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“Invisible Threat: How Airborne Pollution Fuels Antimicrobial Resistance in the EU”

Ilaria Natali

Toulouse School of Economics

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Ilaria Natali*

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Abstract

Recent scientific research suggests that the environment represents an important pathway for the spread of antimicrobial resistance (AMR). This paper is the first to provide causal estimates of the impact of fine particulate matter ($PM_{2.5}$) on AMR diffusion. I focus on EU countries and the period 2002 to 2019. To pin down causal effects, I use an instrumental variable approach that exploits temperature inversions as a source of exogenous shocks to air pollution. I find that a 1% increase in $PM_{2.5}$ leads to about a 0.7% increase in average antibiotic resistance, but there is significant heterogeneity across pathogen-antibiotic combinations in their responsiveness to changes in pollution. I then separately estimate the *direct* impact of pollution on resistance, as well as the impact of an *indirect* channel via antibiotic consumption. When antibiotic use is accounted for, the *direct* influence of air pollution on AMR remains sizable and significant. Finally, I provide a counterfactual analysis assessing the impact of alternative air pollution control policies on resistance and compare their effectiveness vis-à-vis interventions aimed at reducing antibiotic use in humans. Findings imply that air pollution policies can be fruitfully leveraged in the fight against AMR propagation.

JEL Codes: I12, I18, Q51, Q53.

*Toulouse School of Economics (TSE), Université Toulouse 1 Capitole.

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1 Introduction

Antimicrobial resistance (AMR) is currently one of the most pressing public health challenges, imposing immense societal costs and cumbersome pressure on economic systems worldwide. Likely to reach the magnitude of a pandemic in the near future, it is currently causing around 35,000 deaths every year among EU patients only (ECDC (2022)). This figure stands at 700,000 annual deaths globally and could reach 10 million in the absence of adequate policies (O'Neill (2016)). The economic burden attributable to antibiotic-resistant bacteria is estimated to be 1.5 billion annually in the EU alone (ECDC/EMEA (2009)). These costs are related to longer hospital stay, more complex treatment, as well as reduced productivity at work and labor force participation. The World Bank considers AMR as a threat to the global economy that could cause the global annual GDP to fall by up to 3.8% by 2050 (WorldBank (2017)). While overprescribing and overconsumption of antibiotics are deemed to be the main responsible for rising AMR rates,[1] little is known about other potential risk factors. However, recent scientific research suggests that the environment represents an important pathway for AMR propagation.

This paper studies the causal relationship between air quality and the spread of antimicrobial resistance (AMR) in EU countries during the period 2002 to 2019. My identification strategy allows me to estimate both the *total* impact of air pollution on resistance and to disentangle the *direct* and *indirect* channels through which air pollution affects antimicrobial resistance. I further provide a counterfactual analysis estimating the impact of alternative air pollution control policies, and I compare the effectiveness of these policies with that of interventions aimed at regulating antibiotic consumption in humans.

I focus on fine particulate matter, or $PM_{2.5}$ (airborne particulate matter with a diameter of less than 2.5 µm), as a proxy for air quality since this pollutant is found to be the most detrimental to human health and a significant contributor to morbidity and mortality. Concentration levels for this pollutant are considered as a general measure of exposure to air pollution (WHO (2016)), they are extensively used for air-quality assessments and in research evaluating the impact of air

[1] Antimicrobial resistance (AMR) is defined as the ability of bacteria to resist the drugs meant to kill them. Large consumption of antibiotics imposes selective pressure on bacteria that develop resistance as a result of adaptation and natural evolution. AMR implies that even routine hospital procedure may become dangerous and potentially deadly.

pollution on health and economic outcomes.[2] Moreover, the particularly small size of airborne $PM_{2.5}$ particles allows them to easily penetrate the human body. This may also permit the entry of antibiotic-resistant strains via inhalation, facilitating the dissemination of AMR.

To establish causality, I exploit an instrumental variables approach that uses temperature inversions as excluded instruments. Temperature (or thermal) inversions are atmospheric phenomena that occur when a layer of cooler air remains trapped under a layer of warmer air. Under normal atmospheric conditions, there is an inverse monotonic relationship between altitude and temperatures: within the troposphere (the lowest layer of the atmosphere), temperatures decrease as we move up to lower pressure levels at higher altitudes. When a temperature inversion occurs, this relationship is reversed so that the mass of warmer air keeps pollution near the surface, significantly worsening the quality of the air. The relationship between thermal inversions and pollution has been widely documented in the literature. Figures 2 and 3 in Appendix A provide a graphical representation of these phenomena. Because this is a purely atmospheric phenomenon, an inversion can be thought of as producing random (non-anthropogenic) variation in air quality levels. As discussed later in the paper, temperature inversions are among the best meteorological predictors for air quality. Moreover, they do not directly affect health and can only influence resistance via increases in air pollution once the effect of other weather conditions has been appropriately netted out.

The analysis proceeds in a few steps. I first estimate the causal effect of air pollution on average antibiotic resistance. After providing these baseline results, I perform a heterogeneity analysis to investigate whether different pathogen-antibiotic combinations exhibit different sensitivities to exogenous changes in air pollution. In a third step, I distinguish between *direct* and *indirect* channels through which air pollution influences antibiotic resistance. Indeed, the positive shock in air pollution induced by temperature inversions may cause a contemporaneous negative shock in individual health and lead people to use more antibiotics. If this is the case, the baseline estimates capture the *total* impact of pollution on resistance, which encompasses both the *direct* influence of pollution on AMR and the impact of an *indirect* channel through increases in antibiotic use.[3] Since antibiotic consumption in humans is observed, I can introduce this variable into

[2] See literature review below.

[3] In the reminder of the paper, I will use the terms antibiotic consumption, antibiotic sales, and antibiotic use interchangeably, although actual consumption by individuals cannot be observed.

the analysis and separately estimate the contributions of these two (*direct* and *indirect*) channels. To address potential endogeneity in antibiotic consumption, I exploit the exogenous variation in air pollution generated by lagged temperature inversions. Introducing antibiotic consumption allows me to compare the importance of air pollution versus antibiotic consumption in affecting AMR patterns, and it is useful for the counterfactual analysis in the following step. In this final step, I perform a counterfactual analysis focusing on three important EU objectives. First, the EU is currently planning to set the annual limit value for $PM_{2.5}$ concentration at 10 $\mu g/m^3$ to be achieved by 2030. These new rules are meant to make existing standards more closely aligned with the latest World Health Organization (WHO) recommendations that set the limit at 5 $\mu g/m^3$ (WHO (2021)). I consider, therefore, capping $PM_{2.5}$ concentration at 5 $\mu g/m^3$ as the second EU objective under study. Third, another objective the EU is currently trying to achieve is to reduce antibiotic consumption in humans in each Member State by 20% by 2030.

I find that air pollution is an important contributor to the spread of AMR in the EU. Results from the baseline analysis show that a one percent increase in air pollution leads to about a 0.7% increase in the prevalence of AMR. Equivalently, a one $\mu g/m^3$ increase in $PM_{2.5}$ concentration causes average antibiotic resistance to increase by about 0.94 percentage points in the most conservative estimate. However, there is significant heterogeneity across pathogen-antibiotic combinations in their responsiveness to changes in pollution. When introducing antibiotics consumption in the analysis, I find that the coefficient associated with $PM_{2.5}$ concentration decreases, but the *direct* influence of air pollution on AMR remains sizable and significant. Estimated coefficients for pollution now range between 0.24 and 0.34, meaning that a one percent increase in $PM_{2.5}$ causes antimicrobial resistance to increase by 0.24 to 0.34%. Results from the counterfactual analysis show that antibiotic resistance would have been approximately 2.33 percentage points lower, had the EU regulation capped $PM_{2.5}$ concentration at 10 $\mu g/m^3$ during the period under study. An equivalent reduction in resistance would have been obtained by reducing antibiotic use by about 22.6% on average in each country.

The contribution of this paper is two-fold. First, this paper contributes to the growing health economics literature on antibiotics and antibiotic resistance by identifying potential risk factors (other than antibiotic use) driving AMR diffusion. Although research in the medical literature shows a positive and significant relationship between air pollution and resistance, causal evidence

has never been provided before. The IV estimation procedure allows to correct for a number of potential threats to identification related to measurement error in air pollution and omitted variables (Graff Zivin & Neidell (2013)) and provide the first causal estimates of the impact of air pollution on AMR. Second, to the best of my knowledge, the impact of specific environmental policies on the evolution of AMR in the EU has never been previously assessed. This is a timely question to be addressed in light of the EU's recent commitment to reduce both pollution and antibiotics use.

This analysis highlights the critical importance of considering the adverse effects of air pollution on AMR diffusion in cost-benefit evaluations of air pollution reduction policies. Any analysis in this sense would severely underestimate the benefits of imposing stricter pollution standards by overlooking their role in curbing AMR. Establishing causality is essential to accurately inform the cost-benefit assessments of air quality policies based on these estimates.

Related Literature. This paper contributes to a few strands of the health economics literature. First, there exists a well-developed literature on the environmental determinants of health, where the association between air pollution and poor health conditions is widely recognized. Prior work has shown that exposure to air pollution leads to significant increases in mortality rates as well as in the incidence of respiratory infections and cardiovascular diseases (Deryugina et al. (2019); Hicks et al. (2016); Schlenker & Walker (2016); Heutel & Ruhm (2016)). There is also a rich literature focusing specifically on the adverse consequences of air pollution on infant health, as reflected in rates of infant and neonatal mortality and hospitalizations in the US and the developing world (Currie & Neidell (2005); Currie, Neidell & Schmieder (2009); Chay & Greenstone (2003); Arceo et al. (2016); Lleras-Muney (2010)). Jans et al. (2018) show how this association is more important for children in disadvantaged socioeconomic status, while Knittel et al. (2016) show that the presence of suspended particles has a more significant impact on premature and low-birth-weight infants. Moreover, recent studies indicate that air pollution has notably contributed to the diffusion of the COVID-19 pandemic (Austin et al. (2023); Persico & Johnson (2021); Travaglio et al. (2021)).

This paper is also related to extensive research documenting the harmful effects of pollution on economic and labor market outcomes. Several papers explore how poor air quality impacts

productivity, with effects on both low- (Adhvaryu et al. (2022); Chang et al. (2016); Chang et al. (2019); He et al. (2019); Zivin & Neidell (2012)) and high-skilled workers (Holub & Thies (2023); Sarmiento (2022); Heyes et al. (2016); Heyes et al. (2019)). Other studies examine its effects on educational attainment (Ebenstein et al. (2016)) and absenteeism at school (Currie, Hanushek, Kahn, Neidell & Rivkin (2009); Ransom & Pope III (1992)) and at the workplace (Holub et al. (2021); Aragón et al. (2017); Hanna & Oliva (2015)). Some researchers evaluate the impact of air pollution control policies on the labor market (Walker (2013)).

This study further contributes to the emerging literature on antibiotics and antibiotic resistance. Much of the existing research so far focuses on physicians' prescribing and antibiotics consumption (Adda (2020), Huang & Ullrich (2024), Bennett et al. (2014)), on the effectiveness of policies aimed at influencing antibiotic prescriptions (Gökkoca (2022), Ellegård et al. (2018), Bokhari et al. (2024)), and on incentives to spur innovation of novel antibiotics (Majewska (2022), Dubois et al. (2022), Simpkin et al. (2017)), as well on the appropriate size of these incentives (Outterson (2021)). Other studies investigate how physicians' awareness of AMR influences their prescribing behavior (Dubois & Gökkoca (2023), Filippini et al. (2009), Howard (2004)). However, as far as I know, understanding of potential factors determining antimicrobial resistance (other than antibiotic use) is still extremely limited.

Recently, it has been suggested that antibiotics consumption control and stewardship programs alone will not be enough to curb AMR in the future, as the transmission of resistant bacteria and genes through the environment represents a primary driver of AMR (Collignon et al. (2018), Merlin (2020)). One potential environmental pathway is given by the air. Some recent research shows that $PM_{2.5}$ can carry significant quantities of antibiotic-resistant bacteria and antibiotic-resistant genes (Li et al. (2018)).[4] This can be due to the emission of antibiotic-resistant genes (ARGs) from several sources as a result of evaporation or aerosolization (McEachran et al. (2015)).[5] Traffic exhaust can also favor the horizontal transmission of ARGs between bacteria (Zhang et al. (2018)).[6] Hu et al. (2018) find that antibiotic-resistant

[4] Antibiotic resistant genes are genetic sequences enabling bacteria to resist the effects of antibiotics.

[5] Aerosolization is defined as the process through which some physical substance is transformed into small and light particles that can be carried on the air.

[6] Horizontal gene transfer (HGT) is defined as the movement of genetic information between organisms, a process that includes the spread of antibiotic resistance genes among bacteria, fueling pathogen evolution (Burmeister (2015)).

genes were more abundant in $PM_{2.5}$ during days with high smog concentration in Beijing and suggest that this may be because suspended particles provide more adhesion sites for bacteria to remain more stably suspended in the air. Jin et al. (2022) offer a comprehensive overview of these recent findings. Although important, these papers mostly rely on samples of pollutants collected in specific locations at a specific point in time. As a consequence, they cannot quantify the impact of increasing pollution on resistance at a more aggregate level, and nothing can be concluded on the evolution of this relationship over time. One attempt in this direction is given by Zhou et al. (2023). This paper represents the first large-scale study providing correlational evidence on the relationship between pollution and AMR. Besides this, the literature on this topic is still incredibly thin and, to the best of my knowledge, no causal estimates have been provided thus far.

Outline. The rest of the paper proceeds as follows. Section 2 provides background information on $PM_{2.5}$ and its relationship with temperature inversions, as well as a brief description of the EU regulations on air pollution. Section 3 provides an overview of the data collected for this study. In Section 4, I provide descriptive statistics, while in Section 5, I introduce the research design. Baseline results are provided in Section 6, while a heterogeneity analysis across different pathogen-antibiotic combinations is provided in Section 7. Section F first introduces and discusses the role of antibiotic consumption and then discusses results from the counterfactual policy analysis. Section 9 concludes.

2 Background Information

2.1 Fine Particulate Matter ($PM_{2.5}$)

Air pollution is currently the leading environmental threat to human health, causing numerous premature deaths as well as a wide range of diseases in Europe and worldwide. Enhancing air quality standards and reducing pollution levels are priority objectives under the United Nations Sustainable Development Goals (SDGs) that target to substantially reduce pollution-related mortality by 2030.[7] In the calculation of its Air Quality Index, the European Environmental Agency includes pollutants such as ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), particulate matter with diameter of less than ten µm (PM_{10}), and particulate matter with diameter of less than 2.5 µm ($PM_{2.5}$). Among these, $PM_{2.5}$ is predominantly responsible for the adverse health effects associated with air pollution, and no concentration level of this pollutant can be considered safe (WHO (2016)). In 2021, 97% of the EU's urban population was still exposed to concentration levels of fine particulate matter above the WHO recommended limits, with an estimated 240,000 premature deaths attributed to this pollutant alone each year.[8] $PM_{2.5}$ is a complex combination of solid and liquid components with a varied chemical structure that remain suspended in the air. These fine particles can originate from primary (e.g., combustion of fossil fuels or wood, dust from roads and constructions, wildfires) or secondary sources (through chemical reactions of other gaseous pollutants, such as sulfur dioxide, that are produced by power plants or industries). Because these particles are extremely thin (about 1/40th the diameter of a human hair), they have the ability to penetrate deep into the lungs and even enter buildings through doors, windows, and cracks/gaps in building structures.[9] For this reason, particulate matter is a major cause of respiratory and cardiovascular diseases, asthma, acute and chronic bronchitis, and, more in general, physical and cognitive impairment.[10] Due to their exceptionally small size, PM2.5 particles are also likely to transport antibiotic resistant elements from the environment into the human body.

[7] See `https://www.un.org/sustainabledevelopment/health/`.

[8] `https://www.consilium.europa.eu/en/policies/air-quality/`

[9] Hoek et al. (2008) find significant correlation between outdoor and indoor $PM_{2.5}$ concentrations in four European cities.

[10] `https://ww2.arb.ca.gov/resources/inhalable-particulate-matter-and-health`.

2.2 Pollution & Temperature Inversions

Temperature inversions are meteorological phenomena driven primarily by the (vertical and horizontal) large-scale movement of air masses. They also commonly occur overnight as the Earth's surface cools more rapidly than the air above it, resulting in cooler air near the ground being trapped beneath a warmer layer above. This inversion layer limits vertical air circulation, trapping pollutants close to the ground and contributing to poor air quality. The relationship between temperature inversions and poor air quality is well established in the literature. For instance, Gramsch et al. (2014) find significant correlations between thermal inversions and concentrations of black carbon and $PM_{2.5}$. Similarly, Kukkonen et al. (2005) study PM_{10} concentrations in four European cities and identify temperature inversions as the best meteorological predictors for air quality. As a matter of fact, temperature inversions are considered to be co-responsible for some of the most catastrophic pollution events in human history, such as the Great Smog of 1952 in London, the 1948 Donora Smog, or the extreme $PM_{2.5}$ concentration levels observed in Cache Valley in January 2004 (Malek et al. (2006)). Approximately 12,000 excess deaths are attributed to the lethal London fog (Bell & Davis (2001)), while the Donora smoke event led to 20 deaths and left around 6,000 individuals seriously ill (Jacobs et al. (2018)). The Donora incident directly influenced the establishment of the first US Clean Air Act in 1963 (Kuklinska et al. (2015)).

In the analysis of this paper, I will distinguish between winter and summer inversions since these phenomena exhibit high seasonality. Winter inversions are typically more frequent, intense, and persistent than those in summer.[11] Consequently, winter inversions tend to have a more substantial impact on pollution levels and health outcomes than summer inversions. For example, Wallace & Kanaroglou (2009) find that both daytime and nighttime inversions significantly increase concentration levels for $PM_{2.5}$ and NO_2, but this effect is more pronounced during the winter. Silva et al. (2007) also report that strong winter inversions were responsible for the severe air quality deterioration in Utah in 2004.

[11] `https://en.ilmatieteenlaitos.fi/temperature-inversions`.

2.3 EU pollution control policies

The European Union has made efforts to address air quality issues for more than 40 years now, with the first directive on air quality dating back to 1980 (Directive 80/779/EEC). During the following years, additional directives have been approved to regulate and pose limits to the emissions of several pollutants (Kuklinska et al. (2015)). The most recent piece of regulation is the 2008 directive on ambient air quality and cleaner air for Europe (Directive 2008/50/EC), which came into force in June 2010. Regulating levels of particulate matter in the air was one crucial priority of this directive. This regulation imposes a limit value for $PM_{2.5}$ concentration of 25 $\mu g/m^3$ as an annual average to be met as of 2015 (January 1st) and proposes an indicative limit value of 20 $\mu g/m^3$ to be met as of 2020 (January 1st).[12] More recently, in October 2022, the European Commission presented a proposal to merge and revise the previous directives, while in February 2024, the Council and the European Parliament reached a provisional political agreement on this proposal.[13] Among others, the main goal of this revision consists of updating and strengthening the existing standards (target and limit values) to make them more closely aligned with the latest WHO recommendations and the zero-pollution action plan adopted by the EU in May 2021. Indeed, the 2021 World Health Organization (WHO (2021)) air quality guidelines suggest a level of $PM_{2.5}$ concentration not exceeding 5 $\mu g/m^3$, while the zero-pollution action plan aims at significantly reducing air, water, and soil pollution by 2050 to create a toxic-free environment, thus impeding pollution to cause harm to human health and natural ecosystems. For $PM_{2.5}$, the new rules would set the annual limit value at 10 $\mu g/m^3$ to be achieved by 2030.

[12] https://eur-lex.europa.eu/eli/dir/2008/50/oj

[13] https://www.consilium.europa.eu/en/press/press-releases/2024/02/20/air-quality-council-and-parliament-strike-deal-to-strengthen-standards-in-the-eu/

3 Data

The analysis in this paper exploits several sets of national-level data covering 24 European countries for the period 2002 to 2019.[14] The data can be broadly classified into four groups: data on antimicrobial resistance, pollution data, weather data, and information on additional control variables. This information is collected from various sources, with details provided in the following subsections.

3.1 Resistance Data

Antibiotic resistance data are obtained from ResistanceMap (OneHealthTrust (2024*a*)). ResistanceMap is an open-source web-based database providing comprehensive information on antimicrobial resistance (AMR) across various countries globally and spanning the years 1999-2021.[15] These data are sourced from public and private laboratory networks that routinely collect results from AMR tests. Resistance data are presented as percentages, calculated by dividing the number of tested isolates (from blood, cerebrospinal fluid, or both) exhibiting non-susceptibility (intermediate or resistant) to a specific antibiotic class by the total number of tested isolates.[16] The information is harmonized to facilitate comparison across countries.[17] I select data for the 24 European countries and the time period under study, and for 5 bacterial species (*Enterococcus faecalis*, *Enterococcus faecium*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*). In most of the analysis, I consider an aggregate measure of resistance as my outcome variable, given by the average resistance rate across all pathogens and antibiotic classes in each country and year. In the heterogeneity analysis, instead, I consider resistance rates for each pathogen-antibiotic pair.

[14] The dataset covers a total of 24 countries: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Poland, Portugal, Romania, Slovenia, Spain, and Sweden.

[15] The website is made available by One Health Trust, a public health research organization, and, currently, a WHO Collaborating Center for antimicrobial resistance.

[16] Tested isolates are bacteria isolated from samples of blood, cerebrospinal fluid or both. These bacteria are subject to antibiotic susceptibility testing to find out whether they are susceptible (and, hence, can be treated using antibiotics), intermediate (can be treated with antibiotics but may require adjusted dosages) or resistant (and, hence, cannot be treated with antibiotics). Notice that resistance is defined as non-susceptibility to at least one antimicrobial agent in a class, although not all isolates were tested against every antibiotic in that class.

[17] Additional information can be found at `https://resistancemap.onehealthtrust.org/Methodology.php`.

3.2 Pollution Data

Fine Particulate Matter (PM2.5). I focus on $PM_{2.5}$ as the primary pollutant of interest. High-quality $PM_{2.5}$ concentration data are made available by van Donkelaar et al. (2021) for the period 1998-2022.[18] This dataset provides $PM_{2.5}$ concentration measures by employing a 'hybrid' approach that combines satellite aerosol optical depth (AOD) retrievals and chemical transport modeling with ground monitor-based calibration. This methodology is used to compensate for the relative paucity of ground-based monitors and guarantees the high quality of $PM_{2.5}$ global estimates. The dataset provided by these researchers is among the most accurate currently available. I retrieve information on $PM_{2.5}$ annual concentration for European countries from the Annual Global country-level mean $PM_{2.5}$ summary files.

Other Pollutants. To account for other 'criteria' pollutants, I use air quality monitoring station data from the European Environmental Agency's (EEA) database, AirBase. The EEA provides information on readings from a network of monitoring stations. These stations are located in both urban and rural settings to capture concentrations across diverse environments. The World Health Organization (WHO (2021)) identifies particulate matter ($PM_{2.5}$ and PM_{10}), ozone (O_3), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) as the most critical pollutants from a public health perspective. These are also the key criteria pollutants the EU considers in calculating its air quality index and the five main pollutants regulated by European air quality legislation. For this reason, I focus on these pollutants for my analysis. Information is aggregated by considering average concentrations across all monitoring stations for each pollutant in each country and year.

3.3 Weather Data

Temperature Inversions. Gridded data for temperature inversions are collected from NASA's MERRA database (Global Modeling & Assimilation Office (2015)). This database provides information on daily air temperature for 42 pressure levels and each grid cell, with spatial resolution 0.5° x 0.625° (corresponding to about 50 kilometers). I select data for all grid cells

[18] I use version V6.GL.02.

covering Europe and for all altitude levels between the surface (usually 1000 hPa) and 600 hPa. This is because the normal monotonic inverse relationship between temperatures and altitude holds within the troposphere. Beyond that limit, temperatures remain constant or even increase with altitude.[19] I consider two alternative definitions of temperature inversions. First, I say that a temperature inversion occurs if the temperature at the second lowest level of the atmosphere is higher than at the surface (henceforth called surface inversions). In a second definition, I say that a temperature inversion occurs if the temperature at any level above the surface is higher than at the surface. It is important to note that surface pressure typically corresponds to 1000 hPa. However, in some cases, MERRA does not report temperature measures at this pressure level. This is because, in some areas, the land surface may be elevated, or the area may be characterized by a low-pressure system. In these cases, I consider the temperature difference between the lowest level for which the information is available and the level(s) above that one. To build the inversion instruments, I proceed in several steps. First, I aggregate temperature data for each altitude at the NUTS3-region level.[20] Despite being very granular, the resolution of these data does not allow to cover all NUTS3 regions in Europe. When no gridded data point overlies a NUTS3 region, I consider the closest point to the region's centroid for which information is available. When, instead, more than one gridded data point overlies a NUTS 3 region, I consider the average temperature across these points for each pressure level. I then count the number of days during a year in which an inversion has occurred for each NUTS 3 region. I also consider the inversion intensity, defined as magnitude of the temperature difference between different pressure levels. To derive an annual measure of population exposure to temperature inversions (and, hence, to poor-quality air), I aggregate the information by considering a weighted average, where the weights are given by the ratio between the population of each NUTS 3 region and the total country population. This approach allows to capture variation in local population exposure to temperature inversions while ensuring accurate aggregation to the national level. The sets of instruments used in the analysis exploit all the information collected and described above, and is reported in Table 4.

[19] The threshold of 600 hPa has been chosen based on the previous literature (Dechezleprêtre et al. (2019)).

[20] NUTS means Nomenclature of territorial units for statistics, and divides the territory of the EU into regions at three different levels. Hence, NUTS 3 represent the smallest geographical units. There are 1166 NUTS 3 regions in Europe.

Weather Controls. To control for weather conditions, I exploit gridded meteorological data made available by the Joint Research Center of the European Commission, covering all EU member states for a period of 30 years. I extract monthly data for mean air temperatures (°C), max temperature (°C), cumulated daily precipitations (mm/day), and mean wind speed at 10 m (m/s). The spatial resolution for these data is 0.31° x 0.31°, corresponding to 25km x 25 km. Moreover, I include information on specific humidity (g/kg) from the NASA's MERRA database (Global Modeling & Assimilation Office (2015)), with spatial resolution 0.5° x 0.625°.[21] The aggregation is done in a similar fashion as for the temperature inversion data. That is, I first aggregate the information at the NUTS3-region and year level. To measure the country's population exposure to different weather conditions, I then consider weighted averages, where the weights are given by the ratio between the population of each NUTS 3 region and the total country population.

3.3.1 Antibiotics Consumption

Antibiotic consumption data are also obtained from ResistanceMap (OneHealthTrust (2024*b*)) and sourced from the IQVIA MIDAS database. These data provide information on antibiotic sales in 76 countries and from 2000 to 2015. Due to this limitation, the analysis in Section F is constrained to the years 2002-2015. Information is provided in terms of Defined Daily Doses (DDDs) per 1,000 inhabitants[22] and refers to both the retail and hospital sectors. I consider data on consumption for all antibiotics. This includes 18 antibiotic classes: aminoglycosides, broad-spectrum penicillins, carbapenems, cephalosporins, chloramphenicols, glycopeptides, glycylcyclines, lipopeptides, macrolides, monobactams, narrow-spectrum penicillins, oxazolidinones, phosphonics, polymyxins, quinolones, tetracyclines, trimethoprim and combinations, other antibiotics.[23]

[21] Specific humidity is a measure of the moisture content in the air and it is calculated as the mass of water vapor in a given mass of air. It is expressed here in terms of g/kg, that is, the amount of grams of water vapor in a kilogram of air.

[22] A DDD represents the daily dosage of a drug for its main indication in adults.

[23] The interested reader can refer to `https://resistancemap.onehealthtrust.org/MethodologyAU.php` for further information on data and methods used to calculate antibiotic consumption, and on the allocation of specific antibiotic molecules into each class.

3.4 Other Controls

Data for the remaining control variables are downloaded from the World Bank database. I consider the following demographic and health-related variables: population density (people per square kilometer of land area), rural population, population aged 65 and above (percentage over total population), number of international tourism arrivals, per capita healthcare expenditure (in current US dollars), and physicians' density (number of doctors per 1,000 people).

4 Descriptive Statistics

Tables 1 to 3 report descriptive statistics for all the variables used in the analysis of this paper, where the unit of observation is country-year. Our main variables of interest are antibiotic resistance, $PM_{2.5}$ concentration, and antibiotic consumption. Table 1 presents summary statistics for these variables, as well as all covariates and instrumental variables. Table 2 displays the average resistance, pollution, and antibiotic use during the sample period for each country separately. Finally, Table 3 provides resistance figures for each pathogen-antibiotic class combination.

Table 1 shows that the average resistance across all the pathogen-antibiotics combinations under study is 24.4%, even though there is substantial variations across countries and time periods, going from a minimum of zero to a maximum of 71%. From Table 2, we see that resistance rates for some countries, such as Romania and Greece, are exceptionally high. Resistance in Romania equals 48.14%, meaning that about half of the tested bacteria are non-susceptible to antibiotic treatment. This figure is double the average over the whole sample and more than four times larger than the country with the lowest resistance level (i.e, Denmark). As for $PM_{2.5}$ concentration, the average at the EU level equals 13.4 $\mu g/m^3$, but, again, there is substantial variation across countries and years. Most countries in Western Europe (e.g., Germany, France, Austria, Belgium) exhibit concentration levels just above the 10 $\mu g/m^3$ limit that the EU regulation wants to impose in the near future. For Northern European countries plus Spain, instead, the EU policy would be barely binding, while for Sweden and Finland not even the WHO's cap at 5 $\mu g/m^3$ represents a constraint. On the other hand, Eastern European countries, such as Poland, Bulgaria, Romania, and Hungary, represent the high polluters in Europe. The new EU rules would force these countries to reduce pollution concentrations by about half.

Table 1: Descriptive Statistics - All Variables

	Obs	Mean	SD	Min	Max
Main Variables					
Resistance (%)	426	24.40	10.64	0	71
Pollution ($PM_{2.5}$ in $\mu g/m^3$)	432	13.39	4.852	3.600	26.20
Antibiotics Consumption (DDDs per 1,000 inh.)	330	8,646	2,995	3,930	15,908
Covariates					
Population 65+ (%)	432	17.42	2.412	10.68	23.06
Population Density (people per sq. Km)	432	127.8	107.4	17.07	515.1
Rural Population (in 100,000)	432	4.832	5.869	0.0544	20.31
(per capita) Health Expenditure (current US$)	432	2,736	1,942	96.58	7,671
PM10 ($\mu g/m^3$)	424	26.58	9.641	5.765	95.85
SO2 ($\mu g/m^3$)	426	5.119	3.927	0.264	25.40
NO2 ($\mu g/m^3$)	426	22.77	6.318	4.229	44.65
O3 ($\mu g/m^3$)	426	51.48	6.431	8.036	73.57
(mean) Temperature (°C)	432	10.51	2.885	2.938	16.92
(mean) Max Temperature (°C)	432	14.68	3.397	6.366	22.25
(mean) Precipitation (mm/day)	432	57.18	15.45	27.45	128.6
(mean) Wind Speed (m/s)	432	3.089	0.770	1.524	5.321
(mean) Specific Humidity (g/Kg)	432	5.084	1.276	1.003	8.189
Physicians (per 1,000 inh.)	432	3.494	0.800	2.115	6.247
Tourism Arrivals (in 100,000)	432	30.98	43.03	0.805	217.9
Total Population (in 100,000)	432	18.07	22.13	0.446	83.09
Instruments					
# Surface Inversions	432	71.63	27.04	12.31	143.9
# Inversions at any Altitude	432	83.01	30.88	13.57	172.0
# Winter Inversions at any Altitude	432	57.85	24.16	6.29	118.54
Intensity of Inversions at any Altitude	432	1.184	0.301	0.477	2.331
Number of Countries	24	24	24	24	24

Table 2: Descriptive Statistics - Main Variables

Country	Resistance (%)	Pollution ($PM_{2.5}$)	Antibiotic Use (DDDs)
AUSTRIA	17.25	12.95	6,820
BELGIUM	18.02	13.20	11,759
BULGARIA	33.39	22.13	7,929
CROATIA	30.84	17.16	10,009
CZECH REPUBLIC	31.24	16.88	6,965
DENMARK	11.08	10.41	6,134
ESTONIA	15.18	9.08	4,360
FINLAND	11.59	4.99	6,990
FRANCE	19.27	11.31	12,941
GERMANY	22.27	13.17	6,391
GREECE	42.85	16.25	14,114
HUNGARY	28.65	19.26	7,611
IRELAND	23.57	8.11	10,752
ITALY	32.43	14.17	10,972
LATVIA	28.69	13.00	4,673
LITHUANIA	27.66	15.08	7,927
LUXEMBOURG	16.14	12.11	10,892
NETHERLANDS	14.68	13.92	4,290
POLAND	30.83	21.07	9,204
PORTUGAL	29.65	8.97	9,772
ROMANIA	48.14	18.32	11,955
SLOVENIA	21.60	15.72	6,346
SPAIN	20.39	9.82	12,767
SWEDEN	11.30	4.38	5,280

To conclude the discussion about the main variables of interest, EU countries consumed an average of 8,646 DDDs for every 1,000 inhabitants during the time period under analysis, going from a minimum of 3,930 to a maximum of 15,908 DDDs per 1,000 people. Once again, antibiotic consumption across European countries is highly heterogeneous. The largest use of antibiotics is observed in Greece, Spain, and France, with about 14/13,000 DDDs every 1,000 people. Instead, the most moderated use of antibiotics is observed in the Netherlands. The former consume, on average, about three times more antibiotics that the latter.

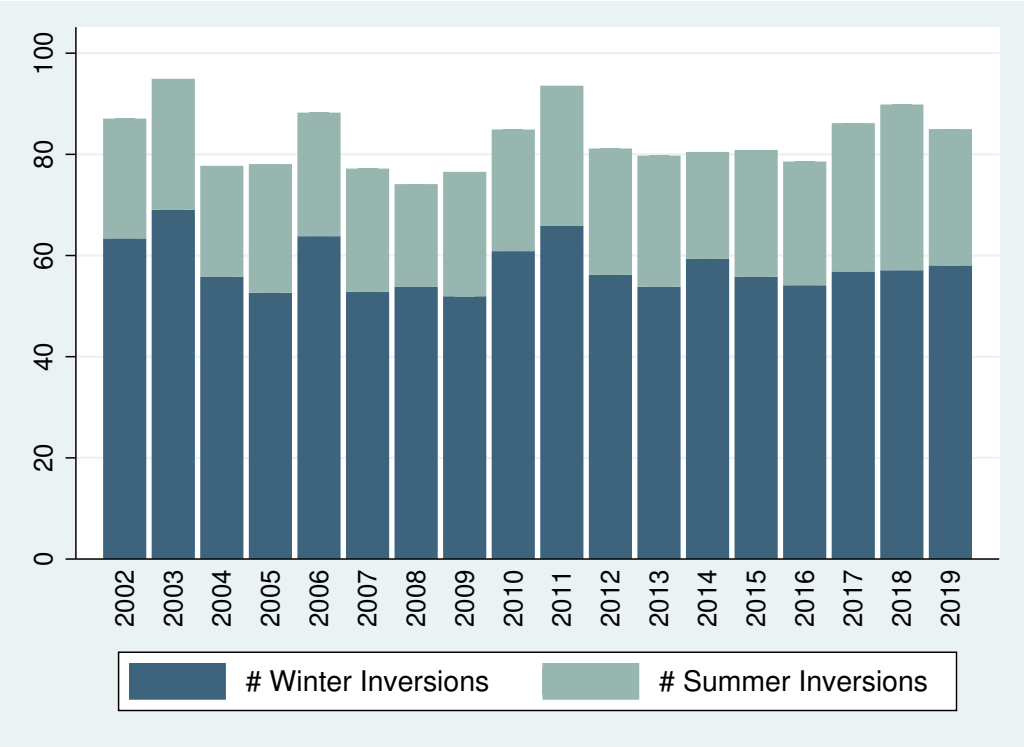
Table 1 also shows that thermal inversions vary widely in frequency and intensity across locations and years. This is important to ensure that the instruments have strong predictive power and well identify exogenous changes in pollution. European countries experience, on average, 83 temperature inversions per year. Among these, 72 occur near the surface. The minimum number

Table 3: Descriptive Statistics - Pathogen-Anntibiotic Pairs

	PATHOGEN				
ANTIBIOTIC	E. Faecalis	E. Faecium	K. Pneumoniae	P. Aeruginosa	S. Aureus
Aminoglycosides			27.50	19.48	
Aminoglycosides (High-Level)	34.43	46.23			
Aminopenicillins	3.30	86.52			
Carbapenems			5.42	23.17	
Ceftazidime				17.90	
Cephalosporins (3rd gen)			32.80		
Fluoroquinolones			31.98	24.34	
Oxacillin (MRSA)					18.77
Piperacillin-Tazobactam				20.76	
Vancomycin	1.30	10.57			
Total	13.01	47.77	24.43	21.13	18.77

of inversions is 14 a year, while the maximum equals 172, revealing substantial spatial and temporal variation. This can also be observed from Figure 4 in Appendix A. Each graph reports the number of thermal inversions at the NUTS 3 level for the most recent year in my dataset (that is, 2019) based on altitude and seasonality. The geographical distribution for the frequency of thermal inversions at any altitude closely mirrors the distribution for surface inversions. There are significant differences in the occurrence of these phenomena across countries, with Scandinavian and Eastern European countries experiencing inversions more frequently than Southern European countries (i.e., Italy and Greece). Due to the seasonal nature of thermal inversions, in the analysis that follows, I distinguish between winter and summer inversions. As mentioned, winter and summer inversions have different characteristics and may affect pollution differently. The two bottom graphs of Figure 4 in Appendix A, highlight differences in the distribution of winter and summer inversions across countries. Winter inversions are more frequent in Northern and Eastern countries, while summer inversions are more frequent in countries such as Spain and France. Moreover, inversions are more likely to take place during the winter than during the summer. This is evident from Figure 1, which reports the average number of winter and summer inversions across countries and for each year. The average number of winter inversions at any altitude is around 58 per year, whereas the average number of summer inversions is 25 per year.

Figure 1: Winter & Summer Inversions



Finally, Table 3 reveals that there is substantial heterogeneity in resistance rates across pathogen-antibiotic pairs in the EU. Among the pathogens under study, Enterococcus faecium and Klebsiella pneumonia exhibit the largest resistance rates, followed by Pseudomonas aeruginosa. Notice that, in the data, a distinction is made between aminoglycoside resistance and high-level aminoglycoside resistance (HLAR). This is because the two bacteria Enterococcus faecalis and Enterococcus faecium are usually resistant to low levels of aminoglycosides, implying that aminoglycosides alone are ineffective in treating infections caused by these pathogens and, hence, they must be used in combination with other antibiotics. High-level aminoglycoside resistance (HLAR) implies that aminoglycosides are ineffective even when used in combination. As can be seen from Table 3, high-level resistance to aminoglycosides is more prevalent in Enterococcus faecium than in Enterococcus faecalis. Moreover, since methicillin is no longer used due to the emergence of resistance, oxacillin (a beta-lactam antibiotic) is rather used to test for methicillin resistance in Staphylococcus aureus strains. This is because the two antibiotics act

in a similar fashion. If the Staphylococcus aureus strain is resistant to oxacillin, then it is said to be Methicillin-resistant Staphylococcus aureus (MRSA). This means that the pathogen is resistant to all beta-lactam antibiotics. Finally, Piperacillin-Tazobactam is a combination between a broad-spectrum penicillin (Piperacillin) and a beta-lactamase inhibitor (Tazobactam). Additional information on each antibiotic and pathogen is given in Table 11 of Appendix B. Due to differences in the prevalence of resistance and in the specific characteristics of each pathogen and antibiotic, causal estimates from my baseline analysis may be hiding important heterogeneity in the sensibility of different pathogen-antibiotic combinations to air pollution. Hence, in Section 7, I study each pair in isolation.

Descriptive statistics for the remaining covariates are also provided in Table 1.

5 Research Design

This section presents the baseline regression model used for the analysis in the rest of the paper, discusses potential endogeneity issues, and describes the IV estimation procedure.

Baseline Regression Model. As my outcome variable takes on nonnegative values and to model non-linearities in the relationship between outcome and regressors, I estimate the following Poisson model:

$$\mathbb{E}\left(R_{ct}\right) = exp(\alpha + \beta_1 log(PM_{2.5})_{ct} + \mathbf{D'_{ct}}\beta_2 + \mathbf{OP'_{ct}}\beta_3 + \mathbf{W'_{ct}}\beta_4 + \beta_5 R_{ct-1} + \gamma_c + \eta_t) \qquad (1)$$

where R_{ct} is the average antibiotic resistance level in country c and year t expressed in percentage terms, while $(PM_{2.5})_{ct}$ is the average particulate matter concentration, measured in $\mu g/m^3$. The coefficient of interest is β_1, and since $(PM_{2.5})_{ct}$ is taken in logarithmic terms, this coefficient can be interpreted in terms of elasticity. Vector $\mathbf{D'_{ct}}$ contains a set of demographic and health-related variables, such as population density, rural population, percentage of population aged 65 and above, number of tourism arrivals, physicians density, and per capita healthcare expenditure. These variables are likely to affect, positively or negatively, resistance rates, and they are of interest per se. For instance, international traveling is recognized to favor the spread of antimi-

crobial resistance, while investment in infection prevention policies is considered an important action to be undertaken to fight AMR.[24] Vector $\mathbf{OP'_{ct}}$ includes other important pollutants that may be correlated with $PM_{2.5}$ concentration and have their own impact on resistance. I consider PM_{10}, NO_2, SO_2, and O_3 concentration levels to encompass all the criteria pollutants included in the European Environmental Agency's Air Quality Index. Vector $\mathbf{W'_{ct}}$ considers a set of weather controls including mean air temperatures, maximum temperatures, precipitations, wind speed, and specific humidity that might correlate with air quality and affect resistance at the same time. For instance, precipitations are know to influence both air pollution and the spread of pathogens (Wu et al. (2016)). For the baseline results in Section 6, I progressively add sets of control variables, and, in the most complete specification, I also include lagged resistance, R_{ct-1}, on the right-hand side to account for the strong time dependence of resistance. In each regression, I further include a set of country and year fixed effects, γ_c and η_t, which allow to control, respectively, for time-invariant country characteristics and for shock or unexpected events common to all EU countries. For example, new air pollution policies have been applied to all EU countries starting from 2010.

In Tables 12 and 13 of Appendix D, I test the robustness of results across different specifications. I first fit the following linear model:

$$\mathbb{E}\left(R_{ct}\right) = \alpha + \beta_1 (PM_{2.5})_{ct} + \mathbf{C'_{ct}}\beta_2 + \mathbf{OP'_{ct}}\beta_3 + \mathbf{W'_{ct}}\beta_4 + \beta_5 R_{ct-1} + \gamma_c + \eta_t \tag{2}$$

Given the specification of equation (2), the magnitude of the coefficient β_1 should be interpreted here as the percentage point increase in resistance induced by a one unit increase (that is, a one $\mu g/m^3$ increase) in the level of $PM_{2.5}$. Moreover, since the dependent variable R_{ct} is expressed in percentage terms, and hence bounded between zero and 100, I also consider a fractional logit model as:

$$\mathbb{E}\left[\log\left(\frac{R_{ct}}{100 - R_{ct}}\right)\right] = \alpha + \beta_1 log(PM_{2.5})_{ct} + \mathbf{C'_{ct}}\beta_2 + \mathbf{OP'_{ct}}\beta_3 + \mathbf{W'_{ct}}\beta_4 + \beta_5 R_{ct-1} + \gamma_c + \eta_t \tag{3}$$

This specification allows to account for non-linearities in the relationship between antibiotic

[24] `https://www.cdc.gov/antimicrobial-resistance/causes/`

resistance and any of the predictors, as well as for the bounded nature of the outcome variable.[25] In equations (2) and (3), all the remaining right-hand side variables are defined as before, and standard errors are clustered at the country level. All regressions are weighted by the country population (Solon et al. (2015)).

When performing the heterogeneity analysis of Subsection 7, the dependent variable is given by resistance levels for each antibiotic-pathogen combination. The rest remains unchanged.

Instrumental Variable Estimation and Identification. Although the set of covariates in equations (1), (2), and (3) above allows me to control for a large pool of potential confounding factors, the estimated values for β_1 cannot be interpreted as causal due to the potential for omitted-variable bias and measurement error. Indeed, air quality is not randomly assigned across geographical areas, and hence, population exposure to pollution is likely to be endogenous. A number of unobservables related to residential sorting and individual behavior may bias the estimation in this resistance equation. Due to residential sorting, individuals with worse baseline health conditions may live in more polluted areas (e.g., people with lower socioeconomic status may live in more polluted countries). These individuals would be more vulnerable and more prone to infections or catching healthcare-associated germs while being treated for other conditions. They are also more likely to consume antibiotics and develop resistance. As a result, some geographical areas may feature higher air pollution and resistance rates due to these underlying mechanisms. By contrast, people living in less polluted areas may be more educated and better informed about the threats posed by antibiotic resistance. This could lead them to be more careful about antibiotic consumption[26] and more likely to adopt preventive measures aimed at curbing AMR, such as improving personal hygiene or paying extra attention to avoid infections.[27] Individual behavior also plays a role. If pollution concentration is predictable, individuals may

[25] To correct for the fact that resistance may equal zero, the left-hand side expression above is adjusted by augmenting both the numerator and denominator by one unit.

[26] Even when controlling for antibiotic sales, individuals may still consume antibiotics without a prescription, for example, because they get it from a friend or family or because they have some spared pills from previous prescription. Moreover, they could be doctor- or pharmacy-shopping. Controlling for this type of phenomena is a regression setting is a challenging task.

[27] According to the US Centers for Disease Control and Prevention, anti-microbial resistant germs can spread not only through antibiotic consumption, but also within healthcare facilities, through the food and the environment, as well as through international traveling. Measures to limit and eradicate AMR include improving personal hygiene, reducing the occurrence of infections, strengthening infection control systems at the national level, as well as enhancing information and awareness about infection prevention and control. See `https://www.cdc.gov/antimicrobial-resistance/causes/` for additional information.

adopt some defensive or avoidance behavior, such as reducing the time they spend outside (thus limiting social interactions).

To address these endogeneity concerns, I implement an instrumental variable approach that exploits random variation in air quality induced by the occurrence of temperature inversions. This type of instruments is widely used in the literature since temperature inversions are found to be excellent predictors of pollution. Since they are purely atmospheric phenomena, they produce non-anthropogenic and unpredictable shocks in air quality. Therefore, they are likely to be orthogonal to long and short-run determinants of health. In other words, thermal inversions determine positive random shocks in pollution that affect AMR while keeping residential sorting and individual compensatory behavior constant. Finally, temperature inversions do not directly affect health, but they can influence resistance through their impact on $PM_{2.5}$ concentration once the effect of other pollutants and weather conditions are netted out.

Weather conditions represent important factors to control for to satisfy the exclusion restrictions as thermal inversions exhibit seasonality, and weather has been shown to directly affect health (e.g., Deschenes & Moretti (2009) and Deschênes & Greenstone (2011)). In the specific context of antibiotic resistance, recent studies find a positive and significant association between temperatures and resistance for several classes of antibiotics and pathogens, both in the US and Europe (MacFadden et al. (2018), McGough et al. (2020)). This is because increasing temperatures facilitate the reproduction of bacteria, the exchange of resistance genes, and the proliferation of infectious diseases. Research also finds that the presence of antibiotic-resistant genes in waters (e.g., rivers and lakes) increases after rainfall episodes (Di Cesare et al. (2017)). Finally, humidity facilitates the spread of bacteria and the occurrence of respiratory infections (Wu et al. (2016)). To isolate the impact of $PM_{2.5}$ on AMR, I further control for other important pollutants that may have their own impact on resistance rates and be themselves affected by temperature inversions.

For the analysis that follows, I build a rich set of instruments, which allows me to exploit all the information at my disposal. In particular, I consider measures of population exposure to inversions near the surface and at any altitude between the surface and 600 hPa. I take into account the seasonality of these phenomena by considering the population exposure to winter inversions, as well as their intensity/strength. The sets of instruments used are displayed in

Table 4: Sets of Instruments

Instruments	
Group A	# of surface inversions, interacted with country dummies
Group B	# of inversions at any altitude, interacted with country dummies
Group C	# of winter inversions, interacted with country dummies
Group D	# of inversions at any altitude and their intensity/strength, interacted with country dummies
Group A'	# of surface inversions and their lags, interacted with country dummies
Group B'	# of inversions at any altitude and their lags, interacted with country dummies
Group C'	# of winter inversions and their lags, interacted with country dummies
Group D'	Intensity/strength of inversions at any altitude and their lags, interacted with country dummies

the upper panel of Table 4. These sets of instruments always include interactions with country dummies to account for potential heterogeneity in the impact of inversions on pollution across countries.[28]

Consumption. Causal estimates from the baseline analysis represent the *total* impact of pollution on antibiotic resistance. However, this *total* causal impact may manifest through different channels. As the positive shock in air pollution induced by temperature inversions may cause a contemporaneous negative shock in individual health, the pollution effect on AMR may partly capture an *indirect* effect through antibiotic use. That is, the unexpected increase in pollution may make some people sicker and lead them to use more antibiotics.[29] If this is the case, the coefficient associated with pollution will encompass both the *direct* influence of pollution on AMR and the impact of an *indirect* channel through increases in antibiotic consumption. Since we observe antibiotic consumption in humans, I can introduce this variable into the resistance equation to disentangle the influence of the two (*direct* and *indirect*) channels. However, the resistance equation would then suffer from endogeneity in the antibiotic use variable. To see this better, it is useful to exploit a graphical representation. Figures 5 in Appendix C illustrate my

[28] This approach allows the impact of inversions on air quality to vary across countries, rather than assuming that the impact is the same across geographical units.

[29] Antibiotics are commonly used for treatment of respiratory disorders such as asthma and bronchitis. Prior research (i.e., Rohlf et al. (2020)) finds that the introduction of low emission zones in Germany reduced air pollution, as well as expenditure in pharmaceuticals for respiratory and heart diseases.

identification strategy. Suppose there exists an omitted variable correlated with both pollution and antibiotic consumption and that also directly affects antibiotic resistance, as depicted in Figure 5 panel (a). Moreover, antibiotic consumption may respond to changes in pollution as explained above. In the baseline analysis (when not explicitly accounting for antibiotic use), the use of temperature inversions as instruments allows me to isolate causal effects, because the exogenous/random nature of these phenomena breaks the correlation between the omitted variable and our variables of interest. However, because antibiotic use is not explicitly taken into account, the estimated coefficient will reflect the impact of both the *direct* and *indirect* channels, as shown in panel (b) of Figure 5. To separate these two effects, it is necessary to introduce antibiotic consumption explicitly into equation (1). Simply controlling for consumption, though, would not be enough since the coefficient for antibiotic use would now pick up the effect of any residual endogenous variation in pollution (that is, any change in pollution that is not related to the temperature inversion shock), as shown in panel (c). To correct for this and separate the two channels, I also instrument for antibiotic consumption by exploiting the exogenous variation created by lagged and twice-lagged inversions. The mechanism, depicted in panel (d), goes as follows. Lagged temperature inversions generate a random shock that affects lagged pollution and, through lagged pollution, lagged AMR. As shown in prior research (Dubois & Gökkoca (2023)), physicians react to increases in past levels of AMR by reducing antibiotics prescriptions. Hence, lagged thermal inversions generate exogenous variation in variables that ultimately affect antibiotic use at time t. The sets of instruments used in this case are similar to those used for the baseline results, and interacted with country dummies. These sets of instruments are displayed in the second panel of Table 4.

Counterfactual Policy. Separating the impact of pollution and antibiotic consumption in humans on AMR allows me to study and compare the role of two major determinants of antibiotic resistance at the EU level. By employing the Poisson model in equation (1), augmented with antibiotic use, I provide, in Section F, a counterfactual analysis considering the evolution of antibiotic resistance under alternative EU pollution control policies during the last couple of decades. I first study a scenario in which the regulator acts by exclusively modifying the pollution policy. I then consider the joint impact of reducing both $PM_{2.5}$ and antibiotic consumption.

Finally, I directly compare pollution and consumption control policies by providing estimates of the reduction in antibiotic use required to obtain the same reduction in resistance induced by the pollution policy. I also compare estimates across EU countries.

6 Baseline Results

Table 5 below shows the baseline results from the Poisson model, while Tables 12 and 13 in Appendix D refer to the linear and fractional logit models, respectively. In each table, columns (1) to (3) employ instrument group A, columns (4) to (6) use instrument group B, and columns (7) to (9) refer to instrument group C. I progressively add controls, and, hence, the most complete specifications are in columns (3), (6) and (9).

In each model and for each instrument group, controlling for weather conditions (mean temperature, max temperature, precipitations, wind speed, and specific humidity) increases the magnitude of the coefficient estimate associated to pollution while accounting for the time dependence of resistance reduces its magnitude. However, the estimated impact of pollution on resistance remains statistically significant and sizable in most specifications. For the Poisson model, estimates in columns (3) and (6) are significant at 5% confidence level and imply that a 1 percent increase in $PM_{2.5}$ concentration leads to approximately a 0.7% increase in antibiotic resistance. Estimates from the linear model, instead, imply that a one-unit increase, corresponding to a one $\mu g/m^3$ increase in $PM_{2.5}$ concentration, causes antibiotic resistance to increase by 0.94 to 1.23 percentage points. For the linear and fractional logit model, results from the Kleibergen-Paap rk Wald F and Hansen J tests are also reported. Each instruments group strongly predicts pollution and widely passes the test of overidentifying restrictions, thus confirming the validity of the instruments.

As for the other controls, the share of individuals over 65 years old in the population is positively and significantly associated with the prevalence of antibiotic resistance. This is consistent with prior research indicating that individuals above 65 years old are among the most vulnerable populations and experience a disproportionate share of AMR-related mortality (OECD (2023)). The elderly are more susceptible to infections as the responsiveness of the immune system tends to decline with age (Montecino-Rodriguez et al. (2013), Keilich et al. (2019)). Moreover, they are

often affected by multiple comorbidities that may require invasive procedures, further increasing infection risks. Diagnosis is also more uncertain in older age groups, complicating timely and accurate treatment (Beckett et al. (2015)). As a consequence, resistance rates are typically higher among geriatric patients (Adam et al. (2013)). The coefficient associated with the number of tourist arrivals is positive and statistically significant, consistent with the idea that tourism and, more in general, international movement of people contributes to the dissemination of AMR at the global level (Bokhary et al. (2021)). There is also a positive and significant relationship between AMR and the size of the rural population. One reason may be that the rural population is more exposed to high quantities of antibiotics used in agriculture and livestock farming (Medina-Pizzali et al. (2021)). Some previous research also shows that individuals in rural areas are substantially more likely to be inappropriately prescribed antibiotics (Yau et al. (2021)). Intuitively, the coefficient for the population density is positive and significant. More densely populated areas mean more and closer contacts and social interactions, favoring the spread of bacteria. Estimates for per-capita health expenditure and physicians' density are negative and significant. This suggests that the quality and efficiency of the healthcare infrastructures, as well as additional investments in infection prevention and control and in stewardship programs, may play an important role in containing the spread of AMR. Finally, the estimated coefficient for past resistance is always positive and significant at 1 % level, confirming the strong time pattern of resistance. This is consistent with epidemiological models (Laxminarayan & Brown (2001)) and with existing empirical evidence (Dubois & Gökkoca (2023)).

Table 14 in Appendix D additionally reports coefficient estimates for the year fixed effects. To conserve space, I exclusively report these estimates for the specification of column (2) of each model in Tables 5, 12, and 13. Estimated coefficients are positive and statistically significant, confirming that antibiotic resistance has increased during the 18 years under study. Table 15 in Appendix D shows results from the three models where pollution is taken as exogenous. Coefficient estimates for these regressions are always smaller than those in the corresponding specifications in Tables 5, 12, and 13. Finally, Tables 16 to 18 in Appendix D report the first-stage results for the linear model in Table 12. Each table refers to one instrument group. The coefficients associated with each instrument, interacted with the country dummies, are mostly positive and significant, confirming the crucial role of thermal inversions in worsening air quality.

Table 5: The Effect of Pollution on Resistance - Poisson Model

	Poisson Model								
Dependent Variable *Resistance*	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
(log) Pollution	0.7653**	1.3065***	0.7167**	0.7427**	1.0660***	0.6728**	0.7145**	0.8141**	0.5296
	(0.3117)	(0.4260)	(0.3317)	(0.3083)	(0.4113)	(0.3192)	(0.2787)	(0.3643)	(0.3358)
Lagged Resistance			0.0140***			0.0135***			0.0128***
			(0.0023)			(0.0023)			(0.0026)
(per capita) Health Expenditure	-0.0001***	-0.0001***	-0.0001***	-0.0001***	-0.0001***	-0.0001***	-0.0001***	-0.0002***	-0.0001***
	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)
Population Density	0.0051**	0.0070***	0.0045**	0.0060**	0.0070***	0.0051**	0.0061***	0.0065***	0.0060***
	(0.0024)	(0.0026)	(0.0020)	(0.0024)	(0.0026)	(0.0021)	(0.0024)	(0.0025)	(0.0023)
Rural Population	0.1497***	0.1349***	0.0828***	0.1562***	0.1445***	0.0958***	0.1648***	0.1603***	0.1094***
	(0.0246)	(0.0299)	(0.0259)	(0.0257)	(0.0294)	(0.0266)	(0.0279)	(0.0305)	(0.0296)
Population 65+	0.0600***	0.0601***	0.0343**	0.0614***	0.0566***	0.0349**	0.0612***	0.0537***	0.0374**
	(0.0169)	(0.0171)	(0.0149)	(0.0172)	(0.0169)	(0.0152)	(0.0171)	(0.0166)	(0.0166)
Tourism Arrivals	0.0040***	0.0042***	0.0046***	0.0042***	0.0042***	0.0046***	0.0041***	0.0043***	0.0051***
	(0.0014)	(0.0014)	(0.0013)	(0.0014)	(0.0014)	(0.0014)	(0.0014)	(0.0013)	(0.0014)
Physicians	-0.2327***	-0.1814***	-0.1114***	-0.2236***	-0.1790***	-0.1071***	-0.2173***	-0.1893***	-0.1075***
	(0.0439)	(0.0458)	(0.0345)	(0.0437)	(0.0449)	(0.0352)	(0.0420)	(0.0436)	(0.0385)
PM10	0.0005	-0.0005	-0.0030	0.0002	-0.0001	-0.0023	0.0008	0.0005	-0.0009
	(0.0024)	(0.0028)	(0.0027)	(0.0025)	(0.0026)	(0.0027)	(0.0023)	(0.0023)	(0.0026)
SO2	-0.0191***	-0.0196***	-0.0167**	-0.0197***	-0.0191***	-0.0163**	-0.0185**	-0.0189***	-0.0154**
	(0.0073)	(0.0075)	(0.0070)	(0.0073)	(0.0074)	(0.0068)	(0.0074)	(0.0071)	(0.0069)
NO2	-0.0011	0.0005	-0.0039	0.0005	0.0022	-0.0024	0.0021	0.0045	0.0002
	(0.0036)	(0.0038)	(0.0033)	(0.0038)	(0.0038)	(0.0033)	(0.0037)	(0.0036)	(0.0036)
O3	-0.0019	0.0007	0.0010	-0.0018	0.0004	0.0011	-0.0017	0.0001	0.0018
	(0.0013)	(0.0017)	(0.0015)	(0.0013)	(0.0017)	(0.0014)	(0.0014)	(0.0017)	(0.0016)
(mean) Temperature		0.1946**	0.1052		0.1604*	0.0958		0.1108	0.0909
		(0.0860)	(0.0686)		(0.0871)	(0.0678)		(0.0851)	(0.0749)
(mean) Precipitation		0.0031**	0.0017		0.0025*	0.0016		0.0020	0.0014
		(0.0015)	(0.0013)		(0.0014)	(0.0012)		(0.0013)	(0.0013)
(mean) Wind Speed		-0.0457	-0.0570		-0.0380	-0.0490		-0.0061	-0.0265
		(0.0651)	(0.0528)		(0.0625)	(0.0531)		(0.0622)	(0.0584)
(mean) Max Temperature		-0.1575**	-0.0871		-0.1404*	-0.0833		-0.1105	-0.0815
		(0.0714)	(0.0570)		(0.0723)	(0.0575)		(0.0704)	(0.0631)
(mean) Specific Humidity		-0.0195	-0.0255*		-0.0168	-0.0246*		-0.0192	-0.0309**
		(0.0169)	(0.0140)		(0.0171)	(0.0145)		(0.0175)	(0.0151)
Observations	419	419	398	419	419	398	419	419	398
Instruments	Group A	Group A	Group A	Group B	Group B	Group B	Group C	Group C	Group C

All regressions include country and year fixed effects and are weighted by the country population. Standard errors in parenthesis.
*** p<0.01, ** p<0.05, * p<0.1

7 Heterogeneity Analysis

Tables 6 and 7 report the results of the heterogeneity analysis. Each column refers to one instrument group, while each panel considers a different pathogen-antibiotic class combination.

Table 6: Heterogeneity Analysis

Dependent Variable *Resistance*	(1)	(2)	(3)	(4)
(a) E. Faecalis - Aminoglycosides				
(log) Pollution	0.6009	0.5155	0.9163**	0.1571
	(0.5417)	(0.4849)	(0.4571)	(0.3122)
Lagged Resistance	0.0087***	0.0077***	0.0078***	0.0080***
	(0.0022)	(0.0021)	(0.0021)	(0.0019)
(b) E. Faecium - Aminoglycosides				
(log) Pollution	0.9194**	1.2419***	0.9340**	0.9379***
	(0.4524)	(0.4137)	(0.3705)	(0.2974)
Lagged Resistance	0.0122***	0.0119***	0.0120***	0.0117***
	(0.0018)	(0.0018)	(0.0018)	(0.0015)
(c) K. Pneumoniae - Aminoglycosides				
(log) Pollution	0.9047	1.1116*	0.0313	0.6011
	(0.6711)	(0.6458)	(0.3847)	(0.3935)
Lagged Resistance	0.0121***	0.0117***	0.0117***	0.0111***
	(0.0023)	(0.0024)	(0.0019)	(0.0017)
(d) K. Pneumoniae - Fluoriquinolones				
(log) Pollution	1.0507*	0.7337	-0.5586	0.1704
	(0.6004)	(0.5499)	(0.4751)	(0.3371)
Lagged Resistance	0.0122***	0.0126***	0.0145***	0.0129***
	(0.0025)	(0.0023)	(0.0019)	(0.0017)
Instruments	Group A	Group B	Group C	Group D

Controls include demographic, pollution and weather variables, as described in equation (1). Regressions are weighted by the country population. Standard errors in parenthesis.
*** p<0.01, ** p<0.05, * p<0.1

I find significant heterogeneity across pathogen-antibiotic pairs in their sensitivity to $PM_{2.5}$ concentration. Aminoglycoside antibiotics, in combination with any pathogen, seem to be the most responsive to changes in fine particulate matter concentration. In particular, estimated

coefficients for combinations of aminoglycosides with Enterococcus faecium and Pseudomonas aeruginosa are all positive and statistically significant, with values ranging between 0.92 and 1.24 for the first pathogen (panel (b)) and between 0.65 and 1.81 for the second pathogen (panel (e)). Combinations with other pathogens are less responsive but still positive and significant for Enterococcus faecalis (panel (a)) and Klebsiella pneumoniae (panel (c)) in some specifications. This is consistent with prior findings by Hu et al. (2018), who show that aminoglycoside-resistant genes are among the most abundant in samples of particulate matter during days with intense smog. One reason why aminoglycoside antibiotics are so responsive to air pollution may be that these antibiotics are non-biodegradable and, hence, they can persist longer in the environment (Chen et al. (2023)).

Changes in pollution levels also cause significant increases in resistance rates for Staphylococcus aureus in combination with Oxacillin (panel (h)). Coefficients are positive and range between 0.61 and 1.03. This result is also consistent with prior studies in the literature. For example, in a recent paper, Psoter et al. (2017) find that increased exposure to $PM_{2.5}$ is associated with larger increases in the risk of acquiring MRSA in young patients with cystic fibrosis. This is worrisome since Methicillin-resistant Staphylococcus aureus (MRSA) is considered one of the *top killer* pathogens, deemed to be responsible for most AMR-related deaths. According to Murray et al. (2022), methicillin-resistant Staphylococcus aureus alone caused 100,000 deaths worldwide in 2019.

I also find positive and significant coefficients for Pseudomonas aeruginosa in combination with Ceftazimide (panel (f)). The most conservative estimate here equals 0.71, while the largest estimate equals 1.13. Ceftazimide is a third-generation cephalosporine used to treat Pseudomonas aeruginosa because particularly effective in treating this pathogen. Ceftazimide is included in the *Watch* group by the WHO AWaRe classification, meaning that the use of this antibiotic entails a high risk of promoting bacterial resistance. For this reason, it is generally considered as a second or third-line treatment option, and growing resistance to this antibiotic presents significant challenges. Fluoroquinolones in combination with Klebsiella pneumoniae (panel (d)) and with Pseudomonas aeruginosa (panel (g)) exhibit smaller coefficients, but they are still positive and significant in some specifications. Finally, for other pathogen-antibiotic combinations (not shown to conserve space), I do not find a significant causal relationship with $PM_{2.5}$ concentration.

Table 7: Heterogeneity Analysis (cont'd)

Dependent Variable *Resistance*	(1)	(2)	(3)	(4)
(e) P. Aeruginosa - Aminoglycosides				
(log) Pollution	1.7802***	1.8121***	1.7488***	0.6543*
	(0.5801)	(0.6393)	(0.6698)	(0.3859)
Lagged Resistance	0.0153***	0.0158***	0.0152***	0.0166***
	(0.0039)	(0.0041)	(0.0042)	(0.0036)
(f) P. Aeruginosa - Ceftazimide				
(log) Pollution	1.1285**	0.9151*	0.0285	0.7124*
	(0.5476)	(0.4810)	(0.5875)	(0.3689)
Lagged Resistance	0.0032	0.0035	0.0045	0.0034
	(0.0029)	(0.0029)	(0.0029)	(0.0025)
(g) P. Aeruginosa - Fluoroquinolones				
(log) Pollution	0.1057	0.3475	0.4300	0.4565*
	(0.4252)	(0.4003)	(0.3427)	(0.2681)
Lagged Resistance	0.0080***	0.0079***	0.0069***	0.0079***
	(0.0023)	(0.0023)	(0.0020)	(0.0023)
(h) S. Aereus - Oxacillin (MRSA)				
(log) Pollution	0.8074**	0.4562	1.0267***	0.6118**
	(0.3462)	(0.3353)	(0.3900)	(0.2726)
Lagged Resistance	0.0180***	0.0176***	0.0183***	0.0190***
	(0.0026)	(0.0024)	(0.0025)	(0.0020)
Instruments	Group A	Group B	Group C	Group D

Controls include demographic, pollution and weather variables, as described in equation (1). Regressions are weighted by the country population. Standard errors in parenthesis.
*** p<0.01, ** p<0.05, * p<0.1

8 Counterfactual Analysis

Table 8 displays results from the model in equation (1), where I also add antibiotic consumption, expressed in terms of DDDs per 1,000 inhabitants. Estimates are reported for each instrument group, both with and without the inclusion of lagged resistance. Both the coefficient associated with pollution and antibiotic use are positive and significant in the most complete specifications of columns (2), (4), (6) and (8). As expected, including antibiotic use in the analysis reduces the magnitude of the coefficient associated with pollution compared to the baseline. This confirms that causal estimates from the baseline encompass the *direct* and *indirect* (through antibiotic consumption) effect of pollution on AMR. Most importantly, we see that, as intuitive, the coefficient associated to antibiotic use in columns (2), (4), (6) and (8) is larger than the one associated with pollution. However, the impact of $PM_{2.5}$ concentration on AMR spread remains sizable. A one percent increase in $PM_{2.5}$ concentration increases resistance rates by 0.24 to 0.0.34 percent, while a one percent increase in the number of DDDs consumed per 1,000 inhabitants increases resistance by 0.30 to 0.34 percent. These results show that pollution represents an important driver of AMR diffusion and a key factor to be leveraged in the fight against antimicrobial resistance.

Table 8: The Effect of Consumption

	Poisson Model							
Dependent Variable *Resistance*	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
(log) Pollution	0.3392**	0.2456*	0.3652**	0.2397*	0.2722*	0.2697**	0.3051**	0.3398**
	(0.1526)	(0.1343)	(0.1552)	(0.1324)	(0.1469)	(0.1249)	(0.1502)	(0.1475)
(log) DDDs	0.3527**	0.3427***	0.2971*	0.3179***	0.2629	0.3016**	0.0044	0.3438**
	(0.1634)	(0.1157)	(0.1643)	(0.1217)	(0.1677)	(0.1208)	(0.1753)	(0.1366)
Lagged Resistance		0.0138***		0.0145***		0.0138***		0.0160***
		(0.0019)		(0.0019)		(0.0018)		(0.0020)
Observations	283	281	283	281	283	281	283	281
Instruments	Group A'	Group A'	Group B'	Group B'	Group C'	Group C'	Group D'	Group D'

Controls include demographic, pollution and weather variables, as described in equation (1). Regressions are weighted by the country population. Standard errors in parenthesis. *** p<0.01, ** p<0.05, * p<0.1

Due to the transboundary nature of pollution, that is the ability of pollution to travel long distances, I also test for the presence and importance of spillovers effects. This is done by following a three-step procedure. First, for each country c, I consider the mean $PM_{2.5}$ concentration across all countries sharing a border with c. Second, I regress this measure over the $PM_{2.5}$ concentration in country c and I take the residuals. This allows me to isolate the portion of pollution in the neighboring countries that are not affected by pollution in the country c and, hence, to avoid potential collinearity due to the presence of both pollution measures in the final regression. Finally, I run the same regressions as in Table (8) by also including the residuals from the previous step. Each instrument group is used here to instrument for both pollution, antibiotic consumption, and the residuals. Results are shown in Table 19 in Appendix E. The coefficient associated with the spillover variables (Residuals) is mostly not significant, and the introduction of this variable leaves the remaining coefficients largely unchanged. The reason may be that spillovers do not play a major role at this level of aggregation.

Table 9 reports the first set of results for the counterfactual analysis. For this counterfactual analysis, I exploit estimates for air pollution and antibiotic consumption from column (6) in Table 8. For each country, the first column displays the resistance rates at the observed levels of pollution, antibiotic consumption, and all the remaining covariates. In the following couple of columns, I consider two specific objectives based on the discussion in Subsection 2.3. That is, I estimate the counterfactual resistance rate, had the EU regulation capped $PM_{2.5}$ concentration at 10 $\mu g/m^3$ or at 5 $\mu g/m^3$ during the period under analysis. Hence, the first counterfactual reflects the EU objective for the year 2030, while the second corresponds to the latest WHO recommendations. The next column, instead, considers a regulation that reduces antibiotic consumption by 20%. The rationale for this is that, in June 2023, the Council of the European Union set a few targets to reduce AMR. Among others, one objective is to reduce antibiotic consumption (in terms of DDDs per 1,000 inhabitants per day) by 20 % in each Member State by 2030.[30] Finally, in the last two columns, I consider the joint impact of each of the two pollution policies together with the consumption policy.

Of course, the impact of the policies under consideration differs across countries, depending on the situation of each specific country. For example, France is a relatively low polluter but a

[30] https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32023H0622(01)

Table 9: Comparison across Counterfactuals

		Pollution Policy only		**Consumption Policy only**	**Pollution & Consumption Policy**	
Country	Resistance ($\hat{R}$)	$PM_{2.5} = 10$	$PM_{2.5} = 5$	$\Delta C = -20\%$	$PM_{2.5} = 10$, $\Delta C = -20\%$	$PM_{2.5} = 5$, $\Delta C = -20\%$
AUSTRIA	16.97	15.79	13.41	15.87	14.91	12.66
BELGIUM	18.49	17.01	14.45	17.29	16.03	13.61
BULGARIA	32.69	26.56	22.55	30.56	25.17	21.38
CROATIA	32.40	28.36	24.08	30.29	26.52	22.52
CZECH REPUBLIC	31.59	27.55	23.39	29.53	25.87	21.97
DENMARK	13.49	13.20	11.27	12.61	12.44	10.62
ESTONIA	16.00	15.93	13.80	14.96	14.88	12.88
FINLAND	10.94	10.94	10.79	10.23	10.25	10.11
FRANCE	20.38	19.48	16.55	19.06	18.19	15.46
GERMANY	24.42	22.52	19.12	22.83	21.20	18.00
GREECE	45.66	40.12	34.07	42.69	37.76	32.06
HUNGARY	29.85	25.19	21.39	27.91	23.46	19.92
IRELAND	24.07	24.06	21.36	22.51	22.54	20.01
ITALY	31.87	29.05	24.67	29.80	27.31	23.19
LATVIA	28.35	26.33	22.36	26.51	24.73	21.00
LITHUANIA	27.32	24.26	20.60	25.54	22.68	19.26
LUXEMBOURG	16.22	15.27	12.97	15.16	14.28	12.13
NETHERLANDS	15.42	14.10	11.97	14.41	13.03	11.07
POLAND	31.41	25.92	22.01	29.36	24.34	20.67
PORTUGAL	31.83	31.56	27.51	29.76	29.57	25.78
ROMANIA	49.09	41.94	35.62	45.89	39.56	33.59
SLOVENIA	23.52	20.87	17.72	21.99	19.54	16.60
SPAIN	19.80	19.53	16.77	18.51	18.38	15.78
SWEDEN	11.09	11.09	11.06	10.37	10.37	10.33
Total	25.09	22.76	19.56	23.46	21.39	18.38

relatively high antibiotic consumer, as can be seen also from the descriptive statistics in Table 2 of Section 4. Hence, while capping pollution at 10 would reduce resistance by 0.9 percentage points (from 20.38 to 19.48), reducing consumption by 20% has a more important effect, as resistance would be reduced by 1.32 percentage points. If we consider, instead, a high polluter, such as Bulgaria, the impact of the pollution policy is more important than the effect of the consumption policy, with a four percentage points differential impact (the counterfactual level of resistance under the pollution policy is 26.56, while under the consumption policy, it is 30.56). Notice also that, in some countries, such as Sweden, Ireland, Portugal, and Finland, the pollution policy has a very limited impact, if any. This is because the cap at 10 is never binding, or it is only binding in a few time periods. Moreover, for countries like Sweden or Finland, even capping at 5 has a minimal impact. As intuitive, the most beneficial effect (that is, the largest reduction in AMR) is obtained when both the pollution and antibiotic consumption policies are applied. Figure 7 in Appendix F plots resistance and counterfactual resistance when $PM_{2.5}$ is capped at 5 $\mu g/m^3$ and antibiotic use is reduced by 20%.

Table 10 reports the same results as Table 9 in the first three columns. In the last couple of columns, I estimate the reduction in antibiotic use that would be required to achieve the same level of resistance as under each of the two pollution policies. On average, capping $PM_{2.5}$ concentration at 10 $\mu g/m^3$ reduces pollution by 2.33 percentage points in the EU, which corresponds to about a 22.6% reduction in antibiotics use. Capping $PM_{2.5}$ at the same level as recommended by the WHO would, instead, be equivalent to reducing antibiotic use by about 51%.

Table 10: Comparison across Counterfactuals (cont'd)

		Pollution Policy only		**Corresponding Consumption Policy**	
Country	Resistance ($\hat{R}$)	$PM_{2.5} = 10$	$PM_{2.5} = 5$	% Reduction ($PM_{2.5} = 10$)	% Reduction ($PM_{2.5} = 5$)
AUSTRIA	16.97	15.79	13.41	-21.38	-54.34
BELGIUM	18.49	17.01	14.45	-24.20	-56.01
BULGARIA	32.69	26.56	22.55	-49.83	-70.78
CROATIA	32.40	28.36	24.08	-35.75	-62.63
CZECH REPUBLIC	31.59	27.55	23.39	-36.65	-63.20
DENMARK	13.49	13.20	11.27	-6.86	-45.06
ESTONIA	16.00	15.93	13.80	-1.40	-38.95
FINLAND	10.94	10.94	10.79	0	-4.52
FRANCE	20.38	19.48	16.55	-14.10	-50.07
GERMANY	24.42	22.52	19.12	-24.52	-57.09
GREECE	45.66	40.12	34.07	-35.06	-62.35
HUNGARY	29.85	25.19	21.39	-43.35	-67.10
IRELAND	24.07	24.06	21.36	-0.20	-33.66
ITALY	31.87	29.05	24.67	-26.60	-57.40
LATVIA	28.35	26.33	22.36	-21.99	-54.85
LITHUANIA	27.32	24.26	20.60	-33.11	-61.39
LUXEMBOURG	16.22	15.27	12.97	-18.20	-52.65
NETHERLANDS	15.42	14.10	11.97	-25.70	-56.84
POLAND	31.41	25.92	22.01	-47.83	-69.81
PORTUGAL	31.83	31.56	27.51	-2.87	-38.89
ROMANIA	49.09	41.94	35.62	-41.61	-66.48
SLOVENIA	23.52	20.87	17.72	-32.80	-60.94
SPAIN	19.80	19.53	16.77	-4.50	-42.49
SWEDEN	11.09	11.09	11.06	0	-1.09
Total	25.09	22.76	19.56	-22.59	-50.87

9 Conclusion

This paper is the first to provide causal estimates of the impact of air quality on the propagation of antimicrobial resistance (AMR). Results show that air pollution is an important driver of increasing AMR rates in the EU, with an influence comparable to antibiotic consumption in humans. Additionally, I find substantial heterogeneity across pathogen-antibiotic combinations in their responsiveness to exogenous changes in $PM_{2.5}$ concentration. Stricter pollution standards would help contain the spread of resistance to some second and third-line antibiotics, thereby preserving their efficacy. Moreover, air pollution control would contribute to limiting the diffusion of some *top killer* resistant bacteria, such as MRSA.

These findings suggest that pollution reduction policies could be effectively leveraged in the fight against antimicrobial resistance. They also emphasize the need to account for the causal impact of pollution on AMR in cost-benefit analyses of air quality improvement policies. Ignoring this impact would likely result in an underestimation of both the health and economic benefits associated with cleaner air.

In terms of future extensions, this paper does not consider yet the impact of antibiotic use in animal farming and agricultural activities. Although prior research in the US identifies human antibiotic use as the main driver of resistance (Adda (2020)), veterinary use still accounts for approximately 60% of total antibiotic consumption in European countries. Future versions of this paper will incorporate veterinary usage data into the analysis. Another valuable extension would involve estimating the economic costs and benefits of alternative pollution reduction strategies. Finally, while this paper focuses exclusively on environmental policies through stricter pollution standards, future research could explore the impact of other types of environmental policies.

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A Temperature Inversions

Figure 2: Inversions: Example 1

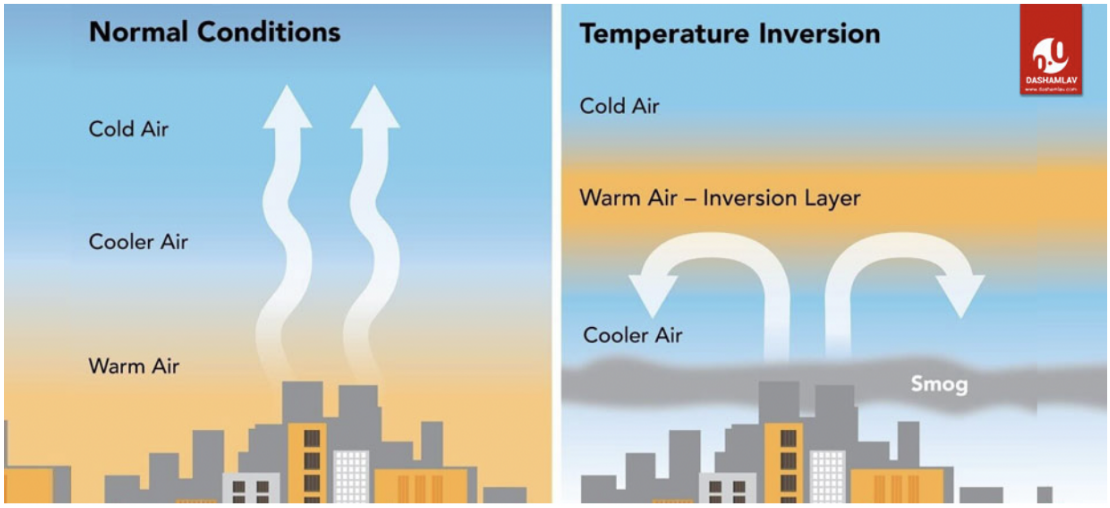
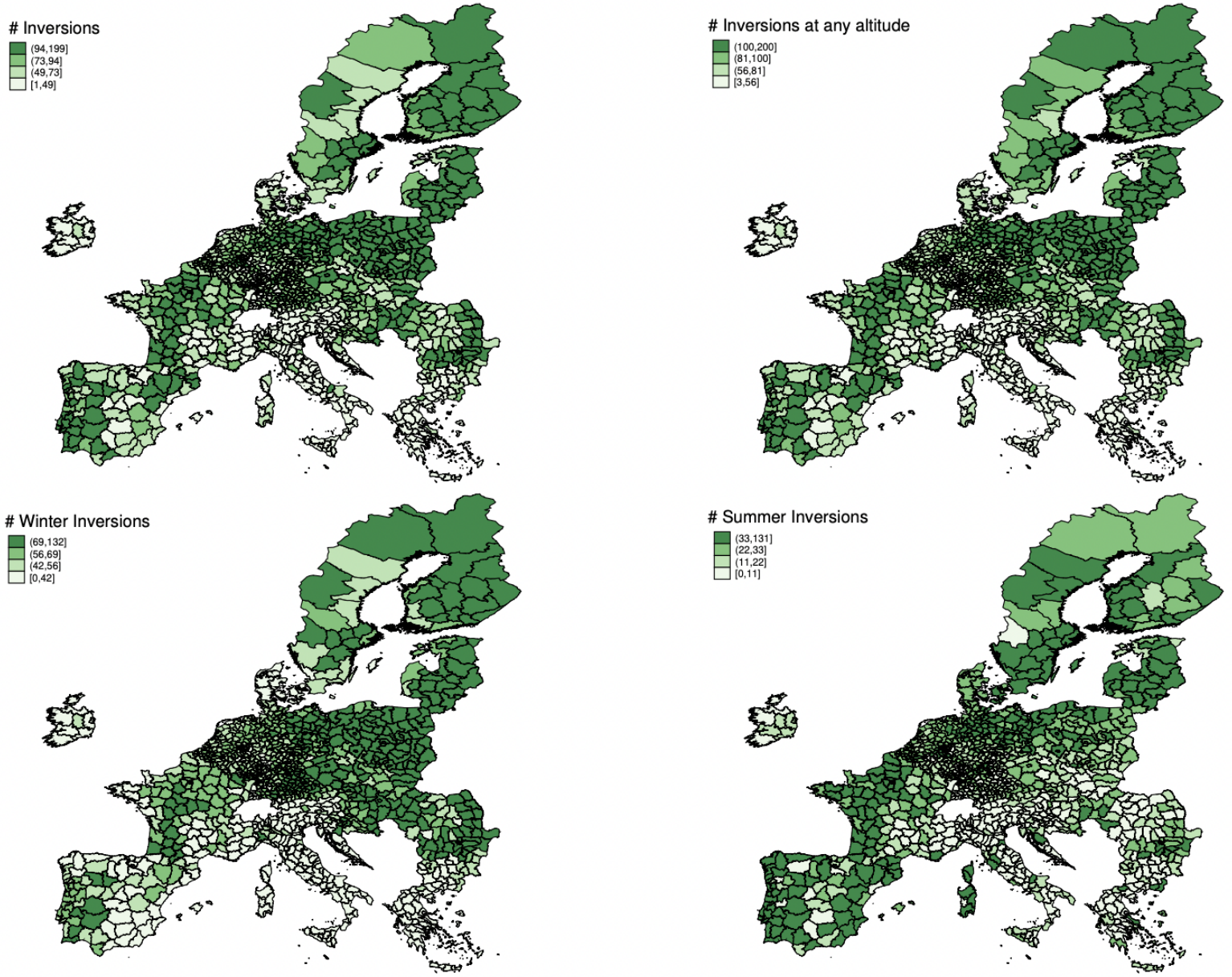


Figure 3: Inversions: Example 2

Figure 4: Temperature Inversions in NUTS3 Regions



B Heterogeneity Analysis - Glossary

Useful definitions:

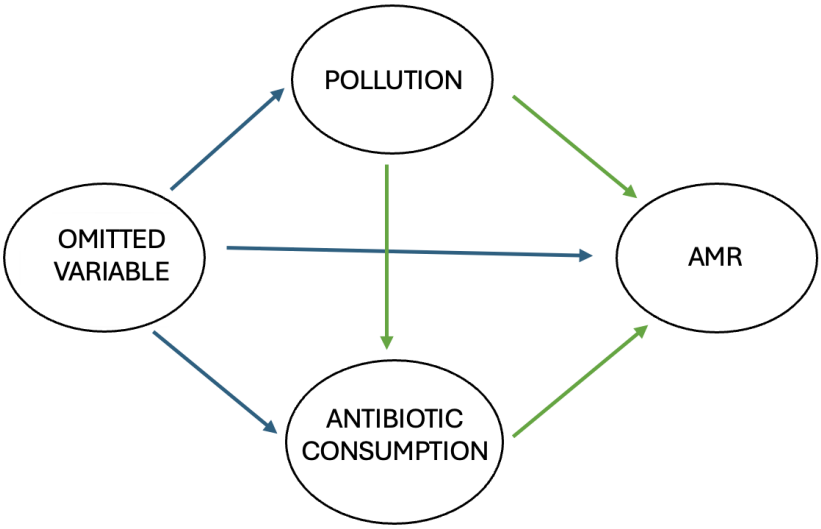
- *Beta-lactam Antibiotics*: these represent a broad class of antibiotics, including several classes under analysis in this paper. These include penicillins, amonipenicillins (amoxicillin, commonly used for respiratory infections, ampicillin), penicillinase-Resistant penicillins (methicillin, nafcillin, oxacillin), broad-spectrum penicillins, cephalosporins, carbapenems, monobactam.
- *Gram-positive and Gram-negative Bacteria*: the distinction between gram-positive and gram-negative bacteria depends on the cell wall structure of the pathogens. This distinction is important because it determines antibiotic susceptibility and pathogenic behavior and it allows to identify the most appropriate antibiotic treatment option. Among the pathogens under study, the *Enterococcus faecalis*, *Enterococcus faecium* and *Staphylococcus aureus* are gram-positive bacteria, while *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are gram-negative bacteria.

Table 11: Antibiotics

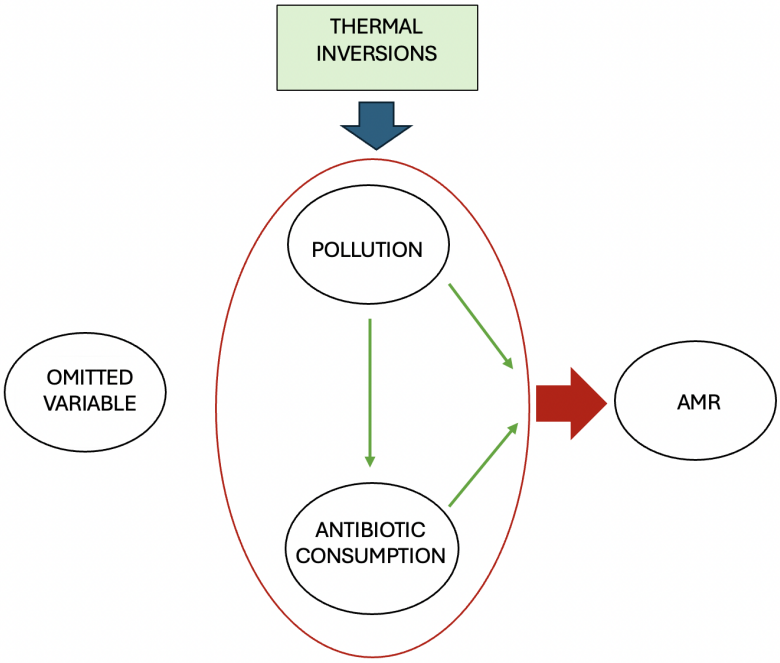
Antibiotic	**Class**	**Sub-class**	**Spectrum**
Aminoglycosides (second-line)	Aminoglycosides	-	Primarly effective against Gram-negative bacteria, and used in combination for Gram-positive bacteria.
Aminopenicillins (first-line)	Beta-lactams	Penicillins	Broad-spectrum. Effective against Gram-positive bacteria (e.g., *Enterococcus faecalis*) and some Gram-negative bacteria.
Carbapenems (third-line)	Beta-lactams	Carbapenems	Broad-spectrum. Effective against Gram-positive, Gram-negative, and anaerobic bacteria. Used for resistant infections.
Ceftazidime (third-line)	Beta-lactams	Cephalosporines (3rd generation)	Broad-spectrum. Particularly effective against Gram-negative bacteria, such as *Pseudomonas aeruginosa*.
Cephalosporines (first-line)	Beta-lactams	Cephalosporines	Gram-positive and Gram-negative bacteria (depending on generation),
Fluoroquinolones (second-line)	Fluoroquinolones	-	Broad-spectrum. Effective against Gram-negative and some Gram-positivebacteria.
Oxacillin (second-line)	Beta-lactams	Penicillins	Narrow-spectrum. Mainly used to treat penicillinase-producing Staphylococcus aureus.
Piperacillin-Tazobactam (second, third line)	Beta-lactams	-	Broad-spectrum. Effective against Gram-positive, Gram-negative, and anaerobic bacteria.
Vancomycin (third-line)	Glycopeptides	-	Narrow-spectrum. Effective against Gram-positive bacteria.

C Instrumental Variable Estimation

Figure 5: Instrumental Variables

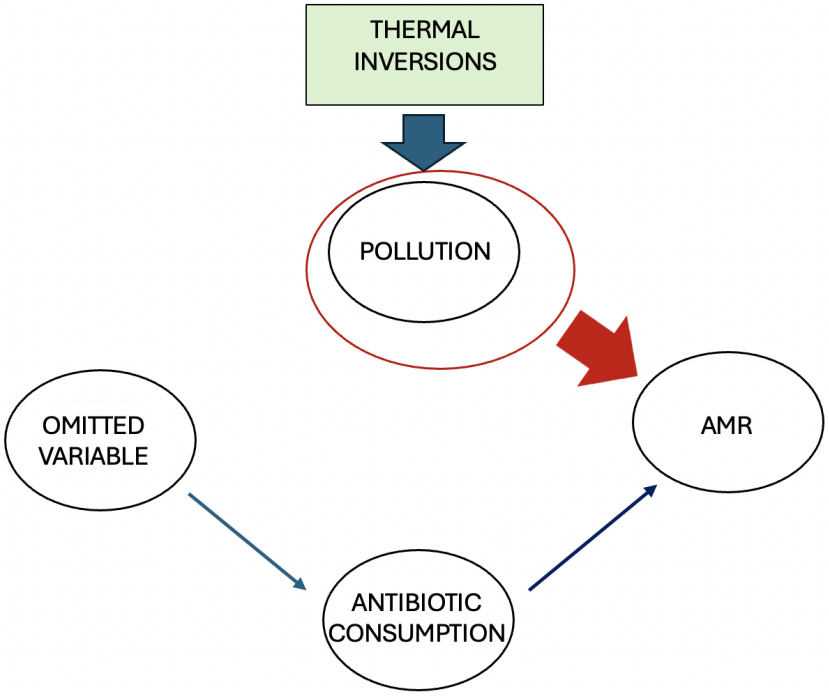


(a) Omitted-variable bias

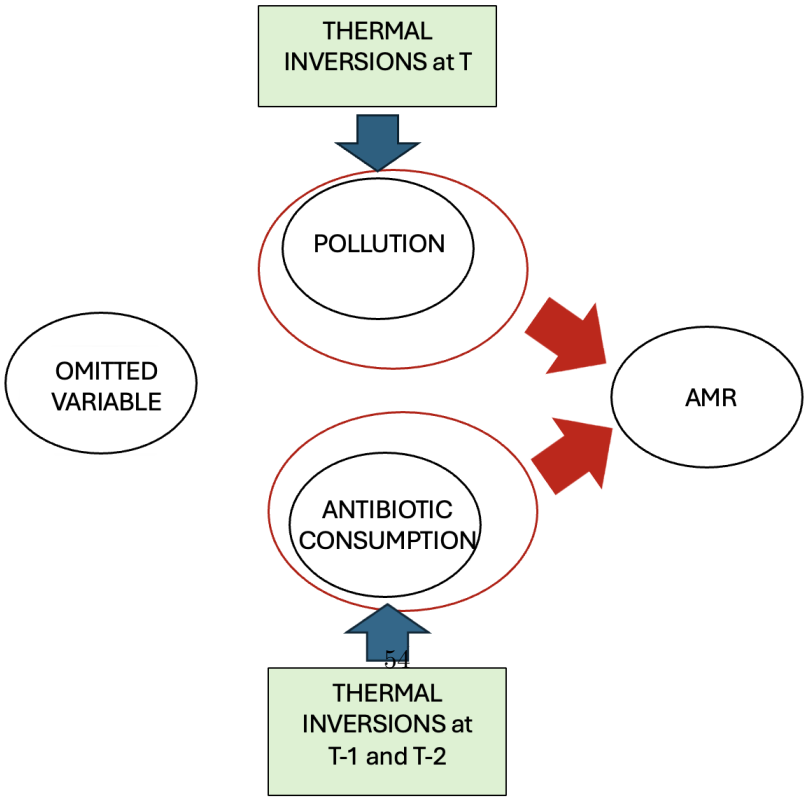


(b) Total impact of pollution

Figure 5 (cont'd): Instrumental Variables



(c) Antibiotic consumption



(d) Causal impact of pollution and antibiotic use

D Baseline Results

Table 12: The Effect of Pollution on Resistance - Linear Model

	Linear Model								
Dependent Variable *Resistance*	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Pollution	1.3624**	1.7164**	1.2284*	1.0537*	1.3227*	0.9350*	1.0871**	1.2422*	0.9573**
	(0.5593)	(0.7717)	(0.6085)	(0.5270)	(0.7278)	(0.5036)	(0.4501)	(0.6558)	(0.4452)
Lagged Resistance			0.4473***			0.4540***			0.4535***
			(0.0839)			(0.0810)			(0.0789)
(per capita) Health Expenditure	-0.0039***	-0.0041***	-0.0017*	-0.0038***	-0.0040***	-0.0016*	-0.0038***	-0.0040***	-0.0016**
	(0.0013)	(0.0012)	(0.0008)	(0.0013)	(0.0012)	(0.0008)	(0.0013)	(0.0012)	(0.0008)
Population Density	0.1237	0.1428	0.1146	0.1238	0.1347	0.1049	0.1237	0.1331	0.1056
	(0.1397)	(0.1468)	(0.0969)	(0.1388)	(0.1460)	(0.0948)	(0.1388)	(0.1455)	(0.0931)
Rural Population	5.2535***	5.2753***	3.5175***	5.2138***	5.2811***	3.5235***	5.2181***	5.2822***	3.5230***
	(1.1413)	(1.1803)	(0.7461)	(1.1487)	(1.1869)	(0.7509)	(1.1367)	(1.1907)	(0.7519)
Population 65+	1.7770**	1.6095*	0.7247	1.6846*	1.5387*	0.6563	1.6946*	1.5242*	0.6615
	(0.8173)	(0.8312)	(0.4407)	(0.8580)	(0.8592)	(0.4537)	(0.8711)	(0.8777)	(0.4724)
Tourism Arrivals	0.0899*	0.0924*	0.1044**	0.0899*	0.0918*	0.1017**	0.0899*	0.0917*	0.1019**
	(0.0493)	(0.0481)	(0.0406)	(0.0488)	(0.0475)	(0.0405)	(0.0489)	(0.0475)	(0.0410)
Physicians	-4.7692***	-4.4535***	-1.6194	-4.7201***	-4.4906***	-1.7010	-4.7254***	-4.4982***	-1.6948
	(1.5926)	(1.4882)	(1.1490)	(1.5796)	(1.4801)	(1.1741)	(1.5651)	(1.4919)	(1.2175)
PM10	0.0301	0.0193	0.0002	0.0545	0.0423	0.0134	0.0518	0.0470	0.0124
	(0.1464)	(0.1147)	(0.0539)	(0.1325)	(0.1027)	(0.0474)	(0.1283)	(0.1004)	(0.0476)
SO2	-0.6141*	-0.7054*	-0.4787	-0.5739	-0.6586*	-0.4387	-0.5783	-0.6491*	-0.4417
	(0.3497)	(0.3666)	(0.3022)	(0.3538)	(0.3722)	(0.2932)	(0.3559)	(0.3713)	(0.2852)
NO2	0.1476	0.1953	0.0217	0.1418	0.1854	0.0213	0.1425	0.1834	0.0213
	(0.1327)	(0.1520)	(0.1069)	(0.1298)	(0.1471)	(0.1052)	(0.1275)	(0.1431)	(0.1051)
O3	-0.0761	-0.0451	-0.0239	-0.0776	-0.0492	-0.0261	-0.0774	-0.0500	-0.0259
	(0.0481)	(0.0473)	(0.0334)	(0.0490)	(0.0482)	(0.0329)	(0.0493)	(0.0491)	(0.0330)
(mean) Temperature		3.0485	3.0300		2.2019	2.3659		2.0289	2.4165
		(3.6282)	(2.4646)		(3.5162)	(2.6798)		(3.4916)	(2.8242)
(mean) Precipitation		0.0358	0.0181		0.0313	0.0135		0.0304	0.0138
		(0.0514)	(0.0464)		(0.0490)	(0.0433)		(0.0487)	(0.0430)
(mean) Wind Speed		1.1906	0.0999		1.2124	0.1894		1.2169	0.1826
		(1.8040)	(1.6656)		(1.7681)	(1.6735)		(1.7618)	(1.7034)
(mean) Max Temperature		-2.8730	-2.6956		-2.3543	-2.3164		-2.2483	-2.3453
		(3.4790)	(2.4666)		(3.3616)	(2.5905)		(3.3062)	(2.6532)
(mean) Specific Humidity		-0.0788	-0.4119		-0.1416	-0.4321		-0.1544	-0.4305
		(0.6786)	(0.4946)		(0.6594)	(0.4680)		(0.6577)	(0.4669)
Observations	419	419	398	419	419	398	419	419	398
Instruments	Group A	Group A	Group A	Group B	Group B	Group B	Group C	Group C	Group C
Kleibergen-Paap rk Wald F	5.8e+04	1.6e+05	1.4e+06	2.9e+06	1.7e+06	1.1e+05	3.9e+04	2.6e+04	1.0e+05
Hansen J	0.4897	0.3718	0.4772	0.3886	0.5049	0.4422	0.6081	0.4302	0.3724

All regressions include country and year fixed effects and are weighted by the country population. Standard errors are clustered at the country level in parenthesis. *** p<0.01, ** p<0.05, * p<0.1

Table 13: The Effect of Pollution on Resistance - Fractional Logit Model

	Fractional Logit Model								
Dependent Variable *(log) Resistance*	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
(log) Pollution	1.1603**	1.3171	0.5544	0.9484*	1.0329	0.4294	1.0173**	1.0460	0.5677
	(0.5543)	(0.8336)	(0.6754)	(0.4937)	(0.7424)	(0.5873)	(0.4463)	(0.6741)	(0.6543)
Lagged Resistance			0.0263***			0.0266***			0.0262***
			(0.0072)			(0.0071)			(0.0071)
(per capita) Health Expenditure	-0.0002	-0.0002	-0.0000	-0.0002	-0.0002	-0.0000	-0.0002*	-0.0002	-0.0000
	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)
Population Density	0.0070	0.0070	0.0044	0.0068	0.0064	0.0040	0.0062	0.0064	0.0044
	(0.0072)	(0.0077)	(0.0054)	(0.0074)	(0.0078)	(0.0052)	(0.0076)	(0.0077)	(0.0051)
Rural Population	0.2567***	0.2522***	0.1586***	0.2601***	0.2592***	0.1611***	0.2698***	0.2589***	0.1583***
	(0.0757)	(0.0803)	(0.0418)	(0.0763)	(0.0797)	(0.0404)	(0.0784)	(0.0799)	(0.0404)
Population 65+	0.1034*	0.1010*	0.0510	0.1014*	0.0998	0.0503	0.1013*	0.0999	0.0511
	(0.0569)	(0.0583)	(0.0313)	(0.0583)	(0.0594)	(0.0319)	(0.0574)	(0.0598)	(0.0320)
Tourism Arrivals	0.0054**	0.0052**	0.0055**	0.0055**	0.0052**	0.0054**	0.0054**	0.0052**	0.0055**
	(0.0026)	(0.0025)	(0.0024)	(0.0026)	(0.0025)	(0.0024)	(0.0025)	(0.0025)	(0.0024)
Physicians	-0.2832***	-0.2461***	-0.0873	-0.2803***	-0.2493***	-0.0885	-0.2759***	-0.2491***	-0.0872
	(0.0922)	(0.0819)	(0.0745)	(0.0911)	(0.0831)	(0.0752)	(0.0872)	(0.0846)	(0.0758)
PM10	-0.0022	-0.0020	-0.0015	-0.0012	-0.0011	-0.0012	-0.0025	-0.0011	-0.0015
	(0.0084)	(0.0076)	(0.0032)	(0.0075)	(0.0066)	(0.0030)	(0.0066)	(0.0064)	(0.0029)
SO2	-0.0163	-0.0195	-0.0120	-0.0161	-0.0194	-0.0118	-0.0187	-0.0194	-0.0120
	(0.0184)	(0.0190)	(0.0141)	(0.0183)	(0.0188)	(0.0140)	(0.0191)	(0.0188)	(0.0142)
NO2	0.0041	0.0056	-0.0025	0.0043	0.0058	-0.0024	0.0052	0.0057	-0.0025
	(0.0093)	(0.0099)	(0.0070)	(0.0093)	(0.0098)	(0.0070)	(0.0099)	(0.0099)	(0.0071)
O3	-0.0006	0.0014	0.0011	-0.0010	0.0006	0.0008	-0.0003	0.0006	0.0012
	(0.0033)	(0.0036)	(0.0024)	(0.0033)	(0.0036)	(0.0023)	(0.0035)	(0.0040)	(0.0027)
(mean) Temperature		0.0531	0.0283		0.0158	0.0119		0.0175	0.0301
		(0.1972)	(0.1362)		(0.1948)	(0.1505)		(0.2011)	(0.1665)
(mean) Precipitation		0.0047	0.0020		0.0042	0.0017		0.0043	0.0020
		(0.0032)	(0.0028)		(0.0031)	(0.0025)		(0.0031)	(0.0025)
(mean) Wind Speed		-0.0426	-0.0440		-0.0312	-0.0383		-0.0317	-0.0446
		(0.0876)	(0.0742)		(0.0922)	(0.0799)		(0.0933)	(0.0859)
(mean) Max Temperature		-0.0672	-0.0464		-0.0429	-0.0363	-0.0560	-0.0440	-0.0474
		(0.1682)	(0.1148)		(0.1674)	(0.1266)	(0.0464)	(0.1731)	(0.1373)
(mean) Specific Humidity		-0.0107	-0.0204		-0.0109	-0.0199	-0.0005	-0.0109	-0.0204
		(0.0311)	(0.0207)		(0.0306)	(0.0211)	(0.0312)	(0.0306)	(0.0213)
Observations	419	419	398	419	419	398	419	419	398
Instruments	Group A	Group A	Group A	Group B	Group B	Group B	Group C	Group C	Group C
Kleibergen-Paap rk Wald F	6.4e+04	1.3e+04	2.3e+05	2.2e+04	2.7e+04	4.4e+05	3.2e+05	2.1e+04	7933.323
Hansen J	0.3491	0.3576	0.3783	0.4875	0.4178	0.3812	0.4391	0.3844	0.4646

All regressions include country and year fixed effects and are weighted by the country population. Standard errors are clustered at the country level in parenthesis. *** p<0.01, ** p<0.05, * p<0.1

Table 14: Baseline Results - Year Fixed Effects

	Linear Model	**Fractional Logit Model**	**Poisson Model**
	(1)	(2)	(3)
Dependent Variable:	*Resistance*	*(log) Resistance*	*Resistance*
Year 2003	5.9572***	0.2688**	0.2231***
	(2.0151)	(0.1253)	(0.0750)
Year 2004	8.9282***	0.4186**	0.3798***
	(3.0382)	(0.1831)	(0.0770)
Year 2005	6.9316**	0.3112	0.2584***
	(3.1586)	(0.2042)	(0.0799)
Year 2006	6.6471**	0.3141	0.2308***
	(2.9553)	(0.1893)	(0.0772)
Year 2007	10.5001**	0.5006*	0.3907***
	(4.1208)	(0.2685)	(0.1023)
Year 2008	9.7886**	0.4477	0.3226***
	(4.2363)	(0.2869)	(0.0988)
Year 2009	10.1867**	0.4554	0.3444***
	(4.2526)	(0.2793)	(0.0978)
Year 2010	8.7809**	0.3574	0.2701***
	(4.1976)	(0.2662)	(0.0965)
Year 2011	13.1625**	0.5992*	0.4294***
	(4.8410)	(0.3150)	(0.1050)
Year 2012	14.2211**	0.6234	0.4814***
	(5.7408)	(0.3752)	(0.1191)
Year 2013	14.0779**	0.5983	0.4604***
	(6.0729)	(0.3991)	(0.1244)
Year 2014	14.9230**	0.6343	0.4607***
	(6.7916)	(0.4437)	(0.1352)
Year 2015	13.2366*	0.5736	0.4555***
	(7.0292)	(0.4429)	(0.1413)
Year 2016	13.1953*	0.5520	0.4449***
	(7.1075)	(0.4699)	(0.1516)
Year 2017	13.3710*	0.5543	0.4559***
	(7.4723)	(0.4958)	(0.1548)
Year 2018	15.5192*	0.6608	0.5215***
	(8.4359)	(0.5755)	(0.1756)
Year 2019	15.5642	0.6627	0.5136***
	(9.5473)	(0.6268)	(0.1944)
Observations	419	419	419

Table 15: Baseline Results - Pollution Exogenous

	Linear Model			**Fractional Logit Model**			**Poisson Model**		
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Dependent Variable	*Resistance*	*Resistance*	*Resistance*	*(log) Resistance*	*(log) Resistance*	*(log) Resistance*	*Resistance*	*Resistance*	*Resistance*
Pollution	0.5555**	0.5883	0.5006*						
	(0.2660)	(0.3492)	(0.2444)						
(log) Pollution				0.5409***	0.6139***	0.3890**	0.3862***	0.4661***	0.3844***
				(0.1739)	(0.2129)	(0.1434)	(0.1412)	(0.1587)	(0.1392)
Lagged Resistance			0.4639***			0.0266***			0.0169***
			(0.0761)			(0.0061)			(0.0026)
(per capita) Health Expenditure	-0.0037**	-0.0037***	-0.0015*	-0.0002	-0.0002	-0.0000	-0.0001**	-0.0001***	-0.0000
	(0.0013)	(0.0012)	(0.0008)	(0.0001)	(0.0001)	(0.0001)	(0.0000)	(0.0000)	(0.0000)
Population Density	0.1239	0.1198	0.0905	0.0063	0.0055	0.0039	-0.0012	-0.0005	0.0010
	(0.1379)	(0.1462)	(0.0953)	(0.0076)	(0.0078)	(0.0046)	(0.0022)	(0.0022)	(0.0018)
Rural Population	5.1497***	5.2918***	3.5324***	0.2666***	0.2697***	0.1619***	0.1420***	0.1370***	0.0921**
	(1.1495)	(1.2185)	(0.7706)	(0.0814)	(0.0837)	(0.0443)	(0.0407)	(0.0410)	(0.0377)
Population 65+	1.5354	1.4064	0.5550	0.0975	0.0981	0.0501	0.0363*	0.0369*	0.0141
	(0.9000)	(0.9044)	(0.4634)	(0.0594)	(0.0610)	(0.0327)	(0.0210)	(0.0209)	(0.0167)
Tourism Arrivals	0.0898*	0.0909*	0.0977**	0.0055**	0.0053**	0.0054**	0.0020	0.0022	0.0027
	(0.0486)	(0.0478)	(0.0437)	(0.0026)	(0.0025)	(0.0024)	(0.0018)	(0.0017)	(0.0018)
Physicians	-4.6410***	-4.5599***	-1.8218	-0.2748***	-0.2539***	-0.0889	-0.1566***	-0.1388***	-0.0421
	(1.5538)	(1.5142)	(1.2506)	(0.0881)	(0.0879)	(0.0786)	(0.0457)	(0.0473)	(0.0355)
PM10	0.0939	0.0851	0.0330	0.0007	0.0003	-0.0011	0.0016	0.0019	0.0002
	(0.1326)	(0.1022)	(0.0480)	(0.0070)	(0.0061)	(0.0029)	(0.0020)	(0.0020)	(0.0017)
SO2	-0.5091	-0.5715	-0.3794	-0.0158	-0.0192	-0.0117	-0.0045	-0.0056	-0.0004
	(0.3252)	(0.3363)	(0.2566)	(0.0180)	(0.0185)	(0.0136)	(0.0073)	(0.0073)	(0.0071)
NO2	0.1326	0.1669	0.0207	0.0045	0.0059	-0.0024	-0.0030	-0.0026	-0.0042
	(0.1271)	(0.1417)	(0.1043)	(0.0091)	(0.0097)	(0.0072)	(0.0034)	(0.0034)	(0.0031)
O3	-0.0800	-0.0569	-0.0292	-0.0019	-0.0006	0.0006	0.0002	0.0008	0.0006
	(0.0506)	(0.0502)	(0.0337)	(0.0032)	(0.0033)	(0.0022)	(0.0022)	(0.0022)	(0.0020)
(mean) Temperature		0.6227	1.3824		-0.0393	0.0066		0.1312*	0.0989
		(3.0628)	(2.4911)		(0.1748)	(0.1384)		(0.0780)	(0.0624)
(mean) Precipitation		0.0231	0.0067		0.0036	0.0017		0.0006	0.0008
		(0.0469)	(0.0425)		(0.0029)	(0.0022)		(0.0013)	(0.0013)
(mean) Wind Speed		1.2531	0.3219		-0.0144	-0.0365		-0.0643	-0.0304
		(1.7207)	(1.5934)		(0.0974)	(0.0826)		(0.0787)	(0.0606)
(mean) Max Temperature		-1.3867	-1.7549		-0.0071	-0.0331		-0.1155*	-0.0775
		(2.8523)	(2.3012)		(0.1526)	(0.1165)		(0.0655)	(0.0544)
(mean) Specific Humidity		-0.2587	-0.4619		-0.0112	-0.0197		-0.0255*	-0.0191
		(0.6121)	(0.4450)		(0.0300)	(0.0210)		(0.0148)	(0.0130)
Observations	419	419	398	419	419	398	419	419	398
R-squared	0.8779	0.8806	0.9202	0.8389	0.8421	0.9032			

All regressions include country and year fixed effects and are weighted by the country population. Standard errors parenthesis. *** p<0.01, ** p<0.05, * p<0.1.

Table 16: Baseline Results - First Stage (Group A)

	Controls				Instruments		
Dependent Variable *Pollution*	(1)	(2)	(3)		(1')	(2')	(3')
(percapita) Health Expenditure	0.0004	0.0005*	0.0003	Inversions*AUS	0.0684***	0.0449***	0.0320***
	(0.0003)	(0.0003)	(0.0003)		(0.0129)	(0.0113)	(0.0106)
Population Density	0.0011	-0.0149	-0.0284**	Inversions*BEL	-0.0161**	-0.0122	-0.0059
	(0.0164)	(0.0149)	(0.0129)		(0.0065)	(0.0075)	(0.0072)
Rural Population	-0.1159	0.0645	0.0471	Inversions*BUL	-0.0344	-0.0622**	-0.0890***
	(0.2246)	(0.2025)	(0.1780)		(0.0241)	(0.0245)	(0.0293)
Population 65+	-0.2174	-0.1405	-0.1924	Inversions*CRO	0.1045***	0.0486*	0.0327
	(0.1503)	(0.1479)	(0.1188)		(0.0210)	(0.0282)	(0.0275)
Tourism Arrivals	-0.0042	-0.0007	-0.0119	Inversions*CZE	0.0469***	0.0346***	-0.0004
	(0.0115)	(0.0114)	(0.0146)		(0.0092)	(0.0100)	(0.0084)
Physicians	-0.1205	-0.2183	-0.3977	Inversions*DEN	0.0427***	0.0401***	0.0376***
	(0.3865)	(0.3449)	(0.2947)		(0.0066)	(0.0060)	(0.0053)
PM10	0.0816*	0.0579	0.0479	Inversions*EST	-0.0373***	-0.0511***	-0.0513***
	(0.0471)	(0.0423)	(0.0401)		(0.0066)	(0.0072)	(0.0068)
SO2	0.0655	0.0468	0.0758	Inversions*FIN	-0.0296***	-0.0521***	-0.0509***
	(0.0647)	(0.0595)	(0.0552)		(0.0079)	(0.0113)	(0.0092)
NO2	-0.0244	-0.0205	-0.0026	Inversions*FRA	0.0121	0.0272**	0.0120
	(0.0347)	(0.0390)	(0.0375)		(0.0158)	(0.0138)	(0.0133)
O3	-0.0149	-0.0180*	-0.0117	Inversions*GER	0.0376***	0.0246**	0.0152
	(0.0116)	(0.0106)	(0.0127)		(0.0097)	(0.0100)	(0.0093)
(mean) Temperature		-1.4959*	-1.8957***	Inversions*GRE	0.0146	0.0044	-0.0088
		(0.7760)	(0.6788)		(0.0117)	(0.0172)	(0.0161)
(mean) Precipitation		-0.0156	-0.0164	Inversions*HUN	0.0948***	0.0719***	0.0769***
		(0.0146)	(0.0147)		(0.0075)	(0.0097)	(0.0112)
(mean) Wind Speed		-0.0154	0.2089	Inversions*IRE	0.0548***	0.0435**	0.0240
		(0.3987)	(0.3437)		(0.0187)	(0.0190)	(0.0191)
(mean) Max Temperature		0.6744	0.9270	Inversions*ITA	0.0244***	0.0298***	0.0219**
		(0.7342)	(0.6430)		(0.0090)	(0.0115)	(0.0107)
(mean) Specific Humidity		-0.1731	-0.0815	Inversions*LAT	-0.0077	-0.0172**	-0.0220***
		(0.1185)	(0.0992)		(0.0074)	(0.0081)	(0.0082)
Lagged Resistance			0.0183	Inversions*LUX	-0.0136	-0.0084	-0.0153
			(0.0150)		(0.0138)	(0.0159)	(0.0161)
				Inversions*NET	0.0258***	0.0157**	0.0193**
					(0.0066)	(0.0076)	(0.0085)
				Inversions*POL	0.1167***	0.1069***	0.0665***
					(0.0142)	(0.0134)	(0.0119)
				Inversions*POR	0.0570***	0.0417***	0.0337***
					(0.0117)	(0.0122)	(0.0093)
				Inversions*ROM	0.0968***	0.0936***	0.0861***
					(0.0298)	(0.0267)	(0.0222)
				Inversions*SLO	0.0602***	0.0303**	0.0080
					(0.0106)	(0.0150)	(0.0126)
				Inversions*SPA	0.0718***	0.0670***	0.0590***
					(0.0170)	(0.0203)	(0.0188)
				Inversions*SWE	-0.0064	-0.0234**	-0.0341***
					(0.0092)	(0.0098)	(0.0088)
Observations	419	419	398				
Kleibergen-Paap rk Wald F	5.8e+04	1.6e+05	1.4e+06				
Instruments	Group A	Group A	Group A				

Table 17: Baseline Results - First Stage (Group B)

	Controls				Instruments		
Dependent Variable *Pollution*	(1)	(2)	(3)		(1')	(2')	(3')
(per capita) Health Expenditure	0.0004	0.0005*	0.0003	AnyInversion*AUS	0.0722***	0.0482***	0.0307***
	(0.0003)	(0.0003)	(0.0003)		(0.0091)	(0.0094)	(0.0074)
Population Density	0.0016	-0.0156	-0.0277**	AnyInversion*BEL	0.0082	0.0080	0.0099
	(0.0155)	(0.0148)	(0.0134)		(0.0064)	(0.0070)	(0.0063)
Rural Population	-0.0607	0.0813	0.0625	AnyInversion*BUL	-0.0271	-0.0516***	-0.0714***
	(0.2299)	(0.2071)	(0.1784)		(0.0167)	(0.0174)	(0.0206)
Population 65+	-0.1861	-0.1150	-0.1702	AnyInversion*CRO	0.0688***	0.0310*	0.0177
	(0.1428)	(0.1459)	(0.1233)		(0.0119)	(0.0177)	(0.0167)
Tourism Arrivals	-0.0039	-0.0016	-0.0111	AnyInversion*CZE	0.0533***	0.0437***	0.0210***
	(0.0110)	(0.0112)	(0.0147)		(0.0072)	(0.0073)	(0.0066)
Physicians	-0.1645	-0.2391	-0.3991	AnyInversion*DEN	0.0342***	0.0336***	0.0299***
	(0.3763)	(0.3362)	(0.2957)		(0.0056)	(0.0051)	(0.0040)
PM10	0.0763*	0.0549	0.0462	AnyInversion*EST	-0.0318***	-0.0444***	-0.0450***
	(0.0445)	(0.0405)	(0.0392)		(0.0052)	(0.0055)	(0.0052)
SO2	0.0525	0.0341	0.0636	AnyInversion*FIN	-0.0252***	-0.0473***	-0.0482***
	(0.0622)	(0.0572)	(0.0532)		(0.0070)	(0.0096)	(0.0081)
NO2	-0.0184	-0.0181	0.0009	AnyInversion*FRA	0.0164	0.0268**	0.0127
	(0.0368)	(0.0394)	(0.0388)		(0.0128)	(0.0106)	(0.0110)
O3	-0.0138	-0.0170	-0.0115	AnyInversion*GER	0.0377***	0.0241***	0.0153**
	(0.0112)	(0.0107)	(0.0129)		(0.0070)	(0.0076)	(0.0069)
(mean) Temperature		-1.4799**	-1.8482***	AnyInversion*GRE	0.0075	-0.0003	-0.0099
		(0.7035)	(0.6281)		(0.0112)	(0.0161)	(0.0162)
(mean) Precipitation		-0.0123	-0.0142	AnyInversion*HUN	0.1068***	0.0805***	0.0740***
		(0.0145)	(0.0148)		(0.0079)	(0.0080)	(0.0094)
(mean) Wind Speed		-0.0481	0.1672	AnyInversion*IRE	0.0477***	0.0399***	0.0237*
		(0.3837)	(0.3282)		(0.0154)	(0.0150)	(0.0143)
(mean) Max Temperature		0.7263	0.9365	AnyInversion*ITA	0.0260***	0.0319***	0.0240**
		(0.6703)	(0.6018)		(0.0099)	(0.0110)	(0.0104)
(mean) Specific Humidity		-0.1760	-0.0759	AnyInversion*LAT	0.0047	-0.0057	-0.0152***
		(0.1193)	(0.1037)		(0.0045)	(0.0055)	(0.0055)
Lagged Resistance			0.0159	AnyInversion*LUX	0.0078	0.0102	0.0020
			(0.0152)		(0.0105)	(0.0109)	(0.0111)
				AnyInversion*NET	0.0248***	0.0165**	0.0150**
					(0.0064)	(0.0072)	(0.0068)
				AnyInversion*POL	0.0955***	0.0849***	0.0545***
					(0.0106)	(0.0091)	(0.0080)
				AnyInversion*POR	0.0497***	0.0357***	0.0295***
					(0.0105)	(0.0109)	(0.0084)
				AnyInversion*ROM	0.0939***	0.0657***	0.0579***
					(0.0247)	(0.0228)	(0.0197)
				AnyInversion*SLO	0.0751***	0.0498***	0.0279**
					(0.0093)	(0.0134)	(0.0112)
				AnyInversion*SPA	0.0618***	0.0561***	0.0499***
					(0.0140)	(0.0178)	(0.0171)
				AnyInversion*SWE	-0.0029	-0.0127*	-0.0216***
					(0.0074)	(0.0076)	(0.0068)
Observations	419	419	398				
Kleibergen-Paap rk Wald F	2.9e+06	1.7e+06	1.1e+05				
Instruments	Group B	Group B	Group B				

Table 18: Baseline Results - First Stage (Group C)

	Controls				**Instruments**		
Dependent Variable *Pollution*	(1)	(2)	(3)		(1')	(2')	(3')
(percapita) Health Expenditure	0.0005**	0.0005**	0.0003	WinterInverions*AUS	0.0754***	0.0516***	0.0343***
	(0.0002)	(0.0002)	(0.0002)		(0.0069)	(0.0069)	(0.0067)
Population Density	-0.0037	-0.0176	-0.0297**	WinterInverions*BEL	-0.0087	-0.0086	-0.0012
	(0.0138)	(0.0138)	(0.0115)		(0.0066)	(0.0081)	(0.0069)
Rural Population	-0.0082	0.0941	0.0873	WinterInverions*BUL	-0.0202	-0.0497**	-0.0928***
	(0.2154)	(0.1940)	(0.1730)		(0.0193)	(0.0233)	(0.0255)
Population 65+	-0.1320	-0.0722	-0.1206	WinterInverions*CRO	0.1094***	0.0666***	0.0511**
	(0.1425)	(0.1427)	(0.1241)		(0.0207)	(0.0247)	(0.0233)
Tourism Arrivals	-0.0060	-0.0031	-0.0147	WinterInverions*CZE	0.0626***	0.0538***	0.0339***
	(0.0100)	(0.0100)	(0.0119)		(0.0071)	(0.0082)	(0.0076)
Physicians	-0.2234	-0.2756	-0.3969	WinterInverions*DEN	0.0279***	0.0305***	0.0260***
	(0.3721)	(0.3510)	(0.3165)		(0.0060)	(0.0054)	(0.0049)
PM10	0.0702*	0.0522	0.0454	WinterInverions*EST	-0.0418***	-0.0570***	-0.0516***
	(0.0419)	(0.0400)	(0.0391)		(0.0063)	(0.0071)	(0.0064)
SO2	0.0546	0.0381	0.0562	WinterInverions*FIN	-0.0334***	-0.0639***	-0.0618***
	(0.0621)	(0.0566)	(0.0531)		(0.0085)	(0.0126)	(0.0104)
NO2	-0.0063	-0.0107	0.0056	WinterInverions*FRA	0.0105	0.0229*	0.0043
	(0.0306)	(0.0328)	(0.0317)		(0.0167)	(0.0132)	(0.0127)
O3	-0.0120	-0.0167	-0.0116	WinterInverions*GER	0.0478***	0.0321***	0.0222***
	(0.0118)	(0.0110)	(0.0141)		(0.0066)	(0.0060)	(0.0061)
(mean) Temperature		-1.3454**	-1.6769***	WinterInverions*GRE	-0.2052***	-0.1477***	-0.0690***
		(0.6387)	(0.5935)		(0.0369)	(0.0376)	(0.0257)
(mean) Precipitation		-0.0146	-0.0154	WinterInverions*HUN	0.1412***	0.1136***	0.1019***
		(0.0141)	(0.0143)		(0.0105)	(0.0105)	(0.0139)
(mean) Wind Speed		-0.0567	0.1843	WinterInverions*IRE	0.0513***	0.0250	0.0112
		(0.4094)	(0.3500)		(0.0149)	(0.0169)	(0.0178)
(mean) Max Temperature		0.6993	0.8552	WinterInverions*ITA	0.0767***	0.0894***	0.0790***
		(0.5820)	(0.5391)		(0.0213)	(0.0206)	(0.0163)
(mean) Specific Humidity		-0.1815	-0.1081	WinterInverions*LAT	-0.0038	-0.0167**	-0.0210***
		(0.1106)	(0.0961)		(0.0100)	(0.0080)	(0.0080)
Lagged Resistance			0.0132	WinterInverions*LUX	0.0254***	0.0119	0.0102
			(0.0144)		(0.0089)	(0.0097)	(0.0104)
				WinterInverions*NET	0.0244***	0.0126*	0.0125*
					(0.0048)	(0.0067)	(0.0069)
				WinterInverions*POL	0.0907***	0.0824***	0.0558***
					(0.0112)	(0.0101)	(0.0085)
				WinterInverions*POR	0.0855***	0.0468**	0.0344**
					(0.0191)	(0.0203)	(0.0174)
				WinterInverions*ROM	0.0719***	0.0365*	0.0277
					(0.0204)	(0.0214)	(0.0200)
				WinterInverions*SLO	0.0747***	0.0510***	0.0307***
					(0.0079)	(0.0127)	(0.0111)
				WinterInverions*SPA	0.1536***	0.1264***	0.1253***
					(0.0268)	(0.0302)	(0.0266)
				WinterInverions*SWE	-0.0245**	-0.0341***	-0.0445***
					(0.0108)	(0.0108)	(0.0102)
Observations	419	419	398				
Kleibergen-Paap rk Wald F	3.9e+04	2.6e+04	1.0e+05				
Instruments	Group C	Group C	Group C				

E Spillovers

Table 19: The Effect of Spillovers

	Poisson Model							
Dependent Variable *Resistance*	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
(log) Pollution	0.3334**	0.2480*	0.3366**	0.2371*	0.2624*	0.2659**	0.2243	0.2273
	(0.1523)	(0.1362)	(0.1516)	(0.1323)	(0.1502)	(0.1280)	(0.1663)	(0.1470)
(log) DDDs	0.2919*	0.3673***	0.2136	0.3167***	0.2238	0.3241***	-0.1362	0.1521
	(0.1748)	(0.1221)	(0.1739)	(0.1222)	(0.1890)	(0.1204)	(0.1820)	(0.1423)
Residulas	-0.0100	0.0072	-0.0230	-0.0009	-0.0053	0.0116	-0.0339**	-0.0297**
	(0.0185)	(0.0146)	(0.0216)	(0.0165)	(0.0192)	(0.0150)	(0.0169)	(0.0149)
Lagged Resistance		0.0139***		0.0145***		0.0138***		0.0150***
		(0.0019)		(0.0019)		(0.0018)		(0.0021)
Observations	283	281	283	281	283	281	283	281
Instruments	Group A'	Group A'	Group B'	Group B'	Group C'	Group C'	Group D'	Group D'

Controls include demographic, pollution and weather variables, as described in equation (1). Regressions are weighted by the country population. Standard errors in parenthesis. *** p<0.01, ** p<0.05, * p<0.1

F Counterfactual

Figure 7: Counterfactual Graph