2nd Health Economics Conference Summaries

Toulouse, June 19 & 20, 2024

CONFERENCE VENUE

Toulouse School of Economics (TSE)
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TSE held its 2nd Health Economics Conference on June 19-20, 2024, in Toulouse, France, following the successful inaugural edition of the conference in 2023.

Like the year before, this conference aimed to explore recent scientific contributions in the **organization and regulation of healthcare and pharmaceutical sectors**. The presentations and discussions covered a wide range of topics, providing a platform for exchanging views on research findings. Conference participants gained valuable insights for shaping future health policies, particularly in the field of health investment and innovation.

Jointly organized by **Jean Tirole, TSE's Nobel laureate and Honorary Chairman, and Pierre Dubois, Director of the TSE Health Center**, the conference brought together over 100 participants from around the world, including political decision-makers, experts and academics.

Below are summaries of the two roundtable discussions and a selection of articles (listed in the order they appeared in the program).

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Policy roundtables

"Which Pricing and Reimbursement Model for Very Costly Innovative Therapies?", roundtable chaired by Pierre Dubois

Recent pharmaceutical advancements, such as gene therapies and mRNA technologies, promise significant progress but come at a high cost, as medicines are increasingly tailored to individual genetic profiles and diseases. How should pricing and reimbursement models be structured in this new landscape? Comprising both practitioners (regulators and industry representatives) and academics (from Europe and the US), this policy roundtable offered diverse perspectives and insights on the topic.

Pricing innovative drugs: insights from the French regulatory framework

At present, the French regulator negotiates with the pharmaceutical industry on two levels: at a macro level, it negotiates with the industry association (LEEM) a set of operational rules ("Framework Agreement") consistent with the general principles set by law; at a micro-level, it negotiates with each pharmaceutical company the specific price of each reimbursed drug on a case-by-case basis.

At this second level, the Economic Committee for Health Products (CEPS) uses the clinical added value of a medicine (as assessed by a scientific committee within the French National Authority for Health (HAS) to negotiate a premium or discount with the manufacturer, relative to the current price in France of comparative products. Philippe Bouyoux (chairman of CEPS) highlighted two specific challenges in pricing costly innovative drugs within this framework. He noted that in recent years manufacturers have demanded increasingly higher prices, often pre-announcing a target "global price", both for the US and Europe. The current practice of the French regulator is to negotiate a lower price by using the price of comparative products in France as a benchmark. However, some scholars consider this to be "free riding" on the US. Philippe noted that "regulated prices" (as in France and the EU in general) are indeed lower than free market prices (as in the US), **but once the price is set, the medicine is available and reimbursed for every patient, thus increasing the volume of sales.** Philippe acknowledged that even within the current framework, innovative drugs are becoming more difficult to price. Gene therapies, for example, are "one-shot products" (administered with a single injection), so a

comparison with more traditional chronic treatments poses additional challenges. Moreover, there is a large degree of uncertainty regarding the long-term effects of gene therapies. To this address uncertainty, the regulator can employ two options: outcome-based payments and cost-effectiveness analysis. The first helps manage the uncertainty mentioned above, though there are concerns about feasibility and availability of the necessary data. Moreover, in focusing too much on establishing the modalities of payment over time, the regulator risks losing sight of its own willingness-to-pay for the drug, which is the most important consideration. The second option, cost-effectiveness analysis, provides a clear metric (the incremental cost effectiveness ratio - ICER) and an in-depth analysis of identified uncertainties, that can guide decision-making, even though France – at odds with the UK, for instance – does not rely on a specific threshold in terms of an acceptable level of ICER.

Competition and international pricing dynamics

For most innovative products, negotiations are extremely complex: the manufacturer uses the publicly disclosed list price as a signal observed internationally, while the regulator pays a lower net price that remains confidential. In some cases, the gap between the two prices can exceed 50%. This generates two forms of information asymmetry. First, a manufacturer considering entry does not observe the net prices of comparative drugs. To foster competition, the regulator attempts to close this gap by the time the patent protection expires, thereby reducing uncertainty and encouraging the entry of generic products into the market. The second form of information asymmetry concerns the regulator's lack of knowledge of the net prices paid by other countries for the same drug. This opacity allows the manufacturer to price discriminate across countries based on their demand, income, demographics, etc., even in the presence of reference pricing. Hence, the lack of transparency in this context reduces price spillovers across countries, which may have an ambiguous effect on prices, timing of entry, and the incentives to innovate.

Challenges in pricing high-cost therapies and their impact on healthcare systems

What sets these innovative therapies apart from traditional drugs is their very high marginal production cost, due to their targeting of individual patients and diseases. This may further complicate the negotiation process, as the manufacturer will not find it profitable to sell the product below a certain price, and the regulator will struggle even more to balance access and affordability. Juliette Moisset (Director of access and economic affairs of LEEM, the professional organization representing the pharmaceutical industry in France) suggested focusing on the following question: is a drug too expensive or just very costly? Currently, the French regulator sets the price of a pharmaceutical drug by considering its annual budget in isolation, looking only at the prices of other comparative drugs rather than the potential savings in terms of healthcare resources in future years. Innovative pharmaceuticals, however, can be very disruptive in terms of hospital procedures and management, entailing different treatments and use of healthcare resources. To correctly assess the expected value of a drug, and then compare it to its current cost, this perspective markedly impacts the healthcare production function and

should be considered very carefully by the regulator. Moreover, Juliette emphasized that pricing decisions are crucial in directing innovation towards specific fields and cautioned that this role can be overlooked if the regulator focuses solely on setting a price relative to comparative drugs.

Evaluating Healthcare Value

Professor David Ridley (health economist at Duke University's Business School), whose research on pharmaceutical innovation has paved the way for policy reform in the US), points out that the debate on cost-effectiveness analysis and the value of care varies between countries. France adopts a values-based approach, although some countries – such as the UK – use lower thresholds to assess value.

Balancing immediate costs with long-term benefits

Pierre noted that paying high prices today could be justified if it results in treatments becoming more routine and cost effective over time. If, on the one hand, the regulator refuses to pay, the process of learning-by-doing could be delayed, as well as the efficiency gains and the development of scale economies. Therefore, if cost-effectiveness is considered endogenous to the regulator's decision, it might be beneficial to design a new framework where the regulator agrees to high prices now in exchange for much lower prices in the future. This would require a long-term commitment from both the regulator and the industry; however, this should be feasible in principle.

The discussion also briefly touched on the recent adoption of a joint Health Technology Assessment group in the EU. While this should accelerate the first step of the negotiation procedure, the pricing and reimbursement decision will remain at the State level. Specific work is required, in this context, to shorten access delays to innovative drugs, especially in France. In conclusion, while the roundtable discussion underscored the complexities of pricing innovative therapies and the need for a framework addressing both immediate costs and long-term benefits, there is room for more dialogue and research to explore potential solutions and develop effective strategies.

"The Use of Health Data, Platforms and Digital Technologies for Innovation", roundtable chaired by Jean Tirole

Moving fast and breaking things, data-crunching technologies are surging across research frontiers. Opening the panel discussion, Claire Biot (VP, Life Sciences & Healthcare, Dassault Systems) explained how medical researchers can now "fail fast and fail cheap", using artificial intelligence to pinpoint the best drug candidates: "You can screen millions of potential compounds and reduce them to 100-200 for testing. You can then reinject the results into your AI model so that it's even more efficient in proposing the next wave of compounds."

Virtual twins

Virtual twins are among the most exciting digital innovations in the health sector, building on the dramatic success of 3D models and shared simulations in car and aircraft design. "Today, 95% of crash tests for cars use virtual twins," said Claire. "Obviously you're going to use real cars at the end, but it's much faster, costs less for materials, it's more sustainable and allows us to explore a much broader design space."

In the future, virtual twins may become a common tool for improving doctors' treatment of their patients. Today, the use of synthetic patients – built using data from previous clinical trials – has already begun to transform analysis and testing of medical products. Claire noted that Dassault has conducted successful 'crash tests' of a cardiac repair device in a sophisticated simulation of the human heart.

AI that delivers

Digital technologies can also drive massive efficiency gains in hospital administration and workflow. "How can we scale clinician time? We don't have enough doctors and nurses. To unlock the equivalent of one free nurse per day per hospital department would be amazing," said Ariel Stern (Health economist, Harvard Business School). "Why do I have to make three phone calls to schedule a medical appointment? Clinical notes, scheduling, even triage, can all be done better with support from AI."

Ingenious tech must not be a distraction from the real challenges for health workers, she warned. "It's vitally important to think about healthcare delivery. What do clinicians want? Not the cool, sexy stuff we can do with algorithms, but what products are useful to improve the workflow of a radiologist's day." Without changes in hospital management, glittering AI innovations will have little value. "If nobody's job description changes, if nobody gets training or incentives to use these new tools, we're in trouble."

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Trust in tech

Are we playing with fire in wielding AI tools that surpass our understanding? As Ariel argued, we do not really know how paracetamol or anesthesia work either. "If we are going to hold medical products to that explainability standard, we have to pull a bunch of very useful, safe drugs off the market. The question, though, is relevant to liability settings: What is the combination of clinical decision-making and algorithm and how does it matter?"

Regulate to innovate

"There is a fight on how to use data, especially in Europe" said **Edwin Morley-Fletcher (President, Lynkeus)**. His eHealth consultancy has been working with the European Commission to facilitate the use of virtual human twins by developing data ecosystems and simulation platforms. He underlined the higher complexity of Europe's data protection, compared to the US, and called for more transparency about regulatory objectives and decisions.

"There is a fight on how to use data, especially in Europe"

Recent indications that Europe may push forward with tougher requirements for fully anonymized data are particularly unclear, he noted, presenting investors with a Sphinx-like riddle that is spreading confusion. "Is the Commission waiting for other things to develop like the European health data space which should come with newer rules? Or is there a strategic choice to make the hindrance of our much stricter data protection rules into something which allows Europe to develop much stronger synthetic data generation mechanisms?"

Encouragingly, as Ariel observed, innovation in regulatory policy itself can also boost R&D. Her keynote lecture showed how the US Food and Drug Administration's targeting of drugs with "breakthrough" potential has reduced clinical development time by about five months.

Data liquidity

Ariel also suggested that federated learning algorithms, designed for use with local datasets and data rules, may help regulators to balance privacy concerns with R&D objectives. "My hope is that we can move away from conversations about data ownership and towards data governance and data stewardship," she said, pointing to German proposals for a national data center that allows access for medical research and other projects that benefit society.

The future of health innovation will depend on access to data, agreed Claire. "We need a business model of the conditions under which stakeholders will be able to share their data; standardization of data so that you can compare across different hospitals, for example, and trust." To achieve these goals, she advocated the use of a sovereign cloud to store sensitive health data within national or EU borders.

Academic presentations

"Transparency and Competition for Influence", Sofia Amaral-Garcia (Joint Research Center - European Commission) with Giacomo Calzolari (European University Institute), Vincenzo Denicolò (University of Bologna) and Mattia Nardotto (Université Libre de Bruxelles)

This paper studies the interplay between delegated decision makers, who are entrusted to act in the best interest of their stakeholders, and third parties, who compete with each other and try to influence the decision makers. This is the case, for example, with pharmaceutical companies that provide gifts or monetary contributions to physicians leading to concerns that this might influence physicians in their prescribing behavior. To discipline the decision makers, transparency regulations have mandated the disclosure of such payments from the pharmaceutical industry. In the example, the prevailing view is that transparency causes patients to be wary of doctors who receive payments, thus incentivizing doctors to accept fewer payments and prescribe fewer sponsored drugs. Hence, transparency should imply a *reduction* in industry payments and their "productivity." However, looking at data on the US anticoagulants market, the authors find that the productivity of payments *increased* after the 2010 Sunshine Act entered into force. This regulation requires companies to report their payments, therefore mandating transparency.

To explain this phenomenon, the authors have developed a new theory of competition regarding influence and transparency. The crucial assumption is that under transparency, a firm can condition payments made to a doctor, not only on how much the doctor prescribes of its drug, but also on how much the doctor receives financially from the rival firm. The model predicts that transparency decreases the total number of prescriptions, has an ambiguous effect on total payments, increases the concentration of prescriptions and payments, and increases the productivity of payments. The increase in polarization is a significant unintended consequence of transparency regulations as it allows firms to divide their sphere of influence, thus hurting competition. These theoretical predictions have been empirically tested and validated within the context of the US anticoagulants market, where the nationwide adoption of transparency resulting from the 2010 Sunshine Act provides a natural experiment. The study is completed by an (ongoing) structural analysis quantifying the welfare effects of transparency.

"Pull Incentives, Market Size and Pharmaceutical Innovation: From Early Preclinical Research to Drug Launch" Pierre Dubois and Ilaria Natali (Toulouse School of Economics)

This work provides new evidence on the causal impact of financial incentives on pharmaceutical companies' willingness to innovate, with a specific focus on the antibiotics market. One important objective is to inform policymakers about the impact of certain healthcare policies. For instance, the Congressional Budget office in the US uses elasticity estimates from studies such as this to evaluate the impact of policies aimed at reducing drug costs. The focus on the

antibiotics market is crucial due to the recent emergence of antimicrobial resistance (AMR), along with the urgent need to provide pharmaceutical companies with appropriate incentives to stimulate the further development of antibiotics. "AMR currently results in approximately 79,000 deaths per year in OECD countries. Beside the human loss, the financial burden associated with AMR is about USD$29 billion due to longer and more complex treatments, while the impact on the labor market equals USD$37 billion," says one co-author. Hence, another important objective of this study is to highlight the effectiveness of pull mechanisms to enhance research and development in the field of antibiotics. Unlike prior studies, the authors consider several measures of innovation following the entire development stream – from preclinical trials to launch – as well as different measures of revenue. They provide the first-ever estimate of the elasticity of innovation effort at each phase in relation to the expected pharmaceutical revenues. The paper also examines the role of risk and uncertainty, focusing on how the expected volatility in revenue shapes pharmaceutical companies' decisions to engage and encourage progress in the drug discovery process. The results show that pharmaceutical companies are more sensitive to profit incentives in the later stages of the development process, while uncertainty about future revenue generally discourages innovation. The development of antibiotics is also responsive to profit incentives, but not at the preclinical trial stage.

"Does Research Save Lives? The Local Spillovers of Biomedical Research on Mortality", Rebecca McKibbin (The University of Sydney) with Bruce A. Weinberg (Ohio State University)

This paper explores the real-world impact of biomedical research on reducing death rates in local communities across the US. This study is significant as the returns on investments in research tend to decrease with time. The authors examine what happens to local mortality rates for 39 different non-contagious diseases when there are sudden changes in funding from the National Institutes of Health (NIH) in the US.

By analyzing data on research publications and mortality rates, they determine that areas receiving more research funding see more significant reductions in death rates. Specifically, a 1% increase in research publications related to a particular disease can lead to a 0.35% reduction in the local death rate for that disease over a decade. This means that research not only advances scientific knowledge but also has tangible health benefits for the communities in which it is conducted.

The findings emphasize that the benefits of biomedical research extend beyond the laboratories and hospitals. When innovative ideas and treatments are developed, they tend to spread and be adopted locally in the first case, demonstrating the power of technological diffusion and local spillover. This study emphasizes the importance of continuing to invest in biomedical research and to ensure that the results are effectively disseminated in order to maximize their positive impact on public health.

"Treatment Effects and Targeting: Evidence from Hospital Antibiotic Stewardship", Edward Kong (Harvard University), with Erica Shenoy and Alyssa Letourneau (Massachusetts General Hospital)

The consumption of antibiotics generates externalities, specifically antibiotic resistance. Controlling such resistance requires the management of antibiotic use. As a result, the share of US hospitals with antibiotic stewardship programs (ASPs) has more than doubled from 2014 to 2019. However, there is much to learn about the effects of such programs. The use of antibiotics is challenging to regulate, as the cost of *not* giving an antibiotic when it is necessary can be higher than the cost of giving an *unnecessary* antibiotic. The paper sheds light on the causal effects of the use of antibiotics on health outcomes in a hospital setting.

The authors use electronic health record data from a large academic hospital and focus on the use of linezolid, which is used in the treatment of Vancomycin-resistant enterococci. When a treating physician wants to use a restricted antibiotic such as linezolid, a request is sent to an ASP pager holder, who either confirms or denies this request. The causal effects of ASP approval versus denial is challenging to identify because of selection into treatment: unobserved disease severity drives both antibiotic use and poorer health outcomes. To overcome this problem, the authors exploit the exogenous variations in the likelihood of approval due to variations in pager staffing from week to week, which they show to be uncorrelated with observable patient characteristics. The authors then use machine learning methods to divide the sample into the treatment and control groups, where the treatment group consists of patients with higher than the predicted linezolid use. In the treatment (but not control) group, there is a negative relationship between the average ASP approval rate and the 30-day mortality rate. The findings enhance our understanding of the outcomes of ASPs and are crucial for the improved design of such programs.

"Who Gains When Medicine Becomes More Precise? Evidence from Genomic Testing in Breast Cancer", Jasmin Moshfegh (Stanford University)

In her paper, Jasmin Moshfegh investigates the impact of genomic testing adoption on breast cancer treatments and health outcomes, while also examining its implications for racial disparities. She uses event study models looking at variations in the timing of patient diagnoses relative to the provider's adoption of the technology. The author finds that patients consulting an oncologist within a year of the oncologist's adoption of genomic testing are more likely to avoid unnecessary treatments, particularly chemotherapy, *without an increased risk of mortality*. However, this beneficial effect is more prevalent in white patients and those with higher socioeconomic status, which cannot be fully explained by differences in patients' access to physicians. Additionally, she proposes two potential mechanisms: first, the differences in patients' medical appropriateness; and second, the racial differences in provider testing decisions, where the former accounts for only 40% of the within-provider Black-white gap using linked cancer registry data. Overall, the adoption of precision medicine improves healthcare efficiency, though with a risk of exacerbating health disparities.

"Optimal Conditional Drug Approval", David Ridley (Duke University) with Giuseppe Lopomo, Peng Sun and Chenxi Xu (Fuqua School of Business)

In 1988, a crowd of protesters gathered in front of the FDA chanting, *"Hey, hey, FDA, how many people have you killed today?"*. They were protesting because thousands of people were dying of HIV-AIDS. They wanted the US Food and Drug Administration to grant faster access to experimental drugs for people with AIDS. In response to calls such as this, the FDA released the *Accelerated Approval* regulations in 1992.

These new regulations allowed for the FDA to grant conditional approval for a drug based on smaller and shorter clinical trials, making innovative treatments available to the market at an earlier time. Following their commercialization, pharmaceutical companies are still required to provide additional evidence and to conduct further trials in order to confirm the anticipated clinical benefits and obtain final approval.

These new rules did not come without criticism. Recently, some FDA advisors resigned, claiming that in some cases there was not enough evidence to safely justify the approval of a drug. They were concerned that payers would waste money on ineffective drugs. Nevertheless, besides making drugs intended to treat serious conditions available to patients earlier, these regulations also provided pharmaceutical companies with stronger incentives to invest in drug discovery for otherwise neglected diseases.

This paper offers recommendations for regulators to improve their existing rules. The main results suggest that the regulator should conditionally approve – with a lower efficacy threshold – in order to encourage investment, especially if testing costs are high. The authors also note that this policy is not incentive compatible when testing costs are privately known. Pharmaceutical companies are often reluctant to report cost information, in which case the regulator should choose a different threshold to prevent firms from misreporting testing costs. Moreover, the regulator should grant conditional approval, even for a limited share of patients, so as to stimulate tests.

Finally, in some cases, the regulator should also commit to a lower efficacy threshold for final approval. The paper also compares these recommendations with two alternative policies. The first option would be for the regulator to pay for Phase III testing costs. However, late-stage testing is extremely costly. The NIH (National Institute of Health) funding is normally reserved for universities conducting early clinical research. Alternatively, the Pay for Success option has the disadvantage of relying on regulator credibility. Furthermore, for this to be effective, the regulator would need to offer a high price since firms discount future revenues.

The conference insights, centered around nine key topics, highlight the pressing need for policies that combine innovation, affordability, and equity in healthcare, with significant implications for health economics. With a view to continuing these high-level discussions, Jean Tirole and Pierre Dubois are pleased to announce that the **3rd edition of the Health Economics Conference,** now become firmly established **in the landscape of health economics in Europe, will take place in Toulouse on 18-19 June 2025. Please save the date!**

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TSE also extends its sincere thanks to the current and future generations of health economists for their valuable contributions to the conference proceedings (including Gokce Gokkoca, Ilaria Natali, Valentina Reig, Giulia Tani, and Xin Zhang).

Further readings : TSE Health Center / Health Conference
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