TSE Health Center

# Economics of antibiotics & antibioresistance journal

March 2025

## Unlocking the power of diagnostic tests

David Bardey, Philippe De Donder and Vera Zaporozhets

## Air pollution and antimicrobial resistance

Ilaria Natali

Economics for the Common Good

# Economics for the Common Good

Dear readers,

The fight against antibiotic resistance is one of the major global challenges facing society and policymakers today. TSE researchers are committed to developing our understanding of this critical issue, drawing on their valuable expertise in the economics of antibiotics and antimicrobial resistance (AMR) and with the support of a variety of public and private actors from the health sector.

In this new edition of our journal, we feature the recent work of David Bardey, Philippe De Donder, and Vera Zaporozhets on the role of diagnostic tests in the effective management of antibiotics. Their research shows how the adoption of companion tests and personalized medicine is shaped by various factors, including financial incentives that influence doctors' behavior, ultimately affecting both the quality of care and associated costs.

We also highlight Ilaria Natali's research on the correlation between air pollution and the spread of AMR. Her study provides key insights into an important question: To what extent could stricter environmental policies help curb this spread and prove as effective as reducing antibiotic consumption?

We would like to thank the partners of the TSE Health Center, especially bioMérieux, Bpifrance and the members of the ARPEGE consortium as well as the CSF Santé, for encouraging our research in this field. Their support and our discussions with them have been instrumental in advancing our work.

Enjoy your reading!

**Pierre Dubois**
***Director, TSE Health Center***

# Past and upcoming events

***Economics of AMR R&D Incentives: The Cost of Inaction and Action***
May 2024 – Paris

Together with Antabio, Beam Alliance and the AMR Action Fund, TSE has organized this symposium for European economists, innovators and policymakers to exchange ideas, questions and views on existing and alternative policy options for R&D on antimicrobial resistance, and to identify research gaps and opportunities for moving the agenda forward.
*See summary of the workshop*

***2nd TSE-CEPR Health Economics Conference***
June 19 & 20, 2024 - Toulouse

Jean Tirole, Nobel Laureate and Honorary President of TSE, and Pierre Dubois, Director of the TSE Health Center, have organized an annual conference on health economics since 2022. It brings together academics from Europe and beyond, as well as decision-makers and experts, who are interested in the organization and regulation of healthcare and pharmaceutical industries. Several sessions have delved into topics related to the economics of antibiotics and AMR.
*Find out more*

**SAVE THE DATE | June 18 & 19, 2025: 3rd TSE-CEPR Health Economics Conference**

# How can we unlock the potential of diagnostic tests?

**Diagnostic tests help doctors to accurately identify medical conditions, guiding effective use of antibiotics and other treatments, preventing the spread of disease, and improving overall patient outcomes. In a new working paper, TSE researchers David Bardey, Philippe De Donder and Vera Zaporozhets review the latest research on the economic incentives to use and develop these powerful tools for a healthier future.**

*Why do diagnostic tests play such a crucial role in modern healthcare?*

Diagnostic tests encompass all the procedures used to reveal what ails patients and how to treat them. In the case of cancer, tests look for genes, proteins, and other biomarkers that can provide information about the patient's specific condition. Our review focuses on companion tests and personalized medicine, which aim to determine a treatment's suitability for the patient.

Companion tests are increasingly important, both in enhancing use of existing treatments and in the authorization of new ones. For instance, around half of cancer drugs that received EU approval between 2015 and 2018 required patients to be screened by a genetic test before treatment.

Although doctors must often invest considerable time and effort in learning to use them, they provide valuable information that enables faster and more precise diagnosis. As medical treatments are rarely safe and effective for everyone, diagnostic tests can reduce risky interventions and unnecessary expenditures by allowing doctors to exclude patients who are unlikely to benefit. Public attention often focuses on overprovision of diagnostic testing but the economic impact of undertesting has been estimated to be as high as 38% of total healthcare spending.

*How do financial incentives influence doctors' behavior?*

Theoretical and empirical research has shown that the behavior of healthcare providers is sensitive to monetary incentives. Various forms of payment and reimbursement schemes – such as fee for service (FFS), capitation (CAP), salary, or payment for performance (P4P) – can impact healthcare providers, who may react by modifying the amount of time or the volume of services they devote to their patients. FFS schemes encourage healthcare providers to supply more visits and other services, inflating healthcare costs. CAP payments and salaries can help to control these expenses, sometimes at the expense of the quality of services offered.

Non-monetary considerations also play an important role. For instance, intrinsic motivations such as altruism may interfere with the influence of monetary incentives on doctors, with unintended effects on quality.

*How do these motivations impact the use of diagnostic tests?*

The use of diagnostic tests also depends on several factors such as doctors' altruism, liability fears, time constraints, income and workload. These can influence the impact of tests on doctors' trade-off between patients' welfare and their own financial rewards.

**Diagnostic tests help doctors to accurately identify medical conditions, guiding effective use of antibiotics and other treatments, preventing the spread of disease, and improving overall patient outcomes**

Some empirical studies find that FFS rules generate too many diagnostic tests, as in China for instance. However, if diagnostic tests reduce the need for doctors' time and services, their use may be discouraged by FFS schemes. In contrast, P4P schemes have been shown to provide better incentives for the use of personalized medicine.

At the same time, altruistic considerations induce doctors to prescribe fewer tests when they are aware of their patients' out-of-pocket costs. This means we also need to consider whether care is being administered in an primary care or hospital setting, as different rules for out-of-pocket costs usually apply.

**Public attention often focuses on overprovision of diagnostic testing but the economic impact of undertesting has been estimated to be as high as 38% of total healthcare spending**

*Which incentives can promote better use of diagnostic tests?*

Finding the optimal incentive schemes requires a very good understanding of the objectives and constraints faced by healthcare providers. Theoretical models usually assume some adverse selection, such as doctors having private information on their own ability or the patients' health situation. Others add a moral hazard element, such as the unobservability of the doctors' diagnostic effort.

These studies stress that any reimbursement rule involves trade-offs. For instance, rewarding good health outcomes may result in higher health expenditures. They also point to counter-intuitive results, suggesting that even costless diagnostic tests should not be mandatory. Similarly, social welfare does not always increase in line with the doctor's altruism, possibly because skilled physicians underuse tests due to overconfidence in their own ability.

Diagnostic tests are used more often when they are well-known and easy to interpret. However, the investment in time and effort necessary to use such tests can play the role of a commitment device, increasing subsequent use and devotion to patients.

The U.S. practice of reimbursing biomarker tests and associated treatments separately has been criticized for encouraging insufficient use of biomarker tests. Research into regulation of diagnostic tests' characteristics shows that minimum standards on the specificity have no impact as doctors already have incentives to recommend tests with low rates of false negatives. In contrast, limiting the sensitivity of the test (i.e., the rate of false positives) can reduce demand and, consequently, unnecessary treatments.

**Finding the optimal incentive schemes requires a very good understanding of the objectives and constraints faced by healthcare providers**

*How can firms be incentivized to develop new tests?*

Incentives to develop tests are much stronger before approval of the linked treatment by the health authorities.

Companion tests increase the likelihood of approval of a drug – and sometimes its price – by restricting use to the patients most likely to benefit. The simultaneous development of test and treatment for metastatic melanoma led to the fastest FDA approval in history. Incentives to develop tests are also weaker after approval due to the reduction in market size. Regulation often prevents manufacturers from raising treatment prices in response.

These obstacles to development are easier to overcome when competition exists between laboratories. Incentives to develop the test are also higher when the average efficiency of the treatment is low. Tests may increase prices by dampening price competition between innovators. However, tests are not always associated with costly treatments as their development may benefit older, cheaper drugs which are off-patent.

Many researchers call for flexible and value-based pricing to reflect the benefits of companion tests. Another possibility is to sponsor research with R&D subsidies. If the treatment price is fixed, P4P reimbursement that depends on the success of the treatment can incentivize test development. Alternatively, procurement design rules or price regulation can be used to align the private and social values generated by biomarkers, taking into account laboratories' private information about the specific groups which can benefit from the test.

*Reference: 'Economic incentives to develop and to use diagnostic test'. Other publications are available to read on the webpage of the TSE Health Center.*

## KEY POLICY INSIGHTS

- Doctors are influenced in part by monetary incentives. FFS schemes tend to inflate healthcare costs, while CAP payments and salaries may contain them at the expense of quality.
- Non-financial motivations matter too. For instance, doctors prescribe fewer tests when aware of their patients' out-of-pockets costs.
- Well-known and easily interpreted tests are used more often. However, investing time and effort in learning to use tests may encourage doctors to use them more.
- Diagnostic tests should not always be made mandatory, even when costless, or reimbursed separately from the relevant treatment.
- Companion tests increase the likelihood that a treatment will be approved. Tests are less likely to be developed after approval because they lack this incentive and reduce market size.
- P4P schemes, procurement design and price regulation can be used to encourage development of companion tests. Incentives are higher if labs compete or if the treatment is not very effective.
- Tests may raise prices by dampening price competition. However, they may also improve the efficacy of cheaper drugs.

# About the authors


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David is a TSE Associate Faculty and Professor at Universidad de Los Andes, Bogotá, Colombia. His fields of interest include health economics, economics of education, economics of insurance, industrial organization, segregation, (applied) contract theory, labor economics, and operational research.

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**Philippe De Donder**

Philippe is a Research Director at the National Center for Scientific Research (CNRS) and a senior researcher at TSE. His research focuses on public economics, political economy, health economics and economics of regulation.

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**Vera Zaporozhets**

Vera is a researcher at TSE and INRAE. Her expertise lies at the intersection of political economy, public economics and environmental economics and natural resources. Her diverse projects are driven by her keen interest in studying the connections between individual preferences, individual actions and the collective choices taken by institutions.

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# Air pollution and antimicrobial resistance

**Reckless overconsumption of antibiotics is a key driver of the rise of antimicrobial resistance (AMR) but little is known about other risk factors. In a new study, TSE's Ilaria Natali provides the first causal estimates of the impact of air pollution on AMR. Her analysis suggests we will severely underestimate the benefits of air quality standards if we overlook their role in curbing the spread of killer genes and bacteria.**

*What is at stake in the fight against AMR?*

AMR is one of the world's most pressing challenges, as bacteria adapt and evolve to resist the drugs that protect us against them. In a post-antibiotic world, even routine hospital procedures may become lethal. In the EU alone, the current annual toll from AMR stands at 35,000 deaths with an economic burden estimated at €1.5 billion. Without adequate policies, the planetary toll could claim 10 million lives every year, far outstripping that of the Covid-19 pandemic. The World Bank considers that AMR could slash global GDP by up to 3.8% by 2050.

*Why has air pollution been linked to these dangers?*

My paper focuses on fine particulate matter (PM2.5), which is the most harmful airborne pollutant to our health and a significant contributor to morbidity and mortality. Recent research shows that PM2.5 can carry significant quantities of antibiotic-resistant genes and bacteria. The tiny size of the particles allows them to easily penetrate the human body via inhalation, facilitating the spread of AMR.

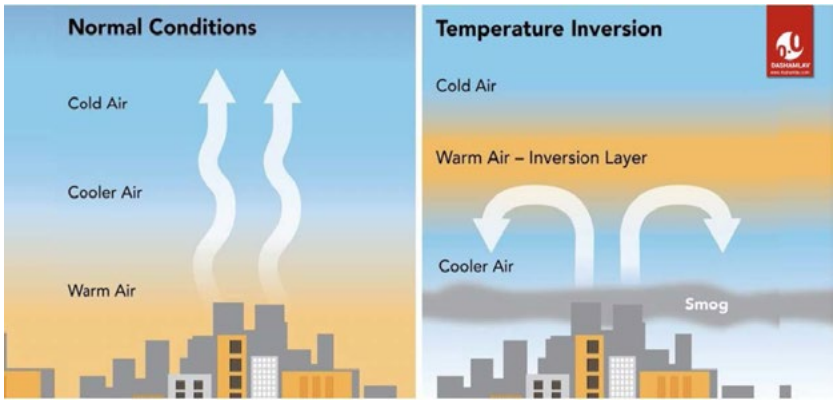
Traffic exhaust can also favor the horizontal transmission of resistance as it has been suggested that suspended particles provide more adhesion sites for bacteria. Researchers have found that antibiotic-resistant genes were more abundant in PM2.5 during days with high smog concentration in Beijing.

*How does your research capture this invisible threat?*

To establish causality, I exploit the random variation in air quality caused by temperature (or thermal) inversions. These are meteorological phenomena that occur when a layer of cooler air remains trapped under a layer of warmer air. Temperature inversions do not directly affect health but can significantly worsen local air quality by keeping pollution near the earth's surface. They have contributed to some of the most catastrophic pollution events in history, such as the 1952 Great Smog in London.

Selecting data for 24 European countries and five bacterial species, I first estimate the causal effect of air pollution on AMR from 2002 to 2019. I then compare the sensitivities of different pathogen-antibiotic combinations to non-anthropogenic changes in air pollution. I also distinguish an indirect channel for AMR diffusion through which the impact of air pollution on individual health leads people to use more antibiotics. Since antibiotic consumption in humans is observed, I can compare its impact on AMR with that of air pollution.

How do temperature inversions impact air quality?



**Air pollution is an important contributor to the spread of AMR in the EU**

I use this framework to conduct a counterfactual analysis of three European environmental and AMR policies. First, I set the annual limit for PM2.5 concentration at 10µg/m3, in line with current EU plans to be achieved by 2030. Second, I lower this cap to 5µg/m3 as recommended by World Health Organization (WHO) guidelines. Third, I reduce human antibiotic consumption in each member state by 20%, mirroring another EU target for 2030.

*What are your key findings?*

My results show that air pollution is an important contributor to the spread of AMR in the EU. I find that a 1% increase in air pollution leads to about a 0.7% increase in the prevalence of AMR. Equivalently, a 1µg/m3 increase in PM2.5 concentration causes average AMR to increase by about 0.94 percentage points in my most conservative estimate.

However, I also find that different pathogen-antibiotic combinations vary considerably in their response to pollution. Stricter pollution standards would help contain the spread of resistance to some second and third-line antibiotics and limit the diffusion of some of the most deadly resistant bacteria, such as MRSA.

When antibiotic consumption is accounted for, the direct influence of air pollution on AMR remains sizable and significant: a 1% increase in PM2.5 causes AMR to increase by 0.24% to 0.34%.

My counterfactual results show that AMR would have been 2.3 percentage points lower, had the EU capped PM2.5 concentration at 10 µg/m3 in the same period. To obtain an equivalent reduction in resistance, the EU would have needed to reduce antibiotic use by about 22.6% in each country.

*How do you plan to extend the scope of your analysis?*

Future versions of this paper will incorporate the impact of antibiotic use in animal farming and other agricultural activities. Although human antibiotic use is the main driver of resistance, veterinary use still accounts for approximately 60% of total antibiotic consumption in European countries.

Another valuable extension would involve estimating the costs and benefits of alternative strategies for reducing pollution. Moving beyond this paper's focus on pollution standards, future research could evaluate other types of environmental policies.

**Stricter pollution standards would help contain the spread of resistance to some second and third-line antibiotics and limit the diffusion of some of the most deadly resistant bacteria, such as MRSA**

City smog: Temperature inversions can trap air pollution

*Reference: "Invisible Threat: How Airborne Pollution Fuels Antimicrobial Resistance in the EU". Other publications are available to read on the webpage of the TSE Health Center.*

## KEY POLICY INSIGHTS

- This research provides the first causal evidence that air pollution is increasing AMR rates in the EU.
- The role of air pollution in driving AMR is almost as important as antibiotic use.
- Anti-pollution measures – in particular, adhering to WHO air quality standards – can dramatically reduce the spread of AMR.
- If cost-benefit analyses ignore the causal impact of pollution on AMR, policymakers will undervalue the benefits of cleaner air.
- Existing estimates on the costs of air pollution are likely to be a lower bound.

# About the author

**Ilaria Natali**

Ilaria is a postdoctoral research fellow at TSE. She is an applied microeconomist with interests in health economics, environmental economics, and industrial organization. Her research studies the socioeconomic and policy determinants of drug consumption and health outcomes, as well as the role of pharmaceutical advertising in the healthcare sector. More recent work focuses on the antibiotics market and the spread of AMR.

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# Previous issues

**#November 2022**

**Can transferable patent extensions solve the market failure for antibiotics?**

In this first issue of the journal, Jean Tirole, Pierre Dubois, & Paul-Henri Moisson propose vouchers for rewarding innovation that could be transferred to another pharmaceutical company, giving it the right to extend the period of exclusivity of one of its drugs.

Find out more

**#November 2023**

**How does antimicrobial resistance impact demand for antibiotics?**

**Can cooperatives aid the search for new antibiotics?**

This issue features research by Pierre Dubois, Gokçe Gokkoca, Paul-Henri Moisson & Jean Tirole. Their findings highlight the collective mechanisms that can ensure that all countries, businesses and global citizens embrace the need to change the way we use antibiotics.

Find out more

# Health Center

## Economics of antibiotics & antibioresistance journal

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