Notable advances 2024

This year saw breakthroughs in stem cell therapy, exposome research and HIV prevention, as well as ever-more-elegant gene-editing tools — while the rise of the incretin agonists continued unabated. Here is our selection of critical developments that moved medicine forward in 2024.

Nutrition

The harms of ultra-processed foods

In February, a large umbrella review and meta-analysis sought to comprehensively evaluate the existing evidence — stemming from myriad epidemiological studies with varying designs and limitations — on associations between ultra-processed foods and health outcomes. The results broadly consolidate previous findings; greater exposure to ultra-processed foods was consistently associated with a higher risk of adverse health outcomes, in particular all-cause mortality, cardiovascular-related mortality, type 2 diabetes and common mental disorders. Grading of the credibility and quality of evidence should help to prioritize associations that warrant further validation through preclinical studies and randomized, controlled trials — which are lacking in this field. Ultra-processed foods are not universally bad, and it will be important for future research to determine the specific processes and components that are harmful to health, and the mechanisms by which they exert their effects. Such evidence will be key to formulating effective public health strategies.

Original reference: *BMJ* **384**, e077310 (2024)

Neurodegenerative disease

From clinical to biological definitions of neurological diseases

February saw the release of revised criteria for the diagnosis and staging of Alzheimer's disease (AD) by the Alzheimer's Association Workgroup, to align with recent scientific advances — including the approval of therapies that target AD pathology, and the development of reliable and accessible biomarkers. The new criteria define 'core' (specific to AD) and 'non-core' biofluid and imaging-based biomarkers; diagnosis now relies on the presence of amyloid and tau, with clinical diagnosis of dementia alone being insufficient for AD diagnosis. Although they are not without controversy, these new criteria are broadly accepted by clinical societies and reflect a shift toward biological definitions of neurological diseases beyond AD. Indeed, two frameworks were published this year that outline biological criteria for the staging of Parkinson's disease — although, unlike those for AD, these are not yet widely accepted or ready for clinical use. Overall, this biological reframing of neurological conditions should better address the priorities of research and clinical care.

Original references: *Alzheimers Dement.* **20**, 5143–5169 (2024); *Nat Med.* **30**, 2121–2124 (2024); *Lancet* **23**, 191–204 (2024); *Lancet* **23**, 178–190 (2024)

Environmental health

Health impacts of microplastic exposure

Microplastics and nanoplastics (MNPs) are everywhere — the oceans, air, soil and food supply — but evidence of their effects on human tissues and organs has been limited mostly to preclinical analyses. In March, a prospective observational study examined carotid plaque specimens from 257 people who underwent a surgical procedure to unblock arteries — and identified MNPs (specifically, polyethylene and polyvinyl chloride) in the carotid artery plaques of more than half of all participants. The presence of these MNPs was associated with a 4.5-fold increased risk of cardiovascular events after almost 3 years of follow-up. These findings do not prove causality, but they are a cause for concern; they highlight the urgent need for further research into the key sources of human exposure to MNPs, their impact on health and the mechanisms underlying these effects.

Original reference: *N. Engl. J. Med.* **390**, 900–910 (2024)

Cancer therapies

First tumor-agnostic approval for an ADC

In April, the HER2-targeting antibody–drug conjugate (ADC) trastuzumab deruxtecan was granted accelerated approval by the US Food and Drug Administration for the treatment of unresectable or metastatic HER2-positive solid tumors. After an initial approval in 2019 for this drug for the treatment of patients with unresectable or metastatic HER2-positive breast cancer, the recent tumor-agnostic approval is based on phase 2 studies in the DESTINY clinical trial series: DESTINY-PanTumor02, DESTINY-Lung01 and DESTINY-CRC02. Promising efficacy data had been reported previously in patients with gastric cancer or non–small-cell lung cancer, which led to specific approvals for those cancers, but recent data have shown benefits across many solid-tumor indications — including gynecological cancers, for which there is a particularly strong need for new treatment options.

Original references: *FDA* https://go.nature.com/4fkvDPg (2024); *J. Clin. Oncol.* **42**, 47–58 (2024); *Lancet Oncol.* **25**, 439–454 (2024); *Lancet Oncol.* **25**, 1147-1162 (2024)

Gene therapy

Prime time for gene editing

Gene-editing tools are evolving rapidly, from the first CRISPR–Cas systems to base editing and, more recently, prime editing. Unlike CRISPR–Cas systems, base editing does not require double-strand breaks; neither does prime editing, and it supports greater editing power — including targeted