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March - April 2022

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Skin cancer

Mobile app and AI speed up diagnoses

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Prognosis

Innovations in life science

Scientists in China using 3D ultrasound imaging have developed a new method to predict foetal weight during pregnancy. The researchers say the new method is more accurate than pre-existing methods which rely on analysis of two-dimensional ultrasound images. Predicting foetal weight during pregnancy is important to prevent a number of potential complications, such as macrosomia. In the study they measured arm volume, thigh volume and abdominal circumference of the foetus and correlated this with actual birth weights in 134 pregnancies to develop an algorithm for predicting birth weight. They then tested the algorithm to check whether it could accurately predict the actual birthweights in 68 pregnancies and found it compared favourably to traditional formulas. They expect the new method of measuring foetal limb volumes will be used in future clinical practice to help avoid complications such as macrosomia.

Also in our focus on ultrasound imaging, we report on a new consensus statement developed by several leading organisations which aims to provide consistency through standardized terminology in diagnostic ultrasound imaging. They point out that the lack of consistent terminology has created many challenges, and they expect that the consensus statement will go some way to resolving them, particularly with terms used to describe simple actions such as transducer movement and imaging planes. Consistent and agreed-upon terminology facilitates communication among medical professionals and ultimately leads to better patient care, they note.

In our focus on oncology, we look at a smartphone app and artificial intelligence developed for GPs to assist them in the early identification of skin cancer. It is hoped the Derm.AI project, as it is called by the scientists at the Fraunhofer Center for Assistive Information and Communication Solutions who created it, will ultimately lead to lower mortality from skin cancer. According to a global burden of disease study published in 2019 more than 62,000 people died from malignant skin melanoma alone. If malignant melanoma is diagnosed early and treated, the survival rate is more than 95% after five years.

Remember to keep a check on our website – *www.MiddleEastHealth.com* – where we regularly post healthcare news from the region and important research updates from the world's healthcare scientists.

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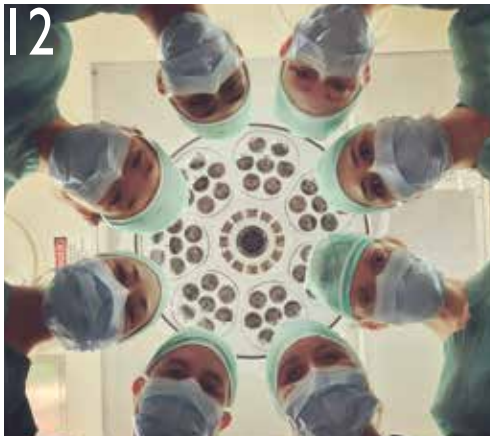

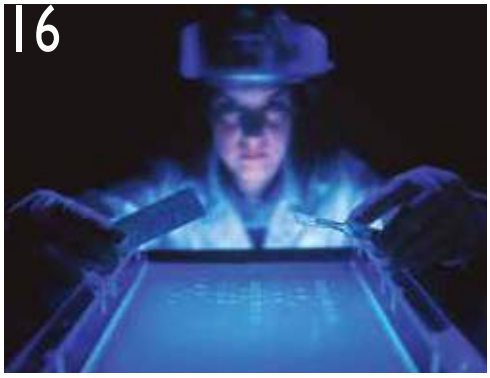

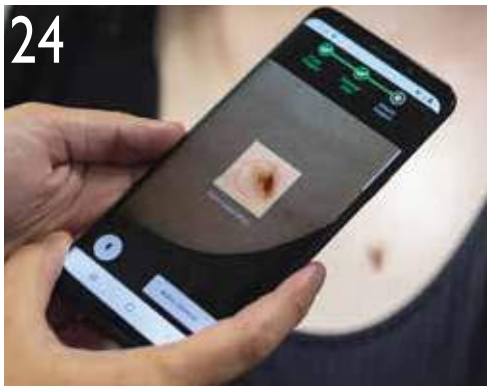

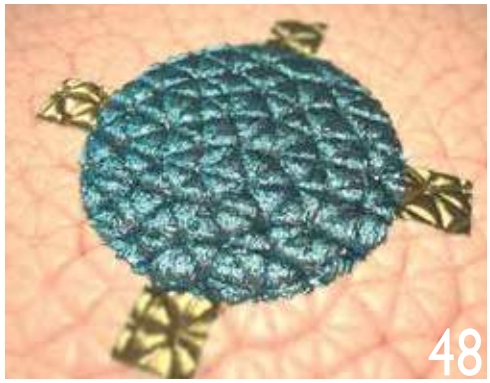

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middle east monitor

Update from around the region

Cleveland Clinic Abu Dhabi tops off new Cancer Center building due to open this year

Cleveland Clinic Abu Dhabi recently completed the exterior construction of its new Cancer Centre, which is due to open later this year.

The final glass panel was fitted to the tenth floor of the facility during a topping-off ceremony attended by Waleed Al Mokarrab Al Muhairi, Chairman of Cleveland Clinic Abu Dhabi and Deputy Group CEO of Mubadala Investment Company; Hasan Jasem Al Nowais, Mubadala Health CEO; and Dr. Jorge Guzman, Cleveland Clinic Abu Dhabi CEO.

Al Muhairi said: "The completion of the Cancer Center's exterior structure represents a major milestone in the construction process and brings us one step closer to start serving patients later this year. When it opens, the Center will provide the highest standards of specialized oncological screening, diagnostics and treatments, ensuring that cancer patients have access to the best and most comprehensive care in the UAE and the region."

The new 19,000 square meter centre is modelled on Cleveland Clinic's Taussig Cancer Center, which is ranked number five for cancer care in the United States. The Abu Dhabi-based Cancer Center is set to bring an integrated and transformative approach to diagnosing and treating the disease in the UAE and the region. Cancer is the third most common cause of death in the UAE and the primary reason patients travel overseas. The new Center will help eliminate the need for patients to travel abroad for treatment.

The Center will have 24 exam rooms, 24 infusion rooms, two procedure rooms, and an area devoted to women's oncology services. The facility will apply a "patient and family-centred" approach to care, which is already well-established in Cleveland Clinic Abu Dhabi's Oncology Institute. MEH

Gargash Hospital collaborates with Meitra Hospital to launch the Centre of Excellence for Bone and Joint in Dubai

Gargash Hospital collaborates with Meitra Hospital to launch the Centre of Excellence for Bone and Joint in Dubai

Gargash Hospital, the UAE's first female Emirati- owned, multi-specialty hospital has will partner with Meitra Hospital, owned by KEF Holdings, to establish a Center of Excellence for Bone and Joint in the UAE.

As part of the partnership, Gargash Hospital will improve orthopaedics treatment with cutting-edge technology, such as the CORI Robotics Surgical System, an advanced hand-held robotics solution for joint replacement surgeries.

"We are delighted to partner with Meitra Hospital. The UAE has always been a step ahead with its innovations and collaborations, and the healthcare sector is further accelerating this space with its advancements. As one of the leading hospitals in the UAE, we are committed to bringing some of the best technologies to this region and are confident that this new centre for bone and joint will help patients access effective and efficient treatments," said Ghada Sawalmah, CEO of Gargash Hospital.

The CORI Robotics Surgical System simplifies the surgical process with pinpoint accuracy to place the knee implants through real-time imaging, carefully treating the soft tissues to attain optimized alignment and balance, which significantly improves the natural function and life expectancy of the knee, over regular, conventional joint replacement surgery.

Faizal E Kottikollon, Chairman of KEF Holdings, said: "We are glad to associate with Gargash Hospital. Meitra has a strong reputation in orthopaedics, and our international launch in Dubai with Gargash Hospital is a significant milestone in bringing quality healthcare to patients in the UAE and GCC." MEH

Ghada Sawalmah, CEO of Gargash Hospital, and Faizal E Kottikollon, Chairman of KEF Holdings, shake hands after signing the collaboration agreement.

London's King's College Hospital to open hospital in Jeddah

An artistic rendering of King's College Hospital, Jeddah

Building on the success of King's College Hospital Dubai, Ashmore Group, a specialist emerging markets investment manager, in partnership with King's College Hospital London and Saudi Bugshan Group, will construct King's College Hospital Jeddah (KCHJ). The hospital is scheduled to open its doors to patients in the second half of 2023.

This is expected to be the first of several similar projects providing Ashmore and King's the platform for further growth in KSA.

KCHJ will be the country's first truly integrated hospital bringing the full benefits of King's College Hospital London to KSA, and playing its role in achieving the Kingdom's 2030 vision in the healthcare sector. The London-based tertiary hospital is part of the world leading UK National Health Service, with a 180 year history of successfully caring for patients with complex conditions. King's is also one of the largest teaching hospitals in the UK. The hospital's 13,000+ staff in London treat over one million patients every year.

King's College Hospital Jeddah, located on King Abdulaziz Road, will have a capacity of 150 beds in the first phase. The hospital will be staffed with over 1000 leading healthcare professionals, sourced from London, KSA and wider region

Clinical innovation and smart technologies will be a prominent feature at the hospital, with 40 medical and surgical specialties and four Centres of Excellence: Women's Health, Metabolic Diseases & Bariatric Surgery, Orthopaedics and Heart & Vascular. The patient-centred care model, staffing and services will all be fully integrated with King's College Hospital London, designed to address a range of complex and critical care requirements unique to the residents of KSA.

Ahsan Ali, Head of Healthcare Private Equity at Ashmore commented: "We stand true to our ambition and commitment to bringing the best of British healthcare to the region in partnership with King's College Hospital London. Following the success of King's hospital and clinics in Dubai, entering Saudi Arabia marks a new chapter for King's and Ashmore, with the first project being a landmark hospital in Jeddah. We expect to follow this with the establishment of similar King's branded facilities, including specialized centres, in other parts of the Kingdom."

Sir Hugh Taylor, Chairman of King's College Hospital, London said: ''We are delighted that King's, in partnership with Ashmore, is expanding its footprint to Saudi Arabia, following on from the success of our hospital and clinics in the UAE. King's College Hospital has a long history of providing outstanding patient care in London and as part of our "Strong roots, Global reach" strategy we remain committed to delivering outstanding care for patients in Saudi Arabia" MEH

Al Ansari Exchange donates AED250,000 to The Reach Campaign to help end Neglected Tropical Diseases

Al Ansari Exchange, the UAE-based foreign exchange and worldwide money transfer company, has donated AED250,0000 (US$68,000) to The Reach Campaign, a fundraising initiative launched to help put an end to neglected tropical diseases (NTDs) in the Middle East and Africa region. The donation brings the company's total contribution to the initiative to AED 3.25 million this year.

Proceeds from the Reach Campaign will go to the Reaching the Last Mile Fund (RLMF) that is being hosted by the multi-donor platform, The END Fund. The RLMF initiative aims to eliminate preventable diseases affecting the most vulnerable communities worldwide, as driven by the personal commitment of His Highness Sheikh Mohamed bin Zayed Al Nahyan, Crown Prince of Abu Dhabi and Deputy Supreme Commander of the UAE Armed Forces.

Mohamed Ali Al Ansari, Chairman of Al Ansari Exchange, said: "We are happy to see that the global community is now paying wider attention to NTDs. We are confident that this increased attention will mobilize more businesses across sectors to donate to the RLMF initiative, which aims to free over a billion people from these diseases by 2030."

"This is not the first time that we are joining hands with the RLMF, and it is not going to be the last. We will continue to help establish a more humane and caring global society according to our Corporate Social Responsibility programmes," he added.

Tala Al Ramahi, Acting Managing Director for the Reach Campaign, said: "World NTD Day is an opportunity for our valued partners to support us in not only raising awareness of NTDs, but to also translate that awareness into action. We are grateful to Al Ansari Exchange for their generous donation to the campaign and their continued commitment to supporting communities that are affected by NTDs."

NTDs are responsible for thousands of preventable deaths each year and can cause impairments that perpetuate the cycle of poverty by keeping millions of adults out of work and children out of school. Complicating efforts towards progress, COVID-19 has further compounded the impact of NTDs on communities over the past years. One out of every five people in the world are impacted by NTDs. MEH

Value partnership: Ole Per Maloy, CEO, Siemens Healthineers, Middle East, Southern & Eastern Africa, and Alisha Moopen, Deputy Managing Director of Aster DM Healthcare, shake hands on the collaborative agreement.

Aster DM Healthcare, Siemens Healthineers set up value partnership to advance healthcare in the GCC

Aster DM Healthcare has entered into a seven-year technology and strategic partnership with Siemens Healthineers to advance sustainable healthcare solutions in the UAE and GCC. To be executed by Eurohealth Systems, the partnership will focus on upgrading technology, digital optimization, training, capacity building and clinical workflow optimization.

Aster DM Healthcare is a leading healthcare provider, which operates 27 hospitals, 118 clinics, 66 labs and 323 pharmacies in the GCC and India.

Commenting on the partnership, Alisha Moopen, Deputy Managing Director of Aster DM Healthcare said: "Technology is changing rapidly. We at Aster want to ensure that we have the most up to date technology, service levels, and integrated work flows that can help us to enhance patient experience as well as offer the highest standards of quality care. We believe in raising the bar in healthcare, and strong partnerships with key stakeholders is the game changer that we see for the industry overall. We are glad to work with Siemens Healthineers on this long-term partnership to improve delivery of patient care in the region."

The agreement centres on a Value Partnership, a long-term performance-oriented relationship which will further enable Aster DM Healthcare to optimize clinical operations and expand their capabilities. The suite of medical technology and services included in the Value Partnership will help ensure continued access to the latest imaging technology and increase service efficiency across multiple sites. The design of the Value Partnership is tailored to the needs of medical professionals and patients which would enable Aster DM Healthcare to help maintain its leading position as an innovator in the market and to increase affordability and access to quality care.

"We are delighted and honoured to enter into this long-term partnership with Aster DM Healthcare, that will optimize workflows, facilitate digital connectivity, and ensure continuous access to the latest imaging technology. This Value Partnership is an excellent example of the innovative power that can be harnessed when like-minded healthcare trailblazers come together to transform care delivery and improve patient experience, which is fully in line with Aster DM Healthcare's mission of providing quality healthcare at an affordable cost.", said Ole Per Maloy, CEO, Siemens Healthineers, Middle East, Southern & Eastern Africa.

Key areas of the partnership include ongoing supply, maintenance, and life cycle management of medical technology across multiple sites, supported by digital solutions to optimize workflows and to enhance clinical delivery. Additionally, to build up and maintain a required knowledgebase across Aster DM Healthcare's entities, Siemens Healthineers will provide educational services for medical professionals to expand clinical capabilities and further empower the medical teams to offer outstanding patient care. MEH

Cleveland Clinic Abu Dhabi introduces PreserFlo MicroShunt procedure to treat glaucoma

Three patients at Cleveland Clinic Abu Dhabi have become the first in the region to receive an innovative outpatient treatment for glaucoma. This follows the hospital introducing a new technology that has the ability to lower eye pressure and effectively treat the progressive damage that glaucoma can cause to the optic nerve, while also reducing or eliminating the reliance on medication in most patients.

Glaucoma is a common eye condition where the optic nerve becomes damaged because of an increased pressure caused by fluid build-up in the front part of the eye.

The new minimally invasive PreserFlo MicroShunt procedure involves inserting a small biocompatible stent into the drainage system of the eye in order to shunt intraocular fluid and lower pressure inside the eye. This procedure enables patients to quickly recover at home. Patients can generally return to normal, non-strenuous activities within a few days, and to a normal lifestyle within a few weeks.

Dr. Jason A. Goldsmith, a Staff Physician in the Eye Institute at Cleveland Clinic Abu Dhabi, who was part of the care team for these patients, said: "Glaucoma is a leading cause of blindness around the world and is also one of the main causes of vision loss in the UAE. The expansion of our minimally-invasive surgical options with the introduction of this novel approach to treat glaucoma means that even patients with advanced disease can be treated safely, with minimum downtime and positive results in most cases."

The new procedure is recommended to patients only after a thorough eligibility assessment that includes a comprehensive eye exam and imaging, and a review of their medical history.

"Incisional surgery is not normally the first step to treat glaucoma, but it becomes necessary when medications do not work for the patient, or if the patient is experiencing significant side effects while taking medications. We generally only recommend incisional glaucoma surgery when the patient is at significant risk of permanent vision loss without surgery," he explained.

In suitable candidates, the new procedure is performed under a local anesthetic and takes about 30-45 minutes, after which the patient is observed for a few hours in clinic and discharged the same day. The patient is prescribed postoperative eye drops, with a follow-up visit scheduled for the next day to assess the success of the operation. MEH

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Saudi Health Council, Sanofi partner to boost diabetes studies and research in the kingdom

The Saudi Health Council, represented by the National Diabetes Centre, signed a memorandum of understanding (MoU) with Sanofi, to collaborate on various initiatives in research and development in the field of diabetes in the kingdom.

The MoU was signed at the the headquarters of the General Secretariat of the Council in the presence of Dr Nahar bin Mazki Al-Azmi, Secretary-General of the Saudi Health Council, and Dr Moatazbellah bin Muhammad Alruwaithi, Assistant Secretary-General, Dr Suleiman bin Nasser Alshehri, Director General of Saudi Diabetes Centre, Tarja Stenvall, Senior Vice President, General Medicines, Key Markets, Sanofi and Niven Al-Khoury, General Manager General Medicines KSA & Gulf MCO at Sanofi.

"This collaboration will serve as a great impetus in offering efficient healthcare initiatives to develop the ecosystem of diabetes management in the country. Sanofi and SHC will collaborate in building the nucleus of scientific research and generating local disease data supported by establishing a comprehensive diabetes research network. In addition, the agreement includes launching a digital tool that aims to improve the efficiency of diabetes management for people living with diabetes in the country. This MoU will include collaboration in the development and implementation of tailored training courses and workshops for physicians and diabetes educators with specific criteria and performance indicators," Dr Al-Shehri said.

Stenvall welcomed the collaboration and highlighted its substantial role in facilitating comprehensive, high-quality healthcare to people living with diabetes.

"Drawing on our unrivalled experience in the fight against diabetes, we are implementing a series of strategic projects in the healthcare sector of Saudi Arabia. We're grateful to the Saudi Health Council for its sustained efforts in coordination with various authorities to prevent and control diabetes as part of its commitment to bolster the country's public health," Stenvall said. MEH

Amana Healthcare partners with UAE IBD Society to provide healthcare for IBD patients

To improve the quality of life of patients in the UAE who are living with Crohn's disease, ulcerative colitis,s and other kinds of inflammatory bowel disease (IBD), Mubadala Health's Amana Healthcare has become the healthcare provider for the UAE IBD Society, collaborating on several stoma-related initiatives, including establishing a support community for IBD patients.

The two parties outlined areas of cooperation to support IBD patients with stomas – an opening in the abdomen that facilitates the removal of waste products from the body. The collaboration will see Amana Healthcare delivering pre-operative stoma education, stoma site marking, and post-operative stoma care at patients' homes.

Under the patronage of His Highness Sheikh Khalifa bin Sultan bin Hamdan Al Nahyan, and established under the Ministry of Community Development, the UAE IBD Society is committed to supporting patients living with IBD conditions, as well as their families and friends through awareness, support and education, as well as being an active voice to advocate for their needs, while helping them lead fulfilling lives.

Dr. Maryam Al Khatry, founder of the UAE IBD Society and a prominent gastroenterologist, said: "Our Society was formed in part to develop the highest international standards of healthcare services for IBD patients and to provide a platform to raise awareness, promote a healthy culture, and encourage the exchange of knowledge and advice. Working with Amana and exchanging expertise ensures the delivery of exceptional healthcare and support for our members. This, together with establishing an IBD stoma community for patients and educating patients and the community about IBD and stomas, will help us to achieve our goals." MEH

Oman International Hospital and Siemens Healthineers partner to develop premier healthcare facility

Integrated Global Healthcare Service (IGHS), the management company for Oman International Hospital, has formed a partnership with Siemens Healthineers to establish a leading private healthcare facility in Muscat.

One of the main objectives of the Oman International Hospital's executive management team is to turn the hospital into a premier private healthcare facility. Their ambition is to be the number one healthcare provider in Oman in areas such as general surgery, cardiology, and orthopaedics.

Commenting on the partnership, Ole Per Maloy, Managing Director Siemens Healthineers Middle East and Southern & Eastern Africa, said: "Siemens Healthineers is proud to support this aspirational and innovative project as a strategic and trusted partner through the provision of state-of-the-art medical solutions and technology, including digital solutions, clinical and strategic consulting, and further supporting the staff with relevant research and development."

In addition, Siemens Healthineers will support the hospital's Board in making optimal management decisions using data analysis and performance optimization. MEH

Sheikh Khalifa Medical City introduces toxicology unit

Abu Dhabi's Sheikh Khalifa Medical City (SKMC) has introduced a toxicology unit for the management and follow-up care of patients who have been poisoned by pesticides, hydrocarbons, chemicals, plants, snakebites, scorpion bites, and insect stings.

Dr Ashraf Mohamed Kamour, Chair of Medicine, SKMC, commented: "Toxicology as a specialty is new to the country, and we are excited to be providing the community with this specialty at SKMC. The unit will function round-the-clock, helping reduce morbidity, improve care, and reduce the average length of stay and possibility of readmission. Recently, a patient was admitted to SKMC experiencing severe iron overdose. Thanks to SKMC's Toxicology Unit, he was treated at SKMC and discharged after 48 hours with no complications." MEH

Mubadala Health partners with BioIntelliSense to activate remote patient monitoring

Abu Dhabi's Mubadala Health will partner with BioIntelliSense to incorporate the company's remote monitoring technologies within Mubadala Health's continuous care model to drive clinical workflow efficiencies, unlock data-driven insights, and enhance the patient experience.

BioIntelliSense's flagship FDA-cleared BioSticker and medical-grade BioButton wearable devices, along with its algorithmic-based data services, will enable Mubadala Health to capture continuous multi-parameter patient data passively and securely across a broad range of physiological leading indicators, such as resting heart rate, respiratory rate, temperature, body position, activity level, sleep, and gait analysis. Using the company's BioCloud analytics and intelligent alerting, Mubadala Health can remotely monitor at-risk, long-term care patient populations and allocate resources efficiently based on a documented clinical need through a centralized command centre using the data from the wearable devices.

Mubadala Health will roll out the new technology across its integrated healthcare network of providers.

Starting with long-term services, Mubadala Health is working to incorporate BioIntelliSense's technology for remote monitoring programmes across orthopaedics, oncology, end-stage renal disease, post-hospital discharge, home healthcare, and elderly primary care.

Hasan Jasem Al Nowais, Chief Executive Officer of Mubadala Health, said: "This partnership is in line with our comprehensive strategy to provide innovative care to our patients and create efficiencies in the way healthcare is delivered. BioIntelliSense's technology will allow our clinicians to access near real-time information on patients' vital signs and symptoms, enabling them to identify changes in health sooner and intervene earlier.

"This strategic partnership will help create fully integrated, continuous care delivery that starts during a patient's hospitalization, enabling monitoring of their health status

throughout their recovery process, and from the comfort of their own home after leaving the hospital."

James Mault, MD, Founder and Chief Executive Officer of BioIntelliSense, said: "The collaboration with Mubadala Health in launching a continuous remote monitoring capability will help providers deliver a new level of care for patients in the UAE. This partnership with Mubadala Health represents a tremendous opportunity to apply the 'BioSticker' and 'BioButton' wearable medical devices across multiple care settings, make early detection simple, and empower care teams with personalized clinical intelligence that enables informed, proactive interventions." MEH

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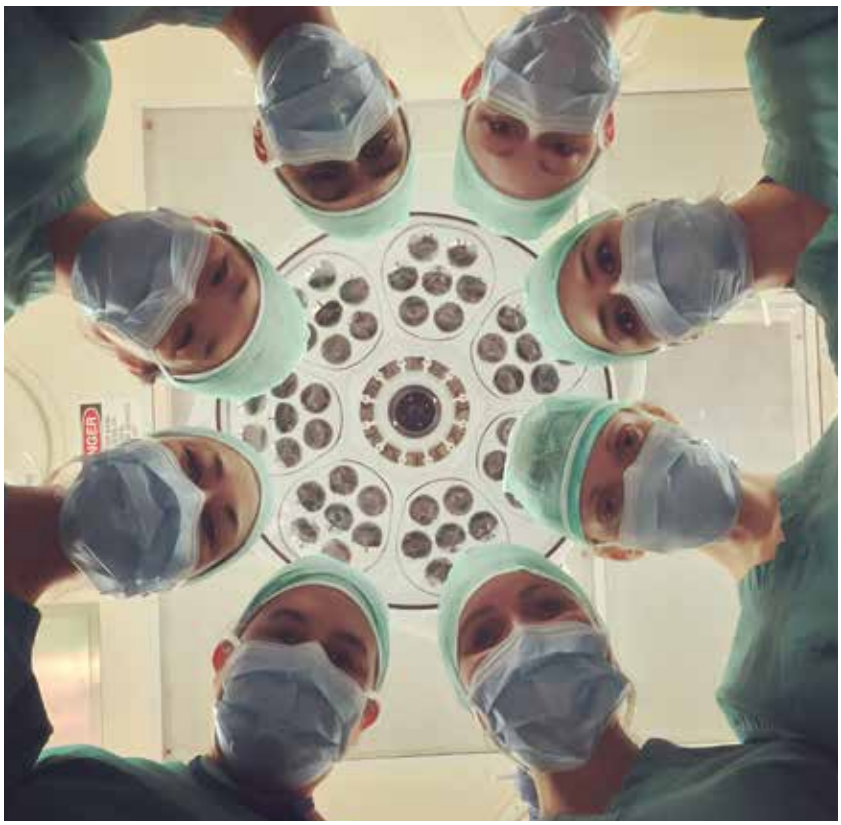
Update from around the globe



New WHO platform promotes global cancer prevention

The World Health Organization's International Agency for Research of Cancer (IARC) [1] has launched the World Code Against Cancer Framework [2], an online platform that will promote prevention globally and the development of Regional Codes to help fight the disease.

Based on current scientific evidence, at least 40 per cent of all cancer cases could be prevented with effective primary prevention measures, and further mortality can be reduced through early detection of tumours.

Dr Carolina Espina, the IARC scientist who leads the project, explains that some risk factors are common worldwide, but some patterns are specific to certain regions and socioeconomic and cultural conditions.

Because of that, the new framework provides a common strategy and methodology to develop recommendations tailored to the context and needs of local populations.

The framework builds on the success of the fourth edition of the European Code Against Cancer.

"This new platform will host existing Regional Codes Against Cancer, such as the European Code… as well as Regional Codes that are currently under development, such as the Latin America and the Caribbean Code Against Cancer, and other future Regional Codes," Dr Espina explained.

The Latin America and the Caribbean Code Against Cancer is expected to be launched in 2023. It will be the first regional adaptation of the European Code Against Cancer.

Rays of Hope Initiative

At the tome of the launch, the International Atomic Energy Agency (IAEA) announced a new initiative, called Rays of Hope, to support Member States with diagnosis and treatment using radiation technologies, beginning with African countries most in need.

In a joint statement, the World Health Organization Director-General, Tedros Adhanom Ghebreyesus, and the IAEA Director General, Rafael Mariano Grossi, explained how low and middle-income countries (LMICs) are disproportionately affected.

By 2040, over 70 per cent of cancer deaths are expected to occur in LMICs.

According to the two officials, recommended interventions for preventing cancer and other noncommunicable diseases have not been adequately implemented, and treatment remains inaccessible in many parts of the world.

"Globally, an estimated half of people diagnosed with cancer may require radiotherapy as part of their care, yet many countries do not have a single radiotherapy machine," they say.

The disparity is particularly acute in Africa where nearly 70 per cent of countries reported that radiotherapy is generally unavailable.

The IAEA and WHO have a longstanding collaboration to support Member States to address their cancer burdens.

The organizations have successfully supported more than 90 governments through imPACT [3] review missions, and through WHO cancer initiatives in cervical, childhood and breast cancers. MEH

References

[1] *https://www.iarc.who.int/*

[2] *https://cancer-code-world.iarc.who.int/*

[3] *https://www.iaea.org/services/review-missions/impact-reviews*

World leaders and experts call for action to protect the environment from antimicrobial pollution

The Global Leaders Group on Antimicrobial Resistance < *http://amrleaders.org/* > have issued a call on all countries to reduce the amount of antimicrobial waste entering the environment. This includes researching and implementing measures to safely dispose of antimicrobial waste from food,

human health and animal health systems, and manufacturing facilities.

The call came ahead of the UN Environment Assembly which took place in Nairobi early March.

The Global Leaders Group on Antimicrobial Resistance includes heads of state, government ministers, and leaders from private sector and civil society. The group was established in November 2020 to accelerate global political momentum, leadership and action on antimicrobial resistance (AMR) and is co-chaired by Mia Amor Mottley, Prime Minister of Barbados, and Sheikh Hasina, Prime Minister of Bangladesh.

They called for all countries to improve measures for the management and disposal of antimicrobial-containing waste and runoff from manufacturing sites, farms, hospitals and other sources.

Antimicrobials given to humans, animals and plants are entering the environment and water sources (including drinking water sources) via wastewater, waste, run-off and sewage. This spreads drug-resistant organisms and exacerbates antimicrobial resistance. The fear is that this will fuel the emergence of 'superbugs' that are resistant to several types of antimicrobial drugs.

The Global Leaders Group calls for all countries to develop and implement regulations and standards to better monitor and control the distribution and release of antimicrobials and drug-resistant organisms into the environment.

Other key actions include:

1. In the manufacturing sector, developing national antimicrobial manufacturing pollution standards to better control and monitor antimicrobial pollution.
2. In the human and animal health sector, enforcing laws and policies to reduce or eliminate antimicrobial use that is not under the guidance of a trained healthcare provider.
3. In food systems, implementing standards to treat and manage discharge from food-animal farms, aquaculture farms and crop fields.

Inaction will have dire consequences

Antimicrobial drugs, including antibiotics, antifungals and antiparasitics, are used in human and veterinary medicine all over the world. They are used to treat and prevent diseases in humans and animals, and sometimes in food production to promote growth in healthy animals. Antimicrobial pesticides are also used in agriculture to treat and prevent diseases in plants.

Current antimicrobial drug usage in humans, animals and plants is leading to a concerning rise in drug-resistance and making infections harder to treat.

Drug-resistant microbes and disease-causing pathogens can pass between humans, animals, plants and food, and in the environment.

Drug-resistant diseases contribute to nearly 5 million deaths every year, according to *The Lancet*. Urgent action is needed to curb the rise and spread of antimicrobial resistance across all countries. Without action, the world is rapidly approaching a tipping point where the antimicrobials needed to treat infections in humans, animals and plants will no longer be effective.

The impact on local and global health systems, economies, food security and food systems will be devastating.

"The connections between antimicrobial resistance, environmental health and the climate crisis are becoming increasingly stark," said Mottley co-chair of the Global Leader Group on Antimicrobial Resistance. "We must act now to protect the environment, and people everywhere, from the damaging effects of antimicrobial pollution."

UN condemns brutal killing of eight polio workers in Afghanistan

The United Nations has condemned the killing of eight polio vaccination workers in four locations in northern Afghanistan on 24 February, the first such attacks since nationwide immunization campaigns resumed last November.

One member of the vaccination transit team was killed in Taloqan district in Takhar province, while four members of house-to-house teams were murdered in two separate incidents in Kunduz city, according to a statement from the UN Country Team.

Two vaccinators and a social mobilizer were killed in Emamsaheb district of Kunduz province.

In the wake of the carnage, the UN immediately suspended the national polio vaccination campaign in Kunduz and Takhar provinces.

Ramiz Alakbarov, the Secretary-General's Deputy Special Representative for Afghanistan, took to Twitter to express condemnation in the strongest terms. He said the attacks and assassinations were a violation of international humanitarian law.

The head of the World Health Organization, Tedros Adhanom Ghebreyeus, has also expressed his profound shock. Four of the health workers were women, he said in a post on Twitter.

"We extend our deepest condolences to their families and colleagues," he wrote, adding that health workers should not be targeted.

The UN Country Team was appalled by the brutality of the killings, noting that this was not the first time health workers have come under attack.

Last year, nine polio workers were killed during national polio vaccination campaigns.

These immunization exercises are a vital and effective way to reach millions of children to protect them against polio, the UN statement said, and depriving them from an assurance of a healthy life is inhumane.

"This senseless violence must stop immediately, and those responsible must be investigated and brought to justice. These attacks are a violation of international humanitarian law."

The UN strongly condemns all attacks on health workers anywhere, stressing that delivery of health care is impartial.

The polio vaccination campaign in

Afghanistan is supported by WHO, together with the UN Children's Fund and other partners.

They planned to target nearly 10 million under-fives across the country this month, with four more rounds scheduled for the rest of the year.

Dr Ahmed Al-Mandhari, WHO Regional Director for the Eastern Mediterranean, said the suspension of the programme in Kunduz and Takhar provinces leaves thousands of children unprotected and exposed to a life-threatening disease that can result in permanent paralysis.

In calling for an end to "senseless attacks" on health workers, Dr. Al-Mandhari pointed out that they are strictly forbidden in all faiths.

"These cowardly acts ultimately only harm innocent children who must be given every opportunity to live safe and healthy lives," he said.

"WHO condemns all attacks on health workers in the strongest terms and appeal to the Taliban Authorities to immediately identify and bring the perpetrators to justice."

Over one billion people at risk of hearing loss, says WHO

A new international standard for safe listening at venues and events was launched ahead of World Hearing Day on 3 March on the theme, *To hear for life, listen with care!* It applies to all places and activities where amplified music is played.

Over 1.5 billion people globally live with hearing loss, and according to recent estimates this number could rise to over 2.5 billion by 2030. The WHO estimates that 50% of hearing loss can be prevented through public health measures.

Prevention is key

According to the UN health agency, many common causes of hearing loss can be prevented, including over-exposure to high volume sounds.

"Millions of teenagers and young people are at risk of hearing loss due to the unsafe use of personal audio devices and exposure to damaging sound levels at venues such as nightclubs, bars, concerts and sporting events," said Dr Bente Mikkelsen, WHO Director for the Department for Noncommunicable Diseases.

"The risk is intensified as most audio devices, venues and events do not provide safe listening options and contribute to the risk of hearing loss,"she added.

The new WHO standard aims to better safeguard young people as they enjoy their leisure activities.

New recommendations

The Global standard for safe listening at venues and events, highlights six recommendations for implementation to ensure that venues and events limit the risk of hearing loss to their patrons, while still preserving high-quality sound and an enjoyable listening experience.

The six recommendations outline:

- A maximum average sound level of 100 decibels.
- Live monitoring and recording of sound levels using calibrated equipment.
- Optimizing venue acoustics and sound systems to ensure enjoyable sound quality and safe listening.
- Making personal hearing protection available to audiences including instructions on use.
- Access to quiet zones for people to rest their ears and decrease the risk of hearing damage.
- And, provision of training and information to staff.

The new standard was developed under WHO's Make Listening Safe initiative [1], which was launched in 2015, and seeks to improve listening practices especially among young people.

WHO noted that hearing loss due to loud sounds is permanent, underlining that exposure to loud sounds causes temporary hearing loss or tinnitus, and prolonged or repeated exposure can lead to permanent hearing damage, resulting in irreversible hearing loss.

Young people can better protect their hearing by:

- Keeping the volume down on personal audio devices
- Using well-fitted, and if possible, noise-cancelling earphones/headphones
- Wearing earplugs at noisy venues
- Getting regular hearing check-ups

Calling for the new global standard to be supported, WHO encouraged governments to develop and enforce legislation for safe listening and raise awareness of the risks of hearing loss.

The UN agency also advised that behaviour change can be motivated by civil society organizations, parents, teachers, and physicians, who can educate young people to practice safe listening habits.

References:

[1] *https://www.who.int/activities/making-listening-safe*

WHO launches new repository on urban health

Over 55% of the world's population live in urban areas – a proportion that is expected to increase to 68% by 2050. This trend calls for strengthened support to address health at the urban level. To this end, WHO's new repository on urban health gives access to a broad range of WHO-generated resources to enhance local action for health.

The repository reflects WHO's renewed commitment to promoting urban health worldwide and includes resources that provide technical support and build capacity, strategic reports and guidelines, health impact assessment tools, and other products relevant to urban health and cities.

The repository is a living resource, open to modifications and additions, and it will be regularly updated when new products become available. It covers topics such as urban planning, housing, environmental issues, transport and mobility, nutrition, physical activity, COVID-19 and many others. The search engine allows users to access existing WHO materials by health topic category, product type, geographical area and year of publication/development.

Some products in the repository relate specifically to urban health (e.g. local urban planning tools), while others relate to broader, cross-cutting issues that impact urban health (e.g. global guidelines on health threats such as air pollution, road traffic injuries, or violence against children that need to be endorsed at national level and implemented locally).

The initial content in the repository is based on a structured, non-exhaustive, technical mapping exercise identifying WHO activities and products across the organization. WHO hopes that users including researchers, practitioners, community actors, government and city officials, NGO reps, private sector agents, civil society members, donors, development partners, multilateral agencies and others in all Member States will find the repository a useful tool in the journey towards better

on the WEB Urban Health Repository
https://urbanhealth-repository.who.int

WHO: Accelerate action to stop obesity

More than 1 billion people worldwide are obese – 650 million adults, 340 million adolescents and 39 million children. This number is still increasing. WHO estimates that by 2025, approximately 167 million people – adults and children – will become less healthy because they are overweight or obese.

On the occasion of World Obesity Day 2022 (March 4), WHO urged countries to do more to reverse this predictable and preventable health crisis.

Obesity is a disease impacting most body systems. It affects the heart, liver, kidneys, joints, and reproductive system. It leads to a range of noncommunicable diseases (NCDs), such as type 2 diabetes, cardiovascular disease, hypertension and stroke, various forms of cancer, as well as mental health issues. People with obesity are also three times more likely to be hospitalized for COVID-19.

Countries need to work together to create a better food environment so that everyone can access and afford a healthy diet. Effective steps include restricting the marketing to children of food and drinks high in fats, sugar and salt, taxing sugary drinks, and providing better access to affordable, healthy food. Cities and towns need to make space for safe walking, cycling, and recreation, and schools need to help households teach children healthy habits from early on.

WHO is responding to the global obesity crisis on many fronts. This includes monitoring global trends and prevalence, the development of a broad range of guidance addressing the prevention and treatment of overweight and obesity, and providing implementation support and guidance for countries.

Following a request from Member States, the WHO secretariat is developing an acceleration action plan to stop obesity, tackle the epidemic in high burden countries and catalyse global action. The plan will be discussed at the 76 World Health Assembly to be held in May 2022.

the laboratory

Medical research news from around the world

Genetic study gives extensive insights into severe Covid-19

The world's largest study of the genetics of critical Covid-19, involving more than 57,000 people, has revealed new details about some of the biological mechanisms behind the severe form of the disease.

Some 16 new genetic variants associated with severe Covid-19, including some related to blood clotting, immune response and intensity of inflammation, have been identified.

These findings will act as a roadmap for future efforts, opening new fields of research focused on potential new therapies and diagnostics with pinpoint accuracy, experts say.

Researchers from the GenOMICC consortium – a global collaboration to study genetics in critical illness – led by University of Edinburgh in partnership with Genomics England, made these discoveries by sequencing the genomes of 7,491 patients from 224 intensive care units in the UK.

Their DNA was compared with 48,400 other people who had not had Covid-19, participants in Genomics England's 100,000 Genomes Project and that of a further 1,630 people who had experienced mild Covid.

Determining the whole genome sequence for all participants in the study allowed the team to create a precise map and identify genetic variation linked to severity of Covid-19. The team found key differences in 16 genes in the ICU patients when compared with the DNA of the other groups.

They also confirmed the involvement of seven other genetic variations already associated with severe Covid-19 discovered in earlier studies from the same team.

The findings included how a single gene variant that disrupts a key messenger molecule in immune system signalling – called interferon alpha-10 – was enough to increase a patient's risk of severe disease.

This highlights the gene's key role in the immune system and suggests that treating patients with interferon – proteins released by immune cells to defend against viruses – may help manage disease in the early stages.

The study also found that variations in genes that control the levels of a central component of blood clotting – known as Factor 8 – were associated with critical illness in Covid-19.

This may explain some of the clotting abnormalities that are seen in severe cases of Covid-19. Factor 8 is the gene underlying the most common type of haemophilia.

Professor Kenneth Baillie, the project's chief investigator and a Consultant in Critical Care Medicine at University of Edinburgh, said: "Our latest findings point to specific molecular targets in critical Covid-19. These results explain why some people develop life-threatening Covid-19, while others get no symptoms at all. But more importantly, this gives us a deep understanding of the process of disease and is a big step forward in finding more effective treatments.

"It is now true to say that we understand the mechanisms of Covid better than the other syndromes we treat in intensive care in normal times – sepsis, flu, and other forms of critical illness. Covid-19 is showing us the way to tackle those problems in the future."

Professor Sir Mark Caulfield from Queen Mary University of London, formerly Chief Scientist at Genomics England and co-author on this study, said: "As Covid-19 evolves, we need to focus on reducing the number of people getting seriously ill and being hospitalised. Through our whole genome sequencing research, we've discovered novel gene variants that predispose people to severe illness – which now offer a route to new tests and treatments, to help protect the public and the NHS from this virus."

The findings have been published in *Nature* [1].

GenOMICC (Genetics of Susceptibility and Mortality in Critical Care) started in 2015 as an open, global consortium of intensive care clinicians dedicated to understanding genetic factors influencing outcomes in intensive care from diseases such as SARS, flu and sepsis.

The consortium is led by the University of Edinburgh, and since 2020 it has been focused on Covid-19 research in partnership with Genomics England and in collaboration with NHS Lothian, the Intensive Care National Audit and Research Centre (ICNARC), and Queen Mary University of London.

The ground-breaking 100,000 Genomes Project was established in 2014 to sequence 100,000 genomes from people with a rare disease or cancer. The Project was completed in 2018 and paved the way for the creation of a new genomic medicine service for NHS England, transforming patient care by bringing advanced diagnosis and personalised treatments.

Reference:

[1] **doi:** *https://doi.org/10.1038/s41586-022-04576-6*

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Discovery of a new ALS and dementia disease mechanism raises treatment hopes

A pioneering new study led by University College London (UCL) and US National Institutes of Health (NIH) scientists has revealed, for the first time, why a common genetic variant worsens disease outcomes for people with the devastating adult-onset neurodegenerative diseases amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD).

Published in *Nature*, the study shows how TDP-43 protein depletion, associated with almost all cases (97%) of ALS and half of FTD cases, corrupts the genetic instructions for the critical neuronal protein UNC13A.

Strikingly, it found that a genetic variant previously associated with disease risk increases the chance of UNC13A's genetic instructions being corrupted among people with the diseases, thereby worsening risk and severity of ALS and FTD.

UNC13A enables neurons to communicate with each other via neurotransmitter release, and data from animal models suggests its loss from neurons can be fatal. The researchers believe that the corruption of UNC13A's genetic instructions in patients may have similarly harmful consequences.

ALS is the most common motor neuron disease and there is no known cure; it affects the brain and spinal cord by attacking the neurons and nerves which control movement, causing them to die.

FTD is a related disease with similar underlying causes; symptoms include language impairment, changes in personality and cognitive difficulties.

Researchers say the discovery raises hope for new treatments; by developing a therapy that blocks the corruption of UNC13A's genetic instructions, disease progression could be slowed for most people with ALS and around half of patients with FTD.

Corresponding author Professor Pietro Fratta (UCL Queen Square Institute of Neurology) said: "The majority of research into gene therapy has focused on genes implicated in familial ALS , but the vast majority of ALS cases are sporadic, with no known family history."

Co-corresponding author Dr Michael Ward (National Institute of Neurological Disorders and Stroke, NIH, US) added: "We have known for a long time that genetic variants in UNC13A cause an increased risk of ALS and dementia, but nobody had figured out why this is the case. Together, our teams showed exactly how this genetic risk factor for ALS interplays with the core disease mechanism, TDP-43 loss, in order to worsen the disease course."

TDP-43 – a key player in ALS and FTD

Arguably the most important protein in ALS research is TDP-43, as in most cases (as well as half of FTD cases), the protein is incorrectly ejected from the cell's nucleus. This prevents TDP-43 from performing its important functions, such as ensuring that mRNA is produced correctly.

Dr Ward said: "We have known for a long time that most patients with ALS, and about half of FTD patients, lose the function of a key protein called TDP-43, wreaking havoc in nerve cells that are affected. But we haven't known how to reverse the most problematic consequences of TDP-43 loss."

As part of the experimental study, the researchers used skin-derived human stem cells to make neuronal cells in dishes and removed the TDP-43 protein from these cells using a new technology based on CRISPR-Cas9, the Nobel-prize winning gene-editing technology.

The scientists were then able to study how these neurons without TDP-43 differed from healthy neurons. They found that the mRNAs for the UNC13A protein were corrupted, meaning the ribosomes in the lab-grown neurons were unable to correctly produce the UNC13A protein. Furthermore, when the team looked at ALS and FTD patient brain samples, they again found that the mRNAs for UNC13A were incorrect, confirming that their experiments replicated the real-world disease process.

Given the essential role UNC13A plays in facilitating neuron communication, its corruption is thus likely to impair neuronal function and contribute to neurodegeneration in those with ALS and FTD.

Genetic variants increase the risk of UNC13A mRNA corruption

The UNC13A gene and its corresponding protein are of longstanding interest to motor neuron disease and FTD researchers, with previous studies showing common genetic variants increase the risk and severity of the diseases, despite being benign in most people unaffected by the diseases (half the population carries one of these variants, which are only harmful in people with ALS or FTD). However, despite over a decade of research, the exact reason for this has remained mysterious, as these variants do not

directly alter the UNC13A protein-coding sequence, but are instead located in a region of 'junk DNA'.

The researchers believe they have uncovered the answer to this critical question: they found that the risk-linked variants greatly increase the chance of the UNC13A mRNA becoming corrupted once the ALS and FTD disease course, and the associated loss of TDP-43 protein, has begun. Thus, patients with these genetic variants are likely to suffer greater loss of UNC13A, resulting in more severe disease.

Co-lead author, PhD student Oscar Wilkins (UCL Queen Square Institute of Neurology and Francis Crick Institute), said: "These results represent a significant breakthrough for several reasons. Firstly, they explain why UNC13A genetic variants increase the risk of motor neuron disease and dementia, a question which has puzzled researchers for over a decade. They are also the first to demonstrate a genetic link specifically between loss of nuclear TDP-43 function and ALS, improving scientific understanding of this central disease mechanism."

Next steps

Professor Fratta said: "We have built on years of genetic research that identified that UNC13A was implicated in motor neuron disease and FTD, and supported it with a new molecular biology finding that confirms that the gene is absolutely fundamental to the disease process.

"We are hoping to carry out trials over the coming years to develop such a treatment that could potentially greatly improve the lives of people living with ALS."

The researchers are confident that with this new information, new therapies for motor neuron disease can be created that stop UNC13A mRNAs from being corrupted in patients.

Reference:

Brown, AL., Wilkins, O.G., Keuss, M.J. et al. TDP-43 loss and ALS-risk SNPs drive mis-splicing and depletion of UNC13A. Nature (2022). *https://doi.org/10.1038/s41586-022-04436-3*

New research findings could help improve bone marrow and stem cell transplantation for patients with blood-related diseases

Hematopoietic stem cells (HSCs) have the capacity to both self-renew and differentiate into all mature blood cell types, making them promising treatments for a variety of diseases. However, the mechanisms involved in engraftment – when the cells start to grow and make healthy blood cells after being transplanted into a patient – are poorly understood. A recent study led by researchers at Massachusetts General Hospital (MGH) and Boston University School of Medicine has revealed the unique signature of genes expressed by HSCs capable of undergoing this process. The findings, published in *Nature Communications* [1], could enable scientists to expand these cells outside of the body or to convert other types of stem cells into cells that can repopulate the blood system.

In adults, HSCs are found in the bone marrow and bloodstream, but before birth, they can be found to a greater extent in the liver, where they multiply, or proliferate, into additional HSCs at a very high rate. Moreover, research in animals has shown that HSCs in the foetal liver are more capable of engraftment than HSCs from bone marrow.

To understand what allows foetal liver HSCs to have these superior proliferation and engraftment characteristics, investigators examined the gene expression patterns that are unique to these highly potent stem cells. They combined this examination with a variety of experimental methods to characterize the protein expression and functionality of those same cells.

"This in-depth analysis revealed that these stem cells express a protein on their surface called CD201 that correlates very closely with this engraftment potential and can be used to isolate functional stem cells away from other cell types," says co-senior author Alejandro B. Balazs, PhD, a principal investigator at the Ragon Institute of MGH, MIT and Harvard. "This will help us improve the process of bone marrow and stem cell transplantation by allowing us to purify these cells."

The enhanced understanding of the genes involved will also help scientists propagate HSCs with high engraftment potential in the lab and manipulate them to more efficiently fight blood cell-related diseases such as sickle cell anaemia, HIV and certain types of cancer.

"Altogether, this work has resulted in a detailed blueprint of the most potent blood stem cells and will lead to a better understanding of why these cells have such an extraordinary regenerative capacity. Such insights will allow us to create safer and more efficient therapies for patients suffering from blood disorders," says lead author Kim Vanuytsel, PhD, a research assistant professor of medicine at Boston University School of Medicine.

Co-senior author George J. Murphy, PhD, an associate professor of medicine at Boston University School of Medicine and co-founder of the BU and BMC Center for Regenerative Medicine (CReM), adds that the team's openly shared resource, which has been made available in an interactive format at *https://engraftable-hsc.cells.ucsc.edu*, will enable new biological insights into engraftment potential and stimulate a broad range of future studies.

Reference:

[1] Vanuytsel, K., Villacorta-Martin, C., Lindstrom-Vautrin, J. et al. Multi-modal profiling of human fetal liver hematopoietic stem cells reveals the molecular signature of engraftment. *Nature Communications*. (2022). *https://doi.org/10.1038/s41467-022-28616-x*

Pets have a positive effect on cognitive health

Owning a pet, like a dog or cat, especially for five years or longer, may be linked to slower cognitive decline in older adults, according to a preliminary study released February 23, 2022, that will be presented at the American Academy of Neurology's 74th Annual Meeting in Seattle, April 2 to 7, 2022 and virtually, April 24 to 26, 2022.

"Prior studies have suggested that the human-animal bond may have health benefits like decreasing blood pressure and stress," said study author Tiffany Braley, MD, MS, of the University of Michigan Medical Center in Ann Arbor and a member of the American Academy of Neurology. "Our results suggest pet ownership may also be protective against cognitive decline."

The study looked at cognitive data from 1,369 older adults with an average age of 65 who had normal cognitive skills at the start of the study. A total of 53% owned pets, and 32% were long-term pet owners, defined as those who owned pets for five years or more. Of study participants, 88% were white, 7% were Black, 2% were Hispanic and 3% were of another ethnicity or race.

Researchers used data from the Health and Retirement Study, a large study of Medicare beneficiaries. In that study, people were given multiple cognitive tests. Researchers used those cognitive tests to develop a composite cognitive score for each person, ranging from zero to 27. The composite score included common tests of subtraction, numeric counting and word recall. Researchers then used participants' composite cognitive scores and estimated the associations between years of pet ownership and cognitive function.

Over six years, cognitive scores decreased at a slower rate in pet owners. This difference was strongest among long-term pet owners. Taking into account other factors known to affect cognitive function, the study showed that long-term pet owners, on average, had a cognitive composite score that was 1.2 points higher at six years compared to non-pet owners. The researchers also found that the cognitive benefits associated with longer pet ownership were stronger for Black adults, college-educated adults and men. Braley says more research is needed to further explore the possible reasons for these associations.

"As stress can negatively affect cognitive function, the potential stress-buffering effects of pet ownership could provide a plausible reason for our findings," said Braley. "A companion animal can also increase physical activity, which could benefit cognitive health. That said, more research is needed to confirm our results and identify underlying mechanisms for this association."

Clinical trial reveals new treatment option for Covid-19 patients progressed to ARDS

A clinical trial conducted by researchers from RCSI University of Medicine and Health Sciences and Beaumont Hospital Dublin has indicated an effective treatment for critically ill COVID-19 patients.

The study, published in *Med*, investigates the effects of using an anti-inflammatory protein, alpha-1 antitryspin (AAT), to treat COVID-19 patients who have progressed to acute respiratory distress syndrome (ARDS).

ARDS is a highly inflammatory state hallmarked by airway damage, respiratory failure and increased risk of death. Treatment options for COVID-19 patients who have ARDS are particularly limited.

AAT is a naturally occurring human protein produced by the liver and released into the bloodstream which normally acts to protect the lungs from the destructive actions of common illnesses.

In this randomized controlled trial, AAT that had been purified from the blood of healthy donors was administered to patients with COVID-19-associated ARDS, with the aim of reducing inflammation.

The results indicated that treatment with AAT led to decreased inflammation after one week. The study also found that the treatment was safe and well tolerated, and did not interfere with patients' ability to generate their own protective response to COVID-19.

This discovery suggests a potentially important role for AAT in the treatment of ARDS and other inflammatory diseases associated with COVID-19.

The study's co-lead author, Dr Oliver McElvaney from the RCSI Department of Medicine and Beaumont Hospital, commented on these novel findings: "We know that patients who are critically ill with COVID-19 are more prone to developing severe inflammation throughout the body, with a disproportionately high rate of progression to ARDS and other serious respiratory issues. We think AAT might be able to provide some protection against the more harmful types of inflammation that arise in severe COVID-19 and other conditions with a similar inflammatory profile."

Professor Gerry McElvaney, RCSI Department of Medicine and Beaumont Hospital, and senior author on the paper, commented: "These early results are encouraging, and will we hope form the basis for a larger trial to see how much of an effect reducing inflammation using AAT has on clinical outcomes such as mortality."

- **doi:** *https://bit.ly/3u0jAAa*

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Scientists develop CINDELA – a new platform for personalized cancer therapy

Killing cancer cells without affecting surrounding normal cells is the most desirable approach for targeted cancer therapy. However, it cannot be easily achieved due to the similarities in the properties between normal and cancer cells. Using CRISPR-Cas9 targeting multiple cancer-specific mutations, researchers at the South Korea's Institute of Basic Science have developed an innovative approach called CINDELA (Cancer-specific INDEL Attacker), which attacks cancer-specific mutations and causes multiple DNA double-strand breaks to specifically induce cancer cell death. It is hoped that CINDELA can become a potential approach for personalized cancer treatments in most tumours.

Diagnosis of cancers may be one of the worst news to patients and their families. Conventional treatment options such as radiation and chemotherapies often kill not only cancer cells but also normal cells, which results in painful side effects. Radiation and chemotherapies destroy cancer cells by producing DNA double-strand breaks in their DNA. Since both treatments target DNA in both normal and cancer cells, radiation and chemo-drugs cannot distinguish between cancer and normal cells. Thus, indiscriminate killing of healthy cells and side effects are unavoidable when using these treatments. Therefore, scientists have long been searching for a method to selectively target only cancer cells without affecting normal cells, which is a crucial requirement for ideal cancer therapy.

There have been two major developments in the biomedical science fields recently. One is cancer genomics, and the other one is the discovery of a site-specific endonuclease, called CRISPR-Cas9 (commonly called genetic scissors). Cancer genomics projects have found that regardless of their origins, most cancer cells accumulate many mutations including small insertion/deletion (InDel) of several nucleotides, single nucleotide changes, and large chromosomal aberrations. CRISPR-Cas9, the discovery which was recognized by the 2020 Nobel Prize in chemistry, is a technology that can be used to make DNA double-strand breaks in a sequence-specific manner.

South Korean researchers in the Center for Genomic Integrity (CGI) within the Institute for Basic Science (IBS) combined these two concepts and proposed a new idea for cancer therapy. By using CRISPR-Cas9 to produce DNA double-strand breaks at cancer-specific mutations that only exist in cancer cells, they proposed a possibility of triggering cell death in cancer cells without affecting normal cells. Three CGI research groups (laboratories led by Myung Kyungjae, Kwon Taejon, and Cho Seung Woo) located in the Ulsan National Institute of Science and Technology (UNIST) teamed up and proved that it is indeed possible.

First, the researchers confirmed that enzyme-driven DNA double-strand breaks using CRISPR were able to induce cell deaths in cancer similar to physical or chemical breaks driven by radiation or chemotherapies, respectively. Then, they performed bioinformatics analysis to identify unique InDel mutations in several different cancer cell lines, including breast, colon, leukaemia, glioblastoma, which are not found in normal cells. Based on this information, they successfully made CRISPR-Cas9 reagents targeting those mutations.

Cancer-specific InDel Attacker

The scientists named this new treatment CINDELA, which stands for "Cancer-specific InDel Attacker." CINDELA was found to be able to selectively kill cancer cells without affecting normal cells. It was discovered that CINDELA-driven cancer cell death was dependent on the number of DNA double-strand breaks created by CRISPR-Cas9. For example, CINDELA reagent which induced 50 breaks in the DNA was much better at killing cancer cells than the reagent that induced only 10 breaks.

In addition to cancer cell line experiments, researchers conducted further animal studies to verify CINDELA's efficacy in living organisms. To do so, tumour cells (colon and lung cancer) were derived from patients and were xenografted into mice. It was found that the CINDELA treatment can substantially suppress the growth of tumours in these mice.

Notably, since CINDELA targets InDel mutations which are generated as byproducts during tumorigenesis, CINDELA can be applied to treat most tumours.

"We believe CINDELA can become a novel therapeutic application for cancer

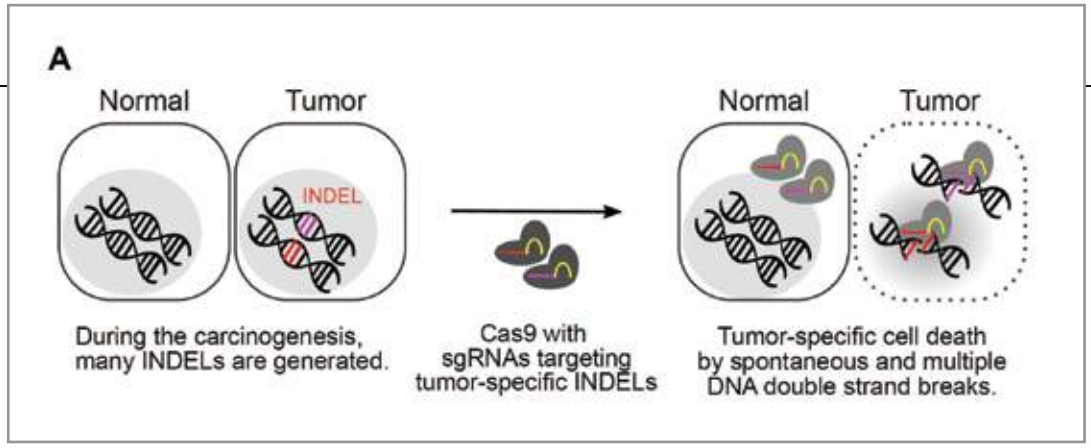

Figure 1. Cancer cells tend to accumulate many mutations during their growth. These include single base substitutions, small insertion/deletions (InDel), and large chromosomal changes. Researchers made CRISPR-Cas9 reagents targeting tumour-specific InDel mutations that can induce numerous double-strand breaks in the DNA of cancer cells, effectively killing them. Because normal cells do not have these cancer-specific mutations, only tumour cells will be destroyed.

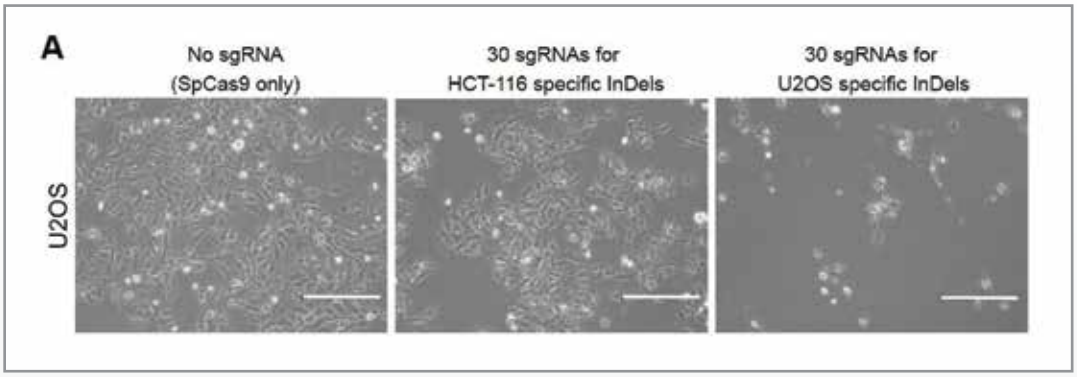

Figure 2. Whole-genome sequence determinations of HCT-116 (colon cancer cells) and U2OS (osteosarcoma cells) revealed that there are many InDel mutations specific for HCT-116 and U2OS. When researchers delivered HCT-116 or U2OS InDel targeting CRISPR-Cas9s to U2OS cells, only U2OS InDel targeting CRISPR-Cas9 caused U2OS cancer cell death, which confirms the high specificity of CINDELA technology.

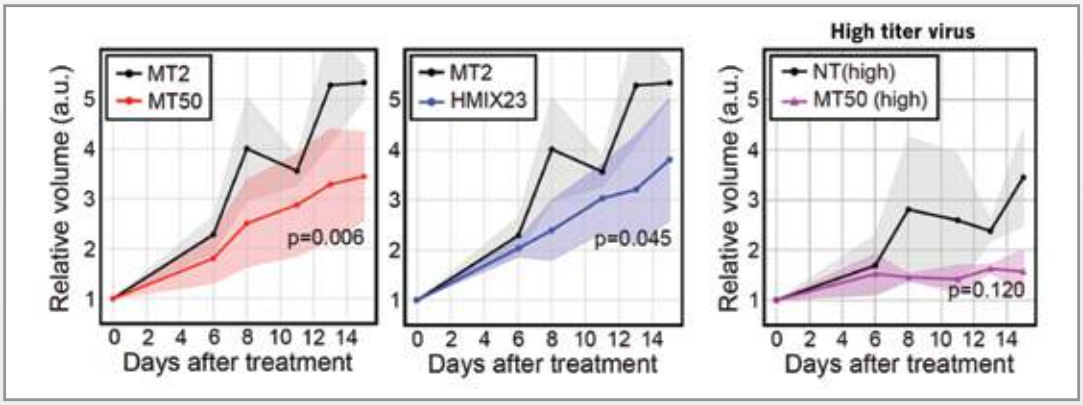

Figure 3. The growth of colon tumours (HCT-116) xenografted in mice was delayed by CINDELA treatment. Compared to the reagent that causes 2 DNA double-strand breaks (MT2), the reagents inducing 50 DNA double-strand breaks (MT50), or HCT-116 specific 23 breaks (HMIX23) had greater ability to reduce the growth of implanted tumours in mice.

treatments as personalized and precision medicine for all cancer patients without severe side effects," the CGI Director Myung explained. As a next milestone, researchers have started applying this technology in tumours directly taken from patients, with research groups having expertise in the relevant technologies, such as gene delivery, companion diagnostic platform, and cancer genomics.

However, one obstacle that researchers had during all these experiments was the delivery of CINDELA reagents to tumours. Although researchers could achieve significant tumour growth inhibition using a high titre of the virus to deliver the CRISPR in mice, as of yet this may not be enough to directly treat human patients. However, such an obstacle is one of the major issues in the current CRISPR-Cas9 field. Researchers believe that in the near future, the development of new delivery systems will eventually help establish CINDELA as a cancer treatment technology for cancer patients.

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doi: *https://doi.org/10.1073/pnas.2103532119*

A mobile app and AI software speed up skin-cancer diagnoses

Skin cancer is a particularly deceptive form of cancer. In the early stages, it looks very much like a harmless mole or birthmark and doesn't cause any pain. One of the most serious types of skin cancer is malignant melanoma, which is most frequently caused by exposure to the sun's UV rays. In 2019 there were approximately 62.8 thousand deaths globally due malignant skin melanoma [1].

However, if caught in time, even melanoma is very likely to be cured. The survival rate is more than 95% after five years, which means that early diagnosis and prevention are even more crucial.

The Fraunhofer Center for Assistive Information and Communication Solutions (AICOS) in Porto and Lisbon has developed a solution to accelerate early recognition. The Derm.AI solution combines smartphone photos of the skin lesion with image-analysis software and artificial intelligence. It provides a swift, first assessment of potentially dangerous changes in the surface of the skin. Dermatologists can access this decision support platform and analyse the cases with increased risk of skin cancer first.

"In recent years, GPs have been increasingly concerned with spotting skin cancer early. People who notice dark spots or other perceptible changes to their skin need clarity quickly. But in regions with few specialists, it often takes a long time to get an appointment for the initial assessment. Often patients also have to travel long distances for these appointments, too. This is where our Derm.AI solution comes in," says Maria Vasconcelos, Senior Scientist at Fraunhofer AICOS.

Standardized photos with a smartphone

The first step is for the GP to photograph the potential problem area on the skin with a smartphone. The Fraunhofer team developed a special app just for this purpose that runs on both iPhones and Android smartphones. The app ensures that the photos are correctly aligned, taken at the right distance and have the correct resolution. The app takes two photos: one close-up of the suspicious area and one from further away to show the area in context. It also helps to correctly align and position the camera. This creates standardized photos with consistent settings for resolution, colour, brightness and contrast. "The standardized shots are easy to compare and can be reliably analysed by specialists," Vasconcelos explains.

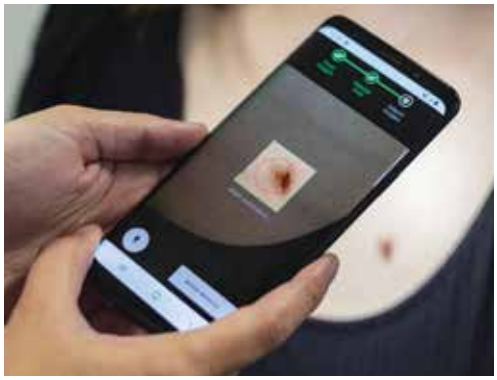
Image analysis with AI

The images obtained at the GP's practice are then sent via the internet to the dermatology department of a hospital. This is where the artificial intelligence software comes into play. It analyses the photos of the skin lesion, compares them to reference data and the data of other patients and provides a risk assessment. The lesion in question is labelled as "normal", "priority" or "high priority". This is not yet a formal diagnosis, it is simply a first assessment which helps prioritize the order in which the potential cases are examined. The doctors can prioritize examining the cases which the AI software has indicated have a high risk, as these need to be quickly confirmed or clarified.

"The software doesn't make a decision; it simply provides a pre-selection based on probability. The actual examination and diagnosis are still in the hands of the dermatologists or skin-cancer specialists," Vasconcelos explains.

After the images are analysed, along with the patient data such as age, gender or previous conditions, the dermatologist at the hospital can either provide feedback to the GP responsible for the patient via teleconsultation or schedule a presential consultation with the patient.

Around 80% of the cases in which patients present themselves at the GP's practice with a suspicious change in their skin prove to be harmless moles or birthmarks, after image analysis and consultation between the doctor and the dermatologist.



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The Derm.AI mobile app photographs suspicious patches on the skin with precisely defined and standardized settings.

This enables GPs to quickly give patients the all-clear, saving them long periods of waiting and an often-long journey to a hospital appointment.

For patients whose skin changes are not clearly identifiable as harmless or for those which indicate a less dangerous form of skin cancer, the GP asks the patient to return, for example in three months, and have another photo taken of the area.

Deep-learning software

During the Derm.AI project, the AICOS researcher and her team developed the algorithm for the image-analysis software. The deep-learning software was fed with image data and information from around 4000 cases. The algorithm also utilized the expert knowledge of dermatologists in the subsequent prioritization. "We had a lot of discussions with GP and dermatologists to really understand what they need. We have received very good feedback from doctors for Derm.AI," Vasconcelos says.

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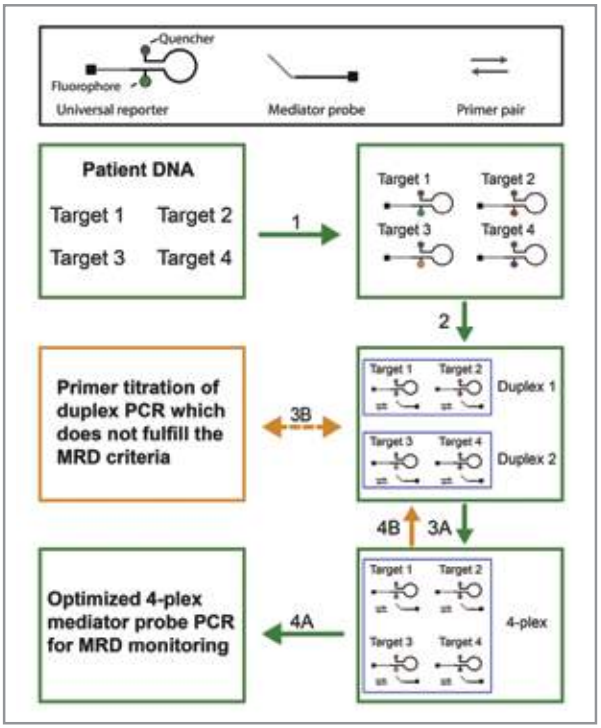
[1] Wei Zhang, Wen Zeng, Aofei Jiang, et. al.Global, regional and national incidence, mortality and disability-adjusted life-years of skin cancers and trend analysis from 1990 to 2019: An analysis of the Global Burden of Disease Study 2019. Cancer Medicine. (July 2021).

doi: *https://doi.org/10.1002/cam4.4046*

Researchers develop new protocol for monitoring acute lymphoblastic leukaemia

Researchers share a new workflow and guidelines for improved monitoring of cancer recurrence in acute lymphoblastic leukaemia patients in *The Journal of Molecular Diagnostics*.



MRD-multiplex workflow for the development of patient-specific 4-plex MP PCR assays through an iterative process. MP PCR-design and -analysis can be done with different software tools already available. In addition, specialized software for multiplex MRD-PCR-design (Assay Manager GNWI mbH, Germany) and standardized analysis (ValidScale Hahn-Schickard e.V., Germany) have been under clinical validation.

The Journal of Molecular Diagnostics

Researchers have developed a new protocol for monitoring acute lymphoblastic leukaemia (ALL), the most common cancer in children, to inform more effective treatment strategies and detect disease recurrence. The personalized mediator probe PCR (MP PCR) uses multiple genomic cancer cell markers in a single assay and is simpler than current techniques. It improves monitoring clonal tumour evolution to detect a relapse sooner and avoid false negative results. Their protocol is detailed in *The Journal of Molecular Diagnostics* [1].

The survival rate for children with ALL has increased impressively to over 80% over the last several decades. However, the prognosis for children whose cancer recurs remains unfavourable. Therefore, minimal residual disease (MRD) monitoring is an important prognostic factor for treatment response and patient stratification. MRD monitoring uses highly sensitive real-time PCR to measure the amount of cancer cells among normal cells.

"MRD markers can disappear during treatment, which can lead to false-negative results and poor decision-making in personalized treatments," explains Principal investigator Cornelia Eckert, PhD, Department of Pediatric Oncology/Hematology, Charité – Universitätsmedizin Berlin, German Cancer Consortium (DKTK) and German Cancer Research Center (DKFZ). Consequently, monitoring at least two independent markers per patient is recommended. Dr Eckert continues: "The current gold standard EuroMRD consortium guidelines call for amplification using singleplex real-time PCR quantification, making testing additional markers more laborious and expensive. They also lead to a higher consumption of patient material."

Personalized MP PCR

To overcome these limitations, Dr Eckert and co-investigators established the personalized MP PCR, an iterative workflow and guidelines for designing multiplex real-time PCRs to monitor up to four MRD markers for ALL simultaneously in one assay. When tested on DNA in bone marrow samples from patients with ALL, the MP PCRs met the EuroMRD gold standard guidelines and level of sensitivity for clinical decision-making.

Co-investigator Michael Lehnert, PhD, Hahn-Schickard Freiburg, explains: "Multiplexing can significantly improve personalized MRD monitoring of patients, because a higher number of MRD markers per patient can be analysed at the same time. Even though these patient-specific sequences of cancer cells only differ in a few DNA nucleotides from healthy cells, our multiplex assay can still distinguish between these DNA sequences. Therefore, a broader range of patient-specific sequences can be included in the assay."

The MRD-MP guidelines are simple and may allow assay standardization across different laboratories. To demonstrate the potential transfer of the duplex MP PCR into a routine diagnostic setting, the new assay was applied in a prospectively assessed patient case in comparison with the gold standard singleplex test. Both fulfilled the EuroMRD guidelines and led to a similar quantitative range and sensitivity.

In order to deal with challenges inherent to multiplex PCR, the researchers developed an efficient iterative workflow for PCR design and optimization. DNA primer titration is only involved and extended if the assay performance is not sufficient in the first step, so that the number of iterations is minimized.

"There is a vast variety of DNA marker sequences unique to each leukaemia," adds first author Elena Kipf, PhD, Hahn-Schickard Freiburg. "The MRD-multiplex workflow provides a systematic and reliable way of effective MRD-MP PCR design and optimization and helps the standardization of personal diagnostics."

While their work demonstrates that multiplex MP PCR has the potential to set a new standard in personalized MRD monitoring, the researchers note it must be clinically validated in a representative cohort of ALL patients.

"Cancer is a fatal disease from which not every patient can be cured," Dr Eckert stresses. "After successful clinical validation, patients could benefit from extended MRD monitoring, leading to more precise predictions of therapy response and better patient stratification and outcomes."

Reference:

Elena Kipf, Franziska Schlenker, Nadine Borst, et. al. Advanced Minimal Residual Disease Monitoring for Acute Lymphoblastic Leukemia with Multiplex Mediator Probe PCR. *The Journal of Molecular Diagnostics* (Jan 2022).

doi: *https://doi.org/10.1016/j.jmoldx.2021.10.001*

Great Ormond Street Hospital for Children
INTERNATIONAL AND PRIVATE CARE

Great Ormond Street Hospital for Children

We've been helping children overcome **rare and complex conditions** ever since we opened our doors in 1852 in London. Our expert team cares for children across 60 different specialties and sub-specialties, the largest of any UK hospital.

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Great Ormond Street Hospital offers personalised therapy for children with cancer

Great Ormond Street Hospital for Children (GOSH) in London became one of the first hospitals in the UK to offer a new pioneering cancer therapy to paediatric patients in 2019. International patients with B-cell acute lymphoblastic leukaemia (ALL) can now receive a new personalised treatment, known as CAR-T therapy.

CAR-T therapies are specifically tailored for individual patients and work by harnessing the patient's own immune system to fight cancer. In a complex manufacturing process, immune cells are taken from a patient's blood and reprogrammed to specifically to target and kill cancer cells.

Tamim, from Saudi Arabia, was one of the first international patients at GOSH to be treated with a CAR-T therapy called Kymriah for his relapsed ALL. "I chose GOSH because Tamim's condition needed urgent treatment," explains Tamim's mum. "This treatment is only available in a limited number of countries and hospitals … the plan was to go to the United States, but we decided to come to GOSH because it would be quicker."

Dr Sara Ghorashian, Consultant Paediatric Haematologist at GOSH, explains: "Rather than being a pharmaceutical drug, this is a cellular product created by taking a patient's immune cells and then genetically-engineering them to recognise the patient's leukaemia."

When asked if she would recommend this form of treatment, Tamim's mother responded: "Of course, it was excellent. There are other forms of gene therapy available that we have tried before, and I noticed they all had some effect on Tamim. With this one, he didn't feel as affected and tired as with the other forms of gene therapy."

Dr Ghorashian says: "The CAR-T cell service at GOSH is a joint service between haematology and the bone marrow transplantation services and contributed to by consultants from each of these teams.

"We have a team of clinical nurse specialists who help coordinate a patient's care, and ward nurses. We also link in with the neurology, endocrine and intensive care departments who regularly review our patients when needed and provide specialist support. Finally, we have a team of therapists, including physiotherapists and play therapists, who support patients and their parents throughout the treatment.

"Tamim has a very resistant disease and he faced a number of complications," explains Dr Ghorashian. "He is a remarkable little boy and recently returned home."

Tamim will return to GOSH for check-ups and the family are hopeful that the treatment is successful.

ALL is a severe form of leukaemia that affects around 600 people per year, most of whom are children between the age of 2 and 5. Although the outlook for children with ALL has dramatically improved over the last decade, 10-15% of patients still do not respond to standard treatments. The new therapy has been shown to be effective in treating patients with particularly aggressive or relapsed cancers where other treatments have failed. MEH

Dr Sara Ghorashian, Consultant Paediatric Haematologist at GOSH.

Tamim, from Saudi Arabia, was one of the first international patients at GOSH to be treated with a CAR-T therapy called Kymriah.

Want to know more about Great Ormond Street Hospital (GOSH) in London?

We've been helping children overcome rare and complex conditions ever since we opened our doors in 1852. Stronger than ever, our team is made up of 300 exceptional and dedicated consultants across 60 specialties. We're a driving force in medical technology and research so we can provide much needed treatment for children across the world.

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Exceptional leaders in the fight against cancer

The Robert H. Lurie Comprehensive Cancer Center

Northwestern Medicine is proud that Robert H. Lurie Comprehensive Cancer Center of Northwestern University at Northwestern Memorial Hospital has received the highest rating of "Exceptional" from the National Cancer Institute (NCI). The Northwestern Memorial Hospital Oncology programme is ranked No. 6 in the U.S. according to *U.S. News & World Report*, 2021-2022, and remains the highest-ranked cancer programme in Chicago and Illinois. Treating more than 10,000 patients each year for both common and rare cancers, Northwestern Memorial Hospital gives patients access to leading-edge technologies and advanced treatments. Services include all surgical interventions, minimally invasive surgery, BMT, CAR-T, chemo, radiation, precision (personalized) medicine, and the only Proton Center in Illinois.

Northwestern Medicine doctors help write the **NCCN patient guidelines** for each cancer type. The Feinberg School of Medicine's Division of Hematology and Oncology in the Department of Medicine is certified by the Quality Oncology Practice Initiative, an affiliate of the American Society of Clinical Oncology, for meeting the highest standards for quality in cancer care.

Innovations in oncology:

- Precision (Personalized) Medicine Programme
- Nano-oncology Center – NM has a very strong nanotechnology programme, and we are doing a study using the gold nanoparticle with conjugated spherical nucleic acid that targets bcl2l12
- Developmental therapeutics
- 3D Printing – Study enabled infertile mice to give birth after ovary implants made with a 3D printer restored fertility. NM scientists hope the research will help restore fertility and hormone production in women who have undergone cancer treatments.
- Proton Center – A global destination for proton therapy treatment

– The Chicago Proton Center is the first and only proton therapy centre in Illinois to bring this innovative radiation treatment to patients. The Northwestern Medicine Chicago Proton Center has treated hundreds of adults and children from the U.S. and multiple countries since it opened in 2010.

Oncology physician pioneers

Dr. Leonidas Platanias – In addition to providing leadership as Director of the Lurie Comprehensive Cancer Center, Dr. Platanias' molecular biology and biochemistry research, spanning more than 20 years and published in more than 250 scientific papers, focuses on signalling pathways in cancer cells and developing novel therapies that target those pathways to treat malignancies. Among his many career honours, Dr. Platanias received the 2013 Seymour & Vivian Milstein Award for Excellence in Cytokine Research. The Milstein Award represents the pinnacle of scientific achievement in cytokine and interferon research. A member of various scientific societies, Dr. Platanias served as president of the International Cytokine and Interferon Society in 2010-2011.

Dr. Maha Hussain - Dr. Hussain is a practicing oncologist, internationally renowned expert, and clinical researcher in genitourinary oncology particularly prostate and bladder cancer. Her clinical research has contributed to impacting the standards of care for patients with metastatic hormone-sensitive and castration-resistant prostate cancer. The research protocol also reduced the risk of developing metastases or death by 71% compared to the standard of care.

Dr. Jayesh Mehta (left) & Dr. Seema Singhal (right) – Northwestern is a destination for myeloma, amyloidosis, and other plasma cell diseases nationally and internationally due to the expertise of Dr. Jayesh Mehta (Chez Family Professor of Myeloma Research, Director, HSCT Program) and Dr. Seema Singhal (Chez Family Professor of Myeloma Research, Director, Myeloma Program) who have been involved with developing cutting-edge treatments in myeloma for the last 20 years. They were the first to use thalidomide and lenalidomide (Revlimid) in myeloma and participated in the earliest clinical trials of all other new drugs in myeloma. Dr. Mehta sees patients with all hematologic malignancies requiring stem cell transplantation and Dr. Singhal's practice is confined to plasma cell disorders.

Dr. Massimo Cristofanilli - Director of the OncoSET Precision (Personalized) Medicine Program. He has led the development of novel diagnostic and prognostic markers in primary and metastatic

– Only proton centre in the U.S. using vertical CT scanner and thoracic treatment chairs that scan and treat patients in the seated position providing better patient comfort and more targeted treatments for head and neck and some thoracic tumours.

– One of only a few U.S. proton centres accredited by the American College of Radiology.

– Among the first proton centres in the U.S. to deploy Pencil Beam scanning technology.

– ioneered a treatment protocol for ocular melanoma patients.

Feature care areas of oncology

a. AIDS-related cancers
b. Blood cancers
c. Brain and spine cancers
d. Breast cancer
e. Colon Cancer Center
f. Dermatologic cancers
g. Gastrointestinal cancers
h. Genitourinary cancers
i. Gynaecologic cancers
j. Head and neck cancers
k. Leukaemia
l. Lung cancer
m. Orthopaedic and rheumatologic cancers
n. Precision medicine and genetic testing
o. Immunotherapy

Northwestern Medicine International Health

Northwestern Medicine International Health helps to connect patients and caregivers to the most advanced medical care at Northwestern Memorial Hospital and its affiliates, while driving innovation and growth in hospitals and clinics worldwide.

With a dual focus on the patient and supporting the global development of healthcare, Northwestern Medicine International Health works to create outstanding patient care worldwide.

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breast cancer. His research is focused on advancing a patient-centred, biology-driven model of cancer care, combining sophisticated tissue and blood-based molecular diagnostic technologies and innovative treatments.

Prior to joining the Lurie Cancer Center, Dr. Cristofanilli was director of the Breast Care Center and deputy director for Translational Research at the Sidney Kimmel Cancer Center at Thomas Jefferson University. He previously served as chair of the Department of Medical Oncology at Fox Chase Cancer Center and executive director of the Morgan Welch Inflammatory Breast Cancer Program and Clinic at the University of Texas MD Anderson Cancer Center.

Dr. Leo Gordon – Dr. Gordon is a world-renown physician in lymphoma. The overarching goal of his translational research is to improve the outcome of patients with lymphoma. He is currently investigating novel signalling pathways in lymphoma, using cell lines and animal model systems. Clinical research interests include the study of novel immune stimulatory strategies following stem cell transplant in lymphoma with collaborators in Israel, Europe, and the US, new approaches to the use of radioimmunotherapy (RIT) in lymphoma, and new treatment paradigms based on the basic investigations described above.

Dr. William Gradishar – Chief of Hematology and Oncology in the Department of Medicine and is among the top 27 academic breast oncologists in the country identified in Forbes Magazine, based on "big data" analysis from Grand Rounds.

Dr. Ryan Merkow - Surgical oncologist at Northwestern Memorial Hospital. His clinical practice focuses on complex upper gastrointestinal malignancies including pancreas, liver, biliary, gastric, small bowel, metastatic colorectal as well as peritoneal surface cancers. He is one of a few surgeons in the United States who is experienced in the application of regional therapeutic techniques, including hyper thermic intraperitoneal chemotherapy (HIPEC) and liver-directed chemotherapy. Dr. Merkow uses advanced minimally invasive surgical techniques including robotic surgery when appropriate. In addition to his clinical practice, he is a health services researcher in the Surgical Outcomes and Quality Improvement Center (SOQIC) in the Center for Healthcare Studies at Northwestern University with a focus on surgical outcomes, quality improvement, and patient safety.

New cellular therapy offers hope for multiple myeloma patients

Andrzej Jakubowiak, MD, PhD, is an internationally known expert in the treatment and research of multiple myeloma.

Although several effective treatments exist for multiple myeloma, patients with this blood cancer face a disheartening reality: Most will experience relapses over several years, and with each relapse, treatment becomes less effective.

"Nevertheless, we continue to add new drugs and new treatment regimens to push that moment patients run out of options further and further away," said hematologist-oncologist Andrzej Jakubowiak, MD, PhD, an internationally recognized expert on multiple myeloma who heads a team of University of Chicago Medicine researchers leading the charge to cure the disease.

Patients with multiple myeloma may have no symptoms for years. When the disease is active – for example, at the time a patient first seeks medical help or when the disease is at an advanced stage –they may experience bone pain, fatigue and even confusion, among other symptoms. Because the cancer comes from plasma cells that normally help fight infections by secreting antibodies, multiple myeloma also weakens patients' immune systems, leading to frequent infections.

New cell-based gene therapy

Dr Jakubowiak, however, is especially excited about the effectiveness of a new cellular therapy called idecabtagene vicleucel (brand name Abecma.)

"Suddenly we have a tool that completely changes the natural history of the advanced stage of this disease," he said.

In March 2021, the FDA approved Abecma as the first cell-based gene therapy for patients with treatment-resistant multiple myeloma. It works by specifically targeting the BCMA receptor on the surface of myeloma cells. Patients with triple-refractory multiple myeloma who have already undergone four or more therapies, including anti-CD38 monoclonal antibody, a proteasome inhibitor and an immunomodulatory drug, are eligible and should discuss the treatment with their doctor.

"We were desperate without this treatment," said Dr Jakubowiak, who directs UChicago Medicine's multiple myeloma programme. "That's why this type of therapy is a game changer."

Multiple Myeloma Research Consortium

UChicago Medicine was chosen as the first hospital in Chicago to offer Abecma because of its expertise in cellular therapy and strong program for treating multiple myeloma, which includes a multidisciplinary clinic devoted to fast-tracking care for new patients. UChicago Medicine is a member of the Multiple Myeloma Research Consortium, an association of 25 academic hospitals dedicated to bringing promising therapies to patients.

UChicago Medicine multiple myeloma researchers are lead investigators and co-investigators on numerous clinical trials and more recently have used innovative treatment regimens to achieve excellent and durable responses – even among patients with advanced stages of the disease.

"This is why patients should receive cellular therapies at a specialized centre," said Benjamin Derman, MD, a hematologist-oncologist specializing in multiple myeloma. "We're increasingly achieving impressive responses at any stage of the disease."

Derman explains that the treatment process with Abecma is similar to the one used to collect stem cells for a transplant but with key differences. Patients are hooked up to a special machine that draws their blood, filters out the T cells, then returns the blood to their body. The T cells are taken to a lab, where over the course of several weeks, they are genetically modified to identify and attack cancerous myeloma cells.

Patients then undergo three days of chemotherapy to knock down any remaining T cells in their body before receiving the modified T cells a few days later. That infusion takes less than 30 minutes.

"In many cases, this is a one-and-done treatment," said Dr Derman. "This does not require continual treatment and allows for a treatment break."

Doctors closely watch patients for side effects in the two weeks after the infusion. One possible secondary effect is systemic inflammation called cytokine release syndrome, which is characterized by a fever, fast heartbeat and low blood pressure. Another is neurotoxicity, when certain elements of the nervous system become temporarily impaired. This can present as tremors, confusion and communication problems.

"There are antidotes for many of these side effects," said Dr Derman. "We can provide this treatment safely and, in most cases, avoid the need for intensive care."

After receiving Abecma, patients in the karMMa clinical trial <*https://www.nejm.org/doi/full/10.1056/NEJMoa2024850*> experienced longer remission periods, improving from three to four months (using the best previous therapies) to roughly a year; some achieved remission for more than 20 months. And while Abecma is not a cure, Derman said the current pace of innovation in multiple myeloma care suggests new treatments should be available by the time the effects of Abecma wear off.

"We keep working to extend patients' lives while making sure they feel well," said Dr Derman. "I think it's something we do really well at UChicago Medicine."

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

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Tiny particles with a big impact

Radiation therapy for cancer treatment with protons and carbon ions

Particle therapy is a highly precise form of radiation therapy that uses beams of high-energy protons or carbon ions to treat cancer. Unlike X-rays or electrons used in conventional radiotherapy, these particles deposit the maximum dose of radiation in the last millimetres of their path and thus directly in the tumour. The underlying physical phenomenon is called the "Bragg peak".

Because of this effect, it is possible to minimize radiation exposure to the healthy tissue around the tumour, making particle therapy an ideal method for treating tumours near radiation-sensitive organs. Side effects and long-term consequences of radiation therapy can be reduced. More than 260,000 patients worldwide have already been treated with particle therapy, and for many indications it is already an established form of therapy. It is used primarily for localized tumours, where local destruction of the tumour cells can lead to a cure or at least long-term survival.

Kaestenbauer/Ettl

Protons are the most widely used worldwide because of the more readily available equipment, while carbon ions require more complex technical equipment. Both particles have the advantage that radiation exposure to healthy tissue can be kept low. Carbon ions, however, have additionally higher biological effectiveness and unleash even greater destructive power in tumour cells. They can be used, for example, to combat tumours that are particularly difficult to treat and do not respond to other types of radiation.

MedAustron, a cancer treatment and research centre located in Wiener Neustadt, Austria, about 50 km south of Vienna, is one of only the six centres worldwide that can use both types of particles for therapy. Its technology branch also serves as a provider of multi-ion facilities.

- For more information, visit: *https://www.medaustron-technology.at*

DTM Medical showcases Signature Cassette Printer for tissue and biopsy cassettes

Print directly onto tissue and biopsy cassettes to increase efficiency, enhance patient safety

Signature Cassette Printer is designed for use in cytology, pathology and histology labs to print high-resolution text, graphics and bar codes directly onto tissue cassettes. That eliminates handwriting or expensive and difficult-to-apply labels and makes the lab workflow more efficient while increasing patient safety. As the cassette printer supports full-colour and black printing with UV- and chemical-resistant ink, only white cassettes need to be stored. That leads to significant cost reduction.

The Signature Cassette Printer is available in two versions: The SCP-M is the standalone, manual printer, loading one cassette at a time by the operator. Print speed is fast, at about six seconds per cassette.

The SCP-R is a completely automated system consisting of a printer and a new upgraded robotic picking system called Autoloader EVO, enabling in addition the use of Sakura Paraform Cassettes. Up to 160 cassettes are automatically loaded by the robotic. Print speed is fast, at about eight seconds per cassette. Labs can first purchase a manual printer and later upgrade that printer with robotics to make it a completely automated system. The same SCP-M printer is simply placed on top of the robotics module and connected via a USB cable.

Unlike other similar printers, Signature Cassette Printer utilises thermal transfer ink ribbons instead of solvent inkjet or laser ablation. There are many advantages to thermal transfer inks, including:

- Virtually silent while printing
- No smell or smoke
- Unlike laser, does not require proprietary cassettes and no fume removal system is required
- No ink tanks or print heads that dry out, need maintenance and have short expiration dates
- Crisp, clear text, graphics and bar codes that won't smear or rub off during or after processing

- The ability to print colour on white cassettes, eliminating the need for coloured cassettes
- Significantly lower acquisition cost than competitive units

Primera's PTLab SE Software, a user-friendly and easy-to-learn program, is included with every printer. Templates can be designed that define the required information on slides or cassettes including fixed and variable fields. Information contained in 2D bar code on the vial or other containers is automatically printed on a number of cassettes that have been ordered for each study. For full integration into existing laboratory information systems, PTLab PE is available as an option.

Together with Signature Slide Printer, Signature Cassette Printer and PTLab Software, DTM Medical provides an advanced and complete labelling solution – all from a single source. Signature printers offer a new and better way for laboratories as well as medical, education and research organizations to process and manage slides and cassettes.

By placing a cassette printer at each grossing station and a slide printer at each microtome station the labs' efficiency is significantly increased while the risk of specimen misidentification is reduced or even eliminated. Labs can certainly afford and cost-justify to do so as the Signature printers cost less than all other monochrome-only slide and cassette printers currently available.

- For more information, visit: *https://dtm-medical.eu*

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Seven predictions for healthcare technology trends in 2022

In the wake of a pandemic, shifting care delivery models, and a surge of clinical content, Wolters Kluwer healthcare experts have identified seven healthcare technology trends for 2022.

While the coronavirus in 2020 dramatically altered the way healthcare is practiced in the U.S. and around the world, 2021 has had its own unique challenges — namely, divergent views on vaccines, powerful COVID-19 variants, and hospitals bursting at the seams as they balance caring for patients with and without the virus.

Technology has proven crucial to keeping the healthcare industry resilient in the face of so many challenges. Simultaneously, the widespread adoption of virtual care delivery along with the rapid pace of vaccine creation and distribution have provided hope for many as the world adjusted to "the new normal".

So, what's in store for 2022?

Our Wolters Kluwer healthcare experts have identified seven healthcare technology trends for 2022 that they anticipate will empower healthcare professionals to continue pushing towards delivering quality care for all.

1. Building trust in an age of digital information overload

With the COVID-19 pandemic came the information epidemic, or "infodemic", so named by the World Health Organization for the influx of false or misleading information throughout social, digital, and physical environments across healthcare.

In 2022, providers will need to focus on increasing access to trustworthy, "high-quality, evidence-based heath content" for themselves and patients, according to Jason Burum, General Manager, Healthcare Provider Segment of Clinical Effectiveness, Wolters Kluwer. Having content that reflects patients' lived experiences and supports clinicians in providing clear, accurate, and accessible health information will be key to building trust with patients in an information-saturated climate.

For Burum, this is a key strategic component currently missing from the digital health space, which has mostly focused on technology innovation and workflow improvements. "Effective, engaging digital health requires more than the right technology," he says, "but a full-fledged experience that informs and motivates consumers towards evidence-based action."

2. Telemedicine becomes a fixture of the healthcare landscape

As social distancing and stay-at-home orders upended the care delivery model, many clinicians and health systems rapidly adopted telehealth and virtual care models – and have seen the benefits it can bring to patient care.

As a result, telemedicine will likely prove resilient well past the pandemic and will establish itself as a permanent and prominent fixture in the healthcare ecosystem, according to Vikram Savkar, Vice President & General Manager, Medicine Segment of Health Learning, Research & Practice.

Looking to 2022, he expects healthcare providers themselves will be among the first to strengthen and formalize training to research and promote telehealth best practices to their clinical teams. He also expects specialties like mental health and urgent care to make a permanent shift to a predominantly virtual model. "Ultimately, I believe that the rise of telehealth will drive more dialogue around modes of access as an issue not only of tech but also of equity in the years to come. This, in turn, will have big impacts in the future of medical practice."

3. Resilience is key to retaining the nursing workforce

Resilience has been one of the biggest challenges in nursing since COVID-19 first appeared. Many nurses were already stressed and burnt out before the pandemic; COVID-19 brought that to the forefront and magnified it. Healthcare organizations will need to proactively foster resiliency and workforce wellbeing to combat the nursing shortage and lack of nursing faculty.

According to Anne Dabrow Woods, Chief Nurse: "2022 will focus on restoring a safe work environment with adequate personal protective equipment, and staffing models that are based on acuity of the patients and competencies of the workforce."

A McKinsey survey from May 2021 found that 22% of nurses indicated they may leave their current position providing direct patient care within the next year. That rate was 15.9% in 2019.

At a time when nurses are needed more than ever, health systems are actively designing and deploying virtual technologies into nursing workflows to reduce burnout and build resilience. They are likely to find an enthusiastic reception. The McKinsey survey also found that more than 40% of frontline nurses have delivered care virtually within the last year, and roughly two-thirds of frontline nurses are interested in providing virtual care in the future.

4. Unstructured health data helps researchers build health equity

The pandemic put a spotlight on health disparities in the U.S. Even with alarming racial and ethnic disparities in COVID-19 infection, many states were not reporting COVID-19 mortality by race and ethnicity.

This greater awareness coupled with new federal reporting mandates will improve data capture in the long term. But Karen Kobelski, Vice President and General Manager of Clinical Surveillance Compliance & Data Solutions, believes that, in the short term, the focus should be on unlocking the 80% of existing healthcare data that remains unstructured. This will be key to making it more actionable for stakeholders across care settings and

it is crucial to gaining big-picture insights into our healthcare disparity problem.

Machine learning tools such as natural language processing and text mining can help health systems reveal valuable health equity insights hidden in unstructured clinical data that is difficult to store, search, analyze, and share across health systems. "2022 will be a pivotal year for making healthcare data help and not hinder the bigger goal of delivering the best care everywhere," says Kobelski.

5. AI-powered technology reduces healthcare-associated infections (HAIs)

In 2022, hospitals will be looking more closely than ever at the effectiveness of infection prevention and control (IP&C) programs powered by artificial intelligence (AI) to better monitor patients in real-time with quick infection risk identification and early clinical intervention.

According to Mackenzie Weise, Infection Prevention Clinical Program Manager for Clinical Surveillance & Compliance: "Data show that while hospitals have allocated more resources to infection prevention and control efforts to contain COVID-19, it has largely come at the expense of controlling other, far too common, healthcare-associated infections (HAIs)."

To gauge the impact COVID-19 pandemic has had on HAI rates in the U.S., the Center for Disease Control and Prevention (CDC) compared 2020 HAI data to that of 2019 which showed significant increases in bacteremia such as MRSA. The CDC concluded these increases were not due to a larger volume of sicker patients but were a result of insufficient surge capacity and other operational challenges.

In response, the agency is investing $2.1 billion to improve IP&C activities across the public health and healthcare sectors. This infusion will help hospitals leverage AI, identify at-risk patients sooner, and allow clinicians to apply evidence-based prevention strategies.

6. Quality improvement accelerates evidence to implementation

In the wake of the pandemic exposing the weaknesses and limitations of medical research's current delivery system, Vikram Savkar anticipates growing interest for tools and solutions specifically designed to shorten the cycle between identification of clinical problems and the implementation of clinical solutions based on evidence.

"Quality improvement research initiatives are key to better patient outcomes and financial performance," he says, "but these are time-intensive programs and it can be difficult to efficiently surface and implement new evidence against the backdrop of a continually evolving clinical practice."

On average, it takes 17 years for newly published research to gain widespread adoption and usage. To accelerate implementation closer to real-time, healthcare organizations will have to find new solutions to translate evidence-based improvements quickly into clinical practice.

7. Virtual simulation and technology transforms nursing education

In 2022, virtual simulation and online learning will become more commonplace in nursing education as classrooms weigh benefits seen during the pandemic. According to Julie Stegman, Vice President, Nursing Segment of Health Learning, Research & Practice, with critical nursing shortages, "the technology can eliminate traditional roadblocks such as a lack of physical training sites as well as staffing challenges by offering flexible solutions for faculty and students".

Virtual simulation has benefits such as knowledge retention and improved clinical reasoning, as well as allowing students to use their sense of touch when practicing physical assessments and hands-on skills such as immunization.

For Stegman, these technologies can strengthen NCLEX and clinical judgement preparation, helping nurses enter the workforce better prepared for clinical decision-making and a diverse patient population.

Healthcare technology to support a healthier, more equitable 2022

Our predictions look to a world where patients and healthcare workers are benefitting from smart, actionable data; flexible work schedules and locations; new ways to collaborate and study together; equitable access to evidence-based information; and new understanding of how innovation, collaboration and automation can improve healthcare delivery to everyone, everywhere. MEH

New 3D ultrasonic method improves accuracy of foetal weight prediction during pregnancy

A potential predictor of complications during pregnancy and birth is foetal birth weight. For example, macrosomia (which is defined as a birth weight greater than 4,000 grams) makes it more difficult for the baby's shoulders to pass through the mother's vagina, and this effect can increase the mother's risk of experiencing vaginal tearing and postpartum bleeding and her likelihood of needing to undergo a caesarean section. It also increases the baby's likelihood of experiencing respiratory problems shortly after birth.

Given the serious problems that macrosomia can cause, obstetricians are keenly interested in techniques that allow them to predict a baby's birth weight before the mother goes into labour. Thus, it should come as no surprise that dozens of research groups have proposed their own methods for predicting foetal weights since the 1980s. Many of these pre-existing methods rely on two-dimensional analyses of ultrasound images of the developing foetus, but accurate evaluation of foetal weight by ultrasound is still challenging owing to foetal and maternal factors.

As Prof. Qing-Qing Wu of Beijing's Capital Medical University notes: "The accuracy of foetal weight predictions is of great significance to clinical work."

A research team at Capital Medical University led by Prof. Wu therefore decided to develop a model for predicting foetal weights based on three-dimensional analyses of ultrasound measurements of foetal limb volumes and abdominal circumferences, in a study published in *Chinese Medical Journal*[1].

The study

For their study, the researchers analysed ultrasound images of the foetuses of 202 pregnant Chinese women whose pregnancies were in the 28th to 42nd week of gestation. All ultrasound scans occurred at the Beijing Obstetrics and Gynecology Hospital between September 2017 and December 2018, and the women gave birth within 7 days of the ultrasound scans. A sonographer with over a decade of experience reviewed three-dimensional ultrasound scans to determine arm volume, thigh volume, and abdominal circumference values. The researchers then computationally generated a model with the arm volume, thigh volume, and abdominal circumference values and actual birthweights from 134 pregnancies and used these data to develop an algorithm for predicting birthweights. The researchers then tested the resulting algorithm to check whether it could accurately predict the actual birthweights for the remaining 68 pregnancies. Then, the algorithm's birthweight-predicting ability was compared with those of traditional formulas, such as the Hadlock, Lee2009, and INTERGROWTH-21st formulas.

Predicting macrosomia

Analyses of the data showed that babies' arm volume, thigh volume, and abdominal circumference values all positively correlated with actual birth weights. This means that babies with greater arm volume, thigh volume, and abdominal circumference values during late foetal development weighed more at birth. Further, an algorithm based on abdominal circumference values and arm volume-to-thigh volume ratios performed well at predicting birthweights. The newly developed algorithm's performance compared favourably with the performance of the traditional formulas, and the novel algorithm outperformed the Lee2009 and INTERGROWTH-21st formulas at predicting macrosomia. Overall, 27 cases of macrosomia occurred, and the newly developed algorithm correctly predicted 87.5% of those cases while correctly predicting the absence of macrosomia for 91.7% of the negative cases.

Conclusion

In conclusion, these findings provide clear evidence that three-dimensional analyses of foetal limb volumes in ultrasound images can provide a basis for accurately predicting foetal weights and the risks of macrosomia. Prof. Wu predicts that the use of such three-dimensional analyses will lead to "foetal limb volumes becoming a parameter for predicting foetal weight" in future clinical practice and medical research. Although the researchers only tested their newly developed algorithm against foetuses in late stages of prenatal development, Prof. Wu predicts that, with further refinements, the algorithm could be used "to assess the growth of the foetus across all stages of prenatal development".

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doi: *https://bit.ly/3t6Em1J*

Early liver diagnosis: the difference is in the details

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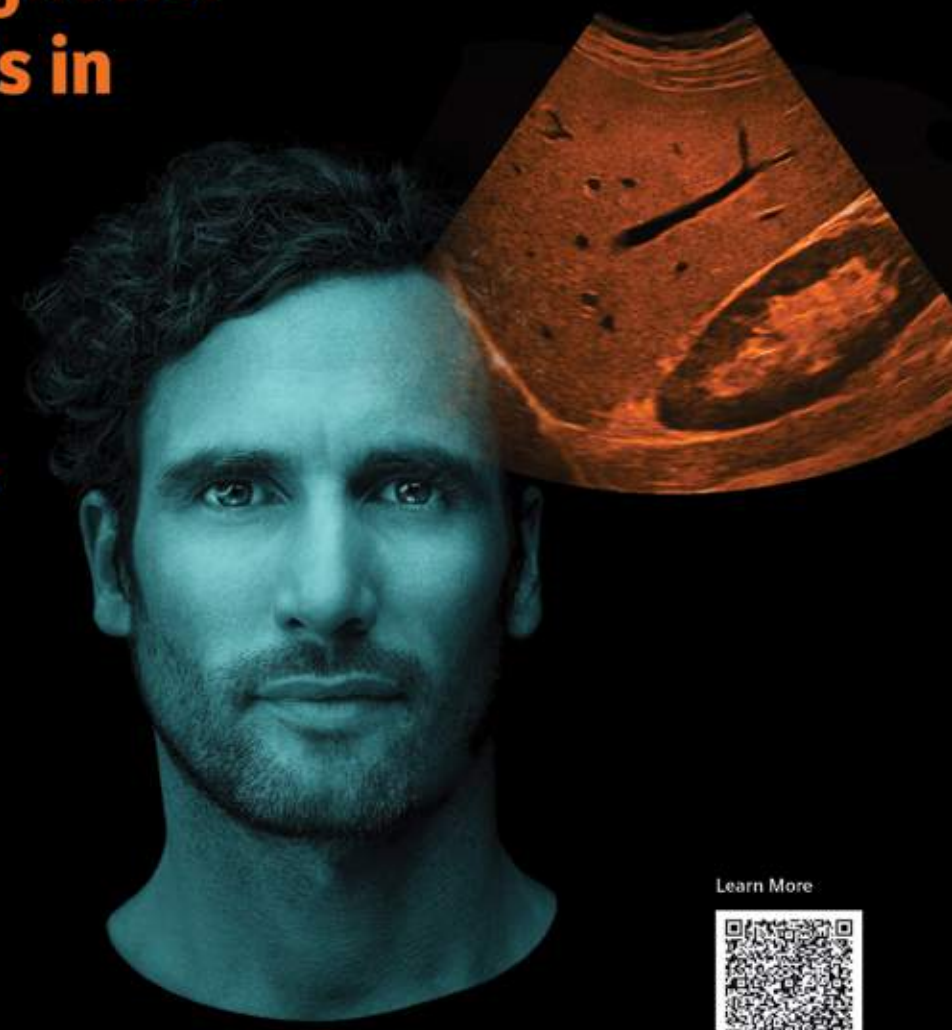

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25%
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1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016 Jul;84-73:(1)64.
* Labyed, Y, PhD. Milkowski, A, MSc. Novel Method for Ultrasound-Derived Fat Fraction Using an Integrated Phantom.
** Data on file. Many variables exist in the customer environment including sonographer techniques, which may affect individual customer experience.

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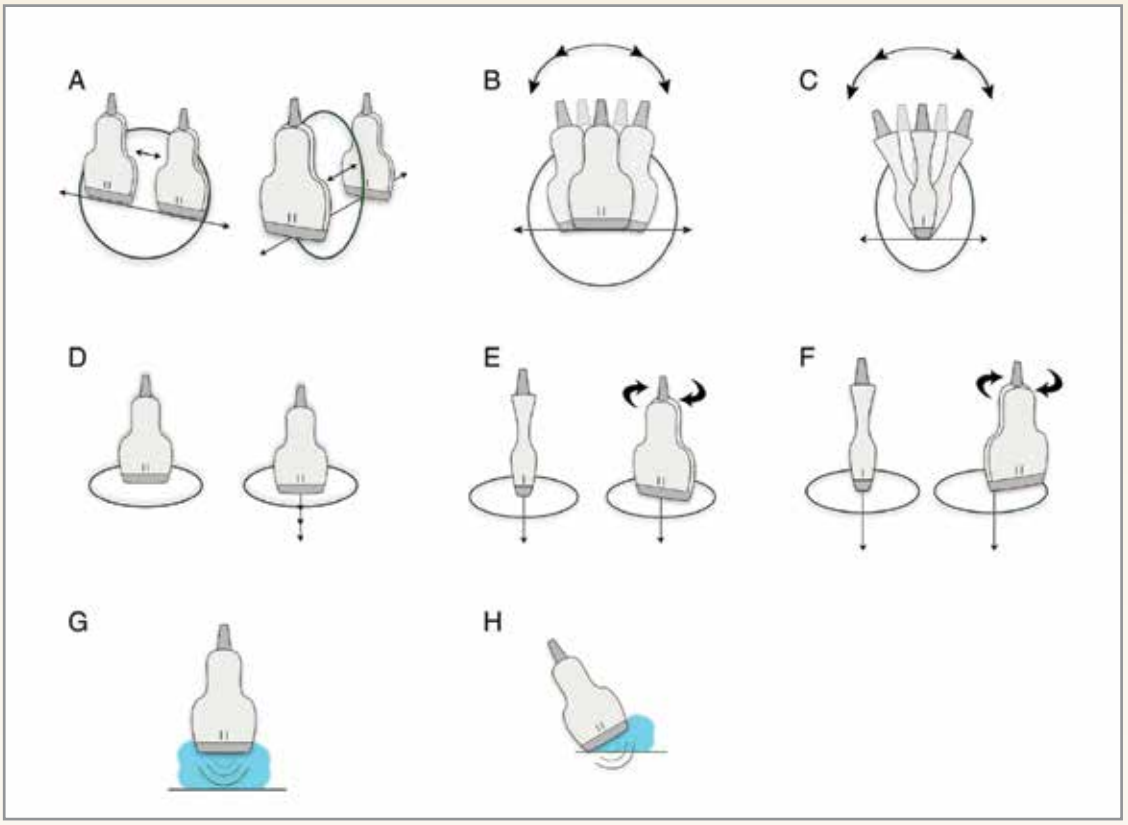

M.M. Hall et. al/JUM

Figure 1: **A**, Slide, **B**, heel-toe, **C**, tilt, **D**, compression, **E**, rotation, **F**, pivot, **G**, standoff, **H**, oblique standoff.

Multiple societies support new consensus statement on musculoskeletal and sports ultrasound terminology

Leading organizations representing sports medicine, radiology, orthopaedics, anaesthesia and pain medicine, and physical medicine and rehabilitation have provided support for a position statement on the Recommended Musculoskeletal and Sports Ultrasound Terminology.

This multidisciplinary expert consensus statement addresses multiple areas of variability in diagnostic ultrasound imaging and ultrasound-guided procedures related to musculoskeletal and sports medicine.

The following societies have endorsed this statement: American Institute of Ultrasound in Medicine, American Medical Society for Sports Medicine, American Orthopaedic Society for Sports Medicine, American Society of Regional Anesthesia and Pain Medicine, Canadian Academy of Sport and Exercise Medicine, European Society of Musculoskeletal Radiology, Society of Interventional Radiology, and Society of Skeletal Radiology. The American Academy of Physical Medicine and Rehabilitation has affirmed the value of the statement.

The document has been co-published in the *Journal of Ultrasound in Medicine* [1] and the *British Journal of Sports Medicine*.

Consistent communication

"The use of ultrasound has increased at a frantic pace and is now used by multiple medical disciplines in the care of musculoskeletal and sports medicine patients, and the lack of consistent terminology has created many challenges," said Mederic Hall, MD, the co-lead author of the statement. "We saw an opportunity to further advance the field by providing a resource which will allow consistent communication whether teaching or reporting."

With the increasing use of ultrasound across disciplines, a lack of consensus regarding standardized terminology can lead to confusion when conveying information between colleagues for clinical and research purposes. Learners can also struggle as different terms are used to describe simple actions such as transducer movement and imaging planes. Furthermore, communication with patients, third-party payers, and the public, also faces these same challenges.

To address these issues, a multidisciplinary expert panel was convened consisting of 18 members representing multiple specialty societies identified as key stakeholders in musculoskeletal and sports ultrasound, resulting in the consensus document.

While other terminology references are available, the focus was on clinically relevant topics in the context of musculoskeletal medicine, where the authors identified frequent variations in terminology used in everyday practice, scientific presentations, and the literature. This concise reference document strives to improve clarity and consistency of communication and reporting.

"As the use of musculoskeletal ultrasound has proliferated, the need for this type of reference has become paramount," said AIUM President and statement co-author Levon Nazarian, MD. "Consistent and agreed-upon terminology facilitates communication among medical professionals and ultimately leads to better patient care."

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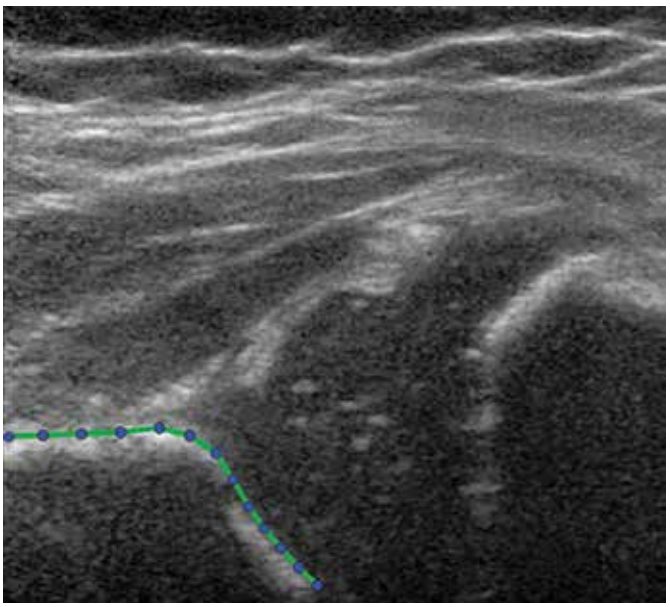
Ultrasound technique predicts hip dysplasia in infants

A technique that uses ultrasound images to determine the depth and shape of the hip socket can accurately predict which infants with hip dysplasia will develop normal hip structure and which remain dysplastic, according to a study in *Radiology*. Researchers said statistical shape modelling improves on existing techniques and could spare many infants from unnecessary treatment.

Developmental dysplasia of the hip occurs when the baby's hip socket is too shallow to cover the head of the thigh bone. In severe cases, the thigh bone can become dislocated from the hip entirely. According to the International Hip Dysplasia Institute, 1 in 10 infants are born with hip instability, meaning the hips can be wiggled in the socket because of loose ligaments. After birth, most will tighten up naturally. One in 100 infants will need treatment for hip dysplasia.



Hip ultrasound image in a 3-month-old girl at baseline. No contrast material was used. The presented hip is outlined with the acetabular shape model, consisting of 13 points.

There is no consensus on how and when to treat stable hip dysplasia (Graf type 2, as determined by the Graf classification system). It is estimated that about 80% of stable Graf 2 hips will develop to normal without treatment. But since there is currently no way to differentiate those that will develop to normal in the future compared to those that will not, a large percentage of stable cases are likely to be overtreated, according to study senior author Ralph J. B. Sakkers, M.D., Ph.D., from the Department of Orthopedic Surgery at the University Medical Center Utrecht in Utrecht, the Netherlands. Overtreatment has significant drawbacks.

"The most important negative consequences of overtreatment are the financial and logistical burdens for parents and society," Dr Sakkers said. "Medical consequences of overtreatment are relatively rare, but the risk is not zero. If there is a rare medical consequence this would probably be avascular necrosis of the hip due to non-proper use of the treatment device."

Avascular necrosis is a disease that results from the temporary or permanent loss of blood supply to the bone.

The Graf classification system is commonly used to evaluate hip dysplasia, but it has limitations. Patients are classified into groups based on acetabular angle appearance on ultrasound images. This angle is derived from the depth and shape of the socket of the hip bone where the head of the femur fits. The Graf system is reported to have a high variability and low agreement in all reported hip dysplasia metrics, and the ultrasound image quality and anatomic appearance of the hip can be affected by probe positioning.

Statistical shape modelling with ultrasound is an alternative method that quantifies the shape of the image of the hip with multiple reference points that each have an X and an Y coordinate in the 2D ultrasound image. It offers potential advantages over existing predictive models.

"By quantifying the shape of the image of the hip with statistical shape modelling, significantly more data are extracted from the ultrasound images as compared to the current methods used," Dr Sakkers said.

For the study, Dr Sakkers and colleagues analysed the predictive power of the technique in 97 infants with stable developmental dysplasia of the hip.

They developed statistical shape modelling on baseline ultrasound images and then correlated the model with persistent hip dysplasia on ultrasound after 12 weeks follow-up and residual hip dysplasia on pelvic X-rays around the age of one year.

The results showed that statistical shape modelling accurately predicted which hips developed to normal or remained dysplastic. It also identified hips that benefitted from treatment with the Pavlik harness, a soft splint that encourages normal development of the hip socket.

Although more research is needed to validate the proof of concept, the study findings support a future role for statistical shape modelling in the clinic.

"The method could be automated after validation, similarly to the current automated determination of the skeletal age on X-rays of the hand," Dr Sakkers said.

The researchers hope to prove the robustness of the method with additional research in other patient populations with stable hip dysplasia according to the Graf classification.

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Artificial intelligence platform offers low-cost, non-invasive option for thyroid cancer screening and staging from ultrasound images

A new study finds that an artificial intelligence (AI) model incorporating multiple methods of machine learning accurately detects thyroid cancer and predicts pathological and genomic outcomes through analysis of routine ultrasound images. The AI model could present a low-cost, non-invasive option for screening, staging and personalized treatment planning for the disease.

Findings from the study[1] were presented at the 2022 Multidisciplinary Head and Neck Cancers Symposium.

"Thyroid cancer is one of the most rapidly increasing cancers in the United States, largely due to increased detection and improved diagnostics. We have developed an artificial intelligence platform that would examine ultrasound images and predict with high accuracy whether a potentially problematic thyroid nodule is, in fact, cancerous. If it is cancerous, we can further predict the tumour stage, the nodal stage and the presence or absence of BRAF mutation," said senior author Annie Chan, MD, Director of the Head and Neck Radiation Oncology Research Program at the Mass General Cancer Center. "If caught early, this disease is highly treatable, and patients generally can expect to live a long time after treatment."

To train and validate the AI platform, researchers obtained 1,346 thyroid nodule images through routine diagnostic ultrasound from 784 patients. The ultrasound images were divided into two datasets, one for internal training and validation, and one for external validation. Malignancy was confirmed with samples obtained from fine needle biopsy. Pathological staging and mutational status were confirmed with operative reports and genomic sequencing, respectively.

Unlike the conventional AI approach, researchers combined multiple AI methods for the model, including (1) radiomics, which extracts a large number of quantitative features from the images; (2) topological data analysis (TDA), which assesses the spatial relationship between data points in the images; (3) deep learning, where algorithms run the data through multiple layers of an AI neural network to generate predictions; and (4) machine learning (ML), in which an algorithm utilizes Thyroid Imaging Reporting and Data System (TI-RADS)-defined ultrasound properties as ML features. "By integrating different AI methods, we were able to capture more data while minimizing noise. This allows us to achieve a high level of accuracy in making predictions," said Dr. Chan.

A multimodal platform utilizing these four methods accurately predicted 98.7% of thyroid nodule malignancies in the internal dataset, significantly outperforming individual AI modalities used alone. By comparison, the individual radiomics model predicted 89% of malignancies ($p<0.001$ compared to the multimodal platform), the deep learning model achieved 87% accuracy ($p=0.002$), and TDA and (ML)TI-RADS were accurate for 81% and 80% of the samples, respectively (both $p<0.001$). On the external validation dataset, the model was 93% accurate for malignancy prediction.

A multimodal model comprising radiomics, TDA and (ML)TI-RADS also was able to distinguish pathological stage (93% accuracy for T-stage, 89% for N-stage, and 98% for extrathyroidal extension). Additionally, the model identified BRAF V600E mutation, which can be treated with targeted therapy, with 96% accuracy.

> If caught early, this disease is highly treatable, and patients generally can expect to live a long time after treatment.

References

[1] https://bit.ly/36fxJBw

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As a result of the health crisis, we're seeing major shifts in the delivery of care, including the transition to telehealth, rapid deployment of temporary field hospitals and clinics, increased call center volumes and remote work.

Transition to telehealth

To reduce physical contact between patients, clinicians and care teams, telehealth is quickly becoming the new normal. Both for primary care and for Covid-19 triage and evaluation, healthcare professionals are using Cisco Webex devices and Cisco Webex meeting and messaging platforms to securely consult with patients virtually.

Rapid deployment of temporary field hospitals

To support a surge in demand for evaluation and testing while mitigating and preventing the spread of infectious disease, healthcare providers are setting up temporary, compartmentalized hospitals and clinics in mobile, pop-up and drive-through locations. By connecting these temporary locations with existing hospital and clinical spaces through Meraki or Cisco networking products, healthcare providers can maintain isolation for high acuity patients. To accelerate deployment, Cisco Customer Experience provides customers with trusted expertise.

Increased call centre volumes

Prior to visiting a hospital, clinic or temporary field hospital, symptomatic patients are being asked to first call a triage hotline. As a result, patients are turning to these contact centre agents to answer questions about symptoms, testing and treatment advice at greater volumes than ever before.

Enabling remote work

Businesses worldwide are implementing work from home mandates. But, what about clinicians and care teams in critical industries such as healthcare? We're seeing many health systems empower both administrators and healthcare staff to work remotely when possible, arming clinicians with tools for telehealth and large-scale video broadcasts for knowledge distribution and health system-wide meetings.

To address these use cases and to share challenges, best practices and resources to keep up with healthcare today, we're launching a new series entitled #HealthcareNow as part of a larger #PublicSectorNow series.

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https://blogs.cisco.com/healthcare/healthcare-now

Revenue Cycle Management for the healthcare industry

By **Amit Agrawalr**,
Senior Director of Operations,
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The Middle East healthcare market is going through rapid transformation with new regulations, laws, systems, processes, and financial dynamics, making Revenue Cycle Management (RCM) a cornerstone in the healthcare industry. The UAE, particularly the emirates of Dubai and Abu Dhabi have led the transformation. The Kingdom of Saudi Arabia also initiated reforming its healthcare system some years ago. Rest of the GCC members are also embarking on transforming their healthcare systems. Bahrain, Oman and Qatar are expected to introduce mandatory health insurance in the near future, so are the northern emirates of UAE.

The UAE healthcare sector is growing at an increasing rate where the overall healthcare spending was 4.27% of GDP in 2018 which is projected to rise to 4.6% by 2026 and 5.1% by 2029 respectively.

Adapting to the fast changing landscape is very challenging but necessary for healthcare providers. Effective RCM function enables a healthcare provider navigate through the rapidly evolving operating landscape and optimize financial performance. It empowers health care providers to focus on their core competency, which is to provide quality healthcare to every patient, while the RCM process takes care of the other factors in a cost-effective manner. Systems such as those provided by ACCUMED, spare healthcare providers spending thousands on the required technology, training staff and process efficiency. It's all about economy of scale.

What is Revenue Cycle Management?

RCM encompasses all administrative and clinical processes in a healthcare facility. RCM tracks patient care beginning with registration, appointment scheduling, insurance eligibility, and ends with the final payment for any given treatment. The goal of the RCM function is to multi-fold and includes: enhancing patient experience during the entire journey of clinical care, maximizing claims reimbursement and revenue, improve cash flow and ensure regulatory compliance.

RCM provides significant operational efficiency to the process of claims management. It aids in speeding up the process of reimbursements, reduces resubmissions of claims, reduces claim denials, and aggregates health information data for the required analysis to benefit stakeholders within the healthcare ecosystem.

For the RCM process to be effective and efficient, the numerous touch points along the patient journey must be managed properly, beginning with front-end such as appointment scheduling and insurance eligibility verification using experienced medical coders and clinical coders. A pre-visit eligibility check is also critical because it allows hospital staff to collect patient information and verify insurance coverage prior to an appointment. This process not only enhances the patient experience but also minimizes potential billing delays and lowers the amount of refused claims owing to insurance ineligibility.

Patient treatment data

The next step of RCM is converting patient treatment data into a format that can be submitted to payers using codes for reimbursement processing. This is now done electronically and includes back-end duties such as coding, claims filing, payment posting, statement processing, and claim management. A well-structured organization enhances time management, communication, regulatory compliance, and the capacity to detect potential coding and billing errors, allowing providers to maximize revenue cycle possibilities at the point of service.

Presently, the processing of claims submitted by health care operators could take from three months to over two years, impacting the cash flow, and cost of capital of the hospital or clinic. A robust RCM function will aid in lowering capital cost by shortening collection cycles and reducing claim rejection rates as it ensures the information provided to the insurance company is accurate, relevant and on time, so the claim is processed without delays.

In mature markets such as North America, RCM has become one of the most popular functions for healthcare providers to outsource, mainly due to combination of complexity and critical importance in managing providers' internal functionalities in an efficient and cost-effective manner. Although RCM still remains at a nascent stage in the Middle East, it is quickly becoming a cornerstone in the healthcare industry.

- For more information, visit: *http://accumed.ae*

Make needlestick injuries history

A large number of all infectious diseases acquired at work in the healthcare sector can be attributed to injuries with medical sharps. Needlestick injuries pose by far the highest risk of infection. More than 50% of all registered cases concern nursing staff, followed by doctors and laboratory staff. However, this does not mean that needlestick injuries represent an unavoidable occupational risk. The correct use of VACUETTE® safety products can virtually eliminate this risk. VACUETTE® safety products comply with the EU Directive (EU 2010/32).

The right safety product for every situation

We offer an extensive range of safety products, allowing the most suitable products to be selected for every market and customer. At Greiner Bio-One, you will find the optimal product for your individual needs as well as every level of safety: from a simple safety product to a premium product.

For daily blood collection routines: VACUETTE® QUICKSHIELD Safety Tube Holder

The VACUETTE® QUICKSHIELD Safety Tube Holder by Greiner Bio-One can be used either with VACUETTE® Multiple Use Drawing Needles or with VACUETTE® VISIO PLUS Needles. With our VACUETTE® QUICKSHIELD Complete and VACUETTE® QUICKSHIELD Complete PLUS, the needles are already assembled. The protective shield is attached directly to the holder. Thanks to the one-handed activation of the protective shield with the aid of a stable surface or the finger or thumb, this product is a winner with its easy handling and extensive protection against injury and infection.

The VACUETTE® QUICKSHIELD Safety Tube Holder offers protection against needlestick injuries with no change to collection technique.

The first step into safety: VACUETTE® SAFETY Winged Set

The VACUETTE® SAFETY Winged Set is a sterile, plastic winged blood collection set. The set consists of a stainless steel needle, colour-coded wings according to needle size, flexible tubing and a plastic safety cover. The version without Luer Adapter as well as the SAFETY Winged Set + Luer Adapter is also suitable for the single-use short-term infusion of intravenous fluids.[1] Each product is equipped with a safety mechanism to reduce the risk of needlestick injuries. After blood collection is completed, the needle is carefully removed from the patient's vein and the safety mechanism is activated immediately afterwards.

SAFETY Blood Collection Set

This product provides a high degree of safety as the safety mechanism is activated while the cannula is still inside the vein. Correct activation by the user is indicated by a clearly audible click. The SAFETY Blood Collection Set thereby provides the best possible protection against needlestick injuries. Visual inspection of the venipuncture through a transparent view window also increases puncture safety. The set can be used for blood collection or infusions for up to five hours.[2] The SAFETY Blood Collection Set is a sterile, single-use winged needle, connected to a flexible tubing, with or without a Luer Adapter or a Luer Adapter with a standard or a blood culture holder.

The gentle touch: VACUETTE® EVOPROTECT SAFETY Blood Collection Set

The safety mechanism with a semi-automatic spring mechanism protects you from the risk of a needlestick injury and makes your daily work easier. Any needlestick injury is one too many. The VACUETTE® EVOPROTECT Safety Blood Collection Set is exceptionally comfortable and intuitive to use. It consists of a winged needle with a safety mechanism, which is suitable for one-handed activation thanks to the special design. Activating the safety mechanism while the needle is still in the vein largely eliminates the risk of needlestick injuries. Extra-thin needle walls of the 21G and 23G cannulas have a positive effect on the flow rate and thus also on the duration of blood collection and infusion.

- For more information, visit: *www.gbo.com*

References

[1] Note: for some product versions, minimum order quantities and lead-up times apply.

[2] Except SAFETY blood collection set with the blood culture holder. MEH

Target-Controlled Infusion anaesthesia: New more universal models

By **James Waterson**, RN, M.Med.Ed. MHE.
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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 compartment 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 mean-average 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 evidence-based anaesthesia, and new near-universal patient models seems primed to change our approach to the management of all patients receiving sedatives and analgesic agents. MEH

Interview

UAE-based neuroscience centre provides multidisciplinary care for kids

Middle East Health speaks to Dr Arif Khan, a paediatric neurologist and founder of Neuropedia, a comprehensive children's neuroscience centre in the UAE, about the centre and the neurological disorders they're seeing and treating.

Middle East Health: When was the paediatric neuroscience centre, Neuropedia, established? Why was it set up?

■ **Arif Khan:** Neuropedia was established in March 2018. It's the first paediatric neuroscience centre in the region and has been providing exceptional services to the local population for the past four years. Whilst there are larger healthcare providers in the region that offer paediatric neurology services, only a few create a welcoming and comprehensive environment that facilitates diagnosis from an interdisciplinary point of view. The multi-faceted nature of neurosciences and its application in paediatrics is often overlooked by a hospital or clinic that focuses on multiple specialties. Neuropedia functions on the concept of creating a self-sufficing cycle of consultation, diagnosis, prognosis, treatment and rehabilitation designed especially for each child.

MEH: Can you tell us a bit more about the centre: What age groups does it serve? How big is it? Which areas does it serve? Are you receiving referrals from outside the UAE?

■ **AK:** We cater to children from birth up to 18 years of age. Our first centre was opened in Jumeirah, Dubai. It has a number of specialities like paediatric neurology, paediatric psychology, developmental paediatrics, educational psychology, paediatric physiotherapy, occupational therapy, speech therapy, behavioural therapy for autism, paediatric dietetics, neurophysiology and clinical genetics.

After having successfully operated for four years, we have recently opened a similar facility in Sahara Healthcare City in Sharjah. We plan to replicate the same reliable and comprehensive service to the population of Sharjah.

We receive international referrals from a number of countries. We have children from Nigeria, Azerbaijan, Pakistan, Oman, Kuwait, Sudan and Egypt being referred to us and following up with us on a regular basis.

MEH: Does the centre specialise in treating specific neurological disorders?

■ **AK:** Being a unique paediatric neuroscience centre, we have demonstrated clinical excellence in diagnosing and treating a number of childhood disorders. Some of the most common disorders that we treat include: autism, ADHD (attention-deficit/hyperactivity disorder), epilepsy, migraine, cerebral palsy, neuropathies, neurogenetic disorders, neuromuscular disorders, sleep problems and many learning conditions like dyslexia, dyscalculia, speech difficulties and behavioural problems.

MEH: There are quite a variety of paediatric neurological disorders. What are the most prevalent disorders presented at Neuropedia?

■ **AK:** Epilepsy forms 30 to 40 percent of our patient presentations. Autism is also seen frequently along with other neurobehavioural conditions like ADHD. We have a number of long-term patients with chronic disorders like cerebral palsy benefitting from the comprehensive rehabilitative services that we offer.

Dr Arif Khan, paediatric neurologist, Neuropedia.

MEH: Are there any significant sex differences in the prevalences of the disorders?

■ **AK:** It depends on the specific neurological conditions. For example, ADHD is seen mainly in boys during childhood but the gender gap narrows in adulthood. Autism, neuromuscular diseases and motor tics are also seen more frequently in boys. Whereas, certain types of epilepsies, migraines and multiple sclerosis is more common in girls.

MEH: Are some of these most prevalent disorders specific to the region or is it similar to other parts of the world?

■ **AK:** Most of these conditions have a similar prevalence in different geographi-

cal regions. However, certain genetic disorders have a higher prevalence in this region due to parental consanguinity. However, not many epidemiological studies have been carried out to look into the exact difference in prevalence.

MEH: For the most prevalent disorders, what treatments are available at Neuropedia?

■ **AK: Epilepsy:** Epilepsy is an extremely common neurological disorder and can be seen in children and adults of all ages. If diagnosed, it can be treated and controlled – thereby significantly improving the quality of life of the patient. At Neuropedia, we have state-of-the-art neurophysiology laboratory facilities to evaluate and investigate the brain's electrical pattern in children. This enables our paediatric neurologists to make an accurate diagnosis, followed by appropriate treatment strategies.

Autism: 1 in 58 children are diagnosed with autism. At Neuropedia we have an interdisciplinary professional team who facilitate the management of autism from diagnosis to treatment, including academic support.

Cerebral palsy: Our expert team of paediatric physiotherapists and paediatric neurologists create a child-centred approach at Neuropedia where every child is given an individualized plan to achieve their functional goal. The co-morbidities associated with cerebral palsy are managed by neurologists, speech therapists, occupational therapists and developmental paediatricians.

MEH: Are you finding that there is significant misinformation / misunderstanding among parents regarding certain neurological disorders? Which disorders are these? What is the misinformation? What do you recommend can be done to correct this?

■ **AK:** I believe misinformation is the biggest threat to medical advances and healthcare improvements. Let's look, for example at epilepsy.

When a child or teenager is diagnosed with epilepsy, the impact of the diagnosis on the child and family is enormous. Children with epilepsy see the disorder through the window of their parents' eyes. The situation for children with this disorder in the developing world remains problematic. The misinterpretation of epilepsy often results in these children being socially ostracized. Many times, they are not brought to the clinic for medical advice and even if they do present, it usually is very late. However, I can see this changing as I have been practicing in this region for nearly seven years. Many parents resort to seeking information on Google. We know that most of the information on Google is not accurate and the websites that offer accurate advice may not be the first ones they come across.

There is a lot of stigma that still exists with seizures and epilepsy. We still see some parents who believe that epilepsy is contagious, some believe that it is a form of disability, some put a metal object in the child's hand in the belief it will stop a seizure, some pour water into the child's mouth during the seizure. These myths and tales must be systematically identified and abolished.

MEH: Have you been finding an increase in certain disorders due to the Covid-19 pandemic?

■ **AK:** The biggest problem that I come across in my clinic post-covid is this new disorder called 'Screen Pandemic'. Children are spending 8 to 10 hours a day on screens and this includes digital learning. This leads to degeneration of social skills, motivation, and physical health, as well as sleep and behaviour problems. We have a number of children coming in with problems such as aggression, insomnia, and lethargy. We need to gradually reverse this pandemic by teaching our children to get outdoors, adopt extra-curricular activities and hobbies and minimize screen time.

We have been seeing increased prevalence of childhood headaches and migraines, as well as increased cases of depression and social anxiety.

MEH: Where does the road ahead take Neuropedia?

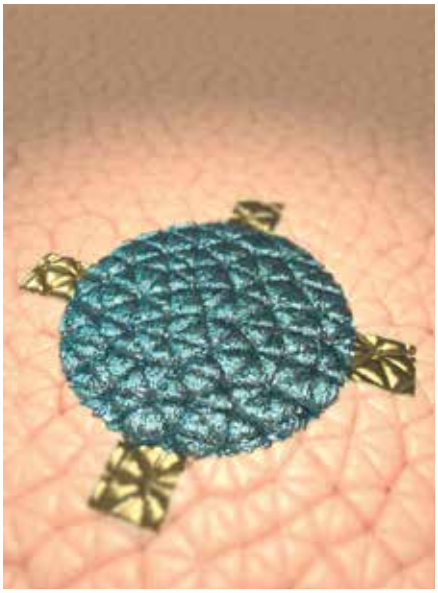
■ **AK:** Our focus on growing and developing Neuropedia goes hand in hand with the Dubai Health Authority's five-year focus on Mental Health and Rehabilitation. This is a personal goal of mine. We believe in treatments based on evidence, experience and consensus that reflect our evolving and adapting nature in this field. We believe our vision of expansion and growth stands for a wider sense of acceptance – a world where neurological illnesses are not shrouded behind legends of curses and old-wives' tales that hinder the scientific and genetic nature of one's being. We wish to be a beacon of light for those parents who experience hopelessness and fear in a warped world with mass hysteria about conditions that make us different.

In five years' time, we hope Neuropedia becomes synonymous in the region for all paediatric neuroscience-based consultations. Having brought light and clarity into the lives of a few since our inception, we see ourselves not only expanding to more cities, but also accepting more patients from overseas thanks to the vision of the UAE leaders who aim to promote medical tourism in the region.

As a paediatric neurologist and a father of three, I am optimistic about the growth of paediatric neuroscience in the region. I only hope that professionals in other specialities follow suit to ensure that the future is always filled with joy, hope and positivity for generations to come.

• To learn more, visit: *https://neuropedia.ae/*

Researchers develop ultrathin films for stretchable, sturdy bioelectronic membranes


Yan et al/UCLA

Artistic representation of a skin transistor made from van der Waals thin films.

UCLA researchers have developed a unique design of ultrathin films for highly flexible yet mechanically robust bioelectronic membranes that could pave the way for diagnostic on-skin sensors that fit precisely over the body's contours and conform to its movements.

Science recently published a paper describing the research co-led by Xiangfeng Duan, professor of chemistry and biochemistry; and Yu Huang, professor and chair of the Materials Science and Engineering Department at the UCLA Samueli School of Engineering.

Held together by van der Waals forces, intermolecular interactions that can only take place at extremely close distances between atoms or molecules, the membrane is stretchable and adaptable to dynamically changing biological substrates, while being breathable and permeable to water and air. The advancement of the durable electronic material could lead to the development of noninvasive electronics for medicine, health care, biology, agriculture and horticulture. The researchers named the material van der Waals thin film, or VDWTF, which could serve as a foundational platform for living organisms to adopt electronic capabilities.

"Conceptually, the membrane is like a much-thinner version of kitchen cling film, with excellent semiconducting electronic functionality and unusual stretchability that naturally adapts to soft biological tissues with highly conformal interfaces," Duan said. "It could open up a diverse range of powerful sensing and signalling applications. For example, wearable health-monitoring devices built with this material can accurately track electrophysiological signals at the organism level or down to the level of individual cells."

The researchers created several demonstrations using the thin films, including a transistor that sat on top of a succulent plant's leaf, whose abundant electrolytes were used to create the electronic circuit. They also created a similar transistor for human skin that used electrolytes-present skin cells to complete the circuit. In addition, the team developed an electrocardiogram that uses small circles of the film placed on a person's right and left forearm and could detect their blinking during meditation.

"Our proof-of-concept demonstrations using the van der Waals thin film really just hint at the myriad possibilities for this new material," Huang said. "The membrane could serve as the connection for human-machine interfaces, enhanced robotics and artificial intelligence-enabled technologies that connect directly. This could open a pathway to synthetic electronic-cellular hybrids – cyborg-like living organisms with electronic enhancements."

The ultrathin, approximately 10-nanometre-think electronic membranes are made of several layers of atomically thin sheets of the inorganic compound molybdenum disulphide. Each sheet is only two to three nanometres thick – more than 10,000 times thinner than the diameter of a piece of human hair.

The key to maintaining the membrane's structural integrity while keeping it thin lies in its unique layered patchwork structure. The layers are not a single continuous sheet but instead are an assemblage of smaller pieces.

Instead of being held in place by rigid covalent bonds, the layers are loosely connected by nonbonding van der Waals forces. This allows the sheets to independently slide and rotate over one another, creating extraordinary pliability while keeping their electronic functionality intact.

The design also enables the membranes to stretch and flex over irregular geometries. The thin films can adhere to soft biological tissues with a snug fit over their micrometre-scale topologies, seamlessly merging with, and actively adapting to, dynamically changing biological substrates, such as skin, without tearing or interfering with the membranes' functionality.

The layered patchwork creates a percolating network of nanochannels, large enough for air and water molecules to pass through them, giving the material its permeability and breathability.

With its unusual combination of high electronic performance and malleability, the van der Waals film addresses many challenges presented by other candidates for bioelectronic thin films, such as inorganic membranes or organic thin films. Those alternatives have been limited by their thickness, lack of stretchability, incompatibility to merge with irregular geometries of biological surface, or by their poor performance in wet biological environments.

The UCLA Technology Development Group has applied for a patent on the technology.

Reference

Highly stretchable van der Waals thin films for adaptable and breathable electronic membranes.
https://doi.org/10.1126/science.abl8941

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