measurable difference for older lymphoma patients

Oncology and later-life care · Source date: November 2026 journal issue; indexed by November 2 · Evidence: Multicenter, open-label, randomized phase 2 trial · Primary source

Older adults with relapsed large B-cell lymphoma may be too medically vulnerable for transplantation. In that setting, therapies need to be judged by what happens after treatment, including the chance of serious toxicity. The DALY 2-EU trial tested a dual CD20/CD19-directed CAR T-cell product, zamtocabtagene autoleucel, against rituximab,

gemcitabine and oxaliplatin chemotherapy in patients deemed ineligible for transplant. The median age was 74.

Across 160 randomized patients at 45 European centers, independently assessed median event-free survival was 6.21 months with CAR T treatment and 2.53 months with chemotherapy (hazard ratio 0.39; 95% CI 0.27–0.58). Serious adverse events were reported in 41% and 66%, respectively, among treated participants. Grade 3 or higher adverse events remained common in both arms (83% and 86%). CAR T treatment caused two treatment-related deaths, including cytokine-release syndrome and hemophagocytic lymphohistiocytosis; one treatment-related death occurred in the control arm.

This is promising evidence in older patients who could not undergo transplantation. Follow-up was relatively short. Manufacturing time, monitoring and caregiver support matter, and the trial does not establish regulatory availability, longer survival or better quality of life.

Clinical position: Promising trial evidence; do not present the product as an approved option without current regulatory confirmation.

03. Liver-cancer patients gain time before progression; survival remains unresolved

Oncology · Source date: November 2026 journal issue; indexed by November 2 · Evidence: Randomized phase 3 trial; overall survival immature · Primary source

For patients with unresectable hepatocellular carcinoma, transarterial chemoembolization (TACE) can contain disease but frequently loses effectiveness. The TALENTACE study asked whether combining on-demand TACE with atezolizumab and bevacizumab would extend the period before disease became untreatable by TACE or the patient died. It randomized 342 people across 40 centers in China and Japan, with preserved liver function and a substantial tumor burden.

Median TACE progression-free survival improved from 7.03 to 11.30 months (hazard ratio 0.71; 95% CI 0.55–0.92). The difference did not translate into a demonstrated overall-survival advantage at the first planned interim analysis: median survival was 34.53 versus 35.38 months, with highly uncertain estimates. Treatment-related deaths were reported in five participants in the combination arm and three in TACE alone. Patients were selected for Child-Pugh A liver function, which limits generalization to the more medically fragile populations encountered in practice.

Longer disease control may come with additional treatment and monitoring. Progression-free survival and overall survival are distinct outcomes. Shanghai Roche Pharmaceuticals sponsored the study.

Clinical position: Specialist-relevant but confirm local standard of care and regulatory/guideline context; OS not established.

04. The next weight-loss drugs are moving quickly. Tolerability still sets the pace.

Metabolic health · Source date: November 2026 journal issue; indexed by November 2 · Evidence: Double-blind, randomized phase 2 trial · Primary source

Mazdutide acts on both GLP-1 and glucagon receptors. In a U.S. phase 2 study at 24 centers, 179 adults with overweight or obesity but without diabetes were assigned to weekly injections of several doses or placebo. This is an important step in the evolution of incretin-based therapies because it examines a distinct biological combination rather than simply increasing a familiar dose.

At 32 weeks, estimated mean weight changes were −7.3%, −15.6%, and −18.1% in the three treatment groups versus −0.9% for placebo. The higher-dose groups generated the largest reductions. However, treatment discontinuation because of adverse effects reached 20% at 16 mg, primarily owing to gastrointestinal problems. The trial's primary analysis used a hypothetical efficacy estimand; it should not be confused with average real-world results in people who stop therapy. It also measured body weight rather than long-term cardiovascular events, muscle function, or survival.

Can people retain strength and daily function as they lose weight? This trial measured weight change; it cannot settle that question. Eli Lilly funded the trial.

Clinical position: Promising investigational obesity therapy, not demonstrated clinical-outcomes superiority over established options.

05. A protective device that has not shown it protects patients routinely

Cardiovascular medicine · Source date: November 2026 journal issue; indexed by November 2 · Evidence: Systematic review and meta-analysis of 8 RCTs · Primary source

When aortic valves are replaced through a catheter, clinicians worry about embolic material reaching the brain. Cerebral embolic-protection devices are designed to catch debris during transcatheter aortic valve replacement (TAVR). Their mechanism is plausible, but a device must ultimately reduce strokes that patients experience. This new synthesis brings together eight randomized trials and 11,692 participants.

Routine protection was not associated with a statistically significant reduction in stroke within two to five days (risk ratio 0.95; 95% CI 0.75–1.19) or at 30 days (RR 0.93; 95% CI 0.57–1.53). Estimates for disabling stroke were imprecise, and the pooled studies differed by device and context. The result does not exclude narrower benefits in carefully selected high-risk patients, but it weakens the case for routine use as a default intervention.

A device can catch debris without reducing strokes. Local risks, patient selection and procedural harms matter when deciding whether a device deserves routine use.

Clinical position: Important negative evidence for routine adoption; specialist-level appraisal and patient selection still matter.

06. The most useful strength program may train several abilities at once

Movement and independence · Source date: November 2026 journal issue; indexed by November 2 · Evidence: Network meta-analysis of 47 randomized trials · Primary source

The ability to rise from a chair, carry something heavy, navigate stairs and recover balance requires more than muscle size. A network meta-analysis assembled 47 randomized trials in older adults and compared exercise programs using grip strength and the Timed Up and Go test. The most favorable rankings involved multicomponent programs paired with nutritional support.

Compared with controls, multicomponent training plus nutrition had the largest reported grip-strength effect estimate (6.39; 95% CI 0.48–12.30); the authors reported a favorable Timed Up and Go estimate of −1.88 (95% CI −2.73 to −1.02) for multicomponent-plus approaches. The abstract does not specify the measurement units for these effect estimates, so we will not assign them. Network comparisons can depend heavily on intervention definitions, the amount of direct head-to-head evidence and assumptions about comparability. They also do not establish that one particular program prevents disability or increases lifespan.

Grip, mobility and meaningful daily tasks deserve to be measured alongside muscle mass. A high ranking in a network comparison is not proof that a particular program preserves independence.

Clinical position: Exercise is established care; precise rankings and nutrition combinations require further appraisal.

07. A small practical choice in menopause care can matter to patients

Women’s midlife and older women · Source date: November 1, 2026 · Evidence: Small randomized noninferiority trial · Primary source

For postmenopausal patients with recurrent urinary tract infections, the way a prescribed topical estrogen treatment is applied can affect comfort and adherence. The TAPER trial randomized 114 participants, mean age 71, to intravaginal estradiol cream or periurethral application and followed them for six months. It asked whether an easier route could preserve prevention benefit.

The proportion without a UTI at six months was 52.6% after intravaginal application and 50.9% after periurethral application. The risk difference was −1.75 percentage points, with a 95% confidence interval from −20.0 to +17.0 points. The trial’s noninferiority margin was unusually permissive at 25 percentage points, the study was unblinded and single-center, and it did not compare estrogen with no treatment. It found more reported vaginal itching at three months in the intravaginal group (24.0% versus 2.4%).

Convenience, tolerability and actual infection recurrence matter. The wide confidence interval does not establish that the two routes work identically for every patient.

Clinical position: Potentially useful for counseling, but a wide noninferiority margin limits certainty; do not extrapolate to untreated patients.

08. An AI system helped pharmacists reach people. It did not yet prove better health.

Clinical AI and care delivery · Source date: November 2026 journal issue; indexed by November 2 · Evidence: Retrospective, propensity-matched quasi-experiment; historical controls · Primary source

A powerful way to evaluate AI is to begin with an actual service problem. Pharmacy teams know that many people eligible for medication therapy management do not take a consultation. Researchers compared a machine-learning targeting system used in 2025 with traditional assignment in a 2024 cohort. After propensity matching, the analysis included 183,888 patient pairs.

The share accepting a consultation was 21.2% with machine-learning targeting versus 12.6% in the historical approach—an 8.6-percentage-point absolute difference, or 68% relative increase. That is meaningful for reach and staff scheduling. But a historical comparison cannot fully remove changes in operations, outreach tactics or patient characteristics, and the measured endpoint was consultation acceptance—not adherence, avoidable hospitalization, adverse medication events, or mortality.

Reaching someone is the start of care. A prospective comparison could ask whether more completed consultations lead to better health and whether all eligible groups benefit. The historical comparison does not establish that the algorithm caused the difference.

Clinical position: Promising operational evidence; no demonstrated clinical-outcome gain or causal AI effect.

09. A brief conversation before surgery may reveal who needs more protection afterward

Dementia, hospital medicine and functional recovery · Source date: November 2026 journal issue; indexed by November 2 · Evidence: Retrospective cohort of 3,353 older surgical patients · Primary source

Frailty and cognitive difficulty are often assessed in separate parts of the medical record. In a cohort of 3,353 patients at least 70 years old undergoing elective noncardiac surgery, researchers combined a Mini-Cog assessment with a Clinical Frailty Scale rating and followed patients for delirium through the first two postoperative days.

The proportion with a positive delirium assessment ranged from 4.2% among patients with neither finding to 24.0% among those with both cognitive impairment and frailty. After adjustment, the combined phenotype had 4.79 times the odds of delirium compared with the intact group (95% CI 3.22–7.11). This is risk stratification, not evidence that the screening

tool—or any one preventive intervention—reduces delirium. Selection, ascertainment and residual confounding are important limitations.

Acute delirium after surgery and a chronic neurodegenerative disease require different assessments. A screening result can inform a conversation about baseline function and discharge support; this study did not test a preventive treatment.

Clinical position: Screening may support risk conversations and prevention planning; no proof of intervention benefit from this cohort.

10. A Parkinson’s experiment suggests another way to protect vulnerable neurons

Neurodegeneration and regenerative biology · Source date: October 30, 2026 · Evidence: Preclinical nonhuman-primate disease model · Primary source

The nervous system depends on ways to remove damaged proteins. One of these, chaperone-mediated autophagy, uses the lysosomal protein LAMP2A to help process selected cellular cargo. Parkinson’s disease is linked to abnormal alpha-synuclein. A new Science Advances study tested whether raising LAMP2A expression could blunt damage caused by injections of patient-derived Lewy-body material in nonhuman primates.

The investigators report protection of dopamine-producing neurons, delayed accumulation or release of pathology-related alpha-synuclein species, and favorable motor and cognitive behavior in the primate model. The retrieved abstract does not give a sample size or clinical treatment effect; none should be invented. The animals did not have naturally developing human Parkinson’s disease, and neither human efficacy nor an acceptable gene-delivery risk profile is established.

The next question is whether the approach can be delivered safely and restore function in people with established disease. Protecting neurons in an induced model does not establish clinical benefit in Parkinson’s disease.

Clinical position: Promising preclinical evidence; no clinical prescribing or longevity claim.

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