

THE LAST DECADES OF LIFE TEND TO BE fraught with frailty and chronic disease, making them less productive years as well as less enjoyable. Furthermore, with every additional disease, the increase in health-care spending is not linear but exponential. In Singapore, annual spending in 2019 on an individual with no disease was S\$3,000 (US\$2,200), with one disease was S\$6,000, with more diseases was S\$16,000 and so on.

This is the puzzle medical Doctor and Professor Andrea Maier is trying to solve as Co-Director of the Centre for Healthy Longevity at the National University of Singapore and founder of the first evidence-based longevity clinic, Chi Longevity, in Singapore's Camden Medical. Her research on the

At current projections, nearly half of Singapore's population will be over 65 by 2050. Planning for a vital workforce means extending not only lifespan, but "healthspan," the duration of life spent free from age-related disease.

"If you asked national governments if they're investing in prevention and health, of course everybody will say yes," Dr. Maier says. "But from a personal perspective, for me as a researcher and physician, nobody has the ecosystem that we have in Singapore. Fifteen years ago, I was applying for grants in Europe to open a healthy longevity clinic and was turned down. People looked at those applications and said, 'what is she doing?' The field wasn't ready. But then Singapore started calling me."

Developing an ecosystem for healthy longevity science means engaging across public and private sectors in three big areas: pre-clinical research with animal models, translating this into the human domain through clinical research and bringing this into practice that can be effective in clinics, with the infrastructure to support it. Dr. Maier and her group address the clinical research and implementation

SOLVING the AGE-OLD PUZZLE

mechanisms of age-related diseases appears in more than 350 peer-reviewed articles. She is a frequent guest on radio and television programs and an invited member of several international academic and health policy committees, including with the World Health Organization.

Singapore, her research base, is a tiny nation geographically, but also one of the world's most densely populated and its healthcare is regarded by some as the envy of the developed world. It's 18 "polyclinics" run by the government have been called "a model of efficiency" by *The New York Times*. From 66 in 1960, the average lifespan has increased to 84 years today.

"Singapore already has one of the longest average lifespans," Dr. Maier says. "It also has a very low fertility rate, which means that at a certain point there is a manpower shortage. Population growth to fix that would take 20 to 30 years at best, and you have to increase the fertility rate to do it. A shorter-term investment would be increasing and investing in the health of the individuals alive now—you and me."

DR. ANDREA MAIER chooses Singapore as a base of operation for groundbreaking work in healthy longevity research and clinical practice. By Brunswick's **SUNITHA CHALAM**.

into practice. While the work is based in Singapore, it has global reach.

One important accomplishment that Dr. Maier points to is the classification of aging as a disease by the World Health Organization—a simple, but profound shift that dramatically improves the outlook for developing clinical applications.

"The WHO has International Classification of Diseases codes, or ICD codes, one for each disease," she says. "We started advocating about 15 years ago that aging and its related conditions needed an ICD code and we finally got it in 2018. Having that code is important because doctors cannot diagnose and treat something that is not recognized as an illness."

AGING CLOCKS

The first age-related chronic diseases typically kick in when an individual is in their 50s, with the first spike in deaths occurring when people hit their 60s and 70s. Often these are related to cardiovascular disease, but as age increases, so do illnesses.



“The question is, ‘How do we prevent the onset of a chronic disease and, if somebody has already one disease, how can we prevent the next disease?’ This is about optimizing health, and interrogating aging processes across the life course,” Dr. Maier says. “This approach is not only reducing healthcare costs, but has other positive results too. The workforce is more vital, the productivity is better and absenteeism is less—that’s the longevity dividend.”

The clinical practice of longevity medicine is increasingly multifaceted, involving earlier, better diagnoses and intervening with supplements, specialized drugs and changes in lifestyle.

“If you look at twins who were separated and grew up in different environments, you can extrapolate how much genetic versus environmental influence there is on lifespan and healthspan,” Dr. Maier says. “The difference between them is a measure of the influence of location and lifestyle. We know from those studies that genetics amounts to roughly 20% of the longevity outcome.”

That means you cannot blame your genes for poor health, leaving much of the problem in the hands of patients and their health advisors, she says. Studies have demonstrated that a change of diet alone can add years to a person’s life—three years for someone in their 80s and a decade or more for those in their 20s.

Bringing this into clinical practice requires diagnostics to measure biological age and then interventions to lower it. Biomarkers measure the state of the human body and how well it is preserved compared to another individual of the same chronological age.

Comparing biological and chronological age can serve as a benchmark against the similar biomarkers of health in their peer group—how does heart function in a 40-year-old compare to others of the same age? Then, interventions tailored to the individual can be developed and the effect can be measured with biomarkers.

“We’ve identified these biomarkers over the past 20 years and we’ve begun to build clocks around them,” Dr. Maier says. “Many people want to know how they’re aging compared to some of their peers, how fast the clock is ticking. We are constantly refining, calibrating these clocks, adding new markers. And the idea is to push the clock hands back, while lowering the incidence of disease through geroprotective interventions.”

The “clocks” include dozens of areas and habits that can affect both the length of a person’s life and the quality of their lives: heart health, hormones,

lipids, blood, sleep, diet, social environment and activity, cognitive sharpness, and the immune system, to name just a few. In some, research results are new and still developing, such as those related to the microbiome.

“The microbiome is important. We carry lots of fungi, bacteria,” she says. “We each have on average 1.5 kilograms of bacteria and fungi in our gastrointestinal system. They are influencing how we feel, the risk of depression, maybe even Parkinson’s disease and dementia.”

RISK AND BENEFIT

Interventions go well beyond eating less and moving more, to include what to eat and when; whether to do intermittent fasting; when to exercise and what kind of exercise to do. Simple changes like changing your pillow or mattress can result in better sleep.

Certain supplements can also play a decisive role. For example nicotinamide mononucleotide or NMN can improve nicotinamide adenine dinucleotide (NAD) levels in cells, which reduce with aging. Dr. Maier showed that individuals who get NMN have higher NAD levels leading to improvements in walking capacity and quality of life. According to Dr. Maier, to get 600mg of NMN in food, you would have to eat 100 cucumbers a day—the big ones.

Supplements and other treatments are only brought into her clinical practice if trials show they work and provide a meaningful beneficial effect that outweighs any potential side effects.

“We absolutely do not have conclusive evidence for stem cell therapies or drips or juices or whatever,” Dr. Maier says. “Even for hyperbaric chambers, there’s no conclusive evidence yet that they can optimize healthspan. So if you choose that, you have to balance whatever the risk is against an unknown benefit.”

Any intervention needs to be based on a thorough assessment of the individual and their genetic and environmental profile. Something that works for one person might not work for another.

“Get to know yourself and act!” Dr. Maier says. “The aim of healthy longevity medicine is to diagnose a person’s biological age and to enable them with cutting edge individualized interventions to optimize their health and healthspan. We need to know what’s good for you.

“I think that is the key message,” Dr. Maier says. “Know who you are and make informed decisions and be clear about risk taking. Treat yourself as you would treat your investments.” ♦

“MANY PEOPLE WANT TO KNOW HOW THEY’RE AGING COMPARED TO SOME OF THEIR PEERS, HOW THE CLOCK IS TICKING.”

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