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# Type 2 Diabetes

## Novel treatment stops insulin dependency

## Alzheimer's Warning

Biomarkers alone not sufficient for diagnosis

## World First

KFSHRC surgeons perform fully robotic left-at-right liver transplant

### In the News

- Cleveland Clinic Abu Dhabi launches renal denervation therapy
- Viatris partners with NYU Abu Dhabi to advance NCD research
- Abu Dhabi DoH designates Sheikh Shakhbout Medical City as Centre of Excellence for Burn Treatments
- In collaboration with KSA, WHO expands digital health cards for Hajj pilgrims
- Egypt achieves WHO malaria-free certification

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# Prognosis

## Aggressive interventions in diabetes treatment

The mounting global burden of type 2 diabetes continues to challenge healthcare systems worldwide, affecting approximately 422 million individuals, according to the World Health Organization. As obesity rates climb and populations age, the relationship between lifestyle factors and metabolic disease demands increasingly sophisticated therapeutic approaches.

Recent developments in diabetes management illustrate a marked shift towards more aggressive interventions, particularly when conventional treatments prove insufficient. The emergence of dual-therapy approaches, such as the combination of endoscopic duodenal ablation with semaglutide administration, demonstrates promising outcomes in insulin-dependent patients. Research presented at UEG Week 2024 showed that this novel approach achieved insulin independence in 86% of participants over two years, potentially revolutionising treatment for those requiring daily insulin therapy.

Particularly noteworthy is the growing evidence supporting early intervention in metabolic disease. Recent findings from the Teen-LABS study reveal that bariatric surgery in adolescents achieves superior outcomes compared to adult interventions, with diabetes remission rates of 55% at ten years post-surgery – significantly higher than the 12-18% observed in adult cohorts. These findings challenge our traditional, conservative approach to metabolic surgery in younger patients.

These developments underscore a crucial paradigm shift in our understanding of lifestyle diseases: timing matters. The superior outcomes observed in early interventions suggest that the traditional 'wait-and-see' approach may need reconsideration. Furthermore, the emergence of minimally invasive techniques like ReCET offers new possibilities for disease modification rather than mere management.

As our therapeutic arsenal expands, the focus must remain on developing strategies that address the root causes of metabolic dysfunction whilst considering patient compliance and quality of life. The challenge ahead lies in translating these promising interventions into widely accessible treatment options whilst maintaining our commitment to evidence-based practice.

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# Cleveland Clinic Abu Dhabi launches renal denervation therapy

Medical specialists at Cleveland Clinic Abu Dhabi have introduced renal denervation therapy, a minimally invasive procedure aimed at treating patients with resistant hypertension who have not responded to conventional treatments.

The catheter-based intervention employs radiofrequency or ultrasound energy to target and disrupt overactive nerves surrounding the renal arteries. These nerves, which play a crucial role in blood pressure regulation, are accessed through a small groin incision under fluoroscopic guidance. The procedure is performed under local anaesthesia and typically requires only a one-day hospital stay.

## Patient selection and therapeutic context

Dr Ronney Shantouf, Staff Physician in Cardiovascular Medicine at the hospital's Heart, Vascular & Thoracic Institute, highlighted the significance of identifying suitable candidates: "We frequently see patients whose surgical procedures are delayed due to uncontrolled high blood pressure. This procedure provides added therapeutic option for patients not responding to medical therapy."

The treatment's efficacy stems from its precise targeting of sympathetic nerve fibres that contribute to blood pressure regulation. Dr Ashraf M. Azzoni, Staff Physician in Cardiovascular Medicine, explained: "This technology allows us to address one of the underlying causes of high blood pressure that conventional treatments may struggle to manage."

## Healthcare delivery implications

The introduction of this procedure represents a significant addition to the cardiovascular treatment options available in the UAE region. The hospital employs a multidisciplinary approach, combining the expertise of interventional cardiologists, vascular surgeons, and anaesthesia specialists to deliver comprehensive care.

Dr George Haber, CEO of Cleveland Clinic Abu Dhabi, emphasised the broader implications: "This procedure marks a major advancement in our cardiovascular care, reinforcing our shared mission to drive innovation and implement tech-enabled health solutions that are transforming the traditional healthcare landscape."

The therapy's implementation is particularly relevant given the World Health Organization's identification of hypertension as a major contributor to premature mortality globally. Patients typically observe improvements in blood pressure control over several months post-procedure, potentially reducing their risk of serious cardiovascular complications such as stroke and heart attack.

The procedure is now available at Cleveland Clinic Abu Dhabi's Heart, Vascular & Thoracic Institute, which operates as part of the M42 group, providing local access to advanced cardiovascular care for patients in the UAE and surrounding regions. MEH


Fahad Bin Dayel, Applications & Health informatics Director, KFSHRC (centre) receives the KLAS Research award.

## Innovation in genomics and nursing informatics earns KFSHRC global recognition

King Faisal Specialist Hospital & Research Centre (KFSHRC) has demonstrated its technological prowess by securing both first and second positions at the 2024 Gartner Eye on Innovation Award for healthcare and life sciences, emerging victorious from a field of 2,700 entries.

The hospital's primary award-winning initiative focuses on implementing pharmacogenomics for personalised medicine delivery, marking a significant advancement in point-of-care treatment optimisation. This programme aims to expand across all medical specialties, enabling treatment protocols tailored to individual genetic profiles.

In parallel, KFSHRC's second award recognised their innovative 3D printing programme, which has enhanced pre-surgical planning capabilities and facilitated the production of bespoke prosthetics. The initiative extends beyond direct patient care, incorporating educational models for medical devices and anatomical representations for surgical simulation.

### Electronic health records transform nursing practice

Further cementing its position at the forefront of healthcare technology, KFSHRC has also received recognition from KLAS Research for its electronic health records (EHR) implementation. The institution secured both the EHR Pinnacle Award for Nurses and the EHR Experience Breakthrough Award, distinguishing itself among 300 healthcare organisations.

The EHR advancement has yielded substantial improvements in nursing satisfaction scores, with KFSHRC being one of only 14 institutions to achieve this level of excellence.

These achievements align with KFSHRC's broader success in international rankings, where it maintains its position as the leading academic medical centre in the Middle East and Africa, ranking 20th globally among the top 250 academic medical centres. The institution has also been recognised as the most valuable healthcare brand in the Middle East according to the 2024 Brand Finance rankings.

The combination of awards reflects a comprehensive approach to healthcare innovation, encompassing genetic medicine and digital health systems. This technological integration aims to enhance both operational efficiency and patient outcomes, while simultaneously supporting medical education and professional development. MEH

## Viatris partners with NYU Abu Dhabi to advance NCD research

Healthcare in Abu Dhabi's is set to benefit from a new collaborative partnership between global healthcare company Viatris and New York University Abu Dhabi (NYUAD), focusing on non-communicable diseases (NCDs). The partnership, announced during the HEAL "Health for All" Conference 2024, aims to enhance research capabilities and improve patient outcomes in the United Arab Emirates.

### Data driven approach strengthens evidence base

The collaboration will leverage the UAE Healthy Future Study's research infrastructure to generate real-world evidence and enhance understanding of NCDs among the Emirati population. This partnership marks a significant step towards building a comprehensive research framework that combines academic expertise with pharmaceutical industry experience.

Commenting on the initiative, Dr Lobna Salem, Chief Medical Officer of Viatris, said: "Our partnership with NYUAD underscores the importance of enhancing global research capabilities. Together, we are advancing the UAE Healthy Future Study, which seeks to provide vital insights into the health of Emiratis."

The memorandum of understanding between the two organisations encompasses several key areas, including real-world analysis, health data dissemination, and digital research capabilities. The partnership will also focus on developing training programmes in research ethics, data analysis, and scientific writing.

NYUAD's Public Health Research Center will play a crucial role in generating evidence-based research in collaboration with other UAE institutions. This research is expected to inform clinical practice recommendations and contribute to the development of targeted healthcare interventions.

Arlie Petters from NYU Abu Dhabi highlighted the potential impact of this collaboration: "This partnership with Viatris represents an important step in our ongoing efforts to address critical public health challenges, particularly in the realm of non-communicable diseases. By combining our academic expertise with Viatris' global healthcare perspective, we are poised to generate meaningful insights and contribute to building a healthier future for the UAE."

The partnership aligns with the UAE's national health agenda and its vision to establish a world-class health system. According to Ayman Mokhtar, regional head of MENA and Eurasia at Viatris, the company's local footprint and partnerships in the UAE demonstrate their commitment to supporting improved patient outcomes through collaboration with leading institutions.

This initiative represents a significant step forward in addressing the growing burden of NCDs in the UAE through evidence-based research and educational initiatives, while fostering the development of local healthcare expertise. MEH


## KFSHRC teams perform world's first robotic left-at-right liver transplant

Surgical teams at King Faisal Specialist Hospital and Research Centre (KFSHRC) have achieved a significant breakthrough in transplant surgery by successfully performing the world's first non-identical, fully robotic liver transplant using a living donor left-lobe graft. This innovative approach represents a substantial advancement in robotic transplant surgery, potentially broadening access to life-saving procedures for patients previously considered unsuitable candidates.

### Technical innovation creates new possibilities

The surgical milestone involved transplanting left-lobe grafts into the right hepatic fossa of two patients using the Da Vinci Xi robotic system. This departure from traditional right-lobe transplantation techniques demonstrates the versatility of robotic surgery in addressing complex anatomical challenges. The procedure was successfully performed on two female patients: a 26-year-old with end-stage liver disease caused by Autoimmune Hepatitis and a 48-year-old diagnosed with Primary Biliary Cirrhosis.

The innovative technique yielded impressive clinical results, with both cases reporting optimal blood flow patterns and minimal blood loss. The confined intraabdominal space, which typically presents significant challenges in traditional transplant surgery, was effectively managed through the enhanced precision and visualisation capabilities of the robotic system. Post-operative recovery was notably efficient, with patients requiring only 2-4 days of intensive care unit monitoring.

### Building on established expertise

This achievement builds upon KFSHRC's growing reputation in robotic surgery. The centre previously made headlines in 2023 by performing the world's first fully robotic liver transplant, subsequently completing 29 such procedures. Their expertise in robotic surgery was further demonstrated in 2024 with the world's first fully robotic heart transplant.

The centre's commitment to surgical innovation is reflected in its recent rankings, securing the top position in the Middle East and Africa and 20th globally among Academic Medical Centres. KFSHRC has also been recognised as the most valuable healthcare brand in the Kingdom and the Middle East according to the 2024 Brand Finance rankings.

This surgical breakthrough represents a significant evolution in transplant medicine, potentially offering new hope to patients who previously had limited options. The success of these procedures suggests that robotic left-at-right liver transplantation could become an important addition to the transplant surgeon's arsenal, particularly in cases where traditional approaches may be contraindicated. MEH

## Abu Dhabi DoH designates Sheikh Shakhbout Medical City as Centre of Excellence for Burn Treatments

Abu Dhabi's largest tertiary hospital, Sheikh Shakhbout Medical City (SSMC), has been designated as a Centre of Excellence for Burn Treatments by the Department of Health – Abu Dhabi (DoH), marking a significant advancement in specialised burn care services in the emirate.

### Advanced treatment capabilities enhance patient care

The newly designated centre houses a state-of-the-art facility featuring 20 ICU beds and a dedicated operating theatre. The centre employs advanced technologies, including allograft skin and biodegradable temporising matrix (BTM), for comprehensive burn management. The BTM technique enables surgeons to remove damaged tissue whilst promoting neovascularisation and collagen production, potentially improving patient outcomes.

In addition to clinical services, the centre has established itself as a hub for burn care education and research. The facility provides accredited continuing medical education programmes and advanced burn care training courses, whilst actively participating in research initiatives to enhance treatment protocols.

H.E. Dr. Noura Al Ghaithi, Undersecretary of the Department of Health – Abu Dhabi, said: "Being designated as a CoE enables healthcare facilities like SSMC to continuously improve, grow


## Dubai prepares to host landmark MedTech regulatory gathering

Senior regulatory experts from across the medical technology sector will gather in Dubai as the Middle East and African region strengthens its position in global healthcare innovation. In their first joint initiative, Mecomed and the Regulatory Affairs Professionals Society (RAPS) have announced the 2025 MEA MedTech Regulatory Summit, addressing critical challenges in medical device regulation. The summit, set for 30 January 2025 at voco Dubai, comes as regulatory systems worldwide adapt to match the pace of technological advancement.

The one-day summit aims to address crucial challenges facing the medical device industry, with particular emphasis on the impact of artificial intelligence and software on regulatory operations. The programme will explore regulatory developments across the Middle East, Africa, Europe and North America, offering attendees insights into evolving global regulatory strategies.

Mecomed's Chief Executive Officer, Rami Rajab, highlighted the region's growing significance: "The Middle East and Africa encompass a growing and diverse MedTech hub in the regulatory community, with rapidly expanding new business opportunities." He emphasised that as companies extend their global reach, there is an increased demand for educational resources and professional development to support growth whilst advancing patient care.

### Professional development meets strategic imperatives

The summit's timing coincides with a period of rapid transformation in medical device regulation. RAPS Executive Director Bill McMoil reinforced the event's strategic importance: "Together, we hope to curate an event that stimulates innovation and solutions for transformation across the region."

The planning committee comprises notable industry figures, including representatives from Boston Scientific Middle East, Edwards Life Sciences, Johnson & Johnson, and BSI, ensuring comprehensive coverage of regulatory challenges and opportunities.

The summit represents a significant step in addressing the complex regulatory requirements facing medical device manufacturers and distributors in the MEA region. It particularly focuses on regulatory reliance implementation, a crucial aspect for companies navigating multiple jurisdictional requirements.

This collaborative initiative between Mecomed, representing medical devices, imaging and diagnostics manufacturers across the Middle East and Africa, and RAPS, the largest global organisation of healthcare product regulatory professionals, demonstrates the industry's commitment to advancing regulatory excellence in the region.

The complete programme agenda and speaker lineup are expected to be announced in the coming weeks, with registration currently open for interested participants. MEH

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and excel while being recognised for their exceptional efforts in providing quality care to patients and community members."

The Centre of Excellence designation follows DoH's comprehensive evaluation framework, which assessed six key indicators: clinical outcomes, patient experience, safety and quality metrics, staff competency, medical education, and research capabilities. Healthcare facilities must meet minimum standard requirements and demonstrate exceptional performance across these domains to achieve the designation.

Dr Marwan Al Kaabi, Acting Chief Executive Officer at SSMC, noted: "The SSMC Burns Centre boasts advanced facilities and infrastructure, a team of multidisciplinary experts, and the provision of the latest effective treatments for severe and complex burns using advanced techniques in skin grafting and membrane restoration."

The centre's multidisciplinary approach encompasses emergency response, acute care, and rehabilitation services. This comprehensive care model aims to support patients throughout their treatment journey, from initial consultation to long-term recovery.

The designation reinforces Abu Dhabi's position in specialist healthcare provision and ensures that complex burn cases in the region have access to evidence-based, multidisciplinary care. The centre's commitment to research, education, and clinical excellence aligns with DoH's broader strategy to enhance healthcare standards across the emirate. MEH

# worldwide monitor

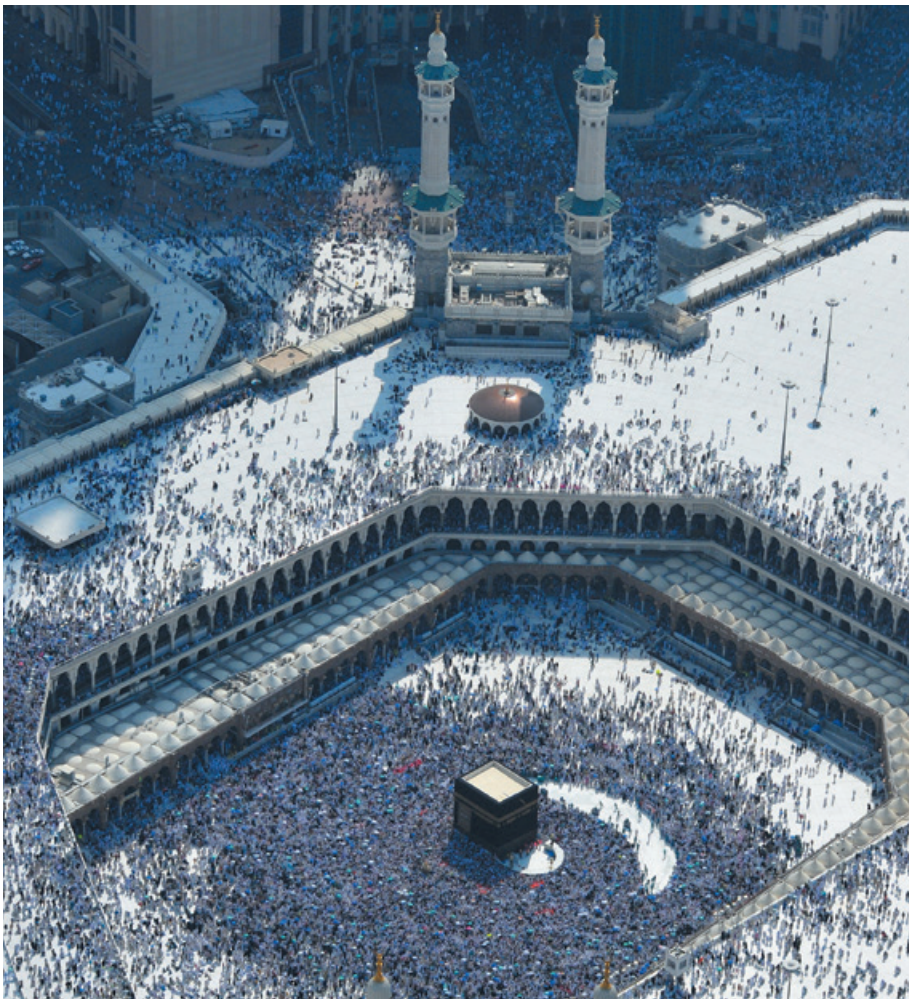
Update from around the globe

## In collaboration with KSA, WHO expands digital health cards for Hajj pilgrims

The World Health Organization (WHO) has broadened its digital health certification initiative for Hajj pilgrims through a new collaboration with Saudi Arabia. The programme aims to support approximately three million annual pilgrims by providing them with digital health cards containing essential medical information.

Following a successful pilot involving 250,000 pilgrims from Indonesia, Malaysia, and Oman in 2024, the initiative is now set to expand. The digital health cards, which operate on WHO's Global Digital Health Certification Network (GDHCN), contain crucial health data including medication requirements, allergies, immunisation records, and pre-existing conditions.

Commenting on the development, Dr Jeremy Farrar, WHO Chief Scientist, said: "Today marks a notable progress in WHO's support to Member States to expand access to safer and person-centred digital health tools for people to improve their access to quality health care when and where they need it."



### Technical infrastructure supports cross-border healthcare

The GDHCN, launched in 2023, employs public key infrastructure encryption to ensure the security and verifiability of health credentials across borders. The system, which originally supported COVID-19 vaccination certificates, now encompasses more than 80 WHO Member States and utilises the International Patient Summary (IPS) ISO standard.

The Saudi Government, along with their digital implementation partner LEAN, provides technical support and data security expertise to countries joining the programme. This collaboration enables participating nations to issue their own national versions of the health card whilst maintaining global standardisation.

### Regional impact and future applications

Dr Hanan Balkhy, WHO Regional Director for the Eastern Mediterranean, highlighted the broader implications: "This exciting partnership between the Kingdom of Saudi Arabia and the World Health Organization to expand the Hajj health card initiative enhances the safety and well-being of millions of pilgrims."

The system's architecture allows for potential future applications beyond pilgrim healthcare. The infrastructure could support cross-border electronic prescriptions, insurance verification, and telemedicine services. Additionally, the standardised approach reduces administrative burden at border controls whilst improving the quality of healthcare delivery.

The digital health card system prioritises individual privacy and patient autonomy. Pilgrims maintain control over their health information, choosing which details to share with authorised healthcare providers. This approach ensures that whilst healthcare providers can access necessary medical information, patient confidentiality is preserved.

The initiative represents a significant step toward standardised international health documentation, particularly beneficial for mass gatherings such as the Hajj, which attracts pilgrims from over 180 countries annually. The system's successful implementation during the pilot phase demonstrates the feasibility of large-scale digital health certification whilst maintaining security and accessibility standards. MEH

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## Egypt achieves WHO malaria-free certification

The World Health Organization (WHO) has certified Egypt as malaria-free, marking a significant public health achievement for the nation of 100 million people. This certification, announced on 20 October 2024, follows nearly a century of sustained efforts to eliminate a disease that has been endemic since ancient times, with genetic evidence found in Egyptian mummies including Tutankhamun.

### The value of sustained intervention

The path to elimination began in the 1920s when Egypt implemented initial vector control measures, including prohibiting rice cultivation near residential areas. A critical moment came in 1930 when malaria was designated a notifiable disease, leading to the establishment of the country's first malaria control station focused on diagnosis, treatment and surveillance.

The country faced significant challenges during its eradication journey. In 1942, cases surged to over 3 million due to multiple factors, including population displacement during World War II and the invasion of Anopheles arabiensis, a highly efficient mosquito vector. Egypt responded by establishing 16 treatment divisions and deploying more than 4,000 health workers.

Dr Tedros Adhanom Ghebreyesus, the WHO Director-General, noted the historic nature of the achievement: "Malaria is as old as Egyptian civilization itself, but the disease that plagued pharaohs now belongs to its history and not its future."

### Sustained vigilance essential for maintaining status

Egypt's certification required proving the interruption of indigenous malaria transmission nationwide for at least three consecutive years, alongside demonstrating capacity to prevent re-establishment. The country maintains free malaria diagnosis and treatment for all residents regardless of legal status, whilst training healthcare professionals nationwide in case detection and screening, including at border points.

Egypt becomes the third country in the WHO Eastern Mediterranean Region to achieve this status, following the United Arab Emirates and Morocco, and the first since 2010. Globally, 44 countries and one territory have achieved this certification.

Deputy Prime Minister Dr Khaled Abdel Ghaffar emphasised the need for continued vigilance: "Receiving the malaria elimination certificate today is not the end of the journey but the beginning of a new phase. We must now work tirelessly and vigilantly to sustain our achievement through maintaining the highest standards for surveillance, diagnosis and treatment, integrated vector management and sustaining our effective and rapid response to imported cases."

The success demonstrates the value of sustained public health interventions and cross-border collaboration, particularly with neighbouring Sudan, in achieving and maintaining disease elimination status. MEH

## Global tuberculosis cases hit record levels since WHO monitoring began

The World Health Organisation has reported an unprecedented surge in tuberculosis (TB) diagnoses, with 8.2 million new cases recorded in 2023, marking the highest figure since the organisation began tracking global TB cases in 1995. The disease has regained its position as the leading infectious disease killer, surpassing COVID-19.

### Funding shortfall hampers progress

The WHO's Global Tuberculosis Report 2024 <*https://bit.ly/3CaRZ75*> reveals a complex picture of both progress and persistent challenges. While TB-related mortality decreased from 1.32 million in 2022 to 1.25 million in 2023, the total disease burden increased to an estimated 10.8 million cases. The report highlights a significant geographical concentration, with five countries accounting for 56% of global cases: India (26%), Indonesia (10%), China (6.8%), the Philippines (6.8%), and Pakistan (6.3%).

The financial landscape remains particularly concerning, with available funding reaching only 26% of the targeted annual amount. Of the US$22 billion annual funding target, merely $5.7 billion was accessible in 2023. Low- and middle-income countries, which shoulder 98% of the TB burden, face the most severe funding constraints.

### Drug resistance presents ongoing challenge

The report identifies multidrug-resistant TB as a continuing public health crisis. Despite treatment success rates for multidrug-resistant or rifampicin-resistant TB reaching 68%, only 44% of the estimated 400,000 affected individuals received diagnosis and treatment in 2023.

WHO Director-General Dr Tedros Adhanom Ghebreyesus expressed frustration at the continuing impact of the disease: "The

fact that TB still kills and sickens so many people is an outrage, when we have the tools to prevent it, detect it and treat it."

### Research funding crisis deepens

The research sector faces significant underfunding, receiving only one-fifth of its $5 billion annual target in 2022. This deficit impedes the development of new diagnostics, drugs, and vaccines. The report also reveals that half of TB-affected households in low- and middle-income countries face catastrophic costs, exceeding 20% of their annual household income, for diagnosis and treatment.

Dr Tereza Kasaeva, Director of WHO's Global Tuberculosis Programme, emphasised the multifaceted nature of the challenge: "We are confronted with a multitude of formidable challenges: funding shortfalls and catastrophic financial burden on those affected, climate change, conflict, migration and displacement, pandemics, and drug-resistant tuberculosis, a significant driver of antimicrobial resistance."

The report identifies five major risk factors driving new TB cases: undernutrition, HIV infection, alcohol use disorders, smoking (particularly among men), and diabetes. Men comprise 55% of TB cases, women 33%, and children and young adolescents 12%.

While the gap between estimated new TB cases and reported cases has narrowed to 2.7 million from the pandemic-era levels of approximately 4 million, significant work remains to achieve the global targets set for 2027. The WHO emphasises the urgent need for governments, global partners, and donors to transform their commitments from the 2023 UN High-Level Meeting on TB into concrete actions, particularly regarding increased funding for research and new TB vaccines. MEH

## Parliamentarians back WHO pandemic agreement at Berlin summit

Medical legislators and health policy makers have united to endorse the World Health Organization (WHO) Pandemic Agreement at the UNITE Global Summit in Berlin. The agreement, which aims to address gaps identified during the COVID-19 pandemic and recent mpox outbreaks, received formal parliamentary backing through a structured statement on 16 October 2024.

### Implementation strategy takes shape

The parliamentary endorsement outlines specific mechanisms for strengthening global health security, with emphasis on equitable access to medical resources during health emergencies. The framework specifically addresses vaccine distribution, treatment protocols, and medical supply chains, particularly for nations with limited healthcare infrastructure.

WHO Director-General Dr Tedros Adhanom Ghebreyesus highlighted the agreement's significance: "The WHO Pandemic Agreement represents a once-in-a-generation opportunity to build a stronger, fairer, and more prepared global health system." He emphasised the importance of ensuring equitable access to vaccines, treatments, and diagnostics across all nations.

### Resource allocation framework emerges

The agreement introduces concrete measures for pandemic preparedness and response, incorporating lessons learned from recent global health challenges. Central to the framework is the establishment of systematic approaches to resource distribution, particularly focusing on nations with constrained healthcare capabilities.

UNITE President Ricardo Baptista Leite stressed the critical role of parliamentary representatives: "Parliamentarians are the voice of the people and have a crucial responsibility in safeguarding public health." He further noted: "The challenges we face today demand a global response. No single country can prevent or combat pandemics alone."

The parliamentary statement delineates four primary commitments: ensuring equitable distribution of pandemic-related medical resources, fostering international cooperation for robust health systems, facilitating legislative implementation of the agreement, and addressing medical misinformation through evidence-based communication.

### Scientific communication strategy develops

The framework specifically addresses the challenge of medical misinformation, incorporating mechanisms for disseminating evidence-based health information. This approach aims to enhance public health communication during future disease outbreaks, ensuring consistent messaging across different healthcare systems.

The summit, conducted in partnership with the World Health Summit, focused on critical health challenges across four domains: human rights and equitable health access, global health architecture and security, healthcare system reinforcement, and sustainable health financing.

Moving forward, parliamentarians will collaborate with WHO and international health organisations to implement the agreement's provisions. The focus remains on developing sustainable financing mechanisms, advancing research capabilities, and building capacity for rapid response to health emergencies. MEH

# the laboratory

## Medical research news from around the world

### Novel 3D navigation system enables multiple miniature robots to traverse blood vessel networks

Scientists have developed a magnetic control system that can independently guide multiple miniature robots through complex three-dimensional vessel networks, potentially enabling simultaneous treatment of multiple disease sites within the body.

Blood vessels inside a brain

Researchers at the Max Planck Institute for Intelligent Systems (MPI-IS) in Stuttgart have created a robotic system capable of deploying and controlling multiple five-millimetre-sized robots within a three-dimensional matrix that mimics blood vessels. The innovation, published in *Science Advances* on 6 November 2024, represents a significant step forward in the field of minimally invasive medical procedures.

#### Clinical implications for stroke treatment

The development holds particular promise for conditions such as stroke, where multiple blocked blood vessels can simultaneously deprive different brain regions of oxygen, leading to rapid cellular damage. Current treatment approaches often struggle with addressing multiple affected sites quickly enough to prevent permanent neurological damage.

The system's ability to deploy several robots simultaneously could substantially reduce procedure times in such critical scenarios. Each magnetic robot, designed in the form of a stent, can flexibly adapt to changes in vessel structure while carrying out functions such as drug delivery or flow diversion.

#### Technical advancement in magnetic control

The research team has overcome a fundamental challenge in magnetic robot control: the ability to manipulate multiple magnetic objects independently within the same magnetic field. "To our knowledge, this is the first case of independent control of more than five robots in 3D lumens under physiologically relevant conditions," says Chunxiang Wang, a PhD student at MPI-IS and first author of the study.

The system employs a rotating permanent magnet with specifically designed influence and rotation regions to enhance usability. By carefully positioning the magnet, operators can selectively activate or deactivate specific robots. The control system has been designed with clinical practicality in mind, featuring an automated path-planning algorithm that allows users to simply input target points, with a robotic arm handling the complex navigation calculations.

"For us it was quite a challenge to control multiple magnetic robots all at once – after all, all magnetic parts are affected by the magnetic field in the same way," explains Tianlu Wang, former postdoctoral researcher at MPI-IS and currently Assistant Professor at the University of Hawaii at Mānoa.

#### Future applications

According to Metin Sitti, former Director of the Physical Intelligence Department at MPI-IS and President at Koç University: "The proposed system has the potential to open avenues for a wide range of biomedical applications by deploying a group of soft robots equipped with diverse functional modules to reach hard-to-access areas deep inside the human body for targeted therapy".

The technology could particularly benefit procedures requiring simultaneous intervention at multiple sites, such as complex vascular conditions or distributed drug delivery requirements. The system's ability to navigate through tortuous vessels while maintaining precise control over multiple robots represents a significant advancement in minimally invasive therapeutic approaches. MEH

**Reference:**

Wang, C., Wang, T., Li, M., et. al. (2024). Heterogeneous multiple soft millirobots in three-dimensional lumens. *Science Advances*. https://doi.org/10.1126/sciadv.adq1951

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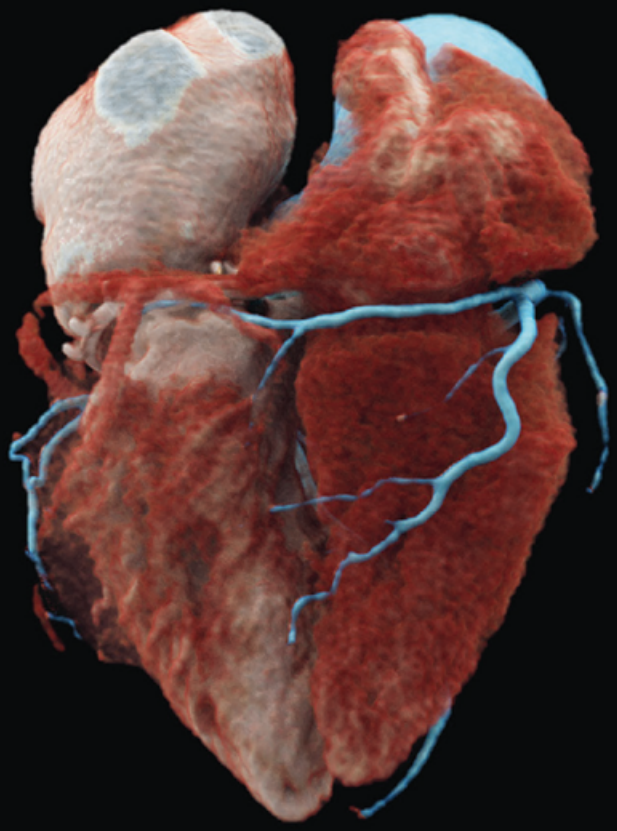

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## Critical flaws found in AI genomic analysis methods

Researchers at the University of Wisconsin-Madison have identified substantial methodological concerns in AI-assisted genome-wide association studies, highlighting risks of false positives and misleading correlations when artificial intelligence is used to bridge data gaps.

A comprehensive analysis by researchers at the University of Wisconsin-Madison's Department of Biostatistics and Medical Informatics has revealed significant methodological flaws in the growing practice of using artificial intelligence to supplement genome-wide association studies (GWAS). The findings, published in *Nature Genetics*[1], demonstrate how AI tools can generate misleading conclusions about genetic associations with disease risk factors.

### Statistical validity under scrutiny

The investigation, led by Associate Professor Qiongshi Lu, identified that machine learning algorithms commonly employed in GWAS can erroneously establish links between genetic variations and disease risks. A particularly concerning example emerged in the analysis of Type 2 diabetes risk factors, where the AI system produced multiple false positive correlations.

"The problem is if you trust the machine learning-predicted diabetes risk as the actual risk, you would think all those genetic variations are correlated with actual diabetes even though they aren't," explains Lu, highlighting the fundamental issue with current approaches.

Large-scale genomic research often relies on extensive databases such as the NIH's All of Us project and the UK Biobank. However, these resources frequently lack complete data sets for specific health conditions, leading researchers to employ AI tools to fill these gaps. The practice has gained significant traction in recent years as advances in machine learning have made such predictions seem more feasible.

### Novel solution proposed

The Wisconsin team has developed a new statistical method designed to enhance the reliability of AI-assisted GWAS. This approach specifically targets the removal of bias introduced by machine learning algorithms when working with incomplete data sets. The researchers have successfully applied this method to improve the accuracy of genetic associations with bone mineral density.

In a parallel study also published in *Nature Genetics* [2], Lu's team identified additional problems with GWAS that utilise proxy information rather than direct data. The research revealed particularly problematic results in studies of late-onset conditions such as neurodegenerative diseases, where family health history surveys are often used as proxy data sources.

### Scale amplifies bias

The increasing scale of genomic research presents its own challenges. "These days, genomic scientists routinely work with biobank datasets that have hundreds of thousands of individuals, however, as statistical power goes up, biases and the probability of errors are also amplified in these massive datasets,"

> The problem is if you trust the machine learning-predicted diabetes risk as the actual risk, you would think all those genetic variations are correlated with actual diabetes even though they aren't.

Lu notes, emphasising the critical importance of maintaining statistical rigour in large-scale genomic research

The findings serve as a crucial reminder of the need for careful methodology in genetic research, particularly as AI tools become more prevalent in scientific analysis. The studies suggest that while artificial intelligence may offer powerful analytical capabilities, its application must be tempered with robust statistical validation methods to ensure accurate results.


**References:**

1. Miao, J., Wu, Y., Sun, Z. et al. Valid inference for machine learning-assisted genome-wide association studies. *Nat Genet* (2024). https://doi.org/10.1038/s41588-024-01934-0

2. Wu, Y., Sun, Z., Zheng, Q. et al. Pervasive biases in proxy genome-wide association studies based on parental history of Alzheimer's disease. *Nat Genet* (2024). https://doi.org/10.1038/s41588-024-01963-9

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## New high-sensitivity troponin test shows promise for early heart attack rule-out

Research conducted at a major US trauma centre demonstrates that a novel high-sensitivity cardiac troponin I assay could enable earlier discharge of patients presenting with suspected acute coronary syndrome, potentially reducing emergency department burden.

A comprehensive study conducted at Hennepin County Medical Center in Minneapolis has evaluated a new high-sensitivity cardiac troponin I assay developed by health technology company Mindray. The research, which focused on more than 1,500 patients presenting with symptoms suggestive of acute coronary syndrome, assessed the assay's capability to facilitate early rule-out protocols in emergency department settings.

### Clinical implications

The findings suggest that approximately 60% of patients presenting with symptoms indicative of acute coronary syndrome could potentially be safely discharged, with many suitable for early rule-out. The study demonstrated that 15% of early presenters could be ruled out based on a single blood test upon hospital arrival, representing a significant advancement in rapid triage capabilities.

### Technical performance

The assay demonstrated high precision and sensitivity across both male and female cohorts. When implementing a traditional two-hour serial testing protocol, researchers found that an additional 30-40% of remaining participants could be safely ruled out, with less than 1% probability of adverse events within a 30-day follow-up period.

Beyond its utility in ruling out acute coronary syndrome, the assay exhibited strong positive predictive characteristics. The research team reported a positive predictive value of approximately 70%, suggesting potential utility in identifying patients requiring immediate admission for suspected acute coronary syndrome.

Professor Fred Apple, the study's principal investigator and medical director in laboratory medicine at Hennepin Healthcare, contextualised the findings: "Our preliminary findings around Mindray's high-sensitivity troponin I test are exciting for emergency medicine — with multiple ways this could be built into algorithmic clinical practice to help avoid overcrowding and enhance triage safety."

He further elaborated on the assay's clinical utility: "Cardiac troponin alone doesn't determine if you have had a heart attack, but it can tell the clinician if the heart has been injured, and when measurements are normal that it is safe to send a patient home."

### Methodology and approval

The study, designated as MERITnI, received Institutional Review Board approval and was conducted alongside existing testing protocols. Standard hospital procedures were maintained throughout, with blood samples drawn for routine clinical practice being simultaneously evaluated using the Mindray high-sensitivity cardiac troponin I assay for research purposes.

The preliminary findings are currently undergoing peer review. Researchers have indicated plans to explore additional applications, including comparative studies of high-sensitivity cardiac troponin I and T assays. These investigations aim to enhance clinicians' ability to differentiate between chronic and acute myocardial injuries, potentially informing more targeted treatment strategies.

> Cardiac troponin alone doesn't determine if you have had a heart attack, but it can tell the clinician if the heart has been injured, and when measurements are normal that it is safe to send a patient home.

The assay's development followed Mindray's acquisition of Finnish company HyTest in 2021, where Professor Apple previously served as a board member. The technology represents a significant advancement in cardiac biomarker testing, with Professor Apple noting: "In 40 years of cardiac biomarker research, this assay is as good, if not better than any cardiac troponin assay I've worked with in my career."

The findings of this research are currently under peer review and are expected to be published in a forthcoming issue of a major cardiovascular journal. MEH

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## Novel 36-gene score predicts cancer treatment resistance

A new polygenic scoring system developed by researchers at the University of Alabama at Birmingham demonstrates superior efficacy in predicting resistance to anti-cancer treatments, particularly in breast cancer patients receiving tamoxifen therapy.

Research led by Professor Anindya Dutta at University of Alabama's (UAB) Department of Genetics has identified a set of 36 genes strongly associated with anti-cancer drug resistance, potentially offering clinicians a more reliable tool for predicting treatment outcomes and tailoring therapeutic approaches.

### Understanding treatment resistance

Cancer therapy resistance remains a significant challenge in oncology, with 50-80% of patients showing suboptimal response to treatment. This resistance contributes to the more than 600,000 cancer-related deaths annually in the United States, highlighting the critical need for better predictive tools in cancer treatment.

The research team's approach involved analysing established cancer cell databases, including the Genomics of Drug Sensitivity in Cancer (GDSC), Cancer Therapeutics Response Portal (CTRP), and the Catalogue of Somatic Mutations in Cancers (COSMIC). By examining 777 cancer cell lines present across these databases, the team identified crucial genetic markers of drug resistance.

### Development of the UAB36 score

The researchers developed a combined polygenic score, termed UAB36, incorporating the 36 genes most strongly associated with drug resistance. Among these, the FAM129B gene emerged as particularly significant, confirming previous experimental findings about its role in drug resistance mechanisms.

The UAB36 score demonstrated superior correlation with anti-cancer drug resistance compared to existing polygenic scores. This was particularly evident in predicting resistance to tamoxifen, a widely prescribed drug for breast cancer treatment.

### Clinical validation

The study's significance extends beyond laboratory findings, with the UAB36 score successfully predicting patient outcomes across three different cohorts of breast cancer patients receiving tamoxifen treatment. Patients with higher UAB36 scores showed poorer survival rates, independent of age and tumour stage, consistent with the score's prediction of increased tamoxifen resistance.

Notably, tumours with elevated UAB36 scores showed enrichment of gene sets associated with multiple drug resistance mechanisms, establishing the score as a potentially valuable biomarker for predicting both anti-cancer drug resistance and survival outcomes.

### What the future holds

While the findings suggest promising applications in personalised medicine, particularly in identifying patients at higher risk of tamoxifen resistance, the researchers emphasise the need for validation through prospective clinical trials.

"This approach should provide promising polygenic biomarkers for resistance in many cancer types against specific drugs and can be improved further by incorporating machine-learning methods in the analysis," says Professor Dutta.

UAB

Professor Anindya Dutta, University of Alabama Department of Genetics

This approach should provide promising polygenic biomarkers for resistance in many cancer types against specific drugs.

**Reference:**

Sahu, D., Rueda, I. A. S., Dutta, A., et. al (2024). Development of a polygenic score predicting drug resistance and patient outcome in breast cancer. *NPJ Precision Oncology*. https://doi.org/10.1038/s41698-024-00714-7

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# WCM-Q program promotes professionalism in medical education in a highly diverse culture

A symposium and webinar series offered by the Division of Continuing Professional Development at Weill Cornell Medicine-Qatar (WCM-Q) addressed the challenges associated with fostering professionalism in medical education in Qatar's highly diverse multicultural context.

The symposium, titled, Fostering Professionalism in Medical Education: Exploring Effective Approaches for Diverse Learners, featured a full day of interactive sessions led by highly experienced WCM-Q faculty and visiting experts from leading medical education institutions in Europe and the US. Sessions focused on identifying and defining the key attributes of professionalism, examining how conceptions of professionalism vary among different cultures, methodologies to assess professionalism, and discussions about how learners develop their professional identities through education and other experiences.

The sessions also explored how assessment data can be used to inform the professionalism remediation process and optimize coaching, and how to design and implement an appropriate remediation plan using coaching skills. The symposium, which was offered for the first time in June this year, is augmented by a regular webinar series on professionalism in diverse learning contexts.

The symposium was directed and presented by WCM-Q faculty members Dr. Amal Khidir, associate professor of pediatrics; Dr. Fatimah Isa, assistant professor of psychology teaching in medicine; Dr. Moune Jabre, assistant professor of clinical obstetrics and gynaecology; and Dr. Mange Manyama, assistant professor of anatomy in radiology.

International and Qatar-based speakers included Dr. Adina Kalet, Stephen and Shelagh Roell Endowed Chair at the Medical College of Wisconsin; Dr. Goran Stevanovski, health professions education consultant and the founder and former director of the Medical Education Department at Ss. Cyril and Methodius University, North Macedonia; Dr. Marianne Mak-van der Vossen, assistant professor of general practice at Amsterdam University Medical Center (UMC); and Dr. Majda Sebah, assistant professor of chemistry in pre-medical education at WCM-Q.

## Coaching model to help develop professionalism

Reflecting on the coaching model that can be used to help healthcare professionals develop professionalism and cultural awareness, Dr. Isa stressed that the aim was to empower healthcare professionals by equipping them with new skills. She said: "To develop and/or improve professionalism in diverse learning environments, it is essential that we reflect on how people from other cultures perceive our behaviour. Also, we need to consider various factors – it is not only about behaviour but also attitude, morals, values, and so on. For this session [at the symposium], I used a model rooted in the Schön reflection model with the humanistic approach and framed it to reflect some ICF (International Coaching Federation) core competencies. This approach empowers healthcare professionals to reflect, explore options, and formulate an action plan to achieve the desired results. The role of a coach is facilitating the process rather than instructing or directing them, and reflection is the key to this coaching process."

The symposium and webinar series were accredited locally by the Ministry of Public Health's Department of Healthcare Professions – Accreditation Section and internationally by the Accreditation Council for Continuing Medical Education (ACCME).

Dr. Manyama explained that professionalism in diverse learning environments is assessed through multiple dimensions that reflect cultural sensitivity and inclu-

Dr. Amal Khidir

Dr. Fatimah Isa

Dr. Mange Manyama

Dr. Moune Jabre

sive practices. "Some of the important aspects evaluated include communication skills, cultural competence, adaptability, collaboration abilities, ethical behaviour, ability to create an inclusive atmosphere, language sensitivity, conflict resolution skills, and receptivity to feedback from diverse sources," he said. "The evaluation process usually focuses on an individual's ability to interact respectfully with peers and instructors from various backgrounds, understand and respect diverse perspectives, adjust approaches based on different cultural contexts, work effectively in diverse teams, and adhere to ethical standards that consider cultural variations."

### Values, behaviours, and relationships

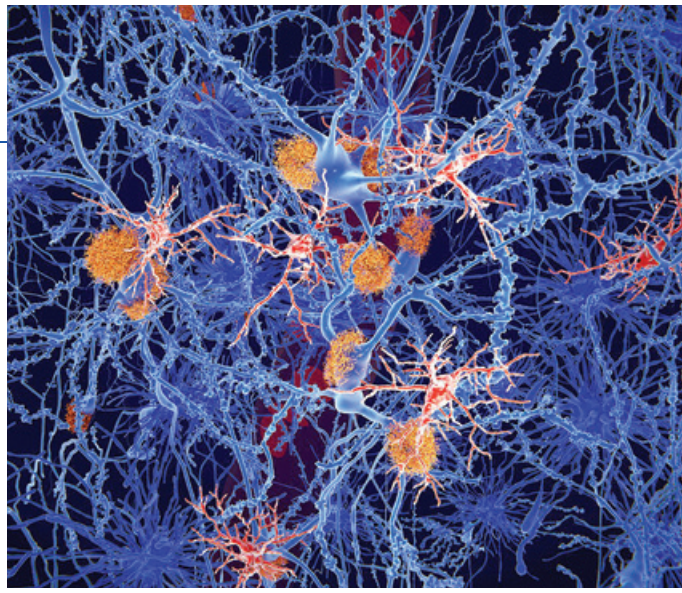
Dr. Jabre said: "Medical professionalism is a set of values, behaviours, and relationships centred on trust, integrity, and accountability, that prioritize patient welfare and societal well-being. It encompasses a commitment to ethical behaviour, compassion, and continuous self-assessment to adapt and grow.

"Clinical experiences, mentorship, and reflection, coupled with regular assessment, feedback and diverse, real-world learning opportunities, foster professional identity formation in trainee physicians. In this way, learners develop the skills necessary to navigate and contribute positively to increasingly multicultural academic and professional environments. Assessment methods may include peer evaluations, self-reflections, case studies, role-playing exercises, and observations of group interactions."

Another of the learning objectives of the program is equip the participants with the skills and knowledge to apply culturally adept coaching skills in interacting with learners. Dr. Khidir said: "The diverse learning environment includes learners, instructors, staff and patients from diverse cultural background; learners in such environment usually acquire humility and soft skills. Exposure to a variety of cultures, styles and professionals from different backgrounds supports the learner's professional identity formation, which is the process that leads to thinking, feeling and acting like a physician. The learner educated in a diverse environment will gain the ability to cope and handle patients from different cultures and backgrounds." MEH

> The role of a coach is facilitating the process rather than instructing or directing them, and reflection is the key to this coaching process.

# The perils of premature Alzheimer's diagnosis: Why biomarkers alone aren't enough



Microglia cells (red) play an important role in the pathogenesis of Alzheimer's disease. Microglia are specialised macrophages that restrain the accumulation of amyloid (orange plaques). 3D rendering.

**New international guidelines warn that relying solely on biological markers for diagnosing Alzheimer's Disease could lead to unnecessary diagnoses in healthy individuals, potentially causing unwarranted psychological distress to thousands of older adults.**

## The controversial path to diagnosis

In a laboratory at Geneva University Hospitals, Professor Giovanni Frisoni contemplates a concerning trend in Alzheimer's Disease (AD) diagnosis. "70% of people with positive biomarkers will never develop AD," he says. "Therefore, why give them this distressing diagnosis?"

This stark warning comes as part of new recommendations published 1 November 2024 in *JAMA Neurology* [1] by an international expert panel, challenging recent diagnostic criteria that would define AD purely through biological markers, without considering cognitive function.

The numbers tell a troubling tale. While only 3% of individuals aged 50-59 have positive biomarkers without clinical symptoms, this figure skyrockets to 40% in those aged 80-89. Under recently proposed American criteria, all these individuals would qualify for an AD diagnosis, despite most never developing cognitive impairment.

## Beyond biomarkers

Lead author Professor Bruno Dubois and colleagues argue that the approach of diagnosing AD without a clinical and biological construct would be "unwarranted and potentially concerning without a clear knowledge of when or whether symptoms will ever develop".

The research team emphasises that Alzheimer neuropathologic changes are necessary but not sufficient for establishing an AD diagnosis. "AD is a clinicopathological entity that should be disentangled from Alzheimer pathological changes, which are frequently observed in postmortem brains of aged individuals who died without any cognitive or functional decline," they write.

## The cancer analogy fallacy

The paper challenges a common argument that compares AD diagnosis to cancer screening. While some advocate for earliest possible diagnosis based on biomarkers alone, similar to in situ cancer detection, the authors argue this analogy fails in sporadic AD cases.

"The lifetime risk of AD dementia in a 65-year-old man who is amyloid-biomarker positive has been estimated at 21.9%, a mere 1.7 times higher than the risk of an individual of a similar age who is amyloid-biomarker negative," the researchers note, highlighting the stark difference from cancer's more predictable progression.

## A new pathway emerges

In response to these concerns, the panel has developed a more nuanced approach. They recommend categorising individuals with abnormal biomarkers into two distinct groups: those with abnormal memory tests who have AD, and those with normal cognitive function who merely have an increased risk of developing the disease.

This distinction is already shaping clinical practice. In Geneva, the Memory Center is pioneering a new patient journey for at-risk individuals, funded by the State of Geneva. Set to launch in early 2025, this comprehensive programme will evaluate all known risk factors, including biomarkers, depression, and social isolation.

## The complexity of diagnosis

The authors highlight the challenge of multiple pathologies, noting that "lesions of different pathological nature are frequently observed postmortem due to the high prevalence of comorbidities and to the synergy between pathologies". They warn that a biomarker-only approach could lead to multiple simultaneous diagnoses of different neurodegenerative diseases in cognitively normal individuals.

Professor Dubois and colleagues emphasise that "the clinical value and utility of these biomarkers or tests differ depending on the context, e.g., research or clinical settings, in which they are used". This distinction is crucial for appropriate patient care.

## The research imperative

The implications of this new categorisation extend beyond clinical practice. By creating better-stratified longitudinal cohorts, researchers hope to quantify the weight of each risk factor more accurately. This could pave the way for more personalised treatments, potentially combining lifestyle modifications, nutritional interventions such as probiotics, and anti-amyloid drugs.

## Societal impact and ethical considerations

The paper raises significant concerns about the societal implications of overdiagnosis. "The resulting psychological and societal consequences of being diagnosed with AD and never developing symptoms can be consequential," the authors warn. They particularly emphasise the risks as blood-based biomarkers become more accessible.

"Given the current availability of blood-based biomarkers for amyloid and tau, an explosion of cognitively normal persons who are labelled as having AD on a purely biological definition of the disease may be expected," they caution, highlighting the potential for increased societal pressure for preventive drug treatments.

### A balanced approach

This shift towards viewing AD as a clinical-biological construct rather than a purely biological entity represents a more balanced approach to diagnosis and treatment. The authors advocate for "Brain Health Services for the Prevention of Dementia" that would offer evaluation of risk, communication of risk, and risk-reduction interventions targeting modifiable factors.

### Looking to the future

The path forward requires careful navigation. The panel emphasises the need for well-designed, long-term observational studies to better understand progression risk in asymptomatic individuals. "The study of groups for whom this information is lacking (e.g., Black, Hispanic, and other ethnic minoritized groups and populations from low- and middle-income countries) is of utmost importance, as their dementia risk factors may differ," they note.

### The human element

Behind the scientific debate lies a profound human impact. The authors stress that diagnostic criteria for AD can have "far-reaching societal, political, organizational, and economic implications". Their recommendations aim to prevent unnecessary psychological distress while maintaining scientific rigour in diagnosis and treatment.

As we move forward in our understanding of Alzheimer's Disease, the challenge lies in balancing technological advances with clinical wisdom. The new recommendations provide a framework for achieving this balance, ensuring that the power of biomarker testing enhances rather than overshadows clinical judgment.

> Given the current availability of blood-based biomarkers for amyloid and tau, an explosion of cognitively normal persons who are labelled as having AD on a purely biological definition of the disease may be expected.

**Reference:**

1. Dubois B., Villain, N., Schneider, L., et. al. (2024). Alzheimer Disease as a Clinical-Biological Construct - An International Working Group Recommendation. *JAMA Neurology*. Published online November 1, 2024. doi: *https://doi.org/10.1001/jamaneurol.2024.3770*

# Portable high-resolution PET scanner could transform early Alzheimer's detection

**Weill Cornell Medicine researchers will develop a portable upright PET scanner that promises unprecedented spatial resolution for detecting early biomarkers of Alzheimer's disease.**

Weill Cornell Medicine researchers have secured a $6.2 million grant from the US National Institute on Aging to develop an innovative portable positron emission tomography (PET) scanner. The five-year project builds upon their groundbreaking Prism-PET technology, which demonstrated sub-millimetre resolution in preliminary phantom studies published in *Medical Physics* in 2023.

### Technical advances target crucial brain region

The new scanner design represents a significant departure from conventional PET systems, incorporating an upright configuration that allows patients to remain seated during imaging procedures. Led by Dr Amir H. Goldan, associate professor of electrical engineering in radiology, the research team aims to achieve unprecedented imaging precision of the transentorhinal cortex – a critical region for early Alzheimer's pathology.

"The transentorhinal cortex is only a few millimetres in size and can be incredibly difficult to accurately image with conventional PET scanners, even with highly specific tau PET tracers," explained Dr Gloria Chiang, director of the Brain Health Imaging Institute at Weill Cornell Medicine.

### Enhanced accessibility through portability

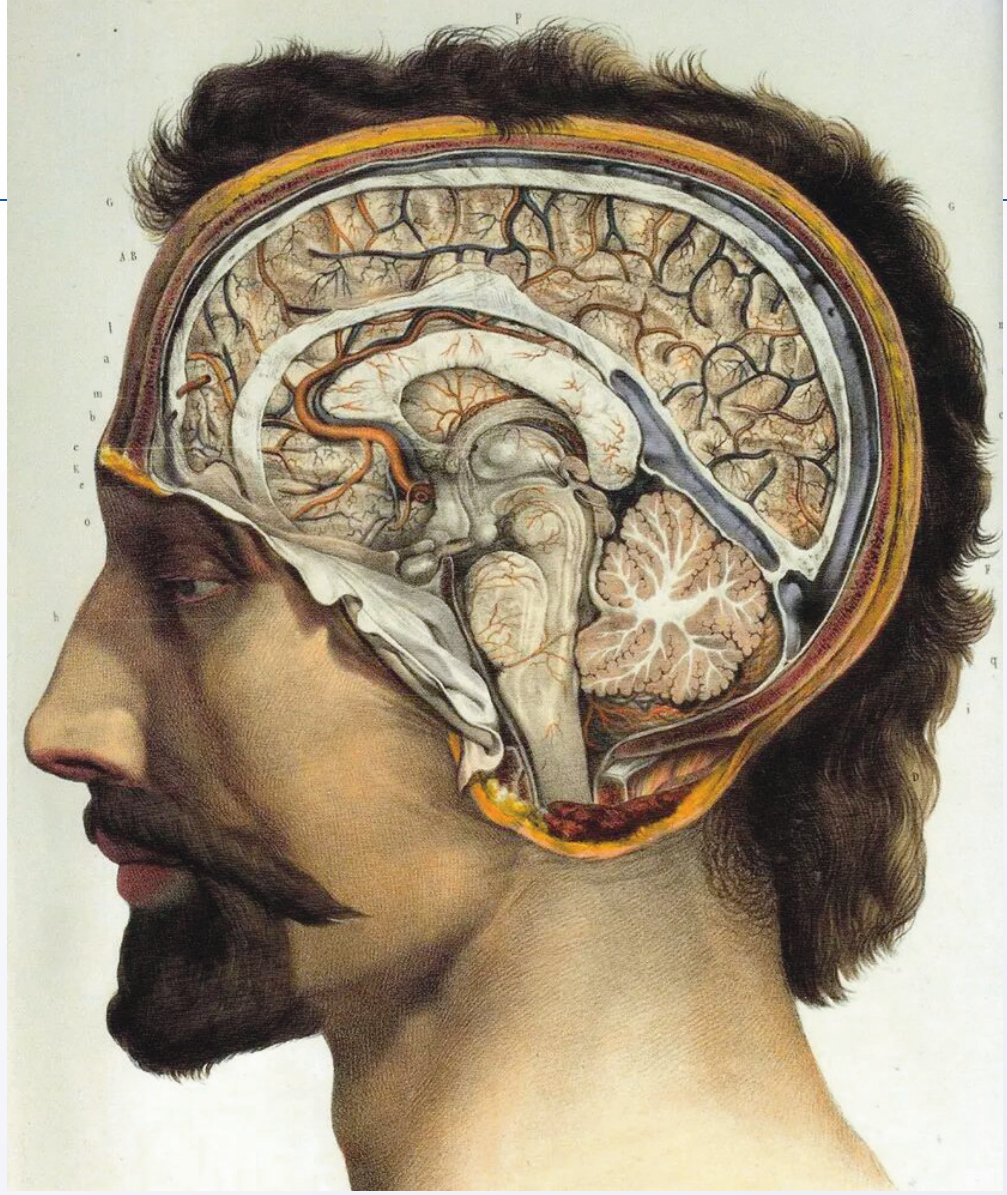
The scanner's compact footprint eliminates the need for dedicated imaging suites, potentially enabling deployment in community hospitals and mobile imaging units.

"We can move it to medical centres that might not have advanced brain imaging, enabling us to provide the highest-level care to more diverse populations," noted Dr Goldan. The development team includes collaborators from the University of California, Davis, with Dr Jinyi Qi serving as co-principal investigator.

### Clinical implications

The system's superior spatial resolution could enable detection of tau tangles within the transentorhinal cortex before clinical symptoms manifest. The research team is additionally developing advanced motion compensation techniques to minimise image degradation caused by patient movement during scanning.

"Our overall goal is two-fold – having the highest performance brain PET scanner available, while also addressing its accessibility and portability to serve the community," said Dr Goldan. "The earlier you can diagnose Alzheimer's disease, the better the chances of therapy being effective."



# Intelligence at age 11 predicts cognitive health at 80: landmark Scottish study reveals secrets of brain ageing

A quarter-century study tracking cognitive abilities from childhood through to older age has provided unprecedented insights into brain ageing, challenging long-held assumptions about cognitive decline and revealing remarkable variations in how individuals' brains age across the lifespan. A paper published 7 November 2024 in *Genomic Psychiatry* [1] looks at lessons learned from this study.

### Lifetime stability of intelligence

One of the most striking findings from the Lothian Birth Cohorts (LBC) studies is that approximately half of the variance in intelligence test scores measured in older age can be traced back to childhood cognitive ability. The research, which followed Scottish individuals born in 1921 and 1936, found correlations of about 0.7 between cognitive test scores at age 11 and those same tests taken in participants' 70s and 80s.

This remarkable stability in cognitive differences across most of the human life course provides important insights into both the persistence of early-life cognitive capabilities and the factors that might influence cognitive change over time. The researchers note that this correlation represents a lower-bound estimate, as it doesn't account for measurement error or the restriction of range in these samples compared with their background populations.

### Brain structure and ageing patterns

The research team's detailed brain imaging studies revealed substantial variations in brain health among people of the same chronological age. Using magnetic resonance imaging (MRI) of participants at age 73, they documented striking differences in both brain atrophy and white matter health, even among individuals born in the same year.

The researchers found that the health of brain white matter – the connecting

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tissues between different brain regions – showed consistent patterns. "People's differences in brain white matter health were modestly associated with cognitive functioning," the authors note in their paper. "Moreover, these two variables change together in a synchronized fashion over time: on average, those with steeper ageing of their brain white matter pathways are those whose general cognitive functioning declines more steeply."

### Survival and cognitive ability

A particularly significant finding from the research relates to the relationship between early-life cognitive ability and longevity. The study found that higher intelligence test scores at age 11 were associated with a better chance of survival to older age and lower risk of death from many major causes of mortality.

The researchers found that a one-standard deviation advantage in childhood cognitive test scores was associated with approximately 20% to 25% lower chance of dying from most major causes of death up to the late 70s. This association remained significant even after accounting for various socioeconomic factors, suggesting a robust link between early cognitive ability and later health outcomes.

### Genetic influences across the lifespan

The study revealed intriguing findings about genetic influences on intelligence. The researchers discovered that genetic factors affecting cognitive ability are not identical in childhood and older age. Their work with the APOE gene, known for its association with Alzheimer's risk, showed that while it had no association with cognitive test scores at age 11, it significantly influenced cognitive performance at age 79.

The team's genome-wide association studies revealed that hundreds of tiny individual genetic associations contribute to intelligence differences, with genetic factors accounting for about two-thirds of the stability in intelligence from childhood to older age but only about a quarter of the changes in intelligence rankings across the same period.

### DNA methylation and ageing

The research team made significant discoveries regarding epigenetic markers of ageing. They found that DNA methylation patterns – chemical modifications to DNA that can affect gene expression – could predict mortality risk. This finding suggests that biological ageing processes may be more accurately measured through molecular markers than chronological age alone.

The study also revealed that these epigenetic patterns were associated with various lifestyle factors, including smoking and body mass index, which in turn showed relationships with brain and cognitive differences. This provides evidence for potential biological mechanisms linking lifestyle choices to cognitive ageing.

### Reverse causation challenges

One of the most thought-provoking findings challenges conventional wisdom about factors affecting cognitive ageing. The researchers discovered that some variables previously thought to be causes of cognitive differences in later life were actually outcomes of early-life cognitive ability.

For example, factors such as physical fitness, social engagement, and certain health markers in older age were found to be partially predicted by childhood intelligence. This suggests a complex relationship between early cognitive ability and later life choices or circumstances that influence brain health.

### The power of longitudinal data

The study's unique strength derives from its use of the Scottish Mental Surveys of 1932 and 1947, which tested almost every child born in 1921 and 1936 in Scotland. This comprehensive baseline allowed researchers to track cognitive changes across entire lifespans with unprecedented accuracy.

The value of this longitudinal approach became particularly evident when examining factors affecting cognitive decline. The researchers found that cross-sectional associations between various lifestyle factors and cognitive ability often disappeared when accounting for childhood cognitive ability, highlighting the importance of having early-life data for accurate interpretation.

### Methodological insights

The research team emphasises that the effect sizes in cognitive ageing studies are typically small. Individual factors like fitness, genetic variants, or lifestyle choices usually contribute about 1% of the variance to cognitive capability in older age, after accounting for youth cognitive ability.

This finding has important implications for both research methodology and public health interventions. It suggests that rather than seeking single large effects, researchers and clinicians should consider the cumulative impact of multiple small influences on cognitive health.

### Future research directions

Looking ahead, the research team continues to follow the surviving members of the 1936 cohort, who are now in their late 80s. This ongoing work promises to provide even more insights into the factors that influence cognitive health in advanced age.

The researchers have also established a brain tissue bank, with some participants consenting to donate their brains after death. This resource will enable future studies to examine the cellular and molecular basis of cognitive ageing, potentially revealing new therapeutic targets for age-related cognitive decline.

### Practical implications

The findings suggest that maintaining cognitive health in later life likely requires a multifaceted approach. While some factors affecting cognitive ageing are fixed (such as genetics and early-life cognitive ability), others are potentially modifiable through lifestyle choices and environmental factors.

The researchers advocate for a "marginal gains" approach to cognitive health, where individuals focus on making multiple small positive changes rather than seeking a single solution. This could include maintaining physical activity, engaging in social and intellectual activities, and managing cardiovascular health.

**Reference:**

1. Deary I. J., & Cox, S. R. Lessons we learned from the Lothian Birth Cohorts of 1921 and 1936. *Genomic Psychiatry*, 1-14. (7 November 2024). https://doi.org/10.61373/gp024i.0076


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# Active navigation shows promise in memory enhancement for neurodegenerative conditions

**New research demonstrates that physical movement through space while learning could enhance episodic memory formation, potentially offering insights for developing non-invasive treatments for conditions such as Alzheimer's disease.**

Recent findings from researchers at the Universitat Oberta de Catalunya (UOC) suggest that active navigation and body movement in immersive environments may play a crucial role in strengthening episodic memory formation. The study, published in *Scientific Reports* on 15 October 2024 [1], explores the relationship between spatial navigation and memory consolidation, offering potential implications for both preventive and therapeutic approaches in neurodegenerative conditions.

## Understanding episodic memory formation

Episodic memory, our ability to mentally revisit past experiences with vivid detail, begins to deteriorate early in the progression of neurodegenerative diseases such as Alzheimer's. The UOC research team, led by Álvaro Pastor and Pierre Bourdin-Kreitz, conducted their investigation at Barcelona's CaixaForum museum, examining how spatial environments and physical movement influence memory organisation and retention.

"The study focuses on how episodic memory works, more specifically on how the spatial environment affects how, and how effectively, memories are organized in our minds," explained Pastor, a cognitive scientist and researcher at the UOC's XR-Lab.

## Methodology and findings

The research team employed both virtual and augmented reality technologies to compare passive and active navigation experiences. Twenty-eight participants explored two floors of the museum, with some using virtual reality while seated and others physically walking through the space using augmented reality. During their exploration, participants were shown AI-generated facial portraits at specific locations.

The results revealed that participants who physically walked through the environment demonstrated superior memory retention both immediately after the experience and during follow-up testing 48 hours later. Notably, information encountered near the stairs connecting the two floors proved particularly memorable, surpassing recall of information presented near visually striking artwork.

"Actively navigating through an environment enables us to collect enough information for our episodic systems to build a sort of cognitive map of our experience, leading to more effective subsequent recall," Pastor noted.

## Innovative methodological approach

The research team's use of AI-generated facial portraits represents a methodological advancement in memory research. These artificially created faces ensured that participants encountered entirely novel stimuli with controlled characteristics.

"By creating artificial faces, we were able to provide participants with images they'd never seen before and ensure their features were uniform, including their facial expression and lighting," Pastor explained, highlighting the importance of such control in studying face recognition within episodic memory formation.

## Therapeutic potential

The findings suggest several potential applications in both preventive and therapeutic contexts. For healthy individuals, the research indicates that incorporating active movement during learning experiences could help maintain episodic memory function over time. In clinical settings, the approach offers promising possibilities for rehabilitation programmes.

The researchers suggest that virtual and augmented reality-based interventions could potentially "slow down the progression of the disease in an inexpensive and easily scalable way". The non-invasive nature of such interventions might also promote better treatment adherence while maintaining patient safety.

## Future directions

The research team is currently expanding their investigation to include additional sensory elements, including the controlled introduction of olfactory stimuli alongside virtual visual presentations. This multimodal approach could further enhance our understanding of memory formation and retention in immersive environments.

The study draws interesting parallels with historical practices, as Bourdin-Kreitz noted: "The idea of walking while learning to increase retention may have been known to mankind since ancient times, at least if we are to believe the story that Aristotle taught his students philosophy while walking through the streets of Athens, and thanks to immersive technologies we can now study this phenomenon in depth." MEH

**Reference:**

1. Pastor A., & Bourdin-Kreitz, P. (2024). Comparing episodic memory outcomes from walking augmented reality and stationary virtual reality encoding experiences. *Scientific Reports*, 14, 7580. https://doi.org/10.1038/s41598-024-57668-w

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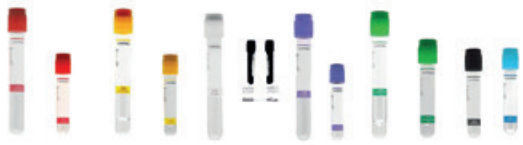

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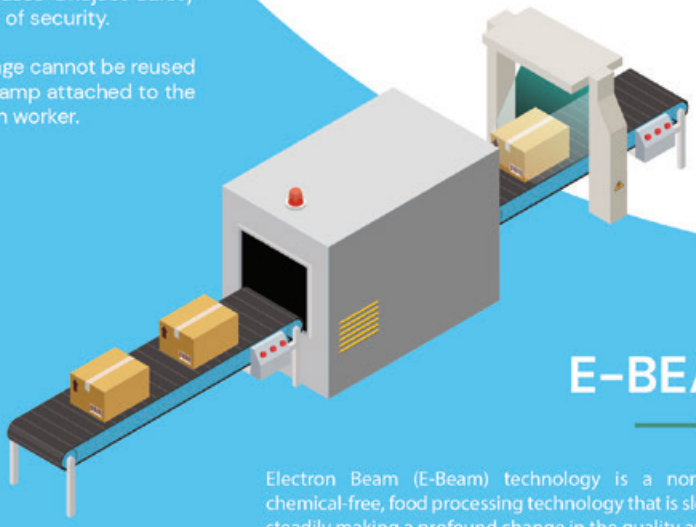

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# World-leading expertise in children's ENT and hearing implant surgery

Evelina London Children's Hospital is a world-leading children's hospital and among the few with the extensive experience, expert surgical skills and advanced facilities needed to perform complex paediatric Ear, Nose and Throat (ENT) surgery.

Our children's ENT service has one of the UK's largest specialist teams, offering life-enhancing care. We perform surgical procedures for common conditions and offer comprehensive treatments in sub-specialist areas such as complex ear surgery and hearing implant insertion where we have in-depth experience and knowledge.

Evelina London is part of Guy's and St Thomas' NHS Foundation Trust, a prestigious, internationally renowned teaching centre. We have a global reputation for exceptional medical and surgical services from before birth to later life.

Evelina London's co-location with St Thomas' Hospital is a significant advantage for patients and their families. With two hospitals on the one central London site, our top-rated ENT surgeons can access expert support should children present with complex hearing issues and associated airway, heart or lung problems. This multidisciplinary team (MDT) approach helps us achieve the best outcomes for our young patients.

## Cochlear implant surgery

We are one of a few centres in the UK that provide every kind of hearing implant surgical solution, including bone conduction, middle ear, cochlear, and auditory brainstem surgery. We also offer middle ear surgery in patients with complex diseases, including advanced cholesteatoma.

Consultant ENT surgeon Nikul Amin said: "We offer a cochlear implant when a patient's hearing levels are so poor that they will not benefit from a regular hearing aid. In children born with significant hearing loss, we aim to start assessments early and provide a cochlear implant by their first birthday."

A cochlear implant is a small electronic device that can help people with severe hearing loss by bypassing damaged parts of the inner ear and directly stimulating the hearing nerve. Unlike hearing aids, which simply amplify sound, cochlear implants convert sound into electrical signals that stimulate the hearing nerve, which then transmits these signals to the brain, allowing the person to perceive sound. However, they are unsuitable for people who lack the necessary cochlea parts or the hearing nerve, as the implant needs these structures to transmit sound signals effectively. Such patients may require an auditory brainstem implant.

## Auditory brainstem implant service

Evelina London is home to the UK's leading paediatric auditory brainstem implant (ABI) service. As one of Europe's most experienced centres, we treat children from the UK and worldwide.

ABI provides a transformative solution for children with profound hearing loss. It can help those who cannot benefit from conventional hearing aids or cochlear implants due to the absence or injury of the cochlear or auditory (hearing) nerve.

The implant bypasses damaged areas by placing electrodes at the first relay station of the hearing pathway in the brainstem, stimulating the auditory brainstem directly and allowing the brain to perceive sound.

Professor Dan Jiang, ENT consultant and skull base surgeon and lead of the Hearing Implant Service, explains "our multidisciplinary team combines expertise from Evelina London, UCLH, and King's College Hospital, and partners with local hearing services, to provide long-term rehabilitation close to home for every patient."

## Complex syndromes and CHARGE

CHARGE Syndrome (CS) is a condition that affects multiple systems in the body, including the heart, eyes, kidneys, and hearing. While some children with CS are suitable candidates for cochlear implants, others may not be, depending on the severity of their medical conditions. In addition to CHARGE, we manage children with other complex issues, such as Down, Usher, and Waardenburg syndromes, which also impact hearing and development.

As a specialist centre, Evelina London has the expertise and experience to evaluate these unique cases and decide whether cochlear implantation is appropriate. Our MDT ensures that each child receives tailored care suited to their specific needs.

In patients whose anatomy isn't suited to a standard device, we can arrange for a specialist manufacturer to make tailored devices through our close relationship with all the major implant manufacturers. We can also provide cochlear implants to a subset of patients with single-sided deafness or sudden hearing loss.

## Treatment for microtia and atresia

Another sub-specialist area is hearing im-

## Recognised as one of the world's best children's hospitals – *US Newsweek for 2025*

plant surgery for children with under-developed outer ears (microtia), absent ear canals (atresia) and narrow (stenotic) ear canals.

Consultant ENT surgeon, Mr Amin said: "The inner ear parts, including the auditory (hearing) nerve, are often normal. So, we can provide hearing surgery that bypasses the absent ear canal. It's challenging because the abnormally small outer ear often means multiple abnormalities in the middle part of the ear, including the hearing bone. We need access to the middle ear and beyond, which includes navigating the abnormal positioning of the nerve supplying the face muscles."

In light of these challenges, the combined expertise of a hearing implant surgeon, plastic surgeon, audiologist and radiologist is needed to determine the best type of hearing provision for the child. The answer is often either a middle ear or bone conduction implant. We provide one of the largest and most experienced MDT approaches to this condition.

### Supporting international patients

Our ability to provide high quality care means we can manage everything from infections associated with hearing loss to surgery and subsequent hearing rehabilitation which can be a long process.

We're building ties with our international partners and hospitals to educate on children's rehabilitation so that care can be continued closer to home with a return to Evelina London for future assessments.

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# Transforming healthcare practice with UpToDate and UpToDate Lexidrug: A case study and interview from the United Arab Emirates

This Expert Insight explores the transformative impact of UpToDate and Lexidrug in addressing clinical complexity with Dr. Khaled Aboeldahab, Head of Long-Term Care and Rehabilitation at Global Care Hospital in Abu Dhabi.

Clinical complexity is increasing at unprecedented rates in the Middle East and the UAE healthcare spending [1] is projected to reach US$30.7 billion (AED112.6 billion) – the highest healthcare spending growth rate in the Gulf Cooperation Council (GCC). Care teams need access to the best resources possible to improve outcomes and control costs. Leadership can identify these resources by prioritizing tools that support tailored treatment plans, facilitate access to real-time information, center the clinician experience, and encourage professional development.

Equipping clinicians to navigate growing clinical complexity is the first step in standardized patient care [2]. When clinicians don't receive the support of evidence-based tools, the risk of variation in care is significantly higher – a gamble that is a loss for patients, clinicians, and provider organizations alike.

To help you better understand how healthcare organizations in the Middle East are revolutionizing healthcare with evidence-based medicine tools [3], we're delving into the transformative impact UpToDate® Lexidrug™ drug information at Global Care Hospital in Abu Dhabi, a facility known for its world class care and commitment to compassion and innovation through the experiences of Dr. Khaled Aboeldahab, expert and founder of the Long-Term Care (LTC) and Rehabilitation at Global Care Hospital in Abu Dhabi.

## Exploring the transformative impact of UpToDate with Dr. Aboeldahab

**Q: Can you provide an overview of your role and involvement with UpToDate and Lexidrug?**

■ **Dr. Khaled Aboeldahab:** As a senior physician, my role involves overseeing clinical practices and ensuring that my medical team has access to the best resources available.

My involvement with UpToDate began in 2021 when we introduced it to address the constant need for reliable clinical information. Recognizing the additional need for detailed drug information, we integrated Lexidrug in 2022. These tools became indispensable in my daily operations, aiding both junior and senior staff in making informed decisions and optimizing medication choices.

**Q: What benefits do you believe UpToDate and Lexidrug bring to the medical field?**

■ **KA:** UpToDate provides a comprehensive, evidence-based resource that supports clinicians in making informed decisions. It helps reduce the unnecessary use of medications, particularly antibiotics, and guides appropriate dosing adjustments. Lexidrug enhances this by offering detailed drug information and interaction checks, crucial for managing complex medication regimens in our long-term care facility. Together, they improve patient care, reduce side effects, and lower healthcare costs.

**Q: What sets UpToDate and Lexidrug apart from other resources in the healthcare industry?**

■ **KA:** UpToDate stands out because of its extensive and continuously updated database of clinical information. The reliability and accuracy of the content, along with its user-friendly interface, make it a superior resource. Lexidrug adds value by providing precise drug information and interaction analysis, essential for our patients with chronic diseases requiring multiple medications. The integration of these tools offers a unified, authoritative source for clinical decision-making.

Dr Khaled Aboeldahab, Head of Long-Term Care and Rehabilitation at Global Care Hospital in Abu Dhabi

**Q: How do you see UpToDate and Lexidrug evolving in the future, particularly in addressing the changing landscape of healthcare?**

■ **KA:** As healthcare continues to evolve, the need for accurate and timely information will only grow. I see UpToDate incorporating more real-time data analytics and predictive tools to further support clinical decision-making. Lexidrug will likely expand its drug databases and interaction checks to include more personalized medicine insights. This evolution will be crucial in addressing emerging healthcare challenges and improving patient outcomes.

**Q: As an advocate for UpToDate and Lexidrug, what key message or recommendation would you offer to your peers in the medical community?**

■ **KA:** I would strongly recommend incorporating UpToDate and Lexidrug into daily practice. These tools are essential for supporting evidence-based medicine and enhancing the quality of care provided to patients. The ability to access reliable information at any time is invaluable. The

tools not only support clinical decisions but also foster a standardized approach to patient care.

**Q: How satisfied are you with your experience with UpToDate and Lexidrug?**

■ **KA:** I am extremely satisfied with both UpToDate and Lexidrug. They have significantly improved clinical practices, reduced medication errors, and optimized patient outcomes. The feedback from my medical team has been overwhelmingly positive, and the support from Wolters Kluwer has been excellent, ensuring any issues are resolved promptly.

**Q: Do you have any additional insights or perspectives you'd like to share about UpToDate and Lexidrug?**

■ **KA:** UpToDate and Lexidrug have become more than just reference tools; they are integral to our practice. Their continuous updates and evidence-based recommendations help clinicians stay at the forefront of medical care, ensuring that patients receive the best possible treatment. They also play a crucial role in training medical students and new staff, making them indispensable in modern medical practice.

**Q: Can you give an example of a time when UpToDate and Lexidrug provided critical information that influenced a patient's treatment plan?**

■ **KA:** Certainly. In one of my previous roles, we had a case where a patient with compromised renal function needed precise dosing adjustments for multiple medications. Using UpToDate and Lexidrug, we were able to tailor the treatment plan accurately, avoiding potential complications and ensuring effective therapy. This precise management was particularly crucial given the advanced age and complex medical conditions of our patients.

**Q: How does using UpToDate and Lexidrug contribute to more efficient use of your time and resources in your practice?**

■ **KA:** UpToDate and Lexidrug save time by providing immediate access to reliable information, reducing the need for extensive searches or consultations. The platform's use of AI minimizes search time. It chooses the exact topic that the physician is searching for based on the physician's specialty and the question asked and can even suggest some differential diagnoses.

These efficiencies allow clinicians to focus more on patient care and less on administrative tasks, thereby optimizing resources. The unified decision-making process also minimizes unnecessary queries and ensures consistent, high-quality care.

**Q: How would you describe the overall impact of UpToDate and Lexidrug on your professional development and patient care?**

■ **KA:** UpToDate and Lexidrug have had a profound impact on both my professional development and patient care. They keep me informed about the latest medical advancements and best practices, which translates to better patient outcomes and continuous professional growth. They also foster a culture of evidence-based medicine within our team, promoting lifelong learning.

The application of AI also contributes to patient safety. Integration with the EMR can raise red flags for severe medication interactions and provide certain advice based on the patient's condition.

**Q: Do you find UpToDate and Lexidrug's mobile apps useful for accessing information on-the-go? Can you share an example?**

■ **KA:** Yes, the mobile apps are incredibly useful. For instance, during a recent patient round, I needed to check a drug interaction. Using the apps, I quickly accessed the information and made an informed decision without delay. This immediacy is crucial in a clinical setting, ensuring timely and accurate patient care.

**Q: Can you discuss any cost-benefit analyses you've encountered where UpToDate and Lexidrug demonstrated clear financial savings for your practice or institution?**

■ **KA:** Implementing UpToDate and Lexidrug has led to significant financial savings, particularly by reducing unnecessary antibiotic use and optimizing medication choices. This has decreased overall pharmacy expenditures and minimized complications, resulting in lower treatment costs. Additionally, morbidity and mortality rates decreased, reflecting improved patient outcomes and cost efficiency.

**Q: How do you see the role of continuous professional development evolving in the Middle East, and how can UpToDate and Lexidrug support this evolution?**

■ **KA:** Continuous professional development is becoming increasingly important in the Middle East. UpToDate and Lexidrug can support this evolution by providing healthcare professionals with access to the latest medical knowledge and best practices, ensuring they remain current in their fields and can deliver high-quality care. These tools are essential for fostering a culture of lifelong learning and evidence-based practice.

● To read more please visit: *http://www.wolterskluwer.com/en/health*

Learn how UpToDate enables clinicians through clinical decision support: *https://www.wolterskluwer.com/en/solutions/uptodate*

**Dr. Khaled Aboeldahab** is the Head of Long-Term Care and Rehabilitation at Global Care Hospital in Abu Dhabi. With a master's degree in Critical Care Medicine from Alexandria University, Dr. Aboeldahab has over two decades of experience in the Gulf region's healthcare sector. His leadership and business development skills have been instrumental in expanding healthcare services and generating significant revenue in his previous roles, including as the CEO of Burjeel Darak Unit. He is currently focused on driving the business development and expansion efforts for healthcare groups across the UAE and Gulf region. Dr. Aboeldahab is also an experienced healthcare consultant, well-versed in critical care, long-term care, and healthcare management.


**References:**

1. *https://www.wam.ae/en/details/1395303163635*
2. *https://www.wolterskluwer.com/en/expert-insights/how-standardized-care-helps-hospitals-and-patients*
3. *https://www.uptodate.com/contents/evidence-based-medicine*

# Novel diabetes treatment shows promise in eliminating insulin dependency

A combination therapy using endoscopic duodenal ablation and semaglutide has demonstrated significant potential in eliminating insulin dependency in type 2 diabetes patients, according to new research presented at UEG Week 2024 in October.

Research presented at the United European Gastroenterology (UEG) Week 2024 in Vienna has revealed promising results from a first-in-human study combining a novel endoscopic procedure with semaglutide administration, potentially offering a new treatment pathway for type 2 diabetes patients dependent on insulin therapy.

## Understanding the treatment approach

The study, which combined ReCET (Re-Cellularization via Electroporation Therapy) with semaglutide administration, demonstrated remarkable success in eliminating insulin dependency in 86% of participants over a 24-month period. The research addresses a significant clinical need, as type 2 diabetes affects approximately 422 million people globally, with many patients requiring daily insulin therapy despite its associated challenges such as weight gain and complex management requirements.

## Mechanism of action

The ReCET procedure represents a significant advancement in endoscopic treatment approaches. It utilises electroporation to ablate the duodenal mucosa through a precisely controlled process that creates irreversible holes in cell membranes, leading to controlled cell death (apoptosis). Unlike traditional ablation techniques, ReCET avoids heat generation, thereby preventing damage to deeper wall layers of the duodenum. This innovative approach appears to enhance the body's sensitivity to endogenous insulin, although researchers note that the exact mechanism requires further investigation.

## Study design and outcomes

The research included 14 participants aged between 28 and 75 years, with body mass indices ranging from 24 to 40 kg/m². Following the ReCET procedure, which was performed under deep sedation, participants followed a two-week isocaloric liquid diet before beginning a graduated semaglutide treatment protocol, eventually reaching a target dose of 1mg weekly.

The results were particularly noteworthy, with 12 out of 14 participants maintaining glycaemic control without insulin therapy through the 24-month follow-up period. All successful cases maintained HbA1c levels below 7.5%, indicating effective blood glucose management.

## Safety and tolerability

The study reported encouraging safety outcomes, with no serious adverse effects from the ReCET procedure. The semaglutide component was well-tolerated by 93% of participants, with only one individual unable to reach the maximum dose due to nausea. All participants successfully completed the ReCET procedure without significant complications.

Commenting on the research, lead author Dr Celine Busch, said: "These findings are very encouraging, suggesting that ReCET is a safe and feasible procedure that, when combined with semaglutide, can effectively eliminate the need for insulin therapy."

## Future research directions

The research team is currently conducting a larger randomised controlled trial, EMINENT-2, which will compare ReCET to a sham procedure while maintaining the same inclusion criteria and semaglutide administration protocol. This follow-up study will include mechanistic assessments to better understand the underlying processes of ReCET.

Dr Busch highlighted a key advantage of the treatment approach: "Unlike drug therapy, which requires daily medication adherence, ReCET is compliance-free, addressing the critical issue of ongoing patient adherence in the management of T2D. In addition, the treatment is disease-modifying: it improves the patient's sensitivity to their own (endogenous) insulin, tackling the root cause of the disease, as opposed to currently available drug therapies, that are at best disease-controlling." MEH

**Reference:**

1. Busch C.B.E, et al. (2024). Durable effects of duodenal ablation using electroporation combined with semaglutide to eliminate insulin therapy in patients with type-2 diabetes; the 24-month results. Paper presented at UEG Week 2024, Vienna, Austria, 14 October 2024.

# Early-life sugar restriction shows long-term protection against chronic disease

New research examining post-World War II sugar rationing data reveals significant reductions in diabetes and hypertension risk when sugar intake is restricted during the crucial first 1,000 days of life, from conception through age two.

A groundbreaking study published in *Science* (31 October 2024) [1] has demonstrated that restricting sugar consumption during pregnancy and early childhood can reduce the risk of developing type 2 diabetes by up to 35% and hypertension by 20% in later life. The research capitalises on the unique circumstances of sugar rationing in the United Kingdom during and after World War II to provide robust evidence of the long-term health implications of early-life sugar consumption.

## Natural experiment from wartime rationing

The research team, led by senior economist Tadeja Gracner from the USC Dornsife Center for Economic and Social Research, utilised the UK's wartime sugar rationing programme as a natural experiment. The programme, which lasted from 1942 to September 1953, restricted sugar consumption to approximately 8 teaspoons (40 grams) per day. Following the end of rationing, sugar consumption doubled almost immediately to 16 teaspoons (80 grams) daily.

"Studying the long-term effects of added sugar on health is challenging," says Gracner. "It is hard to find situations where people are randomly exposed to different nutritional environments early in life and follow them for 50 to 60 years. The end of rationing provided us with a novel natural experiment to overcome these problems."

The researchers analysed data from the UK Biobank, comparing health outcomes of individuals conceived or born just before and after the end of sugar rationing. The findings revealed that those who experienced sugar restrictions during their first 1,000 days of life not only had lower disease risk but also showed delayed onset of conditions when they did develop. For those diagnosed with diabetes or hypertension, the onset was delayed by four and two years, respectively.

## Protective effects begin in utero

A particularly significant finding was that exposure to sugar restrictions during pregnancy alone was sufficient to provide protective effects, accounting for approximately one-third of the observed risk reduction. However, the greatest benefits were seen in individuals who experienced sugar restriction both before and after birth, with protection increasing notably after six months of age when solid foods were typically introduced.

## Contemporary relevance

The wartime sugar rationing levels align closely with current dietary guidelines from the US Department of Agriculture and the World Health Organization, which recommend no added sugars for children under two and a maximum of 12 teaspoons (50g) of added sugar daily for adults. This correlation adds weight to the contemporary relevance of the findings.

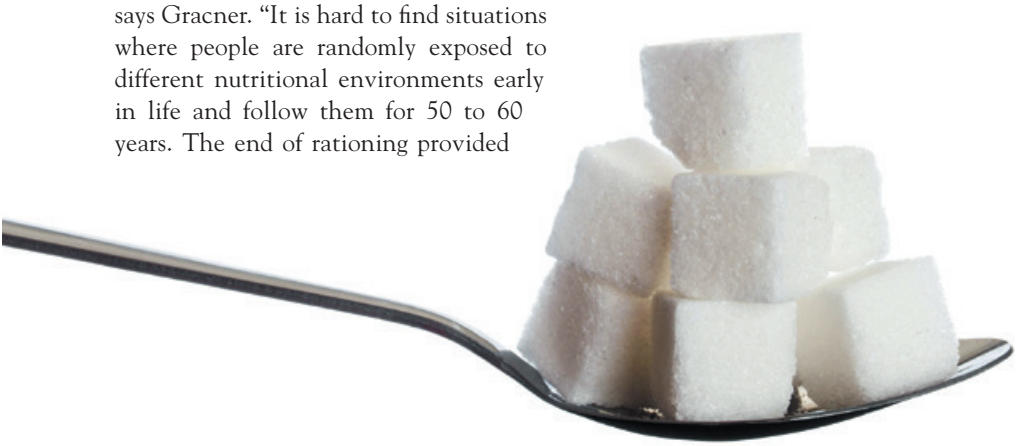
Study co-author Claire Boone of McGill University and the University of Chicago emphasises the practical implications: "Parents need information about what works, and this study provides some of the first causal evidence that reducing added sugar early in life is a powerful step towards improving children's health over their lifetimes."

## Economic implications

The findings have significant economic implications for healthcare systems. Earlier diabetes diagnosis is associated with significantly reduced life expectancy, with each decade earlier diagnosis resulting in a three to four year reduction in life expectancy.

Co-author Paul Gertler of UC Berkeley and the National Bureau of Economics Research draws a stark comparison: "Sugar early in life is the new tobacco, and we should treat it as such by holding food companies accountable to reformulate baby foods with healthier options and regulate the marketing and tax sugary foods targeted at kids."

The research team is continuing their investigations into the broader implications of early-life sugar restrictions, including effects on education, wealth, chronic inflammation, cognitive function, and dementia.



**Reference:**

1. Gracner T, et al. (2024). Exposure to sugar rationing in the first 1000 days of life protected against chronic disease. Science. *https://doi.org/10.1126/5421*

# Adolescent bariatric surgery achieves 55% diabetes remission rate at ten years

New research demonstrates superior diabetes remission rates in adolescents compared to adults following weight-loss surgery, with sustained improvements in multiple obesity-related conditions observed a decade post-procedure.

Major research published in the *New England Journal of Medicine* [1] has revealed compelling long-term outcomes for adolescents who underwent bariatric surgery, showing sustained weight loss and significant resolution of obesity-related conditions ten years post-procedure. The study represents the longest follow-up investigation of weight-loss surgery performed during adolescence.

## Methodology and outcomes

The Teen Longitudinal Assessment of Bariatric Surgery (Teen-LABS) study followed 260 adolescents aged 13-19 years who underwent either gastric bypass or sleeve gastrectomy procedures. After a decade, participants maintained an average body mass index reduction of 20%, with both surgical approaches showing comparable efficacy.

## Diabetes remission superiority

Perhaps the most striking finding was the marked superiority in type 2 diabetes remission rates compared to adult outcomes. The study documented that 55% of adolescent participants who had type 2 diabetes at baseline remained in remission after ten years. This stands in stark contrast to adult outcomes, where recent multi-centre randomised controlled trials have shown remission rates of only 12-18% at seven to twelve years post-surgery.

Commenting on the research, Dr Justin Ryder, Vice Chair of Research for the Department of Surgery at Ann & Robert H. Lurie Children's Hospital of Chicago and lead author, said: "Our study presents impressive outcomes of the longest follow-up of weight loss surgery during adolescence, which validates bariatric surgery as a safe and effective long-term obesity management strategy."

## Broader health improvements

Beyond diabetes outcomes, the research demonstrated substantial improvements across multiple obesity-related conditions. The data showed a 57% reduction in hypertension and a 54% reduction in abnormal cholesterol levels at the ten-year mark.

## Clinical implications

The findings have particular relevance given the current underutilisation of bariatric surgery in adolescents.

Dr Thomas Inge, Principal Investigator of the Teen-LABS study and Surgeon-in-Chief at Lurie Children's, highlighted the timing advantage: "The fascinating part is that when we use these operations in teenagers, the remission of health conditions like diabetes and high blood pressure are more durable than when operations are done later in adulthood."

## Patient perspective

The study included testimonial evidence from participants, including Hillary Fisher, who underwent the procedure at age 16 and was one of the 260 long-term study participants. "I was crushed by the daily issues I faced due to my weight, health problems and bullying in high school," Ms Fisher said. "After many unsuccessful attempts to lose weight, at 260 pounds, we decided bariatric surgery was the answer. It changed my life... the improved health and self-esteem that came with the 100-pound weight loss were important to me and I would certainly do it again."

## Research implications

The research, published in October 2024, provides robust evidence supporting early intervention in cases of severe adolescent obesity, particularly given the enhanced durability of health benefits compared to adult interventions. The findings suggest that the current conservative approach to adolescent bariatric surgery may need reconsideration, given the demonstrated long-term efficacy and safety profile.

The study was supported by the US National Institute of Diabetes and Digestive and Kidney Diseases through multiple grants, alongside additional funding from the National Center for Research Resources and the National Center for Advancing Translational Sciences Clinical and Translational Science Awards Program.

**Reference**

1. Ryder J., et al. (2024). Ten-year Outcomes Following Adolescent Bariatric Surgery. *New England Journal of Medicine*. DOI: https://doi.org/10.1056/NEJMc2404054

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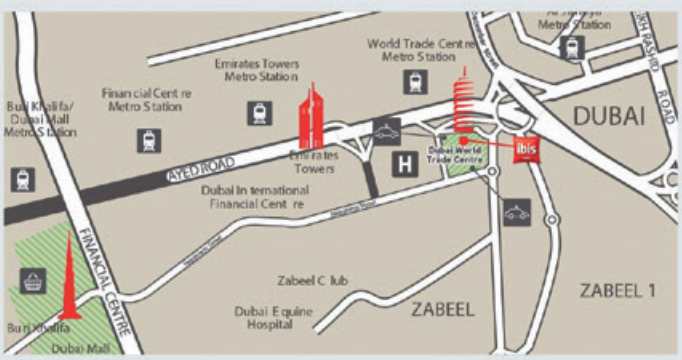

# Type 2 diabetes disrupts key muscle energy protein, study finds

New research from Karolinska Institutet reveals that reduced levels of creatine kinase in muscle cells may explain energy production deficiencies in type 2 diabetes, offering potential new therapeutic targets for metabolic disorders.

## Understanding the creatine connection

Scientists have long observed that individuals with type 2 diabetes (T2D) exhibit impaired energy metabolism in their muscles, but the underlying mechanisms have remained unclear. Now, a groundbreaking study published in *Science Translational Medicine* (9 October 2024) [1] has identified a crucial protein deficiency that may explain this metabolic dysfunction.

The research team, led by Professor Anna Krook from the Department of Physiology and Pharmacology at Karolinska Institutet, discovered that people with T2D have significantly lower levels of creatine kinase in their muscles. This protein plays a vital role in metabolising and converting creatine, a natural compound essential for muscle energy production.

## Consequence rather than cause of disease

The findings help resolve a longstanding puzzle in diabetes research. Previous studies had identified elevated blood creatine levels as a potential risk factor for T2D, raising concerns about creatine supplementation – a popular practice among athletes and fitness enthusiasts. However, this new research suggests that high blood creatine levels are a consequence rather than a cause of the disease.

"The findings indicate that impaired creatine metabolism is a consequence of type 2 diabetes, rather than a cause of the disease," explains Prof. Krook in the study announcement.

## Impact on cellular powerhouses

Through detailed investigations using both human and mouse models, the researchers demonstrated that reduced creatine kinase levels have far-reaching effects on cellular energy production. The study revealed that low levels of this protein impair the function of mitochondria – the cellular structures responsible for energy generation.

These compromised mitochondria exhibited both reduced energy production capacity and increased cellular stress, consistent with the metabolic inefficiencies commonly observed in T2D patients.

## Unexpected findings

The research yielded an unexpected discovery about the relationship between creatine kinase and mitochondrial function. The team found that alterations in creatine kinase levels affected both the structural appearance and energy-producing capabilities of mitochondria, independent of available creatine levels.

"This suggests that although the main role of creatine kinase is to process creatine, it affects mitochondrial function in other ways," notes Dr David Rizo-Roca, the study's first author. The team is now investigating the molecular mechanisms underlying these effects.

## Therapeutic implications

The identification of creatine kinase's role in T2D opens new avenues for therapeutic intervention. Prof. Krook suggests that regulating creatine kinase could potentially become part of the treatment strategy for metabolic diseases, including obesity and diabetes.

Photo: Johannes Frandsén

Anna Krook, Professor at the Department of Physiology and Pharmacology at Karolinska Institutet.

The research represents a significant advance in understanding the relationship between creatine metabolism and diabetes. It suggests that previous concerns about creatine supplementation may need to be re-evaluated in light of the finding that creatine accumulation appears to be a marker of metabolic dysfunction rather than its cause.

The study was conducted in collaboration with Danderyd Hospital and Karolinska University Hospital Huddinge, with funding from several prestigious organisations including the European Association for the Study of Diabetes (EASD), the Knut and Alice Wallenberg Foundation, and the Novo Nordisk Foundation. MEH

**Reference**

1. Rizo-Roca D., Guimarães, D. S. P. F., Pendergrast, L. A., et. al. (2024). Decreased mitochondrial creatine kinase 2 impairs skeletal muscle mitochondrial function independently of insulin in type 2 diabetes. *Science Translational Medicine*. https://doi.org/10.1126/scitranslmed.ado3022

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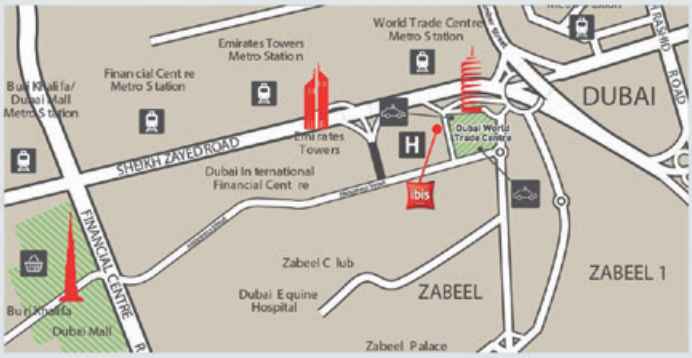


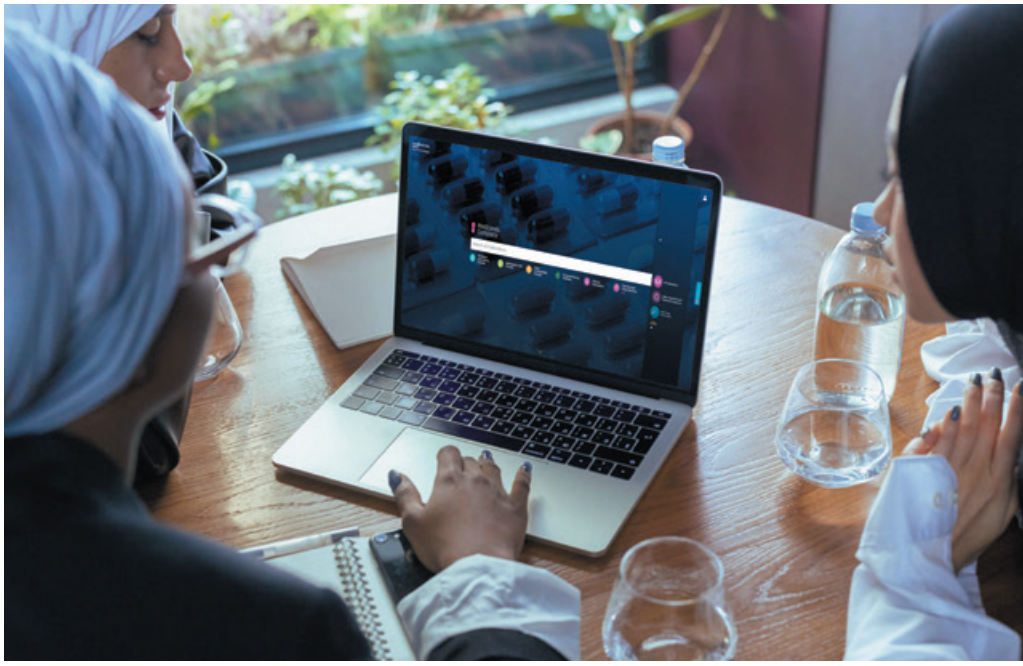
# Pharmaceutical Press shares ways to reduce medication errors and improve patient safety

Medicines are the most common therapeutic intervention in healthcare, and they have now become much more complex. Although patients benefit considerably as a result of living longer and better-quality lives, many experience significant harm due to mistakes or errors in how medicines are used. A medication error is defined as: Any preventable event that causes or leads to inappropriate medication use or patient harm while the medication is under the control of a health professional, patient or consumer.[1]

Medication errors occur frequently in health systems around the world, and, according to the World Health Organization (WHO), nearly 50% of preventable harm to patients globally is due to inappropriate use of medicines and other treatments. A quarter of this preventable harm can be severe or even life-threatening.[1,2]

Even when errors are not harmful or severe, they can drive the cost of care up, and the quality of care down.1 Health professionals do their best to protect patients from harm due to medicines but human factors, such as fatigue and insufficient staffing levels, can play a part. Medication errors that lead to patient harm can negatively impact the mental health of health professionals, and their ability to do their job.[4]

Fortunately, with greater awareness of the scale of the problem, there is now a focus on ensuring a culture of safety in health systems. With the right education, policies, prescribing tools, and reporting and learning systems, errors can be minimised and patients protected.



## Preventing medication errors

Medication errors are a multifaceted problem, there is no one size fits all solution. Rather, tailored approaches to understanding and mitigating the risks are required. Improved systems can help reduce error rates, such as electronic prescribing and automated dispensing. Reporting all drug errors and near misses, regardless of whether the patient came to harm, and having processes to investigate and analyse the data is crucial. It is only by building the baseline evidence that health systems can better understand how errors occur, and how to prevent them.

"Use of medicines has increased because of increased adherence to disease-based guidance. The increase in use also results, however, in increased hazards, errors, and adverse events associated with medicines, which can be reduced or even prevented by improving the systems and practice of medication," WHO, Medication Without Harm, 2023.[1]

## The 5 Rights of medication safety

The "5 Rights" of medication safety can help health professionals who administer drugs to avoid errors.[14]

Best practice dictates that nurses and others carry out the following checks before giving a medication:

> A culture of safety in the health system is necessary to ensure medication safety. With the necessary education, support, and tools, individual health professionals can do much to ensure safe practice.


1. **Right patient:** check the patient's name using two identifiers (e.g. wristband, prescription) and the patient to identify themself if he or she is able.
2. **Right drug:** Check the medication label against what has been prescribed.
3. **Right dose:** Confirm the dose using current references, such as local protocols or British National Formulary (BNF). If necessary, recalculate the dose and have a colleague check it.
4. **Right route:** Check the appropriateness of the route that has been prescribed and confirm with the patient if they are able to take the medicine that way. For example, can they swallow a tablet or capsule.
5. **Right time:** Check the frequency of the prescribed medication and confirm when the last dose was given.

Both the General Medical Council (GMC, 2021)[16] and the Royal Pharmaceutical Society (RPS Competency Framework, 2021)[17] stipulate that health professionals should make use of all available evidence-based resources to keep their knowledge and skills up to date.

In the UK, such resources include those published by the Medicines and Healthcare products Regulatory Agency (MHRA), the National Institute for Health and Care Excellence (NICE), BNF, and BNF for Children, all of which are essential for practice.

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MedicinesComplete brings regularly updated medicines information, and expert guidance on the use and administration of drugs together in one place, helping health professionals to use medicines safely and avoid medication errors.

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# Latest Lancet report reveals unprecedented threats to human health and survival as governments continue fossil fuel investments

## Mounting evidence links health deterioration to climate crisis

The health of billions of people worldwide faces unprecedented threats from accelerating climate change, according to new findings from the 2024 Lancet Countdown Report. The analysis reveals record-breaking levels of heat-related deaths, rising infectious disease transmission, and severe economic losses, while governments continue to invest heavily in fossil fuels rather than redirecting funds towards protecting public health and promoting clean energy alternatives.

The *2024 Lancet Countdown Report on Health and Climate Change* [1] has unveiled disturbing findings about the escalating impact of climate change on global health, with ten out of fifteen health threat indicators reaching unprecedented levels. The comprehensive analysis, involving 122 experts from 57 academic institutions and UN agencies, including the World Health Organisation and World Meteorological Organisation, presents compelling evidence of the direct correlation between climate change and deteriorating health outcomes worldwide.

The report, published ahead of COP29 (held in Baku, Azerbaijan, from 11 to 22 November 2024), documents that 2023 witnessed the highest recorded temperatures, resulting in a significant surge in heat-related mortality. Deaths associated with heat exposure among individuals over 65 increased by 167% compared to the 1990s, substantially exceeding the anticipated 65% increase that would have occurred solely due to demographic changes. This disproportionate impact particularly affects nations with lower human development indices, highlighting the intersection of climate vulnerability and social inequity.

### Quantifying climate impact on daily activities

The data reveals concerning statistics about the impact on daily activities, with people globally experiencing an unprecedented average of 1,512 hours of temperatures that posed at least a moderate risk of heat stress during light outdoor activities such as walking. This represents a 27.7% increase from the 1990-1999 yearly average, adding 328 more hours of potential heat exposure.

The economic implications have been equally severe. The report estimates that 512 billion potential labour hours were lost globally in 2023, marking a 49% increase from the 1990-1999 average. These losses translated to approximately US$835 billion in potential income losses, significantly affecting low and middle-income countries, where the impact reached 7.6% and 4.4% of GDP, respectively.

The analysis also reveals that 61% of global land area experienced an increase in extreme precipitation events during the past decade compared to the 1961-1990 average. These events have heightened the risks of flooding, infectious disease spread, and water contamination. The total yearly economic losses from extreme weather events between 2019-2023 reached US$227 billion, exceeding the GDP of 60% of the world's economies.

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### Disease transmission patterns shift with climate change

The changing climate has created more favourable conditions for the transmission of mosquito-borne diseases. The past decade (2014-2023) saw a 46% increase in transmission risk for dengue fever via Aedes albopictus mosquitoes and an 11% increase via Aedes aegypti compared to 1951-1960 levels. This culminated in over 5 million dengue cases reported across more than 80 countries and territories in 2023, marking an all-time high.

Dr Marina Romanello, Executive Director of the Lancet Countdown at University College London, emphasised the gravity of the situation: "This year's stocktake of the imminent health threats of climate inaction reveals the most concerning findings yet in our eight years of monitoring. Once again, last year broke climate change records – with extreme heat waves, deadly weather events, and devastating wildfires affecting people around the world."

### Financial priorities misaligned with health needs

Despite mounting evidence of health impacts, the report highlights a concerning trend in global financial priorities. In 2023, fossil fuel investments claimed 36.6% of global energy investment, while governments increased fossil fuel subsidies in response to energy price surges following Russia's invasion of Ukraine. In 2022, 84% of analysed countries (72 out of 86) subsidised fossil fuels, reaching a record total of US$1.4 trillion.

The disparity between fossil fuel subsidies and health spending is particularly striking, with subsidies exceeding 10% of national health spending in 47 countries and surpassing 100% in 23 countries. Meanwhile, the Loss and Damage Fund established at COP27 received initial pledges of just US$700 million, less than 0.2% of the estimated annual requirement.

The report reveals that the world's 114 largest oil and gas companies have increased their projected fossil fuel production levels, with emissions expected to exceed 1.5°C-compatible levels by 59% in 2030 and 189% in 2040. More alarmingly, 33 of these companies are projected to exceed their 1.5°C-compatible emissions by over 300% in 2040.

### Environmental degradation compounds health risks

The report presents new data showing that approximately 182 million hectares of forest were destroyed between 2016 and 2022, equivalent to 5% of global tree cover. Russia experienced the most significant losses at 35.8 million hectares, followed by the USA and Canada with nearly 15 million hectares each. This deforestation has severely impacted the Earth's natural carbon dioxide capture capacity.

Furthermore, increasing red meat and dairy consumption contributed to 220,000 additional diet-related deaths between 2016 and 2021, while simultaneously driving a 2.9% rise in agricultural greenhouse gas emissions.

Prof Stella Hartinger, co-author and Lancet Countdown Latin America Director at Universidad Peruana Cayetano Heredia, notes: "Oil and gas companies – supported by many governments and the global financial system – continue to reinforce the world's addiction to fossil fuels. In a world in which survival depends on phasing out fossil fuels, these short-sighted investments set us up for financial turmoil as we pursue a liveable future."

### Signs of progress emerge amid challenges

Despite the overwhelmingly negative trends, some positive developments have emerged. Deaths from fossil fuel-derived air pollution decreased by nearly 7% from 2.25 million in 2016 to 2.09 million in 2021, with 59% of this reduction attributed to coal pollution reduction efforts. Additionally, clean modern renewables now account for 10.5% of electricity generation, almost double the 2016 figure of 5.5%.

The renewable energy sector has shown promising growth, with global investment increasing by 10% in 2023 to US$1.9 trillion, exceeding fossil fuel investment by 73%. Employment in renewables reached a record 13.7 million workers in 2022, representing a 35.6% increase since 2016.

This year's stocktake of the imminent health threats of climate inaction reveals the most concerning findings yet in our eight years of monitoring. Once again, last year broke climate change records – with extreme heat waves, deadly weather events, and devastating wildfires affecting people around the world.

Prof Anthony Costello, Co-Chair of the Lancet Countdown, emphasises the need for systemic change: "Progress towards an equitable and healthy future requires a global transformation of financial systems, shifting resources away from the fossil-fuel based economy towards a zero-emissions future."

UN Secretary-General António Guterres responded to the report's findings, stating: "Record-high emissions are posing record-breaking threats to our health. We must cure the sickness of climate inaction – by slashing emissions, protecting people from climate extremes, and ending our fossil fuel addiction – to create a fairer, safer, and healthier future for all."

The report concludes that growing engagement from individuals, corporations, scientists, and international organisations with climate change and health issues offers hope for positive change, particularly as the health community's leadership could be instrumental in reversing concerning trends and promoting health-centred climate policies at the COP29. MEH

**Reference:**

1. The *2024 Lancet Countdown Report on Health and Climate Change*. https://www.thelancet.com/countdown-health-climate

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