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November - December 2025

Alzheimer's

Researchers link brain disease to metabolic health

Clonal Haematopoiesis

Scientists find causal relationship between blood mutations and metabolic disease

Obesity

New treatment framework prioritises GLP-1 medications

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- JHAH opens to public as Saudi Arabia expands healthcare access
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- Adolescent concussion recovery reveals sex-specific blood biomarker differences
- Breathing difficulty predicts sixfold mortality risk in hospital patients

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THE MORE THE UNEXPECTED:

Jakarta, The Halal Capital of Flavour

The first thing you notice about Jakarta isn't the skyline, it's the food. Coconut rice steams in banana leaves, satay sizzles over charcoal, and long tables spill into the night as families gather past midnight. Wander a little further and chandeliers glow over plates where tradition is shaped into art.

For Muslim travelers, there is comfort in knowing that almost every taste is halal, whether found on sidewalks or behind velvet curtains.

Coffee that tells a story

And like any good story, it often begins with coffee. Jakarta's coffee culture is as layered as its food. In Glodok's Chinatown, Kopi Es Tak Kie has poured its no-frills brew since 1927. Some come for the sweet iced coffee mixed with condensed milk, but the regulars swear by its black coffee, strong and slightly bitter, the kind that lingers long after the glass is empty. The tiled floor and wooden chairs feel unchanged, and every sip carries the weight of old Jakarta.

Across town in Cipete, South Jakarta, Tuku Coffee sparked the city's modern caffeine wave. Its iced latte with palm sugar became a neighborhood hit that grew into a national trend, a drink that balances the roast's depth with a subtle sweetness. From heritage brews to contemporary blends, coffee here is never just about caffeine, it is a window into the city's changing tastes.

Street legends that never fade

Every city has dishes that become part of its daily rhythm, and in Jakarta the streets tell that story best. On the crowded lanes of Pasar Baru in Central Jakarta, Bakmi Gang Kelinci has served its springy chicken noodles since 1957. The soy-rich aroma fills a dining room that feels frozen in time, and for many Jakartans it is the taste of homecoming.

A short ride away in Tanah Abang, the air is thick with the coconut fragrance of Nasi Uduk Kebon Kacang. Plates of rice cooked in santan arrive with crispy fried chicken and fiery sambal, best enjoyed shoulder to shoulder with locals in the late-night rush. Both spots prove that some of the city's greatest meals are still found where the streets hum the loudest.

Restaurants and refined tables

Jakarta's dining scene does not just preserve tradition, it reinvents it. Across the city, restaurants are shaping heritage dishes into experiences that feel fresh without losing their roots.

In Senopati, South Jakarta, Daun Muda Soulfood retells Indonesia's culinary stories with spice and fire. Dishes like Manado's rica-rica or Palembang's rusip come plated with a contemporary touch, but the soul remains deeply rooted in the archipelago. For something more elevated, 1945 Restaurant at the Fairmont Senayan reimagines rendang and satay as fine dining artistry. As Jakarta's first halal-certified luxury restaurant, it proves that heritage and refinement can sit comfortably at the same table.

Jakarta's halal dining culture is more than convenience. It is culture made accessible. From the chatter of Chinatown cafés to the hush of silver-spoon dinners, every sip and every dish offers not only sustenance but also a story, waiting to be tasted.

The more dishes you share, the more memories you create. Every flavour is an invitation to the city's soul.

Kopi Es TAK KIE

Tuku Coffee

Bakmi Gang Kelinci

The more meals you gather around, the more connections you make. Every plate brings you closer to the spirit of Jakarta.

Sate Maranggi by 1945 Restaurant

Nasi Uduk Kebon Kacang

Prognosis

From blood to brain: New evidence reveals unexpected disease connections

In this issue we look at recent studies examining Alzheimer's disease and obesity which demonstrate how diseases previously thought to be separate may be fundamentally linked through shared biological mechanisms.

The University of Florida's research on clonal haematopoiesis challenges conventional thinking about metabolic disease. These blood stem cell mutations, affecting approximately 10% of older adults, actively promote obesity rather than simply resulting from it. In mouse models, DNMT3A mutations caused 1.7-fold faster weight gain and progressive metabolic dysfunction including pre-diabetic glucose levels and fatty liver disease. The bidirectional relationship between blood cell mutations and metabolic disorders suggests that patients may enter harmful feedback loops where each condition worsens the other.

Meanwhile, the European Association for the Study of Obesity has released guidance positioning semaglutide and tirzepatide as primary treatments for obesity and its complications. The framework moves beyond simple weight loss targets, categorising complications into mechanical conditions like sleep apnoea and metabolic conditions including type 2 diabetes and cardiovascular disease. Tirzepatide achieved 16.5% total body weight loss, whilst both medications demonstrated significant benefits for heart failure, diabetes remission and liver disease.

The Alzheimer's research reveals equally important connections. MIT researchers found that daily 40 Hz audiovisual stimulation over two years reduced plasma phosphorylated tau 217 levels by up to 55% in late-onset patients, representing the first demonstration that non-invasive therapy can modify disease biomarkers in humans. Separately, Houston Methodist discovered that Alzheimer's pathology systematically dismantles organised neurovascular structures in adipose tissue, potentially explaining why patients frequently develop concurrent cardiovascular and metabolic complications.

These findings demonstrate that effective treatment requires understanding how different organ systems influence each other. Blood mutations affect fat metabolism, brain disease disrupts peripheral tissue function, and sensory stimulation modifies disease biomarkers. Recognising these connections may enable earlier intervention and more effective treatment strategies across multiple conditions.

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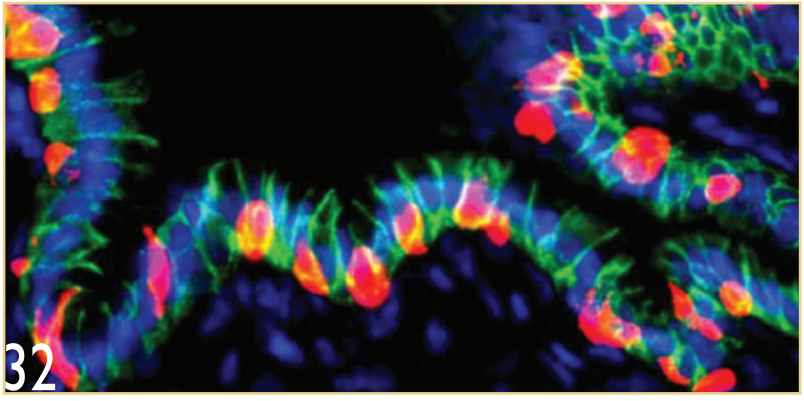

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Update from around the region

Dubai Healthcare City unveils AED1.3 billion infrastructure expansion

Dubai Healthcare City Authority has announced a major development programme comprising a LEED platinum-certified office building and purpose-built medical complex. The projects, scheduled for completion in November 2027, aim to strengthen the city's position as a regional healthcare investment hub whilst advancing sustainability objectives aligned with the UAE Net Zero Strategy 2050.

The Dubai Healthcare City Authority (DHCA) has unveiled a comprehensive AED1.3 billion development plan for Phase 1 of Dubai Healthcare City (DHCC), marking a strategic investment in healthcare infrastructure designed to attract international capital and drive innovation in the sector.

Central to the programme is the district's first LEED platinum-certified office building, designed by P&T Architects and Engineers Ltd. The 13,000-square-metre structure spans three basement levels and nine floors, offering flexible office configurations and ground-floor commercial spaces. The project represents the highest tier of international environmental certification, aligning with the Dubai Economic Agenda D33 and the UAE's national decarbonisation targets.

Purpose-built medical facilities address sector demand

Complementing the office development, Dubai-based Design and Architecture Bureau (DAR) has designed a 5,800-square-metre medical complex featuring two basement levels and five floors. The facility provides adaptable infrastructure for surgical units, laboratory services, diagnostic imaging, outpatient clinics, medical offices, and ancillary services.

The shell-and-core design methodology enables healthcare providers to customise clinical spaces according to operational requirements, whilst smart parking integration and optimised spatial planning address long-term scalability considerations.

Issam Galadari, Chief Executive Officer of Dubai Healthcare City Authority, said: "Our upcoming development plan, starting with these flagship projects, reflects our commitment to contribute to shaping the future of healthcare infrastructure in Dubai. By creating an ecosystem that attracts investments, including FDI, and fosters innovation, while integrating sustainability with world-class design, we are aligning with the Dubai Economic Agenda, D33, and the UAE Net Zero Strategy 2050."

Infrastructure enhancement supports accessibility

The development plan includes multi-storey car parks equipped with electric vehicle charging infrastructure, Salik-integrated smart parking systems, and comprehensive accessibility features designed to accommodate diverse user requirements.

Allae Almanini, Chief Operating Officer at Dubai Healthcare City Authority, added: "Our priority is to deliver infrastructure that enables growth and creates confidence for healthcare providers and investors. These projects will enhance accessibility, sustainability, and efficiency across the community, ensuring that DHCC remains the most attractive healthcare investment destination in the region."

Construction is scheduled to commence in December 2025, with project completion anticipated for November 2027. The phased approach aims to minimise operational disruption whilst delivering modern facilities that meet evolving healthcare sector demands. MEH

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GMU launches clinical simulation institute as cornerstone of UAE's largest healthcare training network

Gulf Medical University has opened the Thumbay Institute of Clinical Simulation at its Ajman campus, establishing a comprehensive training facility that anchors an expanding network of seven specialised simulation centres across medical, dental, physiotherapy, surgical, and veterinary disciplines. The institute aims to standardise skills training and enhance patient safety through high-fidelity clinical scenarios.

Integrated simulation network addresses competency gaps

Gulf Medical University inaugurated the Thumbay Institute of Clinical Simulation on 1 October 2025, creating a centralised hub for practice-based healthcare education. The facility enables students, residents, and practising clinicians to rehearse clinical scenarios using advanced manikins, task trainers, and simulated clinical environments before encountering real patients.

The institute forms the foundation of what GMU describes as the UAE's largest integrated healthcare simulation network, comprising seven facilities: the Thumbay Clinical Simulation Centre, Dental Simulation Centre, Physiotherapy Simulation Centre, Thumbay Surgical Skills Centre, and planned facilities for veterinary medicine and Dubai operations.

Evidence-based training methodology deployed

The facility replicates intensive care units, emergency departments, operating theatres, primary care clinics, inpatient wards, and home-care settings. All training sessions undergo digital recording for structured debriefing, allowing learners to analyse and improve clinical performance through objective assessment.

Prof. Manda Venkatramana, Chancellor of Gulf Medical University, said: "Simulation changes outcomes. It lets our learners make mistakes without harm, learn as teams, and return to the bedside more confident and more prepared. With this institute and our growing network across medicine, dentistry, physiotherapy, surgery, and soon veterinary medicine, GMU is setting a national standard for hands-on health-professions education."

Curriculum extends beyond technical procedures

The training programme encompasses team-based drills, Objective Structured Clinical Examinations (OSCEs), crisis resource management, and procedure training. Beyond technical skills, the curriculum addresses communication, ethics, cultural competence, and leadership under clinical pressure.

International partnerships strengthen credibility

GMU maintains accreditation with multiple international bodies, including the American Heart Association International Training Centre, National Association of Emergency Medical Technicians, Society in Europe for Simulation Applied to Medicine, Royal College of Physicians of the United Kingdom MRCP, Emirates Medical Preparedness and Response Programme (Jaheziya), and Health and Safety Institute.

The institute will serve GMU's undergraduate and postgraduate programmes whilst supporting continuing professional development across the Thumbay healthcare network. Future research directions include human factors analysis, AI-assisted training methodologies, and patient safety outcomes assessment. MEH

JHAH opens to public as Saudi Arabia expands healthcare access

Johns Hopkins Aramco Healthcare has announced its historic expansion beyond the Saudi Aramco community, opening world-class medical facilities to the broader Saudi public for the first time. The move supports Saudi Arabia's Vision 2030's healthcare transformation goals, introducing Centres of Excellence focused on oncology, cardiovascular medicine and other specialties that integrate screening, treatment and research into coordinated patient-centred models.

Dr Howard S. Podolsky, Chief Executive Officer of JHAH

Johns Hopkins Aramco Healthcare (JHAH) has opened its doors to the general public in Saudi Arabia, marking a significant shift in the Kingdom's healthcare infrastructure. The Dhahran-based institution, established through a joint venture between Saudi Aramco and Johns Hopkins Medicine in 2014, will now extend its clinical services beyond its traditional patient base for the first time.

The expansion aligns with Saudi Arabia's Vision 2030 initiative, which prioritises preventive care, innovation and healthcare accessibility across the King-

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dom. JHAH will leverage Johns Hopkins Medicine's clinical standards whilst addressing regional healthcare needs through specialised centres designed to elevate care delivery across multiple therapeutic areas.

Centres of Excellence to set clinical benchmarks

Central to the expansion is the rollout of Centres of Excellence (CoEs) that integrate clinical expertise, innovation and research into multidisciplinary care models. The first of these, the Oncology Centre of Excellence, was unveiled at the Global Health Exhibition 2025 in Riyadh. This centre will focus on breast, prostate and colorectal cancers, integrating screening, diagnosis, treatment, survivorship and palliative care into a unified pathway.

"By extending access to the wider public, we are combining the best of Johns Hopkins Medicine's global standards with our deep understanding of local needs," said Dr Howard S. Podolsky, Chief Executive Officer of JHAH. "Our promise is clear: every patient deserves exceptional care, centred on their unique needs."

Integrated care models and workforce development

JHAH's service portfolio spans cardiology, oncology, orthopaedics, women's health, paediatrics, mental health, neurology and musculoskeletal care. The organisation has integrated remote medicine capabilities, hospital-at-home programmes and AI-powered diagnostic systems into its clinical operations.

Beyond cardiovascular medicine, additional Centres of Excellence are planned to address evolving healthcare priorities across Saudi Arabia and the wider region. The institution continues to focus on precision medicine development and digital healthcare innovation whilst building a skilled national healthcare workforce.

"This is only the beginning of our journey," said Dr Podolsky. "Today, we reaffirm our promise to the people of Saudi Arabia to provide access to globally recognised experts, to harness the power of innovation and research, to develop the next generation of medical professionals, and to ensure every patient receives care centred around their needs." MEH

PureHealth integrates mental health services into AI-powered telehealth platform

PureHealth has launched nationwide virtual mental health services through its Pura app, powered by SAKINA's network of licensed psychologists and psychiatrists. The telehealth initiative addresses significant treatment gaps in the UAE, where up to 80% of mental health cases remain undiagnosed, according to regional healthcare data. The service is available to all UAE residents, including Daman insurance holders.

The UAE's largest healthcare group has expanded its digital health infrastructure with the integration of comprehensive mental health services into its AI-enabled Pura application. The platform now provides direct access to SAKINA's clinical network, the region's largest mental health service provider operating within PureHealth's SEHA hospital network.

Clinical access and service delivery

Users can schedule private consultations with licensed mental health professionals through the application's telehealth interface. The platform combines synchronous video consultations with asynchronous support tools, including guided meditation protocols, educational resources, and structured resilience-building programmes tailored to individual patient profiles.

The initiative targets documented barriers to mental health service utilisation in the Gulf Cooperation Council region. World Health Organization data indicates one in eight individuals globally experiences mental health disorders at any given time. Regional statistics demonstrate that 75% of affected individuals do not seek treatment, primarily due to access limitations and privacy concerns.

Digital health infrastructure integration

The mental health module represents an expansion of PureHealth's existing digital health ecosystem, which encompasses 110 hospitals, 316 clinics, and associated diagnostic facilities across the Middle East. The platform utilises artificial intelligence to facilitate appointment scheduling, symptom assessment, and care coordination.

Shaista Asif, Group Chief Executive Officer at PureHealth, said: "By harnessing the power of digital healthcare and AI, we're not just scaling access, we're personalising care and helping to remove longstanding barriers to mental health support."

Healthcare system alignment

The service launch aligns with UAE national health priorities emphasising preventive care and digital transformation. Dr Zain Al Yafei, Chief Executive Officer of SAKINA, noted: "This launch marks an important step toward enabling earlier intervention and promoting a more proactive, personalised approach to mental health care across the UAE."

The platform is accessible through the Pura application at https://pura.ai, with services available to both private patients and those covered through Daman insurance networks. MEH

- Further information is available at *www.purehealth.ae*.

SEHA CLINICS honoured with six awards for healthcare excellence

SEHA CLINICS, a subsidiary of PureHealth and one of the UAE's largest primary care providers, has received six awards from the Arab Hospitals Federation, including a Platinum Award for Safety and Quality of Care. The recognition highlights the organisation's commitment to patient-centred healthcare across its network of 32 multi-specialty centres serving 3.5 million people annually.

SEHA CLINICS has been recognised with six awards at the sixth edition of the Arab Hospitals Federation's 'Star of Excellence in Patient Experience', held in Abu Dhabi on 17 September 2025. The ceremony, organised under the patronage of Sheikh Nahayan Bin Mubarak Al Nahayan, Cabinet Member and Minister of Tolerance and Coexistence in the UAE, brought together healthcare stakeholders and professionals from across the Arab region.

Platinum recognition for safety standards

The organisation received a Platinum Award for Safety and Quality of Care, reflecting its commitment to maintaining rigorous safety protocols and quality standards across its facilities. The award recognises SEHA CLINICS' systematic approach to patient safety and clinical outcomes across its comprehensive network.

SEHA CLINICS also secured five Gold Awards in categories spanning patient-centred care and community engagement, continuity of care and transition management, leadership governance policy and culture, and accessibility. The awards acknowledge the organisation's integrated approach to healthcare delivery across the emirate of Abu Dhabi.

Integrated care delivery model

Dr Khadija Al Marashda, Chief Executive Officer of SEHA CLINICS, emphasised the organisation's patient-focused approach. "At SEHA Clinics, we take pride in fostering a culture of inspirational leadership, grounded by patient insights and community needs, to preserve and enhance the wellbeing for all residents of Abu Dhabi," she said.

The organisation operates 32 multi-specialty healthcare centres, three dental specialty centres, 19 disease prevention and screening centres, and provides school health services at 250 public schools across Abu Dhabi, Al Ain, and Al Dhafra regions. This infrastructure supports SEHA CLINICS' integration of preventive healthcare with specialised services, underpinned by digital platforms and patient management systems.

Regional healthcare benchmark

Alice Yammine Boueiz, CEO of the Arab Hospitals Federation, noted the broader significance of the recognition. "The success of SEHA CLINICS in winning six Platinum and Gold awards confirms that patient experience has today become a cornerstone of healthcare transformation in the region," she said, highlighting Abu Dhabi's position as a reference model for healthcare systems development across Arab countries.

The awards align with the UAE's strategic focus on developing accessible, prevention-oriented healthcare infrastructure for all residents. MEH

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Update from around the globe

WHO reports 100 countries join climate health alliance as inaction claims half a million lives annually

The global health community is confronting an escalating crisis as climate change drives unprecedented health impacts, with two landmark reports revealing both the devastating toll of inaction and emerging international efforts to build resilient health systems.

The 2025 Lancet Countdown on Health and Climate Change, produced in collaboration with the World Health Organization, documents that 12 of 20 key health threat indicators have reached record levels, whilst simultaneously the Alliance for Transformative Action on Climate and Health has expanded to encompass 100 countries committed to climate-responsive healthcare infrastructure.

Heat-related mortality surges 23% since 1990s

The mortality burden from rising temperatures has intensified dramatically, with heat-related deaths averaging 546,000 annually, representing a 23% increase since the 1990s. Population-level exposure to dangerous heat conditions has expanded substantially, with the average person experiencing 16 days of climate change-attributable extreme heat in 2024. Vulnerable populations face disproportionate risks, with infants and older adults enduring over 20 heatwave days per person – a fourfold increase over two decades.

"The climate crisis is a health crisis. Every fraction of a degree of warming costs lives and livelihoods," said Dr Jeremy Farrar, Assistant Director-General for Health Promotion and Disease Prevention and Care at the World Health Organization. "This report, produced with WHO as a strategic partner, makes clear that climate inaction is killing people now in all countries. However, climate action is also the greatest health opportunity of our time. Cleaner air, healthier diets, and resilient health systems can save millions of lives now and protect current and future generations."

Economic and food security impacts compound health burden

The physiological consequences of climate change extend beyond direct thermal stress. Droughts and heatwaves contributed to 124 million additional people facing moderate or severe food insecurity in 2023, whilst heat exposure eliminated 640 billion potential labour hours in 2024, generating productivity losses equivalent to US$ 1.09 trillion. The economic burden of heat-related mortality amongst older adults alone reached US$ 261 billion.

Fossil fuel subsidies exceed climate finance by threefold margin

Financial allocation patterns reveal a stark disconnect between stated climate commitments and governmental spending priorities. Governments allocated US$ 956 billion to net fossil fuel subsidies in 2023 – more than triple the annual funding pledged to support climate-vulnerable countries. Fifteen nations spent more subsidising fossil fuels than their entire national health budgets, highlighting the structural barriers to health-protective climate policy.

Health systems demonstrate climate leadership capacity

Despite these challenges, emerging data indicate significant capacity for health sector climate action. Health-related greenhouse gas emissions decreased 16% globally between 2021 and 2022 whilst maintaining care quality improvements. WHO data reveal that 58% of Member States have completed health Vulnerability and Adaptation assessments, with 60% having finalised Health National Adaptation Plans.

Urban health systems are advancing risk preparedness, with 834 of 858 reporting cities having completed or planned climate risk assessments. The transition towards renewable energy infrastructure has generated measurable co-benefits, with an estimated 160,000 premature deaths avoided annually between 2010 and 2022 from reduced coal-derived outdoor air pollution alone.

Alliance expansion reflects growing political commitment

The Alliance for Transformative Action on Climate and Health has rapidly expanded since its 2022 establishment to support delivery of the COP26 Health Commitments on Climate Resilient and Low Carbon Health Systems. The addition of Cook Islands, Malaysia and Tuvalu between July and October 2025 brought membership to 100 countries and over 95 partner organisations.

Small island developing states face particular vulnerabilities, with Tuvalu – the smallest WHO Member State – having championed climate and health initiatives for decades. As a rapidly growing economy, Malaysia is building resilience and sustainability across multiple sectors, including healthcare infrastructure.

"We already have the solutions at hand to avoid a climate catastrophe – and communities and local governments around the world are proving that progress is possible. From clean energy growth to city adaptation, action is underway and delivering real health benefits – but we must keep up the momentum," said Dr Marina Romanello, Executive Director of the Lancet Countdown at University College London.

The renewable energy sector achieved record generation of 12% of global electricity in 2024, creating 16 million jobs worldwide. Medical education has expanded to incorporate climate and health competencies, with two-thirds of medical students receiving relevant training in 2024. These developments provide an evidence base for accelerated health-centred climate action ahead of COP30 from 10-21 November in Belém, Brazil. MEH

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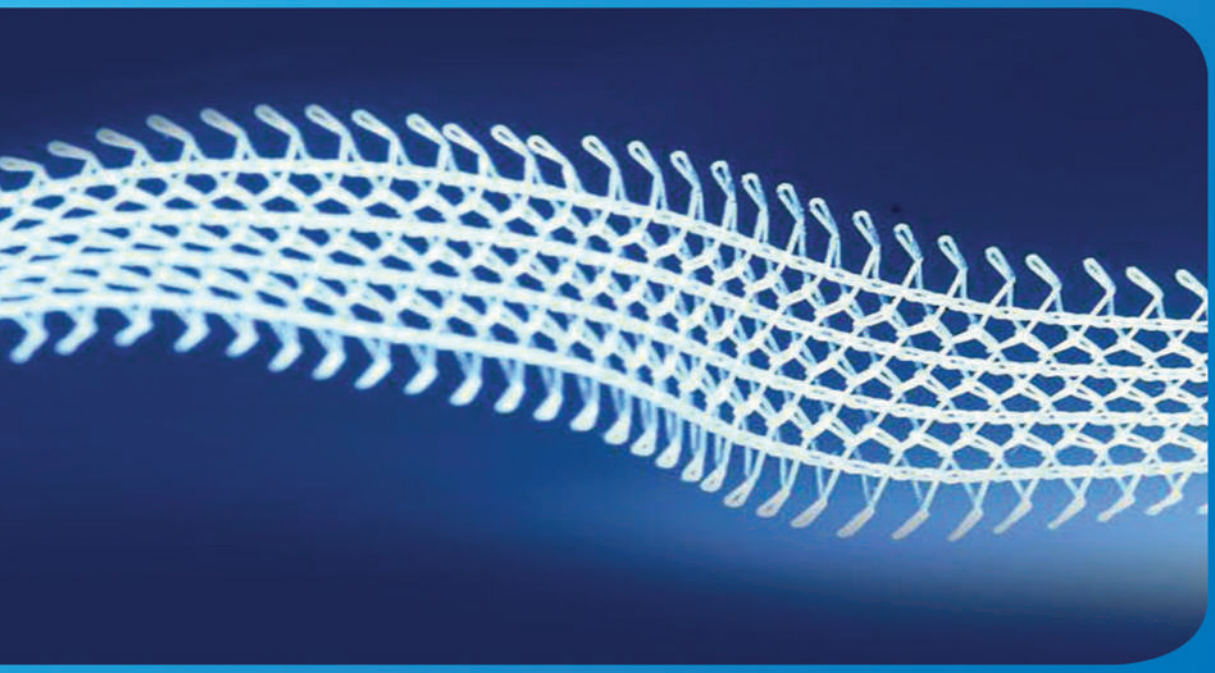

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KFSHRC performs world's first robotic intracranial tumour resection in historic neurosurgical milestone

Surgeons at King Faisal Specialist Hospital and Research Centre (KFSHRC) in Riyadh have completed the world's first robotic intracranial tumour resection, marking a significant advance in neurosurgical technique and patient outcomes. The procedure involved removing a 4.5-centimetre brain tumour from a 68-year-old male patient who presented with severe headaches and cognitive impairment.

Same-day discharge demonstrates clinical efficacy

The patient was discharged fully conscious within 24 hours post-operatively, representing a recovery time approximately four times faster than conventional craniotomy procedures. This rapid recovery profile reflects the reduced surgical trauma associated with robotic-assisted techniques, according to hospital officials.

Dr Homoud Aldahash, Consultant of Skull Base Tumours at KFSHRC, who performed the surgery, noted that the robotic system provided exceptional precision in navigating critical neurovascular structures. "The patient's same-day discharge, fully conscious and without complications, represents a new benchmark for neurosurgical innovation," Dr Aldahash stated.

Technical approach combines robotics with advanced imaging

The one-hour procedure utilised robotic arms guided by a three-dimensional optical system, enabling surgeons to operate with enhanced magnification and visualisation of intracranial anatomy. Advanced image-guided navigation technology facilitated precise tumour removal whilst protecting vital brain structures.

The robotic platform addresses inherent limitations of traditional microscope-based manual resection, where precision depends on surgeon steadiness and visual acuity. Current robotic systems deliver enhanced instrument stability, tremor elimination, and superior visualisation, establishing new standards for safety and precision in neurosurgical practice.

Institutional context and global positioning

Dr Majid Alfayyadh, Chief Executive Officer of KFSHRC, commented on the achievement: "This achievement reflects KFSHRC's growing role in shaping the future of global medicine. It aligns perfectly with our vision, where innovation and patient-centred care define the future of healthcare."

This procedure follows KFSHRC's previous robotic surgical milestones, including the world's first robotic heart transplant and robotic liver transplant. The institution has been ranked first in the Middle East and North Africa region and fifteenth globally amongst the world's top 250 academic medical centres for 2025, and was recognised as the most valuable healthcare brand in the Middle East by Brand Finance 2025.

The successful outcome suggests potential for expanded application of robotic techniques in complex neurosurgical cases, particularly for lesions requiring high-precision manipulation in anatomically challenging locations. MEH

Young leaders declare social isolation a critical public health priority at WHO simulation

Young leaders from more than 40 countries have issued an urgent call to address social isolation and loneliness as a fundamental public health priority, adopting a landmark declaration at the Global Model WHO 2025 in Geneva this week.

The Global Model WHO Youth Declaration on Social Connection, approved by nearly 400 delegates at WHO headquarters, demands national strategies, community investments, and inclusive digital policies designed to foster belonging and reduce loneliness across populations. The declaration emerged from the second in-person Global Model WHO (GMWHO), a partnership initiative between WHO and the World Federation of United Nations Associations (WFUNA) that simulates the World Health Assembly.

Mental health crisis demands systemic response

"Social connection is the missing pillar of global health," said Ida Marchese, Director-General of the Global Model WHO 2025. "Our generation has grown up in an age of digital connection but social disconnection. This declaration is our call to rebuild communities where every person feels seen, valued and supported."

The four-day simulation brought together six youth delegates from each WHO region to examine policies and community strategies informed by the WHO Commission on Social Connection. The Commission's recent report revealed that loneliness affects one in six people worldwide, with rates highest amongst younger populations and in lower-income countries. The condition contributes to an estimated 871,000 deaths annually.

Evidence base strengthens case for intervention

The WHO Commission on Social Connection, co-chaired by Dr Vivek Murthy, the 19th and 21st Surgeon General of the United States, and Ms Chido Mpemba,

Special Adviser on Youth and Women to the African Union Chairperson, has positioned social connection as a vital yet historically overlooked component of well-being. The commission's findings provided the scientific foundation for policy discussions throughout the simulation.

During the closing ceremony, WHO Director-General Dr Tedros Adhanom Ghebreyesus urged delegates to translate their engagement into community action. "When you return home, carry this spirit of connection with you. Bring it to your families, your schools, your communities. To-

UN adopts comprehensive declaration targeting noncommunicable diseases and mental health

Government representatives, gathered at the United Nations in September, adopted a political declaration addressing the growing burden of noncommunicable diseases (NCDs) and mental health conditions, which together account for more than 43 million deaths annually worldwide. The declaration establishes concrete targets for 2030, including reducing tobacco use by 150 million people, bringing hypertension under control for 150 million additional individuals, and expanding mental health care access to 150 million more people.

The document emphasises that NCDs cause 18 million premature deaths each year before age 70, with cardiovascular diseases representing the largest share, followed by cancers, diabetes, and chronic respiratory diseases. Mental health conditions, affecting nearly one billion people globally, commonly co-occur with neurological conditions including Alzheimer's disease, stroke sequelae, Parkinson's disease, and epilepsy. The declaration notes that suicide ranks as the third leading cause of death amongst those aged 15 to 29 years.

Specific disease targets and intervention strategies

The declaration outlines detailed prevention and treatment strategies across multiple disease categories. For cardiovascular disease, member states commit to scaling up early screening, monitoring, and diagnosis, alongside affordable treatment and regular follow-up for individuals at risk or living with high blood pressure. The document emphasises addressing diagnostic gaps of cardiovascular conditions in women.

Cancer prevention measures include promoting early access to affordable diagnostics, screening, treatment, and care, as well as vaccines that lower cancer risk. Specific targets include eliminating cervical cancer through human papillomavirus vaccination coverage for girls and boys, improving screening access particularly for women living with HIV, and ensuring quality treatment access. The Global Initiative for Childhood Cancer aims to achieve at least 60% survival rate globally by 2030.

Mental health interventions focus on scaling up accessibility, availability, and provision of psychosocial and psychological support, alongside pharmacological treatment for depression, anxiety, and psychosis. The declaration calls for developing national suicide prevention strategies, limiting access to means of suicide including highly hazardous pesticides, and reducing stigma through inclusive public education involving people with lived experience.

Economic rationale and resource mobilisation

The declaration highlights that investing in World Health Organization 'Best Buys' could save approximately seven million lives and result in 50 million additional years of healthy life, with a return on investment of at least US$7 by 2030 for every US$1 spent, generating more than US$230 billion in economic benefits between now and 2030.

Member states committed to mobilising adequate, predictable, and sustained resources through domestic, bilateral, and multilateral channels, including international cooperation and official development assistance. Financial protection measures aim to reduce out-of-pocket expenditure for affected individuals and households through policies covering or limiting costs of essential services, diagnostics, assistive products, psychosocial support, and medicines.

Primary healthcare strengthening and universal coverage

The declaration identifies primary healthcare as the foundation for achieving universal health coverage, calling for integrated community-based services covering health promotion, prevention, screening, diagnosis, treatment, and follow-up. Member states committed to expanding primary health facilities' availability of WHO-recommended essential medicines and basic technologies, with a target of at least 80% coverage by 2030.

Specific measures include shifting mental health care resources from specialised institutions to general healthcare services delivered in community-based settings, integrating NCD responses with communicable disease programmes including HIV/AIDS and tuberculosis, and ensuring continuity of care during emergencies and humanitarian settings.

The declaration establishes operational targets requiring at least 80% of countries to implement multisectoral integrated policies on NCDs and mental health by 2030, alongside surveillance and monitoring systems for tracking progress. Member states committed to transparent accountability mechanisms and regular reporting through Sustainable Development Goals review processes, with the Secretary-General requested to submit a progress report by the end of 2030 to inform the next high-level meeting in 2031. MEH

gether, by building stronger human bonds, we can create healthier societies," he said.

Youth diplomacy shapes health policy discourse

WFUNA Secretary-General Aziel Goulandris emphasised the broader implications of the declaration for global health systems. "This shows the power of youth diplomacy to shape healthier societies. Connection strengthens not only individuals but the global systems we rely on. The world cannot achieve health for all without social health for all," Goulandris noted.

The simulation addressed multiple health policy domains, including mental health, vaccine hesitancy, health and migration, digital health, and artificial intelligence. However, delegates consistently reinforced that mental and social health are interdependent, with inclusion, empathy, and participation serving as essential components of global health infrastructure alongside clinical interventions and technology.

The declaration concludes with a commitment to action: "By acting with empathy, courage, and intentionality, we can transform isolation into belonging, silence into conversation, and indifference into collective care." MEH

Bridging borders: How regional collaboration is advancing vNOTES

Dr. Wael Hosni: German Board-Certified Consultant Obstetrician & Gynecologist, Group Chief of Obstetrics & Gynecology at HMS Hospitals in Dubai, and Vice President of the Emirates Obstetrics & Gynecology Society. He has pioneered the clinical introduction of vNOTES in Germany, the UAE, and most recently Egypt.

The landscape of gynecologic surgery has undergone a profound transformation over the past three decades. What began as large abdominal incisions evolved into conventional laparoscopy, significantly reducing surgical trauma and accelerating patient recovery. Today, we stand at the threshold of the next paradigm shift: vaginal Natural Orifice Transluminal Endoscopic Surgery (vNOTES) – an advancement that merges laparoscopy with vaginal surgery to eliminate abdominal incisions entirely and combines the advantages of both procedures.

vNOTES allows access to the pelvic and abdominal cavities through the vagina using a specialized endoscopic port. The result is a procedure that is very precise and scarless. vNOTES combines the best features of both transvaginal and laparoscopic surgery, permitting women to undergo gynecologic procedures with the shortest recovery, the least amount of pain, and the most favorable cosmesis.

International experience and early adoption

The international expansion of vNOTES has been shaped by experts in the field of minimally invasive gynecologic surgery who adopted the technique early and helped refine its clinical application. Among them is Dr. Wael Hosni, a German board-certified gynecologic surgeon recognized for his expertise in minimally invasive surgery. Dr. Hosni was one of the first three surgeons in Germany to introduce vNOTES in the country and implement it into routine gynecologic practice in 2021.

After relocating from Europe to the United Arab Emirates, he became one of the first gynecologic surgeons to perform vNOTES in the region in 2022, broadening the minimally invasive surgical options available to patients.

In addition to his clinical work, he has lectured extensively at international congresses and has trained surgeons across Europe and the Middle East in adopting the scarless vNOTES technique.

Introducing vNOTES in Egypt: A national initiative

In November 2025, the Egyptian Society for Minimally Invasive Surgery (MISSE) invited Dr. Wael Hosni to introduce vNOTES to Egypt — a country with a rapidly evolving minimally invasive gynecology landscape and one of the highest academic surgical training outputs in the region.

The introduction of vNOTES in Egypt followed a structured, multistage implementation strategy designed to ensure safe adoption:

1. **Educational Webinar**
   More than 160 surgeons and experts from Egypt and the region attended a live online webinar that presented the evidence, clinical indications, perioperative management, surgical steps and patient benefits of vNOTES.
2. **Hands-On Workshop**
   A fully booked workshop provided practical training using specialized vNOTES simulators, with emphasis on instrument handling, anatomical orientation, and case selection.
3. **First Live Transmitted vNOTES Surgery**
   The workshop concluded with the first vNOTES surgery in Egypt, performed live by Dr. Wael Hosni and transmitted to all workshop participants, demonstrating the surgical steps in real time.

This stepwise model of education, simulation-based training, mentorship and live surgeries demonstrated success in providing a safe and scalable pathway for introducing vNOTES into new healthcare systems.

Collaboration and regional leadership

This milestone represents more than the introduction of a new surgical technique – it marks a significant collaboration between two leading professional bodies in women's health. The initiative was driven by the joint efforts of Dr. Wael Hosni, Vice President of the Emirates Obstetrics and Gynecology Society (EGOS), and Prof. Dr. Fady Moiety, President of the Egyptian Society for Minimally Invasive Surgery (MISSE). Their collaboration reflects a growing regional commitment to advancing minimally invasive gynecologic surgery and strengthening cross-border professional exchange. By aligning the expertise and resources of both societies, the project has established a model for regional cooperation and created momentum for future joint initiatives aimed at improving surgical excellence and women's health across the region.

The future of minimally invasive gynecologic surgery

The evolution of minimally invasive gynecologic surgery has progressed through distinct milestones. Conventional laparoscopy marked the first major shift away from open surgery, followed by the emergence of robotic-assisted surgery. Today, vNOTES represents the newest advancement in this continuum.

These milestones are not intended to replace one another; rather, they complement each other, expanding the spectrum of minimally invasive options and allowing surgeons to select the most appropriate approach for each individual patient.

The expansion of vNOTES signals a paradigm shift in the field of gynecologic surgery. With growing clinical evidence, increasing surgeon training, and strong regional collaboration, vNOTES is poised to become an integral part of minimally invasive gynecologic surgery. MEH

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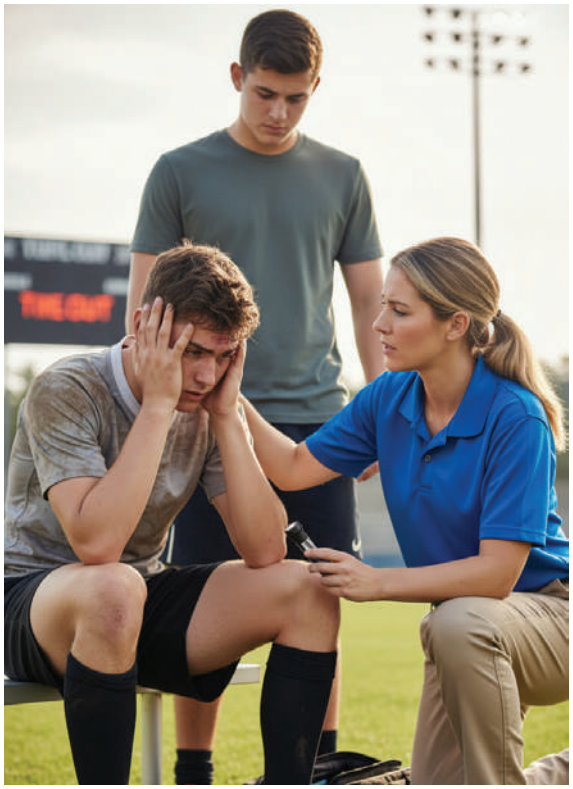
Adolescent concussion recovery reveals sex-specific blood biomarker differences

Researchers have identified significant sex-based differences in blood biomarker levels during adolescent concussion recovery, with females showing elevated tau proteins and distinct symptom-biomarker associations compared to males. The findings from the multi-site CARE4Kids study suggest hormonal and biological factors may influence neurological recovery trajectories in young people.



A comprehensive analysis of 305 adolescents aged 11 to 18 years has revealed that biological markers of brain injury behave differently in males and females during the subacute recovery period following concussion. The research, published in the *Journal of Head Trauma Rehabilitation*, examined plasma samples collected 7 to 35 days after injury alongside detailed symptom assessments, uncovering sex-specific patterns that could inform more personalised treatment approaches.

Higher tau levels in female adolescents

The study found that female adolescents demonstrated significantly higher levels of tau protein (mean 6.18 pg/mL versus 4.55 pg/mL in males) and lower phosphorylated tau to total tau ratios after adjusting for age, body mass index, and days post-injury. No significant sex differences emerged for other biomarkers including glial fibrillary acidic protein (GFAP), neurofilament light chain (NFL), or ubiquitin C-terminal hydrolase L1 (UCH-L1).

"This study highlights sex-specific biomarker differences during adolescent concussion recovery and the importance of understanding how sex differences may influence symptom burden and recovery trajectories," the authors stated in their conclusion.

The research team measured five established markers of neuronal and astrocytic injury: GFAP, NFL, UCH-L1, tau, and phosphorylated tau at threonine 181 (p-tau181). These proteins serve as objective indicators of brain tissue damage, inflammation, and ongoing repair processes following traumatic brain injury.

Distinct symptom-biomarker associations by sex

Perhaps more striking than the baseline differences were the divergent relationships between biomarker levels and post-concussion symptom severity in males and females. The study utilised the Post-Concussion Symptom Inventory, 2nd Edition (PCSI-2), which assesses symptoms across four domains: physical, emotional, cognitive, and fatigue.

In females, elevated levels of NFL and UCH-L1 were significantly associated with more severe emotional symptoms. However, in males, lower levels of these same biomarkers correlated with greater physical symptoms and overall symptom burden – a counterintuitive finding that challenges existing assumptions about biomarker interpretation.

Elevated p-tau181 levels were associated with increased cognitive symptoms in both sexes, though the relationship was stronger in males. The authors noted that these sex-specific patterns "suggest that sex may moderate the relationship between biomarkers and symptom burden in adolescents following concussion."

Hormonal influences on recovery

The research team proposed that the elevated tau concentrations and altered tau phosphorylation patterns in females may reflect bidirectional interactions between hormonal regulation and concussion pathology. Previous work has suggested that injury during the luteal phase of the menstrual cycle – when progesterone levels peak – is associated with poorer recovery outcomes in females.

"Our finding of higher tau concentrations and lower p-tau181/tau ratio in females may reflect a bidirectional relationship between hormonal regulation and concussion pathology," the authors explained. "Oestrogen and progesterone fluctuations across the menstrual cycle may influence tau phosphorylation, while brain injury may in turn affect endocrine function."

This interpretation aligns with prior research from the same team demonstrating distinct temporal patterns in circulating tau levels among young female athletes with concussion compared to their male counterparts.

Implications for clinical practice

The findings underscore the need for sex-stratified approaches to concussion assessment and management in adolescents. Female adolescents are already known to experience more severe post-concussion symptoms and recovery periods approximately 1.7 times longer than males, yet

current clinical assessments rely predominantly on subjective symptom reporting.

The study recruited participants from outpatient settings across multiple institutions participating in the Concussion Assessment, Research, and Education for Kids (CARE4Kids) consortium. All participants had sustained a concussion diagnosed according to Concussion in Sport Group criteria and reported at least one symptom exceeding their pre-injury baseline.

Future research directions

The authors acknowledged several limitations, including the wide biomarker collection window and incomplete menstrual status data. They emphasised the importance of future studies incorporating hormonal assays and pubertal staging to clarify how endocrine factors modulate neuroinflammation and recovery.

"Future research should examine hormonal influences on biomarker profiles and prolonged symptomatology," the authors concluded, adding that "expanding validated, sex-stratified paediatric reference ranges is also necessary to improve clinical interpretability."

The CARE4Kids study will continue to follow participants and collect biomarker measurements at three months post-injury, providing opportunities to track longitudinal changes and identify biological signatures associated with symptom resolution or persistence. MEH

Reference:

Pasini, M., Gioia, G., Rivara, F., et. al. (2025). Sex differences in subacute blood biomarker levels and associations with post-concussion symptom severity in adolescents with concussion. *Journal of Head Trauma Rehabilitation*, 40(6), 420–428. https://tinyurl.com/36kz7s8y

Breathing difficulty predicts sixfold mortality risk in hospital patients

A simple nursing assessment of patient-reported breathlessness during hospitalisation can identify those at dramatically elevated risk of death, with post-admission dyspnoea linked to a sixfold increase in mortality compared with patients reporting no breathing difficulty, according to research published in *ERJ Open Research*.

Researchers at Beth Israel Deaconess Medical Center conducted a retrospective cohort study of 9,785 consecutive hospital admissions between March 2014 and September 2016. The team analysed nursing assessments in which patients rated their breathing discomfort on a 0-to-10 scale at least once per shift throughout their hospital stay.

The investigation revealed that 18% of patients reported dyspnoea upon admission, whilst an additional 10% developed breathing difficulty after admission. Most strikingly, patients who developed dyspnoea after admission faced a 5.9% mortality rate during hospitalisation, compared with just 1% amongst those who never reported breathing difficulty.

"Dyspnoea is easy to measure, prevalent, distressing, and predictive of subsequent adverse outcomes," the authors wrote. "Ongoing periodic dyspnoea assessment is needed both for adequate symptom management and to predict risk."

Mortality risk extends beyond discharge

The predictive power of patient-reported dyspnoea extended well beyond the immediate hospital stay. Patients who reported breathing difficulty at any point during hospitalisation demonstrated 50% greater mortality during the following two years compared with those reporting no dyspnoea. This risk intensified for patients still experiencing breathlessness upon discharge, who faced a 2.6-fold increased risk of death within two years.

The study also revealed a quantitative relationship between dyspnoea severity and outcomes. Patients rating their worst breathlessness above 3 out of 10 during hospitalisation carried six times the risk of in-hospital death compared with those reporting no dyspnoea, and twice the risk compared with those experiencing milder symptoms.

"Documentation of patient-reported dyspnoea opens the possibility of individualised diagnostic and therapeutic actions," the researchers noted in their published findings.

Pain shows markedly different pattern

Whilst dyspnoea demonstrated robust mortality prediction, patient-reported pain told a different story. Although nearly three times as common as dyspnoea, with approximately three-quarters of patients reporting pain at some point during hospitalisation, pain showed no significant association with mortality either during admission or in the two years following discharge.

The researchers found that pain was associated with several adverse outcomes including intensive care transfer, rapid response team activation, and extended length of stay. However, its predictive value for mortality remained statistically insignificant even after adjusting for multiple comparisons.

Implementation requires minimal resources

The practical implications of the research are particularly noteworthy given the minimal burden of dyspnoea assessment. Nurses reported that documenting patient breathlessness required less than one minute per patient and did not increase their overall workload. The assessment takes place whilst patients are ordinarily seated or recumbent, using a simple numerical rating scale anchored by "unbearable" at 10 and featuring intermediate descriptors of mild, moderate, and severe positioned according to validated word scaling data.

Physiological integration versus localised injury

The authors proposed that dyspnoea's

superior predictive power stems from its integration of information from multiple interoceptors monitoring cardiopulmonary gas exchange mechanisms throughout the body. This richness of physiological information compensates for any variability in patient perception and reporting.

In contrast, pain typically signals localised injury to skin, muscle, or bone rather than systemic threats to vital organ systems. The study's pain data did not distinguish between somatic and visceral pain, potentially masking relationships that might emerge with more granular categorisation.

Clinical applications and future directions

The findings suggest several potential clinical applications, including using dyspnoea explicitly as a trigger for rapid response teams, as a criterion for enhanced monitoring or telemetry, and as an indicator for discharge planning and goals-of-care discussions. The data particularly highlight concern for patients discharged whilst still reporting breathlessness, who experienced much of their elevated mortality risk within the first 150 days post-discharge.

The researchers acknowledged limitations including the single-centre setting and potential inconsistencies in assessment methodology. They suggested that electronic collection with standardised queries might strengthen the associations between dyspnoea and adverse outcomes even further. MEH

Reference:

Stevens, J. P., Schwartzstein, R. M., Sheridan, A. R., O'Donnell, C. R., Baker, K. M., & Banzett, R. B. (2025). Patient-reported dyspnoea predicts 6-fold hospital mortality. *ERJ Open Research*, in press. https://doi.org/10.1183/23120541.00804-2025

Mussel-inspired adhesive sponge offers rapid control of internal bleeding

South Korean researchers have developed a bioabsorbable composite haemostatic sponge that combines mussel adhesive protein with decellularised extracellular matrix to halt internal organ bleeding. The material addresses critical limitations in current haemostatic agents by providing strong tissue adhesion whilst naturally degrading in the body.

Uncontrolled intraoperative bleeding from solid organ injuries remains a significant cause of perioperative mortality. Injuries to the liver or spleen present particular challenges due to the difficulty of achieving haemostasis in visceral tissues. Existing haemostatic agents frequently demonstrate inadequate adhesion to bleeding sites or persist in tissues without degradation, potentially leading to secondary complications.

A composite approach to haemostasis

Researchers at Pohang University of Science and Technology (POSTECH) have addressed these limitations by developing a composite sponge that integrates mussel adhesive protein with decellularised extracellular matrix (dECM). The material exhibits dual functionality: immediate mechanical haemostasis through blood absorption and tissue adhesion, followed by biological wound support through controlled degradation.

When applied to a bleeding site, the sponge rapidly absorbs blood whilst adhering firmly to tissues through the mussel adhesive protein component. Following haemostatic achievement, the material undergoes natural biodegradation and absorption, exposing the dECM component which supports tissue regeneration. The dECM activates intrinsic coagulation pathways, accelerating clot formation and promoting wound stabilisation.

Performance in anticoagulated models

The research team evaluated the sponge's efficacy in a warfarin-treated liver injury model, which simulates clinically relevant anticoagulation scenarios. The material demonstrated strong adhesion to injured tissue surfaces and achieved significant reductions in both bleeding time and total blood loss compared to conventional haemostatic materials.

Histological analysis revealed that the composite sponge induced minimal inflammatory response and tissue damage whilst promoting enhanced wound stabilisation during early healing phases. These properties suggest potential advantages in reducing postoperative complications and supporting faster recovery.

"This composite sponge can stop bleeding quickly and safely even in severe internal injuries that were previously difficult to control," said Professor Hyung Joon Cha of POSTECH, who led the study. "By reducing the need for additional surgeries and supporting faster recovery, it has the potential to greatly improve patient care."

Clinical implications

The development addresses two fundamental challenges in surgical haemostasis: achieving adequate tissue adhesion in the presence of active bleeding, and ensuring complete material resorption without chronic foreign body response. The combination of immediate mechanical haemostasis with biological wound support through controlled degradation represents a potentially significant advancement in managing internal organ bleeding.

The research, published in Advanced Healthcare Materials on 14 October 2025, was led by Professor Hyung Joon Cha (Department of Chemical Engineering, POSTECH) and Professor Jinah Jang (Department of Mechanical Engineering and Convergence IT Engineering, POSTECH), with graduate student Hyegyo Cha. The work received support from the National Research Foundation of Korea (Ministry of Science and ICT) and the Alchemist Project (Ministry of Trade, Industry and Energy). MEH

Reference:

Cha, H., Jang, J., Cha, H. J. et. al. (2025). Absorbable adhesive composite hemostatic sponge based on decellularized extracellular matrix and mussel adhesive protein for internal bleeding control. *Advanced Healthcare Materials*. https://doi.org/10.1002/adhm.202502994

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Baxter: Innovating for impact across the Middle East, Türkiye & Africa (META) region

How Baxter is redefining healthcare delivery through connected care, leadership, and sustainability

In today's dynamic healthcare landscape, innovation is no longer a luxury, it's a necessity. Baxter, a global leader in medical technology, is embracing this reality with a bold transformation that is reshaping patient care across the Middle East, Türkiye, and Africa (META). With a legacy of over 90 years, Baxter's mission to save and sustain lives is being reimagined through cutting-edge technologies, strategic partnerships, and a deep commitment to regional healthcare development.

At the core of Baxter's innovation strategy is its shift toward connected care. Baxter is bringing devices, systems, and data together to enable the very best care – across hospital, outpatient, home, and pharmacy settings. Its connected solutions, such as smart infusion platforms, vital signs monitors, and infection surveillance tools, are designed to reduce manual charting, deliver timely safety alerts, and connect broader care teams via mobile apps. These technologies are helping healthcare providers streamline workflows, improve patient safety, and reduce cognitive overload among clinicians – an increasingly urgent challenge as burnout and staffing shortages rise globally.

In the META region, Baxter's impact is amplified through partnership. The company's joint initiatives with ministries of health and local stakeholders align with national healthcare visions, such as Saudi Arabia's Vision 2030. These efforts include clinical training, medical education, and community outreach programs that build local capacity and improve patient outcomes. As part of its commitment to shaping the future of healthcare, Baxter actively participates in strategic conferences across the region, including the Global Health Exhibition in Saudi Arabia last October – an influential platform that brings together global leaders to drive innovation, investment, and transformation in healthcare.

Baxter's culture is built on purpose-driven leadership, innovation, and a deep commitment to our mission of saving and sustaining lives. In the META region, this is reflected in how Baxter operates – with agility, integrity, and a focus on high-growth segments such as clinical nutrition, advanced surgery, and connected care that address the region's evolving healthcare needs.

Wafic Faraj, General Manager, Baxter Middle East Türkiye & Africa

"At Baxter, we are proud to touch the lives of millions of people worldwide every day. Our culture is rooted in collaboration, responsibility, and innovation. In the META region, our operations are focused on delivering integrated care solutions – from pharmaceutical products and medical devices to capital equipment – across the entire continuum of care. This diversified portfolio allows us to meet the needs of patients and providers with precision and purpose," says Wafic Faraj, General Manager, Baxter Middle East Türkiye & Africa

This leadership commitment is also reflected in Baxter's corporate responsibility strategy, which is grounded in ethics, inclusion, sustainability, and community investment. One of the most impactful partnerships in the META region is that between the Baxter International Foundation and UNICEF, aimed at expanding access to safe water in Egypt. This initiative reflects a shared commitment to advancing health and well-being in one of the region's most vulnerable populations.

In essence, Baxter's journey in the META region is a compelling story of innovation with purpose. The company is not just introducing new technologies, it's building ecosystems of care that are smarter, more inclusive, and more resilient. As healthcare systems across the region continue to evolve, Baxter's role as a trusted partner and innovator will be instrumental in shaping a healthier future.

For healthcare professionals, policymakers, and industry leaders, Baxter's model offers a blueprint for how global expertise can be localized to meet regional needs. It's a reminder that meaningful innovation is not just about what's new, it's about what works, where it matters most.

- For more information, visit: *www.baxter.com* MEH

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GBU-PH88-250001 (v1.0) 07/2025

New obesity treatment framework prioritises GLP-1 medications as first-line therapy

The European Association for the Study of Obesity has released comprehensive guidance positioning semaglutide and tirzepatide as primary treatments for obesity and most complications. The framework, published in *Nature Medicine*, represents a paradigm shift towards complication-focused prescribing rather than weight loss alone, with recommendations based on systematic meta-analysis of randomised controlled trials.

An international team of obesity experts has developed the first treatment algorithm that uses the presence or absence of obesity-related complications as the primary factor guiding medication selection, marking a fundamental shift in how clinicians approach pharmacological obesity management.

The framework, published in *Nature Medicine* on 2 October 2025, establishes semaglutide and tirzepatide – both incretin-based therapies – as first-line treatments for nearly all obesity presentations, reflecting their superior efficacy compared to existing alternatives.

"Even though there are several options on the market, the reality is that semaglutide and tirzepatide are so effective that they should be the first choice in almost all cases," says co-first author Dr Andreea Ciudin from Vall d'Hebron University Hospital, Barcelona.

The guidance comes at a critical juncture as the number of obesity medications continues to expand, offering clinicians an increasingly complex array of therapeutic options with distinct mechanisms of action. The authors developed their algorithm through systematic review and network meta-analysis of randomised controlled trials, incorporating evidence published up to 31 January 2025.

Complication-centred approach transforms prescribing strategy

The treatment algorithm diverges from traditional weight-loss-focused frameworks by categorising obesity-related complications into two distinct disease subtypes: "fat mass disease", characterised by altered mechanical forces, and "sick fat disease", involving dysregulated metabolic, endocrine, inflammatory and immune responses.

"It is the first framework guided by the presence or absence of obesity-related complications, since weight loss is not the only goal of treatment when complications are present," explains Professor Barbara McGowan from Guy's and St Thomas's Hospital NHS Foundation Trust, London, who co-led the research alongside Dr Ciudin and EASO President Professor Volkan Yumuk.

For patients without established complications, where weight reduction remains the primary objective, the meta-analysis demonstrated clear hierarchies in medication efficacy. Both tirzepatide and semaglutide achieved total weight loss exceeding 10% versus placebo at endpoint, with tirzepatide showing the highest efficacy at 16.5% total body weight loss. By comparison, phentermine-topiramate achieved 8.8%, liraglutide 4.2%, naltrexone-bupropion 4.8%, and orlistat 3.0%.

The authors note in their publication that "tirzepatide and semaglutide should be considered the medications of choice when a substantial total body weight loss is required. When a lesser degree of weight loss is the target, other medications can be considered, including liraglutide, naltrexone-bupropion, and phentermine-topiramate."

Evidence base supports targeted complication management

The systematic analysis examined specific obesity-related complications across multiple organ systems, with medications evaluated based on demonstrated improvement or remission of these conditions rather than weight loss alone.

For obstructive sleep apnoea, classified as a fat mass disease, tirzepatide emerged as the sole first-line recommendation, though the authors acknowledge this rests on a single randomised controlled trial. The medication demonstrated significant OSAS remission with an odds ratio of 2.9 and clinically meaningful reductions in the apnoea-hypopnea index.

In knee osteoarthritis, another mechanical complication, semaglutide showed superior pain reduction compared to liraglutide, with a weighted mean difference of -8.6 points on validated pain scales. This evidence positions semaglutide as first-line therapy for patients with obesity and symptomatic knee osteoarthritis.

Among sick fat diseases, the metabolic and cardiovascular complications showed particularly robust evidence favouring incretin-based therapies. For prediabetes and type 2 diabetes, tirzepatide achieved diabetes remission with an odds ratio of 15.6, followed by semaglutide at 12.3 and liraglutide at 6.8. All three medications also demonstrated significant effects on normoglycaemia restoration in prediabetic patients, with semaglutide showing an odds ratio of 19.6.

Cardiovascular protection emerges as key differentiator

The meta-analysis revealed particularly compelling cardiovascular outcome data for semaglutide. In patients with established cardiovascular disease, semaglutide reduced major adverse cardiovascular events with an odds ratio of 0.78, establishing it as the recommended first-line agent for this population. Naltrexone-bupropion, despite cardiovascular safety data availability, showed no significant cardiovascular benefits with an odds ratio of 0.88.

For heart failure, both tirzepatide and semaglutide demonstrated reductions in hospitalisation risk, with odds ratios of 0.45 and 0.23 respectively. The authors note that evidence encompasses both preserved and reduced ejection fraction phenotypes, though they caution that "data collected are, however, still insufficient to provide individual recommendations for these two distinct conditions."

Liver disease treatment shows developing evidence

In metabolic dysfunction-associated steatohepatitis (MASH), tirzepatide currently holds the strongest evidence base for MASH remission, with an odds ratio of 11.8 versus 2.0 for semaglutide in trials published before the evidence cut-off date. However, the authors acknowledge an important caveat: the phase 3 ESSENCE trial, published after 31 January 2025, demonstrated that semaglutide achieved significant improvements in MASH and liver fibrosis comparable to tirzepatide.

"Notably, the phase 3 ESSENCE trial, not included in the present algorithm because it was published after 31 January 2025, showed that semaglutide was associated with a significant improvement in MASH and liver fibrosis similar to tirzepatide," the authors note in their paper, indicating that future algorithm updates will likely recommend semaglutide as co-first-line therapy for Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD).

Implementation challenges and economic considerations

The guidance acknowledges substantial economic barriers to implementation, particularly concerning the high costs of tirzepatide and semaglutide. However, the authors argue for a broader perspective on healthcare economics.

"The cost of not treating obesity and adipose tissue dysfunction at early stages – thus enabling the progression to complications and end-organ damage – should be weighed equally in health policy and clinical decision-making," the research team emphasises.

Recent health policy initiatives, including caps on out-of-pocket payments and government price negotiations, represent evolving efforts to improve medication affordability, though access remains inconsistent across healthcare systems.

Personalised medicine and clinical judgment remain essential

Despite the algorithm's evidence-based framework, the authors stress that clinical decision-making must extend beyond protocol adherence to encompass individualised patient assessment.

"Tailoring treatment to the individual is a complex task that must consider several factors, including the severity of adiposity, the presence and extent of complications, comorbidities and concurrent therapies. Socioeconomic context, patient values, expectations, and personal goals must also be considered," says Professor McGowan.

Dr Ciudin adds: "Although no treatment algorithm can replace the nuanced clinical judgment required for such comprehensive assessments, this tool can serve to support therapeutic decision-making in obesity."

The framework identifies significant evidence gaps, noting that most medications have not undergone specific evaluation for individual complications. The authors highlight growing potential for obesity medications to influence conditions including chronic kidney disease, neurodegenerative disorders, polycystic ovary syndrome, certain cancers, and mental health conditions, though direct evidence remains limited.

Implications for clinical practice and future research

The algorithm's publication signals a maturation of obesity pharmacotherapy, moving from broad weight-loss approaches towards precision medicine targeting specific pathophysiological mechanisms. The conceptual framework distinguishing fat mass disease from sick fat disease may influence future drug development priorities and clinical trial design.

"This new class of GLP-1 agonists and GIP/GLP-1 dual agonists is completely transforming care of obesity and its complications," Dr Ciudin says.

Professor Yumuk emphasises the dynamic nature of the guidance: "Given the rapid advances in the field of medications to treat obesity, EASO intends to update the present treatment algorithm regularly to incorporate the latest available evidence."

The framework's limitation to BMI ranges of 27-40 kg/m² reflects current evidence constraints, with minimal data available for patients with BMI exceeding 40 kg/m² and no data supporting medication use below 27 kg/m². This highlights priorities for future research as obesity medication indications potentially expand.

Long-term safety data remain incomplete for newer agents, particularly regarding rare serious adverse events including certain malignancies. Ongoing pharmacovigilance and extended follow-up studies will prove essential for comprehensive risk-benefit assessment as these medications achieve widespread clinical adoption.

The publication establishes a new standard for evidence-based obesity treatment decision-making, whilst acknowledging that optimal patient outcomes require integration of algorithmic guidance with individualised clinical assessment and shared decision-making. MEH

Reference:

McGowan, B., Ciudin, A., Baker, J. L., et. al. (2025). Framework for the pharmacological treatment of obesity and its complications from the European Association for the Study of Obesity (EASO). *Nature Medicine*, 31, 3229–3232. *https://doi.org/10.1038/s41591-025-03765-w*

Taming the twin epidemics: Obesity and diabetes – how Imperial College London Diabetes & Endocrine Centre leads with innovation and access

The prevalence of obesity continues to surge across the world and in the region, with consequent increases in type 2 diabetes, cardiovascular disease, and metabolic complications. For physicians and health systems, the question is no longer if to intervene – but how to deliver safe, effective, and sustainable obesity care that reduces diabetes burden.

At Imperial College London Diabetes & Endocrine Centre, we believe obesity is a treatable chronic disease. Our mission is to provide evidence-based, patient-centred management, combining lifestyle, behavioural support, cutting-edge pharmacotherapy, and seamless integration into regional reimbursement frameworks. The result: better glucose control, weight loss, and long-term metabolic health.

The role of modern obesity medications

In recent years, glucagon-like peptide-1 (GLP-1) receptor agonists, and combination therapies (e.g. GLP-1 plus complementary agents), have revolutionised obesity care. These medications help reduce appetite, slow gastric emptying, and improve insulin sensitivity – offering sustained weight loss beyond what lifestyle changes alone typically achieve. In randomised trials, many patients lose 10–15 % (or more) of baseline weight, with corresponding reductions in HbA_1c, blood pressure, and lipid abnormalities.

However, the real-world effectiveness depends on proper patient selection, monitoring, dose titration, and integration with nutrition, exercise, and behavioural support. That is why a multidisciplinary obesity pathway is essential – not just prescribing a drug and hoping for the best.

Landmark policy increases access to care

In Abu Dhabi, a landmark policy now allows Thiqa insurance coverage for obesity medications (OMM: obesity management medications) in eligible patients. Under the policy, adult patients with BMI ≥ 30 (with one or more comorbidities) may qualify for reimbursement of GLP-1 agonists or other pharmacotherapies – provided they follow the standard non-surgical management pathway.

This is a transformative shift: it lowers financial barriers and opens access for nationals to best-practice obesity care within the public health framework.

The Thiqa Obesity / Personalised Weight Management Programme

To fully leverage this coverage, Abu Dhabi's Department of Health (DoH) and the Abu Dhabi Public Health Centre (ADPHC) have recently launched a Personalised Weight Management Programme for eligible Thiqa members (age ≥ 18) diagnosed as overweight or obese. This is the first programme of its kind in the region.

Key features include:

- Holistic 360° care: Initial screening (BMI, metabolic assessments), structured behavioural and lifestyle coaching, psychological support, and medical interventions when indicated.
- Digital monitoring and accountability: Participants track progress with mobile tools (such as the 'Sahatna' app) to monitor daily activity, weight trends, sleep, stress, and more.
- Reimbursement incentive model: Reimbursement is tied to sustained participation and goal attainment, encouraging adherence.
- Flexible duration: Begins with a structured 16-week core phase but extends beyond a year for individuals needing longer-term support.

For Thiqa cardholders, access to medically indicated obesity medications under the programme is a powerful enabler – it bridges the gap between lifestyle efforts and metabolic risk control.

Real impact on diabetes outcomes

Weight loss of 5–10 % is well known to produce meaningful reductions in HbA_1c, insulin resistance, and even induce remission in early-stage type 2 diabetes. When paired with GLP-1–based therapies, the glycaemic benefits are magnified.

> This is a transformative shift: it lowers financial barriers and opens access for nationals to best-practice obesity care within the public health framework.

At Imperial College London Diabetes & Endocrine Centre, patients on integrated care and pharmacotherapy routinely achieve sustainable weight loss alongside improved blood glucose control, reduced cardiovascular risk, and enhanced overall wellbeing. Many are able to reduce or even discontinue glucose-lowering medications within months, maintaining results over time.

By positioning obesity as a therapeutic target rather than a lifestyle choice, Imperial College London Diabetes & Endocrine Centre enables individuals to achieve transformative outcomes – reducing diabetes complications and improving long-term health across the UAE and beyond.

About Imperial College London Diabetes & Endocrine Centre

Established in 2006 by Mubadala Investment Company in partnership with Imperial College London, the Centre has been a trusted leader in diabetes and endocrine care for nearly two decades. With over 70 specialised professionals across four branches in Abu Dhabi, Al Dhafra, and Al Ain, the Centre provides world-class care, research, and education to over one million people.

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Breakthrough: Scientists find blood mutations drive obesity and metabolic disease in causal relationship

Researchers have identified a bidirectional causal relationship between clonal hematopoiesis driven by DNMT3A mutations and metabolic disorders. The study, published in the *Journal of Clinical Investigation* on 30 September 2025, demonstrates that blood stem cell mutations actively promote obesity, type 2 diabetes and metabolic dysfunction-associated steatotic liver disease, rather than merely arising as a consequence of poor metabolic health.

University of Florida Health Cancer Center investigators have challenged the prevailing paradigm regarding the relationship between age-related blood cell mutations and metabolic disease. Their findings suggest that clonal haematopoiesis, a condition affecting approximately 10% of older adults, may represent an underappreciated driver of chronic metabolic disorders rather than simply a consequence of obesity and inflammation.

Reversing the causality paradigm

"Most people don't think about the blood as causing obesity and related diseases, but our surprising findings highlight that there's a causal relationship between mutations in blood stem cells and metabolic diseases," said lead author Bowen Yan, Ph.D., a research assistant professor in the Department of Pharmacology and Therapeutics at the University of Florida College of Medicine.

The research team, led by senior author Olga Guryanova, Ph.D., employed a sophisticated bone marrow transplantation model to investigate the specific impact of DNMT3A mutations on metabolic health. DNMT3A, encoding DNA methyltransferase 3A, represents the most frequently mutated gene in clonal haematopoiesis, yet the distinct functional consequences of different mutation types had remained incompletely characterised.

Epidemiological foundation

The investigators initiated their study with meta-analysis across non-obese individuals from the UK Biobank and All of Us cohorts, identifying an association between clonal haematopoiesis and incident obesity risk. For DNMT3A-associated clonal haematopoiesis specifically, the hazard ratio for developing obesity was 1.14 (95% CI 1.01-1.27), providing epidemiological support for a potential causal relationship.

Previous epidemiological studies had established associations between clonal haematopoiesis, particularly driven by TET2 loss, and conditions including overweight, type 2 diabetes and chronic liver disease. However, these observational data could not definitively establish causality or distinguish whether clonal haematopoiesis represented a cause or consequence of metabolic dysfunction.

Experimental model design

To address this mechanistic gap, the research team created chimeric mice with 20% of haematopoietic cells carrying either Dnmt3a heterozygous loss-of-function (Dnmt3a+/-) mutations, Dnmt3a+/R878H mutations (equivalent to the human Arg882His variant), or wild-type control cells. The remaining 80% comprised wild-type support cells, mimicking a clinically meaningful large clonal haematopoiesis clone observed in human patients.

Eight weeks post-transplantation, following haematopoietic reconstitution and engraftment confirmation, mice were randomised to either high-fat, high-glucose "Western" diet or normal chow. This experimental design enabled the investigators to isolate the specific contribution of DNMT3A mutations to metabolic phenotypes whilst controlling for genetic background and environmental factors.

Differential mutation effects on obesity

The study revealed striking differences between loss-of-function and Arg882His mutations. Control mice harbouring Dnmt3a+/- haematopoietic cells exhibited 1.7-fold faster body weight gain compared to wild-type controls ($p<0.001$), accompanied by moderately increased food intake and subcutaneous white adipocyte hypertrophy. The Dnmt3a+/R878H mice displayed an intermediate phenotype between wild-type and loss-of-function groups.

High-fat diet exposure accentuated these differences dramatically. Mice with Dnmt3a+/- clonal haematopoiesis progressed to overweight and obese states earlier than wild-type controls. After six weeks of high-fat diet feeding, these animals exhibited significantly elevated plasma leptin ($p=0.011$) and resistin levels ($p=0.048$), consistent with increased adiposity and metabolic dysfunction.

Notably, even without dietary challenge, plasma leptin demonstrated mild elevation in both Dnmt3a+/- and Dnmt3a+/R878H clonal haematopoiesis animals six months post-transplantation. The authors noted this finding "suggesting a direct obesogenic effect of Dnmt3a-CH," independent of dietary factors.

Glucose metabolism impairment

The metabolic consequences extended beyond adiposity. Mice maintained on high-fat diet displayed impaired glucose metabolism characterised by elevated fasting blood glucose and insulin levels, alongside compromised glucose tolerance. The glucose dysregulation proved particularly severe in the Dnmt3a+/- cohort.

On normal chow, almost half of Dnmt3a+/- clonal haematopoiesis mice achieved pre-diabetic fasting glucose levels seven months post-transplantation, despite maintaining normal plasma insulin concentrations and glucose tolerance. These observations indicated progressive beta-cell dysfunction and insulin resistance developing even under standard dietary conditions.

Inflammatory mechanisms

The mechanistic basis for these metabolic phenotypes appeared rooted in altered

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Selected Safety Information: Lansulin 100 units/ml solution for injection in a pre-filled pen (insulin glargine): Indications: Treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above. **Posology and method of administration:** Lansulin contains insulin glargine, an insulin analogue, and has a prolonged duration of action. Lansulin should be administered once daily at any time but at the same time each day. The dose regimen should be individually adjusted. **Special warnings and precautions:** •Traceability: the name and the batch number of the administered product should be clearly recorded. • Insulin glargine is not the insulin of choice for the treatment of diabetic ketoacidosis. Instead, regular insulin administered intravenously is recommended. •In case of insufficient glucose control or a tendency to hyper- or hypoglycaemic episodes, the patient's adherence to the prescribed treatment regimen, injection sites and proper injection technique and all other relevant factors must be reviewed before dose adjustment is considered. • Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand, type, origin and/or method of manufacture may result in the need for a change in dose. •Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered. **Hypoglycaemia:** The time of occurrence of hypoglycaemia depends on the action profile of the insulins used and may, therefore, change when the treatment regimen is changed. Due to more sustained basal insulin supply with insulin glargine, less nocturnal but more early morning hypoglycaemia can be expected. Particular caution should be exercised, and intensified blood glucose monitoring is advisable in patients in whom hypoglycaemic episodes might be of particular clinical relevance. Patients should be aware of circumstances where warning symptoms of hypoglycaemia are diminished. The warning symptoms of hypoglycaemia may be changed, be less pronounced or be absent in certain risk groups. Such situations may result in severe hypoglycaemia prior to the patient's awareness of hypoglycaemia. The prolonged effect of subcutaneous insulin glargine may delay recovery from hypoglycaemia. If normal or decreased values for glycated haemoglobin are noted, the possibility of recurrent, unrecognised (especially nocturnal) episodes of hypoglycaemia must be considered. Adherence of the patient to the dose and dietary regimen, correct insulin administration and awareness of hypoglycaemia symptoms are essential to reduce the risk of hypoglycaemia. Factors increasing the susceptibility to hypoglycaemia require particularly close monitoring and may necessitate dose adjustments. Intercurrent illness: requires intensified metabolic monitoring. In many cases urine tests for ketones are indicated, and often it is necessary to adjust the insulin dose. Patients with type 1 diabetes must continue to consume at least a small amount of carbohydrates on a regular basis, even if they are able to eat only little or no food, or are vomiting etc. and they must never omit insulin entirely. Insulin antibodies: the presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia. Medication errors: have been reported in which other insulins, particularly short-acting insulins, have been accidentally administered instead of insulin glargine. Insulin label must always be checked before each injection to avoid medication errors between insulin glargine and other insulins. Combination of insulin glargine with pioglitazone: patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. Contraindications: Hypersensitivity to the active substance or to any of the excipients. Undesirable Effects: Hypoglycaemia.

Selected Safety Information: InsuRapid®100 units/ml solution for injection in a pre-filled pen (insulin aspart): Indications: treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above. **Posology and method of administration:** The potency of insulin analogues, including Insulin aspart, is expressed in units, whereas the potency of human insulin is expressed in international units. InsuRapid dosing is individual and determined in accordance with the needs of the patient. It should normally be used in combination with intermediate-acting or long-acting insulin. InsuRapid can also be used if intravenous administration of insulin aspart, by physicians or other healthcare staff, is applicable. When injected subcutaneously (sc) into the abdominal wall, the onset of action will occur within 10– 20 minutes of injection. The maximum effect is exerted 1-3 hours after the injection. The duration of action is 3-5 hours. **Special warnings and precautions:** Before travelling between different time zones, the patient should seek the doctor's advice since this may mean that the patient has to take the insulin and meals at different times. **Hyperglycaemia:** Inadequate dosing or discontinuation of treatment may lead to hyperglycaemia and diabetic ketoacidosis. Usually the symptoms include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as diabetic ketoacidosis, which is potentially lethal. **Hypoglycaemia:** Omission of a meal or unplanned, strenuous physical exercise may lead to hypoglycaemia. Care should be taken to match insulin doses with food intake, physical activities and current blood glucose level in order to minimise the risk. Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement. In case of hypoglycaemia or if hypoglycaemia is suspected Insulin Aspart must not be injected. After stabilisation of patient's blood glucose adjustment of the dose should be considered. Patients whose blood glucose control is greatly improved may experience a change in their usual warning symptoms of hypoglycaemia, and should be advised accordingly. Usual warning symptoms may disappear in patients with longstanding diabetes. A consequence of the pharmacodynamics of rapid-acting insulin analogues is that if hypoglycaemia occurs, it may occur earlier after an injection when compared with soluble human insulin. Since insulin aspart should be administered in immediate relation to a meal, the rapid onset of action should be considered in patients with concomitant diseases or treatment where a delayed absorption of food might be expected. Concomitant illness usually increases the patient's insulin requirements. Concomitant diseases in the kidney, liver or affecting the adrenal, pituitary or thyroid gland can require changes in the insulin dose. When patients are transferred between different types of insulin medicinal products, the early warning symptoms of hypoglycaemia may change or become less pronounced than those experienced with their previous insulin. **Transfer from other insulin medicinal products:** should be done under strict medical supervision. Changes in strength, brand, type, origin and/or method of manufacture may result in the need for a change in dose. Patients transferred to insulin aspart from another type of insulin may require an increased number of daily injections or a change in dose from that used with their usual insulin medicinal products. If an adjustment is needed, it may occur with the first dose or during the first few weeks or months. **Injection site reactions:** may occur and include pain, redness, hives, inflammation, bruising, swelling and itching. Continuous rotation of the injection site within a given area reduces the risk of developing these reactions. Reactions usually resolve in a few days to a few weeks. On rare occasions, injection site reactions may require discontinuation of insulin aspart. **Skin and subcutaneous tissue disorders:** Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. **Combination of insulin aspart with pioglitazone:** If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs.

Selected Safety Information: InsuMix 100 units/ml suspension for injection in a pre-filled pen (30% soluble insulin aspart and 70% insulin aspart crystallised with protamine): Indications: treatment of diabetes mellitus in adults, adolescents and children aged 10 years and above. Posology and method of administration: InsuMix dosing is individual and determined in accordance with the needs of the patient. Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control. In patients with type 2 diabetes, InsuMix can be given as monotherapy. InsuMix can also be given in combination with oral antidiabetic medicinal products and/or GLP-1 receptor agonists. Special warnings and precautions: Insulin aspart must not be administered intravenously, as it may result in severe hypoglycaemia. Intramuscular administration should be avoided. Insulin aspart is not to be used in insulin infusion pumps. Before travelling between different time zones, the patient should seek the doctor's advice since this may mean that the patient has to take the insulin and meals at different times. Hyperglycaemia: Inadequate dosing or discontinuation of treatment, especially in type 1 diabetes, may lead to hyperglycaemia and diabetic ketoacidosis. Usually, the first symptoms of hyperglycaemia develop gradually over a period of hours or days. They include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, loss of appetite as well as acetone odour of breath. In type 1 diabetes, untreated hyperglycaemic events eventually lead to diabetic ketoacidosis, which is potentially lethal. Hypoglycaemia: Omission of a meal or unplanned, strenuous physical exercise may lead to hypoglycaemia. Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement. In case of hypoglycaemia or if hypoglycaemia is suspected, insulin aspart must not be injected. After stabilisation of the patient's blood glucose, adjustment of the dose should be considered. Compared with biphasic human insulin, insulin aspart may have a more pronounced glucose lowering effect up to 6 hours after injection. This may have to be compensated for in the individual patient through adjustment of insulin dose and/or food intake. Patients whose blood glucose control is greatly improved, e.g. by intensified insulin therapy, may experience a change in their usual warning symptoms of hypoglycaemia and should be advised accordingly. Usual warning symptoms may disappear in patients with longstanding diabetes. Tighter control of glucose levels can increase the potential for hypoglycaemic episodes and therefore require special attention during dose intensification. Since insulin aspart should be administered in immediate relation to a meal, the rapid onset of action should be considered in patients with concomitant diseases or treatment where a delayed absorption of food might be expected. Concomitant illness, especially infections and feverish conditions, usually increases the patient's insulin requirements. Concomitant diseases in the kidney, liver or affecting the adrenal, pituitary or thyroid gland can require changes in the insulin dose. When patients are transferred between different types of insulin medicinal products, the early warning symptoms of hypoglycaemia may change or become less pronounced than those experienced with their previous insulin. Transfer from other insulin medicinal products: Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type, origin (animal insulin, human insulin or insulin analogue) and/or method of manufacture (recombinant DNA versus animal source insulin) may result in the need for a change in dose. Patients transferred to insulin aspart from another type of insulin may require an increased number of daily injections or a change in dose from that used with their usual insulin medicinal products. If an adjustment is needed, it may occur with the first dose or during the first few weeks or months. Injection site reactions: As with any insulin therapy, injection site reactions may occur and include pain, redness, hives, inflammation, bruising, swelling and itching. Continuous rotation of the injection site within a given area reduces the risk of developing these reactions. Reactions usually resolve in a few days to a few weeks. On rare occasions, injection site reactions may require discontinuation of insulin aspart. Skin and subcutaneous tissue disorders: Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site from an affected to an unaffected area, and dose adjustment of antidiabetic medications may be considered. Combination of insulin aspart with pioglitazone: Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind if treatment with the combination of pioglitazone and insulin aspart is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. Avoidance of accidental mix-ups/medication errors: Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between insulin aspart and other insulin products. Insulin antibodies: Insulin administration may cause insulin antibodies to form. In rare cases, the presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia. Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Contraindications:. Hypersensitivity to the active substance or to any of the excipients. Undesirable Effects: Hypoglycaemia.

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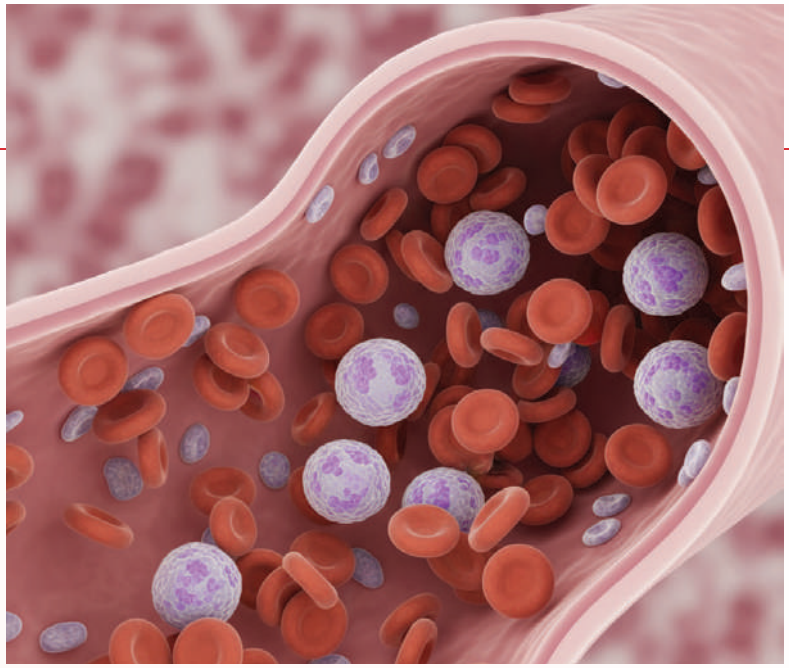

myelopoiesis and inflammatory responses. Dnmt3a+/- clonal haematopoiesis mice demonstrated increased abundance of donor-derived inflammatory monocytes in spleens and peripheral blood compared to wild-type competitor cells within the same recipient, with the most pronounced differences observed under high-fat diet conditions. The Dnmt3a+/R878H group exhibited an intermediate phenotype.

Following 10 weeks of high-fat diet exposure, Dnmt3a+/- clonal haematopoiesis mice displayed elevated inflammation-related cytokines including MIP-1α, CXCL1, IL-1α and IL-15, although classical pro-inflammatory mediators IL-1α and IL-6 showed less perturbation. This suggests a distinctive inflammatory signature associated with DNMT3A loss-of-function mutations.

Hepatic manifestations

The meta-inflammatory state manifested prominently in hepatic tissue. Even on normal chow, both Dnmt3a mutation groups exhibited greater lobular hepatic inflammation with prominent immune infiltration compared to wild-type controls. The Dnmt3a+/- clonal haematopoiesis animals specifically developed metabolic dysfunction-associated steatotic liver disease characterised by enlarged and numerous macrovesicular fat droplets.

Under high-fat diet conditions, the Dnmt3a+/- cohort progressed to severe metabolic dysfunction-associated steatotic liver disease with marked hepatitis, reflected in elevated non-alcoholic fatty liver disease activity scores and extensive fibrosis. This hepatic progression mirrors the natural history observed in human metabolic liver disease, suggesting translational relevance of the model.

Clinical implications

"Mutations in the blood system are driving these conditions," explained Guryanova. "Clonal haematopoiesis is usually a silent condition, but if you know you have it, you're better aware of the risks it's associated with. Our hope is that knowing these risk factors would allow us to manage chronic conditions more efficiently, either with drugs or personalised lifestyle and diet interventions."

The findings carry particular significance given obesity has surpassed smoking as the most substantial preventable cancer risk factor. Guryanova noted: "With the ability to predict the risk of obesity and metabolic disease and better manage it, we could also eventually mitigate the risk of developing cancer."

Bidirectional pathophysiology

The authors emphasised their data support a bidirectional relationship between clonal haematopoiesis and metabolic disease. Whilst previous research focused on inflammation and obesity driving expansion of clonal haematopoiesis clones, these findings demonstrate the reverse causality. The authors stated: "While previous studies focused on inflammation and obesity driving expansion of the CH clone, our findings indicate this relationship is bidirectional wherein CH directly contributes to obesity and metabolic syndrome, suggesting a vicious molecular etiology cycle."

This conceptual framework has implications for understanding disease progression. Patients with clonal haematopoiesis may enter a positive feedback loop wherein blood cell mutations promote metabolic dysfunction, which in turn may further expand the mutant clone through inflammatory mechanisms, accelerating both haematological and metabolic disease.

Mutation-specific considerations

The differential impact of DNMT3A loss-of-function versus Arg882His mutations represents an important finding. Whilst the Arg882His variant shows enrichment in acute myeloid leukaemia, most clonal haematopoiesis-associated DNMT3A alterations comprise loss-of-function mutations. The authors noted these mutation types "may not be fully mechanistically equivalent," with loss-of-function mutations demonstrating more pronounced metabolic effects in their model.

This observation underscores the importance of detailed, mutation-specific investigation of clonal haematopoiesis in human disease. The authors urged "detailed mutation-and gene-specific investigation of CH in human chronic disease pathogenesis, risk stratification, and mitigation through pharmacologic, lifestyle, and dietary interventions."

Future directions and therapeutic potential

The research team plans to investigate the mechanisms by which these mutations drive disease progression and to evaluate potential therapeutic interventions. Yan indicated they will test whether medications commonly used for diabetes treatment and newer weight loss drugs might reverse or prevent diseases caused by these blood cell changes.

The potential for simple blood tests to identify at-risk individuals represents a translational goal. Early identification of patients with pathogenic clonal haematopoiesis clones could enable preventive strategies including dietary modification, lifestyle interventions, or pharmacological approaches before overt metabolic disease develops.

The findings highlight clonal haematopoiesis as an emerging risk factor for chronic metabolic disease that warrants consideration in risk stratification models and may represent a novel therapeutic target for preventing obesity-related complications. MEH

Reference:

Yan, B., Yuan, Q., Buttigieg, et. al. (2025). Clonal hematopoiesis driven by Dnmt3a mutations promotes metabolic disease development in mice. *Journal of Clinical Investigation*. https://doi.org/10.1172/JCI197100

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Special warnings and precautions: Effects on skeletal muscle have been reported in rosuvastatin-treated patients with all doses and in particular with doses >20 mg. The reporting rate for rhabdomyolysis associated with rosuvastatin in post-marketing use is higher at the 40 mg dose. In post-marketing experience with ezetimibe, cases of myopathy and rhabdomyolysis have been reported. However, rhabdomyolysis has been reported very rarely with ezetimibe monotherapy and very rarely with the addition of ezetimibe to other agents known to be associated with increased risk of rhabdomyolysis. If myopathy is suspected based on muscle symptoms or is confirmed by a creatine phosphokinase (CPK) level, rosuvastatin/ezetimibe and any of these other agents that the patient is taking concomitantly should be immediately discontinued. All patients starting therapy with rosuvastatin/ezetimibe should be advised of the risk of myopathy and told to report promptly any unexplained muscle pain, tenderness or weakness. In few cases, statins have been reported to induce de novo or aggravate pre-existing myasthenia gravis or ocular myasthenia. rosuvastatin/ezetimibe should be discontinued in case of aggravation of symptoms. Recurrences when the same or a different statin was (re-) administered have been reported. Creatine kinase (CK) should not be measured following strenuous exercise or in the presence of a plausible alternative cause of CK increase which may confound interpretation of the result. If CK levels are significantly elevated at baseline (>5xULN) a confirmatory test should be carried out within 7 – 5 days. If the repeat test confirms a baseline CK >5xULN, treatment should not be started. Before treatment: Caution should be exercised in patients with pre-disposing factors for myopathy/rhabdomyolysis. In such patients the risk of treatment should be considered in relation to possible benefit and clinical monitoring is recommended. If CK levels are significantly elevated at baseline (>5xULN) treatment should not be started. Whilst on treatment: Patients should be asked to report inexplicable muscle pain, weakness or cramps immediately, particularly if associated with malaise or fever. CK levels should be measured in these patients. Therapy should be discontinued if CK levels are markedly elevated (>5xULN) or if muscular symptoms are severe and cause daily discomfort (even if CK levels are </=5x ULN). If symptoms resolve and CK levels return to normal, then consideration should be given to re-introducing rosuvastatin or an alternative HMG-CoA reductase inhibitor at the lowest dose with close monitoring of the patient. There have been very rare reports of an immune-mediated necrotising myopathy (IMNM) during or after treatment with statins. An increase in the incidence of myositis and myopathy has been seen in patients receiving other HMG-CoA reductase inhibitors together with fibric acid derivatives. The combination of rosuvastatin and gemfibrozil is not recommended. The benefit of further alterations in lipid levels by the combined use of rosuvastatin with fibrates or niacin should be carefully weighed against the potential risks of such combinations. The 40 mg dose of rosuvastatin is contraindicated with concomitant use of a fibrate. rosuvastatin/ezetimibe should not be used in any patient with an acute, serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis. It is recommended that liver function tests be carried out prior to, and 3 months following, the initiation of treatment. Rosuvastatin should be discontinued or the dose reduced if the level of serum transaminases is greater than 3 times the upper limit of normal. The reporting rate for serious hepatic events in post-marketing use is higher at the 40 mg dose. In patients with secondary hypercholesterolaemia caused by hypothyroidism or nephrotic syndrome, the underlying disease should be treated prior to initiating therapy with rosuvastatin. Due to the unknown effects of the increased exposure to ezetimibe in patients with moderate or severe hepatic impairment, rosuvastatin/ezetimibe is not recommended. Rosuvastatin should be used with caution in patients who consume excessive quantities of alcohol and/or have a history of liver disease. Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with higher doses of rosuvastatin, in particular 40 mg, where it was transient or intermittent in most cases. Proteinuria has not been shown to be predictive of acute or progressive renal disease. The reporting rate for serious renal events in post-marketing use is higher at the 40 mg dose. An assessment of renal function should be considered during routine follow-up of patients treated with a dose of 40 mg. Some evidence suggests that statins as a class raise blood glucose and in some patients, at high risk of future diabetes, may produce a level of hyperglycaemia where formal diabetes care is appropriate. This risk, however, is outweighed by the reduction in vascular risk with statins and therefore should not be a reason for stopping statin treatment. Patients at risk (fasting glucose 5.6 to 6.9 mmol/l, BMI > 30 kg/m2, raised triglycerides, hypertension) should be monitored both clinically and biochemically according to national guidelines. In the JUPITER study, the reported overall frequency of diabetes mellitus was %2.8 in rosuvastatin and %2.3 in placebo, mostly in patients with fasting glucose 5.6 to 6.9 mmol/l. Exceptional cases of interstitial lung disease have been reported with some statins, especially with long term therapy. If it is suspected a patient has developed interstitial lung disease, statin therapy should be discontinued. Severe cutaneous adverse reactions have been reported with rosuvastatin. At the time of prescription, patients should be advised of the signs and symptoms of severe skin reactions and be closely monitored. If signs and symptoms suggestive of this reaction appears rosuvastatin/ezetimibe must be discontinued immediately and an alternative treatment should be considered. If the patient has developed a serious reaction with the use of rosuvastatin/ezetimibe, treatment with rosuvastatin/ezetimibe must not be restarted in this patient at any time. Increased systemic exposure to rosuvastatin has been observed in subjects receiving rosuvastatin concomitantly with various protease inhibitors in combination with ritonavir. Consideration should be given both to the benefit of lipid lowering by use of rosuvastatin/ezetimibe in HIV patients receiving protease inhibitors and the potential for increased rosuvastatin plasma concentrations when initiating and up titrating rosuvastatin doses in patients treated with protease inhibitors. The concomitant use with certain protease inhibitors is not recommended unless the dose of rosuvastatin is adjusted. The safety and efficacy of ezetimibe administered with fibrates have not been established. If cholelithiasis is suspected in a patient receiving rosuvastatin/ezetimibe and fenofibrate, gallbladder investigations are indicated and this therapy should be discontinued. Anticoagulants: If rosuvastatin/ezetimibe is added to warfarin, another coumarin anticoagulant, or fluindione, the International Normalised Ratio (INR) should be appropriately monitored. Rosuvastatin/ezetimibe must not be co-administered with systemic formulations of fusidic acid or within 7 days of stopping fusidic acid treatment. In patients where the use of systemic fusidic acid is considered essential, statin treatment should be discontinued throughout the duration of fusidic acid treatment. There have been reports of rhabdomyolysis in patients receiving fusidic acid and statins in combination. The patient should be advised to seek medical advice immediately if they experience any symptoms of muscle weakness, pain or tenderness. Statin therapy may be re-introduced seven days after the last dose of fusidic acid. In exceptional circumstances, where prolonged systemic fusidic acid is needed, the need for co-administration of rosuvastatin/ezetimibe and fusidic acid should only be considered on a case by case basis and under close medical supervision. Pharmacokinetic studies show an increase in exposure of rosuvastatin in Asian subjects compared with Caucasians. Rosuvastatin/ezetimibe is not recommended for use in children and adolescents of less than 18 years of age, due to insufficient data on safety and efficacy. Rosalus Plus contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. Contraindications: Hypersensitivity to the active substances or to any of the excipients. Pregnancy, breast-feeding and in women of childbearing potential not using appropriate contraceptive measures. Active liver disease or unexplained persistent elevations in serum transaminases and any serum transaminase elevation exceeding 3x the upper limit of normal (ULN). In patients with severe renal impairment (creatinine clearance <30 ml/min). In patients with myopathy. In patients receiving concomitant combination of sofosbuvir/velpatasvir/voxilaprevir. In patients receiving concomitant combination of ledipasvir/sofosbuvir In patients receiving concomitant ciclosporin. The 40 mg / 10 mg dose is contraindicated in patients with pre-disposing factors for myopathy/rhabdomyolysis. Undesirable effects: Diabetes mellitus, headache, dizziness, constipation, nausea, abdominal pain, diarrhoea, flatulence, myalgia, ALT and/or AST increased, asthenia and fatigue.

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Engineered human stomach cells demonstrate insulin production in diabetic mice

Researchers have transformed human stomach cells into functional insulin-secreting cells within living mice, offering a potential therapeutic strategy for type 1 diabetes.

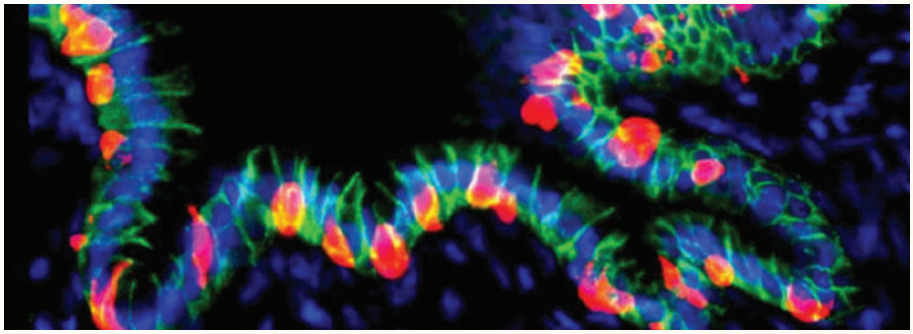
Type 1 diabetes affects approximately 9.5 million people globally due to insufficient insulin production by pancreatic beta cells, requiring lifelong blood glucose monitoring and insulin administration.

Cellular reprogramming approach

Xiaofeng Huang from Weill Cornell Medicine and Qing Xia from Peking University investigated whether human gastric tissue could undergo cell conversion previously demonstrated in mice. Researchers utilised genetically engineered human stomach organoids with an inducible system allowing controlled transformation into pancreatic beta-like cells. Following transplantation into mice, organoids survived and integrated with host vasculature for up to six months.

Functional insulin secretion

Upon activation of the genetic switch, transplanted human stomach cells successfully converted into insulin-secreting cells exhibiting gene and protein expression profiles characteristic of pancreatic beta cells. When tested in diabetic mice, insulin secreted by the transformed cells contributed to blood glucose regulation and ameliorated diabetic symptoms.



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Grafted hGO-NPM generates insulin+ cells.

The findings suggest that a patient's own stomach cells could potentially be converted to insulin-secreting cells directly within the body, though additional studies are essential. Key questions include cell longevity, physiological responsiveness, and immunological considerations. This research expands the therapeutic toolkit for type 1 diabetes beyond traditional islet transplantation.

Reference:

Huang, X., & Xia, Q. (2025). Modeling in vivo induction of gastric insulin-secreting cells using transplanted human stomach organoids. *Stem Cell Reports*. Published online 6 November 2025. *https://doi.org/10.1016/jstemcr.2025.102708* MEH

Lifestyle factors amplify cardiovascular benefits of GLP-1 receptor agonists in type 2 diabetes

Adults with type 2 diabetes who combined healthy lifestyle habits with GLP-1 receptor agonist therapy achieved substantially greater cardiovascular risk reduction compared to those using medication alone.

Type 2 diabetes doubles cardiovascular disease mortality risk, with incidence more than doubling in the United States over two decades. Whilst GLP-1 receptor agonists have demonstrated cardiovascular benefits, their interaction with lifestyle factors has remained incompletely characterised.

Lifestyle assessment

Xuan-Mai Nguyen and colleagues from the Department of Veterans Affairs Boston Healthcare System analysed data from the Million Veteran Program, examining over 63,000 participants with type 2 diabetes. Researchers evaluated adherence to eight healthy lifestyle factors: appropriate nutrition, physical activity, smoking abstinence, adequate sleep, limited alcohol intake, stress management, social connection, and absence of opioid addiction.

"Lifestyle modifications are recommended as the cornerstone for preventing and managing Type 2 diabetes," said Dr Nguyen. "Our study's findings suggest that people with Type 2 diabetes taking GLP-1 receptor agonists can improve their heart health even more by adding and maintaining healthy lifestyle habits."

Combined intervention effects

The analysis, encompassing 418,513 person-years of follow-up, revealed that participants adhering to all eight lifestyle factors demonstrated a 63% lower risk of major adverse cardiovascular events compared to those following one or fewer. GLP-1 receptor agonist use alone conferred a 20% risk reduction. Veterans taking GLP-1 receptor agonists whilst maintaining at least six healthy lifestyle habits experienced a 50% reduction in cardiovascular events compared to participants not using these medications who followed three or fewer factors.

Chiadi E. Ndumele, chair of the American Heart Association's Council on Lifestyle and Cardiometabolic Health, noted that "These findings suggest that a healthy lifestyle really complements the powerful effects of GLP-1RAs. Rather than medications versus lifestyle, healthcare professionals should really be emphasising both."

The preliminary research was presented at the American Heart Association's Scientific Sessions 2025 on 3 November. MEH

Pulsed electromagnetic field therapy improves glucose control in type 2 diabetes patients with central obesity

Non-invasive magnetic field stimulation that mimics exercise effects has demonstrated efficacy in improving glucose control among type 2 diabetes patients with excess abdominal adiposity.

The treatment, termed magnetic mitohormesis, uses pulsed electromagnetic fields to activate metabolic pathways typically triggered by endurance exercise, potentially offering therapeutic benefits to patients unable to engage in regular physical activity.

Therapeutic approach

"We often tell patients with diabetes to exercise because it helps control blood sugar, but we found that most people (over eight out of 10 in our study) do not exercise regularly," said Dr Tan Hong Chang, Senior Consultant in the Department of Endocrinology at Singapore General Hospital. "Many of our patients cannot do so easily due to age, health problems, or other barriers. This treatment could give similar benefits to exercise."

The study enrolled 40 adults with poorly controlled type 2 diabetes at Singapore General Hospital. Participants underwent weekly 10-minute sessions for 12 weeks, during which a specialised chamber device delivered gentle magnetic field pulses to leg muscles. No adverse effects were reported.

Targeted benefits in central obesity

Whilst overall diabetes control did not improve significantly across all participants, researchers identified a marked response in individuals with central obesity. Nearly 90% of patients in this subgroup achieved improved glycaemic control, with haemoglobin A1c declining from 7.5% to 7.1% over three months. Patients with central obesity may respond more favourably due to impaired cellular function and elevated circulating lipids.

"The NUS team has pioneered the novel use of magnetic pulses to trigger lasting physiological changes – without drugs, genetic modification, or surgery," said Professor Alfredo Franco-Obregón from the National University of Singapore. "The findings align with our previous work showing that fat tissue responds very well to the magnetic muscle treatment."

The research, supported by Singapore's Agency for Science, Technology and Research and QuantumTX Pte Ltd, emphasises that larger randomised controlled trials are necessary.

Reference:

Tan, H.C., Franco-Obregón, A., et al. (2025). Investigating the metabolic benefits of magnetic mitohormesis in patients with type 2 diabetes mellitus. *Journal of Clinical Medicine*, 14(18), 6413. Published 11 September 2025.

https://doi.org/10.3390/jcm14186413

Global type 2 diabetes burden projected to reach 800 million cases by 2045

Type 2 diabetes has escalated from a rare condition to a global epidemic within three decades, with current cases exceeding 530 million adults worldwide and projections indicating nearly 800 million by 2045. The study authors call for bold action with policy focused on prevention and early detection.

Type 2 diabetes,, accounting for more than 90% of all diabetes cases, has become one of the top ten causes of global mortality whilst contributing substantially to cardiovascular disease.

Geographic disparities

Zhang and colleagues' analysis reveals marked geographic variation. Whilst prevalence remains elevated in North America and Europe, the steepest increases are occurring in Asia and Africa. China and India account for more than one-third of global cases. Sub-Saharan Africa is experiencing some of the fastest growth rates, creating the dual challenge of managing both infectious diseases and escalating non-communicable conditions.

Epidemic drivers

The epidemic results from demographic ageing, dietary pattern shifts, reduced physical activity, and early-life nutritional exposures. By 2050, the proportion of the global population aged over 60 will nearly double. Urbanisation has normalised diets rich in processed foods and sugary beverages, whilst sedentary behaviour has increased sharply. Early-life malnutrition predisposes individuals to diabetes decades later.

Economic implications

Type 2 diabetes imposes substantial burdens on health systems through cardiovascular, renal, ophthalmic, and neurological complications. Globally, approximately 10% of all health budgets are devoted to diabetes. In the United States, more than half of lifetime costs address complication management. In lower-income countries, late diagnosis and poor care access drive high levels of preventable disability and death.

Prevention imperative

Despite these statistics, type 2 diabetes remains among the most preventable major chronic diseases. Large trials demonstrate that intensive lifestyle interventions can reduce diabetes onset in high-risk individuals by up to 58%, with recent evidence showing disease remission is achievable. However, most healthcare systems allocate resources primarily to managing advanced disease whilst underfunding prevention. The authors call for decisive action, emphasising that the global trajectory can be altered with bold policy focused on prevention and early detection.

Reference:

Zhang, L., et al. (2025). Global risk factors, epidemiology, and disease burden of type 2 diabetes. Science *China Life Sciences*.

https://doi.org/10.1007/s11427-024-3036-4

From insight to impact: How clinical decision support is powering precision medicine in the Middle East

As healthcare systems across the Middle East accelerate their digital transformation journeys, a new paradigm is emerging – one that blends precision medicine, artificial intelligence (AI), and clinical decision support (CDS) to deliver safer, smarter, and more personalized care. At a recent executive Think Tank hosted in Dubai, healthcare leaders, clinicians, and digital health experts gathered to explore how clinical decision support solutions are enabling this transformation.

Precision medicine: A 360-degree view of the patient

"Precision medicine is not just about genomics – it's about integrating behavioural, environmental, and clinical data to deliver truly personalized care," said Dr. Osama Elhassan, PhD, FIAHSI, Chairman of ZIMAM Digital Health Association. "We're moving from a one-size-fits-all model to a 4P approach: personalized, predictive, preventive, and participatory."

This shift is being accelerated by national initiatives like the UAE Genome Project, which has sequenced over one million Emirati genomes, and by the growing adoption of CDS tools that translate complex data into actionable insights at the point of care.

Empowering clinicians with evidence-based precision

At the heart of this transformation is evidence-based clinical decision support. Used by millions of clinicians globally, these tools provide real-time, peer-reviewed guidance across a wide range of specialties.

"Clinical decision support has become our clinical compass," said Dr. Ibrahim Abu-Gheida, Chief Medical Officer of Burjeel Cancer Institute and the Clinical Director of the Department of Radiation Oncology at Burjeel Medical City. "It's not just about convenience – it's about confidence. Our clinicians feel reassured knowing they're making decisions backed by the latest evidence."

Christian Cella, Vice President and General Manager, International segment, Wolters Kluwer Health, emphasized the role of CDS in reducing variability in care: "Whether you're in Abu Dhabi or Addis Ababa, clinical decision support ensures that every patient receives care aligned with global best practices."

Precision in prescribing

Medication safety is a cornerstone of precision medicine – and a persistent challenge. "We're seeing an explosion of new drug approvals, complex regimens, and pharmacogenomic considerations," noted Jordan Fulcher, Clinical Solutions Consultant, Wolters Kluwer. "That's where clinical decision support tools come in."

These tools offer comprehensive drug information, IV compatibility data, and patient education materials, while also providing real-time alerts for drug interactions, contraindications, and dosing errors – integrated directly into the electronic medical record (EMR).

Dr. Manal Al Nemari, Digital Health Adoption Lead, Chapter Lead, Accountable Care, Clinical Data & Automation Lead, Ministry of Health, Saudi Arabia highlighted the impact: "With advanced clinical decision-support technologies, we've dramatically reduced override rates and elevated alert relevance. This isn't just about flagging potential risks – it's about leveraging intelligent automation and real-time data to guide clinicians toward safer, evidence-based alternatives, ultimately transforming patient safety and care quality."

AI and CDS: A responsible partnership

While generative AI tools like ChatGPT are gaining popularity, experts at the Think Tank cautioned against their use in

Dr. Manal Al Nemari, Digital Health Adoption Lead, Chapter Lead, Accountable Care, Clinical Data & Automation Lead, Ministry of Health, Saudi Arabia.

clinical decision-making without rigorous validation.

"AI can hallucinate. Clinical decision support doesn't. Enhanced AI search in UpToDate® doesn't generate new content – it retrieves trusted, editor-reviewed answers word for word," said Fulcher.

From clicks to clinical impact

Beyond point-of-care support, clinical decision support solutions also offer powerful analytics. "We're not just tracking usage – we're translating it into insights," said Fulcher. "We can show hospitals what clinicians are searching for, how that aligns with prescribing patterns, and where there are gaps in knowledge or compliance."

Integration and accessibility: Meeting clinicians where they are

To maximize impact, clinical decision support tools must be embedded into clinical workflows. "The ideal solution is one click away – within the EMR, mobile app, or even Microsoft Copilot," said Fulcher. "We're building a hub-and-spoke model where trusted content is accessible wherever clinicians need it."

Dr. Ahmed Al-Dammas, Chief Data Officer at the Saudi Council of Health Insurance, stressed the importance of seamless access: "If it's not integrated, it's not used. Single sign-on, mobile optimization, and HL7 integration are no longer nice-to-haves – they're must-haves."

While the clinical benefits are clear, the financial case is equally compelling. "CDS tools reduce adverse drug events, shorten hospital stays, and improve formulary compliance," said Dr. Abu-Gheida. "That's real ROI – especially in value-based care models."

Dr. Osama Hassan added: "If we want to move from fee-for-service to outcomes-based reimbursement, we need solutions that link decisions to results. Wolters Kluwer's UpToDate® and Medi-Span® do exactly that."

Looking ahead: A shared vision for safer, smarter care

As the Think Tank concluded, one message resonated: precision medicine is a team sport. It requires collaboration across clinicians, technologists, regulators, and solution providers.

"We're not just building tools – we're building trust," said Fulcher. "And that trust is what turns insight into impact." MEH

The original article is published on *WoltersKluwer.com* here: *https://tinyurl.com/ysx99ynw*

> We're seeing an explosion of new drug approvals, complex regimens, and pharmacogenomic considerations. That's where clinical decision support tools come in.

Innovative Korean medical expertise expands to the Middle East

Expanding breast cancer knowledge through Korea-UAE collaboration

Breast cancer remains one of the most pressing health challenges in the Middle East, consistently ranking among the most frequently diagnosed cancers in women across the region. To strengthen professional capacity in this area the Korea Health Industry Development Institute (KHIDI), the Korean Breast Cancer Society (KBCS) and the Department of Health – Abu Dhabi (DoH) partnered to deliver a five-part online seminar series between April and August 2025.

Korea has reaffirmed its position as a global hub for advanced breast cancer care through the successful completion of the "Current Breast Cancer Treatment Trends & Case Studies in Korea" seminar series. Over 2,600 healthcare professionals from the UAE and across the Middle East participated in this educational programme.

The programme went beyond a traditional academic exchange. It was formally linked to Continuing Medical Education (CME) credits in Abu Dhabi and designed to provide practising clinicians and healthcare decision-makers with practical insights that can be applied directly in patient care. Of particular significance, the seminar engaged not only regional healthcare professionals but also key decision-makers at DoH-Abu Dhabi. Building on this year's success, the series is planned to continue next year.

Ten leading Korean specialists delivered lectures representing the nation's top medical institutions – Seoul National University Hospital, Korea University Anam Hospital, Ewha Womans University Seoul Hospital, Samsung Medical Center, Yonsei Severance Hospital, Seoul St. Mary's Hospital, Bundang Seoul National University Hospital, Asan Medical Center, and CHA Gangnam Medical

Center – reflecting the collective strength of Korea's multidisciplinary and patient-centred oncology care.

Participants heard from these breast cancer consultants who discussed a broad spectrum of topics including surgical and radiation therapy advances, robotic-assisted surgery, and the integration of targeted therapy and immunotherapy in clinical practice. Presentations were anchored in real patient case studies, offering participants a closer look at how new approaches are being applied in day-to-day oncology care.

Feedback from attendees emphasised the relevance of the sessions. Many highlighted the value of learning about treatment innovations through concrete clinical examples, noting the potential to adapt these strategies within their own healthcare systems. Attendees responded positively, stating that "it was a valuable opportunity to learn about the latest medical technology trends in breast cancer treatment from Korea. The case-based presentations are expected to provide practical guidance that can be applied in clinical settings."

KBCS and GBCC: Driving academic and clinical excellence

Founded in 1999, the Korean Breast Cancer Society (KBCS) has become one of Asia's most influential professional organisations in oncology, uniting surgeons, oncologists, radiologists, pathologists, and researchers to improve breast cancer outcomes through education, research, and international collaboration.

Since 2007, KBCS has organised the Global Breast Cancer Conference (GBCC), now recognised as one of the world's largest breast cancer meetings in Asia, drawing participants from more than 40 countries each year. GBCC serves as a key platform for sharing innovations in clinical practice, translational research, and patient advocacy.

Through these initiatives, Korea has fostered a global reputation for combining scientific rigour, advanced technology, and holistic patient care – a reputation further strengthened by this latest collaboration with the UAE healthcare community.

Comprehensive and evidence-based breast cancer care

The seminar series explored the full spectrum of modern breast cancer management – from prevention to survivorship. The opening lecture reviewed the epidemiology of breast cancer in Korea and emphasised the importance of early detection, digital imaging, and genetic testing in identifying premenopausal cases, which remain proportionally higher than in Western countries.

Subsequent sessions addressed systemic therapy before and after surgery, highlighting the optimisation of neoadjuvant and adjuvant treatments based on molecular subtype and individualised risk. Presentations also covered endocrine therapy strategies for both pre- and postmenopausal patients, incorporating insights from global trials such as SOFT and TEXT that have shaped current international guidelines.

Innovation in surgery and radiotherapy

Korea's leadership in surgical innovation was demonstrated through advances in oncoplastic and robotic-assisted breast surgery, including the robotic nipple-sparing mastectomy (RNSM) using the da Vinci Single-Port system. This approach enhances precision, minimises tissue damage, and improves cosmetic outcomes – reflecting Korea's philosophy that quality of life is integral to cancer recovery.

In radiotherapy, Korean clinicians presented data on hypofractionated schedules, which safely reduce treatment sessions while maintaining equivalent oncologic outcomes. These advances enable more efficient use of resources and better patient convenience, a model adaptable to healthcare systems in the Middle East.

Genetic insights, fertility preservation, and survivorship

The programme also highlighted Korea's expertise in genetic counselling and fertility management for young breast cancer patients. Sessions discussed germline mutation testing, PARP inhibitors, and the integration of fertility preservation techniques such as oocyte and ovarian tissue cryopreservation. These strategies embody a comprehensive, multidisciplinary model that safeguards both oncologic safety and reproductive potential.

Digital transformation and global collaboration

Beyond clinical excellence, Korea's hospitals are implementing AI-based clinical decision tools, digital education platforms, and metaverse-enabled patient programmes to enhance communication and shared decision-making. The strong engagement and positive feedback from Middle Eastern participants underscored the growing potential for sustained exchange and collaboration.

The series was also made accessible through the Medical Korea Academy (MKA) e-class, KHIDI's global online education platform for healthcare professionals. The platform is open to physicians, nurses, medical students, hospital managers, IT specialists, and government health officials. Another MKA e-class session started September 15 and runs to November 30, 2025, with free access worldwide < *https://mka-eclass.or.kr* >.

Looking ahead

A KHIDI official remarked: "This seminar represents an important milestone in strengthening healthcare cooperation between Korea and the Middle East, built on Korea's excellent clinical outcomes in breast cancer treatment. Moving forward, KHIDI will work closely with DoH-Abu Dhabi and other partners to identify new areas of interest and continue organising online seminars in the coming year."

Looking ahead, KHIDI and DoH-Abu Dhabi plan to continue their collaboration. Future seminars will likely broaden the focus beyond breast cancer to other high-burden cancers in the region, such as stomach, colorectal, and thyroid cancer, reflecting shared healthcare priorities and thereby reinforcing the global healthcare cooperation network.

Encouraged by this success, KBCS and KHIDI plan to expand educational partnerships through the Medical Korea Academy e-Class and future joint forums, promoting mutual growth and medical innovation between Korea and the UAE.

Through the combined leadership of KBCS and GBCC, Korea continues to advance precision, compassion, and collaboration in breast cancer care – offering the Middle East a trusted partner in shaping the next era of oncology excellence. MEH

Human brain scans reveal hidden drainage pathway around ventral meningeal artery

Researchers have identified a previously unrecognised cerebrospinal fluid drainage route along the human brain's middle meningeal artery using MRI scans and tissue analysis. The finding suggests that ventral regions of the protective brain membranes play a more active role in clearing brain waste than previously thought, with potential implications for understanding neurological diseases.

Scientists have mapped what appears to be a distinct cerebrospinal fluid (CSF) clearance pathway in the ventral regions of the human brain, according to research published in *iScience* on 4 October 2025. The study combines dynamic MRI imaging with detailed tissue analysis to characterise lymphatic-like structures surrounding the middle meningeal artery (MMA), an area that has received limited attention compared to better-studied drainage routes along the brain's upper surface.

The research team, led by Dr Onder Albayram from the Medical University of South Carolina, used contrast-enhanced MRI to track fluid movement in five healthy adults over six hours. They observed a delayed signal enhancement pattern around the periphery of the MMA that peaked at 90 minutes after contrast injection – substantially later than in other brain regions examined.

Delayed drainage patterns suggest non-vascular clearance

Whilst most anatomical compartments analysed showed rapid signal peaks at 30 minutes, consistent with typical vascular patterns, the MMA-peripheral region demonstrated a distinctly slower enhancement profile. "The MMA-peripheral exhibited significantly higher signal intensity than the MMA-lumen at all time points," the authors report in their paper, adding that this pattern "closely paralleled the parasagittal dura, a structure known to participate in meningeal lymphatic drainage."

The team conducted systematic comparisons of signal intensity across five regions: the MMA lumen, MMA periphery, nasal septum, parasagittal dura, and deep cervical lymph nodes. Statistical analysis revealed that the MMA-peripheral showed significantly lower signal intensity than the nasal septum at 30, 90, and 180 minutes, but exhibited no significant differences compared to the parasagittal dura at any timepoint.

"These findings support the hypothesis that the MMA-peripheral exhibits distinct clearance kinetics relative to intravascular and mucosal compartments, but shares signal decay behaviour with other dural regions, such as the parasagittal dura," the authors state.

Tissue analysis confirms lymphatic vessel presence

To validate their imaging observations, the researchers performed detailed anatomical mapping of dural tissue surrounding both dorsal and ventral segments of the MMA obtained from a neurologically intact cadaver. Using two complementary techniques – immunofluorescence confocal microscopy and Hyperion imaging mass cytometry – they identified robust expression of canonical lymphatic markers in the tissue.

The analysis revealed PROX1-positive, PDPN-positive, and LYVE1-positive lymphatic-like structures aligned along the MMA, particularly enriched in ventral segments near the foramen spinosum. "We identified robust expression of canonical lymphatic markers – PROX1, PDPN, and LYVE1 – within the periosteal dura, particularly in the ventral segment, where signal intensity increased progressively towards the bony interface," the authors report.

The lymphatic architecture showed distinct organisational patterns across different dural layers. Inner dura displayed anterior-posterior alignment, middle layers followed a superior-inferior axis, and outer dura revealed more complex, multidirectional lymphatic patterns. The researchers also observed lymphatic marker-positive cells within the tunica media of the MMA arterial wall itself, raising questions about potential interactions between vascular and lymphatic systems.

Molecular heterogeneity in lymphatic markers

Interestingly, the tissue analysis revealed divergent expression patterns amongst the lymphatic markers examined. Whilst PROX1 and PDPN showed strong, consistent expression, LYVE1 was notably faint and discontinuous, particularly in ventral regions.

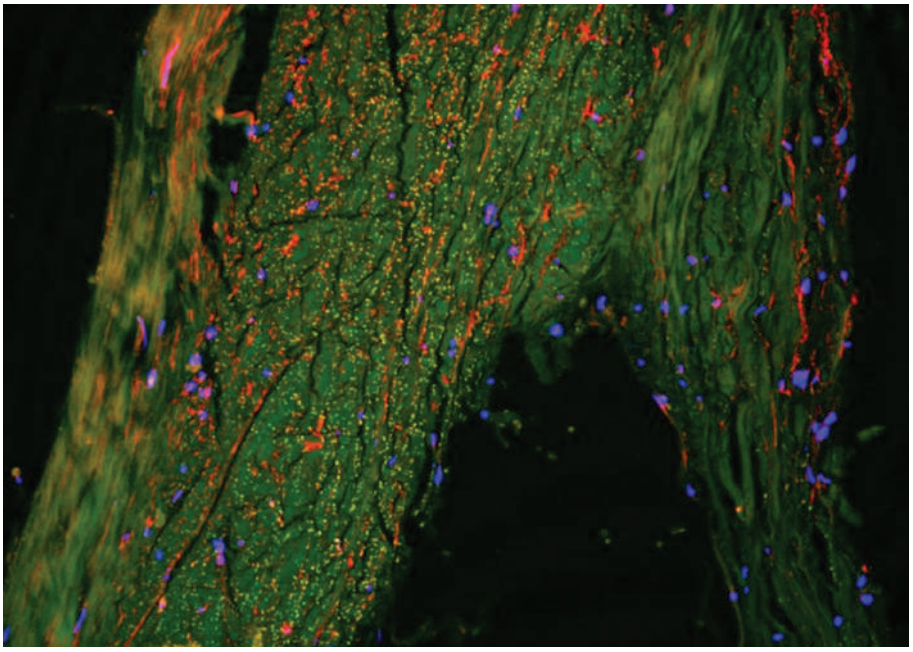
"This divergence likely reflects functional and developmental heterogeneity within human meningeal lymphatic vessels," the authors explain. "While PROX1 and PDPN are well-established markers of lymphatic endothelial identity, with PDPN also linked to mesenchymal-like properties, LYVE1 is more closely associated with classical lymphatic endothelium and is often downregulated in pre-collecting or specialised lymphatic structures."

This molecular variability underscores the complexity of the meningeal lymphatic system and highlights the importance of using multiple markers for accurate identification of these structures in human tissue.

Bridging animal models and human physiology

The findings represent a significant step towards translating preclinical research on meningeal lymphatics to human anatomy. Animal studies, particularly in rodents, have established the ventral meningeal region – including areas around the MMA

Medical University of South Carolina. Image courtesy of Dr Onder Albayram



Microscope image showing lymphatic vessels (red) in the brain's outer protective layer, the dura. These vessels form a rich and complex network that helps drain waste from the brain.

Medical University of South Carolina. Photo by Julie Taylor

Dr Onder Albayram in his lab at the Medical University of South Carolina.

and pterygopalatine fossa – as critical sites for CSF and interstitial fluid drainage. However, direct evidence in humans has been limited.

Clinical implications and future directions

The identification of this ventral drainage pathway could have important implications for understanding various neurological conditions. The meningeal lymphatic system is thought to play crucial roles in clearing metabolic waste, maintaining fluid homeostasis, and regulating immune surveillance in the brain. Dysfunction in these pathways has been implicated in ageing, neurodegeneration, and traumatic brain injury.

However, the researchers emphasise several important limitations. The MRI cohort consisted of only five participants imaged at five timepoints over six hours, which constrains both temporal resolution and generalisability. The histological validation was performed on a single postmortem specimen, though the use of two complementary imaging platforms strengthens confidence in the anatomical observations.

The authors are careful to note that their dynamic MRI data provide indirect evidence of fluid transport pathways inferred from signal enhancement kinetics rather than direct tracer tracking or flow measurements. "The delayed enhancement around the MMA-peripheral is consistent with slower clearance dynamics, which may reflect lymphatic involvement; however, alternative explanations, such as interstitial diffusion or perivascular retention, cannot be excluded," they state.

Regarding the lymphatic marker-positive elements detected within arterial media and periosteal surfaces, the researchers stress that "our data reflect marker localisation alone and do not establish a functional role in perivascular drainage or vessel remodelling. It remains possible that these lymphatic elements contribute to tissue homeostasis or immune surveillance rather than fluid clearance."

Advancing the anatomical atlas of brain drainage

Despite these caveats, the study provides valuable multimodal evidence for organised lymphatic architecture in the human ventral dura. "To our knowledge, this is a comprehensive study to characterise ventral meningeal lymphatic architecture and CSF-ISF flow patterns in the healthy human brain," the authors state. "We identify a distinct lymphatic network adjacent to the MMA and propose that this region functions as a previously unrecognised ventral outflow hub in central nervous system fluid clearance."

The research establishes a methodological foundation for future investigations into meningeal drainage pathways. The authors suggest that larger, demographically diverse cohorts with higher temporal sampling, automated segmentation techniques, and live tracer tracking studies will be needed to definitively establish the functional role of ventral drainage in humans.

As research into brain fluid dynamics continues to evolve, this integrated anatomical framework combining in vivo imaging with high-resolution tissue analysis represents an important step towards understanding how the human brain maintains its complex fluid environment – knowledge that could ultimately inform therapeutic approaches for a range of neurological conditions. MEH

Reference:

Albayram, M., Richmond, S. B., Yagmurlu, K., et. al. (2025). Meningeal lymphatic architecture and drainage dynamics surrounding the human middle meningeal artery. *iScience*, 28(11), 113693. *https://doi.org/10.1016/j.isci.2025.113693*

The Picower Institute for Learning and Memory

Diane Chan (left) and Li-Huei Tsai (right) discuss the research in MIT lab where volunteers receive 40Hz stimulation and their response is measured using EEG.

Long-term gamma wave therapy shows promise in slowing Alzheimer's decline

A two-year pilot study of five patients with mild Alzheimer's disease has demonstrated that daily 40 Hz audiovisual stimulation is safe and may slow cognitive decline, particularly in late-onset cases. Three female patients showed significant improvements in key cognitive scores compared to matched controls, whilst two also exhibited substantial reductions in plasma phosphorylated tau levels.

Researchers at the Massachusetts Institute of Technology and Massachusetts General Hospital have published findings suggesting that extended use of gamma frequency sensory stimulation may offer cognitive and biomarker benefits for patients with mild Alzheimer's disease, marking the longest clinical evaluation of this non-invasive therapeutic approach to date.

The open-label extension study, published in *Alzheimer's & Dementia* on 4 November 2025, followed five participants who received one hour of daily 40 Hz light and sound stimulation over approximately 30 months. The intervention employs a technique called Gamma Entrainment Using Sensory (GENUS) stimuli, which aims to restore disrupted neural oscillations characteristic of Alzheimer's pathology.

Differential responses between patient groups

The study revealed a notable divergence in treatment response between late-onset Alzheimer's disease (LOAD) and early-onset Alzheimer's disease (EOAD) patients. Three female participants with LOAD maintained robust electroencephalography (EEG) responses to the 40 Hz stimulation throughout the study period, with increases of 109%, 164%, and 113% over baseline measurements. In contrast, two male participants with EOAD showed steep declines in their 40 Hz EEG power, falling to 38% and 32% of baseline levels.

"No adverse events occurred over the study period," the authors reported in their findings. The three LOAD patients "showed less decline in Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR), and Functional Assessment Scale (FAS) scores compared to matched controls from National Alzheimer's Coordinating Center (NACC), Alzheimer's Disease Neuroimaging Initiative (ADNI), and Longitudinal Early-Onset Alzheimer's Disease Study (LEADS)."

The cognitive improvements in LOAD participants proved statistically significant when compared to control distributions, with p-values of 0.02, 0.02, and 0.01 for MMSE, CDR-SOB, and FAS scores respectively. These measures assess global cognitive function, dementia severity, and everyday functional capacity.

Biomarker reductions suggest pathological impact

Perhaps the most striking findings emerged from plasma biomarker analysis. Two of the three LOAD participants provided longitudinal blood samples, and both demonstrated reductions in plasma phosphorylated tau 217 (pTau217) concentrations following approximately two years of daily stimulation. The decreases measured 47% and 19% respectively, remaining substantial even after normalisation to total plasma protein (55% and 19%).

"Notably, such a reduction in plasma pTau217 in response to a non-invasive intervention has not previously been demonstrated in humans," the authors stated in their discussion, "and the pTau217 reduction observed here suggests that long-term GENUS treatment may

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potentially reduce amyloid pathology, as has been shown in clinical trials of anti-amyloid antibodies."

The pTau217 biomarker has emerged as a highly sensitive indicator of Alzheimer's pathology, strongly correlating with amyloid burden and demonstrating diagnostic accuracy superior to many traditional markers.

Mechanistic foundations and preclinical evidence

The therapeutic rationale for gamma frequency stimulation stems from observations that Alzheimer's disease disrupts neuronal network oscillations, particularly in the gamma band (30-80 Hz). These disruptions have been documented in both animal models and human patients. Prior research using mouse models of Alzheimer's disease demonstrated that 40 Hz visual and auditory stimulation could decrease amyloid levels and ameliorate cognitive impairment, with combined audiovisual stimulation producing enhanced effects.

The current study participants used devices consisting of a 2-foot by 2-foot LED panel and speaker delivering synchronised 40 Hz light and sound, with a centrally mounted tablet providing entertainment during the hour-long sessions. All five participants had mild Alzheimer's disease at baseline, confirmed by plasma pTau217 values above the diagnostic threshold of 6.8 pg/mL.

Circadian rhythm improvements observed

Actigraphy measurements conducted over two-week periods at each assessment timepoint revealed improvements in sleep-wake patterns for several participants. Intra-daily variability, which reflects fragmentation of circadian rhythm, decreased in four participants following initiation of 40 Hz stimulation. Inter-daily stability, indicating the strength of coupling to environmental cues, improved in two of five participants.

These findings align with previous shorter-term studies reporting sleep quality improvements in Alzheimer's patients receiving gamma frequency stimulation, suggesting a potential role for GENUS in stabilising circadian patterns disrupted by the disease process.

No significant brain volume differences detected

Structural MRI analysis assessed volume changes in temporal lobe structures known to show atrophy with Alzheimer's progression, including the hippocampus, amygdala, and middle and inferior temporal gyri, as well as ventricular dilation. Whilst volume changes in open-label extension participants tended to be less severe in LOAD patients compared to matched controls from the NACC and ADNI databases, these differences did not reach statistical significance.

Previous studies of gamma stimulation and repetitive transcranial magnetic stimulation have reported slowed volume loss in Alzheimer's-affected brain structures, though these assessments covered only three to six months. The current study's extended timeframe may have introduced greater variability in structural measurements.

Study limitations and future directions

The authors acknowledged several limitations inherent to the open-label design. "This extension study followed an open-label design and did not include any controls," they noted, though this limitation was partially addressed through the use of well-matched participants from three large national databases. The researchers emphasised that NACC, ADNI, and LEADS databases "are sufficiently large and diverse to allow matching of participants on sex, age, and cognitive status."

Another constraint involved the confounding of sex and age of onset, with all LOAD participants being female and all EOAD participants being male. The authors emphasised age of onset as the more biologically meaningful distinction, given well-established differences between EOAD and LOAD in brain network involvement and clinical phenotype, with EOAD typically showing a more aggressive disease trajectory.

The limited sample size, whilst appropriate for a pilot extension study, prevents definitive conclusions about efficacy. However, the findings provide sufficient evidence to support larger-scale investigation. "These results provide the rationale for larger long-term studies of 40 Hz audiovisual stimulation in LOAD patients," the authors concluded, "and underscore the utility of nationwide AD studies such as NACC as a source of no-treatment controls."

Clinical implications and research trajectory

The study represents an important milestone as the first to link long-term 40 Hz therapy to changes in Alzheimer's disease biomarkers in human patients. The convergence of improved cognitive scores, maintained EEG responses, and reduced pTau217 levels in LOAD participants suggests potential disease-modifying effects warranting rigorous evaluation.

The differential response between LOAD and EOAD patients raises important questions about treatment stratification and optimal patient selection. The authors suggested that broad pathological differences between these disease subtypes could contribute to differential responses, noting that "future research should explore predictors of treatment response, such as genetic and pathological markers."

The high compliance observed in this study, with participants willing to use the device daily for two years, demonstrates the feasibility of long-term at-home treatment. This practicality represents a significant advantage over many experimental Alzheimer's interventions requiring frequent clinical visits or invasive procedures.

As the field moves forward, the authors emphasised that "future research should prioritise large-scale long-term follow-up studies as well as shorter-term randomised controlled trials to derive optimal treatment parameters and investigate the mechanistic underpinnings of GENUS." MEH

Reference:

Chan, D., de Weck, G., Jackson, B. L., et. al. (2025). Gamma sensory stimulation in mild Alzheimer's dementia: An open-label extension study. *Alzheimer's & Dementia*, 21(10), e70792. https://doi.org/10.1002/alz.70792

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Researchers find Alzheimer's pathology damages neurovascular structures in adipose tissue, linking brain disease to metabolic health

Houston Methodist researchers have uncovered a previously unknown mechanism linking Alzheimer's disease to cardiovascular and metabolic complications. Using advanced three-dimensional imaging in mouse models, the team demonstrated that the neurodegenerative condition systematically dismantles the organised neurovascular structures within adipose tissue, potentially explaining why patients frequently develop concurrent heart disease, stroke and diabetes alongside cognitive decline.

Brain disease extends reach beyond neural tissue

Alzheimer's disease has long been recognised primarily as a disorder of the brain, characterised by amyloid plaques, neurofibrillary tangles and progressive cognitive deterioration. However, research published in the *Journal of Lipid Research* on 25 October 2025 reveals that the disease's pathological influence extends far beyond the central nervous system, disrupting critical communication networks between the autonomic nervous system and peripheral adipose tissue.

The study, led by Stephen Wong, Ph.D., the John S. Dunn Presidential Distinguished Chair in Biomedical Engineering at Houston Methodist, employed sophisticated whole-mount immunostaining and three-dimensional confocal microscopy to visualise the structural organisation of neurovascular bundles within subcutaneous white adipose tissue. Key contributors included Li Yang, Ph.D., a research associate, and Jianting Sheng, Ph.D., an assistant research professor of computational biology and mathematics in radiology.

"By disrupting the connection between the nervous system and fat tissue, the disease may impair the body's ability to manage energy," explained Li Yang, highlighting the metabolic implications of these structural changes.

Neurovascular architecture in adipose tissue

In healthy adipose tissue, sympathetic nerve fibres run in close parallel alignment with blood vessels, forming organised neurovascular bundles that serve as conduits for both hormonal signalling and neural control. These structures are fundamental to the brain-fat communication axis, enabling the central nervous system to regulate lipid metabolism, energy expenditure and thermogenesis through sympathetic innervation.

The researchers utilised anti-endomucin antibodies to label blood vessels and anti-tyrosine hydroxylase antibodies to identify sympathetic nerve fibres. In wild-type control mice at 25 weeks of age, confocal imaging revealed tightly coordinated neurovascular bundles throughout the subcutaneous adipose depots, with sympathetic nerves maintaining intimate spatial proximity to the vascular network.

Progressive structural deterioration in Alzheimer's model

The investigation employed 5XFAD mice, a well-established transgenic model of Alzheimer's disease that develops aggressive amyloid pathology and cognitive deficits. Comparative analysis between age-matched 5XFAD and wild-type animals revealed striking differences in adipose tissue neurovascular organisation.

The research team documented four progressive stages of structural deterioration in the Alzheimer's disease model. Initially, neurovascular bundle decoupling occurred, with sympathetic nerve fibres beginning to separate from their associated blood vessels whilst maintaining some degree of parallel orientation. This progressed to complete loss of spatial proximity and co-localisation, where nerves and vessels became spatially disorganised within the adipose tissue architecture. Ultimately, the most severely affected regions displayed near-complete abrogation of sympathetic nerve signals, suggesting extensive denervation of the adipose depot.

High-resolution three-dimensional reconstructions provided unprecedented visualisation of these structural changes, offering the first comprehensive view of how Alzheimer's disease pathology manifests in peripheral metabolic tissues.

Stephen Wong, Ph.D., the John S. Dunn Presidential Distinguished Chair in Biomedical Engineering, Houston Methodist.

Autonomic dysfunction extends metabolic consequences

The disruption of neurovascular bundles in adipose tissue carries significant implications for whole-body metabolic regulation. Sympathetic innervation of fat depots plays a crucial role in lipolysis, adipokine secretion and thermogenic activation of brown and beige adipocytes. Loss of these neural connections would be expected to impair the body's capacity to mobilise stored energy, respond to metabolic stress and maintain glucose homeostasis.

"Alzheimer's disease induces autonomic nervous system dysfunction (dysautonomia), which exacerbates cardiovascular and metabolic comorbidities, yet the role of dysautonomia in metabolic dysregulation remains underexplored," the authors note in their published work, emphasising the novelty of investigating peripheral autonomic manifes-

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tations of this neurodegenerative condition.

The autonomic nervous system comprises both sympathetic and parasympathetic divisions that operate largely outside conscious control, regulating cardiovascular function, gastrointestinal motility, thermoregulation and metabolic processes. Dysautonomia in Alzheimer's disease has been documented through various clinical manifestations, including orthostatic hypotension, heart rate variability abnormalities and impaired cardiovascular reflexes. However, the cellular and structural basis for these autonomic disturbances has remained poorly characterised.

Clinical implications for comorbidity patterns

Epidemiological studies have consistently demonstrated that Alzheimer's disease patients experience elevated rates of cardiovascular events, metabolic syndrome and type 2 diabetes compared with age-matched cognitively normal individuals. These associations have typically been attributed to shared risk factors, including hypertension, dyslipidaemia and insulin resistance, or to the challenges of disease management in cognitively impaired populations.

The Houston Methodist findings suggest an alternative mechanistic explanation: that Alzheimer's pathology directly compromises the neural circuits governing metabolic homeostasis. This disturbance could help explain why individuals with Alzheimer's often experience issues such as stroke, heart disease, diabetes, high blood pressure and other health complications alongside cognitive decline.

The progressive nature of neurovascular bundle disruption observed in the 5XFAD model parallels the clinical trajectory of Alzheimer's disease, raising the possibility that metabolic dysfunction may intensify as neurodegeneration advances. This temporal relationship warrants investigation in longitudinal clinical studies that track both cognitive and metabolic parameters throughout disease progression.

Therapeutic implications and research directions

"These insights open new avenues for research into how treating or preventing autonomic dysfunction might improve overall health outcomes for people with Alzheimer's," stated Wong and Sheng, pointing towards potential interventional strategies.

Several therapeutic approaches targeting autonomic function merit consideration based on these findings. Pharmacological enhancement of sympathetic signalling through beta-adrenergic agonists could potentially compensate for denervation-induced metabolic impairment. However, systemic sympathetic activation carries cardiovascular risks that would require careful risk-benefit assessment in elderly populations with pre-existing cardiac disease.

Alternative strategies might focus on preserving or restoring neurovascular architecture before extensive degeneration occurs. Neurotrophic factors, anti-inflammatory agents or vascular protective compounds could theoretically maintain the structural integrity of adipose tissue innervation. Such interventions would likely require initiation during prodromal disease stages to prevent irreversible neural loss.

The findings also suggest that metabolic biomarkers related to adipose tissue function, such as adipokine profiles or measures of lipolytic capacity, might serve as peripheral indicators of autonomic dysfunction in Alzheimer's disease. Such markers could potentially aid in early detection or monitoring of disease progression through minimally invasive sampling.

Methodological advances enable discovery

The study's success depended critically on technical innovations in tissue preparation and imaging. Whole-mount immunostaining of adipose tissue presents substantial challenges due to the tissue's high lipid content and three-dimensional complexity. The research team adapted previously published protocols to achieve adequate antibody penetration and optical clearing whilst preserving structural relationships between cellular and extracellular components.

High-resolution confocal microscopy with 20X objectives enabled capture of neurovascular architecture across millimetre-scale tissue volumes with micron-level resolution. The resulting three-dimensional datasets permitted quantitative analysis of nerve-vessel spatial relationships and structural integrity that would be impossible to assess through conventional two-dimensional histological sections.

These methodological advances open opportunities for broader investigation of adipose tissue innervation in various metabolic and neurological disorders, potentially revealing common or distinct patterns of neurovascular disruption across disease states.

Future research priorities

The Houston Methodist study establishes a foundation for multiple lines of investigation. Mechanistic studies are needed to determine whether adipose tissue denervation results from direct Alzheimer's pathology affecting peripheral sympathetic neurons, from loss of central autonomic regulation due to brain neurodegeneration, or from systemic factors such as inflammation or vascular dysfunction.

Translation to human subjects represents another critical priority. Post-mortem examination of adipose tissue from Alzheimer's patients could confirm whether similar neurovascular disruption occurs in human disease. Advanced imaging techniques, including positron emission tomography with tracers for sympathetic innervation, might enable assessment of adipose denervation in living patients.

Reference:
Kwong, M., Sheng, J., Yang, L., & Wong, S. T. C. (2025). Alzheimer's disease disrupts intra-adipose neurovascular contact. *Journal of Lipid Research*, 66(10), 100886. https://doi.org/10.1016/j.jlr.2025.100886

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Polar physical changes pose significant global health threats beyond melting ice

Researchers present a comprehensive framework linking Arctic and Antarctic transformations to worldwide disease burden, from vector-borne illnesses to cardiovascular mortality, urging urgent interdisciplinary action to integrate polar tipping points into health impact assessments and clinical preparedness strategies.

Climate change in Earth's polar regions represents an underexplored yet critical driver of global health risks, with cascading effects extending far beyond the Arctic and Antarctic, according to new research published in *Ambio*.

An international team led by Professor Gail Whiteman from the University of Exeter Business School has developed a novel conceptual framework mapping pathways through which polar physical changes amplify health risks. Their scoping review of 89 peer-reviewed studies reveals that current climate models systematically underestimate health consequences of polar transformations.

"Polar change is not a distant crisis," said Netra Naik, research fellow at Arctic Basecamp and lead author. "Our review of the research shows that melting ice sheets, rising sea levels and shifting weather patterns have complex consequences that extend far beyond the Arctic and Antarctic – affecting food security, disease burden and health infrastructure."

Cardiovascular and renal disease burden escalating

The Arctic is warming at approximately four times the global average. The authors note this warming may contribute to increased frequency of severe El Niño episodes, worsening heatwaves especially across tropical areas. Cardiovascular mortality increases by 2.1% per 1°C rise, equating to approximately 376,000 additional deaths worldwide. Heat stress nephropathy, a form of chronic kidney disease from repeated heat exposure, emerges as a global concern.

In 2023, extreme heat contributed to a 167% surge in heat-related deaths amongst people over 65. Each 1°C mean temperature increase associates with 1% rise in early-term births, approximately 134,000 additional preterm births worldwide.

Sea level rise contaminating water supplies

By 2050, 41 nations are projected to experience inland saltwater intrusion extending at least 1 kilometre. "This salinity rise has also been linked to a range of health challenges, notably pregnancy complications such as pre-eclampsia and postpartum infant morbidity," the authors write. Rising sea levels increase salt concentration in aquifers, causing arsenic release into water supplies, thereby increasing cancer likelihood.

Vector-borne diseases expanding into new territories

Polar warming fundamentally alters disease ecology globally. Warmer temperatures enable vectors to thrive in new regions, driving malaria to higher altitudes in Colombia and Ethiopia, and facilitating outbreaks of dengue, chikungunya, Japanese encephalitis and West Nile virus. By 2050, dengue is projected to expand into Amsterdam, Berlin, London and Stockholm.

Milder winters followed by cold snaps with reduced snow cover in subarctic Finland and Sweden lead to increased nephropathia epidemica outbreaks, a hantavirus infection causing fever, kidney dysfunction and flu-like symptoms.

Arctic communities face compounded threats

Arctic populations, approximately 4 million people of whom 10% are Indigenous groups, already face high rates of chronic conditions and food insecurity. Permafrost thaw releases harmful biological, chemical including mercury and radioactive substances, contaminating water, soil and food chains. Communities dependent on marine mammals face heightened risks including neurological disorders, cognitive dysfunctions and immune impairments.

Permafrost thaw may release dormant viruses including the 1918 influenza virus and Anthrax spores. Ocean warming and acidification challenge key species such as oysters, clams and fish, reducing food provision whilst negatively affecting mental health.

Extreme weather amplifying disease transmission

Arctic warming weakens the jet stream, causing prolonged extreme weather. Flooding contaminates water sources, increasing cholera, *Vibrio vulnificus* infections and leptospirosis. Flooding caused over 100,000 pregnancy losses annually across 33 countries from 2010 to 2020. Arctic wildfire frequency tripled from 2001–2010 to 2011–2020, releasing particulate matter contributing to 25,000–55,000 premature deaths annually.

Rising temperatures beyond 3°C link to anxiety, depression and suicide increases, with 2% increase in mental health problems associated with cumulative 1°C temperature rise over five years. Displacement disrupts cultural practices amongst Indigenous populations, leading to anxiety, depression and identity loss.

Urgent call for interdisciplinary collaboration

"Ignoring these potential drivers of disease and death is not an option," said Professor Whiteman. "We need stronger international collaboration between climate scientists, health professionals, and data experts to prevent harm and prepare our systems for the challenges ahead."

The study forms part of the "Effects of Polar Climate Change on Global Health and Healthcare" project, conducted by the University of Exeter, Arctic Basecamp and the World Economic Forum, funded by the Wellcome Trust.

Reference:
Naik, N., Bot, K., Whiteman, G., et. al (2025). A framework for assessing global health impacts of polar change: An urgent call for interdisciplinary research. *Ambio*. https://doi.org/10.1007/s13280-025-02255-0
Published online: 7 November 2025

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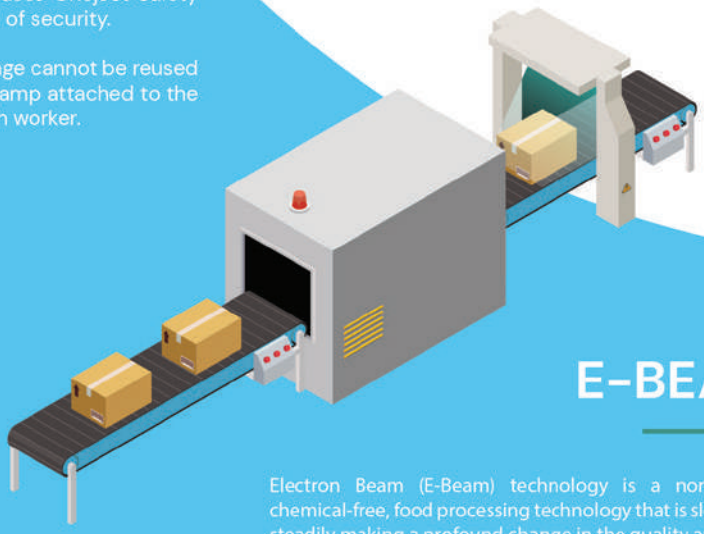

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