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Major study reveals risk of metastasis

Surgical innovation

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WHO, UNICEF warn of perfect storm of conditions for outbreak among children

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Prognosis

Autonomous robotic surgery

Imagine having a robot do your surgery. There are robots that assist in surgery such as the Da Vinci system, but not a robot that can do the surgery on its own. Now in a major first step towards completely autonomous robotic surgery, a team at Johns Hopkins University have a developed a surgical robot that has performed the first known autonomous laparoscopic soft tissue surgery with minimal human assistance. The robot, called STAR – for Smart Tissue Autonomous Robot – was developed to perform intestinal anastomosis and was put through a series of tests on 'phantom' tissue and subsequently on five pigs, where it executed the procedure with high precision. The team notes that it performed the procedure with a higher quality than those performed by expert surgeons. You can read more about this innovation in our focus on surgery in this issue.

Also in this issue, we report on a major global study which reveals the risk of metastasis of breast cancer. The study also shows that certain women face a higher risk than others, including women diagnosed with breast cancer at a younger age, those diagnosed with larger tumours at initial diagnosis and those with specific types of breast cancer.

Continuing our focus on women's health, we report on preliminary research which shows that women who enter menopause very early, before age 40, were found to be more likely to develop dementia of any type later in life compared to women who begin menopause at the average menopause onset age of 50 to 51 years. The researchers call on clinicians to be aware of a woman's age at menopause onset and closely monitor for cognitive decline in those who reached menopause before age 45.

Worldwide measles cases increased by 79% in the first two months of 2022, compared to the same period in 2021, which has prompted the WHO and UNICEF to issue a warning of potentially large outbreaks of the vaccine-preventable disease as communities relax social distancing practices and other preventive measures for COVID-19. The WHO emphasised that now is the time for immunisation services to get back on track and launch 'catch-up' campaigns to prevent an imminent major resurgence of measles.

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Middle East Health is published by Hurst Advertising FZ LLC, Dubai Media City, License Number: 30309 UAE National Media Council - Approval Number: 2294781.

Middle East Health online www.MiddleEastHealth.com

Middle East Health is printed by Atlas Printing Press. www.atlasgroupme.com

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middle east monitor Update from around the region



Cleveland Clinic Abu Dhabi ranked UAE's top hospital in Newsweek's World's Best Hospitals 2022 list

Cleveland Clinic Abu Dhabi has been recognized as the top hospital in the UAE in this year's World's Best Hospitals index, which is compiled by *Newsweek* and Statista Inc. Cleveland Clinic Abu Dhabi was positioned within the top 150 global hospitals in the ranking, which evaluates over 2,200 hospitals from 27 countries around the world.

Waleed Al Mokarrab Al Muhairi, Chairman of Cleveland Clinic Abu Dhabi and Deputy Group CEO of Mubadala Investment Company, said: "I would like to congratulate the entire team at Cleveland Clinic Abu Dhabi on this achievement. It is thanks to their commitment and collective efforts that we are now recognized as one of the best hospitals in the world."

Tom Mihaljevic, M.D., Cleveland Clinic CEO and President, said: "Ranking among the world's best hospitals is affirmation of our caregivers' continued commitment to providing patients with the best care anywhere. It solidifies Cleveland Clinic's international reputation for safe, highquality care. The world looks to Cleveland Clinic for innovative solutions to the greatest challenges in healthcare."

Hasan Jasem Al Nowais, CEO of Mubadala Health, added: "Cleveland Clinic Abu Dhabi has always been a leader in offering quality care, education, and research, as well as a regional pioneer when it comes to healthcare innovation. Having the UAE's number one hospital within the Mubadala Health network should be a source of pride and inspiration for all of our healthcare facilities."

Cleveland Clinic Abu Dhabi CEO, Jorge Guzman, M.D., said: "We are delighted to be positioned so highly on this prestigious list, a veritable who's who of the best hospitals from around the world. The rankings are compiled by collating feedback from medical healthcare professionals and patients, relating to two key objectives of ours: to be the best employer in the healthcare sector and the most trusted provider of patient care in the UAE and the wider region. This recognition is a testament to our continuous focus and commitment to bring world-class care closer to home, to advance the UAE healthcare sector, and to always put patients first."

The rankings are based on three data sources: online surveys of more than 80,000 medical experts from around the world; results from publicly available patient experience surveys; and medical key performance indicators, including patient safety, infection prevention measures, and doctor-to-patient ratios. Cleveland Clinic Abu Dhabi and other top hospitals were recognized for their ability to deliver highquality patient care and conduct critical medical research despite the ongoing global pandemic.

US\$1.8bn joint venture established to build neutron therapy hospital, medical university in UAE

A joint venture agreement has been signed between Royal Strategic Partners in Abu Dhabi with the MIG group based in Dubai and the Austrian Star Energy company to build a neutron therapy hospital in addition to a medical university and a convention centre with the initial investments into the project of AED 6.6 billion (US\$1.8 billion).

Mahmood Al Redha, Chairman of MIG Group, said the joint venture with their Austrian partners will allow the UAE companies to build state-of-the-art medical facilities, which consist of a university hospital for neutron cancer treatment and a medical university that will be the main hub for research and development of the latest technologies to treat advanced cancer in the GCC region.

The project will be implemented in two phases. The first phase is the implementation of a pilot project in Abu Dhabi for the hospital, the medical university, and the convention centre, and the second phase will see the expansion of the project in areas facing a deficit in the production of electricity and thermal energy and a shortage of fresh water, or to use it as an alternative to power generation instead of expensive diesel or other expensive energy sources.



Dubai's Neuro Spinal Hospital installs UAE's first Cyberknife for cancer treatment

Dubai's Neuro Spinal Hospital (NSH) has installed the UAE's first robotic Cyberknife radiosurgery centre for cancer treatment. The Cyberknife targets tumours with submillimeter accuracy without damaging healthy tissue. It provides cancer patients with a safer treatment option that can sometimes replace surgery. Cancer pateints can now access this advanced care without the need to travel abroad for treatment.

"We are proud to bring world-class healthcare services to Dubai and believe our next-generation hospital will be a game-changer for the United Arab Emirates and the region's medical industry. Our aim is provide patients of the region access to the highest expertise together with the latest medical technologies available internationally, and with that in mind the NSH has been a pioneer in its field since its inception in 2002, introducing the first Brain Suite in the region and second worldwide, and lately the first Cyberknife Centre in the UAE. Investing in the new hospital and technology represents our continued faith in the resilience of the region's economy and the vision of its leadership, as well as a testament to our ongoing drive towards healthcare innovation in the UAE," said Prof. Abdul Karim Msaddi, Chairman and founder of the Neuro Spinal Hospital.

NSH has witnessed an inflow of patients from the GCC and Africa in line with HH Sheikh Mohammad's vision of making Dubai a hub for medical tourism. The hospital features spacious smart rooms, green spaces and open gardens for a more healing environment.

Emirates Health Services sets up advanced patient experience management solution

Emirates Health Services (EHS), the largest health organization in UAE, in cooperation

with Emitac Healthcare Solutions has implemented SEDCO's patient experience management solution in 126 centres and more than 700 healthcare departments across the country. These centres include primary healthcare centres, specialized healthcare centres, preventive medicine centres, blood donation centres, and hospitals.

The advanced patient experience management solution streamlines the patient journey at every touchpoint from pre-arrival to post-service, while automatically routing patients across the different centres and healthcare departments to ensure smooth operations, reduce waiting time, and provide a stress-free patient experience. The features of the solution include mobile appointment booking and check-in, sms notifications, instant e-ticket issuance, queue management, digital signage system, and central management and business intelligence system.

An added benefit of the solution is to provide the healthcare authority with realtime data to plan and use their resources more efficiently by delivering insights into the day-to-day operations, identify areas of improvement, provide analysis of historical data, manage staff distribution, promote better communication within each department and overall provide a blueprint of a patient's journey in the entire healthcare facility.

The SEDCO system also streamlines prebooked and walk-ins, where EHS patients can issue a ticket for an appointment, pharmacy, lab, and radiology orders, ensuring a smooth routing across all of the organization's facilities.

The system's smart digital signage is integrated with an audio announcement system to call the next patient in queue. The digital screens also display healthcare tips and targeted ads to promote new medical services.

With a live dashboard and an advanced reporting system, EHS can centrally monitor each healthcare facility, operation, and KPIs such as service quality, utilization, and turnaround time.

Worldwide monitor Update from around the globe



Global Fund urges the world to boost the fight against malaria

The Global Fund is calling for renewed commitment in the fight against malaria, a disease that now kills one child every minute. After years of steady declines, malaria cases and deaths are on the rise mainly due to stalled funding and disruptions caused by the COVID-19 pandemic.

In 2020, there were an estimated 241 million malaria cases and 627,000 malaria deaths worldwide. This represents about 14 million more cases in 2020 compared to 2019, and 69,000 more deaths. Approximately two-thirds of these additional deaths were linked to COVID-19 disruptions.

In addition, climate change-related fluctuations in rainfall, temperature and humidity may shift malaria transmission to areas that may not be adequately resourced or prepared to prevent, detect, and treat the disease.

"More than ever before, the Global Fund needs to support countries in their efforts to revitalize and sustain the fight against malaria," said Peter Sands, Executive Director of the Global Fund. "We must seek to provide better and more equitable access to all health services, vastly increase funding for malaria programs, invest in new approaches and innovations and make better use of existing tools. This year, with the Global Fund's Seventh Replenishment conference, the world has an opportunity to invest more to protect our hard-won gains against malaria and get back on track to end the disease by 2030. This will save millions of lives – the vast majority of them children under 5."

The Global Fund's commitment to introducing and expanding the delivery of new tools has helped transform the fight against malaria. Innovative approaches to partnerships, financing, and catalytic investments – which include the rapid introduction, scale-up, and targeted delivery of new malaria interventions, improved supply chains, and stronger surveillance and lab capacity – have helped reduce malaria deaths rates by 47% since 2002.

In the fight against malaria, both the next-generation insecticide-treated nets and the new malaria vaccine are needed as well as the expanded use of other core malaria prevention tools, such as seasonal malaria chemoprevention to protect children under 5 and mosquito net distributions.

The Global Fund provides 56% of all international financing for malaria programs (39% of total available resources) and has invested more than US\$16 billion in malaria control programs to date. In countries where the Global Fund invests, malaria deaths have dropped by 26% between 2002 and 2020. In the absence of malaria control measures, deaths would have increased by 84% in the same period. Malaria death rates – deaths as a proportion of the population – have dropped by 47% between 2002 and 2020.

From January 2021, the Global Fund has increased malaria grants by 23% on average and is committed to deploying about US\$4 billion to fight the disease over the next three years.

U.S. President Joe Biden will host the Global Fund's Seventh Replenishment conference later this year. The Global Fund's target is to raise at least US\$18 billion to fund its next three-year cycle of grants. A successful Replenishment would save 20 million lives, cut the death rate from HIV, TB and malaria by 64% and strengthen systems for health to build a healthier, more equitable world. In the fight against malaria, a successful Replenishment would cut malaria deaths by 62%, reduce malaria cases by 66%, and eliminate malaria from an additional six countries by 2026.

The Global Diabetes Compact: a promising first year

One year ago, the WHO and the Government of Canada, launched the Global Diabetes Compact – an ambitious new initiative to galvanize efforts around the world to both reduce the risk of diabetes, and ensure that all people diagnosed with diabetes have access to equitable, comprehensive, affordable and quality treatment and care.

Those responsible for the conception of the Compact were under no illusions about the immensity of the challenge.

"The fact that 100 years after the discovery of insulin, a life-saver for many people with diabetes, the treatment was still out of reach for millions of people who needed



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it, was a clear signal that 'business as usual' was no longer an option," said Dr Bente Mikkelsen, Director of the Department of Noncommunicable Diseases at the World Health Organization. "The enthusiasm that we saw among political leaders at the highest levels for the Global Diabetes Compact showed us that the motivation for a radical scale-up of efforts was widely supported."

The critical nature of scaling-up efforts to prevent and treat diabetes was made clear by the adoption by WHO Member States of a historic resolution on diabetes at the World Health Assembly in May last year. The Resolution recommends the integration of prevention and treatment of diabetes into primary health services, the development of pathways for a substantial increase in access to insulin, the promotion of convergence and harmonization of regulatory requirements for diabetes medicines and technologies and improved diabetes monitoring and surveillance. Furthermore, it asks WHO to advise Member States on how to ensure the uninterrupted treatment of people living with diabetes in humanitarian emergencies. This important milestone provides a global mandate for diabetes efforts for the next decade.

Meanwhile work was underway to ensure that WHO had access to leading experts to provide technical advice on matters relating to WHO's work on diabetes. The result was the establishment of a Technical Advisory Group on Diabetes in August. The Group, chaired by Professor Amanda Adler, Professor of Diabetic Medicine and Health Policy at Oxford University, met for the first time in September 2021.

The importance of engaging a broader community beyond technical experts was very clear when the Compact was established, and in November, the first Global Diabetes Compact Forum was held. With more than 50 participants from nongovernmental organizations, academic institutions, philanthropic foundations and business associations, the Forum provided an opportunity for the exchange of information on ongoing and future activities and the sharing of ideas on future endeavours that could be organized collectively for greater impact.

A new report published by WHO in the lead-up to World Diabetes Day in November highlighted the alarming state of global access to insulin and diabetes care, finding that high prices, low availability of human insulin, few producers dominating the insulin market and weak health systems are the main barriers to universal access.

Recommendations made in the report for addressing these issues included boosting human insulin production, introducing pooled procurement mechanisms to bring down prices and improving transparency in price-setting. As part of efforts to address these and other issues relating to the insulin market, WHO has embarked on dialogues with the private sector on medicines and technologies for diabetes care, the last of which was held in September 2021. While these early discussions have served as a basis for setting out goals and potential activities to reach them, WHO will continue to encourage and ask the private sector for commitments and contributions with the aim of dramatically improving access to insulin and health technologies in low- and middle-income countries, as well as in humanitarian emergencies.

The establishment of the Compact and its associated coordination activities have given added impetus to diabetes efforts within ministries of health around the world. WHO regional and country office staff have used the opportunity to support countries in their efforts, providing technical guidance and support for advocacy efforts.

Reflecting on the year since the launch of the Compact and looking ahead, Dr Mikkelsen said: "In the past 12 months we have established the foundations that will enable us to collectively work towards the goals of the Global Diabetes Compact. But this is just the start. We look forward to building on the achievements of this first year with our partners around the world to make a real difference to the lives of people with diabetes. They are counting on us."



MoU signed for a new era of One Health collaboration

The four international agencies, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE), the UN Environment Programme (UNEP) and the World Health Organization (WHO), have signed a groundbreaking agreement to strengthen cooperation to sustainably balance and optimize the health of humans, animals, plants and the environment.

On 17 March 2022, the heads of the four organizations – QU Dongyu, the Director-General of FAO, Monique Eloit, the Director-General of OIE, Inger Anderson, the Executive Director of UNEP, and Tedros Adhanom Ghebreyesus, the Director-General of WHO – signed a Memorandum of Understanding for joint One Health works, by which UNEP joined the former Tripartite (FAO, OIE and WHO) as an equal partner to form a new Quadripartite Collaboration for One Health.

The new Quadripartite MoU provides a legal and formal framework for the four organizations to tackle the challenges at the human, animal, plant and ecosystem interface using a more integrated and coordinated approach. This framework will also contribute to reinforce national and regional health systems and services.

Quadripartite Memorandum of Understanding https://www.fao.org/3/cb9403en/cb9403en.pdf

the laboratory

Medical research news from around the world

How creative arts therapy helps young cancer patients through their treatment journey

As a former dancer and dance instructor, CU Cancer Center member Jennifer Raybin, PhD, knows the power the creative arts hold to help people through challenging times. As a nurse practitioner who led the Palliative Care Program at Children's Hospital Colorado, she knows the creative arts can be especially helpful for children and young adults with cancer. Creative activities help patients deal with symptoms, improve their mood, and even ease disease and treatment symptoms like pain, nausea, and fatigue.

"When I got my master's at Yale, I explored dance movement therapy for adolescents with cancer," Raybin says. "My lifelong dream has been to blend art and science, and to show the scientists that art makes you feel better."

Raybin has taken a step closer to that dream with the publication of her study "Quality of Life Outcomes with Creative Arts Therapy in Children with Cancer" in the *Journal of Pediatric Oncology Nursing*^[1]. In partnership with Patricia Mowry, licensed dance/movement therapist in the Ponzio Creative Arts Therapy Program at Children's Colorado, Raybin implemented her study with patients. Raybin applied scientific investigation to the creative arts therapy (CAT) conducted by Mowry.

Raybin looked at how participation in creative arts therapy improved quality of life for cancer patients ranging in age from 3 to 17. During their treatment, patients worked directly with Mowry, who applied individualized interventions designed to help patients express and process emotions. These included making cloth minime dolls, repurposing radiation masks into art, creating playful movement using props such as balls, scarves, and a parachute as in-the-moment adaptation to loss of physical functioning, and applying yoga breathing exercises to control pain.

The importance of posture

Raybin enrolled 98 children and their

parents in the study. Eighteen patients received no creative arts therapy, 32 received a low dose of CAT, and 33 received a high dose. Children who experienced CAT – and the parents who observed their children – reported significantly better quality of life. Additionally, Mowry observed that patients' posture seemed to change several times during the course of their treatment, reflecting their changing mood and sense of self. Raybin's objective study proved this hypothesis to be true.

"We looked in the physical therapy literature and found a posture measure," Raybin says. "We looked at the kids' posture over time. At first, I thought, 'For sure this won't turn out to be significant'. And lo and behold, it did. It is related to quality of life. We compared that posture measure to surveys, and the kids that were more hunched over also had worse quality of life and chose a sadder face on the Faces scale."

The study's results – that creative arts therapy results in a better quality of life for young cancer patients – is especially important as paediatric cancer is the leading cause of death from disease in children in the U.S.

"I am really passionate about not just throwing medicines at these kids," Raybin says. "They are so tired of taking medication for their symptoms. It's important to think about the mind-body connection and any kind of integrative and complementary therapies we could add that can help them process the physical and psychological symptoms."

Creative Arts Therapy

Creative Arts Therapy, which is conducted by a trained therapist who in this case is also a licensed professional counsellor, is greatly different than personal art making, dancing or music making. Those activities have also been associated with improved quality of life, but they are not guided by a trained clinician. Creative arts therapists assess patients' psychological needs and in-



tentionally apply interventions.

For the next phase of her research, Raybin hopes to do a multi-site study of creative arts therapy programs, aiming to prove their value so that they become a more standard part of care for young cancer patients.

"A lot of places have art therapy, but it's almost always philanthropically funded," she says. "My dream is that it would be paid for by insurance, that we could say, 'You should pay for this as much as you should pay for chemo'.

"Curing cancer isn't enough," she adds. "Creative arts therapy helps patients negotiate the physical and psychological issues surrounding serious illness, while providing an enjoyable aspect to otherwise difficult treatment."

Reference:

^[1] doi: https://bit.ly/3MUPS7v



Researchers develop smartphone-powered microchip for at-home medical diagnostic testing

A University of Minnesota Twin Cities research team has developed a new microfluidic chip for diagnosing diseases that uses a minimal number of components and can be powered wirelessly by a smartphone. The innovation opens the door for faster and more affordable at-home medical testing.

The research is published in *Nature Communications*^[1]. The researchers are also working to commercialize the technology.

Microfluidics involves the study and manipulation of liquids at a very small scale. One of the most popular applications in the field is developing "lab-on-a-chip" technology, or the ability to create devices that can diagnose diseases from a very small biological sample, blood or urine, for example.

Scientists already have portable devices for diagnosing some conditions – rapid COVID-19 antigen tests, for one. However, a big roadblock to engineering more sophisticated diagnostic chips that could, for example, identify the specific strain of COVID-19 or measure biomarkers like glucose or cholesterol, is the fact that they need so many moving parts.

Chips like these would require materials to seal the liquid inside, pumps and tubing to manipulate the liquid, and wires to activate those pumps – all materials that are difficult to scale down to the micro level. Researchers at the University of Minnesota Twin Cities were able to create a microfluidic device that functions without all of those bulky components.

"Researchers have been extremely successful when it comes to electronic device scaling, but the ability to handle liquid samples has not kept up," said Sang-Hyun Oh, a professor in the University of Minnesota Twin Cities Department of Electrical and Computer Engineering and senior author of the study. "It's not an exaggeration that a state-of-the-art, microfluidic lab-on-a-chip system is very labor intensive to put together. Our thought was, can we just get rid of the cover material, wires, and pumps altogether and make it simple?"

Many lab-on-a-chip technologies work



A University of Minnesota Twin Cities research team has developed a new microfluidic chip for diagnosing diseases that uses a minimal number of components and can be powered wirelessly by a smartphone.

by moving liquid droplets across a microchip to detect the virus pathogens or bacteria inside the sample. The University of Minnesota researchers' solution was inspired by a peculiar real-world phenomenon with which wine drinkers will be familiar – the "legs", or long droplets that form inside a wine bottle due to surface tension caused by the evaporation of alcohol.

Using a technique pioneered by Oh's lab in the early 2010s, the researchers placed tiny electrodes very close together on a 2 cm by 2 cm chip, which generate strong electric fields that pull droplets across the chip and create a similar "leg" of liquid to detect the molecules within.

Because the electrodes are placed so closely together (with only 10 nanometres of space between), the resulting electric field is so strong that the chip only needs less than a volt of electricity to function. This incredibly low voltage required allowed the researchers to activate the diagnostic chip using nearfield communication signals from a smartphone, the same technology used for contactless payment in stores.

This is the first time researchers have been able to use a smartphone to wirelessly activate narrow channels without microfluidic structures, paving the way for cheaper, more accessible at-home diagnostic devices.

"This is a very exciting, new concept," said Christopher Ertsgaard, lead author of the study and a recent CSE alumnus (ECE Ph.D. '20). "During this pandemic, I think everyone has realized the importance of at-home, rapid, point-of-care diagnostics. And there are technologies available, but we need faster and more sensitive techniques. With scaling and high-density manufacturing, we can bring these sophisticated technologies to at-home diagnostics at a more affordable cost."

Oh's lab is working with Minnesota

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startup company GRIP Molecular Technologies, which manufactures at-home diagnostic devices, to commercialize the microchip platform. The chip is designed to have broad applications for detecting viruses, pathogens, bacteria, and other biomarkers in liquid samples.

"To be commercially successful, in-

home diagnostics must be low-cost and easy-to-use," said Bruce Batten, founder and president of GRIP Molecular Technologies. "Low voltage fluid movement, such as what Professor Oh's team has achieved, enables us to meet both of those requirements. GRIP has had the good fortune to collaborate with the University of Minnesota on the development of our technology platform. Linking basic and translational research is crucial to developing a pipeline of innovative, transformational products."

Reference: ^[1] doi: https://bit.ly/38V0a92

Changes in blood fats and other markers of heart health and diabetes detectable from age of six in children with overweight, Danish study finds

A new study being presented at this year's European Congress on Obesity (ECO) in Maastricht, the Netherlands, and published simultaneously in *Obesity Research & Clinical Practice*^[1], has revealed that changes in blood fats and other markers of heart health and diabetes are detectable from the age of six in children who have overweight.

The study of almost 1,000 Danish children also established that routine dental check-ups provide a good opportunity to measure BMI.

"The prevalence of childhood obesity is high and the short-term and long-term complications of childhood obesity are numerous," says the study's first author, Dr Christine Frithioff-Bøjsøe, of the Children's Obesity Clinic, European Centre for Obesity Management, Copenhagen University Hospital Holbaek, Holbaek, Denmark.

"Overweight in early childhood often tracks into adolescence and adulthood and is associated with a higher risk of heart disease, liver disease, type 2 diabetes and other metabolic conditions in later life. As a result, the early identification and treatment of overweight provides a crucial opportunity to improve a child's health for years to come."

The study which was led by Dr Frithioff-Bøjsøe, Prof Jens-Christian Holm and colleagues at the Children's Obesity Clinic, set out to discover if it is practical to use existing contacts in primary healthcare sector to detect overweight from an early age.

Dental assistants and public health nurses were trained in measuring weight and height and carried out BMI assessments during routine appointments in dental clinics (children in Denmark are entitled to regular dental appointments from as early as the age of one) and in health visits in schools.

The dental assistants recruited 335 preschool children (age 2.5 and 5 years old) into the study. A further 657 school-age children (6-8 years old) were recruited by public health nurses, taking the total number of participants to 992 (494 boys).

All the children had their BMI assessed at the start of the study. A sub-group of 392 children had their blood pressure measured and gave a blood sample, which was tested for a range of cardiometabolic risk markers.

The BMI assessments and other tests were repeated approximately a year later.

At the start of the study, the proportion of children with overweight was 13.7% in both groups (pre-school children and schoolchildren).

Differences in cardiometabolic risk markers between children with and without overweight were minor in the pre-schoolers.

In the schoolchildren, however, there were clear differences in the blood test results between those with overweight and those in the normal weight range.

Schoolchildren with overweight had significantly higher levels fasting glucose, insulin, triglycerides and alanine aminotransferase, which can indicate a higher risk of type 2 diabetes, cardiovascular disease and liver disease.

Levels of overweight hadn't changed in the pre-school children when they were measured again around a year later but had risen to 17% in the schoolchildren.

The study's authors say that their re-

search shows that it is practical to use existing health services, including dental clinics, to evaluate the degree of overweight in a general paediatric population.

Dr Frithioff-Bøjsøe adds: "We also overcame barriers identified in other studies which include concerns about a lack of adequate training, offending patients and caregivers and stigmatisation of the child."

The researchers say that even though the risk marker levels measured in the study were still in normal range, the increases are still a concern, particularly at such a young age.

Dr Frithioff-Bøjsøe explains: "By the age of 11, 15-20% will exhibit overweight and a large group will subsequently exhibit high blood cholesterol levels, fatty liver disease or prediabetes, as well as a severely affected quality of life. So, detecting these changes early would be a major advance in preventing the development of disease."

The authors conclude: "We found rises in risk markers for heart and liver disease and diabetes in schoolchildren with overweight. These changes were not detectable just a few years earlier in pre-schoolers with overweight and suggests that preschool – as early as 2.5 years of age – could provide a critical window to detect and manage overweight.

"This would, in turn, allow weight loss interventions to start early, and reduce the risk of a child with overweight becoming an adult, or even an adolescent, with overweight and other conditions such as type 2 diabetes."

Reference:

^[1] doi: https://bit.ly/37l3nOI



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Robot performs soft tissue surgery with minimal human help

Performance of robot exceeds expert surgeons in preclinical models

What if your next surgery was planned and performed by a robot? A team at Johns Hopkins University is working to turn this idea into reality.

The concept of robot-assisted surgery is not new: several systems have already been developed and are being used to treat human patients. One example is the da Vinci surgical system, a laparoscopic device with robotic arms that are remotely controlled by a surgeon. This system is not autonomous - the robot does not perform any surgical tasks independently. Other robotic systems with higher levels of autonomy have been developed, such as the TSolution One, which uses a robot to precisely cut bone according to a pre-specified plan. Existing autonomous robotic systems have largely been used to assist in surgeries involving hard tissues, such as drilling into bone for hip or knee implants. But these systems haven't been used for soft tissue surgeries, which pose unique challenges, like accounting for unpredictable tissue motions that occur when the patient breathes, or size limitations of the surgical tools.

Now, National Institute of Biomedical Imaging and Bioengineering (NIBIB)-funded researchers are developing an autonomous robot that can perform bowel surgery with minimal assistance from a surgeon. What's more, the robot outperformed expert surgeons when compared head-to-head in preclinical models. A study detailing the development of this robot, which showcases the first known autonomous laparoscopic soft tissue surgery, was recently published in *Science Robotics*^[1].

"Surgical outcomes are highly dependent on a surgeon's skill and experience, and even one missed stitch in a bowel surgery could lead to internal leak and infection," said Moria Bittmann, Ph.D., programme director in the division of Discovery Science & Technology at NIBIB. "This preclinical work is an important step towards autonomous robotic surgery in soft tissues, which could provide increased efficacy and safety in human patients, independent of the surgeon."

Smart Tissue Autonomous Robot

The robot, called STAR (for Smart Tissue Autonomous Robot), was developed by Axel Krieger, Ph.D., and his colleagues at Johns Hopkins University. So far, the robot has been developed to perform intestinal anastomosis - where two pieces of small intestine are sewn together to form a single, continuous section - under the supervision and guidance of a surgeon. Krieger explained how the robot performs the procedure: After the surgeon manually exposes the tissue edges, STAR takes images and develops a plan for suture placement based on the shape and thickness of the tissue. Once the human operator approves of the plan, STAR independently stitches the tissue together. If the tissue deforms or moves beyond a set threshold, STAR asks the surgeon if a new surgical plan should be created. This process is repeated until the robot completes the entire procedure.

"By incorporating novel suturing tools, imaging systems, machine learning algorithms, and robotic controls, the STAR system is equipped to overcome the challenges of autonomous laparoscopic surgery in soft tissues," said Krieger. "STAR can visualize a surgical scene, generate a surgical plan, and then execute those plans with high accuracy and precision." He noted, however, that STAR is not meant to replace surgeons. "Autonomous robots, like STAR, are designed to be incorporated into the surgical workflow alongside surgeons, enhancing the performance of precise, repetitive tasks and ultimately improving surgical consistency from patient to patient."

Performance evaluation

To evaluate how well STAR performed

compared with expert surgeons, the researchers used "phantom" bowel tissues as a model system. Synthetic small intestine was mounted to a linear stage that was programmed to move back and forth, Krieger explained, which simulated breathing motions that would occur during surgery. Also during these experiments, the phantom tissue was randomly rotated and deformed, requiring STAR or the surgeon to pause, regroup, and complete the procedure, he said. STAR performed the procedure on phantom tissues five times, and four surgeons performed the procedure two different ways - twice using traditional manual laparoscopy, and twice using a different robot-assisted system.

When compared with the expert surgeons, STAR had fewer mistakes and was more consistent in suture spacing and depth. Additionally, when the researchers flowed viscous liquid through the resected phantom bowels, they found that the flow was the most laminar (smooth and streamlined) in the tissues reconstructed by STAR, indicating a higher quality anastomosis than those performed by the expert surgeons.

Finally, STAR's performance was evaluated in a large animal model. Intestinal anastomosis was performed on five pigs; for four of the animals, the procedure was performed via STAR, and for the fifth animal, the procedure was performed via traditional manual laparoscopy. Similar to the phantom experiments, STAR made fewer mistakes compared with the expert surgeon. Additionally, when the researchers analyzed how well the resected bowels had healed seven days after surgery, there was no observable difference in wound healing between the two different surgical methods.

"Our results indicate that STAR is more consistent and accurate than expert surgeons when performing suturing tasks," said Krieger. He noted that their findings demonstrate the potential for autonomous surgical robotics to enhance surgical care –



Study author Hamed Saeidi, Ph.D., observes as STAR performs laparoscopic anastomosis.



Lead author Axel Krieger, Ph.D., inspects the anastomosis performed by STAR on the phantom tissues.

which could lead to more predictable and consistent patient outcomes.

"While many may feel hesitant about having a machine perform a specialized task that is traditionally performed by a human, robotic systems have the potential to improve patient outcomes in medical settings," said Krieger. "Just like the public has embraced the gradual influx of cruise control, lane assist, and self-parking features in automobiles – which will eventually lead to self-driving cars – I think we will see a similar progression in the field of medical robotics."

Reference

^[1] H. Saeidi, J.D. Opfermann, M. Kam, S. et. al. Autonomous robotic laparoscopic surgery for intestinal anastomosis. Science Robotics 2022 7 (62). doi: https://www.doi. org/10.1126/scirobotics.abj2908

Bariatric surgery reverses low testosterone levels in male teens with obesity

Findings underscore benefits of bariatric surgery to the health and fertility of young men treated for obesity

Bariatric surgery not only treats obesity and reverses Type 2 diabetes, but a new study now shows that it also reverses low testosterone levels in teen males with obesity. The finding is important because in addition to reducing inflammation and increasing insulin sensitivity, weight loss after bariatric surgery may also influence sexual and fertility functions. Results were published in the *European Journal of Endocrinology*^[1].

This is the first major study to examine how weight loss after bariatric surgery affects testosterone in adolescent boys. Obesity in adolescent boys can often lead to hypogonadism, as shown by lower-than-normal testosterone concentrations, which may lead to sexual difficulties and reduced fertility.

"It is remarkable that testosterone levels more than doubled and in fact normalized in most adolescent boys who underwent bariatric surgery, and this was maintained up to five years," said study co-author Thomas Inge, MD, PhD, Surgeon-in-Chief and Director of Adolescent Bariatric Surgery Program at Ann & Robert H. Lurie Children's Hospital of Chicago, and Professor of Surgery and Pediatrics at Northwestern University Feinberg School of Medicine. "This testosterone response was greater than that expected in adults undergoing these same operations and adds to the growing list of benefits of using bariatric surgery in teenagers with severe obesity."

The study involved 34 teen males with severe obesity who were enrolled in Teen-Longitudinal Assessment of Bariatric Surgery, a prospective, NIH funded observational study. These teens underwent bariatric surgery and were followed for five years. Prior to surgery, only 27 percent of participants had normal free testosterone levels. Two years later, 80 percent had normal levels, and five years later, 67 percent maintained normal free testosterone levels, presumably due to some weight regain.

The study, which was led by Dr Paresh Dandona's team in the Division of Endocrinology at the University of Buffalo, also showed dramatic reductions in inflammation and insulin resistance, which provides hope that adolescent males with severe obesity who undergo bariatric surgery may have a better outlook for future metabolic health and fertility.

"The rise in testosterone levels paired with improvement in insulin sensitivity after bariatric surgery point to benefits in improving glucose metabolism, fertility, lipid metabolism, bone mineralization, and muscle mass. These changes can help decrease morbidity over the lifespan related to obesity-related complications," said Ellen Kim, MD, paediatric endocrinologist and Medical Director of the Interdisciplinary Weight Management Program at Lurie Children's, as well as Associate Professor of Pediatrics at Northwestern University Feinberg School of Medicine.

Reference:

Dhindsa S., Ghanim H., Jenkins T., et. al. High prevalence of subnormal testosterone in obese adolescent males: reversal with bariatric surgery. *European Journal of Endocrinology*. 1 Feb 2022; 186(3):319-327. doi: https://doi.org/10.1530/EJE-21-0545

Better assessment of risk from heart surgery results in better patient outcomes

A large international study has found an important new benchmark for measuring the risk of death for patients undergoing heart surgery, of which there are two million adults a year globally.

Levels of troponin (a type of protein found in heart muscle) have been used for years, through a blood test, to measure the risk of death and serious complications in patients presenting with symptoms of a heart attack. However, this test is not commonly measured after heart surgery.

With limited data on patients undergoing coronary artery bypass grafting or open-heart surgery such as valve repairs and replacements, recommendations by medical experts varied widely (from 10 times to 70 times or more the laboratory normal value) regarding troponin levels that define heart attack and important heart injury after heart surgery.

This study, published in the *New England Journal of Medicine*, assessed patients having heart surgery, measured troponin before and daily for the first few days after surgery, and assessed death and the incidence of major vascular complications – such as heart attack, stroke or life-threatening blood clot – after heart surgery.

"We found that the levels of troponin associated with an increased risk of death within 30 days were substantially higher – 200 to 500 times the normal value – than troponin levels that surgical teams are currently told defines the risk of a patient having one of the most common complications after heart surgery – myocardial injury, a heart muscle injury associated with increased deaths," said the study's lead investigator, P.J. Devereaux.

He is a senior scientist at the Population Health Research Institute of McMaster University and Hamilton Health Sciences (HHS), a professor of medicine and health



PJ Devereaux, professor of medicine and health research methodology at McMaster University and lead author of the study.

research methodology at McMaster University, and a cardiologist at HHS.

Landmark findings

The study found that by 30 days after heart surgery, 2.1% of patients had died, and 2.9% had experience a major vascular complication, such as heart attack, stroke, or life-threatening blot clot.

The study involved 15,984 adult patients with an average age just over 63 years undergoing cardiac surgery. Patients were from 12 countries, with more than a third of the countries being outside of North America and Europe.

"This study is a landmark for the health

teams taking care of patients after cardiac surgery. For the first time, we have a marker that is fast and reliable for the monitoring of these patients after cardiac surgery," said André Lamy, a study investigator, PHRI scientist, professor in McMaster's department of surgery, and heart surgeon at HHS.

"Our findings will help further studies look at the timing of treatments and procedures to improve patient outcomes after heart surgery," said investigator Richard Whitlock, PHRI scientist and associate chair, research, professor of McMaster's department of surgery, and heart surgeon and intensive care doctor at HHS.

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we have a partnership with Fortius Clinic, which brings together some of the UK's leading experts in the field of joint replacement.

15 US medical societies develop best practices to manage acute pain in complex surgical patients

The American Society of Anesthesiologists (ASA) and 14 leading medical specialty organizations in the United States have established seven guiding principles to better address the perioperative treatment of acute pain in complex surgical patients. The principles were established during a second-of-its-kind landmark pain summit hosted by ASA.

"Every surgical patient deserves adequate pain relief that aims to prevent opioid reliance, chronic pain and other negative outcomes, but it may be more challenging to achieve this in certain patient populations," said ASA President Randall M. Clark, M.D., FASA. "The new principles were created to build upon an original set established last year during our first pain summit, but specifically address patients undergoing surgery with chronic pain, those taking opioids preoperatively, and those with substance use disorders. The new principles give the perioperative care team more guidance to care for these particularly complex patients."

In February 2021, ASA convened 14 medical specialty organizations for a virtual pain summit to collaborate on a resource for acute surgical pain care. The participating organizations reached consensus on seven foundational principles for the perioperative treatment of acute pain, published in *Regional Anesthesia* & *Pain Medicine*^[1]. To build on the best practices and knowledge shared in the first pain summit, a second virtual summit on February 26, 2022 was convened, to establish guiding principles to address complex surgical patients.

The seven new principles, which will be developed into a resource for clinicians and other care team members, recommend: 1. If clinicians identify a positive screen for substance use preoperatively, a more detailed assessment tool should be utilized to risk stratify patients for additional support or referral for treatment when indicated.

2. In conducting a preoperative evaluation, if a patient is identified as having chronic pain, opioid tolerance, or a substance use disorder, clinicians should coordinate with the patient's care team, including consultation with a pain medicine, behavioural health, or addiction medicine specialist.

3. For patients on long-term opioid therapy preoperatively, clinicians should coordinate with the patient's prescribing clinician and continue the baseline opioid dose in the perioperative period with supplemental analgesia as needed for postoperative acute pain.

4. Clinicians should work with patients who have opioid tolerance on an individualized tapering plan for postoperative opioids, coordinating with the long-term opioid-prescribing clinician, with the goal of return to the preoperative dose or lower as soon as possible.

5. For patients prescribed opioids at discharge following surgery, clinicians should inform them and their caregivers about the risks, signs and management of opioidinduced respiratory depression; that they must avoid concurrent use of medicines with sedative effects and alcohol while taking opioids; and when to call for emergency assistance.

6. For patients identified as having significant risk of opioid-related adverse drug events or severe uncontrolled perioperative pain, clinicians should consult a pain specialist or anaesthesiologist preoperatively.

7. For patients identified as benefitting

from additional consultation with a pain medicine, behavioural health, or addiction medicine specialist, clinicians should utilize telehealth options if in-person consultation is not available.

In addition to ASA, participating medical organizations include:

• American Academy of Orthopaedic Surgeons

• American Academy of Otolaryngology-Head and Neck Surgery

• American Association of Neurological Surgeons

• American Association of Oral and Maxillofacial Surgeons

• American College of Obstetricians and Gynecologists

- American College of Surgeons
- American Hospital Association
- American Medical Association
- American Society of Addiction Medicine

American Society of Breast Surgeons

American Society of Plastic

Surgeons

• American Society of Regional Anesthesia and Pain Medicine

- American Urological Association
- Society of Thoracic Surgeons

"The next step for this multi-society consortium and effort is to establish how we can help institutions implement both sets of guiding principles into their practices," said Dr. Clark.

Reference:

^[1] Mariano E. R., Dickerson D. M., Szokol J. W. et. al. A multisociety organizational consensus process to define guiding principles for acute perioperative pain management. *Regional Anesthesia & Pain Medicine* 2022;47:118-127.

doi: http://dx.doi.org/10.1136/rapm-2021-103083

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Stanford Medicine

The case of the vanishing brain tumour

The brain is a new frontier for cancer immunotherapy

By Krista Conger

It was around 2010 and neurosurgeon Michael Lim, MD, was taking a patient to the operating room to remove a brain tumour. Prior to the surgery, the patient received an experimental drug to stimulate his immune system to attack his cancer, which had begun as kidney cancer and metastasized.

"I remember taking him to the OR and thinking this was going to be a routine case," recalled Lim, now chair of the Stanford University School of Medicine's Department of Neurosurgery.

"I took his tumour out. But when the pathology report came back, it indicated the mass was just inflammatory cells and no active cancer. And over the next months, the tumours in his body started to melt away. My interest was piqued by that finding and I became very interested in that drug."

The drug, which became known as Opdivo, belongs to a new class of medications called checkpoint inhibitors. Although our immune systems are honed to recognize and kill developing tumours, the tumours can evade them by exploiting biological safety valves called checkpoints, which normally tamp down any overactive immune responses that could lead to autoimmune disorders or inflammation.

Lim, who trained at Stanford Medicine but was working at Johns Hopkins University School of Medicine at the time, wondered if checkpoint inhibitors might also be effective against tumours that start in the brain, like glioblastomas.

Although subsequent experiments in mice and clinical trials in patients uncovered some significant stumbling blocks, Lim said he is excited to see a way forward for patients with the devastating cancer.

"It's clear that brain cancers are different from other types of cancers," Lim said. "For example, we've found that, although all tumours suppress the immune response



in the microenvironment, tumours that originate in the brain cause a global immune suppression that affects the whole body. This makes it very hard to induce an immune response to the tumour."

Targeting the culprits behind the immune suppression — a class of cells called myeloid cells — could reverse this phenomenon, researchers believe.

Another approach focuses on reviving a kind of immune cell called a T cell that leads the charge against cancers but can become exhausted and ineffective over time.

A series of experiments in Lim's lab suggested that combining a checkpoint inhibitor with a molecule to combat T cell exhaustion is safe.

A study of the combo's effect on patients confirmed the treatment's safety and found it resulted in longer survival times for some of the participants.

"Now we're going back to the lab bench to try to learn why some patients responded to the combination treatment and some didn't," Lim said. "We hope to go on to a larger clinical trial. There's so much amazing science here at Stanford — we're able to go from the bench to bedside and back to the bench to solve these problems."

Lim and his colleagues hope to one day see outcomes for glioblastoma patients that are similar to those experienced by patients with metastatic brain cancer.

"Glioblastoma is such a malignant disease. I've treated hundreds of these patients, and every conversation I've had with them fuelled me to try to do better for them. Each one gives me a new sense of urgency," he said.

"Right now, we are understanding cancer at a level we've never achieved before. As we learn how to assess a patient's tumour, we can become more and more precise with the therapies we can offer. We're not just wielding blunt tools anymore. I'm optimistic and excited about the future for these patients."

• This article was originally published in *Stanford Medicine* magazine, Oct. 14, 2021.

The stethoscope of the future

In 1818, French physician Rene Theophile Hyacinthe Laennec was inspired by children playing with tubes to communicate and listen to each other and, borne out of his frustrations with the traditional practice of placing his ear on the chests of his patients to listen to their breathing, he went on to invent the stethoscope.

It is hard to believe that a 200-year-old creation is still used daily in modern medical care, and yet, the ubiquitous stethoscope is so synonymous with the healthcare industry it is seen hanging around the necks of physicians in every corner of the world.

In a generation where we have seen the invention of home computers, the telephone, the internal combustion engine, light bulbs, atomic bombs, the internet, self-driving cars and space travel, the mainstay of a physician's basic kit remains the same. Until today.

In 2021, Abdul Latif Jameel Health and Butterfly Network entered into a distribution partnership to bring the innovative Butterfly iQ+ ultrasound device to a potential 2 billion people in the Middle East, North Africa, Turkey and India. From underserved communities in the USA, to remote areas of Africa, more than 4.7 billion people lack access to medical imaging^[1]. The Butterfly iQ+ is the world's only single probe, whole-body, handheld imaging device which can help physicians in the field, in rural communities, and in difficult medical situations.

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The Butterfly iQ+ is democratizing healthcare, one scan at a time, a vision that is shared and supported by Abdul Latif Jameel Health.

According to Dr. Peter Weimersheimer, Vice President, Clinical Implementation, Butterfly Network Inc., who addressed healthcare professionals recently at the Arab Health conference in Dubai, UAE, in studies which assess the accuracy of clinicians doing assessment with a stethoscope, that accuracy is never 100%.

He said: "The reality is that most patient evaluations ultimately result in a test being ordered. There has been great diagnostic technology developed which has transformed modern medicine – the CT scan, the MRI, and now, the Butterfly iQ+."

Fusing semiconductors, artificial intelligence, and cloud technology, Butterfly has made it possible to usher in a new era of medical imaging and with it, healthcare from a device that costs significantly less in time and money, than current ultrasound imaging.

The product is designed to dramatically help trained practitioners who need to quickly assess a patient's condition and provide clinical answers faster and has the potential to expand the capabilities of practitioners working outside of hospitals in developed, underdeveloped and remote areas.

Dr. Akram Bouchenaki, Chief Executive Officer, Abdul Latif Jameel Health, said: "At Abdul Latif Jameel Health, we believe access to health is a basic human right, and it is our mission to accelerate that access throughout the world. Utilizing technology helps us in achieving that mission, and Butterfly is an example of how a truly groundbreaking innovation can bring diagnostics to the patient, wherever they are in the world, quickly, efficiently,







and seamlessly. The opportunities to improve health equity are incredibly motivating in driving us forward."

• For more information on the Butterfly iQ+:

email butterfly@aljhealth.com or visit www.aljhealth.com.

References:

^{1.} https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5704652/#R3

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Bringing medical imaging up to speed with other health-tech advances, the Butterfly iQ+ is the world's only single probe, whole-body, handheld imaging device which can help physicians in the field, in rural communities, and in difficult medical situations. In 2021, Abdul Latif Jameel Health and Butterfly Network entered into a distribution partnership to bring the innovative Butterfly iQ+ ultrasound device to a potential 2 billion people in the Middle East, North Africa, Turkey and India.

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Major global study reveals risk of breast cancer spreading to other parts of the body

The risk of early breast cancer spreading to another part of the body ranges from 6% to 22%, according to the first results of a large and detailed global study of metastatic breast cancer presented at the Advanced Breast Cancer Sixth International Consensus Conference (ABC 6) in Lisbon, Portugal in November last year.

The study also shows that certain women face a higher risk than others, including women diagnosed with breast cancer at a younger age, those diagnosed with larger tumours at initial diagnosis and those with specific types of breast cancer, for example those called luminal B.

Around 2.3 million people are diagnosed with breast cancer each year around the world, but this is the first study of its kind to investigate how many of these patients go on to develop advanced breast cancer (ABC). Researchers say the new study sheds light on the extent of ABC, who is most at risk and what treatments are needed.

The research was presented by Dr Eileen Morgan from the International Agency for Research on Cancer (IARC). She said: "Breast cancer is the most common form of cancer in the world. Most women are diagnosed when their cancer is confined to the breast or has only spread to nearby tissue. But in some women, the cancer will grow and spread to other parts of the body or come back in a different part of the body several years after the end of their initial treatment. At this point the cancer becomes much harder to treat and the risk of dying is higher. However, we don't really know how many people develop metastatic breast cancer because cancer registries have not been routinely collecting this data."

Meta-analysis

The new findings are part of a meta-analysis of the available literature. This means the researchers gathered together the data from as many different studies as they could find on breast cancer and whether it spreads to other parts of the body. By combining lots of data together, researchers can get the most reliable information on the overall risk of metastasis and how it varies for different groups of patients.

This analysis included tens of thousands women who between them took part in more than 400 studies from North and South America, Europe, Africa, Asia, and Oceania. This ongoing meta-analysis will allow the researchers to look at many factors and how they influence the risk of metastasis, but they began by studying women's age when they were diagnosed with breast cancer, and the different types and stages of breast cancer. They also looked at whether rates of metastasis have changed over time.

Risk of metastasis

The analysis shows that the overall risk of metastasis for most breast cancer patients is between 6% and 22%. This is a range that reflects the level of risk for half of the women in the analysis, with only a quar-



Dr Eileen Morgan from the International Agency for Research on Cancer.

ter of women having a higher risk and a quarter of women having a lower risk (the interquartile range). Researchers say the range is broad because the risk varies a great deal depending on different risk factors. For example, women first diagnosed below the age of 35 years, have a 12.7% to 38% risk of their breast cancer coming back and spreading to other parts of the body, while women aged 50 years or older have a risk of 3.7% to 28.6%.

Dr Morgan said: "This may be because younger women have a more aggressive form of breast cancer or because they are being diagnosed at a later stage."

Among the different types of breast cancer, women diagnosed with luminal B cancer (hormone-receptor positive and tends to grow faster) had a 4.2% to 35.5% risk of metastasis compared to 2.3% to 11.8% risk in women diagnosed with luminal A can-



cer (hormone-receptor positive and tends to grow slower).

The study suggests that rates of distant recurrence, meaning breast cancer coming back after initial diagnosis and spreading to other organs, have decreased over time from women first diagnosed in the 1970s and '80s to more recent diagnoses, but some of this may be due to the time lag between a first diagnosis of breast cancer and the appearance of metastases.

The researchers will continue to work with the data they have gathered to try and quantify how many women are living with advanced breast cancer around the world, to look for other factors that may alter the risk and to monitor how the risk is changing over time.

Knowledge gap

Dr Shani Paluch-Shimon, a member of the Scientific Committee for ABC 6, Director of the Breast Unit at Hadassah University Hospital, Israel, who was not involved with the research said: "There has been a knowledge gap about how many people are living with advanced breast cancer around the world. This study is a step towards filling that gap. The researchers have already been able to give the first reliable estimate of how many breast cancer patients go on to develop advanced disease in contemporary cohorts and identify some of the groups, such as younger women, who face a higher risk. The second part of this study will define how cancer registries can collect adequate data about relapses so that we may know how many patients with metastatic cancer there are in each country.

"This information is, of course, important for patients who want to understand their prognosis. But it's also vital at a public health level for those of us working to treat and prevent advanced breast cancer to help us understand the scale of the disease around the world. It will help us identify at-risk groups across different populations and demonstrate how disease course is changing with contemporary treatments. It will also help us understand what resources are needed and where, to ensure we can collect and analyse quality data in real-time as this is key for resource allocation and planning future studies." There has been a knowledge gap about how many people are living with advanced breast cancer around the world. This study is a step towards filling that gap.

Women's Health

Early menopause may raise risk of dementia later in life



Wenting Hao, M.D., a Ph.D. candidate at Shandong University in Jinan, China

Women who enter menopause very early, before age 40, were found to be more likely to develop dementia of any type later in life compared to women who begin menopause at the average menopauseonset age of 50 to 51 years, according to preliminary research presented at the American Heart Association's Epidemiology, Prevention, Lifestyle & Cardiometabolic Health Conference 2022, in Chicago in March this year.

"Our study found that women who enter menopause very early were at greater risk of developing dementia later in life," said Wenting Hao, M.D., a Ph.D. candidate at Shandong University in Jinan, China. "Being aware of this increased risk can help women practice strategies to prevent dementia and to work with their physicians to closely monitor their cognitive status as they age."

Dementia involves changes in the brain that impair a person's ability to remember, make decisions and use language. Alzheimer's disease is the most common type of dementia, while the second most common is vascular dementia, which is the result of disruptions in blood flow to brain cells caused by strokes or plaque build-up in arteries supplying blood to the brain. Both of these types of dementia are more common with age. Diseases affecting specific parts of the brain can also lead to dementia, and a person can have dementia due to more than one disease process.

In the current study, the researchers analysed the potential relationship between age at menopause onset and the diagnosis of dementia from any cause. Health data was examined for 153,291 women who were an average age of 60 years when they became participants in the UK Biobank (between 2006 and 2010) were examined. The UK Biobank is a large biomedical database that includes genetic and health information on a half million people living in the United Kingdom.

The investigators identified the diagnosis of all types of dementia including Alzheimer's disease, vascular dementia and dementias from other causes. They calculated risk of occurrence in terms of the age at which the women reported having entered menopause, compared with the women who began menopause at average age of menopause onset, which is 50-51 years (51 years is the average age for menopause onset among women in the U.S.). The results were adjusted for factors including age at last exam, race, educational level, cigarette and alcohol use, body mass index, cardiovascular disease, diabetes, income and leisure and physical activities.

The analysis found:

• Women who entered menopause before the age of 40 were 35% more likely to have been diagnosed with dementia.

• Women who entered menopause before the age of 45 were 1.3 times more likely to have been diagnosed with dementia before they were 65 years old (called presenile or early-onset dementia).

• Women who entered menopause at age 52 or older had similar rates of dementia to those women who entered menopause at average age of menopause onset, which is the age of 50-51 years.

Although post-menopausal women are at greater risk of stroke than pre-menopausal women, and stroke can disrupt blood flow to the brain and may result in vascular dementia, in this study the researchers did not find an association between age at menopause and the risk of vascular dementia.

How to reduce the risk of dementia

"Dementia can be prevented, and there are a number of ways women who experience early menopause may be able to reduce their risk of dementia. This includes routine exercise, participation in leisure and educational activities, not smoking and not drinking alcohol, maintaining a healthy weight, getting enough vitamin D and, if recommended by their physician, possibly taking calcium supplements," Hao said.

The researchers suggest that lowered oestrogen levels may be a factor in the possible connection between early menopause and dementia.

"We know that the lack of oestrogen over the long term enhances oxidative stress, which may increase brain ageing and lead to cognitive impairment," Hao said.

Call to clinicians

Healthcare clinicians who care for women should be aware of a woman's age at menopause onset and closely monitor for cognitive decline in those who reached menopause before age 45.

"Further research is needed to assess the added value of including the timing of menopause as a predictor in existing dementia models," Hao said. "This may provide clinicians with a more accurate way to assess a woman's risk for dementia."

The study has several limitations. Researchers relied on women's self-reported information about their age at menopause onset. In addition, the researchers did not analyse dementia rates in women who had a naturally occurring early menopause separate from the women with menopause induced by surgery to remove the ovaries, which may affect the results. The data used for this study included mostly white women living in the U.K. and may not generalize to other populations.



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London's Cromwell Hospital provides world-class women's health services

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Our hospital welcomes international patients with embassy sponsorship, international health insurance and those paying for their own treatment. Having welcomed patients from over 140 countries through our doors, we are the only private hospital in the UK to have a bullet proof luxury suite with a history of treating prime ministers and presidents.

At Cromwell Hospital, we put women's health and wellbeing as our top priority, and we continuously strive to provide world-leading healthcare services and offer personalised support every step of the way. Because some conditions require prompt intervention, our rapid access clinics provide fast access to expert care and a range of diagnostic tests for female patients with different conditions including polycystic ovary syndrome (PCOS), endometriosis, uterine fibroids, and adenomyosis.

Our Gynaecology Rapid Access Clinic and our International Centre for Endometriosis offer cutting-edge facilities for our female patients.

Gynaecology Rapid Access Clinic

At Cromwell Hospital, our Gynaecology Rapid Access Clinic enables you to see a consultant gynaecologist and access any diagnostics you need, in the shortest time possible.

The rapid nature of the clinic is specifically designed to give you peace of mind and, if needed, fast access to onward support or treatment.

In many cases, we can offer next day appointments with leading specialist consultants. Any tests can also often be carried out on the same day, within our specialist women's health centre adjacent to Cromwell Hospital – the 'Well Woman Centre' – with test results coming back in as little as 2-5 working days.

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ic, we provide fast and efficient investigations for a range of different gynaecological symptoms and conditions including:

• a cervical smear abnormality

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• a clinical abnormality of your cervix, vulva or vagina

• pelvic pain including period and premenstrual pains

• feeling constantly bloated or discomfort in your

If you're experiencing any of these symptoms or have received an abnormal smear result, you may self-refer to the clinic, or be referred by your GP.

The International Centre for Endometriosis

Endometriosis can have a significant impact on a patient's quality of life, causing a wide range of debilitating symptoms including considerable pain. The variation in symptoms can make diagnosing endometriosis difficult in a primary care setting, with patients waiting on average seven years before receiving an endometriosis diagnosis.

The International Centre for Endometriosis at Cromwell Hospital is highly reputable for the advanced management of complex endometriosis. The Centre brings the best experts in endometriosis together to provide a thorough robust approach to this condition which can have a serious impact on quality of life, fertility, bowel and bladder.

The Centre is led by Mr Amer Raza who is a consultant gynaecologist with vast experience in treating complex endometriosis. Mr Raza is also co-founder and director of CCMIG (Chelsea Centre of Minimal Access Gynaecology).

At Cromwell Hospital's International Centre for Endometriosis, our aim is to provide patients with rapid access to a diagnosis, and a tailored and comprehensive treatment plan to set them on a path to recovery.

Endometriosis symptoms are wide-ranging and can vary in severity too. The most common symptoms of endometriosis are:

• pelvic pain – which is usually worse during your period

• significant period pain

• pain when going to the toilet during your period

- pain during or after sexual intercourse
- fertility issues

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Obesity significantly increases heart failure risk among women with late menopause

While women who enter menopause before age 45 are known to be at higher risk for heart failure, obesity significantly increased heart failure risk among women who experienced late menopause – at age 55 or older, according to new research published in the *Journal of the American Heart Association*^[1], an open access, peerreviewed journal of the American Heart Association.

A woman's body produces less oestrogen and progesterone after menopause, changes that can increase the risk for cardiovascular diseases including heart failure, according to the American Heart Association. Menopause typically occurs between the age of 45 and 55, however, the average age for natural menopause has increased by 1.5 years over the past six decades, according to some research. In the National Health and Nutrition Examination Survey (NHANES) 1959-2018 - surveys providing nationally representative estimates of the United States - the prevalence of early menopause (before age 45) was 12.6% and late menopause (after age 55) was 14.2%.

Previous research has found that women who experience early menopause are at heightened risk of heart failure. Heart failure is diagnosed when the heart is unable to pump sufficient blood and oxygen to allow the body organs to function well.

"There is a gap in knowledge about the possible influence of late menopause – occurring at age 55 or older – on the incidence of heart failure," according to lead study author Imo A. Ebong, M.D., M.S., an associate professor of medicine in the division of cardiovascular medicine at the University of California Davis, in Sacramento, California.

"We know that obesity increases the risk of developing heart failure, and the onset of menopause is associated with increased body fatness," said Ebong. "In our study, we investigated if and how obesity affects the relationship between menopausal age and the future risk of developing heart failure."

Atherosclerosis Risk in Communities Study

Investigators analysed health data for nearly 4,500 postmenopausal women participating in the Atherosclerosis Risk in Communities (ARIC) Study. ARIC is a long-term research project that began enrolling participants in 1987, focused on measuring the associations between known and suspected heart disease risk factors and the development of heart disease among adults in four diverse communities in the United States: Forsyth County, North Carolina; Jackson, Mississippi; the suburbs of Minneapolis; and Washington County, Maryland. Six follow-up visits were completed by 2019.

For this analysis, participants were grouped by how old they were when the entered menopause: younger than 45 years; 45-49 years; 50-54 years; and 55 years and older. The average age of study participants was 63.5 years at the fourth visit. Women with a heart failure diagnosis before the fourth study visit were excluded from in the analysis for this study.

Among many baseline measurements and assessments conducted at the fourth follow-up exam, the women provided their age at menopause, and their weight was measured. They were then classified by weight, into one of three groups: normal weight (if body mass index – BMI – was between 18.5 - 24.9 kg/m2); overweight (if BMI was between 25.0 – 29.9 kg/m2); and obese (if BMI was 30 kg/m2or higher). In addition, abdominal obesity was noted if waist circumference was 35 inches (89 cm) or more at the navel.

The heart failure risk potentially attributed to obesity as measured by BMI or waist circumference was calculated after adjusting for multiple other health and lifestyle risk factors for heart disease, including other conditions such as Type 1 or Type 2 diabetes, hypertension, kidney function, inflammation, left ventricular hypertrophy, and prior heart attack. During an average follow-up of 16.5 years, about 900 of the women had developed heart failure that resulted in either hospitalization or death.

The analysis found significant connections for menopausal age, BMI and waist circumference and heart failure risk:

• For every six-point increase in BMI the risk of developing heart failure increased 39% for the women in the menopause-before-age-45 group; 33% for those in the age 45-49 group; and doubled (2.02 times higher) in women in the late menopause group (age 55 or older). Higher BMI was not associated with increased heart failure risk in women who reached menopause between ages 50-54.

• For every 6-inch (15.24 cm) increase in waist circumference, the risk of developing heart failure almost tripled (2.93 times higher) among the women who entered menopause at age 55 years or older.

• Waist circumference did not significantly raise the risk of heart failure for women in any of the other menopausal age groups.

"We had expected that the effect of obesity on heart failure risk would be greatest among women who had experienced early menopause. This was not so," Ebong said. "The detrimental effects of obesity on heart failure risk was greatest among women who experienced late menopause."

The information from the study may be helpful when screening for heart failure and counselling postmenopausal women about heart failure prevention, according to Ebong.

"A woman's age when she enters menopause is an important factor, and women should share this information with their physicians to guide in estimating their risk of developing heart failure," Ebong said. "Women with early menopause should be informed of their increased risk and counselled to adopt healthy lifestyle and behavioural changes. Women with late menopause should be particularly counselled to maintain a healthy body weight and prevent obesity to decrease their risk of future heart failure." The current study is limited because it did not include enough women to analyse separately for different types of heart failure.

"Our analysis should be repeated according to heart failure subtypes, preserved and reduced ejection fraction heart failure, to more clearly understand heart failure risk estimation and provide guidance on screening and prevention programmes," said Ebong.

Reference

^{1.} Imo A. Ebong, Machelle D. Wilson, Duke Appiah, et. al. Relationship Between Age at Menopause, Obesity, and Incident Heart Failure: The Atherosclerosis Risk in Communities Study. Journal of the American Heart Association 2022;11:e024461.

doi: https://doi.org/10.1161/ JAHA.121.024461

Underweight and overweight women at higher risk of successive miscarriages

A new study has shown that underweight and overweight women are at a significantly higher risk of experiencing recurrent miscarriages compared to those of average weight.

A research team led by the University of Southampton assessed the link between women's lifestyle and risk of recurrent pregnancy loss, defined as women having two or more consecutive early miscarriages. The systematic review and meta-analysis study has been published in the journal *Scientific Reports*^[1].

Miscarriage is the most common complication of early pregnancy, affecting between 15% and 20% of all pregnancies. Recurrent pregnancy loss is a complex disease and although often attributed to numerous medical factors and lifestyle influences, the cause is deemed "unexplained" in around 50% of cases.

The results of this latest study found that there are higher occurrences of successive miscarriages in mothers who are underweight (having a Body Mass Index score of less than 18.5), overweight (having a BMI between 25 and 30) and obese (having a BMI above 30). The study's first author, Dr Bonnie Ng, MRC Fellow in Clinical and Experimental Sciences at the University of Southampton said: "Our study included sixteen studies and showed that being underweight or overweight significantly increases the risk of two consecutive pregnancy losses. For those with BMI greater than 25 and 30, their risk of suffering a further miscarriage increases by 20% and 70% respectively."

The research team also set out to assess the impact of factors such as smoking and consumption of alcohol and caffeine. However, they were unable to establish conclusively whether these have any impact or not due to inconsistencies of the results from a small number of studies and heterogeneity in women taking part in them.

Whilst recognising that more observational and clinical research is needed to establish the full extent of lifestyle choices, the authors conclude that weight is a risk factor that can be modified to reduce the risk.

"Our findings suggest that having an abnormal BMI exacerbates a woman's risk of suffering from repeated miscarriages, and so clinicians really need to focus on helping women manage this risk factor," said Ying Cheong, Professor of ReproducOur findings suggest that having an abnormal BMI exacerbates a woman's risk of suffering from repeated miscarriages.

tive Medicine at the University of Southampton and senior author on the paper.

Reference:

Ka Ying Bonnie Ng, George Cherian, Alexandra J. Kermack, et. al. Systematic review and meta-analysis of female lifestyle factors and risk of recurrent pregnancy loss. *Scientific Reports* Vol 11, Article number: 7081 (2021). doi: https://go.nature.com/3kKHVWm



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Becton Dickinson

Target-Controlled Infusion anaesthesia: New more universal models



By James Waterson, RN, M.Med.Ed. MHE. Becton Dickinson. Medical Affairs Manager, Middle East & Africa

In simple terms Target-Controlled Infusion (TCI) means that instead of setting a dose-rate on the pump, the pump is programmed to target a required plasma concentration or effect-site concentration. A TCI pump automatically calculates how much drug is needed during induction and maintenance to maintain the desired effect-site or plasma concentration.

A TCI algorithm (the 'target' and plan on which the pump relies to deliver appropriate induction and maintenance rates to maintain anaesthesia without overdosing the patient) is based on pharmacokinetic (PK) and pharmodynamic (PD) models and on Absorption, Distribution, Metabolism, and Excretion of medications by the body.

For example, the effect-site concentration of Propofol required to produce loss of consciousness is about 3 to 6 mcg/ml, depending on the patients' demographics. Patients waking from anaesthesia generally have a blood concentration of around 1-2 mcg/ml, although this is dependent on other drugs given during anaesthesia.

Adequate analgesia with Remifentanil is generally achieved with 3-6 ng/ml. A Remifentanil infusion of 0.25-0.5 mcg/kg/ min in an 'average' man – 70 kg, 170 cm, 40 years old – produces a blood concentration of around 6ng/ml after 25 minutes.

PK models are based on body compartments

Conventionally the body compart-

ment that the drug is injected into is V1 (plasma/blood), the next compartment is the 'vessel-rich' or 'fast re-distribution' compartment and is characterized as V2 (heart, liver, etc.). The final compartment, which is anatomically 'vessel-poor' and 'slow' in terms of re-distribution, is V3 (fatty tissue).

Drug distribution and the metabolism/ elimination of each drug in each compartment is also part of each TCI model, as is the pharmacodynamics of the time taken between the plasma and effect-site effect.

Computer simulations and mathematical modelling of infusion schemes based on the above theories of compartments and clearances give models for both Target Plasma Concentration (Cpt) and Target Effect Concentration (Cet) and these can be incorporated into specialist infusion pumps.

The Marsh model for Propofol requires only age and weight to be programmed in the pump. The Schnider model is an alternative model for Propofol and has advantages in elderly patients as it is based on a lean body mass (LBM) calculation for each patient. Elderly patients receive a lower induction and maintenance dose, which can assist with hemodynamic stability.

The Remifentanil Minto model uses age, height, gender and weight, and determines LBM for its calculations.

TCI pumps deliver the infusion at a constantly altering rate, but it is useful to think of this one infusion as being a meanaverage of three continually calculated infusion rates: a constant rate to replace drug elimination and two exponentially decreasing infusions to match drug removed from central compartments to other peripheral compartments of distribution.

Key features of an ideal TCI infusion system or pump are:

• Critical information such as decrement time, current Cet or Cpt and respective targets, current dose rate and concentration and type of agent being infused can be displayed at the same time on one screen.

• Patient parameters used during the setting-up of infusions appear on one screen to avoid the need for shuttling through multiple screens to check vital information.

• An Induction Time adjustable from seconds to minutes to allow for a gentle induction for patients with cardiovascular conditions or established hypotension.

Obese patients have previously presented a problem for 'classic' TCI, and the physiological differences between paediatrics and adults had required separate models for children.

Now, however, we have the Eleveld model for both Propofol and Remifentanil, and the Kim-Obara-Egan Remifentanil model which are much more universal and can potentially allow TCI in age ranges from 6 months to 99 years of age, and from 2.5 to 215 kg.

TCI, with its emphasis on evidencebased anaesthesia, and new near-universal patient models seems primed to change our approach to the management of all patients receiving sedatives and analgesic agents.



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Global clinicians want more precision in medication screening tools

Today's patients are presenting with ever-increasing degrees of complexity in their comorbidities and medication regimens. Global clinical leaders say a key component to patient safety is medication safety screening, but many feel their current solution isn't sophisticated enough to meet their health system's demands.

According to a recent Medi-Span survey ^[1] of more than 300 clinical leaders across 39 countries, 95% of respondents felt a medication safety screening solution would be useful. Despite this, only 44% of those surveyed currently have a solution integrated with their electronic health record (EHR) system.

Medication decision support can help clinicians reduce prescribing, dispensing, and medication administration errors. But with nearly half of clinicians lacking the appropriate data and tools, and many of those that have solutions in place describing them as only adequate or satisfactory, it is clear that clinicians and healthcare IT leaders are craving more maturity from medication decision support systems and greater precision from EHR-integrated patient safety screening.

Reducing medication errors through precision screening

Medication errors and healthcare-related adverse events ^[2] occur in 8-12% of hospitalizations in the European Union. Additionally, evidence shows that 50% to more than 70% of serious harm caused by such errors in the EU can be prevented through comprehensive systemic approaches to patient safety.

Medication decision support solutions can help mitigate those events by providing alerts and supporting content to inform clinician decisions at key moments in the patient care process. Accordingly, among the top benefits of a medication screening solution, survey respondents listed:Alerts and reminders within the

workflow

• Reducing drug interactions and adverse events

- Preventing dosing errors
- Providing guidance of severity
- Preventing compatibility errors

While the healthcare professionals surveyed rated their satisfaction with their current medication safety screening solution when using basic patient data (such as age, weight, or gender) at a 6.4 out of 10, that number dipped to 4.9 when respondents were asked to consider how well their solution uses more advanced patient data. Many noted that one of their biggest causes of frustration with their solu-

tion was the lack of personalized, precision screening that took into account additional patient factors such as:

- Conditions/ comorbidities
- Pharmacogenomics
- Lab results

What do clinicians look for in their tools?

Patient safety was the primary reason clinicians surveyed – whether from Mexico, South America, the Middle East, Asia Pacific, or Australia – offered for why they valued medication screening tools. The top three most valuable benefits of medication screening cited by respondents were:

1. Improved patient safety and quality of care

2. Information within workflow to improve decision making

3. Time-saving and workflow efficiency When asked to rate how important certain factors were in selecting the right medication screening solution, respondents selected their top criteria and scored them on a scale of 0-5:

• Content quality: 4.6

• Workflow optimization (or alerts appearing at the right place, right time): 4.03

- Patient-centric alerts: 4.01
- Frequency of content updates: 3.6
- Granularity of drug information: 3.4
- Visionary vendor: 2.87

Are you ready for the next generation of healthcare IT?

Medication screening solutions are evolving and maturing to adapt to the needs of modern healthcare.

A first-generation solution allows for basic screening, but it does not connect to patient data for personalized alerts, nor does it provide alerts at key moments within the workflow. A second-generation solution will add in minimal patient data and moderate drug information granularity to increase precision. With a more developed third-generation solution, you see more sophisticated data allowing for greater alert precision and efficiency of feedback. It isn't until the fourth generation of development that medication decision support delivers more advanced and granular drug and



patient data, the latest available evidence, efficient just-in-time alerting, and analytic insights to optimize impact.

Of the clinicians surveyed who had already implemented medication screening, the largest percentage – 44% – were comfortable that they were using an advanced third-generation solution. Only 8% reported that they had a fully developed fourth-generation medication decision support solution.

Even so, 21% said that they were still using a first-generation solution. Without the decision support clinicians need at the time, place, and level of sophistication they are seeking, many health systems find that the challenges of reducing errors and lessening demands on the workforce are exacerbated. Taking the steps to upgrade a health system's medication decision support system and workflow integration can have a lasting positive effect on clinician experience and on resulting care quality and outcomes.

Teaching hospital reduces medication errors

See how one teaching hospital helped reduce medication errors and relieved pressure on staff with Medi-Span advanced medication decision support.

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https://www.wolterskluwer.com/en/expertinsights/nckuh-data-solution-helps-reducemedication-errors-relieve-staff-pressure

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 https://www.euro.who.int/en/healthtopics/Health-systems/patient-safety/dataand-statistics





Start-up funding is key to innovation in MedTech \$1 million awarded to biotech breakthroughs

Travelling to the United States for health care can be relatively expensive, but the key reason patients go to the United States for treatment is in large part because of the exceptionally advanced level of care that is available – innovative, evidence-based treatments that in many cases are not available in other parts of the world.

One of the main reasons why leading hospitals in the US are in a position to offer such advanced levels of care is because there is significant and broad spend on medical research in the US across the wide spectrum of healthcare. In addition, there is solid support for start-ups in the industry – to help them bring new tech to the market, for example. And there are many examples of this being announced across the country on a seemingly weekly basis.

The following story of the recent announcement of financial awards for ten biotech projects in the Boston area is a good example of what can be found happening in cities across the country on a regular basis and continues to be one of the main driving forces that ensure the United States remains a leading destination for the most cutting-edge diagnostics and treatments.

Innovation Discovery Grants

This year the Bank of America joined with Mass General Brigham as presenting sponsor at the World Medical Innovation Forum in Boston. The organisers say the Forum – established in 2015 – was set up "in response to the intensifying transformation of health care and its impact on innovation". The Forum, they say, is rooted in "the belief that no

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matter the magnitude of change, the centre of health care needs to be a shared, fundamental commitment to collaborative innovation with industry and academia working together to improve patient lives."

At the Forum the annual Innovation Discovery Grants (IDG) were awarded.

Ten biotech advancements from Mass General Brigham were awarded this highly competitive grant. Each of the potential patient care and healthcare delivery breakthroughs received \$100,000 toward ongoing development and future commercialization, based on the potential to improve health outcomes, meet articulated milestones, and attract follow-on investment as assessed by independent industry experts.

Ravi Thadhani, MD, Chief Academic Officer, Mass General Brigham, explained: "The Innovation Discovery Grants support translation of biotech research from the lab to real-world products whereby they can help more patients."

Since IDG's inception, 65 research projects have been awarded a combined \$4.2 million, and together have raised more than \$199 million to further their development. This includes 14 new companies actively developing IDG-supported technologies and 19 license agreements.

Chris Coburn, Chief Innovation Officer, Mass General Brigham, noted: "Advancements in biotech are redefining the future of medicine. These grants recognize the tremendous commitment to spark innovation throughout Mass General Brigham and translate invention to the front lines of care."

The Mass General Brigham Harvard faculty receiving this year's IDG awards are:

■ A Novel Convection Enhanced Delivery System for Brain Malignancies --Miles Cunningham, MD, PhD, McLean Hospital. Convection Enhanced Delivery (CED) is a method in which a large volume of therapeutic agent under hydrostatic pressure is infused directly within diseased brain tissue. CED is being investigated primarily for glioblastoma multiforme (GBM), an aggressive brain cancer that leads to approximately 200,000 deaths worldwide each year. Typically, patients live only a few months following diagnosis. There have been no significant improve-



ments in treatment for GBM in 40 years. The proposed CED System addresses conventional CED shortcomings by replacing a large, cumbersome delivery tube with multiple precision micro-cannulas. These small tubes are positioned strategically in 3-D arrays using sophisticated surgical planning software and rapid prototyping to fabricate a patient-specific system within 1-2 days of diagnosis. GBM represents but one indication for this system, other indications include inoperable epilepsy and traumatic brain injury.

FastLine: Single-handed Venous Access Device - Hilary Gallin, MD, Massachusetts General Hospital. FastLine is a device that enables placement of a central line with one hand using intuitive, ergonomic movements to enable real-time troubleshooting and allow the use of ultrasound in the other hand throughout the entire procedure. The device eliminates poorly controlled movements that occur with the traditional placement technique and is designed to maximize control and dexterity. It also aggregates almost every required component of the procedure into one device with a safety needle, increasing central line kit organization and decreasing risk of contamination or needlesticks. FastLine will reduce complications, decrease procedure time, improve the patient experience, and serve to reduce the \$2 billion spent on managing patient injuries arising from the 5 million central line placements in the U.S. alone each year.

Development of KRAS Degraders in Cancer – Vid yasagar Koduri, MD, PhD, Brigham and Women's Hospital. Mutation in the KRAS (Kirsten Rat Sarcoma

virus) gene are the main drivers of lung, colon, and pancreatic cancer, which together kill 230,000 annually in the U.S. Treatment regimens are arduous, only partially effective, and cost (in aggregate) hundreds of millions of dollars. The preponderance of data from studies in cell, animal, and patient-derived models of disease indicate that therapeutically targeting KRAS would be an enormous advance in the treatment of these cancers. The proposed research program uses a newly developed positive-selection screening platform as a tool to identify protein degraders of KRAS (rather than inhibitors) as potential therapeutic agents. This approach has been validated as a game-changer in other cancers such as multiple myeloma.

Restoring Tumor Immunogenicity in Glioblastoma Multiforme (GBM) - Arpita Kulkarni, PhD, Brigham and Women's Hospital. This program features a novel drug that may change the paradigm for glioblastoma (GBM) therapy. Traditional treatments for GBM (chemotherapy, radiation, and surgical resection) have remained unchanged for decades, and the prognosis for GBM patients is grim. While emerging cancer therapies (e.g., allogenic cell therapies) are being developed, so far, they remain unsuccessful in clinical trials, in addition to being very expensive and highly variable in outcomes between patients. This program has engineered and patented a new therapeutic that can cross the blood-brain barrier, induce tumour immunogenicity in models of GBM and other solid cancers, as well as synergize with cell therapies. Such a multi-pronged approach has never been tested in the clinic and could markedly improve outcomes in

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GBM while also improving the activity of cell therapy.

Developing First-in-Class mRNA Methyltransferase Inhibitor -- Li Lan, MD, PhD, Massachusetts General Hospital. The goal of this study is to develop IND-enabled compounds targeting mRNA methyltransferase and validate their effectiveness in cancer therapy. The ultimate goal is to target a newly identified mRNA-dependent repair pathway and mRNA methylating enzymes in DNA repair in cancer therapy. This could lead to effective therapeutic strategies for around 90 percent of breast and ovarian cancer patients without HRD, as well as effective therapeutic strategies for other cancers. These first-in-class mRNA methyltransferase inhibitors for cancer treatment have a high potential for the cancer drug market and the treatment of a large population of cancer patients.

Auditory Mirror Therapy for Tinnitus - Clas Linnman, PhD, Spaulding Rehabilitation Network. Current healthcare cost for tinnitus (ringing in the ears) in the U.S. is estimated at \$17 billion. About one in ten adults suffer from tinnitus, yet there are no FDA approved drugs or devices. The proposed technology provides a new type of treatment for tinnitus that is non-invasive, affordable, and low risk. This neuromodulatory therapy is based on disruption of multisensory integration. Like mirror box therapy for phantom pain, in this therapy, sound at the left ear is transmitted to the right ear canal, and sound at the right ear is transmitted to the left ear canal. Implemented in a wearable pair of headphones, a pilot trial of "auditory mirror therapy" (AMT) indicates that brief use of the headphones significantly and substantially reduced tinnitus. The effects of AMT will be verified in a larger, placebo-controlled study of persons with tinnitus. The technology can be implemented as a separate device, added to current hearing aids, or as a software application for microphone-equipped wireless earbuds, with the potential to help many with tinnitus.

■ Noninvasive Diagnosis of Middle-Ear Pathologies – Hamid Motallebzadeh, PhD, Massachusetts Eye and Ear. According to National Institute on Deafness

and Other Communication Disorders, approximately 15% of American adults (37.5 million) aged 18 and over report some trouble hearing, among which, over 50% of the cases are related to conductive hearing loss. Wideband tympanometry is a promising cost-effective tool for noninvasively probing the status of the ear. However, interpreting its complex outcome to provide reliable indicators of middle-ear pathologies has proven challenging. This project aims to automate objective differential diagnoses of middle-ear pathologies by taking advantage of powerful pattern-recognition capabilities of machine learning to infer details about the middle-ear status from clinical data. This tool could reduce the need for exploratory surgery, improve the specificity of preoperative preparations, and provide a low-cost tool for postoperative monitoring. This tool helps spot features that the human eye has difficulty identifying, which can help avoid subjective interpretations in differential diagnosis of the middle ear and conductive pathologies.

Small-Molecule MMP Inhibitors for Allergic Inflammation - Jin Mo Park, PhD, Massachusetts General Hospital. Current allergy medications, ranging from corticosteroids to cytokine receptor-blocking antibodies to JAK inhibitors, are effective in only subsets of patients, produce partial responses, and often encounter treatment resistance. More importantly, they directly interfere with the workings of the immune system and can cause harmful side effects. The inadequacy of current medications to address these problems and the deficiency of new solutions prevent the pharmaceutical and healthcare industry from creating effective allergy treatment options for large patient populations. This project aims to develop small-molecule inhibitors of a specific protein-degrading enzyme as topical therapeutics for atopic dermatitis (AD), asthma, and other allergic inflammatory diseases. Preliminary data show that this enzyme plays a key role in driving allergic inflammation.

Neutralizing Antibody to FSTL3 as an Immunotherapy in Ovarian Cancer – David Pepin, PhD, Massachusetts General Hospital. High-grade serous ovarian cancer is the most lethal gynaecologic malignancy, accounting for 70% of ovarian cancer-related deaths, and affecting over 14,000 women in 2020. The treatment options for these patients are limited, particularly for patients that do not respond to chemotherapy or PARP inhibitors, and the survival rates have remained low. The advent of immunotherapies, such as immune checkpoint blockade (ICB), has brought a paradigm shift in the treatment of many cancers, sometimes providing curative responses. Unfortunately, immune checkpoint blockade therapies have not been successful in ovarian cancer, which is generally resistant to these agents. Our technology consists of a neutralizing antibody to FSTL3, which we hypothesize drives this resistance, that would be used in combination with immune checkpoint blockade therapy and alongside the current standard of care for ovarian cancer. We expect that this technology will significantly increase the response rate of ovarian cancer to immune checkpoint therapies and lead to significantly better outcomes.

Circulating Microparticle Proteins Predict Pregnancies Complicated by Placenta Accreta Spectrum - Hope Yu, MD, Brigham and Women's Hospital. Placenta accreta spectrum, or PAS, is a potentially life-threatening pregnancy complication that occurs in approximately 1 in every 1000 - 2000 pregnancies. There is no biomarker test for PAS currently, and diagnostics rely on imaging studies and assessment of clinical risk factors. Despite these efforts, approximately 50% of PAS cases remain unidentified prior to delivery. The proposed product is a blood test to assess a woman's risk of PAS using circulating microparticle (CMP) proteins. The research team has previously identified a CMP protein panel that distinguishes pregnancies affected by PAS from unaffected pregnancies. This test would be used at the end of the second trimester with a woman's routine outpatient blood work. Implementation of a blood test using this CMP protein panel has potential to improve the antenatal detection of PAS and is critical in global efforts to reduce maternal morbidity and mortality.

Despite the pandemic, UChicago Medicine performed a record number of transplants in 2021, mirroring a nationwide trend



Transplant surgeon Angelica Perez-Gutierrez, MD



For the second year in a row, the University of Chicago Medicine performed a record number of organ transplants despite the unprecedented challenged faced by hospitals during the COVID-19 pandemic.

Transplant teams at the Hyde Park-based academic health system reached an institutional record of 346 transplant surgeries in 2021, a 42% increase from the previous year. That far surpassed the 244 transplants performed in 2020, which also had set a record.

"Even though 2021 was an exceptionally difficult time for hospitals around the world, there continued to be patients with endstage organ failure who needed life-saving surgeries," said John Fung, MD, PhD, co-director of UChicago Medicine's Transplant Institute. "This work wouldn't have been possible without the selflessness of organ donors and donor families whose gifts gave our patients a chance at a new life."

Kidney, pancreas and heart transplants charted the greatest increases between 2020 and 2021. The number of kidney transplants at UChicago Medicine doubled in 2021 to 174. There also were 11 pancreas transplants, a 120% increase over 2020. Sixty-one heart transplants were performed in 2021, a 36% increase over the previous year. The heart transplant figure also set a new state record, surpassing the high-water mark set by Northwestern Medicine with 56 transplants in 2018.

Last year's increase mirrors a nationwide transplant trend. Hospitals across the U.S. performed a record number of organ transplants in 2021, according to the United Network for Organ Sharing (UNOS), increasing 5.9% over 2020. Kidney, liver and heart transplants were at all-time highs, UNOS reported.

More donated organs

A growing supply of donated organs may be fuelling the trend. More people than ever before chose to donate organs in 2021, UNOS data showed. For the 11th consecutive year, the number of deceased organ donors grew, soaring to 14,000 people in 2021, a 10.1% increase over 2020.

While donor organs vary in quality, Valluvan Jeevanandam, MD, director of UChicago Medicine's Heart and Vascular Center, said the health system's experience with difficult and unusual transplant cases has given his team the expertise to safely and effectively utilize a wider pool of donor organs.

"It's taken years of investment, development and dedication from our staff to cultivate a transplant program that can provide these kinds of life-saving surgeries,"said Jeevanandam, who has performed more than 1,000 heart transplants. "We're honoured that so many patients and families trust us to perform these surgeries."

Shortest wait time for transplants

Federal statistics released in July 2021 showed UChicago Medicine's heart transplant program had a 100% first-year survival rate and the shortest wait time for transplants, making it the best in the country, according to the data from the Scientific Registry of Transplant Recipients (SRTR). Half the people on UChicago Medicine's waiting list received a new heart in 1.1 months, compared to the national average of 6.9 months.

The SRTR data also showed that UChicago Medicine had the highest percentage of African American heart transplants in the country at 42.2%.

UChicago Medicine's leading-edge reputation for transplant surgeries dates back to 1904, when a cardiac surgeon developed the technique for joining severed ends of blood vessels. That procedure eventually made organ transplantation possible. The medical centre continued advancing the field by pioneering the study of bone marrow transplantation. UChicago Medicine performed the first successful living-donor liver transplant in the world, the first segmental and split-liver transplants in the U.S. and the first pancreas transplant in Illinois.

Since then, UChicago Medicine has also performed 12 of the country's 34 heart-liver-kidney transplants, including the historic "double-triple" in 2018 — back-to-back triple organ transplants. In 2020, the hospital did one of the country's first transplants on a patient who required a new heart because of damage from COVID-19.

• For more information, visit https://uchicagomedicine.org/global



The new Technogym Dubai

The world's leading brand in equipment and digital solutions for fitness and wellness unveils the new Dubai building to offer consumers and industry operators the possibility to live the Technogym experience

Technogym, the world-leading brand in equipment and digital services for fitness, sport and health, present in the Emirates for over 20 years, has opened its new boutique and Technogym Experience Centre in Dubai, located in Jumeirah Beach Road near the Burj Al Arab in an exclusive shopping and luxury area. The new building is the largest Technogym Experience Centre overseas and the perfect place for both consumers and industry operators to live, firsthand, the Technogym Experience supported by cutting-edge design, superior biomechanics, digital technologies, and personal training.

Biocircuit

The most exciting feature however is the Biodrive. Thanks to the latest innovation, combining research from the aeronautical industry, Technogym has developed the ultimate resistance training solution. The Biodrive can replicate up to 7 different resistance types, for example eccentric overload, and even a built-in spotter! This Biodrive is able to generate adaptive resistance adjustments in response to movement (i.e., position, velocity and acceleration). This method is the foundation of how Biocircuit works.

Despite of all of the great innovations,

the real added value is that members can now access a personalised plan specific to their ability level and matching their goals & needs. Biocircuit has five types of workouts (plus has the potential to customise your own plans) to cater for a variety of needs, ability levels and demographics, all of this squeezed into a sub 30-minute workout (variations are available)!

Whether your goal is to "Start Moving", "Stay Young", "Lose Weight", "Tone Your Body", or "Boost Performance" Biocircuit has you covered. Each programme works on a specific repetition range, tempo and even type of resistance (viscous, inertia free, eccentric overload) to match the demand of the programme to achieve a specific outcome. This means that you can have up to 12 people at any given time working under a time and repetition-based circuit, each with a different programme and with different training history at any time.

• Biocircuit is available at the Technogym Dubai, in the wellness center on the 1st floor.

Point of reference for all clients

The Technogym Dubai building has been designed to be the point of reference for all

Technogym clients, partners and stakeholders. With more than 1000 sqm space it is a great place to discover the Technogym ecosystem comprising connected smart equipment, digital services, on-demand training experiences and apps that allow every user to access a completely personalized training experience anytime and anywhere: at home, at the gym, on-the-go. The centre will have also a room that can accommodate up to 40 people to leverage the educational component of Technogym solutions. Here clients can be trained and operators can run seminars and workshops.

Guidance on all solutions

For industry operators, trainers and professionals, Technogym Dubai is available for meetings, consultancy and guidance on all solutions for different businesses: fitness clubs and sports centres, hospitality, health, rehabilitation and real estate. Technogym will also host seminars and educational activities for industry operators to inform them of all the different applications of the Technogym Ecosystem for sports, wellness and fitness, as well as the latest digital technologies and newest training solutions and formats chosen by the best teams and athletes worldwide.









Technogym's new Excite line

Technogym is the world's leading wellness

company, with its innovative Italian de-

sign, cutting-edge technology, high quality,

and easy-to-use products that are seen and

The new Excite line makes training more fun and inspiring for any age or fitness level with lots of workouts and entertainment options.

Technogym Live

Technogym Live is the new digital user interface that empowers Excite consoles. Born to inspire people to embrace exercise and make it a part of their daily lives, it helps achieve results in a fun and motivating way.

Technogym Coach

Built into every piece of equipment, Technogym Coach will motivate and guide you, so you get the most out of your exercise time. With engaging new content on our consoles, achieving results has never been this much fun.

Choose your Technogym Session, based on your personal goals, and the virtual trainer will guide you through a one-on-one session, offering encouragement and suggesting the level of intensity, which you are free to follow or change. There are six Sessions to each goal-based training series.

Each Technogym Routine contains a variety of movements and exercises, whose intensity is automatically set up by the equipment. You will receive step-by-step guidance either by video, if you are on the Routine-dedicated screen, or by pop-up messages, if you are enjoying entertainment content.

Completely redesigned for extra clarity, the new dashboard keeps all your stats in one place: calories, distance, pace, heart rate and much more.

Mobile connectivity

Technogym has mobile connectivity so you can go about your daily life while exercising: browse the internet, connect with friends on social media or watch an episode of your favorite Netflix series.

Space-saving

Technogym provides more room with less footprint. The redesigned Excite range brings you everything you love about exercising in the least possible space.

and sport teams, as well as being the official supplier of the Olympic Games since 2000, the brand also boasts ongoing collaborations with acclaimed Archistar designers like Antonio Citterio. At the heart of the brand lies its unique concept of 'wellness'. The Technogym lifestyle is committed to promoting regular exercise, a balanced diet and positive mental approach – that translates into everything the company does from products to digital fitness services to interior design.

Technogym

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Skill Run

Skill Run is the first ever treadmill with Multidrive Technology for effective power and cardio conditioning. The variety of on-board video-guided routines and specific workouts for skill training enables elite athletes and demanding fitness enthusiasts to achieve outstanding performances every time.

Skillbike

Skillbike is the indoor cycle that simulates the dynamics of hill climbing, enabling cycling professionals and enthusiasts to experience the emotion and challenge of outdoor riding in an indoor environment.

Skillmill

With Skillmill you are the engine. Your stride sets the pace and drives you toward more challenging goals. A single piece of equipment that improves your power, speed, stamina and agility, so you can achieve more from your training.

UNICEF and WHO warn of 'perfect storm' of conditions for measles outbreaks among children

Reported worldwide measles cases increased by 79% in the first two months of 2022, compared to the same period in 2021, as WHO and UNICEF warn conditions ripe for serious outbreaks of vaccine-preventable illnesses.

An increase in measles cases in January and February 2022 is a worrying sign of a heightened risk for the spread of vaccinepreventable diseases and could trigger larger outbreaks, particularly of measles affecting millions of children in 2022, warn WHO and UNICEF.

Pandemic-related disruptions, increasing inequalities in access to vaccines, and the diversion of resources from routine immunization are leaving too many children without protection against measles and other vaccine-preventable diseases.

The risk for large outbreaks has increased as communities relax social distancing practices and other preventive measures for COVID-19 implemented during the height of the pandemic. In addition, with millions of people being displaced due to conflicts and crises including in Ukraine, Ethiopia, Somalia and Afghanistan, disruptions in routine immunization and CO-VID-19 vaccination services, lack of clean water and sanitation, and overcrowding increase the risk of vaccine-preventable disease outbreaks.

Almost 17,338 measles cases were reported worldwide in January and February 2022, compared to 9,665 during the first two months of 2021. As measles is very contagious, cases tend to show up quickly when vaccination levels decline. The agencies are concerned that outbreaks of measles could also forewarn outbreaks of other diseases that do not spread as rapidly.

Apart from its direct effect on the body, which can be lethal, the measles virus also weakens the immune system and makes a child more vulnerable to other infectious diseases like pneumonia and diarrhoea, including for months after the measles infection itself among those who survive. Most cases occur in settings that have faced social and economic hardships due to CO-VID-19, conflict, or other crises, and have chronically weak health system infrastructure and insecurity.

"Measles is more than a dangerous and potentially deadly disease. It is also an early indication that there are gaps in our global immunization coverage, gaps vulnerable children cannot afford," said Catherine Russell, UNICEF Executive Director. "It is encouraging that people in many communities are beginning to feel protected enough from COVID-19 to return to more social activities. But doing so in places where children are not receiving routine vaccination creates the perfect storm for the spread of a disease like measles."

In 2020, 23 million children missed out

on basic childhood vaccines through routine health services, the highest number since 2009 and 3.7 million more than in 2019.

As of April 2022, the agencies report 21 large and disruptive measles outbreaks around the world in the last 12 months. Most of the measles cases were reported in Africa and the East Mediterranean region. The figures are likely higher as the pandemic has disrupted surveillance systems globally, with potential underreporting.

Countries with the largest measles outbreaks since the past year include Somalia, Yemen, Nigeria, Afghanistan, and Ethiopia. Insufficient measles vaccine coverage is the major reason for outbreaks, wherever they occur.

"The COVID-19 pandemic has interrupted immunization services, health systems have been overwhelmed, and we are now seeing a resurgence of deadly diseases including measles. For many other diseases, the impact of these disruptions to im-

Top 5 countries with reported measles cases in the last 12 months, until April 2022 ^[1]

Country	Reported Measles cases	Rate per million cases	First dose measles coverage (%), 2019 ^[2]	First dose measles coverage (%), 2020 ^[3]
Somalia	9,068	554	46	46
Yemen	3,629	119	67	68
Afghanistan	3,628	91	64	66
Nigeria	12341	58	54	54
Ethiopia	3039	26	60	58



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Olaa Badran, 5 years old, got vaccinated during the UNICEF-supported immunization campaign in the Community College IDP camp in Marib City, Yemen, in November 2021. UNICEF measles and polio immunization campaigns ensure that all children from 6 months to 10 years of age are fully protected from measles and polio diseases.

munization services will be felt for decades to come," said Dr Tedros Adhanom Ghebrevesus, Director-General of the World Health Organization. "Now is the moment to get essential immunization back on track and launch catch-up campaigns so that everybody can have access to these life-saving vaccines."

As of 1 April 2022, 57 vaccine-preventable disease campaigns in 43 countries that were scheduled to take place since the start of the pandemic are still postponed, impacting 203 million people, most of whom are children. Of these, 19 are measles campaigns, which put 73 million children at risk of measles due to missed vaccinations. In Ukraine, the measles catch-up campaign of 2019 was interrupted due to the COVID-19 pandemic and thereafter due to the war. Routine and catch-up campaigns are needed wherever access is possible to help make sure there are not repeated outbreaks as in 2017-2019, when there were over 115,000 cases of measles and 41 deaths in the country - this was the

highest incidence in Europe.

Coverage at or above 95% with two doses of the safe and effective measles vaccine can protect children against measles. However, COVID-19 pandemic-related disruptions have delayed the introduction of the second dose of the measles vaccine in many countries.

As countries work to respond to outbreaks of measles and other vaccine-preventable diseases, and recover lost ground, UNICEF and WHO, along with partners such as Gavi, the Vaccine Alliance, the partners of the Measles & Rubella Initiative (M&RI), Bill & Melinda Gates Foundation, and others are supporting efforts to strengthen immunization systems by:

• Restoring services and vaccination campaigns so countries can safely deliver routine immunization programmes to fill the gaps left by the backsliding;

 Helping health workers and community leaders communicate actively with caregivers to explain the importance of vaccinations;

• Rectifying gaps in immunization cov-

erage, including identifying communities and people who have been missed during the pandemic;

• Ensuring that COVID-19 vaccine delivery is independently financed and well-integrated into overall planning for immunization services so that it is not carried out at the cost of childhood and other vaccination services;

• Implementing country plans to prevent and respond to outbreaks of vaccinepreventable diseases and strengthening immunization systems as part of COV-ID-19 recovery efforts.

References:

^[1] Source: Provisional data based on monthly data reported to WHO as of April 2022

^[2] Source: WHO/UNICEF estimates of national immunization coverage, 2020 revision.

^[3] Source: WHO/UNICEF estimates of national immunization coverage, 2020 revision.



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FEATURES

Intelligent measure algorithm
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Quick installing
Easy operation
Recording and searching
Auto audio alarm

S Temperature Measurer	ment	
Measurement Range	: 30 ~ 45°C	
S Accuracy	: 0.5°C @ 30~45°C	
S Effective distance	: 0.15 ~ 4m	
Infrared Camera		
Resolution	: 256 x 192pixels	
S Image Frame Rate	: 25Hz	
Focal Length	: 3.2mm	
S Field of View	: 56° x 42°	
S F#	: 1.1	
Visual Camera		
Resolution	: 1280 x 720pixels	
S Focal Length	: 4.4mm	
Environmental		
Operating Temperature	: 10 ~ 50°C	
Storage Temperature	:-20~60°C	
Physical Characteristic	C	
Output	: mini USB	
Size	: 80 x 80 x 14.2mm	

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