Juliana Chan – Founding Director, GemVCare

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Dr Juliana Chan, one of Asia's leading endocrinologists, is also the founding director of GemVCare, a company that provides data to medical professionals to advise patients on diabetes prevention, diagnosis, and treatment based on genetic profiling. In conversation, she discusses some of the key differences in how diabetes manifests in Asian versus European populations and the importance of region-specific research; why early detection of diabetes, and stratifying patients into subtypes using biomarkers and algorithms ensures that they receive the right drug at the right time; and the importance of a holistic approach to diabetes management, combining medication with lifestyle changes, patient education, and team-based care to achieve better health outcomes.

In the increasingly competitive Asian clinical trials space, what advantages does Hong Kong still have?

I believe we still have a competitive edge in two key areas. Firstly, phase I clinical trials remain crucial, especially as Hong Kong promotes biotech and drug discovery. We have been conducting extensive genomic research for the past 30 years, which has resulted in a significant database of multi-omic data. This positions us well to use data mining and AI to identify drug targets, new indications, and companion diagnostics. Our scientists are well-equipped to discover human-relevant drug targets using big data and multi-omic information. For instance, in the area of diabetes and its complications, we have a comprehensive database that continues to provide valuable insights.

Furthermore, there are distinct genetic differences between Asian and European populations. For example, our 30 years of research have shown that diabetes manifests itself earlier in Asian populations due to genetic variations in beta cell biology. Asians generally have lower beta cell capacity and a less effective insulin pathway to manage the high caloric intake prevalent today, leading to an earlier onset of diabetes. This early onset means a longer duration of exposure of body organs to adverse internal environment, increasing the likelihood of complications such as heart disease, kidney disease, stroke, and cancer. These genetic and physiological differences, like a propensity for central obesity, highlight the unique needs and vulnerabilities of the Asian population, further underscoring our competitive advantage in conducting region-specific research and clinical trials.

Does the need for early detection and treatment imply that patients should receive diabetes medicines earlier in their disease progression?

The first stage is to find and treat patients early. This is crucial, and it is where biomarkers and algorithms come into play, increasing the precision in detecting those at risk and classifying them into subtypes. This ensures that the right drug is administered at the right time for the best outcome.

The strategy involves early detection, risk stratification, and appropriate medication. For instance, we now have nine medications for diabetes, but you cannot prescribe them randomly. It is essential to characterize the patients and select the right drug at the right moment. Asian populations, for example, respond particularly well to drugs that support beta cell function and often need insulin.

Additionally, newer drugs like semaglutide and GLP-1 agonists, targeting obesity; can prevent the rapid burnout of beta cells. Identifying those who are especially vulnerable is key to treating them more precisely and effectively.

This also ties into the cost-effectiveness of treatments. Every person is unique in their risk factors and outcomes. Even in high income countries, it is not sustainable to administer these expensive drugs to everyone and that not all patients will benefit or accept these new medications which are not without side effects. The 20-80 rule is quite applicable here, where 20-30 percent of patients account for 70-80 percent of the complications. These patients would benefit most from innovative treatments. Therefore, focusing on early detection and tailored treatment for these individuals is both medically and economically advantageous.

How is the diabetes-affected population being mapped in Hong Kong and what is the interaction with the Hong Kong Hospital Authority patient database for clinical trial purposes?

In Hong Kong, with a population of 7.3 million, nearly 900,000 people have diabetes, all registered within the Hospital Authority (HA) system. This extensive database highlights Hong Kong's unparalleled medical informatics, making it an ideal place for conducting innovative scientific research. The specificity of drugs like glucokinase activators, tailored for particular genetic profiles prevalent in the population, underscores the importance of research on precision medicine and data management.

Recently, HA has provided anonymized data to academic researchers for analysis to discover knowledge for translation. I established the Hong Kong Diabetes Register in 1995 as a research-driven Quality Improvement (QI) programme because I needed to understand how my patients were progressing. The aim was to systematically identify risk factors and complications and use that data to help patients understand whether they are meeting their targets. This systematic assessment is crucial for chronic and silent diseases like diabetes, where self-management is essential and early control of risk factors can reduce costly long-term complications.

Patients need to take ownership of their health, but they cannot do that if they are unaware of their condition. That is why it is important to provide them with their data, so they know what actions they need to take. Simply prescribing medications like semaglutide is not enough if patients continue unhealthy lifestyles. While semaglutide can be a fantastic drug, it is not a cure-all. It is an aid that should be part of a comprehensive approach, including lifestyle changes.

Globally, there is a perception that GLP-1 is the ultimate solution, but it is not. It is incredibly expensive and even US patients are struggling to afford it. While these drugs are a breakthrough, they must be part of a multi-component strategy. Diabetes management involves behaviour, cognition, and emotion, requiring a care team working together with the patient at the centre, supported by medications and personalized information. Genetic markers and digital solutions complement these efforts, helping patients understand their condition, set targets, and manage their future risks. This holistic approach maximises the benefits of medical expertise, advanced technologies and treatments.

Will the Hong Kong Hospital Authority set up a data-sharing infrastructure to facilitate research?

Through the universities and the Hong Kong Science and Technology Park, the HA is establishing secure infrastructures and mechanisms to enable researchers to use these valuable data to generate new knowledge for creating solutions, while protecting data privacy. GemVCare is a good example of this, but there is a broader context to consider. There are two sets of operations: the R&D and the translation part. We need both discovery and translation to be effective. Using databases gathered over 30 years during clinical practice with ethical approval, patient consent and hundreds of millions of dollars of research funds, the CUHK researchers had discovered biomarkers, algorithms, drug targets, outcome models, and translated them into diagnostic tools and digital solutions to bring precision medicine to practice with ongoing research to develop novel drug targets.

For phase I clinical trials and other clinical trial developments, the electronic medical record (EMR) system is crucial. With our publicly subsidised healthcare system, Hong Kong is in an excellent position to leverage EMR to identify individuals for various trials. This allows us to design trials in a more pragmatic and cost-effective manner, which is a significant strength for Hong Kong.

Every patient attending the HA could potentially participate in clinical trials. It is essential to highlight that participants in clinical trials often receive superior care and achieve better outcomes than those receiving usual care. This is due to the team-based, protocol-driven care they receive in a clinical trial setting with close monitoring and intensive follow-up.

Moreover, the data from these trials not only aids pharmaceutical companies in developing new drugs but also creates jobs and improves the working environment for doctors and other health care professionals. This has been the foundation of my career over the last 30 years as a clinical pharmacologist. I have learned from my patients, understood drug mechanisms and interactions, and grasped the broader ecosystem of drug development.

For Hong Kong to fully utilise its substantial investment in healthcare, it should consider replicating this setting in every major hospital with investment and manpower. This would involve integrating clinical trials into everyday practice, thus fostering a robust environment for continuous medical advancement and patient care.

What exactly is GemVCare, the company that you have founded?

GemVCare can be considered a translational unit, but it encompasses much more. In a nutshell, GemVCare is a bio-AI IT platform. We use biobanks and advanced information technology to stratify individuals into different risk categories and subtypes of diabetes, providing tailored solutions such as lifestyle changes and pathway-targeted medications. Our aim is to bring precision prediction, prevention, diagnosis and treatment into real practice. Essentially, we act as a hub, collaborating with various stakeholders.

We established GemVCare as a commercial entity in 2014, initially funded by a government start-up fund. We licensed databases, biomarkers, and a disease management platform that we have developed over the last 20 to 30 years. These tools have proven utility in identifying individuals at risk of conditions like diabetes and its complications, enabling early interventions to prevent disease onset and subsequent complications.

Our approach is to make these tools widely accessible, leveraging an IT platform for scalability. We work closely with healthcare partners, including clinics and hospitals. Our technologies identify at-risk individuals through simple tests involving saliva samples, finger-prick analysis, and a few questions. We can identify the top 20 percent of people most likely to develop diabetes in the next decade and collaborate with doctors to provide preventive measures.

These measures may include affordable medications like metformin or lifestyle modifications. We also partner with companies providing continuous glucose monitoring (CGM) and functional foods with scientific backing. Additionally, we work with pharmaceutical companies to offer drugs like GLP-1 analogues to those at high risk, aiming to prevent a diabetes onset altogether.

Our goal is to intervene early in individuals with genetic risks, addressing lifestyle and environmental factors that contribute to disease development. By identifying and managing pre-diabetes early, we aim to prevent the progression to full-blown diabetes and avoid complications like stroke and kidney failure often due to delayed diagnoses or suboptimal care.

How much have clinical trials for diabetes changed in recent years?

Clinical trials for diabetes have indeed evolved significantly. One area where Hong Kong can make a real difference is in the cardiovascular-kidney outcome trials, which follow a standardized protocol with specific criteria and endpoints. These trials are essential but also incredibly costly, often reaching up to one billion USD dollars to develop a single drug for registration before

marketing for clinical use.

Hong Kong's strength lies in its ability to leverage its dense population and robust infrastructure to recruit and retain patients more efficiently. Successful clinical trials hinge on three key components: rapid recruitment, effective randomization, and retaining participants.

In Hong Kong, the HA-EMR system is a major asset. It ensures comprehensive data capture and helps prevent patient dropout. The geographical compactness of Hong Kong also plays a crucial role, allowing us to recruit patients quickly and keep them engaged in the trial.

Additionally, the use of genetic markers and other advanced tools enables us to identify patients who are most likely to benefit from specific treatments. This targeted approach not only improves trial outcomes but also accelerates the development process, making Hong Kong a leading hub for diabetes clinical trials.

And how have clinical trial sponsors' requests changed?

While the basic structure of clinical trials, especially for registration purposes, remains similar with randomization and specific endpoints, there is a growing need for more cost-effective and efficient trial designs. The ultimate focus is still on events like death and hospitalization, but there is a call for new methodologies to streamline the process.

Hong Kong is uniquely positioned to meet this demand. With its dense population, robust infrastructure, and numerous opportunities, it can serve as an ideal location for designing trials tailored to Asian populations. By leveraging these strengths, such as using outcome models to assess treatment cost-effectiveness in different patient segments to help study design, applying biomarkers and algorithms to select patients through EMR for trial enrolment and capturing all care processes and clinical outcomes using ICD-codes, we can conduct trials more effectively and efficiently, ultimately translating into more affordable medications for patients.

This is not to mention the use of English as the scientific language of communication and the many key opinion leaders from Hong Kong who have unique clinical insights and promulgate these trial results. This should be Hong Kong's aspiration moving forward.

What is the strategic importance of collaboration with the Greater Bay Area in clinical trials and having the possibility of tapping a larger population pool?

We see collaboration with the Greater Bay Area (GBA) as vital, but this requires alignment and resource mobilization. Key opinion leaders and innovative study designs are crucial for advancing clinical trials in the region. In addressing the collaboration with the GBA, it is imperative to leverage resources effectively. Key opinion leaders play a crucial role in innovative study design, especially with initiatives like the ‘One Plus One’ initiative by Department of Health, which promotes multi-centre studies within the GBA. Levering Hong Kong’s capacity for R/D with broader implementation in mainland China is a strategic move for companies and investors. This approach enables registration to capture the GBA’s sizable population. However, such endeavours require concrete policies and the involvement of seasoned clinical trial experts, like those in our oncology and diabetes research groups, to unleash the enormous potential in Hong Kong and GBA.

How are precision medicine and innovative strategies being implemented to improve clinical trials?

We have long awaited this opportunity, recognizing Hong Kong’s capacity for swift and innovative action. For instance, our precision medicine efforts capitalize on genetic markers to tailor treatments effectively. Clinical trials must be methodical and systematic, contrasting with the brief patient encounters typical in routine care. My own journey underscores the transformative power of clinical trials in deepening our understanding of diseases like diabetes, building patient-doctor relationships and refining treatment protocols for better patient outcomes. Precision medicine is about matching the right drug with the right pathway, using genetic markers to identify the best candidates for specific treatments, especially in the pre-event stage, for prevention.

How do these advancements impact patient treatment and healthcare infrastructure?

For example, young people with diabetes often have multiple causes such as autoimmunity, common and rare genetic variants. By identifying young patients with autoimmune or genetic markers for type 1 diabetes early when they still have residual beta-cell function, we can use insulin early to optimize glucose control along with other treatments like semaglutide, if they are also obese, to preserve beta-cell function and avoid treatment escalation. Sanofi has developed a drug to prevent type 1 diabetes, and we can use these genetic markers to identify at-risk individuals and test this drug in Hong Kong and GBA to delay the disease’s progression. Our understanding and technology allow us to segment patients accurately and work with pharma companies to ensure the right patients receive the right drugs. In this jigsaw, the missing piece is

to assemble a team of doctors in each major hospital, supported by nurses and other staff, to run these trials systematically.

This approach not only benefits patients by providing tailored treatments but also supports the development of new therapies and the growth of Hong Kong as a biotech and innovative care centre. We have many doctors, but they often see patients for just five minutes. Thirty years ago, I saw my patients in a clinical trial setting, which drastically reduced their risk of death by 80percent compared to random care. This experience highlighted the power of team-based, structured care, which was the motivation behind developing the diabetes register as a QI program. My entire career started with clinical trials, allowing me to appreciate diabetes's complexity and the importance of engaging patients through a team and protocol-based approach whilst develop databases and biobanks to make discoveries.

As a final note, what future developments are planned to further enhance the clinical trials ecosystem?

Today, clinical care is often fragmented due to large volumes of patients, many with urgent and complex problems which are often preventable in the first place. We should turn these challenges into opportunities by transforming care. To reform this, we need to build centres/units with the necessary infrastructure supported by a knowledgeable team. These resources can be created through clinical trials where we can fully exploit the potential of existing medications while develop and evaluate new medications and technologies.

Pharma companies would support this because it provides evidence that these drugs save lives and reduce costs supported by data that can be shared globally. In a clinical trial setting, doctors can build biobanks and collaborate with basic and data scientists to discover new biomarkers and drug targets. At the same time, they will work with other healthcare professionals to conduct phase one, two, and three studies, supported by the right ecosystem. This approach would attract investors, including the government and pharma companies, transforming Hong Kong into a biotech and innovative care centre. It is not just about building the infrastructure; It is about creating a comprehensive package, with the right people. This would ensure better patient outcomes, continuous drug discovery, and a thriving biotech industry.

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