Silver Age:
Aging Better
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Silver Age: Aging Better through research

According to United Nations estimates, by 2050 there will be a three-fold increase in the number of people over the age of 80. There are two ways to interpret this forecast: to some it represents a financial, social and economic risk, while, without ignoring the inherent challenges, we see this primarily as an opportunity. This evolution implies that more of us will have longer and better lives, made possible by advances in hygiene, health, technology... in other words, scientific progress in the broadest sense.

“By 2050 there will be a three-fold increase in the number of people over the age of 80.”

For these octogenarians, their family and friends, their communities, and also for the health system that supports them, one crucial issue predominates: will these extra years be ones of good health? When we consider, for example, that the UN predicts that 65 million people will suffer from Alzheimer’s disease in 2030 at a cost of around 3,000 billion euros, the growing urgency of this question becomes clear.

With these rising numbers, two issues arise: first, the risk of developing critical diseases increases with age, and second, due to advances in medical treatment and prevention, these critical diseases which were once often fatal have become chronic: one can live for many years after suffering a stroke or a heart attack as is the case with Alzheimer’s or Parkinson’s disease. The “chronicization” of critical diseases is a major challenge for healthy aging. While living as long as possible is desirable, every effort should be made to ensure we age in the best possible way, albeit with one or more chronic diseases.
“We rely on research to tailor our products to the needs of those we cover.”

With the goal of healthy aging in mind, AXA is studying specific solutions to address the “silver tsunami”, particularly regarding associated chronic diseases. Scientific research is an essential part of this process.

“Every effort should be made to ensure we age in the best possible way, albeit with one or more chronic diseases.”

Researchers have largely contributed to a better understanding of yesterday’s incurable diseases and are contributing to the improvement of care in this area. We rely on their work to understand the general and local issues of aging, and to tailor our products to the needs of those we cover.

In this guide we have set out to highlight the work of these researchers. We hope that it will provide some of the key insights for healthy aging.

Marine Habart
Group Life, Savings & Health Chief Risk Officer, AXA

Christophe Mugnier
Group Head of Life, Savings & Health Insurance & Risk Management, AXA
“Health awareness is a decisive factor in successful aging.”

China’s population is aging faster than that of any other country, partly due to major healthcare improvements, while longevity in Hong Kong is now the highest in the world. Similarly, old-age dependency ratios are increasing across Europe. Norman Yao and Somesh Chandra, AXA specialists in Hong Kong and European markets respectively, describe the evolution in elderly care in these regions.

You are both working in very different geographical areas. What are the main changes in societal aging?

**Somesh Chandra:** Life expectancy is increasing throughout Europe, which isn’t front-page news. However, the retirement age remains around 60, while birth rates are declining. And because the greatest healthcare costs occur in our later years this means the financial burden on the state and individuals is increasing.

**Norman Yao:** Life expectancy in Hong Kong has definitely changed over the years. Particularly for women who are now at the top of global longevity rankings. In mainland China, health conditions continue to improve as the country undergoes rapid economic growth, accompanied by increasing health awareness, food quality, medical care, etc.

How is the rising number of elderly people impacting social structures and healthcare systems?

**NY:** The traditional family concept is still very much maintained in modern Chinese society. It continues the custom of families supporting their elderly relatives. Families may provide this care themselves, or by paying for care workers or home care services. In Hong Kong, the need for healthcare and elderly home care services is changing, along with the need for longer-term financially sustainable solutions to provide the necessary funding. The Hong Kong government is unlikely to take on a much larger burden in terms of retirement and healthcare provision, so the private sector will play a more critical role. Demand for Long-Term Care insurance is expected to increase in the future to support the growing nonagenarian population.

“Successful aging requires the right care at the right time and at the right place.”

**SC:** In Europe, the need for healthcare is growing. First, new innovations are increasing the quality of health outcomes, thus driving further investment; second,
Awareness on health is increasing in today’s digital world, driving higher consumption; we also observe a shift from public to private care. In the meantime, the number of very elderly hospitalized patients is growing rapidly. Most of these hospitalizations relate to acute infectious diseases and heart-related conditions. This is putting a lot of pressure on public healthcare and on insurance premiums as healthcare becomes more expensive and more people need treatment or care.

The concept of successful aging means living longer, but also being in good health and remaining independent. What steps would you say are necessary to achieve it?

**NY:** Health awareness is a decisive factor in successful aging. Today’s young people are much more health-aware than previous generations; for example, many use devices to track exercise and well-being. Insurers are even starting to offer discounts on insurance premiums to people who lead healthier lifestyles.

**SC:** Successful aging requires the right care at the right time and at the right place. To achieve this, a focus must be placed on preventive care, which includes taking the relevant vaccinations at the right time and undergoing regular health checkups.

**What is the role of insurance?**

**NY:** Due to the increasing strain on public hospitals, most of Hong Kong’s working population have their own medical insurance or group coverage from their employers. In Mainland China some insurers are branching out of their core business areas by operating elderly care homes or day care facilities. Entire retirement towns have been built to provide accommodation as well as medical treatment facilities.

“In mainland China some insurers are branching out of their core business areas by operating elderly-care homes or day care facilities.”

**SC:** At AXA we are helping to address the issue by increasing awareness and helping people keep fit through well-managed lifestyles with insurance products that integrate data collected from connected devices. This can reduce non-communicable diseases, which account for 80% of healthcare costs. We are also creating savings-led products to help customers save in their younger years, giving them access to quality healthcare when they are older. Research in this field is vital for spreading awareness and identifying cost-effective and efficient care solutions.
CHAPTER 01

Caring today
New ways towards better aging
How can we age better? This apparently simple question encompasses many different issues. To begin with, the chronicity of critical illnesses. Today, those who have had cancer, a stroke, or developed a neurodegenerative disease (Alzheimer’s, Parkinson’s) may go on to live well into old age. At the same time, social protection systems have become strained due to population aging. How can we confront the harsh realities of demographic change and financial constraints, while improving care for seniors? Professors Carol Jagger and Evrim Didem Günes, and Doctor Milena Pavlova, experts in this field, weigh in on this major challenge.

Can you explain the shift from an emphasis on “life expectancy” to “health expectancy”?

Carol Jagger: As life expectancy has increased we have seen a growth in the number of people reaching old age. The over 85s are now the fastest growing section of most Western populations. This has led to an increase in age-related diseases, particularly dementia and disability. The focus has therefore moved from simply extending life to extending the quality of remaining years as measured by health expectancy. We are trying to extend healthy years by more than the increase in life expectancy to enable a compression of morbidity. However, most countries are undergoing a morbidity expansion, where the life expectancy gain is made up of more unhealthy years.

An important aspect of this shift is the changing burden from critical illnesses to chronic illnesses. What does this imply for older people?

CJ: Stroke is a good example of this phenomenon as mortality from stroke has fallen for many years, meaning that more people are living with the after-effects. Given that age is one of the strongest risk factors for such illnesses, as life expectancy further increases, we are more likely to develop more than one of these conditions, termed multi-morbidity.

Evrim Didem Günes: The role of the patient in regard to chronic disease is becoming extremely important. Patients must make a continuous effort to follow medical therapies, such as taking regular medication and maintaining a healthy lifestyle. This means they have a significant impact on their own health.
outcomes. I believe this aspect makes personalized medicine and care an important avenue for the future.

“The shift to chronic illness has major implications on the relation between the patient and the healthcare system.”

Prof. Didem Günes

The shift to chronic illness also has major implications on the relationship between the patient and the healthcare system. Chronically ill patients interact with healthcare systems for longer periods - follow-up visits, prescription renewals, new chronic conditions, etc. This interaction may last for a very long time, considering that the risk of developing chronic diseases starts to rise during our 40s and 50s. Moreover, chronic illnesses can mostly be addressed at the primary level by a care team involving professionals other than physicians, such as nurses, dietitians, and physical therapists.

What does this mean for healthcare systems?

CJ: Most of the world’s healthcare systems were set up when few people survived to be very old, so multi-morbidity was rare. Now it is much more common. In our "Newcastle 85+" study, all participants had at least one disease and the average was

AXA Award | Koç University | Turkey

Prof. Evrim Didem Günes is the Associate Professor of Operations Management at the College of Business Administration and Economics in Koç University, Istanbul. Her research focuses on healthcare operations management and behavioral operations management. She is interested in problems related to preventive care, primary care, and chronic care management. Her work provides insights on how to optimize the organization of chronic care management to improve health outcomes and limit costs. Prof. Günes has received support from AXA to focus on chronic care management and collaborate with new researchers. Through this work she aims to understand and model patient and physician behavior in the context of chronic diseases, and to find ways to use this information to manage services better.
3 for men and 4 for women. This is a serious issue because our health systems do not take into account the interrelationship between diseases and common risk factors. We need to revise our systems to treat older people more holistically.

Milena Pavlova: Western societies have extensive long-term state-supported structures, but governments are facing spending restrictions and maintaining care services is therefore becoming a challenge. There is a need to stimulate informal care provision. In contrast, long-term care in Eastern European countries is largely family-based; therefore, new forms of long-term care are required due to the decrease in family size and increase in the number of working women. Enabling current systems to provide care for more and more people while preserving the basic principles of efficiency and equity are contradictory trends that challenge the sustainability of care provision.

How can we make long-term care more sustainable?

MP: A sustainable care system improves population health through more affordable, easily accessible and better-quality services, including the provision of long-term care services to older and chronically sick individuals. Such a system must respond to demographic, social, political and economic stressors and remain functional for future generations. To achieve this, we have to overcome a number of challenges, including a double aging problem - declining birth rates coupled with increasing life expectancy - and the changing labor market.

EDG: Important changes in care delivery systems can be considered as levers to define a chronic care management system. This system should have mechanisms for managing follow-up visits and ways to monitor patients between visits, deploying a team-based care approach and empowering patients to manage their own conditions. Physicians should be provided with the right incentives to offer the right type of care to chronically ill patients. We
are using mathematical and economical models to understand and describe the mechanisms in such systems. These models are frequently inspired by particular diseases and cases, but they are also generalizable in many ways and can provide insights on overall improvements.

**What is the role of research in improving older people's lives?**

**MP:** My research focuses on the financial side of the healthcare sector and other economic aspects, such as access, equity, preferences and satisfaction. In the health and care sector it is important to motivate societal engagement among a wide variety of stakeholders, bringing them together to co-create solutions to meet social needs effectively and efficiently.

Healthcare actors have diverse needs, attitudes, preferences, beliefs and behaviors, but these different perspectives can nevertheless come together when adequate incentives are provided. We have completed several studies as part of my AXA-funded project that have led to some key policy-related recommendations. These include creating a standardized European indicator database to monitor long-term care systems; facilitating the development of social support networks to reduce the need for institutionalized care and to sustain long-term care provision; designing and implementing pay-for-performance reimbursement mechanisms to stimulate improved provider performance; and fostering the spread of innovations, such as the use of ambient assisted living techniques to make it possible for older persons to live longer independently.

"In the health and care sector it is important to motivate societal engagement among a wide variety of stakeholders, bringing them together to co-create solutions to meet social needs effectively and efficiently.”

**Dr Pavlova**

**CJ:** Good research is crucial to improve older people's lives. Very old people are rarely included in clinical trials, so we don’t have realistic estimates of the efficacy of many medications for the elderly. We also need to replicate analyses: if findings across countries are shown to differ, meta-analyses can help to discover why - and therefore what - works best in what situation. We have recently produced projections of multi-morbidity and care needs in England to 2035 using our PACSim model that stands for the Population, Aging and Care Simulation. It shows that the numbers of older people with
multi-morbidity (2+ diseases) will increase by 86% between 2015 and 2035, while people with 4+ diseases (complex multi-morbidity) will more than double.

With regard to dependency, we found very different pictures for men and women. Men will have a compression of dependency in 2035, living an extra 4.2 years independently, with a reduction in years with care. For women, most of their extra years will be with low-level dependency and they will have almost a year more of 24-hour care in 2035 compared to 2015.

What factors can have a positive impact on aging?

**EDG:** I am working to understand customer and service provider behavior with the objective of improving service delivery systems. For example, I investigate the test ordering behavior of physicians in high workload environments, as well as patient behavior in response to appointment delays and availability of treatment and care options.

We are looking into the "patient activation" concept. It is a fairly new concept that could be described as a care system that enables the patients to self-manage their illnesses and to be involved throughout the entire curing process. We investigate this concept and the links with access to healthcare and health outcomes, based on data from chronically ill patients. We are also using a mathematical model to determine the optimal care service level provided to patients with multiple co-morbidities. Another part of my research looks at incentive contracts for primary care physicians to enable better care coordination for chronic diseases. My first general recommendation would be to include patients in the care process as much as possible and to improve patient activation and engagement with their disease management.

**CJ:** The usual messages are very important: we need to keep physically and mentally active, be socially engaged, eat a healthy diet and not be overweight. Physical activity is especially important for women as they have lower muscle mass and strength than men. This means they reach the threshold for carrying out daily living activities earlier than men and therefore have a greater prevalence of disability. Perhaps the most important aspect is to recognize that aging is malleable – we can change our aging trajectory, even at quite old ages. It is important that older people in long-term care facilities are helped to keep active.

"Perhaps the most important aspect is to recognize that aging is malleable – we can change our aging trajectory, even at quite old ages."

**Prof. Jagger**

What about technological innovations?

**EDG:** Technology can play a central role in monitoring the activities and even the health of patients. Existing mobile apps can track activities and help manage the daily routines of patients as well as their
interactions with the healthcare system. Care teams can use these technologies to save costs but, more importantly, to improve patient monitoring and patient control over their own health. Moreover, the availability of big data makes it possible to develop estimations over the course of a disease for a particular patient, which can then be used to personalize treatment.

**MP:** Digitalization in healthcare is vital and many strategies are being implemented. We must make the most of big data: networks of insurers, hospitals and public health departments can combine and analyze their data to improve patient health and prevent the spread of diseases. Electronic medical records are also a key innovation. Many governments, in Austria and Estonia for example, have attempted to develop medical record systems that apply the concepts of patient-centered care and personalized medical treatments, which are improving quality and efficiency in healthcare.

However we should not forget that there are important barriers to digitalization. For example, government efforts and investments in digitalizing health records easily run into opposition from medical doctors, get low-level responses from patients, and raise considerable concerns for privacy advocates due to their sensitive nature. The dilemma for governments is how to ensure that healthcare digitalization continues while preventing abuse of information technology, such as privacy concerns. The closer involvement of all parties, including insurers, service providers and patient organizations in digitalization initiatives will be vital for success.

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**Dr Milena Pavlova**

**AXA Award | Maastricht University | The Netherlands**

Dr Milena Pavlova is a Health economist at the Maastricht University in the Netherlands. Her research provides evidence on good and innovative practices to help European societies make informed choices about healthcare and long-term care systems. Dr Pavola’s AXA project examines systems of long-term care for older persons in Europe, exploring the future of such systems and their sustainability.

One of Dr Pavola’s main areas of research is in social and policy innovations that can help transform existing health and care systems into sustainable solutions for the future. Her work focuses on how to improve population health and well-being through more affordable, easily accessible and better-quality services and products, and on ways to ensure that future generations can continue to enjoy such benefits.
What are the implications of the trend towards increased longevity?

The increase in longevity, both in France and internationally, has led to an aging population and results in a profound social transformation: a disrupted family structure, the need to rethink the world of work, a sharp increase in the number of people in their 90s and even their 100s. These factors are driving us to adapt our health and care facilities.

What are the consequences for social welfare systems?

This aging population creates various disruptions for social welfare systems, primarily for pension or dependency care systems and particularly those operating on a pay-as-you-go basis with an increasingly unsustainable burden of intergenerational support required from the younger generations. In addition, it is to be expected that the costs borne by health systems will increase: medical expenses will rise sharply for those over the age of 50, and medical inflation will be more pronounced in the older age groups. This is largely related to the prevalence of specific chronic conditions, but also, paradoxically, to the better management of these conditions.

How can the insurance business model adapt to these changes?

Our business model as an insurer is being impacted; we must therefore adapt our cover and services to better take into account both the elderly and the chronically ill, while limiting medical inflation as much as possible (for example via our healthcare networks). We should ensure price stability, particularly for our retail customers who are significantly affected by these changes.

“Support for seniors is at the heart of our strategy.”

How does an insurance company such as AXA cope with aging and the "chronicization" of age-related diseases? Didier Weckner, Deputy CEO AXA France Health and Employee Benefits, President of AGIRC-ARRCO, a supplementary pension organization that covers 30 million working people and retirees in France, and President of GIP Union Retraite (which brings together French mandatory, basic and supplementary pension organizations), explains how innovation and proactive approaches can meet these challenges.

"Support for seniors is at the heart of our strategy."
How can better access to care for all be achieved?

As an insurer, our great strength is to be able to pool risks, which makes it possible to cover as many people as possible. Moreover, we strive to be able to meet the variety of needs within the care system. This is the essence of our "from payer to partner" strategy – going further than paying claims, to become a partner of our customers in their care requirements.

“We must adapt our cover and services to better take into account both the elderly and the chronically ill.”

Consequently, our dependency products provide coverage against the risk of severe dependency at affordable rates. Similarly, we offer an array of innovative services in our portfolio, which allows our policyholders to benefit from services that would be difficult to offer without this extensive pooling. For instance, teleconsultation is included in all our health contracts (group and individual) and provides remote access to a doctor. Through our networks, we enable our policyholders to benefit from controlled rates for optician services, dentistry and hearing aids - which are particularly important needs for seniors. We go even further by including alternative medicine, which can prevent and treat musculoskeletal disorders.

Are there other ways to maximize access to health coverage?

Today’s workforce is tomorrow’s retired population. As we cater to the corporate market, we can reach large segments of the population and follow them over time. We offer our corporate customers a number of services, including the Préventelis program in France, which offers preventive medicine in companies, the H4D station, which performs a number of remote medical measurements, and we provide support to employees after a long-term sick leave when they return to their jobs.

What role do you assign to technology in your strategy for seniors?

Care for seniors is at the heart of many of our projects and is a strategic focus. Home automation and, more generally, connected objects open many possibilities: prevention and detailed monitoring of health status, the possibility of performing remote check-ups, early detection of fragile health or a decline in activity... But there are currently two main obstacles: the price of these innovations which is still very high, and the low rate of use and distrust of technology. Our challenge is to remove these barriers.

Didier Weckner
Deputy CEO AXA France Health and Employee Benefits
Curing tomorrow
Tackling critical diseases through science and innovation
Does medical innovation and its underlying science hold the key to better aging? Both have radically altered life expectancy, for instance through better imaging technologies, precise delivery of active molecules, and new forms of care. Will they soon be used to treat conditions that were once fatal, and remain incurable today? Professors Luisa De Cola, Abdul Barakat, and Mickael Tanter, holders of AXA Chairs, explain how a cross-disciplinary scientific approach can drive advances in healthcare, particularly when it comes to age-related diseases.

Critical diseases are increasingly turning into chronic diseases. How can research and innovation help to better live with such diseases and maybe even cure them?

**Abdul Barakat:** Our lab’s research originally focused on cardiovascular disease, and we are now initiating a new direction into the neurovascular field, which includes Alzheimer’s disease. We use the physical laws and the understanding of mechanical factors such as pressure, shear force and flow in blood vessels to better understand those chronic diseases, but also to implement improved solutions for the patients.

As a concrete example, every year millions of patients worldwide have stents inserted into blocked arteries to restore blood flow. However, the performance of stents and other implantable endovascular devices is far from optimal. We are devising methodologies to optimize the design and performance of stents through the understanding of fluid mechanics with the goal of minimizing complications.

**Mickael Tanter:** We are also working with physics to give medicine novel techniques for medical imaging and therapy, mostly based on ultrasonic waves. Over the past twenty years, there has been a radical transformation in the methods for emitting ultrasound and processing the echoes reflected by our organs. This has led to the emergence of ultrafast ultrasound at thousands of frames per second. More recently, we have even been able to perform non-invasive deep imaging at micron-scale spatial resolution. This technology relies on the emission of broad ultrasound waves that cover entire regions of interest in a single shot, enabling a huge amount of information to be collected on the functioning body. Various medical applications ensue, such as spotting a tumor and checking its evolution in terms of vessel evolution, mechanical properties and quantitative hemodynamics or such as better quantifying and understanding the cognitive impairments due to Parkinson’s and Alzheimer’s diseases in elderly patients as well as autistic disorders in young ones.
After completing her studies in Italy, Professor Luisa De Cola undertook post-doctoral research at the Virginia Commonwealth University in the US. Her independent professional career started in the Netherlands, where she worked in close partnership with Philips Research. She then moved to Germany to work in the nanomaterials field.

Prof. De Cola has worked in France since 2013, where she heads the AXA-University of Strasbourg Supramolecular Chemistry Chair. This branch of chemistry involves the study of complex structures made by self-assembling of small molecular components. Prof. De Cola works in collaboration with the Research Institute against Digestive Cancer, the hospital of Strasbourg and Mario Negri Institute in Milano, to create new hybrid materials with therapeutic applications that are fundamental in curing cancer and other age-related diseases such as Alzheimer’s. She is the co-founder of SiBreaX, a company that develops silicate-based nano and microparticles and injectable hydrogels for biomedical applications.

**Luisa De Cola:** My projects relate to the development of materials that can be used to understand and eventually cure diseases such as cancer, Alzheimer’s and other neurological diseases. One of these materials are the hard and porous nanoparticles that we use to entrap drugs and biomolecules. We design these little containers to be able to penetrate the cells and to be sensitive to external stimuli, so that we can disintegrate them into small pieces after they reach the place where they should deliver the therapeutic content (RNA, peptides, drugs, etc.), making it easier to treat patients with drugs or biomolecules that are otherwise difficult to deliver. This technique, called vectorization, might help treating several diseases, including cancer, by blocking the growth of the tumor and hopefully killing it.

**Your projects seem to be at the crossroads between many scientific areas. Is a pluri-disciplinary approach necessary to tackle age related chronical diseases?**

**LDC:** Most modern research is at the interface with two or more disciplines. We must constantly learn new things that we did not originally study – which for me is what makes my work so rewarding – so that we have a clear and complete picture of the problem. We must study beyond the boundaries of our training. We need to know how to talk to other scientists and listen and understand each other, in order to plan experiments together, without being afraid to propose unusual solutions.

We collaborate with biologists, medical doctors, physicists and engineers, because we need different skills to tackle the same problem. An example of this is our work with hydrogels - soft materials formed by polymers able to trap large amounts of water. We are currently working on hydrogels that become solid only after injection into the body, via a
To innovate in our area, we constantly need to further our knowledge in the fundamental aspects of physics and biology. What we do is known as "cellular mechanobiology", which involves studying the role of mechanical factors such as pressure and shear forces in cardiovascular and neurovascular disease. Mechanical factors are just as important as biological ones in regulating cell and tissue structure and function, but how this occurs remains poorly understood. We then apply these findings in innovative solutions such as our work on stents I mentioned earlier.

"Biomedical studies and clinical translation enable us to verify the potential and future impact of our innovations."

Prof. Tanter

More generally, I think that the current exponential evolution of technologies will lead to major changes in the understanding of diseases. Real progress requires the frontiers between research and medicine to be abolished. A transdisciplinary approach has often been a key aspect of major scientific advances throughout history. For instance, in 1665, Robert Hooke, a renowned physicist, detected compartments in plants using one of the microscopes he invented and coined the word “cell” for these compartments, which became the name of the fundamental entity of biology and medicine. Moreover, Marie Curie was awarded Nobel Prizes in both physics and chemistry, while her inventions found fantastic applications in radiotherapy and radiology. Today, transdisciplinary research is ever more crucial.
**AB:** Since some medical developments will raise major ethical questions, we must ensure that ethics experts are closely involved. A transdisciplinary approach is vital if we are to achieve major breakthroughs and develop technologies to improve patient health.

**LDC:** Innovation is part of any research. We need creativity and originality to produce science and advance our knowledge. The main difference between applied and basic research is the approach to the problem. I like to work on practical problems, so I work with end users - the people who can test my discoveries - and put them into practice. When we design a new material, we know the properties it must have if we want it to address a specific problem. Basic research is needed to allow us to produce the correct components and know how to glue them together. There is no applied research without basic science! And there can be no innovations without support for fundamental advancement.

> “There is no applied research without basic science! And there can be no innovations without support for fundamental advancement.”

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**Prof. De Cola**

**AB:** I believe we are on the cusp of a revolution. Tomorrow’s medicine will be much more personalized, targeted, connected and evolutionary. This will happen due to the application of cutting-edge technologies to medical products such as 3D bioprinting, nanoscience, flexible electronics, machine learning, fast computing and connected devices. Developing the systems to make tomorrow’s medicine a reality will require collaborations between experts in these technologies along with experts in these technologies along with scientists and medical doctors.

**MT:** Our research strategy follows the thoughts of Sydney Brenner, winner of the 2002 Nobel Prize in Physiology or Medicine, who said: “Progress in science depends on new techniques, new discoveries and new ideas, probably in that order”. For us, fundamental wave physics is a means to access unexplored areas of biology and medicine, creating the playground for discoveries in other fields, both for the fundamental understanding of disease and the development of innovative treatments.

My laboratory, Physics for Medicine Paris has built its research strategy at the interface between physics and medicine. It would make no sense for us to develop new techniques in physics without demonstrating their benefit for biomedical research. Biomedical studies and clinical translation enable us to verify the potential and future impact of our innovations. We work closely with more than twenty hospitals, institutes and laboratories from other disciplines to cross-fertilize physics and medicine.

To what extent are innovation and new technologies fueling the more fundamental aspect of your research?

**MT:** Our ultimate goal is to integrate innovative imaging modes into devices for fundamental medical research and clinical
practice for an improved understanding, detection, diagnosis and treatment of diseases. Ultrafast ultrasound is a non-invasive method capable of capturing - in real time - many physiological events that cannot be observed at lower frame rates, such as the mechanical vibrations of tissues, blood streams and muscular contractions.

One of our latest techniques is functional ultrasound imaging of brain activity, which detects very subtle blood flow variations in brain vessels associated with neuronal activity. It provides a way to develop portable - and soon, wearable - systems able to image the brain activity in real time at high spatiotemporal resolution. Many applications of the technique are envisioned. It could reveal biomarkers of neurological disorders for Parkinson's and Alzheimer's diseases and, even more interestingly, neurodevelopmental diseases in the early years of life. Defining such biomarkers could enable early disease detection and improved monitoring of treatment efficacy.

**AB:** We are working on the development of artificial arteries with realistic physiological dimensions and flow conditions. These provide platforms within which devices can be deployed and cellular responses monitored in real-time. We also use these systems to study pathological processes under highly controlled conditions.

**“To innovate in our domain, we need to constantly further our knowledge in the fundamental aspects of physics.”**  
Prof. Barakat

**LDC:** Supramolecular materials are my third research focus. Our aim is to understand the formation and disassembly of elements that are responsible for diseases such as Alzheimer’s and, more recently, we are looking on how to reconstruct virus capsides. The assemblies of molecules are the result of weak interactions that glue the components together and can be broken down and reassembled, giving them a dynamic character. We design these molecules to emit light or change color when they form assemblies, so we can monitor the processes underway and, ultimately, mimic and understand the process behind Alzheimer’s and Parkinson’s.

**How are you bringing your research closer to patients?**

**AB:** We hope to have our first product, a smart “guidewire”, ready for deployment in 2020. This device provides clinicians with precise, instantaneous and non-invasive identification of blood clot composition in stroke patients. Not only is this information invaluable for determining the best method to remove such clots, but our sensor technology is also able to overcome the limitations of conventional vascular imaging techniques. We aim to use the same technology to equip a number of other devices including flow diverters and stents, and we are examining its potential for cancer treatment.

**MT:** Functional ultrasound imaging is already operational as a means of improving patient care for newborns. Certain technical developments are required to transfer this technique to adults: while infants have soft membranous gaps between cranial bones, the fully formed skull is an obstacle to ultrasound transmission. However, we are working on solutions and hope to deliver functional...
transcranial ultrasound imaging within the next few years. We are also pursuing fundamental studies in collaboration with neurobiologists to optimize our technology for the investigation of brain function in relation to disease. For instance, we are studying the neuroscience behind social interaction in the context of autism spectrum disorders. We will also develop prototypes to simultaneously record and process the brain activity in two individuals interacting with each other and study the differences between autistic and non-autistic individuals.

**LDC:** In order to test our materials we need in vivo work, which is very expensive. Government funding is insufficient for this purpose and we therefore rely on private individuals and companies such as AXA for financial support. I firmly believe that our objectives and approach will inspire someone to help us take the next steps forward. The journey ahead is long, but it is definitely worth taking.

Currently our research on age-related disease is in its infancy, because most of our work is related to the treatment of acute illness and tumors. Once we can show that our technology is capable of delivering a wide range of drugs more efficiently and effectively than currently possible, then it will surely prove a valuable tool for treating other illnesses, too.

**Prof. Mickael Tanter**

**AXA Chair on Physics for Medicine and Biology | ESPCI ParisTech | INSERM | France**

Physicist Mickael Tanter is Research Professor at the French Institute of Health and Medical Research (INSERM) and director of the Physics for Medicine Paris Laboratory of the Industrial Physics and Chemistry Higher Educational Institution (ESPCI Paris). Professor Tanter holds the AXA Chair on Physics for Medicine and Biology. His research aims to improve medical knowledge through the use of groundbreaking technologies invented by physicists.

Prof. Tanter graduated from the French graduate school of engineering SUPELEC. He was awarded a PhD for his work on the application of time reversal acoustics for the treatment of brain tumors. His research led to the creation of several MedTech companies, including Supersonic Imagine, which produces an ultrafast ultrasound imaging system for the diagnosis of cancer; CardiaWave, a startup for non invasive treatment of cardiac valves using ultrasonic shock waves; and more recently Iconeus, the first company commercializing an ultrasonic neuroimaging device.

Prof. Tanter's objectives are to develop innovative imaging concepts, new therapeutic approaches and smart sensors for healthcare, focusing on cancer, cardiovascular diseases and neuroscience.
Fostering new perspectives
Fundamental research in aging and critical disease
By tirelessly exploring the complexity of life and decrypting the genetic factors behind longevity and brain development, research leading the way in understanding the keys to longevity and treating age-related diseases. What is the connection between aging and serious diseases? Will it be possible to repair brain cells to treat Alzheimer’s or Parkinson’s? When it comes to aging in good health, do genetics have a more significant impact than environment and experience? Research led by Professor Pierre Vanderhaeghen and Doctor Peter Joshi tackles these important questions.

How do you define aging?

Peter Joshi: Aging is the biological process characterized by deterioration in our bodies as time progresses. This process leads to the breakdown of our biological systems and their performance, such as our eyesight or our ability to recover from influenza, along with a general increase in frailty, disease susceptibility and mortality.

To understand more about the aging process, my team and I are particularly interested in studying people who live beyond the age of 90. These people have usually aged well. For example, some have not suffered a major disease before the age of 85. These “super seniors” may hold important clues to healthy aging within their DNA.

Pierre Vanderhaeghen: Defining aging is a very difficult question to answer from my perspective as a neuroscientist. All living species or cells undergo aging, from plants to humans, and that includes the neurons in our brain. But what happens at the molecular level, beyond phenomenology, remains largely obscure.

“There is a fascinating mystery to understand here: how can single cells in our brain survive for decades without much change in their functionality?”

Prof. Vanderhaeghen

One intriguing aspect about neurons in our brain is that they are as old as we are, since in most cases neurons in the adult brain do not regenerate.

There is a fascinating mystery to understand here: how can single cells in our brain survive for decades without much change in their functionality? This is contrary to what happens elsewhere in our bodies.
How does the aging process impact our brain and neural system?

**PV:** A major impact is the loss of plasticity in the connections, or synapses, between neurons. This makes the neural circuits function in a more rigid way, with less reactivity towards changes in the environment. De facto this makes the brain more vulnerable to physical or psychological injury.

In addition, there is the process of neurodegeneration, which is characterized by the loss of synapses and then neurons. While young people can be struck by neurodegeneration, it occurs naturally in the elderly; the most common forms of Alzheimer’s disease occur as a result of neurodegenerative processes. Such diseases are presently incurable: the neurons progressively degenerate and eventually die.

To what extent are the biological processes associated with aging genetically determined?

**PJ:** I am leading a large-scale study to shed light on the underlying genomic and biological mechanisms of healthy aging. I am looking at how variation in DNA among humans influences how we age and how long we live. To do this we are examining the lifespans of around one million people, many of whom are dead, and inferring the DNA they carried from their living children.

DNA controls our detailed cellular processes to a great degree. However, current estimates suggest that less than one sixth of the variability in human lifespans is genetically determined.
determined. So far, the genes we have pinpointed that affect lifespan account for even less variation – perhaps only 1%. We explain this result by the fact that our studies have not yet been carried out on a large enough scale to detect small effects.

**How do you access information on this scale?**

**PJ:** We use data from UK Biobank, a major international health resource that stores the full anonymized genetic profiles of more than 500,000 people. We interpret an enormous amount of lifespan and genomic data available, then apply statistical tests to highlight the genes of special interest.

**What are the links between genes, lifespan and critical illnesses such as cancer, Alzheimer’s and Parkinson’s?**

**PJ:** Genetics can provide a great deal of information about the biological pathways of a disease, as it is very useful to have a thorough understanding of how the genes interact. At this stage, my research has mainly revealed how these diseases affect lifespan through genetic effects.

**“We have pinpointed 12 DNA regions affecting lifespan, five of which were new. The regions are mainly involved in Alzheimer’s disease, smoking-related cancer or heart disease.”**

**Dr Joshi**

We have pinpointed 12 DNA regions affecting lifespan, five of which are new. The regions are mainly involved in Alzheimer’s disease, smoking-related cancer or heart disease. We have also used DNA as a basis for making predictions about whether people might live longer or shorter lives. In our predictions, we found that if we take one hundred people and use our lifespan score to divide them into ten groups, on average, the top group will live five years longer than the bottom one.

**PV:** The major research goal in our laboratory is to unravel some of the key mechanisms that control the development of the cerebral cortex (the outer layer of the cerebrum, which plays an important role in consciousness) - from stem cells to neuronal circuits - in a direct link with human brain evolution and diseases.

We have identified dozens of genes which are only present in the human genome that contribute to our brain's development and function. One family of such genes, called Notch2NL, is key in controlling the expansion capacity of neural stem cells and is therefore likely to be critical in the control of brain size, specifically in our species. Moreover, when these genes are mutated, patients are affected with brain defects and neuropsychiatric conditions.

**To what extent is the study of brain development a key element to the understanding of age-related diseases?**

**PV:** Our projects are focused on the developmental mechanisms that control some of the key, species-specific features of the human cortex and how they relate to human evolution and diseases. For instance, the enlargement of the surface and thickness
of the cortex is mainly due to a higher number of cortical neurons, due to differences in the mechanisms underlying the generation of these neurons.

We also know that neuronal specification and differentiation are linked to neuronal diversity, increased relative size of specific layers and areas, increased neuronal connectivity and prolonged developmental plasticity.

**What tools are you using to study something as complex as the human cerebral cortex?**

**PV:** Our primary tools include innovative models of brain development that we have pioneered in our laboratory, which use human pluripotent stem cells. Such cells are self-replicating and capable of producing any cell required by the body to counter a wide range of diseases.

We apply these tools to understand the mechanisms underlying human-specific diseases such as certain forms of cognitive disorders and degeneration. Moreover, we explore whether and how nerve cells generated from pluripotent stem cells could be used to repair damaged parts of the brain following degeneration, stroke or trauma.

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**Dr Peter Joshi**

**AXA Fellow | The University of Edinburgh | United Kingdom**

Dr Peter Joshi investigates the still largely mysterious genomic and biological basis of human lifespan. His objective is to contribute to a better understanding of how longevity is genetically determined, providing invaluable knowledge for medicine and healthcare systems. In 2017 he was awarded an AXA Fellowship to support his research in this area and had the opportunity to be a visiting scientist at the Institute of Social and Preventive Medicine at the Lausanne University Hospital, Switzerland.

Dr Joshi graduated in mathematics prior to working as an actuary in life insurance, and later undertook a PhD in complex trait genetics in humans at the University of Edinburgh, UK. He then became a Chancellor’s Fellow in the Usher Institute for Population Health Sciences and Informatics at the University of Edinburgh. His PhD research program focused on human aging, using genomics as a tool to elucidate biological pathways.
We understand that aging is a process that stretches across multiple scientific fields. To what extent do we need to adopt a transversal approach to tackle the issue of age-related diseases?

**PJ:** An interdisciplinary approach will ultimately be necessary; however, the specifics of human aging are not well understood at the moment. We therefore first need insights from within specific fields.

**PV:** All biological and medical questions require the adoption of a multi-level approach, from genes to cells, from cells to organs, from organs to bodies, from individuals to societies. I agree with Peter: it is important to note that single-focused studies are often the best way to generate scientific breakthroughs. These innovations then have multi-disciplinary consequences and benefits.

How can your research help in solutions to healthier aging?

**PJ:** My particular interest is in the mathematical application of survival models to human lifespan. By pinpointing regions of the genome that affect lifespan, we can gain a better understanding of how longevity is genetically determined, which is invaluable for medicine and healthcare systems.

I am also aiming to conduct a larger study that will investigate aging pathways and thus help better understand the accretion of susceptibility to diseases such as Alzheimer’s and Parkinson’s.

**PV:** In our research of therapies to enable the replacement of lost or dysfunctional cortical neurons to treat neurological diseases, we recently tested embryonic stem cell-derived cortical neurons in an experimental model of neurotoxic lesioning in the adult mouse cortex. We found that human visual cortical cells differentiated from embryonic stem cells can be transplanted and can integrate successfully into the lesioned mouse adult visual cortex.

However, it remains unclear whether transplanted neurons can integrate into a complex circuit (i.e. the real human brain) and contribute to the genuine restoration of lost function. Indeed, the functional characterization of transplanted neurons in the context of brain repair, as well as their impact on host circuitry function and plasticity, appears as a major, yet unreached milestone to the road of effective and reliable cell replacement therapies of the adult brain. To address this question, we are testing how transplanted neurons display connectivity and functional properties in host circuits that indicate physiological integration.
“Only by studying aging at the molecular level can we delay the process…”

A growing body of evidence indicates that telomeres, nucleotide sequences at the ends of our chromosomes, have a major impact on our health and longevity. Maria A. Blasco, Director of the Spanish National Cancer Research Center (CNIO), Head of Telomeres and Telomerase Group at CNIO and former member of the AXA Research Fund’s Scientific Board, is convinced that telomeres hold the key to healthy aging.

**Shortening telomeres shorten lifespan**

Why are telomeres so critical? “DNA is the most important part of our cells because it holds all of the information necessary for a living organism to function. DNA is packed into chromosomes inside the nucleous of each of our cells, and these chromosomes are protected by structures known as telomeres, which are located at the ends of chromosomes. Unfortunately, our telomeres erode at every cell division. So as our telomeres shorten, DNA damage becomes more likely.” explains Dr Blasco.

There are many molecular pathways that maintain our cells in a young state and the role of telomeres is one of the most important. Human life expectancy is extending but age-related diseases are having an increasing impact because they are associated with molecular pathways that have remained unchanged for thousands of years. “Only by studying aging at the molecular level can we devise therapies and delay the process,” says Dr Blasco.

**Understanding the links between aging, genes and lifestyles**

Increasing our understanding of telomere shortening holds great potential for the development of therapeutic strategies to tackle many age-related diseases including cancer, cardiovascular and neurodegenerative illnesses. “We have demonstrated this in the laboratory. When we delay molecular aging in mice, we delay age-related diseases, including cancer, and the animals live longer and healthier lives. We have recently shown that we can stop the progression of pulmonary fibrosis, which is a lethal age-related illness in humans”, explains Dr Blasco.

Her work has advanced our knowledge on the considerable influence of genetic and lifestyle factors on maintaining telomere length, as she describes it: “Environmental factors are also key in this process. While smoking, obesity and stress accelerate shortening, physical exercise appears to have a protective effect on telomeres.”

Maria Blasco  
Director of the Spanish National Cancer Research Center (CNIO)  
Head of the Telomeres and Telomerase Group
"The challenge of making ‘better aging’ a reality is immense."

As we age, the risk of developing many diseases, such as heart disease, cancer and Alzheimer’s, substantially increases. Why does this happen and is it possible to alter the process? Thomas Kirkwood is Professor of Medicine and Associate Dean of the Institute for Aging at Newcastle University and president of the AXA Research Fund’s Scientific Board. His research focuses on aging and the factors that influence longevity. He is a Fellow of the Academy of Medical Sciences, a Senior Investigator of the UK National Institute for Health Research and has received several international prizes for his research.

How would you define aging and longevity?

Aging is a process of progressive, generalized impairment of bodily and mental functions that eventually results in a growing risk of illness and death. Longevity is the measure of how long the individual can survive within the context where aging takes place, which may be expressed either as the particular longevity of an individual or the average longevity of a population.

How has research evolved over the past decades? What have been the groundbreaking discoveries?

I have been conducting research on aging for 45 years, along with other topics such as the emerging use of mathematical sciences in bioinformatics, genomics and other forms of ‘big data’. I have found it particularly valuable to be able to combine different disciplinary approaches to address this extremely complex and challenging topic.

Over recent decades there has been a growth in the recognition of the importance of longevity and aging as fields for research. During these decades there have been many individual advances and groundbreaking discoveries. Among the most important advances has been the recognition that aging is not programmed, in the sense that the body does not have mechanisms that are there for the purpose of ending our lives. Instead, the body is programmed for survival, but aging occurs because this programming was not sufficient to make us survive indefinitely.
“Over recent decades there has been a growth in the recognition of the importance of longevity and aging as fields for research.”

From this insight comes the understanding that aging is caused by the gradual accumulation of faults and damage in the cells and organs of the body. And also that the aging process is more malleable than once thought, so factors like lifestyle and socioeconomic conditions can make the individual age faster or slower than average.

What is the current state of research on better aging?

The challenge of making ‘better aging’ a reality is immense. Aging research is now a very wide field with many important sub-fields, frontiers and perspectives. At the biological level, much research is focused on the mechanisms of damage and the pathways regulating the body’s response to this damage.

At the individual level, there is great interest in identifying the important factors that influence aging trajectories. Aging begins very early in life, even if the effects are not obvious until later. Therefore, it is important to identify factors that can help an individual have the best chance to remain healthy and independent for as long as possible.

What role could the AXA Research Fund play in supporting this research?

The AXA Research Fund cannot support all these projects by itself, but it can and does make an important contribution by supporting transformative projects and helping to share the results with the wider world. All the projects we have funded through the AXA Research Fund on aging and longevity are important and inspiring. They are also very diverse, as is appropriate for such a wide-ranging topic.

What about ethical issues? Do we have the right to live longer?

Ethical issues are always important. We are all living longer because of the efforts of previous generations. There is nothing unethical per se in the desire to live longer, but ethical problems would certainly arise if new possibilities to do so are available to some but not all.

There is already a strong ‘social gradient’ in longevity and health, which is a deep problem. On average, people in lower socioeconomic groups become ill and die younger than people in higher socioeconomic groups. There is an ethical imperative to find ways to reduce, and if possible, eliminate, this social gradient.

“There is already a strong ‘social gradient’ in longevity and health, which is a deep problem.”
Besides, there is a technological issue: molecular design, nanotechnologies, big data, machine learning... all these fields have potential relevance for future health and longevity. The challenge is to find ways to use them to the best advantage for individuals and society.

Despite continuous progress, the scientific world faces a crisis of growing global mistrust, particularly climate skepticism. Will this have an impact in your field?

Distrust in expert knowledge is indeed troubling, and the field of longevity and aging is affected like every other. The essential quality of academic research is integrity, and this is fundamental to everything we do as scientists. I am privileged to work among the community of scientists for whom integrity is strongly respected as the key guiding principle. Only by holding true to the fundamental principles of integrity, and sharing openly the nature of our research, can we hope to overcome the current mistrust of expert knowledge.

“The AXA Research Fund is addressing this challenge by promoting high quality scientific communication with key opinion formers and the general public.”

Thomas Kirkwood
President of the AXA Research Fund’s Scientific Board

The AXA Research Fund is addressing this challenge by promoting high quality scientific communication with key opinion formers and the general public. By establishing itself as a beacon of good practice in promoting engagement and corporate social responsibility, the AXA Research Fund can be a bastion against ill-informed mistrust.
About
the AXA Research Fund
The AXA Research Fund: Supporting scientific research to build a better future

Since our inception in 2008, our mission has been to support outstanding researchers committed to contributing to some of the most important issues facing our planet. Going beyond AXA’s mission as an insurer to cover and manage risks, through a one-of-a-kind private sector initiative, the AXA Research Fund aims at funding top-tier research in the areas of environment, health, socio-economics and new technology. Through our support, we seek to contribute to solutions that help better anticipate, mitigate and reduce the impact of risks in these fields, potentially transforming risk into opportunity.

We also have the objective of ensuring that science plays its role in contributing to public debate. The AXA Research Fund provides our partner researchers with the tools and networks to help disseminate their findings to a larger audience so as to enlighten decision making for a better future.

“Through our support, we seek to contribute to solutions that help better anticipate, mitigate and reduce the impact of risks.”

Marie Bogataj
Head of the AXA Research Fund
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Abdul Barakat
Ecole Polytechnique | AXA Chair for Cardiovascular Cellular Engineering, since 2010

Prof. Abdul Barakat is the Director of Research at the French National Center for Scientific Research (CNRS), AXA Professor of Mechanics and Biology and holder of the AXA Chair for Cardiovascular Cellular Engineering at Ecole Polytechnique. His research focuses on combining engineering concepts and mechanical factors with an understanding of cardiovascular disease, especially in relation to aging.

Luisa De Cola
University of Strasbourg | AXA Chair in Supramolecular Chemistry, since 2009

Prof. Luisa De Cola heads the AXA-University of Strasbourg Supramolecular Chemistry Chair. As the co-founder of SiBreaX, a nanoparticle-based solution company, and as a scientist, she designs materials that can be used to understand and ultimately cure age-related critical diseases.

Evrim Didem Günes
Koc University | AXA Award in 2016

As Associate Professor of Operations Management at the College of Business Administration and Economics in Koc University, Istanbul, Evrim Didem Günes is specialized in preventive care, primary care and chronic care management. She has received support from AXA to focus on chronic care management. Through her work she aims to understand and model patient behavior in the context of chronic disease.

Carol Jagger
Newcastle University | AXA Chair on Longevity and Healthy Active Life

As the holder of the AXA Chair on Longevity and Healthy Active Life at Newcastle University, Prof. Carol Jagger studies multiple factors that contribute to “healthy aging”, including attitudes towards life and socioeconomic factors. Her work crosses the interface between demography and epidemiology, focusing on future trends in aging.

Peter Joshi
University of Edinburgh | AXA Fellowship in 2017

Dr Peter Joshi is Chancellor’s Fellow in the Usher Institute for Population Health Sciences and Informatics at the University of Edinburgh, UK. He investigates how longevity is genetically determined through the study of genomic and human lifespan. In 2017 he was awarded an AXA research fellowship to support his research in the understanding of human aging.

Maria Blasco
Spanish National Cancer Research Center (CNIO) | Former AXA Research Fund Scientific Board Member

Dr Maria A. Blasco is a renowned molecular biologist devoted to the study of telomeres and telomerase and their role in cancer and longevity. Since 2011, she has also been the Director of the Spanish National Cancer Research center (CNIO) in Madrid.
Milena Pavlova
Maastricht University | AXA Award in 2016
As a Health economist at the Maastricht University in the Netherlands, Dr Milena Pavlova explores good practices that can help European societies make informed choices about long-term care systems. Through her work, Dr Pavlova intends to provide governments and other stakeholders with the information they need on healthcare systems.

Mickael Tanter
ESPCI Paris | INSERM | AXA Chair in Physics for Medicine and Biology, since 2017
Prof. Mickael Tanter is Research Professor at French Institute of Health and Medical Research (INSERM) and director of the Physics for Medicine Paris Laboratory of the Industrial Physics and Chemistry Higher Educational Institution (ESPCI Paris). He holds the AXA Chair on Physics for Medicine and Biology. His work focuses on biomedical ultrasound, which he develops to foster new therapeutic approaches and diagnosis methods, especially for cancer, cardiovascular diseases and neurological disorders.

Pierre Vanderhaeghen
Université Libre de Bruxelles | AXA Chair in Neurosciences and Longevity, since 2012
Holder of the AXA Chair in Neurosciences and Longevity at the Université Libre de Bruxelles, Prof. Pierre Vanderhaeghen is specialized in developmental and stem cell neurobiology. He leads a research group that studies the mechanisms of development the cerebral cortex and their links with human brain evolution and disease. He aims to use this knowledge to understand better human-specific components of brain diseases and to design innovative approaches towards brain repair.