Health economics: innovation and costs

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Toulouse School of Economics

# **Our health** is our wealth



TSE continues in excellent health at the start of 2022. Following the success of our research centers for Digital economics, Energy and Climate, and Sustainable Finance, we are delighted to have recently opened the TSE Health Economics Center led by Pierre Dubois. Two other new centers, focusing on Competition Policy and Regulation and on Infrastructure and Network, are now also up and running.

The ravages of the Covid-19 crisis have been at the forefront of everyone's minds over the past two years, but we should not forget that our societies must confront many other pressing health challenges. In this magazine, you can learn about research by the TSE community on health issues such as the impact of social norms on intergenerational diseases, our willingness to pay for air quality, how mathematical models can help fight cancer (a research project in partnership with the University Toulouse 3 Paul Sabatier and the IUCT Oncopole), the impact of scientific evidence on doctors and their prescriptions, as well as how poor countries can get lower prices for pharmaceutical drugs.

You can also read exclusive interviews with bioMérieux chairman and CEO Alexandre Mérieux on the challenges facing the diagnostics industry as well as with Leem general director Philippe Lamoureux on imminent technological revolutions and how France and Europe should view the pandemic as a warning against underinvestment in health research and innovation.

This issue also celebrates the 10th anniversary of our educational programs. Since its inception, TSE has strived to offer France and the world a research and education center in economics to rival the very best universities. Our successes would not have been possible without our strong scientific community and its shared values of ambitious scientific development, a world-class independent governance that is unique in the French university system, and the unrelenting support of our partners. We are grateful for such invaluable contributions and proud of what we have accomplished. But ambition is at the core of the TSE project and we must always aim higher.

I wish you a great read, good health, and every success in 2022.

Christian Gollier. **TSF** Director

# News

# Health economics

# Campus

**Biannual magazine** of the Toulouse School of Economics

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## News

#### Marion Desquilbet to lead expert group on research independence

TSE researcher Marion Desquilbet has been appointed head of a working group of the National Commission on Ethics and Alerts in Public Health and the Environment (cnDAspe). The group will formulate recommendations to promote the impartiality and integrity of scientific and technical expertise on health and the environment.

#### Franco-German roundtable on climate

On October 18, TSE Director Christian Gollier discussed the Fit-for-55 plan — which aims to reduce EU emissions by at least 55% by 2030 — with François Cabaret, Head of Global Market Forecast at Airbus, and Ottmar Edenhofer, Director and Chief Economist of the Potsdam Institute for Climate Impact Research.

#### TSE opens its doors to future students

Come and visit TSE on February 12 from 9:30am to 5pm and discover everything there is to know about our programs, applications and job prospects.

#### Sébastien Gadat on fighting cancer with mathematics

As part of 'Celebrate Science' week, the TSE-UT1C professor held a conference on his joint work with the Toulouse Cancer Institute – Oncopole on the use of mathematical models to help health professionals target cancer cells. More on page 14.

#### In praise of Jean-Jacques Laffont

Laurent Linnemer wrote a beautiful article about Jean-Jacques Laffont, honoring his work and legacy, which has been published in *Annals of Economics and Statistics.* 

#### TSE researchers discuss the rise of AI

At a special event in December, Jean-François Bonnefon (TSE-IAST-CNRS), Dana Pizarro (TSE-UT1C) and César Hidalgo (TSE-ANITI) exchanged ideas with the audience on the future impact of AI on our societies.

#### TSE joins the fight on antibiotic resistance

A new multidisciplinary consortium, ARPEGE, brings together Antabio, bioMérieux, Hospices Civils de Lyon, and TSE to find solutions to the growth of antibiotic resistance. ARPEGE has received close to €7 million in funding from the French government.

## Prizes & Awards



#### TSE building wins international recognition

The TSE building achieved second place at the CEMEX Building Award 2021 held on November 11 in Mexico. The award aims to promote innovative construction projects with a high sense of sustainability and social well-being. Congratulations to architects Yvonne Farrell and Shelley McNamara.

#### Mathias Reynaert receives Green Finance prize

Banque de France's annual Green Finance award highlights research on making financial flows compatible with low greenhouse gas emissions and sustainable development. Mathias has conducted extensive research on collusion and emissions in the automotive industry.

#### **TSE Director wins two EGRIE awards**

Christian Gollier scooped two EGRIE (European Group of Risk & Insurance Economists) awards this year. He won the 2021 SCOR/TSE-P Award for the best paper published in The *Geneva Risk and Insurance Review* thanks to his paper "Pandemic economics: Optimal dynamic confinement under uncertainty and learning." He also picked up the Harris Schlesinger Prize for Research Excellence for his paper: "On the underestimation of the precautionary effect in discounting".

## In Memoriam

#### Yves Aragon - 1944-2021

Yves joined University Toulouse 1 Capitole in 1970 and was director of the specialized graduate diploma (DESS) in statistics and econometrics from 1992 to 2005. Yves was interested in many areas of statistics, including surveys, nonparametric and spatial statistics, and time series. He co-authored papers with many colleagues, including Jean-Jacques Laffont. Dynamic, benevolent, competent, and always in a good mood, Yves was an exceptional colleague and teacher. We will keep him in our hearts.

#### Michel Moreaux - 1941-2021

Michel was a Professor Emeritus at University Toulouse 1 Capitole – TSE. At nearly 80 years old, he continued his research on renewable resources and environmental economics. He played a major role with Jean–Jacques Laffont in laying the foundations for the TSE project, dedicating his energy and enthusiasm to the development of Toulouse as a vibrant hub for world-class research in economics. He was a brilliant, insatiable economist who will be missed by the scientific community and his colleagues.



**Newcomers** 

# Welcome to our promising new colleagues

TSE is proud to welcome its new faculty members for the academic year 2021-22.

# Professor



Koen Jochmans **Econometrics** and empirical economics

> Koen Jochmans is a professor

of Econometrics who joined TSE from the University of Cambridge. specializing in issues related to panel data and network data. His research has received the support of the European Research Council through a Starting Grant. He currently serves as Associate Editor for Journal of Business & Economic Statistics, Econometrics Journal and Journal of Applied Econometrics, having previously supported Journal of Econometrics in the same capacity.

## Assistant Professors



Anouch Missirian Environmental **Economics** 

Anouch Missirian is an environmental

economist who studies agriculture and land use, and when ecological and economic processes collide. Anouch received her PhD from Columbia University and worked as a postdoctoral fellow for a year at UC Santa Barbara before joining TSE. She studied Biology and Ecology at the École normale supérieure in Paris and received a masters degree in Environmental, Energy and Resource Economics from AgroParisTech.





Sabrine Bair **MINES** ParisTech Finance **FIT IN Initiative** 

Sabrine is a Post-Doc who has studied the

impact of the use of information and communication technologies on farmers in Africa. She completed her PhD at the École des Mines ParisTech.



Ozvilmaz UC. Santa Barbara Finance **FIT IN Initiative** 

Hakan Özyilmaz completed his

PhD at the University of California. Santa Barbara. His research is in household finance, behavioral economics and experimental economics. He designs laboratory experiments to study boundedly rational behavior with the goal of informing policy and economic



Antonio (Tonv) Silveti-Falls is a mathematician studying nonsmooth optimization and its applications to machine learning and, in particular, to the theory of deep learning. He received his PhD in Mathematics from Université de Caen Normandie.

# Visiting professors





Deryugina Gies College of Business University of Illinois Industrial Organization





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**Cyrille Combettes** received a PhD in Machine Learning from Georgia Tech, where he worked on developing efficient algorithms for constrained optimization. Prior to that, he received a MSc. in Applied Mathematics from École Centrale Paris and a masters in Business Analytics from MIT.

#### Antonio Silveti-Falls

Université de Caen Normandie MADS

David Martimort EHESS Theoretical **Economics** 

#### Julian Reif

Gies College of Business -University of Illinois Industrial Organization



PhD **Students** 

Lin Fang

**Guillem Foucault** Llopart

**Javier Gonzalez** Morin

**Pascal Heid** 

Pablo Mileni Munari

**Emil Tobias Mortensen** 

**Juan Pal** 

Valentina Reig

Giovanni Rizzi

Xin Zhang

Yanyan Zhang

Hanlin Zhao

# Health economics: innovation and costs

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n Good

Health

# Health and the common good

While medical practitioners, vaccine developers and epidemiologists have naturally been the first port of call in the current crisis, economic expertise will be essential to manage the costs, incentivize firms, and help governments to finance medical research as efficiently as possible. The pandemic has also raised concerns about the sustainability of our health care systems and supply chains. Here again, economists have a crucial role in finding ways to reduce inefficiencies in a complex regulatory environment where private and public providers interact with different intermediaries, regulators, and public or private insurers.

With the opening of the new Health Center in 2021, TSE is radically expanding its footprint in this area. For more than a decade, TSE researchers have been focused on health-related topics including medical innovation, ageing, pharmaceutical regulation, food and nutrition. Combining this expertise with private and public partners' financial support and knowledge, the Center aims to encourage collaborations involving economists and a wide range of disciplines such as epidemiology, medicine, psychology, and biology. Their research will help public and private organizations to address health issues and improve quality and access to care around the world.

Today, more than 20 TSE-IAST researchers have an interest in healthrelated research. Led respectively by myself, Philippe De Donder, Jean-Marie Lozachmeur, Céline Bonnet, and Nour Meddahi, the Center will focus on five main research areas: Pharmaceutical industry and regulation; Innovation in health; Public healthcare, long-term care and ageing; Food and healthy behavior; and Economics of pandemics.

As evidenced by the research highlighted in this issue, the breadth and scale of modern health challenges is intimidatingly large. But TSE health economists are excited by the opportunity to apply their skills and learning in service of the common good. And we have been delighted with the immediate engagement of our partners and the international research community in the Center's activities, including our first scientific workshops on 'The Economics of Antibiotics' and 'The Future Of Food Supply Chains'.

We look forward to welcoming you at future events and wish you an enjoyable read.

**Pierre Dubois Director**. TSE Health Center

**Pierre Dubois** 

The Covid-19 crisis has focused attention on the immediate difficulties posed by the epidemic. But many other complex health challenges, often interconnected, have been burning in the background for some time. Among these, modern health care systems must address a host of problems stemming from new phenomena that include digitalization, obesity and other epidemics, pollution, antibiotic resistance, and demographic change, as well as opportunities coming from innovative

'Economists have a crucial role in finding ways to reduce inefficiencies in a complex regulatory environment where private and public providers interact with different intermediaries



'The future of health care holds many promises. Yet, our societies will reap the benefits from digital health, artificial intelligence and genetics only if they achieve the right balance. This will require a balance between innovative but expensive treatments and affordability of healthcare, and also between the innovation imperative and fair access to drugs and health care across social classes, regions and countries.

It is up to health specialists within and outside academia to help invent intelligent regulation. TSE is well placed to contribute to this exciting endeavor, thanks to its tradition of excellence in industrial organization, innovation economics, regulation and public finance. Its well-established culture of interaction with industry experts and public policymakers guarantees that the rigor of its research is matched by relevance for policy debates. Our sister institution, the multi-disciplinary Institute for Advanced Study in Toulouse, brings the broader social science angle and sheds a new and relevant light on societal challenges associated with health trade-offs.

I am looking forward to being part of this intellectual adventure!'

#### Jean Tirole

Honorary chair of TSE and IAST, 2014 Nobel laureate

# Can social norms give us healthier children?

Catarina Goulão Researcher, INRAE - TSE Increasing life expectancy has encouraged the belief that we can expect to be at least as healthy as our parents. In a new working paper written with Agustín Pérez-Barahona (THEMA, CY Cergy Paris Université & Ecole Polytechnique), TSE's Catarina Goulão examines the interplay between this widespread social norm and the fallout from our unhealthy lifestyles. Her analysis suggests policymakers might take advantage of such a dynamic to protect future generations.

The deadliest epidemic sweeping the globe is not Covid-19. Today, non-communicable chronic diseases (NCDs) – including cardiovascular and respiratory diseases, cancers, and diabetes - account for more than 70% of worldwide deaths. However. the WHO estimates that 80% of premature deaths from NCDs are preventable. Although they are not biologically infectious, NCDs can spread due to the social transmission of unhealthy behavior. Recent research on epigenetics suggests that the NCD risk factors - such as junk food, smoking, and physical inactivity - may affect the health of subsequent generations.

In a 2014 study published in Journal of Public Economic Theory, Catarina and Agustín propose an economic model for understanding how such epidemics spread across generations. In their theoretical framework, adults' consumption choices have an impact on their health capital in old age. which is in part inherited by their offspring and affects their offspring's probability of developing an NCD. As they do not take into account the full cost of their behavior on the next generation, parents choose lower health conditions and higher unhealthy activities than what would be socially optimal.

Despite major past and present health threats, life expectancy has been increasing steadily for the past two centuries. Individuals are also living in better health for longer. In their latest working paper. Catarina and Agustín build on their 2014 model to examine how social norms might affect the intergenerational dynamics of an NCD epidemic. In this context, offspring compare their own health capital with that of their parents. Crucially, they are influenced by a social norm that leads them to expect to be at least as healthy as the previous generation. Although it imposes a cost on the individual, the strength of this inherited norm encourages households to make healthier choices. The benefits cascade down generations.

'Social norms induce households to invest more in health, leading to higher levels of health capital and less consumption'

By enhancing health capital and reducing the probability of contracting an NCD, the presence of the social norm can counterbalance the negative effects of parents' unhealthy choices. If further adjustments are required, Catarina's research suggests that taxes on unhealthy activities can be used, forcing households to take into account the impact of their individual choices on future generations' welfare. 'Social norms induce households to invest more in health, leading to higher levels of health capital and less consumption,' she writes.

'Individual choices then get closer to the optimal allocation, and it only requires a lower level of corrective tax to make individuals internalize the intergenerational externality.' The resulting tax revenue can be used to subsidize healthy activities.

Catarina's latest working paper underlines the importance of considering the interplay between 'sin' taxes and health-related social norms. The potential for social norms to act as a lever to enhance the effectiveness of fiscal policies is particularly important, given that sin taxes tend to be regressive. As Catarina and her TSE colleague

# 80.7

The average life expectancy in the OECD was 80.7 years in 2017, 10 more than in 1970. Individuals are also living in better

health for longer: in 2019, the average person was expected to live five more healthy years than in 2000.

Helmuth Crémer observe in their 2016 paper ('Earmarking and the political support of fat taxes', *Journal of Health Economics*), unhealthy goods such as junk food and cigarettes tend to be disproportionally consumed by lowerincome individuals.

Social norms can help an economy to escape a health capital trap, Catarina's model suggests. But strong social norms may not be necessary if health care and medical technology is sufficiently advanced, reducing the level of health capital below which individuals have a high probability of developing an NCD.

'This effect is not exclusive to NCDs,' she notes. 'In 2020, and in the absence of medical technology to deal with the Covid-19 virus, nations worldwide were forced to impose an extreme level of the 'social norm' and impose lockdown to minimize social interactions."

Though a careful analysis is still required, countries in which screening was available and infected individuals were identified have not (to the best of our knowledge) imposed lockdowns, even though strict rules of social interaction were imposed, such as the use of masks or minimum physical distancing.'

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How can mathematics improve

our understanding of cancer

patients? TSE math professor

Sébastien Gadat joined forces

with a Toulouse-based team of

biologists, medical researchers

and computer scientists to

immune system's defenses.

investigate ways to boost our

and help doctors to treat

#### How does mathematics research interact with the real world?

In 2021, we can collect data on just about everything, but ultimately the objective is to understand the phenomenon observed, to decide and to predict. The contribution of mathematics is to analyze the evolution of this phenomenon, to simplify it as much as possible, and eventually to simulate it using computer tools.

Mathematics has an extremely diverse set of tools for dealing with real-world problems. It's not just analysis, geometry, and algebra: There are a whole bunch of disciplinary fields within each of these areas. For

'This work has been inspired by mathematical models that describe how ant colonies quickly converge towards a place of interest once it has been found

instance, differential equations allow us to describe the evolution of certain quantities over time; and statistical probabilities allow us to understand chance and describe random processes.

#### In the eyes of a mathematician, what does a patient's struggle with cancer look like?

In essence, the problem is extremely simple. There are large clusters of cancerous cells that grow and are hidden all over the body. On the other side, the immune system has small cytotoxic killer cells that can attack and destroy certain cancer cells. Immunotherapy tries to boost these immune mechanisms. Such therapies are less traumatic than surgery or chemotherapy, since it is the body itself that interacts with its cancer.

All cells divide - even tumor cells. unfortunately - and this division occurs at random times. We can describe this division process using exponential laws, which tell us the probability that a division will occur after a given time, say 10 minutes. The mathematician also has to understand the geometry of the growth of a tumor cluster, which is roughly spherical with an inert core and an outer layer that can feed and grow.

In particular, the mathematician needs to understand the killer cells' random movement. These trajectories have mathematical properties that are radically different in 3D than in 2D, with many more possibilities of movement. Once a killer cell has encountered the tumor. its ability to fight the tumor is also random. How many tumor cells can a killer cell destroy? What is the probability of killing one, or multiple cancer cells?

#### How does the mathematician then proceed?

To understand the evolution of this simple system - killer cells against tumors - we study the biologist's data and develop a simple model that is as close as possible to the reality, isolating the fundamental behaviors. We then lean on mathematical tools that can be used in many fields - weather, medicine, economics, physics, traffic studies -

and obviously artificial intelligence. At the end of the mathematical study, we had a model of the tumor's growth, a model of the movement of each of the killer cells in the body, and a model of the interaction between the killer cell and the tumor. There was a lot of dialogue between with the biologists to estimate all the parameters; and with the computer scientists to obtain convincing simulations. With methods that exploit the law of large numbers, we could then calculate the probabilities of therapeutic success.

#### What were your key results?

Using a statistical test, we discovered that there were actually two subpopulations of killer cells, some that killed less than others. This finding was later confirmed by the biologists. We were even able to identify the proportions of how many were in each category.

Mathematically, we found that what really helps the success of immunotherapy is to increase the number of encounters between killer cells and the tumor. This is much more important than boosting the immune

## Immunotherapy



Health

'Mathematically, we found that what really helps the success of immunotherapy is to increase the number of encounters between killer cells and the tumor. This is much more important than boosting the immune system itself '

> system itself. Highly mobile killer cells are more effective than addressive killer cells with a high kill rate.

#### What future research directions were suggested?

At the end of the study, some new questions appeared. Once a killer cell has found the tumor, if it were able to direct the other killer cells. wouldn't that improve the treatment? Chemotaxis allows cells to leave chemical traces for other cells, and biologists are trying to use this process to improve immunotherapies.

This work has been inspired by mathematical models that describe how ant colonies quickly converge towards a place of interest once it has been found. Once we know where there is good cheese, we are attracted by the smell!

#### **•** FIND OUT MORE

Sébastien's presentation 'Mathématiques contre le cancer' at the recent Fête de la Science in Toulouse is available to view (in French) on Youtube. For more of his research on applied statistics and probability, see www.tse-fr.eu

For decades, bioMérieux has been a world leader in the field of in vitro diagnostics. The French company is dedicated to providing diagnostic solutions to improve healthcare worldwide.

Interview

TSE and bioMérieux have joined forces through the TSE Health Center, launched last year, which will aim at developing and using new tools to address guestions of regulation and organization of healthcare and innovation. The two institutions also recently announced their participation in the ARPEGE project, whose objective is to fight antimicrobial resistance. To discuss these partnerships, as well as the pandemic and its impact on the healthcare industry, Alexandre Mérieux, chairman and CEO at bioMérieux, answered the questions of TSE Mag.

#### What are bioMérieux's current challenges?

Alexandre Mérieux: The COVID-19 pandemic has highlighted the essential role of diagnostics for healthcare systems as well as the value of diagnostics in implementing targeted health policies, optimized patient management, and epidemiological surveillance. This epidemic has also emphasized the need to rapidly develop both fast and reliable tests and decision-support tools using scientific and clinical data. In this context, innovation is the most important challenge in the field of diagnostics in order to respond to the major public health issues that we are facing, such as the fight against Antimicrobial Resistance (AMR).

'Diagnostics remain a key tool to fight infectious diseases'

Alexandre Mérieux Chairman & CEO, bioMérieux

### 'Covid-19 has accelerated the decentralization of tests to get as close as possible to the patient'

#### What impact has the COVID-19 crisis had on your group?

The pandemic mobilized the healthcare community and fostered remarkable commitment from our employees, who worked tirelessly in an exemplary spirit of collaboration to respond to the medical emergency. In just a few months, we developed four complementary molecular biology tests and two serological tests. I would say that we felt useful and engaged, and we were able to demonstrate our agility. Medical diagnostics have shown their importance across the continuum of care. The group's strong performance in this extraordinary context have enabled us to help those in need by bolstering our philanthropic activity and creating an endowment fund.

Interview



#### How will testing for COVID-19 evolve?

The situation is still difficult in many countries and diagnostics remains a key element in the fight against the pandemic. In the long term, COVID-19 will continue to be monitored and will remain among the viruses detected by our respiratory panels. The continuum of care components - prevention, diagnostics, treatment - will be crucial. Diagnostics will be useful to the vaccination strategy in monitoring the immunity of vaccinated individuals over time, and in guiding booster vaccination strategies in the longer and shorter term.

In addition, mass vaccination has not yet been made available to all populations around the world. In some countries, diagnostics is still the main tool to fight the pandemic. Our role as a global player in in vitro diagnostics is to promote access to these diagnostic innovations in lowand middle-income countries.

We are also constantly monitoring the emergence and evolution of new variants. In 2021, we launched a tool to assist in the sequencing analysis of positive patient samples, further preparing ourselves to adapt our tests so that they continue to meet the needs of clinicians and biologists.

'We are moving towards personalized medicine where the role of diagnostics will be central, both for rapidly identifying pathogens and characterizing the host's response to infection

#### What is your analysis of current trends in the diagnostics sector?

The pandemic has accelerated one of the major trends for in vitro diagnostics, which is the decentralization of tests to get as close as possible to the patient: into local healthcare professionals (clinicians, pharmacists, nurses, etc.), at public places, or even directly at home.

Being as close as possible to patients also means taking their needs into account to develop with them our solutions for the future. We are therefore forging increasingly close relationships with patient associations.

#### What future innovations do you predict for your industry?

Healthcare data will play an increasingly central role in the coming years. As far as diagnostics is concerned, the data are more and more numerous and complex. They are also a source of additional information to move towards an "augmented" diagnosis, thereby improving patient care.

Technologies are evolving towards greater speed, automation, and integration. This will allow laboratory personnel to better focus on highvalue activities. The digitalization of patient health data will promote fluidity in the management of the patient's care.

The role of diagnostics will increasingly go beyond the laboratory stricto sensu, bringing it closer to clinicians and patients. In the field of infectious diseases, we are moving towards personalized medicine where the role of diagnostics will be central, both for rapidly identifying pathogens and characterizing the host's response to infection.

## 'We are constantly monitoring the emergence and evolution of new variants'

In addition, we will have to eradicate diseases that are still far too prevalent - such as malaria and tuberculosis - for which early access to diagnostics and treatments is key.

#### What do you expect from this new partnership with TSE?

TSE has launched, with bioMérieux's support, a research initiative on health economics and diagnostic technologies. Our joint ambition is to develop innovative thinking on health economics issues and to make the results publicly available. With an initial duration of three years, the initiative will focus on Antimicrobial

## 'Our joint ambition with TSE is to develop innovative thinking on health economics issues and to make the results publicly available<sup>r</sup>

Resistance and the economic evaluation of diagnostic innovation.

#### What advice would you give to a TSE student?

You have the chance to be part of an internationally renowned school with excellent research laboratories. Make the most of it. Be curious. Be open to various fields of expertise and approaches. Work in collaboration with others to find your path, your project, while enjoying yourself and serving the common good.

> **•** FIND OUT MORE www.biomerieux.com www.tse-fr.eu/health

'Since the real-time air quality index became available in 2013, many Chinese citizens have adopted self-protection measures such as particulate-filtering masks and household air-purifiers

#### Henrik Andersson Associate Professor of **Economics** TSE - UT1C

# How much are we willing to pay for clean air?

With a global death toll of more than 7 million people every year, air pollution is almost as lethal as smoking or junk food. But saving lives will not be without costs. Written with Yana Jin (William & Mary) and Shiqiu Zhang (Peking University), a new study by TSE's Henrik Andersson aims to guide policymakers in their allocation of resources by measuring the preferences of individuals in the fast-changing, highly polluted streets of Beijing.

#### Why is China a key battleground in the fight against air pollution?

Most environmentally caused illnesses and fatalities occur in the megacities of highly populous emerging economies, of which Beijing is a prominent example. In recent years, China has implemented large-scale, often costly policies to control air pollution. However, regulatory impact analysis has seldom been used to evaluate environmental policies in China and other developing countries. Such an approach is urgently needed to ensure efficient resource allocation. Due to its size, and as an example to others, China's policies can also have a global impact, not least by affecting the prospects for climate change mitigation.

#### How can we measure the impact of public policy on our health?

Benefit-cost analysis needs a common metric, and it's usually money. No easily available prices exist for health benefits, but they can be monetized by estimating the preferences of the affected population. The appropriate measure is an individual's willingness to pay (WTP), elicited using individuals' choices in markets or survey answers to hypothetical scenarios. The monetary value for the prevention of one premature death is usually referred to as the value of a statistical life (VSL), whereas the equivalent for a non-fatal health outcome can be referred to as the value of a statistical illness (VSI).

#### What were the objectives of your study?

One of our main objectives was to elicit individual preferences about reduction of health risks from air pollution in Beijing. The majority of studies on monetizing health preferences have been conducted in developed countries, where environmental problems are often less severe. In addition, existing empirical findings are unlikely to accurately reflect the preferences of individuals in China today. Pollution and income levels in China have changed due to rapid development, and public awareness of pollution risks has increased.

A second objective was to examine whether preferences depend on the type of illness (stroke, heart, or lung disease). This is of high research and policy relevance, because if preferences differ it would suggest that VSL and VSI should be differentiated based on illness type.

Our third objective was to study the impact of self-protection on public attitudes. Since the real-time air quality index became available in 2013, many Chinese citizens have adopted self-protection measures such as particulate-filtering masks and household air-purifiers. We estimate this latent self-protection and examine its effect on individual preferences for public programs.

'As people become wealthier and more aware of pollution, we may expect increased selfprotection and demand for public health policies'

#### What is your message to policymakers?

Our empirical analysis uses choice experiments to examine WTP for public measures to improve Beijing's air quality. As expected, respondents prefer programs that have an effect sooner rather than later, prevent more illnesses and/or deaths, and cost them less. More importantly, we find robust evidence that preferences do not vary by illness type. This suggests Beijing's policymakers should use the same values (VSL and VSI) for different illnesses.

We also find that income, education, gender and other factors related to risk vulnerability are good predictors of self-protection, and that respondents who engage more in self-protection have stronger preferences for public intervention. As people become wealthier and more aware of pollution, we may therefore expect increased self-protection and demand for public health policies. Our results suggest a higher willingness to pay (\$1.58 million for VSL; \$0.23 million for VSI) than earlier estimates in China and other

# 7.2 million

An estimated 7.2 million premature deaths in 2017 were due to environmental factors. **3.4 million** of which were due to fine particulate (PM2.5) and ozone pollution. 92% of all pollution-related mortalities occur in low- and middleincome countries

developing countries, but still far less than those for developed countries. This implies that VSL and VSI are likely to increase rapidly in societies with strong economic growth and high pollution, strengthening the role of pollution control and public health policies.

Our approach and estimates can support regulatory impact analysis beyond China, in both emerging and developed countries. Understanding whether preferences depend on illness type, and how self-protection influences preferences for public intervention, will be essential to protect all citizens from air pollution.

#### **•** FIND OUT MORE

'Do preferences to reduce health risks related to air pollution depend on illness type?' was recently published in Journal of Environmental **Economics and Management.** For more research by Henrik on the valuation of health risks, see www.tse-fr.eu

Health

How can the poor afford medicine?

Yassine Lefouili Director of TSE Partnership Professor of economics at TSE - UT1C Patients in the developing world often face soaring prices for essential medicines, even in the absence of patent protection. Yassine Lefouili discusses his latest research, coauthored with his TSE colleagues Pierre Dubois and Stéphane Straub, which suggests that centralized purchasing by the public sector can significantly lower pharmaceutical prices for those in need.

# How much do prices of medical drugs vary around the world?

Across low and middle income countries, the prices of essential medicines, such as cancer treatments, HIV antiretrovirals, and antibiotics, display substantial variations, with local prices sometimes many times higher than the lowest international reference level for generic equivalents. For example, among a group of nine common molecules purchased by the countries included in our analysis, the average price across countries varies by a factor of 16. Even within countries, the data show variations of up to 300% across procurement channels. High prices deplete public health budgets and generate shortfalls in access, especially for the poor.

**Drug prices** 

# How can pharmaceuticals be made more affordable?

Pooled procurement – whereby several buyers, either institutions in a single country or health agencies across countries, consolidate their purchases – is a key mechanism that has been used to reduce prices. However, economic research on the issue of affordable access to drugs has mostly concentrated on patents. Such studies analyze the tradeoff between the potential costs of restrictive patent policies that result in monopolistic prices, excluding many poor and uninsured patients, and the potential benefits of faster diffusion of new drugs in markets with stronger patent protection.

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But patents cannot explain the large markups being charged, given that most drugs purchased in developing countries are off-patent branded generics. Our research suggests that other factors – such as suppliers' market power and buyers' size, and the type of procurement mechanism – play a crucial role in determining local prices, especially for off-patent drugs.

# How does your paper evaluate the benefits of pooled procurement?

We first develop a model in which several firms offer differentiated products through a centralized or decentralized procurement process. We assume that public buyers gain bargaining power when they coordinate. Under fairly general assumptions, we show that centralized procurement leads to lower prices.

## 'Consistent with our model's predictions, our main finding is that centralized procurement allows public buyers to obtain lower prices'

We then analyze exhaustive data – from 2015 to 2017 – for seven developing countries: India, the Philippines, Senegal, Serbia, South Africa, Tunisia, and Zambia. The external validity of many existing studies is undermined by their focus on limited sets of drugs, mostly targeting high-profile infectious diseases such as HIV/AIDS, TB and malaria. In contrast, our paper considers sales quantities and expenditures for a much larger variety of drugs – including antibiotics, antihypertensives, and contraceptives.

Our empirical strategy exploits the rich variation in the way drugs are procured in our sample. For the Philippines, Serbia, and South Africa, the channels of drug procurement even vary within specific therapeutic areas; for example, specific HIV antiretrovirals are purchased centrally, while other purchases are decentralized. We also observe different purchase mechanisms being used simultaneously within molecules. In a final step, we estimate the role of suppliers' concentration, which varies substantially from single sellers to highly competitive environments.

#### What are your key findings?

Consistent with our model's predictions, our main finding is that centralized procurement allows

public buyers to obtain lower prices. However, we also find that the reduction is smaller when suppliers have more market power. Indeed, the effect vanishes when the public sector faces a high concentration of suppliers for a given product.

# What are some of the implications of your research?

Providing better and cheaper access to drugs in developing countries will require careful analysis of the market structure for drug procurement. We suggest that the price reductions in our results may be driven by two complementary mechanisms. First. demand-side concentration may enhance public buyers' bargaining power, allowing them to extract lower prices. In addition, centralized buyers are likely to purchase larger auantities, securing price discounts on larger orders. These two channels are hard to disentangle, as they occur simultaneously. Further research is needed to identify the nature of market interactions between buyers and sellers, and to separate their effect from that of transaction size.

Our results also have important policy implications regarding supply-side concentration. Simple, reducedform estimations of the impact of increasing supply-side competition show large potential increases in the quantity of drugs that public sectors could purchase for a given budget.

> FIND OUT MORE 'Pooled procurement of drugs in low and middle income countries' was recently published in European Economic Review. For more research by Yassine, Pierre and Stéphane, see www.tse-fr.eu

Health



Philippe Lamoureux, Leem general director

#### How is the French pharmaceutical industry faring in the face of the pandemic?

Pharmaceutical companies have demonstrated their resilience and potential throughout the pandemic. I salute the commitment of all the employees in our sector, who have worked tirelessly, under all circumstances, to ensure that treatments are available to patients. Our industry has thus distinguished itself as one of the five strategic sectors for recovery from the crisis in France. This is through the stability of recruitments in the country, the maintenance of the level of exports and our strong contribution to France's trade balance surplus, and the increase in investments (€9 billion in 2020, i.e., +15%), in research and development and in the industrial fabric. Pharmaceutical companies are looking to the future and offer hopeful prospects.

However, the health crisis has highlighted France's decline in place in Europe in several areas: pressure on mature healthcare products, which has led many France.

The solution to catch up is multifactorial. It is essential to strengthen industrial incentives for investment, to simplify market access conditions, to strengthen cooperation between public and private research, and to provide drug policy through a modern, simple, agile and better coordinated administrative organization. All the parameters of the healthcare system must be considered together. This is how France will regain its attractiveness and competitiveness in an increasingly competitive international environment.

'The technological revolutions about to take place hold great promise' Leem (Les Entreprises du médicament) is the professional organization of pharmaceutical companies operating in France. Its general director, Philippe Lamoureux, argues that the Covid-19 crisis is a warning to France and Europe of the short-sightedness of failing to invest and attract investors in health research and innovation.

research and innovation. In 10 years, France has fallen from first to fourth drug production, R&D, clinical trials, taxation, etc. This is due in particular to excessive regulation and economic companies to relocate – the tax and regulatory conditions no longer allow them to manufacture their drugs in

Finally, there is another issue that came to the attention of public authorities during the Covid crisis: 80% of the raw materials for medicines consumed in Europe come from China and India. The answer to this issue of pharmaceutical sovereignty can only be found on a continental scale, on which we must implement economic models that allow us to assume higher labor costs and environmental standards. But we must guard against the temptation to withdraw: the "global" dimension of our industry is the primary condition for its innovative dynamism.

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Relocating without deglobalizing: that is our objective.

The measures announced in 2021 at the CSIS "Innovation Santé 2030" and ratified in the 2022 LFSS social security financing laws, are in line with this objective. The major investments in academic and basic research, the boost to clinical research and industrial policy, and the radical transformation of market access mechanisms are all very good news. It is essential to extend these reforms and to transform our country's assets into competitive advantages.

'One of the challenges for our sector is to know how to deal with the unprecedented wave of innovations that is coming'

# How has the pharmaceutical industry been perceived through this crisis?

This period has put pharmaceutical companies in the spotlight. They demonstrated an exceptional capacity to react, mobilize, innovate, take risks and be resilient. We can be proud of that, especially given the scale of the challenge.

Very quickly, our laboratories got down to work to produce new vaccines. Today, promising new treatments are available to patients. These efforts reflect the exceptional mobilization of all the research teams and, more broadly, of all the players in the sector. So the way our industry is viewed has changed dramatically thanks to the leading role it has played in the fight against the pandemic.

These results are confirmed by the reputation survey we conducted last September, in partnership with lpsos. Indicators are up on all fronts. The image of pharma has clearly improved among the general public (41% positive image in 2021 vs. 28% in 2019). Its usefulness is no longer in question for nearly 100% of respondents.

# What do you think will be the major trends in the industry in 2022?

Unfortunately, the Covid crisis is not yet behind us. Research, development and production of effective vaccines and treatments against this mutant virus will continue to mobilize drug companies this year.

The year 2022 will also be marked by major political deadlines that will be decisive for the future of our industry, in particular for healthcare innovation in France and the prevention and management of future pandemics.

To begin with, the French Presidency of the European Union during the first half of 2022 will be a unique opportunity to create a true Union of public health; I am delighted about this. The issue of health sovereignty must be addressed at the European level, in particular through the

## 'Relocating without deglobalizing: that is our objective'

Interview

strengthening of industrial health policy and the strategic positioning of the Union. In this context, we support the establishment of the European Health Emergency preparedness and Response Authority (HERA).

Prevention will also be at the heart of European political priorities, in particular the fight against cancer, the fight against antibiotic resistance, or to protect the mental health of young vulnerable people.

The technological revolutions that are about to take place hold great promise. One of the challenges for our sector is to know how to deal with the unprecedented wave of innovations that is coming: the contraction of the drug budget that we have been witnessing for the past dozen years will no longer be the case. The 2023 PLFSS legislation will be decisive in this respect.

Another major trend is digital health. The European Health Data Space will make it possible to pool a very rich and useful database to improve diagnoses, while establishing legislative conditions to protect data and anonymity.

In the context of the French presidential elections in April, Leem has also presented a platform of proposals to the candidates on behalf of the sector, structured around the following four objectives: Make France the European leader in pharmaceuticals by providing massive support for research and innovation; Make the pharmaceutical industry the spearhead for reindustrialization; Make patient access to treatment a top national priority; and Reform pharmaceutical policy for greater simplicity and efficacy.

Our ambition is to ensure that health remains at the heart of the debates and political priorities of the next presidential term. While waiting for the verdict, Leem's proposals can be compared with those of the candidates, all of which have been detailed during the campaign, at www.lasantecandidate.fr

# How can French and European regulation foster pharmaceutical innovation?

As the crisis has shown, the French ecosystem is penalized by its lack of clarity and visibility, even though these are essential components for the development and availability of healthcare innovations. These are recognized factors in France's loss of attractiveness to industrial promoters. It is urgent to simplify this ecosystem, to make it predictable and supported with the appropriate budget.

Let's take the example of the LFSS laws, which are subject to the principle of annual budgeting. This short-term vision of drug expenditure regulation prevents the regulator from anticipating the arrival of innovative technologies and their (potentially cost-saving) impact on the organization of care. This is an aberration. Multi-year budgeting could be included in a legal framework, taking into account the projected needs for financing drug expenditure over the longer term.

'We must consolidate the early and/or accelerated access mechanisms implemented in recent years and actively participate in the deployment of European regulation for the assessment of health technologies' It is not just a question of the budget, but also of health priorities. We hope that the future Health Innovation Agency will make it possible to define a clear ambition and steering system for research at national level.

Furthermore, we must not forget the issue of access to innovation, which is fundamental for patients. We must consolidate the early and/ or accelerated access mechanisms implemented in recent years and actively participate in the deployment of European regulation for the assessment of health technologies, which aims to promote cooperation between Member States on the assessment of clinical data (effective implementation in 2024).

#### Leem has been a partner of TSE since 2019. What role can economists play in the pharmaceutical industry?

Spending on drugs is by nature a highly administered expense, in a social security budget that must be constrained. However, the management of this expenditure is today purely budgetary and we have seen the limits of this approach during the Covid-19 crisis. Drug expenditure, which represented 14% of health insurance expenditure in 2011, will only represent 11% in 2021. The adequacy between the budget and France's pharmaceuticals needs is never questioned. The objective of reducing social deficits, which has obsessed health policy in recent years, has overshadowed a question that is becoming critical today: what is the right level of investment to face the challenges of innovation, the relocation of essential medicines, the aging of the population, and the chronification of diseases? Economists can help us to understand the limits of a purely budgetary logic and, with a global vision of the system, to support the need for change. The response to drug issues must be holistic to be relevant. To put it simply, we expect economists to help us ask the right auestions.

# How do doctors respond to evidence?

Pierre Duboi Director, TSE Health Center

To uphold the Hippocratic oath, doctors face difficult decisions about prescriptions that depend on their judgment, subjective experience and medical knowledge. These choices impact not only their patients, but national health systems and finances. In a new paper written with Tuba Tuncel (HEC Montreal), TSE's Pierre Dubois investigates the impact of new public health guidelines on physicians' behavior.

When prescribing treatments, doctors face challenging costbenefit trade-offs that depend on their evaluation of drug efficacy and patient condition. Recent studies provide evidence of the influence of physicians' skills, beliefs and preferences on these decisions. Doctors may also update their prescribing behavior as medical iournals publish new evidence and public health authorities adjust their recommendations. But papers studying the impact of new information on prescriptions are sparse.

Among such studies, Berez et al. (2018) find that the use of pulmonary artery catheters declined after the release of evidence on their ineffectiveness but that older physicians' use of the device was influenced by the practices of junior colleagues. In light of information about the futility of a common knee surgery, Howard et al. (2017) show that physicianowned surgery centers have been slower to abandon the practice than physicians working in hospitals. Howard and Hockenberry (2019) show that older physicians were slower to respond to evidence that routine episiotomy is unnecessary.

To study how public health recommendations affect physicians' decision-making, Pierre and Tuba's paper exploits French panel data containing exhaustive prescriptions made by a representative sample of 386 general practitioners to more than 110,000 depressed patients

from 2000 to 2008. Results revealing an increase in suicidal thinking among children and adolescents taking selective serotonin reuptake inhibitors (SSRIs) prompted the release of new guidelines by public health authorities in 2004.

Compared with other antidepressants and older patients, the researchers found the public health warning decreased the average probability of a prescription of SSRI drugs to kids and adolescents. However, such 'difference-in-difference' estimation cannot disentangle the effect of the warning on physicians' preferences for different types of drugs. To estimate these preferences, the researchers develop a model of physicians' prescribing behavior using their extensive data set. This allows them to test not only whether

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changing scientific information also whether it affects physicians differently.

of their propensity to prescribe different antidepressants, and that they respond very differently to government warnings. Many with 62% continuing to prescribe the antidepressant to kids and in favor of either serotonin and norepinephrine reuptake inhibitors (SNRIs) or other nonantidepressants. 'One important result is that the reduction in the SSRIs before the warning,' says Pierre. 'The wide variety in physicians' responses suggests that some of them interpret the warning as 'good' or 'bad' news adolescents.

What would happen if prescriptions of SSRI drugs to kids and adolescents were banned? The researchers conduct a counterfactual simulation to compare the effects of a ban and a warning. Perhaps unexpectedly, the outright ban leads to a lower level of substitution to other antidepressants and a higher level of substitution towards drugs other

#### 'The wide variety in physicians' responses suggests that some of them interpret the warning as 'good' or 'bad' news'

affects physicians' prescriptions but

The empirical results suggest that physicians vary a great deal in terms physicians ignored the SSRI warning, adolescents. Prescription of SSRIs to kids and adolescents decreased probability of prescribing SSRIs to all patients was larger but also more heterogeneous for physicians with a higher probability of prescribing for age groups other than kids and

than antidepressants. In other words, after a warning, a physician is more likely to substitute an SSRI with another antidepressant. 'These results call into question the interpretation of drug warnings and recommendations by physicians, Pierre concludes, 'and show how heterogeneous reactions can occur in relationship to physicians' ex ante preference for the different possible treatments.'

Pierre's research highlights how physicians can respond to new information in very different ways, with important impacts on treatment decisions. 'Physician beliefs are crucial to explaining their heterogeneous prescribing behavior and are also directly affected by both scientific knowledge and personal experience with their patients,' the authors write. 'Our new approach and results shed light on how to evaluate the impact of medical warnings on physicians and on their wide heterogeneity of responses."

#### **•** FIND OUT MORE

Identifying the effects of scientific information and recommendations on physicians' prescribing behavior' was recently published in Journal of Health *Economics.* For more research by Pierre on health and pharmaceuticals, see www.tse-fr.eu

10 years of TSE's educational programs

TSE started receiving students in 2011 with a training program that has won high praise from companies and institutions over the past decade. To begin with, however, few believed in the potential of this hybrid project, between the Grande École and the university, and it took all the will of the early pioneers to get it off the ground. TSE researchers David Alary, Marie-Francoise **Calmette and Christine Maurel** look back at the challenges of the early days.

# How did the TSE educational programs start?

Marie-Françoise Calmette: I was elected director of the Faculty of Economics in 2008. The day after the election, Bruno Sire came to see me with a project he had been thinking about for a long time: creating a school of economics that would take advantage of the prestige of our research center. At the time, TSE's research was world-renowned, with thinkers like Jean-Jacques Laffont, Jean Tirole and Jacques Crémer, but our teaching was not on a par with this excellence, or at least was not perceived as such.

**David Alary:** Bruno Sire came from the IAE, which later became TSM, so he already had this vision of an integrated school. For him, it was no longer possible to have this separation between economics bachelor's degrees at the faculty and "TSE" master's degrees that only a few of the most successful students managed to obtain, alongside international students.

## What were the structuring discussions?

MFC: The main sticking point was the selection of students, desired by the professors to ensure a level

commensurate with the school's reputation, but discouraged by the University, which should be inclusive and open to all. I remember tense discussions on the subject, and in particular a very difficult meeting in December 2008, which led to a compromise agreement the next day: no selection in the first year of study, but selection for entry into the third vear. This system was inspired by the Grandes Ecoles and has remained in force since the creation of the school. There remained the problem of students who had obtained their first and second year of study but who did not meet the conditions for entry into the school's third year, and how to guide them so that they could continue their studies.

**DA:** In 2011, when the school was created, master's graduates worried their degree would be devalued with the arrival of this new formula. I think, in the end, they have benefited from the update.

**MFC:** The financing of the school seemed extremely difficult and conditioned the implementation of advanced teaching techniques. It was difficult to sell the project because of its uniqueness, not only at the regional level but also at the national level. In 2010, the State called for applications to the IDEFI

project – Initiatives of Excellence in Innovative Training – and, as luck would have it, our project perfectly met the expectations. This funding allowed TSE to come to life, thanks to the hard work of Hélène Billy, general secretary at the time. Christian Gollier, Jacques Crémer, and Joël Echevarria. We all invested a lot of time and effort. I remember the day of the hearing, in front of the jury, at the end of the session, Joël Echevarria spoke in Catalan with one of the members of the jury, and I knew then that we were on the right track. In the end, TSE tied for first place in the IDEFI and won €7 million in funding, a miracle for this extremely ambitious project.

Christine Maurel: This funding enabled us to improve student support, particularly in selective courses in eco-law and eco-maths, and to change the way we teach in all courses. We introduced continuous assessment, well before other schools and universities did, to encourage regular and sustained effort by students throughout the year.

This funding has also strengthened our teaching team, allowing us to offer limited enrollment courses starting in L2, the launch of projectbased learning in L3 (a pedagogical innovation that contributes to the employability of our students), the development of interactive courses, with quizzes, and courses in English. As early as 2011, the school also offered its students the opportunity to take a gap year before M2, and in 2013 we made internships mandatory in M1 and M2. We have gradually been able to strengthen the administrative support team to offer better services to our students and alumni.

# What do you remember about this adventure?

MFC: Things are changing rapidly in higher education - this project would not have been born 10 years earlier. TSE is an unprecedented success in France, not only from the point of view of research but, and this is truly exceptional, also in terms of teaching. Combining selective highlevel education and the University was a particularly challenging task. To see what TSE has become, 10 years later, makes me extremely proud of the work accomplished. I hope that we have shown the way for future similar projects of excellence within the University.

**CM:** It was a great challenge and a great adventure. I think that we have succeeded: the employability of master's graduates is excellent,

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and students' evaluations of the courses are improving year after year. We have been able to keep this ground-breaking spirit: pedagogical innovations are very often tried out!

# What is a remaining challenge for TSE?

**MFC:** We have not succeeded in totally solving the problem of the location. We had succeeded in obtaining from the University that all TSE activities take place at Manufacture des Tabacs but this quickly became too cramped for the institution. The new building made it possible to accommodate all the researchers and doctoral students in a very comfortable way. Unfortunately, we also lost this unity of places between students and researchers.